CHAPTER 13

IMMUNITY

Major Concepts:

Number of allotted teaching periods: 12

More than 2000 years ago, the Greek historian **Thucydides** observed that occasionally someone contact a disease, recovers and never catches the particular disease again, the person has become immune (resistant) to subsequent infection. In 1796 an English country doctor **Edward Jenner** hypothesized that cowpox somehow conferred protection against smallpox.

The body's response to foreign molecules, such as the production of antibodies directed against a specific **antigen**, is called an **immune response**. The term **immune** is derived from Latin word *immunis* meaning "safe" or free of burden. **Immunity** is the ability to resist damage from foreign substances such as microorganisms and harmful chemicals e.g. toxins released by microorganisms. **Immunology** is the study of immunity and the defence mechanism of the body.

Defences Against Microbial Invasion

The human body has three lines of defences against microbial attack:

(1) First line of defence – the **external barriers** that keep microbes out of the body. (2) Second line of defence – the **nonspecific internal defence** (innate immunity) that combat all invading microbes. (3) Third line of defence – the specific (adaptive immunity) or **immune system** that directs its assault against specific microbes.

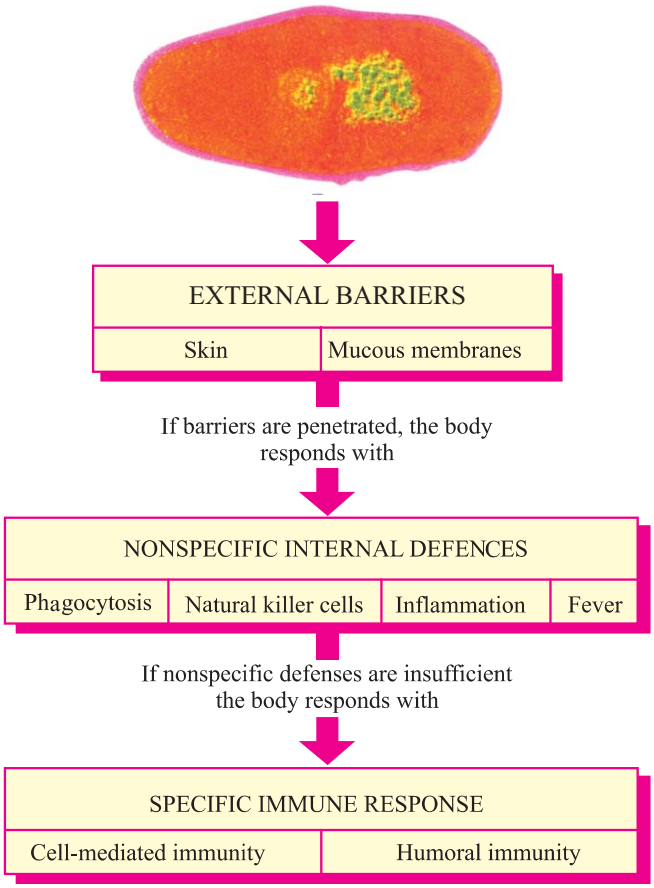


Fig 13.1 Levels of defence Against Infection

13.1 FIRST LINE OF DEFENCE

The first and obviously best, defence is to keep microbes out in the first place. The human body has two surfaces exposed to the environment: the **skin** and the **mucous membranes** of the digestive and respiratory tracts. These surfaces are barriers to microbial invasion.

Structural Features of Human Skin

The skin is made up two-layers **dermis** and **epidermis**. The dermis is dense, irregular connective tissue. Nerve endings hair follicles, smooth muscles, glands and lymphatics extend to the dermis. The epidermis is stratified squamous epithelium separated from dermis by basement membrane. Most cells of epidermis are **keratinocytes**, which produce a protein mixture called **keratin**. Other cells of the epidermis include **melanocytes**, which contribute to skin colour and **Langerhan cells**, which are part of immune system. The major glands of skin are the **sebaceous glands.**

Sebaceous glands located in the dermis, are simple or compound alveolar glands that produce **sebum**, an oily, and white substance rich in lipids. Most sebaceous glands are connected by a duct to the upper part of the hair follicles from which the sebum oils the hair and the skin surface. This prevents drying and provides protection against some bacteria. There are two types of sweat glands i.e merocrine and apocrine.

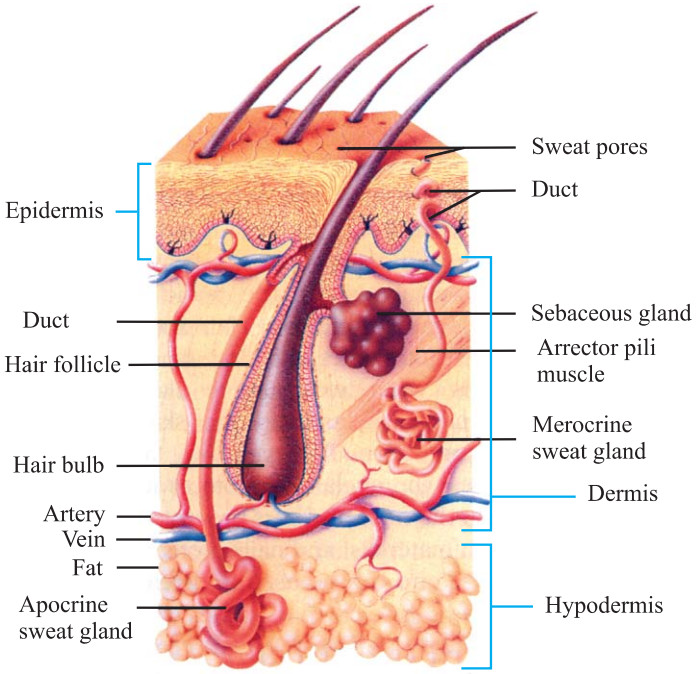


Fig: 13.2 Glands of Skin

The Intact Skin is both a Barrier to Entry and Inhospitable Environment of Microbial Growth

