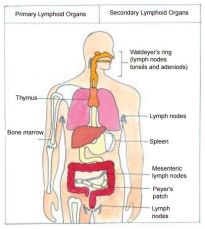

Fig. 3.2: Lymphoid organs in man

UNIT 7

THE IMMUNE SYSTEM

Structure

7.1 INTRODUCTION

You know that it is very important to have a good diet to sustain a good health and avoid diseases. The food items we consume should have proteins, carbohydrates and lipids as the essential components. You have got familiar with the details of these and a few more biomolecules and their metabolism in the previous units. Another important aspect related to good diet is a good immunity. We know that a person with good immunity is liable to reduce the infections and hence the diseases. In this unit we have discussed many concepts and aspects related to immunity and immune system of a human body.

The unit starts with some basic concepts like defining immunity and the levels of defense system. The types of immunity have been explained giving the difference between the innate and the acquired types. The important terms like the antigen and the antibodies have been described giving their types. The “immune system" is a general term for a complex series of cells, factors and processes that provide a specific response to antigens. The components of

the immune system have been discussed giving the mechanism of operation of the immune responses. A good account of the antigen-antibody interaction is also covered to give a complete description of the immune system.

The next and the last unit of this course deals with the most important aspect of heredity involving the informational molecules viz., DNA and RNA.

Expected Learning Outcomes

After studying this unit you should be able to:

- define immunity and describe the levels of defense present in the body;
- describe and differentiate the innate and acquired types of immunity;
- list the types of cells and organs of the immune system;
- elaborate the origin of immune system and the process of its operation;
- describe the cellular immunity and the humoral immunity and the role of T and B lymphocytes.
- define and describe the structure of antigen and antibody; and
- explain the process of antigen-antibody interaction.

7.2 IMMUNITY AND THE LEVELS OF DEFENSE

All of us are familiar with the word immunity which is used commonly for an individual's resistance to any infection. The word 'immunity' comes from a Latin word '*immunis*' meaning free or exempt. We often experience that one person may have severe cold and cough while the other person never suffers from cold although both have the same chances for exposure. This is because of the resistance towards the infection in one person is better than that in the other and we say that the person has a better immunity as compared to the other. Thus, **immunity** can be defined as the ability of an organism to resist a particular infection or toxin by the action of the immune system. The study of the immune system provides the foundation for the very interesting subject called "**immunology**."

Edward Jenner, the pioneer of smallpox vaccination and the father of immunology was an English physician.

Louis Pasteur also developed the overall principle of vaccination and contributed to the foundation of the field of immunology.

The modern definition of immunity includes all "*those physiological mechanisms that enable the animal to recognise materials as foreign to itself and to neutralise, eliminate or metabolise these with or without injury to its own tissues*".

Immunity may also be regarded as the result of the fight of two opposite forces—the infected organism on one hand and the host on the other hand. The result may be complete immunity, partial immunity or total absence of immunity. Most of us fall in the category of partial immunity.

Organisms causing the disease are termed **pathogens**, and the process by which they induce illness in the host is called **pathogenesis**. The human pathogens can be grouped into four major categories based on their characteristics viz., viruses, fungi, parasites, and bacteria. A list of these pathogens and the diseases caused by them is given in Table 7.1.

Table 1.1: Major groups of human pathogens and the diseases caused

Pathogens	Disease
Viruses	
Poliovirus	Poliomyelitis
Coronavirus	COVID 19
Human Immunodeficiency Virus (HIV)	AIDS
Rubeola Virus	Measles
Fungi	
Candida albicans	Candidiasis
Tinea corporis	Ringworm
Protozoa	
Plasmodium species	Malaria
Entamoeba histolytica	Amoebic colitis
Bacteria	
Mycobacterium tuberculosis	Tuberculosis (TB)
Vibrio cholerae	Cholera

Our body has certain mechanisms to counter the attack of these pathogens that is called the **defense mechanism**. Let us understand these mechanisms also called the levels of immune defense.

7.2.1 Levels of Immune Defense

There are three lines of defense or the barriers in the body that must be overcome by a pathogen before it can cause an infection or disease. These are explained in the following paragraphs.

(a) Mechanical Barriers: These are the **first line of defense/barriers**. Our body is surrounded by both pathogenic and non-pathogenic organisms which through various portals like, water, milk, food, air, vectors etc. try to enter the body but are stopped by many efficient mechanical barriers, which would restrict the entry of such microbes. These mechanical barriers are:

- **Intact skin**: Although unbroken or intact skin is a good mechanical barrier and does not allow any organisms to enter the tissues, sometimes the organisms gain their entry through the hair follicle or opening of sweat gland or through the skin if it is injured or there is any cut or wound.

- **The conjunctivae**: The conjunctivae are the thin membranes that cover the inner surface of the eyelid and the white part of the eyeball. These are protected by the motion of the eyelids and the constant washing of the eye balls with shedding tears/secretions, still the organisms may enter through the conjunctivae.

- **Mucous membranes and mucous secretions**: The mucous secretions of respiratory, digestive and urinogenital organs form a

protective covering to mucous membranes. Secretions from the sweat glands, gastric juice and vagina hold many microorganisms and make them reduce their infectivity. Peristalsis, that is rhythmic contractions of the intestine, also help in trapping the microbes into mucous and other such secretions. These secretions whether acidic as in sweat, gastric, juice, vaginal or alkaline as in bile, keep the bacterial flora of the alimentary canal under check. Although the mucous membranes of the genitalia are protected from most bacteria, yet several organisms can invade the body through sexual intercourse (organisms of gonorrhea, syphilis, AIDS, etc.).

Turbinate bone is the inside walls of the nose with 3 pairs of long thin bones covered with a layer of tissue that can expand.

- **Mechanical arrangement of the organ structures**: Turbinate bone in the nose also forms a line of defense. The bacteria when they enter through nose, they either stick to the mucous surface of the nose or they take a longer time to reach the alveoli because of its structure. By the time they reach the alveoli, most of the organisms die and very few succeed in entering the organ.
- **Other barriers**: Coughing, sneezing, shedding tears, perspiring, salivating etc. also help mechanically to remove the pathogenic organisms from the entry point. It may be mentioned here that lysozyme, an enzyme present in most secretions (tears, saliva and mucous) of the body, acts as a chemical barrier.

