Notes

30

IMMUNOBIOLOGY : AN INTRODUCTION

We all get infections, but some of us fall sick more frequently than others. This is related to the immune system. Proper functioning of immune system protects us from the infections. On the other hand its malfunctioning provides opportunity to infectious agents for causing diseases. Besides protection from infection, immune system also performs a number of other functions. It is about all this that you will learn in this lesson.

OBJECTIVES

After completing this lesson, you will be able to :

- *define the term immunity;*
- *explain the concept of "self" and "non-self";*
- *describe the types of defence mechanisms in the body;*
- *describe the types of immunity;*
- *list and describe various cells of the immune system;*
- *differentiate between cellular and humoral immunity; innate and acquired immunity;*
- *describe various components of the immune system;*
- *explain the concept of immunization (vaccination) and list various types of vaccines.*

30.1 IMMUNITY

Immunity is broadly defined as "the capacity of the body to recognize materials as foreign to itself and to neutralize, eliminate or metabolize them with or without injury to its own tissues".

Immunobiology is the study of organization and functioning of immune system. Immune system provides 'immunity' (protection against diseases).

Jenner, the father of immunology

Edward Jenner (1749-1823) is considered to be the father of modern immunobiology. He demonstrated that inoculation of cowpox crusts afforded protection to humans against smallpox. He observed that milkmaids who recovered from cowpox never contracted the disease smallpox. Hence the name vaccination from the Latin word "Vacca" for cow came into beng. The milkmaids and the vaccinated individuals were protected from smallpox virus. Such protection gave them what is called `immunity' to smallpox, although Jenner neither knew the actual causative agent of this disease nor the actual mechanism of protection.

Concept of "Self' and "Non-Self"

The basis of the above mentioned protection was the ability of the immune system of the milkmaid and vaccinated individuals to distinguish between **'self** (their own tissues) and **'non-self'** components of the outsiders i.e. the smallpox virus) in this context.

An individual induces a physiological response (immune response) to substances that are different from self components. For example an immune response is induced against pathogens (bacteria, virus, fungi and parasites) attacking body of the host.

Let us now learn about the different ways by which the body defends itself from pathogens and other harmful substances.

30.2 DEFENCE MECHANISMS IN THE BODY

There are four defence mechanisms in our body :

1. Immunity to defend the body from infections.
2. Metabolic defence to metabolize and detoxify foreign chemicals.
3. Stoppage of bleeding (Haemostasis) and thus preventing blood loss.
4. Resistance to stress mainly through release of hormone.

Immunological defence is the most important defence mechanism. It provides protection against various infective agents e.g. virus, bacteria, fungi and parasites and also against the development of a tumour.

Thus immunological defence serves three main functions :

1. Defence against microorganisms.
2. Recognition and destruction of mutant cells (Surveillance).
3. Removal of damaged or non functional cells to maintain normal state (Homeostasis).

INTEXT QUESTIONS 30.1

1. Who is considered as father of immunobiology?

   .....

2. What are the three main functions of immunological defence?

   (i) .....

   (ii) .....

   (iii) .....

3. Define immunology.

   .....

30.3 IMMUNE SYSTEM

By now, you are aware that immunity to infection is one of the most important factors facilitating survival of an individual. Immunity is mainly provided by a complex network of cells, tissues and soluble factors. This network is collectively referred to as the **'immune system'.** Cells participating in the immune response are organized into discrete **'lymphoid tissues and organs'** and spread throughout the connective tissues of non-lymphoid organs.

1. Tissues and Organs involved in the Immune System

Lymphoid organs are divided into two groups :

(i) Central lymphoid organs or primary lymphoid tissue. Example : Thymus and bone marrow.