The outer surface of the skin consists of dry dead cells having keratin. Consequently, most microbes that land an the skin cannot obtain the water and nutrients they need. **Secretion** from sweat glands and sebaceous glands also cover the skin. These secretions contain acids and natural antibiotics such as **lactic acid** that inhibit the growth of bacteria and fungi. These multiple defences make the unbroken skin an extremely effective barrier against microbial invasion.

Digestive Tract : Role of Acids and Enzymes

The gastrointestinal tract (GIT), is covered by mucous membrane, which protects the G1T. (a) In the stomach hydrochloric acid is secreted by **oxyntic** or **parietal cell**. It kills the microorganisms (b) **Zymogen cells** or principal cells secrete gastric enzymes, which digest the microorganisms. (c) Intestinal and pancreatic juice also secrete enzymes, which digest the microorganism.

Role of Respiratory Tract

The nasal cavity cleans the air. The vestibule is lined with hairs that trap some of the large particles of dust in the air. The air comes into contact with the mucous membrane lining the nasal cavity. This mucous membrane consists of pseudostratified ciliated columnar epithelium with goblet cells, which secrete a layer of mucus. The mucus traps debris in the air and the cilia in the surface of the mucous membrane sweep the mucus posteriorly to the pharynx, where it is swallowed and eliminated by the digestive system. The trachea is lined by mucous membrane. The cilia propel mucus and foreign particles towards the larynx, where they enter the pharynx and are swallowed.

The **nasal turbulence mechanism** (see glossary) for removing particles from air so effective that almost no particles larger than 6 micrometeres in diameter enter the lungs through the nose. Of the remaining particles, many that are between 1 and 5 micrometers settle out in the small brochioles as a result of gravitational precipitation. Particles smaller than 0.5 micrometres in diameter remain suspended on the alveolar air and are later expelled by expiration

The cilia and mucus present in the bronchus and bronchioles are the system's clearing elements.

13.2 SECOND LINE OF DEFENCE - The Nonspecific Defences

Three nonspecific internal defences are mustered against microbes that penetrate the skin or mucous membranes. These defences are nonspecific because they attack wide variety of microbes, rather than targeting specific invaders as the immune response does. First, the body has a standing army of **phagocytic cells** that destroy microbes and **natural killer cells** that destroy cells of the body that have been infected by viruses. Second, an injury with

combination of tissue damage and relatively massive invasion of microbes provokes an **inflammatory response**. Third, if a population of microbes proceeds in establishing a major infection, the body often produces fever, which slows down microbial production and enhances the body's own fighting abilities.

13.2.1 KILLING CELLS OF BLOOD

Constantly patrolling your body are white cells called **phagocytes**. A phagocyte is a cell that destroys other cells by engulfing and ingesting them. This process is called **phagocytosis**. Two types of blood cells are phagocytes: macrophages and neutrophils.

Macrophages

Monocytes are formed in bone marrow. Monocytes have short life i.e. only 10-20 hours. Macrophages are derived from monocytes or the monocytes that that leave the blood are called **macrophages**. From bone marrow, through blood, macrophages are transported to the areas of the body where they are needed. Macrophage can engulf large particles, even the whole red blood cells, or occasionally even malarial parasites. Macrophages after digesting particles can extrude the residual products. Macrophages are beneath the free surfaces of