(b) Phagocytes: Phagocytes belong to the second line of defense. These also form a part of innate immune system that you will learn later. If the microorganisms (pathogens) succeed in passing the first line of defense and enter the deeper tissues, they are attacked by the specific cells of the body called phagocytes or **natural killer** (NK) **cells,** which include the cells of the **reticuloendothelial system** (RES). These phagocytes ingest the microbes and destroy them in few minutes.

(c) Antibodies: Antibodies form the third level of defense. Here you should know that antibodies are specific substances produced in response to antigenic material. Antigens are specific substances which when introduced into the body give rise to the production of antibodies. They are produced in the body to help fight against disease causing pathogens. These form a part of adaptive immune system explained later. If the organisms succeed in passing through the second line of defense also, then the body tissues produce antibodies which act against the pathogens and kill them. The antibodies, apart from destroying the infectious pathogen also neutralise any toxin, which may have been formed in the body.

If the antibody production in the body is slow and quantity produced is insufficient to destroy the organisms or neutralize their toxins, the organisms overcome the specific resistance of the host, they invade the tissues, start multiplying very rapidly, injure the tissue cells, cause irritation, pain, swelling, redness and finally lead to **inflammation**. The swelling and redness are due to dilation of the blood vessel of the affected part. However, if the antibodies are produced in large quantities, the pathogen may be killed.

In the following subsection you will study the types of immunity.

7.3 TYPES OF IMMUNITY

The immunity is broadly of two types viz., natural and acquired immunity. These are further subdivided into different types as depicted in Fig. 7.1. These types are briefly explained in the following subsections.

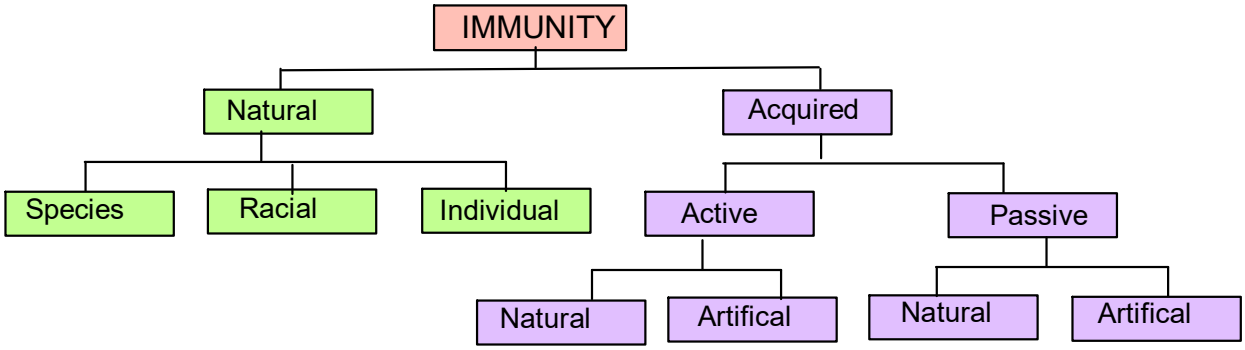

Fig. 7.1: Type of immunity

7.3.1 Innate Immunity

The innate immunity is also known as natural, native or inherited immunity. It is called so because it depicts the immunity we are born with and is the first line of defense. It is nonspecific in nature meaning it protects a person from all the antigens. Innate immunity acts as a barrier that keeps harmful antigens or pathogens from entering the body. It is present since birth therefore it is generally passed on from one generation to the other. A child may possess resistance to certain diseases to which mother is immune to. That is why breast-feeding is very important because child obtains immunity from the mother. Natural immunity is divided into the following three subtypes:

Species Immunity: It means immunity among the members of a particular species. Many diseases which occur in human beings do not occur in animals and vice-versa. For example, diseases such as measles, mumps, polio, syphilis, leprosy, cholera etc., are found only in human beings. This type of immunity is largely due to differences in body temperatures, although metabolic, chemical, physiological and anatomical differences between the different species also play an important role.

Racial Immunity: It means immunity present among the races of the same species. Some are immune to certain diseases while other members are susceptible. For example, in human beings Jews are immune to tuberculosis but Negroes are more susceptible to it. On the other hand, Negroes have high degree of immunity to malaria, dysentery, yellow fever than whites. Complete racial immunity is very rare. Races differ from one another primarily in degree of immunity. This type of immunity partly depends on the **some** physiological differences that exist between different individuals and partly depends upon the nutrition, cleanliness, differences in mode of life, and genetics of the **members**.

Individual Immunity: It means immunity present among the individuals of the same species and same race. It varies with the different individuals of the

same species and same race. The resistance of the same individual may also vary from day to day and time to time. An individual may be very susceptible to one disease organisms and very resistant to another. An individual in good health may never catch cold but if he is weak and exhausted he could catch cold frequently. Individual Resistance of an individual also depends upon the physical state of the individual and varies with other factors such as diet, fatigue and exposure etc.

7.3.2 Acquired Immunity

The immunity acquired during life time of an individual is known as acquired immunity. It is associated with the presence of specific circulating antibodies. Acquired immunity differs from innate immunity in two respects as given below.

i) It is not inherent in the body, it is acquired during lifetime.

ii) It is specific for a single type of microorganism.

Acquired immunity is of two types viz., Active and Passive

Active Acquired Immunity

If the patient actively participates in making his antibodies, the immunity is called active acquired immunity. There are two methods of acquiring active immunity i.e., Natural and Artificial.

a) Natural Active Immunity: It may be acquired in two ways as explained below.

