UNIT 16 : IMMUNOLOGY

Structure

16.1 INTRODUCTION

This unit deals with the systematic study and scope of **Immunology**. The importance of different factors responsible for immunity is explained. The detailed account of specific response has also been given. Specific role played by the lymphocytes has been explained as also the structure and function of different types of antibodies.

Objectives

After studying this unit you should be able to:

- define immunity,
- explain hypersensitivity,
- explain specific immune response,
- discuss cellular and humoral immunity and the role of T and B lymphocytes,
- discuss the structure of different classes of antibodies, and
- explain the function of different antibodies.

16.2 DEFINITION OF IMMUNOLOGY

Before giving a detailed account, it is important to know and understand the word immunology. Immunology is the study of processes used by the host to maintain the constancy in his internal environment when confronted with foreign substances. The systematic study of immunology starting with the principle, mechanism and application will give a clear and overall picture in the area.

The concept of immunology was derived from the study of resistance to infection. It was for centuries that recovery from illness was accompanied by the ability to resist reinfection by the same disease. In recent years contribution to immunology have come from the basic

sciences e.g. biochemistry, anatomy, a developmental biology, genetics, pharmacology and pathology as well as from the study of clinical research.

16.3 IMMUNITY AND HYPERSENSITIVITY

It will be useful to distinguish the two words **immunity** and **hypersensitivity** in relation to the foreign substances or infection by a given microbe. Immunity refers to the relative resistance of the host to reinfection by a certain microorganism. In other words the host already develops the ability to destroy that microbe. Another way to destroy the foreign microbes by the host cell is altered reactivity of the host. This reactivity gives more noxious effect known as hypersensitivity or allergy. One response by the host is beneficial and other is harmful. These two facts can be generalised in the sense that immunity means protection from infectious agent and allergy is a generalised reaction of the host to a foreign substance.

Based on the terms used above and other experiences, the precise definition of immunity would include all those physiological mechanisms that enable the animal to recognise materials as foreign to it self and to neutralise, eliminate or metabolise them with or without injury to its won tissues". Now this response of immunity may be classified into two categories symbol ã 1) Nonspecific immune responses and 2) Specific immune responses.

The details of specific immune response will be discussed in the forthcoming part. Immunity is not the same in all individuals. Certain microorganisms infect one individual, while another resists the same disease. This means that there are factors which control this phenomenon. The following section will throw light on the factors which modify the immune response.

SAQ 1

Fill in the blanks

Immunity refers to the .....A.... of the host to reinfection and each individual has ....B.... immunity against various microorganisms.

16.4 FACTORS WHICH MODIFY THE IMMUNE RESPONSE

Following factors are responsible for modifying the immune mechanism.

16.4.1 Genetic Factor

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

16.4.2 Age Factor

Chronologic age influences immunity. A hypofunctional state of the immune system occurs in the very young and very old. These two ages are susceptible to numerous infections. One group has incompletely developed immune system and in the other there is deterioration of many immunologic functions.

16.4.3 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. Recently a new acquired immune deficiency syndrome (AIDS) has been described in homosexual males and other groups which has been associated with the recurrent opportunistic infection and malignancy. The occurrence of syndrome is due to the factors such as lifestyle, environment, intravenous drug used and transfusion.

Pathogens :

Microorganisms such as bacteria which infect an animal or plant and produce a disease.

16.4.4 Anatomic Factors

The first line of defense against invasion by microbes is usually provided by the skin and mucous 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 burns is a well known clinical finding.

16.4.5 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 pepsinogens 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 digestion and produce disease. Ciliary action in the respiratroy tract is another important physiological mechanism of resistance. Normal urine flow clears bacteria from urinary tract preventing infection. The obstructed urinary tract or respiratroy tract is more susceptible to infection. **Lysozyme** is an enzyme that has been shown to have **bactericidal activity.** The enzyme is found in many types of cell and body fluid including tears and functions by virtue ot **mucolytic properties** that cleave acetyl-amino sugars of bactaerial cell wall.

Typhoid bacilli :
A bacterial strain responsible for producing typhoid.

Bacterial activity :
Ability to kill bacteria.

Another set of protective functions are provided by tissue **mucoproteins** which prevent attachment of certain viruses to the host cells. A family of proteins, the **interferons**, originally thought to inhibit viral replication are now know 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. They contain a greater portion of carbohydrates.