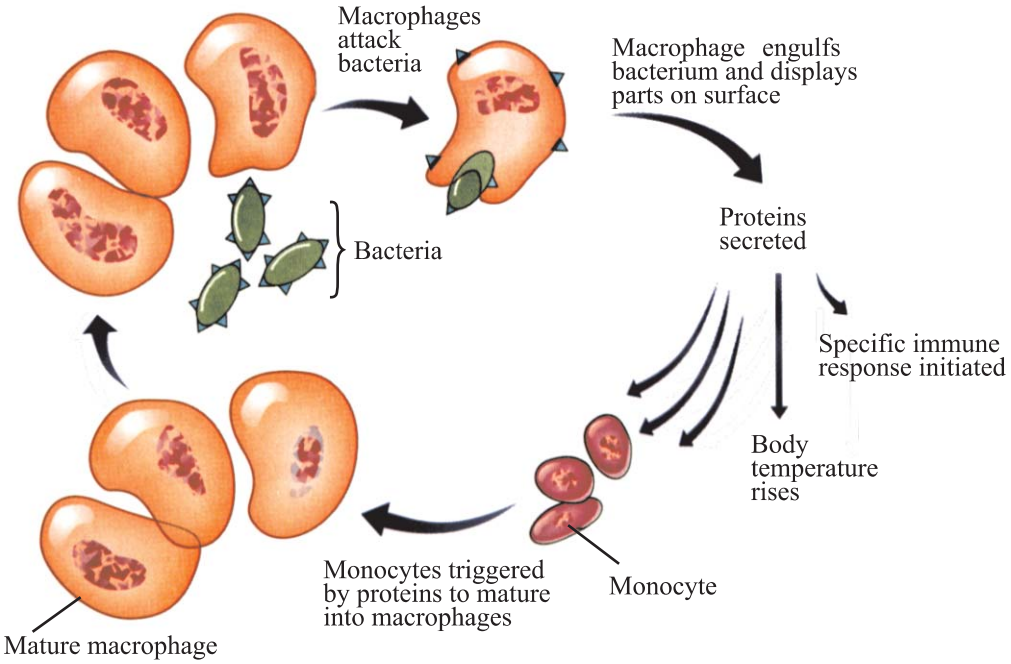


Fig. 13.3 Activation of the Immune Response

the body and provide protection by trapping and destroying microorganisms entering the tissue.

The macrophages secrete many different proteins. Some of these proteins trigger the maturation of monocytes into macrophages, thereby increasing their numbers. Another protein interleucin-1 signals the brain to raise the body temperature, producing fever. The higher temperature aids the immune response and inhibits the growth of invading microorganisms.

Neutrophils

These are a type of granular leukocytes, which are mobile and squeeze between cells of capillary walls. They move like *Amoeba* forming pseudopodia . The life of neutrophils once released from the bone marrow is 4-8 hours circulating in blood and 4-5 days in tissue. In serious infections, life span is shortened to few hours, because they proceed rapidly to infected area to perform their duty and they often die after a single phagocytic event. Neutrophils also release lysosomal enzymes that kill microorganisms and also cause damage and inflammation.

Natural Killer Cells

Natural killer cells are another class of white blood cells. In general, natural killer cells do not directly attack invading microbes. Instead, natural killer cells strike at the body's own cells that have been invaded by viruses. Virus infected cells usually bear some viral proteins on their surfaces. Natural killer cells recognize and kill cancerous cells. Natural killer cells do not eat their victims; they strike from the outside. Their weapons are proteins that they secrete into the plasma membrane of the infected or cancerous cell. Killer cells also secrete enzymes that break up some of the molecules of the target cell, as a result the target cell soon dies.

13.2.2 PROTECTIVE PROTEINS

The **complement system** often simply called complement is a number of plasma proteins. Once a complement protein is activated, it activates another protein, and the result is a set series of reactions. Complement is activated when microbes enter the body. It "complements" certain immune responses and this accounts for its name. For example, it is involved in and amplifies the **inflammatory response** because **complement proteins** attract **phagocytes** to the scene.

Another series of reaction is complete when complement proteins (perforin-1) result in a membrane attack complex that produces **holes** in the bacterial cell walls and plasma membranes of bacteria. When K^+ ions leave,

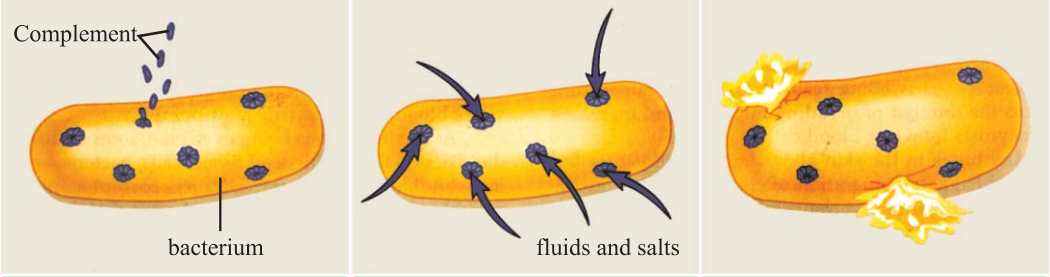


Fig. 13.4 Action of the complement system against a bacterium

fluids and salt enter bacterial cell to the point that it bursts.

How the Interferons Inhibit the Ability of Viruses to Infect Cells?

Cells of immune system secrete a remarkable number of regulatory proteins known as **cytokines**. When infected by viruses, cells respond by secreting cytokines called interferons. Interferons are a heterogeneous group of lipoproteins. They inhibit the growth of viruses by blocking the translation of viral proteins. Because **interferons** are produced within a few hours of the initiation of viral replication, they may act in the early phase of viral diseases to limit the spread of virus.

13.2.3 INFLAMMATORY RESPONSE

The inflammatory response is a major component of the non-specific defence. Any damage to tissue, whether caused by an infections microorganism or by physical injury, even just a scratch or an insect bite triggers this response. Inflammation can be localized or systemic. **Local inflammation** is an inflammatory response confined to a specific area of the body.