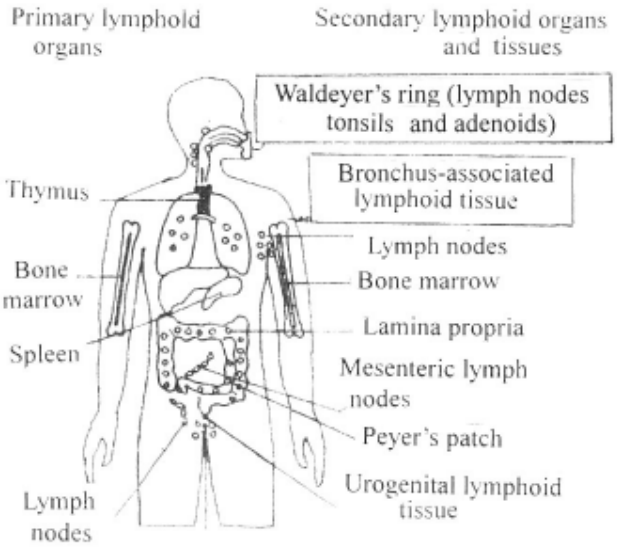

Fig. 30.1 Major lymphoid organs and tissues.

(ii) Peripheral lymphoid organs or secondary lymphoid tissue. Examples spleen, Payer's patches, tonsils, lymph nodes and mucosa-associated lymphoid tissue (MALT), which is associated with the respiratory system, urogenital and alimentary canal (Fig. 30.1).

2. Cells of Immune System

(i) Lymphocyes (Lymphoid cells)

All these are initially derived from the hemopoietic (blood cell producing) stem cells of bone narrow. Stem cells mean undifferentiated cells which can undergo unlimited division and can give rise to one or several different cell types. Bone marrow stem cells also differentiate to produce **erythrocytes (red blood cells), thrombocytes (blood platelets), granulocytes** and **monocytes (white blood cells).**

(ii) The macrophage

These are derived from monocytes.

Lymphocytes are the major cell types responsible for performing the immune functions. About 10^{12} lymphocytes constitute the mature lymphoid system in humans. Functionally, lymphocytes are divied into two sub-classes:

(i) B-cells or B-lymphocytes

(ii) T-cells or T-lymphocytes

Morphologically, these cells cannot be differentiated, but functionally these are distinct. Cells of immune system are differentiated on the basis of presence or absence of specific cell surface markers.

(a) B-Cells (B-lymphocytes)

Main functions of B-cells

1. Initiate antibody-mediated immune response.
2. Transform into plasma cells which secrete antibodies.

Origin of B-Cells

"B" stands for Bursa. Studies in birds showed that the bursa of Fabricius, a hind-gut lymphoid organ was the site of early development of antibody-producing cells. These cells are therefore termed as 'B-cells' ('B' derived from bursa of Fabricius). B-cells mature in the bone marrow and then are carried by the blood to the peripheral lymphoid organs. In mammals, B-cells lineage are initially generated in foetal (embryonic) liver. This process begins during the 8^{th} week of human gestation (pregnancy). The foetal liver continues to be the major site for production of the B-cells, until well into second trimester (4-6 months of pregnancy). Stem cells then populate the bone marrow and thereafter the B-cells are continuously produced in the bone marrow throughout the life (Fig. 30.2).