Interferon :
A substance that is produced by cells infected with a virus and has the ability to inhibit viral growth.

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 parasite and are directed solely at the parasite. The major thrust of the following section will be to examine the specific resistance and to show how good health depends upon their proper functioning.

SAQ 2

a. What is the reason of high susceptibility to various infections in very young and old population?

---

b. What are the digestive constituents of gastric juice?

16.5 SPECIFIC IMMUNE RESPONSE

The specific immune response is concerned with the recognition and ultimate disposal of foreign substance in a highly discriminatory fashion. The final outcome of the encounter between host and a foreign substance is dependent upon the properties of the substance and also upon properties of the host. At this point, it is necessary to introduce and define the term **"antigen".**

Antigens are "foreign" chemical substances (i.e., not normally present in the animal) that elicit a response by the body's immune system. The antigens may be proteins, e.g., milk proteins, bee venom, haemoglobin molecules, bacterial toxin, and the chemical components of microbial flagella, pili and capsules. The key features 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 six to eight amino acid residues or may be an oligosaccharide moiety. Some polysaccharides may also function as antigens. 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. It is believed that before birth the proteins and polysaccharide of body cells make contact with and inactivate immune system cells that might later respond to them. The responsive cells are easily paralysed in the fetal stage. Thus the individual becomes tolerant towards its onw constituents or "**self**" and later will respond only to outside 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 the respiratory tract and penetrate through skin via arthropode bite, injections and wounds. Once they enter in the body, the antigenic nature of a substance is determined by such factors as dose and size of the antigen, ability of phagocytes to degrade the antigen and proper functioning of the immune system.

SAQ 3

What is a hapten ?

16.6 ORIGIN OF THE IMMUNE SYSTEM

"Immune system" is a general term for a complex series of cells, factors and processes that provide a specific response to antigens. The system starts developing approximately two months after conception. At that time, **stem cell** 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