Inflammation literally means "setting on fire". The fig. 13.5 shows the chain of events that make up the inflammatory response, in case where a pin has broken the skin and infected it with bacteria. The first thing that happened when a tissue is injured is that the damaged cells release chemical alarm signals such as **histamine**. The chemical sparks the mobilization of various defences. Histamine for instance induces neighbouring blood vessels to dilate and blood vessels start leaking. Blood flood to the damaged area increases, and blood plasma passes out of the leaky vessels into the interstitial fluid of the affected tissues. The major results of the inflammatory response are to disinfect and clean injured tissues. The white blood cells mustered into the

area engulf bacteria and the remains of the body cells killed by them or by the physical injury are left. Many of the white blood cells die in the process. The **pus** that collects around a wound consists largely of microbes, tissue debris,

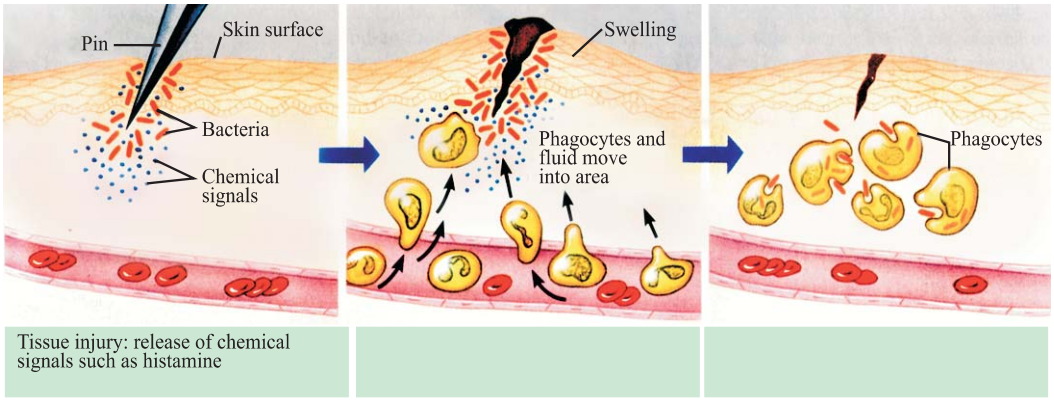


Fig. 13.5 The Inflammatory Response

and living and dead white blood cells. The inflammatory response also helps to prevent the spread of infection to the surrounding tissues.

The body may react with one or several inflammatory weapons for instance the number of white blood cells circulating in the blood may increase. Another response is **fever**.

13.2.4 TEMPERATURE RESPONSE

Fever, which means a body temperature above the usual range of normal, can be caused by abnormalities in the brain itself or by toxic substances that affect the temperature-regulating centers. Some causes of **fever** are bacterial diseases, brain tumors, and environmental conditions that may terminate in heatstroke.

Effect of Pyrogens: Many proteins, breakdown products of proteins, and certain other substances, especially lipopolysaccharide and toxins released from bacterial cell membrances, can cause the set-point of the **hypothalamic thermostat** to rise. Substances that cause this effect are called **pyrogens**. It is pyrogens released from toxic bacteria or pyrogens released from degenerating tissues of the body that cause fever during disease conditions. When the set point of the hypothalamic temperature-regulating center becomes increased to a higher level than normal, all the mechanisms for raising the body temperature are brought into play, including heat conservation and increased heat production. Within a few hours after the set-point has been increased to a higher level, the body temperature also

Several experiments have suggested that interleukin-1 causes fever by first inducing the formation of one of the prostaglandins. When drugs block prostaglandin formation, the fever is either completely abrogated or at least reduced. In fact, this may be the explanation for the manner in which aspirin reduces the degree of fever because aspirin impedes the formation of prostaglandins from arachidonic acid. It also would explain why aspirin does not lower the body temperature in a normal person because a normal person does not have any interleukin-1. Drugs such as aspirin that reduce the level of fever are called antipyretics.

approaches this level.

The Ways Fever Kills Microbes

Certain white blood cells in responding to the infection, release hormones collectively called **endogenous pyrogens** (self produced fire makers). **Pyrogens** travel in the blood stream and raise the thermostat's set point, triggering behaviours that increase body temperature: shivering increased fat metabolism or feeling cold so more clothing is put on. Pyrogens also cause other cells to reduce the concentration of iron in the blood.

Fever has both beneficial effects for the body's defences and detrimental effects on the invading microbes.1) Many bacteria require more iron to reproduce at temperature of 38^0C or 39^0C than at 37^0C, so fever and reduced iron in the blood combine to slow down their rate of reproduction. (2) Simultaneously, fever increases the activity of phagocytic white blood cells that attack bacteria, they rely producing a shorter and less serious infection. (3) When viruses invade certain cells of the body they synthesize and release a protein called interferon. It travels to other cells and increases their resistance to viral attack. Fever increases the production of inteferons. (4) The higher body temperature may directly inactivate the virus particles,

Skills: Initiating and Planning

- **Justify the inflammatory response in arthritis as an example of a misdirected immune response.**

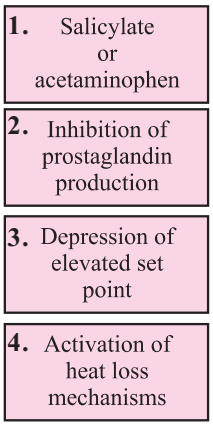
In this disease, autoantibodies are formed against IgG (antibody or immunoglobin of class G). These autoantibodies are called rheumatoid factors. The agent that induces these autoantibodies is unknown. Within the inflamed joints, the synovial membrane is infiltrated with T cells, plasma cells and macrophages and the synovial fluid contains high levels of macrophage- produced inflammatory cytokines.

Skills: Initiating and Planning

- **Justify why the physician prescribe antipyretic drugs, when fever is a nonspecific defense against microbial infections**

Antipyretic Therapy

Antipyretic create their effects by inhibiting prostaglandin production in the hypothalamus, which has the effect of blocking set point elevation and maintaining the set point at nearer normal levels.