Immunity acquired as a result of an attack of disease: An individual may become immune to certain infectious diseases by actually contracting them and recovering. It is entirely specific which means if a person recovers from small pox; he is immune only to small pox but this does not prevent him from contracting typhoid or mumps. This immunity of the body is due to the presence of antibodies which the body develops as a part of the reaction or response to the presence of invading bacteria or other poisons (toxins). In some diseases, the antibody production is so great that the immunity may persist for the life time of the individual. The diseases of this type are typhoid, diphtheria, measles, mumps, small pox, whooping cough. On the other hand, there are some diseases such as pneumonia, influenza, gonorrheae, dengue fever, and streptococci infections, where antibody formation is not prolonged and thus there is only temporary resistance. Second and third attacks are also possible.

Immunity acquired subconsciously on account of subclinical infections: This type is also called the immunity acquired by carriers. It develops gradually subconsciously after repeated exposure to small doses of the infecting organisms. The doses of such pathogens or toxins although are not sufficient to give rise to the disease, yet they are enough to stimulate the production of antibodies. Such persons are not suffering from the disease but they are carriers of the disease. Infectious diseases such as diphtheria, yellow fever and typhoid affect children more frequently and more seriously than adults. The adults develop immunity to such diseases.

b) Artificial Active Immunity: This type of immunity is acquired by immunising agents i.e. antigens such as vaccines or toxoids. It is a method to protect persons against infections to which they may be exposed in future. The antibodies formed are similar to those formed by a natural infection. In this method the vaccines are given by injections into the superficial layer of skin or into the subcutaneous tissue. A single injection of antigen results in the formation of small quantity of the antibody. It has been found that for an effective immunity against many diseases, two or more injections are required which are given at intervals of one to several weeks.

If the immunity is acquired artificially by the introduction of an antigen or toxoid into the body in the form of vaccine and the antigen stimulates the individual to develop specific antibodies, it is called the **artificial active immunity**.

Passive Acquired Immunity

If the patient does not participate in making his/her antibodies, the immunity given from outside is called **passive acquired immunity**. Here the patient is immunised by prepared antibodies and the body cells do not take any part in the production of antibodies. There are two methods of acquiring passive immunity.

Natural Passive Immunity: It is a temporary immunity passed on from mother to the baby before birth. The antibodies from the maternal blood through the placenta or mother's milk enter the fetus. Mothers immune to diphtheria may transfer diphtheria antitoxins to infants. It is sometimes called as **congenital immunity**. This immunity lasts for few months and protects infants from diphtheria, tetanus, measles, mumps, small pox etc.

Artificial Passive Immunity: It is the immunity produced in an individual by intramuscular injection of readymade antibodies (sera). In this case, antibody is prepared by injecting antigen in some other anima to immunize. Then some of the serum from the blood of this immune animal is injected in the person to be artificially immunised. The greatest disadvantage of the artificial passive immunity is that antibodies are rapidly excreted and gradually disappear from the blood. Thus the immunity lasts for a short time. The greatest advantage is that protection is possible immediately when the person is very ill.

SAQ 1

Correct the following terms:

a) Phagocytes - First line of cellular defense

b) Lysozyme – Mechanical barrier

c) Entamoeba histolica - Cholera

d) Inflammation – fast antibody production

SAQ 2

Choose the correct answer for the following statement.

Innate immunity or the natural immunity is called so because,

a) It is the immunity present right from birth and is the first line of defense.

b) It is specific in nature.

c) It cannot be passed from one generation to the other

d) It is not dependent on the individual's physical state.

7.4 THE IMMUNE SYSTEM

You are well aware that the environment in which we live contains a large variety of infectious organisms such as bacteria, viruses, fungi, protozoa or helminth parasites. These organisms enter in our body and cause infections which may be sometimes fatal but fortunately our body has an immune system which protects us from these infections. **"Immune system"** is a general term for a complex series of cells, factors and processes that provide a specific response to antigens. Let us first study the cells and the organs involved in the immune system.

7.4.1 Cells and Organs of the Immune Systems

The immune system consists of cells viz., leukocytes, dendritic cells, and macrophages and different lymphoid organs viz., primary and secondary lymphoid organs. Coordination amongst all of them is required for the development of a full immune response. Blood vessels and lymphatic systems connect these organs, tissues, and cells uniting them into a functional whole. A very brief idea of the types of cells and the organs is given here in view of the scope of the course.

Cells of the Immune System

The total leukocyte count in blood of humans is 4000-11,000/mm^3.

Leukocytes: The leukocytes are also called white blood corpuscles/ cells or WBCs. These are mainly involved in immune responses, recognising and neutralising invaders such as bacteria, viruses, and cancerous cells. The leukocytes are of two types viz., agranulocytes and granulocytes. **Agranulocytes** are characterised by the absence of granules in their cytoplasm and include **lymphocytes** and **monocytes**. The lymphocytes further include B lymphocytes, T lymphocytes and Natural killer cells.

Granulocytes are white blood cells that are characterised by the presence of granules in their cytoplasm. They are also called polymorphonuclear leukocytes (PMN or PML). These include neutrophils, eosinophils and basophils.

Dendritic Cells: Dendritic cells (DCs), are named for their appearance which resemble the dendrites of nerve cells. DCs are derived from the bone marrow and are found in epithelia, all organs, and lymphoid tissues of the body.

Macrophages: Monocytes remain in the blood for 8 hours and then migrate into the tissues where they differentiate and become macrophages.

Organs of the Immune System

Organs of the immune system or organs that participate in the immune response are present at diverse locations in the body. Depending on the function these are classified into primary and secondary lymphoid organs as shown in Fig. 7.2.