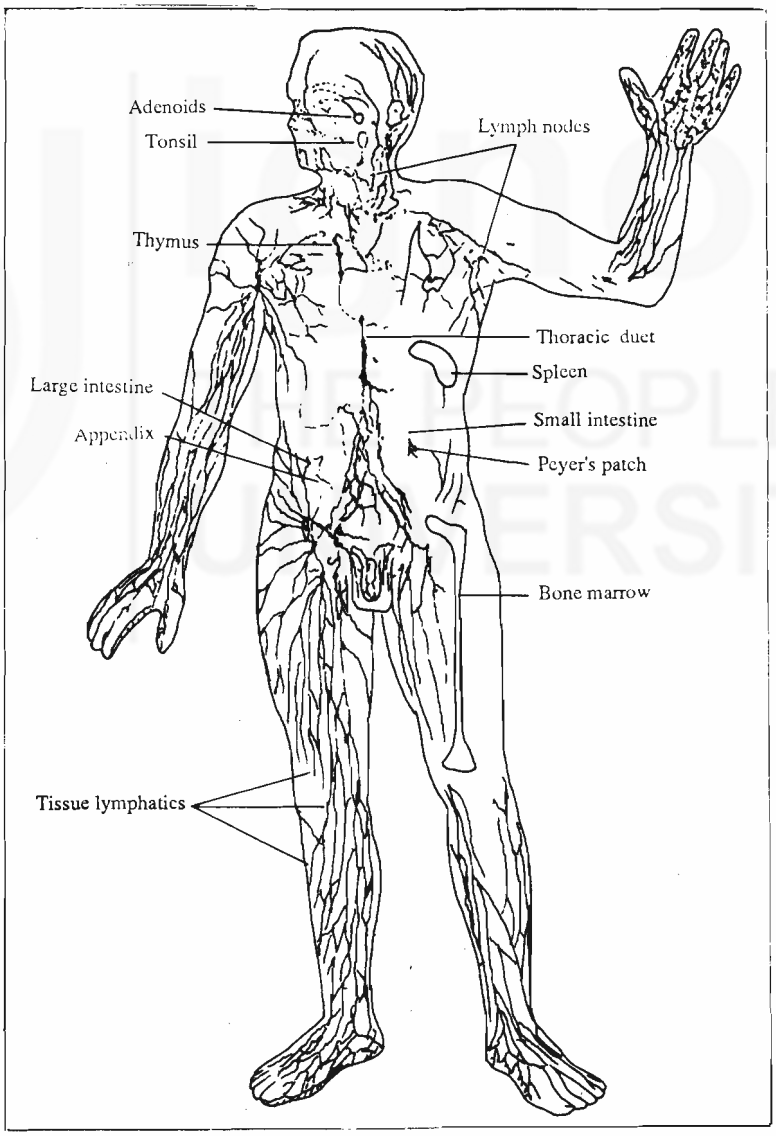

Fig. 16.1 : The human lymphatic system consists of lymphocytes, lymphatic organs. Lymph vessels, and lymph nodes located along the vessels. The lymphatic organs are illustrated and the preponderance of lymph nodes in the neck, axilla and groin is apparent.

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 (Fig. 16.1).

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 distinguish them from the T-lymphocytes. Like T-lymphocytes, B-lymphocytes moves through the circulation to colonise the lymph nodes and other lymphoid tissues. Both 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-lymphocyte is smaller than that of the B-lymphocyte.

SAQ 4

How are T and B lymphocytes formed?

16.7 HOW THE IMMUNE SYSTEM OPERATE

As soon as an antigens enters the lymphatic system, the immune process begins. The antigens are phagocytised 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 macrophages present the antigenic determinants to T-lymphocytes and B-lymphocytes. The lymphocytes gather about the macrophages and interaction then takes place between the antigenic determinants and specific receptor sites on lymphocytes. At this point, the immune process diverges depending upon whether T-lymphocytes B-lymphocytes are stimulated. Two forms of immunity, namely cellular immunity and humoral immunity, are possible depending upon the type of lymphocytes taking part in the process.

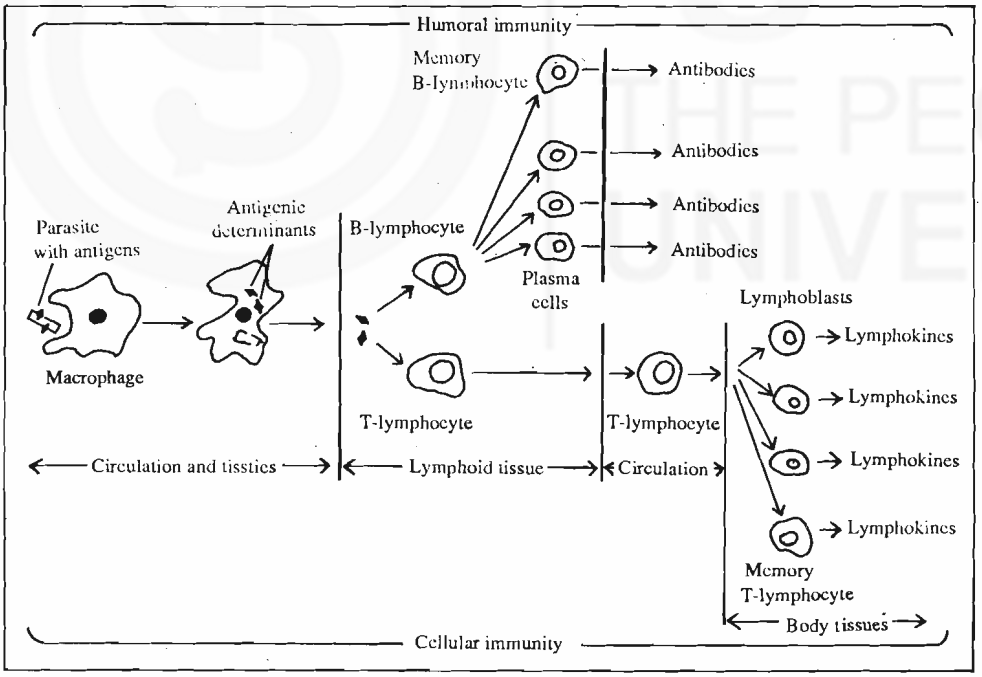

Fig. 16.2 : A generalised overview of the operation of the immune system. Antigens are engulfed by phagocytes and the antigenic determinants are preserved and delivered to the lymphoid tissue. If the T-lymphocytes are stimulated, they leave the lymphoid tissue and travel to the antigenic site in the 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.