Pharmaceutical Intervention in Fever

13.3 THE THIRD LINE OF DEFENCE – The Specific Defences

The third line of defence or specific defence mechanism or immune system recognizes and defends against invading microbes and against cancer cells. Specific defence mechanisms depend on the lymphatic system and its cells. Substances that stimulate specific immunity are antigens (large molecules) and haptens (small molecules). Specific immunity historically has been divided into two types: **Humoral immunity** and **cell-mediated**. Early investigators of the immune system found that, when plasma from an immune animal was injected into the blood of a nonimmune animal, the nonimmune animal became immune. Because the process involved body fluids (humors), it was called **humoral immunity**. It was also discovered that blood cells transferred from an immune animal could be responsible for immunity and this process was called **cell-mediated immunity**.

It was also known that immunity results from the activities of lymphocytes called B and T cells. B cells give rise to cells that produce proteins called **antibodies**, which are found in the plasma. Because antibodies are responsible, **humoral immunity** is now called **antibody mediated immunity**.

Monocytes, T cells and B cells as Components of Immune System

The human blood cells consists of: (a) Polymorphonuclear neutrophils (b) Polymorphonuclear eosinophils (c) Polymorphonuclear basophils(d) Monocytes (e) Lymphocytes

Monocytes

From bone marrow or lymphoid tissues monocytes are transferred (10 to 20 hours transit time) through the capillary into tissues. Once in the tissue they swell and attain a larger size to become tissue **macrophages** and in this form, they can live for months or even for years unless they are destroyed by performing phagocytic function. Macrophages secrete about 100 different compounds including **interferons** and enzymes that destroy bacteria. When macrophages are stimulated by bacteria, they secrete **interleukins**, which activate B cell and helper T cells. Interleukins also promote a general response to injury, causing fever and activating other mechanisms that defend the body against invasion.

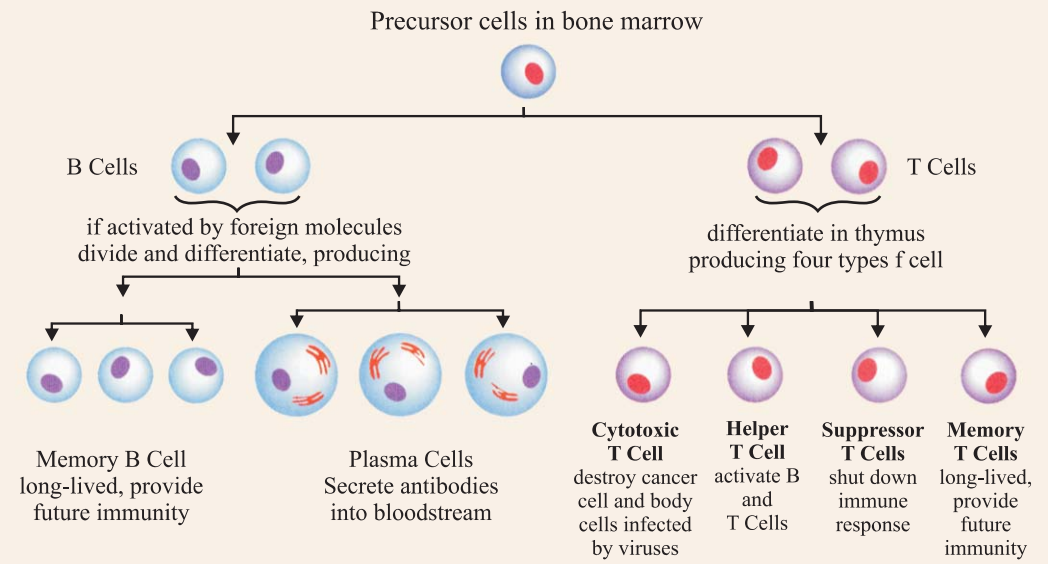


Fig. 13.6 The Major Cells of Immune System and Their Roles in the Immune System

T Cells and B Cells

Immune responses depend on two main groups of white blood cells: phagocytes and lymphocytes. **Phagocytes** include neutrophils and macrophages (monocytes). **Lymphocytes** spend most of their time in tissues and organs of lymphatic system. Three main types of lymphocytes are: T lymphocytes or T cells, B lymphocytes or B cells and natural killer (NK) cells.

T Cells are Responsible for Cellular Immunity

T cells originate from stem cells in the bone marrow. After early embryonic development, the newly forming T cells migrate to **thymus gland** for processing. (The 'T' in cells stands for *thymus derived*). The thymus

makes T cells immunocompetent that is capable of immunological response. Two main categories of T cells have been identified. The first group, known as **CD8** cells because they have surface marker designated **CD8**, include cytotoxin T cells and suppressor T cells. **Cytotoxic T cells** also known as **killer T cells** recognize and destroy cells with foreign antigens on their surface. Among their target cells are virus-infected cells, cancer cells and foreign tissue grafts. T cells kill their target cells by releasing a variety of cytokines and enzymes. **Suppressor T cells** release **cytokines** that inhibit the activity of other T cells and B cells. **Helper T cells** also known as **CD4** cells because they have a surface marker designated **CD4**. Helper T cells secrete substances that activate or enhance the immune response.