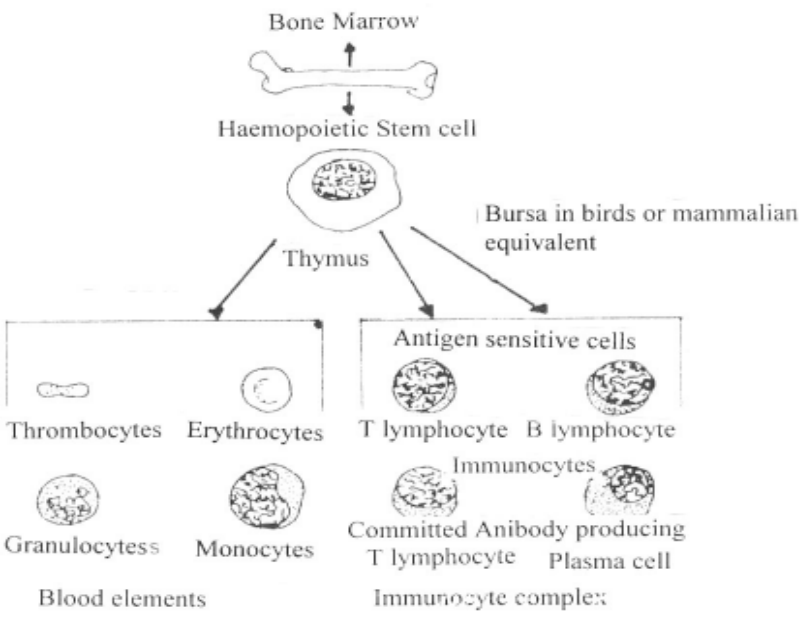

Fig. 30.2 Origin of B and T Cells

Characteristics of B-cells

(i) B-cells display **immunoglobulin** as an integral proteins *of* their cell membranes.

(ii) This surface immunoglobulin (antibody) acts as the receptor for antigen specific to it.

(iii) B-cells are responsible for the production of antibodies. Activated B-cells transform into plasma cells (Fig. 30.3). You will learn about 'antigen' and 'antibody' in the next section of this lesson.

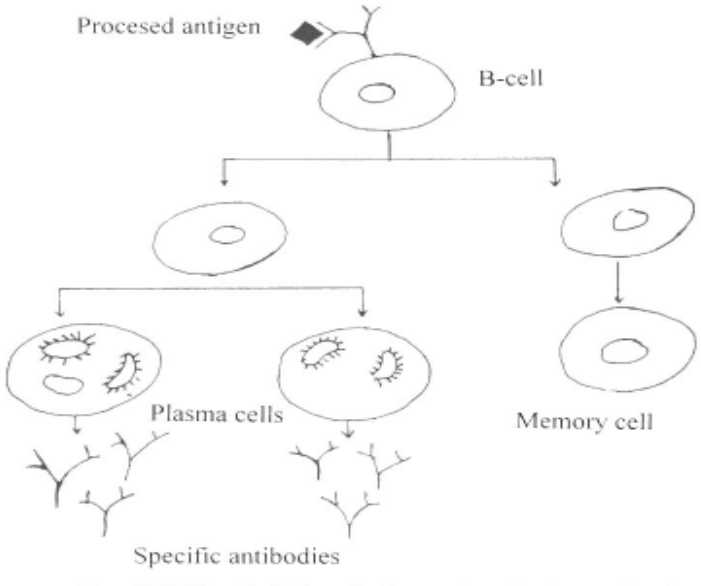

Fig. 30.3 B-cell differentiation and antibody production.

Plasma cells produce thousands of antibody molecules per second before they die in a day or so.

Some of the B-cells progeny do not differentiate into plasma cells but rather become 'memory cells' which produce antibodies in the event of the antigen re-appearing again in future.

(b) T-Cells (T-lymphocytes)

In contrast to B-cells, other lymphocytes leave bone marrow in an immature state during foetal and early stages of life. These are carried to the 'thymus', mature in this organ, and then they migrate to the peripheral lymphoid organ. These cells constitute the second major class of lymphocytes, the T-lymphocyte or T-cells. 'T' derived from thymus. Production of T-cells is completed early in life, but like B-cells, they also undergo mitosis in peripheral lymphoid organs, the daughter cells being identical to the original T-cells.

Main functions of T-cells

(i) Regulate immune response.

(ii) Mediate cell-mediated immune (CMI) response.

(iii) Induce B-cells to produce antibody.

T-cells are functionally classified into three categories (T_H, T_C, T_S)

1. Helper T-cells (T_H)

Promote response of B-cells resulting in antibody production (activate other T-cells).