16.7.1 Cellular Immunity

When T-lymphocytes are responsible for immunity, it is known as **cellular immunity**. It is also known as cell-mediated immunity or tissue immunity (Fig. 16.2). The mechanism by which this immunity develops is as follows :

The antigens of many fungi, protozoa and selected viruses and bacteria stimulate the T-lymphocytes and sensitise them. 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) draw phagocytes to the antigen site.

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

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

iv) Macrophage activating factor (MAF) increase the mobility of phagocytes and the amount of lysosomal enzymes in each.

The overall effect of all these factors is to increase the efficiency of phagocytosis of antigen and bring about a specific response to 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 remains in the tissue. These cells are called **memoryT-lymphocytes.** Whenever that antigen reappears in the tissue, the memory cell will rapidly revert to lymphoblasts that secrete lymphokines to eliminate the antigen. This is one reason for long term immunity to disease. Cellular immunity is an important factor in resistance to bacterial disease such as leprosy and tuberculosis and fungal diseases. Certain antigens stimulate a type of T-lymphocyte known as the killer T-lymphocyte which help in the lysis of infected cells after contacting them.

Two other types of T-lymphocytes, **helperT-lymphocytes** and **suppressor T-lymphocytes** are also stimulated in certain immune responses. Helper T-lymphocytes binds to antigen and assist the response of B-lymphocytes to the antigens. Suppressor T-lymphocytes interfere with the function of B-lymphocytes and prevent an exaggerated immune response.

16.7.2 Humoral Immunity

Humoral immunity is governed by stimulated B-lymphocytes, which is stimuated by the lelper 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 are protein molecules called antibodies. Abtibodies 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 for two to three days or 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 as **memoryB-lymphocytes.** These memory cells remain in the lymphoid tissues for many years and becomes active when the same antigen reappears.

SAQ 5

a. Name the substance which is produced by lymphoblast and what is its nature.

---

b. What will happen if suppressor T-lymphocytes exceed the helper T-lymphocytes?

We have explained the second form of immunity that is called humoral immunity. Let us now study the structure and types of antibodies produced by plasma cells and the process by which they interact with antigens and provide specific resistance.

16.8.1 Structure of Antibodies

The basic antibody molecules consists of four polypeptide chains two identical 'heavy' or H chains and two identical 'light' or L chains (Fig. 16.3).

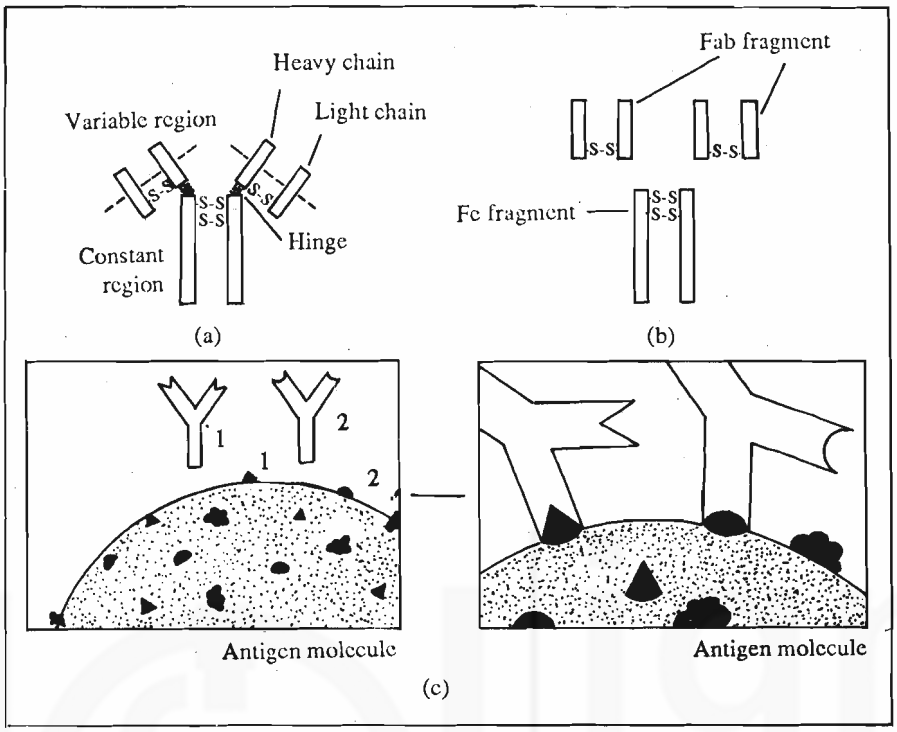

Fig. 16.3 : Structure of the antibody molecule. (a) The antibody molecule consists of four chains of proteins: two light chains and two heavy chains connected by disulfide linkages. The heavy chains bend at a hinge point. The variable region is that portion of the molecule where the amino acids vary from one antibody to another. (b) On treatment with the enzyme papain, cleavage occurs at the hinge point and three fragments result. Two are Fab fragments, and the third is the Fc fragment. (c) The reaction between antibody and antigenic determinants in an antigen molecule. 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.