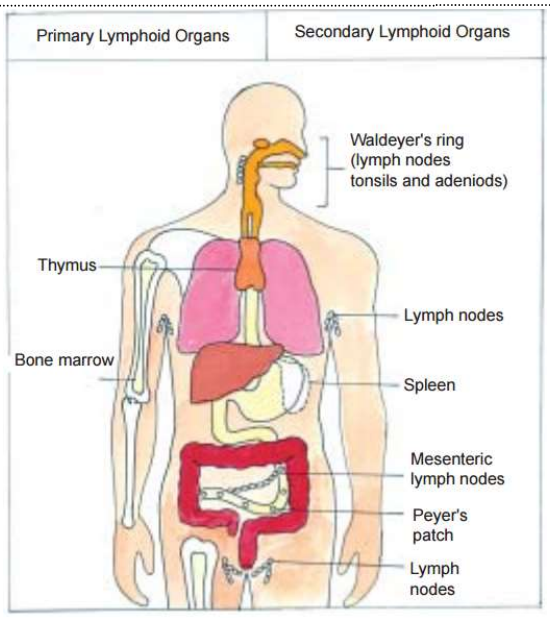

Fig. 7.2: Cells and Organs of the immune system

Primary lymphoid organs

The primary lymphoid organs include the bone marrow and thymus. As you know these are the organs where the cells of the immune system originate and mature.

Bone marrow: All blood cells including B and T lymphocytes originate from the bone marrow in humans. In the developing embryo initially, they develop from the yolk sac and then by the fetal liver. The bone marrow is the site of B-cell maturation.

Thymus: The site of maturation of T cells is the thymus. Thymus is situated above the heart and is bilobed which is further divided into lobules.

A **lymph** is a modified fluid tissue containing 94% water and 6% solids.

Lymphatic System

The lymphatic system consists of a network of lymph vessels and lymphoid organs, especially the lymph nodes. Lymph flows in lymphatics that are thin-walled vessels that carry lymph and are similar to blood vessels that carry blood.

Secondary Lymphoid Organs

The secondary lymphoid organs are the organs where the cells of the immune system actually fight off pathogens and foreign substances. These are located along the lymph vessels. These include the lymph nodes, the spleen, the tonsils, and certain tissue in various mucous membrane layers in the body.

The epidermis is composed of specialised epithelial cells called keratinocytes which secrete cytokines and when activated can function as antigen-presenting cells.

Lymph node: Lymph nodes are bean-shaped and are densely populated with lymphocytes, macrophages, and dendritic cells. The immunological response to the antigen(s) present in the lymph begins here.

Spleen: The spleen is a large secondary lymphoid organ present on the left side of the abdomen. It plays a major role in producing an immune response to blood-borne antigen(s). It filters the blood and traps the antigen present in the blood.

Mucosal-Associated Lymphoid Tissue (MALT): As the mucosal lining of the respiratory system, gastrointestinal and genitourinary tracts are most prone to microbial exposure, these sites are protected by mucosal-associated lymphoid tissues. Tonsils are an example of MALT.

Cutaneous-Associated Lymphoid Tissue (CALT): These relate to the skin as an important physical barrier to the external environment, and is the largest immune organ.

7.4.2 Origin of Immune System

Stem cells are the cells that give rise to other cells to perform different functions in the body.

The immune system starts developing approximately two months after the conception. At that time, stem cells arise in the bone marrow and differentiate into the **erythropoietic** cell and/or the **lymphopoetic** cells. The former become erythrocytes and the latter change into lymphocytes of the immune system.

The lymphopoietic cells have a choice to follow either of two courses. Some pass through a specialised organ of the thoracic cavity called the thymus. Within the thymus, the lymphopoietic cells are modified to form thymus dependent lymphocytes or T-lymphocytes or T-cells. After they emerge, the T-cells move through the circulation and colonise the lymph nodes, like spleen, tonsils and other lymphoid tissues.

Other lymphopoietic cells that pass through fetal liver or bone marrow in humans are modified to B-lymphocytes or the B-cells. B-cells have a chemical substance on their surfaces that distinguishes them from the T-lymphocytes. Similar to T-lymphocytes, B-lymphocytes move through the circulation to colonise in the the lymph nodes and other lymphoid tissues. Both the types of lymphocytes play important roles in the immune system. The points of accumulation of these lymphocytes are the lymph nodes where they encounter all the antigens. The population of T-lymphocytes is smaller than that of the B-lymphocytes.

Immunity is not the same in all individuals. Certain microorganisms infect one individual, while other individual resists the same disease. This means that there are many factors which control this phenomenon. The following subsection will focus on the factors which modify the immune response.

7.4.3 Factors which modify the Immune Response

Following factors are responsible for modifying the immune mechanism.

Genetic Factor: The immune response is under genetic control and varies from one individual to the other. Also, there are biological differences, e.g., in susceptibility to tuberculosis.

Age Factor: Chronologic age influences immunity. A hypofunctional state of the immune system occurs in the very young and very old age. These two ages are susceptible to numerous infections. One group (children) has incompletely developed immune system and in the other (old persons), there is degeneration of many immunologic organs and therefore functions.

Environmental and Nutritional Factors: There is a general increase in susceptibility to diseases under poor living conditions, which may be related to a greater exposure to pathogens as well as diminished resistance caused by malnutrition. In studies, conducted in children in developing countries, nutritional deprivation at an early age has been shown to be associated with the developmental failure of the immune response.

Anatomic Factors: This is first line of defense against invasion by microbes and is usually provided by the skin and mucosal membranes. These tissues act in a normal size by providing a physical barrier to invasion. The intact skin appears to be a more effective barrier than the mucous membrane. The increased susceptibility to infection following bums is a well-known clinical finding.

Physiological Factors: The main digestive constituents of gastric juice, secreted by gastric gland of stomach, are hydrochloric acid, mucin, rennin, and pepsinogen. The acid acts on pepsinogen to produce pepsin which functions best in an acid medium. The acidity of stomach contents also kills unwanted bacteria and other organisms that have been ingested with the food. Some bacteria such as *typhoid bacilli* are not affected; they survive the digestion and cause the disease. Ciliary action in the respiratory tract is another important physiological mechanism of resistance. Normal urine flow clears bacteria from urinary tract preventing infection. The obstructed urinary tract or respiratory tract is more susceptible to infection. **Lysozyme** is the enzyme that has been shown to have bactericidal activity. The enzyme is found in many types body fluid including tears. They function by virtue of mucolytic properties that cleave acetyl-amino sugars of bacterial cell wall and thus kill them.