2. Cytotoxic T-cells (T_C)

Kill virally infected cells and tumour cells.

3. Suppressor T-cells (T_S)

Suppress helper T-cells and may also be B-cells to limit/regulate activity of the latter.

Thus we see that T-cells mediate two general types of immunological functions : **effector** and **regulatory**.

Structurally, T-cells are differentiated on the basis of presence or absence of some specific surface molecules (T-cell receptors). B-cells and T-cells work in cooperation.

INTEXT QUESTIONS 30.2

1. Name the **two** categories of immune cells.

   (i) .....

   (ii) .....

2. Name the organ found in birds where B-cells are produced.

   .....

3. Write the **two** main functions of B-cells.

   (i) .....

   (ii) .....

4. Name the cells responsible for synthesis of antibodies.

   .....

5. What is the function of T-helper cells?

   .....

30.4 ANTIGEN AND ANTIBODY

While discussing about 'self' and 'non-self, we got a broad idea of **antigen**. Let us learn more about it.

30.4.1. Definition and Properties of an antigen

An antigen is any foreign molecule that can trigger a specific immune response.

Most antigens are either **proteins** or very large **polysaccharides**. Another term 'immunogen' is also used for antigen. However, there is a slight difference between the two. Immunogen describes a molecule that provokes an immune response while antigen describes a molecule which reacts with the antibody produced.

Paratopes and Epitopes : The part of antibody molecule which makes contact with the antigen is termed the **paratope**. The part of antigen molecule that makes contact with paratope is called the **epitope**. There may be a series of epitopes on an antigen. Such epitope clusters are called 'antigenic determinant'.

Requirements for becoming an antigen :

l. Substance should be foreign to the host.

2. Molecular weight of molecule should be 10,000 Dalton or more.

3. It should possess chemical complexity.

30.4.2 Antibody : Definition and properties

Antibody is a protein molecule produced in animals in response to an antigen.

Antibodies belong to the category of proteins called immunoglobulin. Each antibody molecule is composed of four interlinked polypeptide chains. The two long chains are called heavy chains, and the two short chains are called light chairs An antibody has a "stem" called "Fc" portion which comprises the lower half of the two heavy chains, and two "prongs' (the amino acid sequences that bind antigen).

The amino acid sequences of Fc portion are identical (constant) for all antibodies of same class. In contrast amino acid sequences for antigen binding site vary from antibody to antibody in a given class (Fig. 30.4)

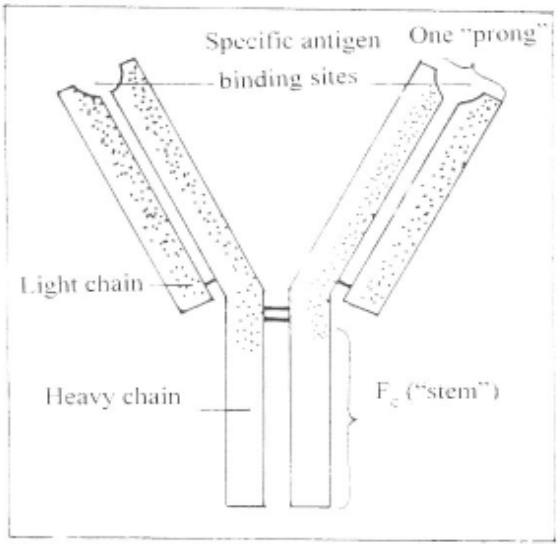

Fig. 30.4 Antibody structure

30.4.3 Type of immunoglobulins

- There are five major classes of antibodies (or immunoglobulins) distinguished by the amino acid sequences in the heavy chains. These classes are designated as Ig, IgA, IgE, IgG and IgM (1g = Immunoglobulin)
- They also differ in their molecular weight and function.
- IgG is found in highest concentration (almost 75% of the total immunogloblulins in humans).
- Antibodies are produced by plasma cells which are differentiated B-cells. Each B-cell type produces antibodies which react with a particular epitope of antigen.
- Secreted antibodies travel all over the body through blood and reach antigens of the kind that stimulate the immune response, combine with antigens (Fig. 30.5) and then direct an attack (by phagocytes cells which eat up foreign material) and complement that eliminate the antigen or the cells bearing them.