These 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. When antibody is treated with papain, a proteolytic enzyme, it gets hydrolysed to give two fragments. One is known as Fab fragment or 'fragment-antigen-binding'. This protein is able to combine with the antigenic determinant. The second fragment is Fc fragment or 'fragment and to be crystallised'. This part of antibody combines with phagocyte and neutrilises viral receptor sites.

16.8.2 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 as follows: (Fig. 16.4).

i) **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 size. Because of its size, IgM remains in circulation. The percentage of IgM is 5-10% of the total antibodies in the serum.

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

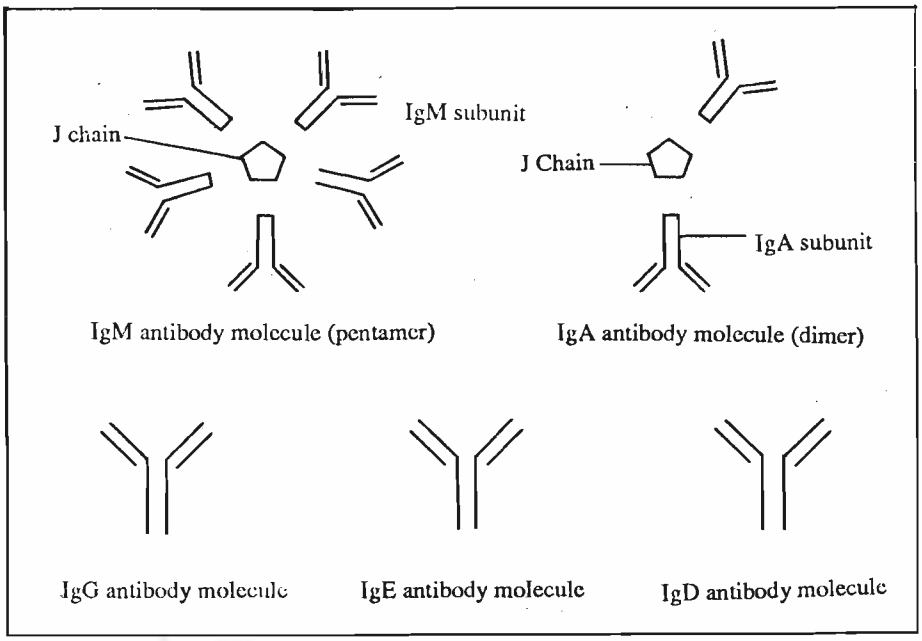

Fig. 16.4: The structures of five types of antibodies. Note the complex structures of IgM (a pentamer) and IgA (a dimer), IgG, IgE, and IgD consist of monomers, each composed of two heavy chains and two light polypeptide chains.

iii) **Immunoglobulin A**—This antibody represents about 15-20% of the human serum immunoglobulin pool. One form of this antibody is serum IgA that exist in the serum. The second form accumulate in body secretion and is referred to as **Secretary IgA.** This antibody provides resistance in the respiratory and gastrointestinal tract by inhibiting the attachment of parasites to the tissues.

iv) **Immunoglobulin E**—This antibody plays a major role in allergic reactions by sensitizing cells to certain antigens. This class may play a role in active immunity to helminthic parasites, but in Western countries it is more commonly associated with immediate hypersensitivity diseases such as asthama and hayfever.

v) **Immunoglobulin D**—This 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.

SAQ 6

a. Name the linkage by which two chains of antibody are joined together.

---

b. Which class of antibody is maximally present in the serum.

16.8.3 Antigen-Antibody Interaction

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. Certain antibodies are known as neutralizing antibodies which react with viral capside (coat of protein surrounding the genome) and prevent viruses from entering their host cells. Another type of

antibodies known as **antitoxin** destroy the toxin molecules by neutralizing them. Agglutinins are antibodies which react with antigens on the surface of organisms such as bacteria. This action causes clumping or agglutination of organism and enhances phagocytosis. Another form of antibodies are precipitins. These antibodies react with dissolved antigens and convert them to solid precipitates. In this form antigens are usually inactive and more easily phagocytized (Fig. 16.5).