Typhoid bacilli : A bacterial strain responsible for producing typhoid.
Bactericidal activity : Ability to kill bacteria.

Another set of protective functions are provided by mucus tissue **mucoproteins** which prevent attachment of certain viruses to the host cells. The **interferons**, a family of proteins, originally thought to inhibit viral replication are now known to have much broader cellular effects and are receiving increasing attention.

Mucoproteins: One of a group of proteins found in the globulin fraction of blood plasma. These contain a greater portion of carbohydrates.

Interferon: A substance that is produced by cells of immune system and infected cells during the immune response.

In addition to the above non-specific barriers against infection there are also some specific forms of resistance. These are produced in response to a particular infectious agent and act specifically at that agent. In the following subsection you will be able to understand the specific immune response while studying the types of immune system.

7.4.4 Types of Immune System

The immune system response is classified into two categories: **Nonspecific** or **innate** immune responses and **Specific** or **Adaptive or Acquired** immune responses. Both of these responses function side by side and protect the host from any infectious agent exposed to the body from any route.

The Innate Immune System

The innate immune system consists of mechanical barriers and phagocytes, the natural killer cells (NK) which protect the body from entry of any infectious agent. These agents when try to enter the body, are first stopped by mechanical barriers which form the first line of defense mechanism. If these

Complete Antigen: If antigen when introduced into the body of the host is capable of stimulating antibody production, it is called complete antigen, e.g. proteins, polysaccharides.
Partial Antigen (Hapten): If antigen when introduced into the body of the host is not capable of stimulating antibody production in the host but produces specific reactions with the antibody, it is called as partial antigen.

microorganisms succeed in passing the first line of defense and enter the tissues, they are attacked by the phagocytic natural killer cells (NK) which form the second line of defense. These phagocytes ingest the microbes and destroy them within some time. The innate immune system is not antigen specific and also does not have memory. It does not even have the ability to improve resistance on repeated exposure to the same antigen.

Specific or Adaptive Immune Response

When the pathogens have breached or crossed the innate immune system and enter the deeper tissues, adaptive immune system becomes active and protects the host from invading organisms. The adaptive immune system is antigen specific and it has memory. It has the ability to remember the chemical nature of the infecting organism. It becomes more and more vigorous on repeated exposure to the same antigen. The adaptive immune system consists of lymphoid cells and lymphoid organs.

The specific immune response is concerned with the recognition and ultimate removal of foreign substance or invading infectious agent in a highly specific sequence. The final outcome of the encounter between host and a foreign substance is dependent upon the chemical properties of the substance and also upon properties or the type of the of the host. At this point, it is necessary to introduce and define the term **“antigen”.**

Antigens are “foreign” nonself chemical substances (available in organisms phylogenetically away from the host i.e. not normally present in the host) that elicit a response by the immune system. The antigens maybe proteins, e.g., milk protein, egg white, bee venom, haemoglobin molecules, bacterial toxin, and the chemical components of microbial flagella, pili and capsules. The key feature of an antigen is an area of activity called the **antigenic determinant**. This is located on the surface of the antigen molecule and may consist of few (approximately six to eight) amino acid residues or may be an oligosaccharide moiety. Some polysaccharides may also function as antigens usually have a molecular mass of over 10,000 Daltons. This large size of antigen suggests that they may have a variety of determinants. Smaller molecules may also be made antigenic by combining them with some tissue proteins or polysaccharides. These small molecules are called **haptens.**

Note that an individual does not normally elicit an immune response against its own proteins or polysaccharides. On the other hand, the same compounds may function as antigens in another individual or other organism. It is believed that before birth, the proteins and polysaccharides of body cells make contact with and inactive immune system cells that might later respond to them. The responsive cells are easily made inactive in the fetal stage. Thus the individual becomes tolerant towards its own constituents or **‘self’** and later will respond only outside (or foreign) antigens which are interpreted as **“nonself”.** This theory is known as **“specific immunologic tolerance”.**

Antigens enter the body through a variety of ways, including passage through mucous membranes of respiratory tract and penetrate through skin via insect, snake bite, injections and wounds. Once they enter in the body, the antigenic nature of a substance is determined by such factors as chemical nature, dose and size of the antigen, ability of phagocytes to take up and degrade the antigen for proper for the effective immune response.

SAQ 3

Fill in the blanks with appropriate words

a) All blood cells arise in the……

b) The tissue …… prevent attachment of certain viruses to the host cells.

c) The two primary lymphoid organs are ……. and …….

d) The immune system starts developing about ……..after conception.

e) The key feature of an antigen is an area of activity called …….

7.5 How the Immune System operates

As soon as an antigen enters the lymphatic system, the immune process begins. The antigen is phagocytosed by macrophages, monocytes or polymorphonuclear cells and major portion of the antigenic material is digested. The phagocytes preserve the antigenic determinants and transport them to the immune system in the lymphoid tissue. At the lymphoid tissue, the tissue, the macrophages present the antigenic determinants to T-lymphocytes and B-lymphocytes. The lymphocytes come close to the macrophages and interaction takes place between the antigenic determinants of the digested antigen and specific receptor sites on lymphocytes. At this point, the immune response depends upon whether the T-lymphocytes or the B-lymphocytes are stimulated or not.

If the T-lymphocytes are stimulated, they will multiply and leave the lymphoid tissue and travel to the antigenic entry site in the tissue, where they become lymphoblasts. The latter produce lymphokines that attract phagocytes to engulf the antigens. If the B-lymphocytes are stimulated, they remain in the lymphoid tissue and convert to plasma cells that produce antibodies. The antibodies enter the circulation, where they interact with antigens and encourage phagocytosis.

Two forms of immunity, namely cellular immunity and humoral immunity are possible depending upon the type of lymphocytes taking part in the process.