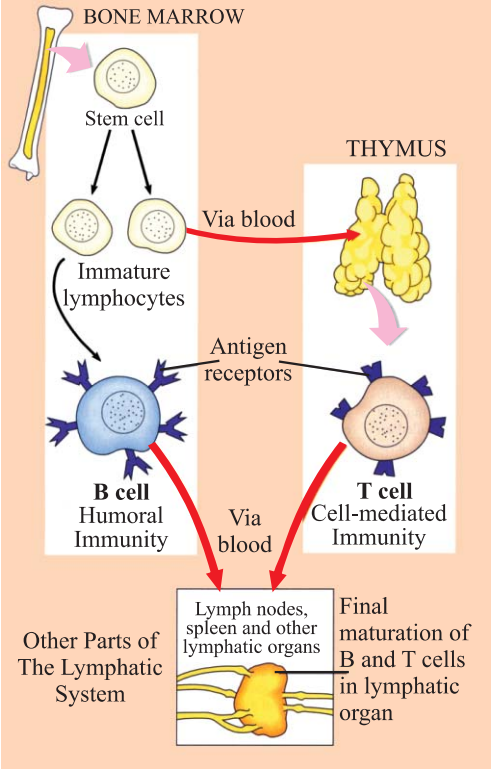


Fig: 13.7 The Development of B cell and T cells

B Cells

B cells are differentiated in bone marrow (hence the name B cells) Each B cells carries receptors needed to bind with a specific type of antigen. After binding with specific type of antigen the B cells develop into **plasma cells**, the cells that are specialized to secrete antibodies. A plasma cell can produce more than 10 million molecules of antibody per hour.

13.3.1 INBORN AND ACQUIRED IMMUNITY

The two basic types of immunity are (a) inborn or innate immunity (b) acquired immunity. If microorganisms breach the first line of defence i.e. skin and mucous membrane then the **innate part** of the immune system is available to destroy the invaders. Because the components of the innate or inborn immunity are fully active, they can function immediately upon entry of the microorganisms. The ability of the innate immune system to kill microorganisms is not specific. Highly specific protection is provided by the **acquired (adaptive) part** of the immune system, but it takes several days for this system to become fully functional. The two components of the acquired immune system are **cell-mediated immunity** and **antibody mediated (humoral) immunity**.

Table 13.2 Main Component oif Innate and Acquired Immunity

Immunity	Humoral immunity	Cell-mediated immunity
Innate	Complement, neutrophils	Macrophages, natural killer cells
Acquired,	B cells, Plasma cells	Helper T cells, cytotoxic T cells

Science Titbits

In 1717 Mary Montagu, the wife of an English ambassador to the Ottoman Empire, observed local women inoculating their children against smallpox. **Edward Jenner** observed and studied Miss Sarah a milkmaid who had previously caught cowpox and was found to be immune to smallpox.

Types of Acquired Immunity ---Active and Passive Immunity

There are two ways to acquire adaptive immunity: (a) Active Immunity (b) Passive Immunity. Both types may be acquired naturally or artificially. Providing immunity artificially is called **immunization**.

Natural Active Immunity: This is the kind of immunity, which is obtained as a result of an infection. The body manufactures its own antibodies when exposed to an infectious agent. Because memory cells, produced on exposure to the first infection, are able to stimulate the production of massive quantities of antibody when exposed to the same antigen again, this type of immunity is most effective and generally persists for a long time, sometimes even for life.

Artificial Active Immunity (Vaccination): This is achieved by injecting (or less commonly administering orally) small amounts of antigen, called the **vaccine**, into the body of an individual. The process is called **vaccination**. The antigen stimulates the body to manufacture antibodies against the antigen. Often a second, booster injection is given and this stimulates a much quicker production of antibody which is long lasting and which protects the individual from the disease for a considerable time. Several types of vaccine are currently in use.

Critical Thinking

Why do you think it is important that there are phagocytes constantly circulating in the blood stream and in the body tissues?

Passive Immunity

In passive immunity antibodies from one individual are passed into another individual. They give immediate protection, unlike active immunity, which takes a few days or weeks to build up. However, it only provides protection against infection for a few weeks, for the antibodies are broken down by the body's natural processes, so their number slowly fall and protection is lost.

Natural Passive Immunity

Passive immunity may be gained naturally. For example, antibodies from a mother can cross the placenta and enter her foetus. In this way they provide protection for the baby until its own immune system is fully functional. Passive immunity may also be provided by colostrum, the first secretion of the mammary glands. The baby absorbs the antibodies through its gut.

Artificial Passive Immunity

Here antibodies which have been formed in one individual are extracted and then injected into the blood of another individual which may or may not be of the same species. They can be used for immediate protection if a person has been; or is likely to be, exposed to a particular disease. For example, specific antibodies used for combating tetanus and diphtheria used to be cultured in horses and injected into humans. Only antibodies of human origin are now used for humans. Antibodies against rabies and some snake venoms are also available. Antibodies against the human rhesus blood group antigen are used for some rhesus.