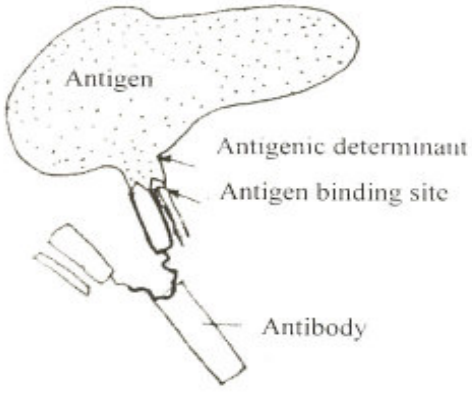

Fig. 30.5 Antigen-antibody binding

30.5 TYPES OF IMMUNE RESPONSES

Broadly, immune responses can be classified into two categories : **Non-specific immune responses** and **specific immune responses**.

1. **Non-specific immune responses** are those which non-selectively protect against foreign substances or cells without having to recognize their specific identities. Phagocytosis (engulfing, of particulate matter) by macrophages and extracellular killing by proteins known as 'complement'. They are two non-specific types of immune responses.
2. **Specific immune responses** (adaptive immune response) depend upon the immunological recognition of the substances or cells to be attacked. Specific immune responses are again of two types :

   (a) **Cell mediated immune responses :** Mediated by cytotoxic T-cells and natural killer cells. These constitute major defence against intracellular viruses and cancer cells.

   (b) **Antibody-mediated or humoral immune responses :** These responses are mediated by antibodies secreted by plasma cells, which arise from activated B-cells. They constitute major protection against bacteria and viruses in the extracellular fluid.

The above two differ from each other as shown in Table 30.1

Both cell mediated and antibody mediated immune responses are facilitated by helper T-cells and inhibited by suppressor T-cells (Fig. 30.6)

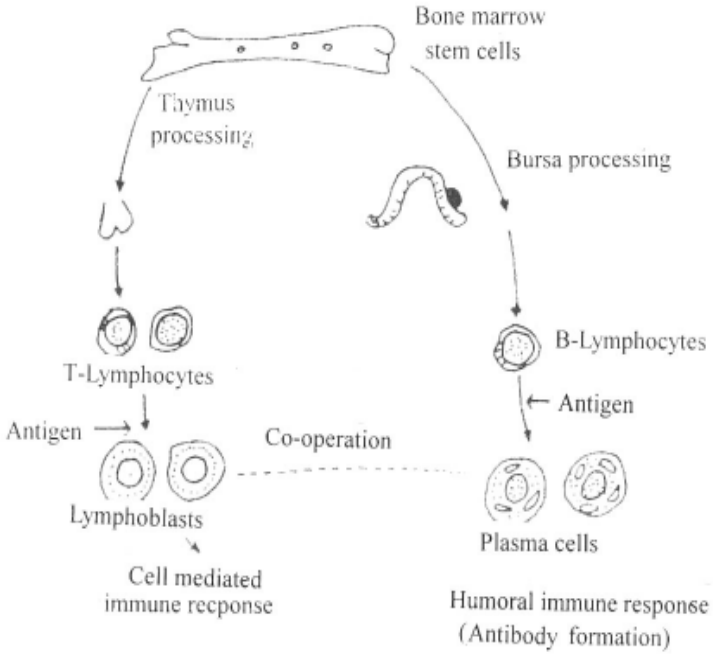

Fig. 30.6 Cell-mediated and humoral immune responses

Table 30.1 : Differences between cell-mediated and humoral (antibody mediated) immune responses