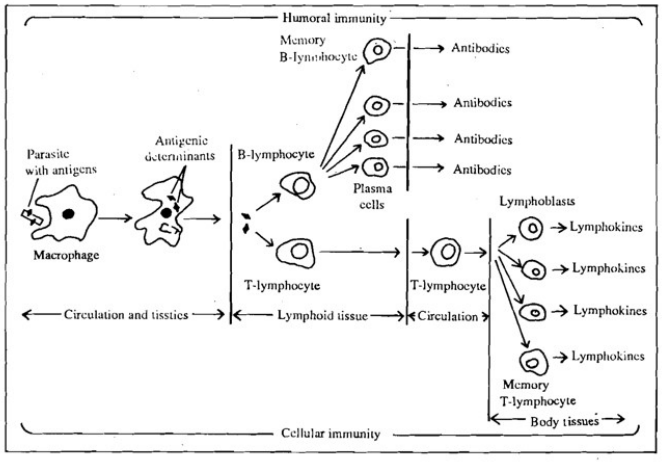

Fig. 7.3: A generalised overview of the operation of the immune system.

7.5.1 Cellular Immunity

When T-lymphocyte are responsible for immunity, it is known as **cellular immunity.** It is also known as cell-mediated immunity or tissue immunity (Fig. 4.2). The mechanism by which is immunity develops is as follows:

The antigens of many fungi, protozoa and selected viruses and bacteria stimulate the T-lymphocytes and sensitise them. The sensitised T-lymphocytes then enter the circulation and migrate to the site where the antigen was detected. The pool of lymphocytes increases at the particular site. At the antigen site the lymphocytes revert to immature cells, called **lymphoblasts,** which produce a series of low molecular weight proteins known as **lymphokines.** These lymphokines are extremely active and can be classified into different categories, depending upon the function they perform.

i) One lymphokine known as **chemotactic factor** (CF) draws phagocytes or macrophages to the antigen entry site.

ii) Migration inhibition factor (MIF) prevents macrophages from moving away.

iii) Macrophage aggregation factor (MAF) causes phagocytes to clump or aggregate together at that site.

iv) Macrophage activating factor (MAF) increase the mobility of phagocytes and release of lysosomal enzymes by each of them in that area.

The overall effect of all these factors is to increase the efficiency of phagocytosis of antigen and bring about a specific immune response to the antigen and prevent the disease.

Once the antigen has been eliminated, the lymphokines disappear rapidly. However, the person will remain immune to future effects of that antigen because a colony of identical T-lymphocytes remaining in the tissue. These cells are called **memory T-lymphocytes.** Whenever that antigen reappears in the tissue, the memory cells get activated and rapidly revert to lymphoblasts that that secrete lymphokines to eliminate the antigen. This is one reason for long term immunity to diseases. Cellular immunity is an important factor in resistance to bacterial disease such as leprosy and tuberculosis and fungal disease. Certain antigens stimulate a type of T-lymphocyte known as the killer T-lymphocyte which help in the lysis of infected cells with the help of B-lymphocytes and prevent an exaggerated immune response.

7.5.2 Humoral Immunity

Humoral immunity is governed by stimulated B-lymphocytes, which is stimulated by the helper T-lymphocytes. The B-lymphocytes do not enter the circulation but they remain in the lymphoid tissue and multiply to form a clone of cells called **plasma cells.** Plasma cells are two to three times the size of B-lymphocytes. Their principal products (secreted by them) are glycoprotein molecules called as antibodies. Antibodies are synthesised and released into the circulation at a rate of several thousand molecules per second. The term humoral immunity is used because the interaction between antibodies and

antigens occurs in the blood stream. Plasma cells continue to produce antibodies until the antigenic stimulation comes to an end. At this point the plasma cells die off and are replaced by a second clone of B-lymphocytes called **memory B-lymphocytes.** These memory cells remain in the lymphoid tissues for many years and becomes active when the same antigen reappears.

SAQ 4

Name the substance which is produced by lymphoblasts. What is its nature?

Let us now study the structure and types of antibodies produced by plasma cells and the process by which they interact and provide specific resistance.

7.6 Antibodies

Antibodies are specific substances produced in the body in response to antigenic material to fight disease germs. These serve as protective agents against organisms and kill them. The antibodies may be found in the fluid part of the circulating blood (plasma and serum) as well as in certain tissues and are mostly produced in the body in reticuloendothelial cells located in bone marrow, liver, spleen, nodes etc. Antibody may be univalent or multivalent. Univalent antibody is one in which each molecule of antibody combines with one molecule of antigen. A multivalent antibody is one in which each molecule of antibody combines with two or more molecules of antigen.

7.6.1 Structure of Antibodies

The basic antibody molecules consist of four polypeptide chains viz., two identical '**heavy**' or **H** chains and two identical '**light**' or **L** chains. These two chains are joined together by sulphur to sulphur (disulfide) linkage to form **Y** shaped structure. Each heavy chain consists of about 400 amino acids while each light chain has about 200 amino acids. Constant and variable regions exists within each polypeptide chain. The amino acids in the constant regions of both light and heavy chains are virtually identical among various antibodies. The amino acids of variable region vary among the hundreds of thousands of different antibodies. The variable regions of light and heavy chain combine to form a highly specific, three dimensional structures which gives the specificity for a particular antigen. In other words it will recognise only the antigen of its own kind. The arms of antibody are identical so that a single antibody molecule may combine with two antigen molecules. This can be seen clearly in Fig. 7.3 (a).

When the antibody (IgG) is treated with papain, a proteolytic enzyme, it gets hydrolysed to give three fragments by getting cleaved at the hinge point. One is known as Fab fragment or 'fragment-antigen-binding' which are two in number. This protein is able to combine with the antigenic determinant. The second fragment is Fc fragment or 'fragment and to be crystallised' and it is one in number as seen in Fig. 7.3 (b). This part of antibody combines with phagocytes and neutralises viral receptor sites.

The reaction between antibody and antigenic determinants in an antigen molecule is shown in Fig. 7.3 (c). Each antibody molecule has two reactive sites complementary to an antigenic determinant. Antibodies 1 and 2 each react with different antigenic determinants at the variable end.