13.3.2 CELL-MEDIATED AND ANTIBODY MEDIATED IMMUNITY

Cell-Mediated Immune Response

The activation of helper T cells by interleukin-1 and the binding of antigen to these activated helper T cells unleash a chain of events known as the **cell-mediated immune response**. The main event of this response is that **cytotoxic T cells** (cell poisoning cells) also known as natural killer (NK) cells, recognize and destroy infected body cells. When a helper T cell has been activated it produces a variety of chemical substances collectively called **lymphokines**. One type of lymphokine attracts macrophages to the site of infection and another inhibits their migration away from it. Another type of a lymphokine stimulates T cells that are bound to foreign antigens to undergo cell division many times. This cell division produces enormous quantities of T cells capable of recognizing the antigens specific to the invader. Each type

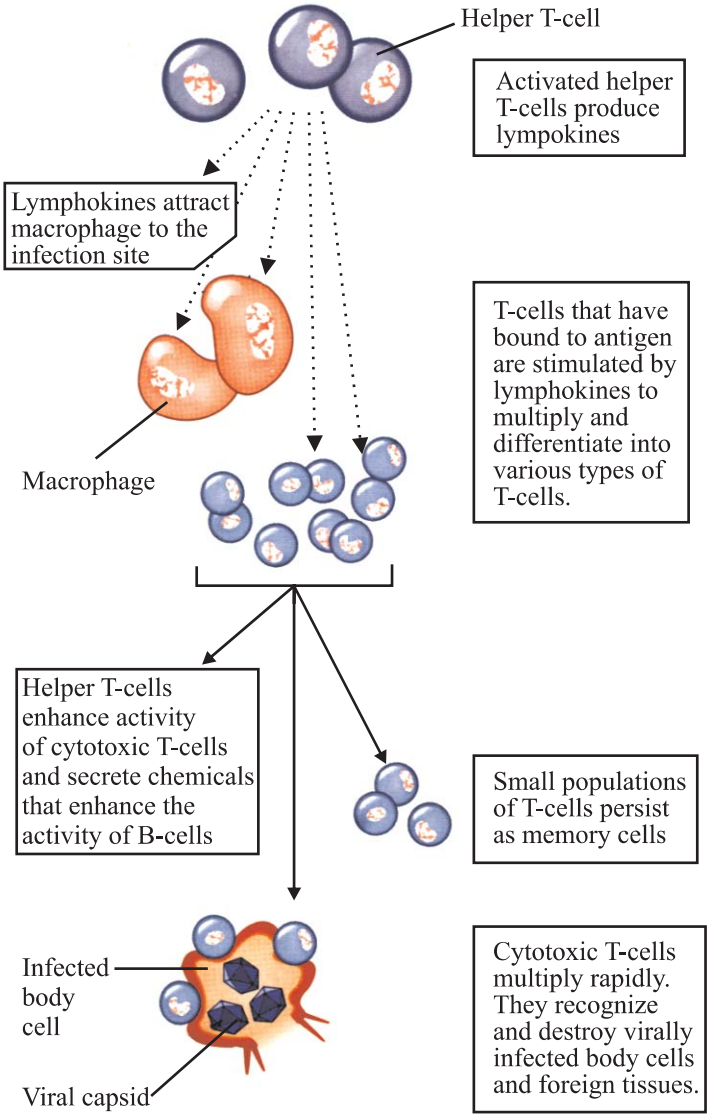


Fig. 13.8 Cell Mediated Immune Response

of activated T cell does have a specific job. Because the entire cell binds to the infected cells (by means of specific cell-surface proteins), this response is called **cell-mediated**.

The Antibody Mediated Immune Response

When helper T cells are stimulated to respond to foreign antigens they activate the cell-mediated immune response and activate a second, more long range defence called the **antibody mediated immune response**. Depending

upon the types of antigen present, the helper T cells may stimulate either or both of the immune response.

The key players in antibody–mediated immunity are the lymphocytes called **B cells** or **B-lymphocytes**. The B cells are named after a digestive organ in birds called Bursa of Fabricus, in which these lymphocytes were first discovered. However, B-cells mature in the bone marrow of the humans. The antibody response is sometimes called the **humoral response**, which refers to the fact that B cells secrete antigen that specific chemicals into the blood stream – one of the body fluids called "**humours**" long ago.