Cell-mediated immune response	Humoral immune response
1. Killing of intracellular organisms.	1. Antibodies specifically combine with antigen which stimulate their production.
2. Destruction of tumour cells	2. The combination of antibody with antigen may result in clumping molecules or particles, their toxicity may be neutralized, their uptake and digestion by phagocytes may be facilitated.
3. Rejection of graft tissue.	3. Combination of antigen with antibody may also cause lysis of cellular antigens present on the red blood cells or bacteria.
4. Delayed type of hypersensitivity reaction after contact with certain antigen.	

INTEXT QUESTIONS 30.3

1. Name the part of antigen which makes contact with antibody.

   .....

2. How many types of immunoglobulins are known? (Give only the number).

   .....

3. Name the immunoglobulin found in highest concentration.

   .....

4. Which type of immune response is responsible for the killing of cancer cells?

   .....

30.6 TYPES OF IMMUNITY

There are two main types of immunity : (i) Natural or innate (i.e. genetic, from birth), and (ii) Acquired (i.e. developed during life time).

A. Natural or Innate Immunity

A healthy individual himself from potentially harmful microorganisms by a number of very effective mechanisms. These mechanisms are termed **innate** or **natural immunity.** Innate defence consists of three main components :

(i) Physical barriers (preventing entry of germs)

(ii) Phagocytic cells and (Dealing with germs which enter)

(iii) Soluble components (complement)

(i) Physical Barriers

It is the first line of defence. It means preventing the entry of pathogens into the body. (Fig. 30.7).

Skin : The outer tough layer of skin is formed of keratin and is almost impermeable to germs. Sebaceous glands in the skin generate an acidic environment by producing lactic acid which kills many pathogens.

Epithelial lining of various organs : The respiratory tract, the alimentary tract (the gut) and the urino-genital tract have an exterior epithelial cell layer covered by a protective mucous lining. In the respiratory tract, cilia covering to the external surface of the epithelial cells continually beat upwards towards the nasopharynx and this helps to expel particles and pathogens. Epithelial cells are constantly renewed and their removal expels pathogens lodged on their surface.

Body secretions : Body secretions such as sweat and secretion from eyes also ward off pathogens. Other body fluids contain molecules which are bactericidal that is capable of killing bacteria (e.g., spermine in seminal fluid, hydrochloric acid in gastric juice, etc.).

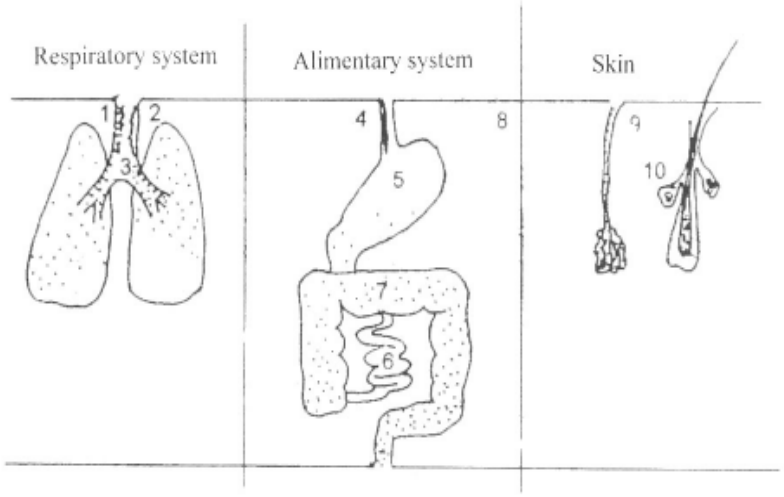

Fig. 30.7 Natural physical barriers to infections

If the germs somehow enter the body by evading physical barriers of the body, the other two main defence mechanisms come into play – **phagocytosis** and the **bactericidal effect** of soluble chemical factors collectively known as **complement system** which are described below. .