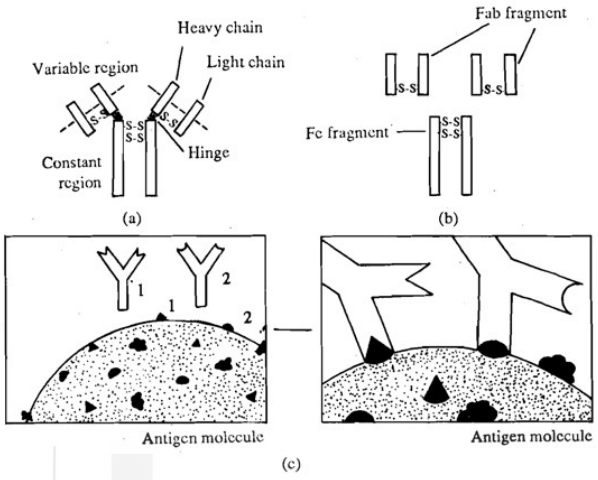

Fig. 7.3: Structure of the antibody molecules.

7.6.2 Types of Antibodies

Different types of antibodies have been identified based on differences in heavy or H chains. The five classes of immunoglobulins (Ig) are explained in brief below and shown in Fig. 7.4.

Immunoglobulin M- This is the first antibody which appears in the circulation after stimulation of B-lymphocytes. It is the largest antibody in terms of of size. Because of its size, IgM remains in circulation. The percentage of IgM is 5-10 % of the total antibodies in the serum. Note the complex structures of IgM seen as a pentamer (each unit is connected with disulfide bond to other unit) and one J chain which makes it available in secretions in the body (secretory IgM).

Immunoglobulin G- This is major immunoglobin in normal human serum accounting for 70-75% of total immunoglobulin pool. IgG appears 24-48 hours after antigen stimulation. This antibody is of the secondary immune response. It provides long term resistance to disease as a product of the memory B-lymphocytes. It has a monomer.

Immunoglobulin A-This antibody represents about 15-20% of the human serum immunoglobulin pool. This antibody IgA exist in the serum The second from accumulate in body secretion and is referred to as **Secretory IgA.** is a dimer, with one J chain joining them. This antibody provides resistance in the respiratory an gastrointestinal tract by inhibiting the attachment of parasites to the tissues.

Immunoglobulin E- This antibody IgE plays a major role in the allergic reactions by sensitising T cells to certain antigens. This class may play a role in active immunity to parasitic infections and is also commonly associated with immediate hypersensitivity diseases such as asthma and hay fever. It is a monomer.

Immunoglobulin D-This antibody IgD accounts for less than 1% of the total plasma immunoglobulin but it is present in large quantities on the membrane of many circulating B-lymphocytes. Similar to IgD and IgE it has a monomer.

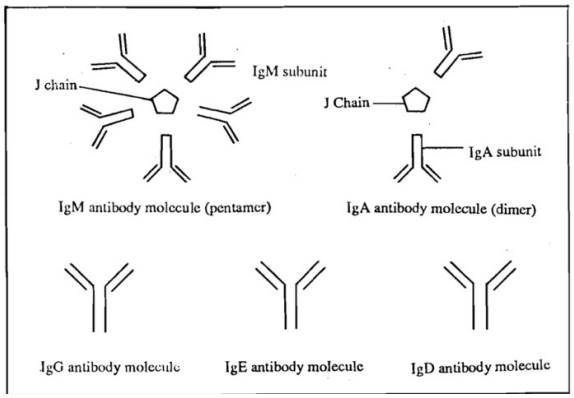

Fig. 7.4: The structures of five types of antibodies. Each composed of two heavy chains and two light polypeptide chains.

7.6.3 Antigen-Antibody Interaction

When molecules of an antigen and an antibody are brought together in a solution, they cause specific reactions known as antigen-antibody reactions. A number of different antigen-antibody reactions have been observed in test tube experiments (*in vitro*) and in humans as well as in animals (*in vivo*). These reactions depend on numerous factors such as nature of antigen, environmental conditions and the origin of antibody etc. The reactions are very useful in the laboratory diagnosis of various diseases.

For the development of specific resistance, antibodies interact with antigens in such a way that antigen is altered. This alteration may result in death of the microorganism that possesses the antigen. There are different modes of antigen-antibody interaction. These are indicated in Fig. 7.5.

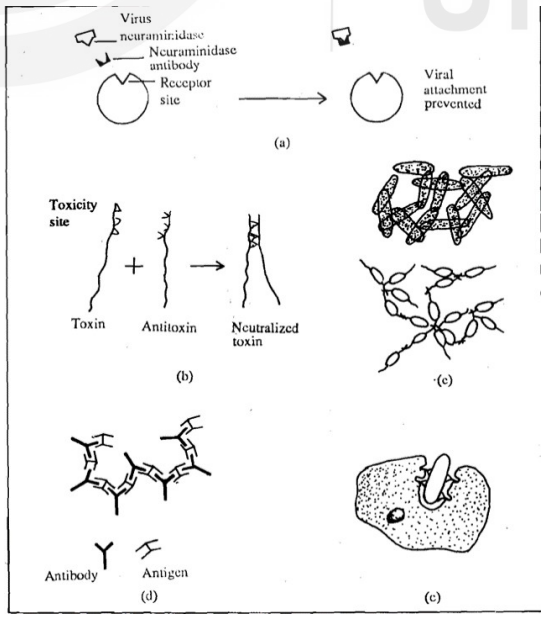

Fig. 7.5: Five different mechanisms by which antibodies interact with antigens and alter them.

The five mechanisms of antigen-antibody interactions with the type of antibodies involved, are given in brief below.

Neutralizing antibodies: These antibodies react with viral capside (coat of protein surrounding the genome) and allow hydrolysis using the enzyme **neuraminidase** to prevent viruses from entering their host cells.

Antitoxins: These antibodies combine specially with toxins and neutralise the toxicity site of the toxin.

Agglutinins: These are the antibodies which react with antigens on the surface of organisms such as bacteria. This action causes or agglutination of organism and thus enhance phagocytosis.