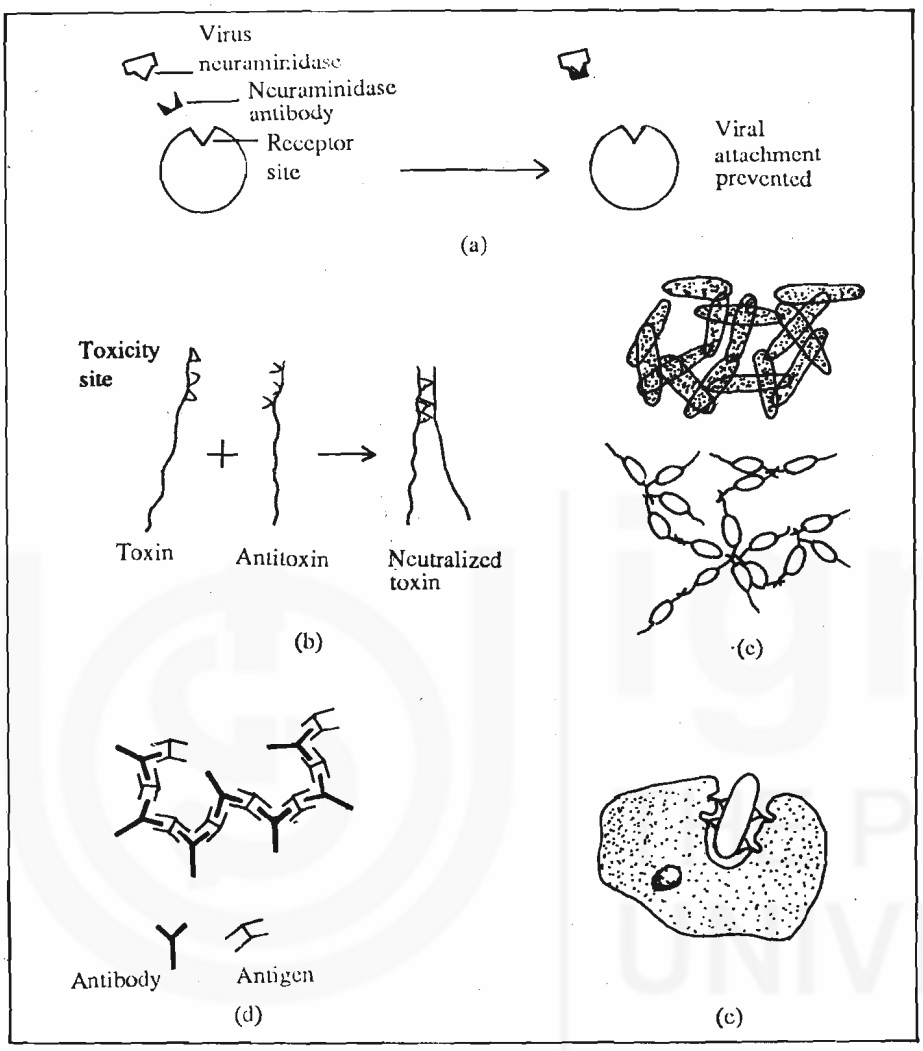

Fig. 16.5: Five different mechanisms by which antibodies interact with antigens and alter them. (a) Neuraminidase antibodies react with neuraminidase and prevent viral attachment to cells. (b) Antitoxins combine specially with toxins and neutralise the toxicity site of the toxin. (c) Agglutinins combine with antigens on the cell surface and bind the cells together or restrict movement by binding with flagellar antigens. (d) Precipitins combine with dissolved antigens and form latticelike arrangements that precipitate ont of solution. (e) Opsonins encourage phagocytosis by forming a bridge between parasites and receptor sites on the phagocyte.

SAQ 7

How do the antibodies alter the antigens infecting to the body.