(ii) Phagocytic Cells

When the micro-organisms or inert particles such as colloidal carbon enter the tissue fluid or blood stream, these are very rapidly engulfed and destroyed by phagocytic cells. Such cells may either be circulating in body fluids or may be fixed in some tissues. This phenomenon is called phagocytosis (literally meaning 'eating' by the cell). The engulfment and destruction/digestion of microorganisms is assigned to two major types of cells named as **microphages** and **macrophages**.

- **Microphages** are the polymorphonuclear leucocytes (or neutrophils which are white blood cells) smaller in size and short-lived.
- **Macrophages** are mononuclear phagocytes large in size and long-lived. These are found in virtually all the organs and tissues. But particularly these are found in large numbers in lung, liver and spleen.

Important features of phagocytic cells

1. They are actively phagocytic.
2. They contain digestive enzymes to breakdown engulfed material.
3. They are an important link between innate and acquired immunity (described below). These pass on antigen or their products to the lymphoid cells for their further processing.

(iii) Complement System

The group of proteins known as 'complement' provides another innate immunity mechanism for killing microbes without prior phagocytosis.

> Complement system is an extremely complex system consisting of at least 20 proteins.

Some of the complement components are designated by the letter 'C' followed by a number. The most pivotal and most abundant component is C_3. Complement component may also act as **opson** in (e.g. $C_3$6). Opson is that type of antibody whose binding to antigens on virus or bacterium facilitates their subsequent ingestion by the phagocytic cells. Such antibodies can also cause direct destruction of microbes by making their membrane leaky.

B. Acquired Immunity

It is the immunity mediated by lymphocytes and characterized by antigen specificity and memory.

An acquired immunity may be brought about in an individual in two main ways:

1. By infection so that antibodies are produced against the infective agent and by deliberate artificial immunization. This is termed **actively acquired immunity.**
2. By transfer from an actively immunized individual through blood, serum component etc. This is called **passively acquired immunity.**

(i) Actively acquired immunity

Actively acquired immunity due to infection falls into two general categories.

(i) Some infections, such as diphtheria, whooping cough, smallpox and mumps usually induce a life time immunity i.e. a patient once recovered does not get the disease subsequently.

(ii) Other diseases such as common cold, influenza, bacillary dysentery and pneumococcal pneumonia confer immunity for a shorter period, sometimes only for a few weeks.

(ii) Passively acquired immunity

It may be developed in the following ways :

1. Transfer of antibodies (e.g. IgG) from mother into foetus across the placenta.
2. Breast fed children also receive antibodies from the mother's milk.
3. Pooled human immunoglobulin is also used as source of antibody in a number of cases including measles infection and infectious hepatitis.
4. Human immunoglobulin is also given to patients with a congenital inability to make antibody globulin.

30.7 ACTIVE IMMUNIZATION (VACCINATION)

People had observed in the past that individuals who recovered from certain diseases are protected for life time from recurrences. This gave rise to the concept of immunization. Edward Jenner introduced vaccination in 1796 using cowpox to protect against smallpox.

The objective of vaccination is introduce the attenuated germs into the body. The boty then generate specific population of memory cells. These memory cells can rapidly increase in number on the renewed contact with the same antigen and more antibodies can be produced to provide protection against infection.

30.7.1 Type of Vaccine

Three main types of vaccines are available :

1. Killed organisms as vaccines : Examples : typhoid, cholera, pertussis (whooping cough), rabies and poliomyelitis.
2. Live attenuated (weakened) organisms as vaccines; Examples: BCG, rubella, measles and polio.

   Attenuation mimics the natural behaviour of the organism without causing disease. The actively multiplying organism provides a sustained antigen supply.
3. Toxoid vaccines : Examples: diptheria and tetanus.

   Toxoid is a chemically or physically modified toxin that is no longer harmful but retains immunogenicity.