Precipitins: These antibodies react with dissolved antigens and convert them to larger aggregates (solid precipitates). In this form antigens are usually inactive and more easily phagocytosed.

Opsonins: These antibodies encourage phagocytosis by forming a bridge between parasites and receptor sites on the phagocyte thus enhance the action of phagocytosis.

You may try to answer the following SAQ now.

SAQ 5

Fill in the blanks with appropriate words:

a) Antibodies are produced by …….

b) Two identical ……chains and two identical…….chains.

c) The percentage of IgM in circulation with respect to total antibodies is …….. and that of IgG is ……

d) …… is the class of immunoglobulin present maximally in serum out of total immunoglobulin pool.

7.7 SUMMARY

- Immunity can be defined as the ability of an organism to resist a particular infection or toxin by the action of the immune system. There are three major levels of immune defense viz., the Mechanical Barriers, the Phagocytes and the Antibodies.
- There are two main types of immunity i.e., innate or natural and acquired/adaptive. The innate immunity is the one which we have right from the time of birth. Species, Racial and Individual are the subtypes of this immunity. The acquired immunity is the immunity acquired during lifetime of an individual. The active and passive acquired immunity are its two types which are further divided into natural and artificial types.
- The immune system functions through some cells and organs which when work in coordination develop an immune response. The cells include

leukocytes, dendritic cells, and macrophages. The lymphoid organs are of two types depending upon their functions. The primary lymphoid organ includes bone marrow and thymus. The secondary lymphoid organs are responsible for fighting off the pathogens and the foreign substances. These include the lymph nodes, spleen and the lymphoid tissues. The lymphopoietic cells give rise to T- lymphocytes and B-lymphocytes depending on whether these are modified in the thymus or the bone marrow.

- The immune response is modified by the genetic, age, anatomic, environmental and physiological factors. The immune systems may be nonspecific (or innate) and specific (adaptive or acquired) type. The innate immune system consists of mechanical barriers and phagocytes, the natural killer cells which protect the body from entry of infectious agents. When these have breached the innate immune system and enter the deeper tissues, adaptive immune system becomes active and protects the host from invading organisms. It is antigen specific, and it has memory.
- Two forms of immunity, namely cellular immunity and humoral immunity are possible depending upon the type of lymphocytes taking part in the immune process. When T-lymphocyte are responsible for immunity, it is known as cellular immunity. Humoral immunity is governed by stimulated B-lymphocytes (which produce antibodies) which is further stimulated by the helper T-lymphocytes.
- The immune system activates helper T-lymphocytes which help to activate the B-lymphocytes to produce specific glycoproteins, called as antibodies, against the antigen and release them into the blood stream. There are five different types of antibodies which are always found in the globulin fraction of the blood serum and are called immunoglobulins.
- The antibodies have a high specific affinity for the antigen. When molecules of an antigen and an antibody are brought together in a solution, they cause specific reactions known as antigen-antibody reactions. For the development of specific resistance, antibodies interact with antigens in such a way that antigen is altered. This alteration may result in death to the microorganism that possess the antigen. There are different modes of antigen-antibody interaction.

7.8 TERMINAL QUESTIONS

1. What are lymphokines and what is the basis of categorizing them?
2. Name the linkage by which two chains of antibody are joined together.
3. List the three types of levels of defense.
4. Define an antigen and a hapten.
5. Differentiate between Active and Passive Immunity.
6. Differentiate between Innate and Adaptive Immune System.

7.9 ANSWERS

Self Assessment Questions

1. a) Second line of cellular defense

   b) Chemical barrier

   c) Amoebic colitis

   d) Fast antibody production (overcoming the specific resistance of the host)

2. a)

3. a) bone marrow

   b) mucoproteins

   c) bone marrow and thymus

   d) two months

   e) antigenic determinant

4. Lymphokines. These are protein in nature.

5. a) Plasma cells

   b) Heavy 'H' chains, light 'L' chains

   c) 5-10 % and 70-75%.

   d) IgG

Terminal Questions

1. The modified T-cells produce lymphokines which are low molecular weight proteins and actively take part in developing the cellular immunity. The lymphokines are categorized depending upon the function they perform. The lymphokines which perform the function of drawing phagocytes to the antigen sites is known as chemotactic inhibition factor (MIF). Similarly other type of lymphokine which increases the mobility of phagocytes and amount of lysosomal enzyme is known as macrophage activating factor (MAF).

2. This is known as disulfide linkage.

3. The three lines of defense are a) Unbroken/ intact skin (mucous membranes and secretions) (b) Phagocytes, and (c) Antibodies.

4. Antigens are specific substances which when introduced into the body give rise to the production of antibodies. They are produced in the body to help fight disease causing pathogens. These form a part of adaptive immune system.

   Haptens are small molecules which serve as antigens when combined with tissue proteins or polysaccharides, produce immune response.

5.	**Active Immunity**	**Passive Immunity**
i.	Produced actively by immune system of host	The host's immune system does not participate
ii.	Body cells take part in the production of antibodies, i.e. active immunity is acquired after infection or inoculation.	Cells of the body do not take part in the production of antibodies. Readymade antibodies are injected.
iii.	Immunity lasts for long time	Immunity lasts for short period, i.e. for few days.
iv.	Immunity is not effective immediately.	Immunity is effective immediately.
v.	It takes some time to develop the antibodies in the system.	No time is lapsed to get the antibodies.
vi.	Immunological memory present	No immunological memory.
vii.	No inheritance of immunity	May be acquired from mother.

6.	**Innate immune system**	**Adaptive immune system**
i.	It forms the first and second line of defense in the body.	It forms the third line of defense in the body.
ii.	Cells involved are phagocytes the natural killer cells (NK).	The cells involved are B and T cells.
iii.	It is not antigen specific.	It is antigen specific.
iv.	It does not have memory.	It has memory, ability to remember the chemical nature of infecting organism.
v.	Resistance not improved on repeated exposure to the same antigen.	Resistance improves and becomes more and more vigorous on repeated exposure to the same antigen.