16.9 SUMMARY

The immunology refers to a systematic study of developing specific immunity or resistance (immunie response) in an individual to a particular infection after an initial exposure to that infection. Age, environments and nutritional status of the individual affect his immune response. There are also some racial and individual differences. Animals, including humans, possess some non-specific defences against infection. These include physical barriers against the entry of pathogenic microorganisms, like skin and mucous membranes, and physiological conditions, e.g., acidic pH in stomach which destroys several bacteria. When any pathogenic micobes succeed in crossing these barriers, they come up against macrophages which can literally engulf and destroy the invader. Some biomolecules, mostly proteins and polysaccharides, which are also found on the surface of microbes, have the property of activating the immune system of the host, i.e., the animal. These are called antigens and those parts of their molecular structure which are responsible for this property are called antigenic determinants. The macrophages carry these determinants to special cells of the immune system which gets activated thereby. The latter developes during the fatal stage of the individual and is directed against "foreign" or "non-self" materials only. The proteins and other potential antigens present in the body before the immune system is developed are recognised as "self" and the system does not react to these. The immune system consists of two types of lymphocytes (lymph cells), namely the T-lymphocytes and the B-lymphocytes. Activated T-cells converge on that site of the body where the antigen was first detected. They get converted into lympho blasts and produce a series of small molecular weight proteins, the lymphokines, which assist the macrophages. After elimination of the antigen, a colony of identical T-lymphocytes persist in the tissue. These are called the memory T-lymphocytes and provide immunity in the event of reinvasion by the same micro-organism. This is called the cellular of cell-mediated immunity. Two other types of T-cells are also activated, namely the helper T-lymphocytes and the suppressor T-lymphocytes. The former help activate the B-lymphocytes which produce specific proteins, called 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 blood serum and are called immuno-globulins. The antibodies have a high specific affinity for the antigen, which may be free or on the microbe surface. The later clump together around the antibodies and are eliminated. This is referred to as the humoral immunity. A colony of activated B-lymphocytes also outlives the infection. These are called memory B-cells which produce more antibodies in the event of re-infection with same micro-organism and thus provide a prolonged immunity. The ratio of the helper and suppressor T-cells regulates the intensity of response of the B-cells. An excessive population of the helper cells leads to a stronger response and allergic symptoms.

16.10 TERMINAL QUESTIONS

1. (A) Tick (√) the correct answer.

   i) The pH of gastric juice is

   (a) basic (b) acidic (c) neutral (d) exactly 10.2

   ii) Stem cells arise in

   (a) Erythrocytes (b) Lymphocytes (c) bone marrow (d) red blood cells. ( )

   (B) Write 'T' for true and 'F' for false against the following statements.

   i) Lysozymes have bactericidal activity. [ ]

   ii) B-lymphocyte is identical to T-lymphocyte. [ ]

2. What are lymphokines and what is the basis of categorizing them?

3. Fill in the blanks

   i) Antibodies are produced by .....

   ii) Two identical ..... and two identical ..... are present in antibodies.

   iii)

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

16.11 ANSWERS

Self Assessment Questions

1. (A) relative resistance
   (B) different
2. a. Very young and old persons have a hypofunctional state of immune response and this is the reason of having susceptibility to various infections.
   b. The main digestive constituents of gastric juice are hydrochloric acid, rennin and pepsinogens.
3. Haptens are small molecules which serve as an antigens when combined with tissue proteins or polysaccharides.
4. When lymphopoeitic cells pass through thymus, they become T-lymphocytes and those passing through fetal liver and bone marrow become B-lymphocytes.
5. a. Lymphokines. They are proteins in nature.
   b. Body will become susceptible to various infections. Normally the suppressor T-lymphocytes interfere with exaggerated immune response. However, with fewer helper T-cells the function of B-lymphocytes will be impaired.
6. a. Thei is known as disulfide linkage.
   b. IgG is the class of immunoglobulin present maximally in serum out of total immunoglobulin pool.
7. Antibodies have specific sites for interaction with antigens and they form antibody-antigen complex in order to destroy the antigens.

Terminal Questions

1. (A) - (1) - b (2) - C
   (B) - (i) - T (ii) - F
2. The modified T-cells produce lymphokines which are low molecular weight proteins and actively take part in developing the cellular immunity. The lymphokines are categorised depending upon the function they perform. The lymphokine which perform the function of drawing phagocytes to the antigen sites is known as chemotactic factor and one which prevent macrophages in moving away is known as migration 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).
3. (i) Plasma cells
   (ii) Heavy 'H' chains, light 'L' chains
   (iii) 5-10% and 70-75%.

NOTE