30.7.2 Important Vaccines – BCG, DPT and MMR

- BCG = Bacille Calmette Guerin (Calmette and Guerin were the scientists who contributed in the development of tuberculosis vaccine).
- DPT is a triple vaccine (or antigen) for diptheria and tetanus toxoids and for pertussis *Bordotella pertussis,* the whooping cough organism.
- MMR vaccine = Attenuated strain of measles, mumps and rubella).

Another class of vaccines termed as **polysaccharide vaccines** are available comprising vaccines for influenza, meningitis and pneumonia. In these vaccines the relevant immunogenic portions of the organism are used.

Vaccines of future : against Malaria, Leprosy, Anthrax, AIDS

INTEXT QUESTIONS 30.4

1. Mention two physical barriers of the body.

   .....

2. Macrophages are found in large numbers in the following organs :

   (i) .....

   (ii) .....

   (iii) .....

3. Give two examples of each of the following:

   (i) Killed organism vaccine .....

   (ii) Live attenuated organism vaccine .....

   (iii) Toxoid vaccine .....

WHAT YOU HAVE LEARNT

- There are various types of defence mechanisms in our body. Immunity defends us against infections.
- Immune system is a complex network of cells, tissues and soluble factors working in close co-ordination.
- Thymus and bone marrow are the central or primary lymphoid organs.
- Lymphocytes which are the major cells performing immune functions are of two main types - B-lymphocytes and T-lymphocytes.
- B-cells are transformed into plasma cells which produce antibodies.
- Foreign molecule which triggers an immune response is called antigen.
- Antibodies (immunoglobulins) are of five types, of which 1gG is found in the highest concentration.
- There are two main types of immune responses — specific and non-specific.
- Specific immune responses can be either cell-mediated or antibody (humoral)-mediated.
- There are two types of immunity — natural or innate and acquired.
- Vaccination is a type of actively acquired immunity.
- There are three types of vaccines – (i) killed organisms as vaccines, (ii) live attenuated organisms as vaccines, and (iii) toxoid vaccines.

TERMINAL QUESTIONS

1. Define the term immunity.
2. What are the main defence mechanisms operating in our body?
3. 'Immune system is a complex network of cells, tissues and soluble factors'. Justify this statement.
4. Describe the process of antibody production.
5. List main functions of T-cells.
6. Draw a schematic diagram of the structure of antibody.
7. What are the main physical barriers of the body?
8. Describe important features of phagocytic cells.
9. Give one main difference between passively acquired immunity and actively acquired immunity.
10. Define the process of attenuation.
11. Name two toxoid vaccines.
12. What do the following abbreviations mean?

    (i) BCG (ii) DPT (iii) MMR

ANSWER TO INTEXT QUESTIONS

30.1 1. Edward Jenner

2. Broadly immunological defence serves three functions :

   (i) Defence against microorganisms.

   (ii) Homeostasis i.e. removal of damaged (non functional) cells to maintain normal state.

   (iii) Surveillance i.e. recognition and destruction of mutant cells.

3. Study of organisation and function of the immune system.

30.2 1. (i) Central or primary lymphoid organs.

(ii) Peripheral or secondary lymphoid organs.

2. Bursa of Fabricius.

3. Main functions of B-cells:

   (i) Initiate antibody mediated-immune response.

   (ii) Transform into plasma cells which secrete antibodies.

4. Plasma cells/B-cells

5. Promote response by B-cells resulting in antibody production and also activate other T-cells.

30.3 1. Epitope

2. Five

3. Immunoglobulin G

4. Cell-mediated immune response

30.4 1. (i) Skin

   (ii) Epithelial cell layer of respiratory system.

2. (i) Lung

   (ii) Liver

   (iii) Spleen

3. (i) Typhoid vaccine, Pertussis vaccine.

   (ii) BCG, Rubella vaccine.

   (iii) Diphtheria vaccine, Tetanus vaccine.