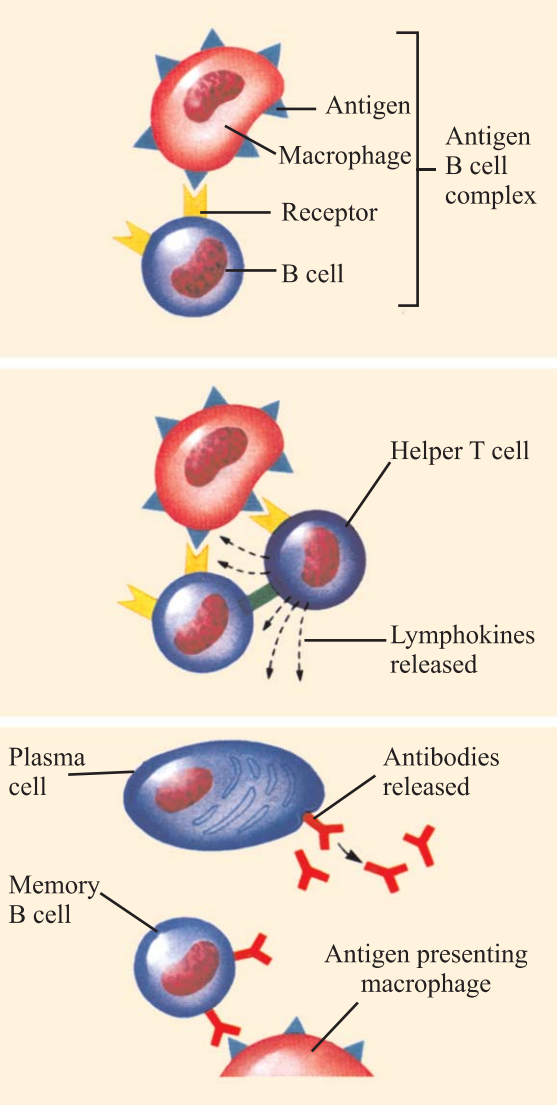


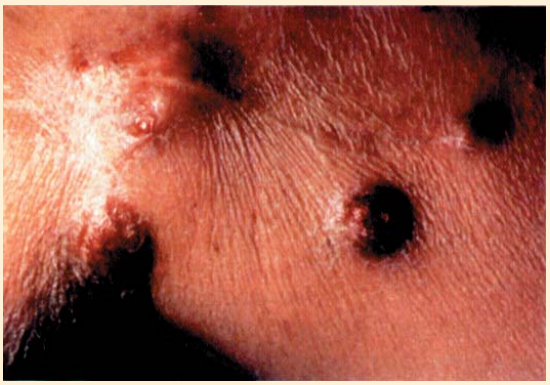
Fig.13.9 Antibody-mediated response

On their surface B cells have about 100,000 copies of a protein receptor that binds to antigens. Because different B cells bear different protein receptors, each recognizes a different, specific antigen. At the onset of a bacterial infection for example, the receptors of one or more B cells bind to bacterial antigens. The B cells may bind to either free bacteria or bacterial antigens displayed by macrophages. These antigen-bound B cells are detected by helper T cells, which then bind to the antigen –B cell complex (fig. 13.9). after binding, the helper T cells release lymphokines that trigger cell division in the B cells. After about 5 days and numerous cell divisions, a large clone of cells is produced from each B cell that was stimulated to divide.

Malignant Melanoma

The presence of tumour infiltrating lymphocytes (TIL) amid the tumour cells in the stroma and overlying epidermis is a constant feature of melanoma, the deadliest skin cancer. These lymphocytes are mostly cytotoxic cells. They can kill melanoma cells. This specific killing can be facilitated by monoclonal antibodies against CD4, CD8, T cells receptors and against class 1 human leukocyte antigens. This indicates that these cytotoxic cells can recognize melanoma cells through the T cells receptors in a human leukocyte antigen class 1. Therefore, these cells and their products are important in killing in melanoma. TILs are not strong enough to control certain types of tumors such as those of malignant melanona.

Gene therapy is the treatment of genetic disorder by the insertion of normal genes into the cells of a patient. In 1991 doctors injected genetically engineered cells into the thigh of a melanoma patient in an attempt to use gene therapy to help his immune system to destroy the cancer. Researchers first remove TIL cells from the patient and inserted a gene that codes for the protein tumor necrosis factor (TNF). This protein kills tumor cells by preventing them from establishing a blood supply. The engineered TIL cells were then returned to the patients bloodstream to seek out and invade the malignant melanoma tumors. As each genetically altered TIL cell finds and enters a tumor, it is able to attack the tumor with the TNF. The engineered TIL cells, in effect, becomes a factory that makes the tumor-killing protein inside the tumor itself.



Malignant Melanoma

Science, Technology and Society Connections

Describe malignant melanoma as due to the inability of tumor-infiltrating lymphocyte (TIL) to control the tumor of skin cancer and correlate it with the scientific advancements of inserting a gene of tumor necrosis factor in the lymphocyte.

Then the B cells begin producing and secreting copies of the receptor proteins that respond to the antigen. These receptor proteins are called **antibodies** or **immunoglobulins**. The secreting B cells are called **plasma cells**. After B cells become plasma cells they live only for a few days but secrete a great deal of antibody during the time. Antibodies do not destroy a virus or bacterium directly, but rather it destruct them by the mechanism of complement or macrophages.

Memory Cells

A person who overcomes a disease often remains immune to future encounter with that specific disease for many years. Retaining immunity is the function of **memory cells**. Plasma cells and cytotoxic T cells do the immediate job of fighting disease organisms, but they usually live only for a few days. **B** and **T memory cells**, on the other hand, may survive for many years. If foreign cells bearing the same antigens re-enter the body, they will be recognized by the appropriate memory cells. These memory cells will multiply rapidly, generate huge populations of plasma cells and cytotoxic T cells, and produce a second immune response. In the first encounter with a disease microbe, only a few B and T cells respond. Each of these however leaves behind hundreds or thousands of memory cells. Further, memory cells respond to antigen much more rapidly than their progenitor B and T cells could. Therefore, the second immune response is very rapid.

Structural Model of an Antibody Molecule

A typical antibody is a Y-shaped molecule in which the two arms of the Y are binding sites. This shape emits the antibody to combine with two antigen molecules, and allow formation of antigen-antibody complexes. The tail of the Y performs functions such as binding to cells or activating the complement system.

The antibody molecule consists of four polypeptide chains: two identical long chains called **heavy chains**, and two identical short chains called **light chains**. Each chain has a **constant segment**, a functional segment, and a **variable segment**. In the constant segment, or **C region**, of the heavy chains, the amino acid sequence is constant within a particular immunoglobulin class.

The **C region** may be thought of as the handle portion of a door key. Like the pattern of bumps and notches at the end of a key, the variable segment, or **V region**, has a unique amino acid sequence. In B-cell receptors the variable region of the immunoglobulin protrudes from the B cell, whereas the constant region anchors the molecule to the cell.

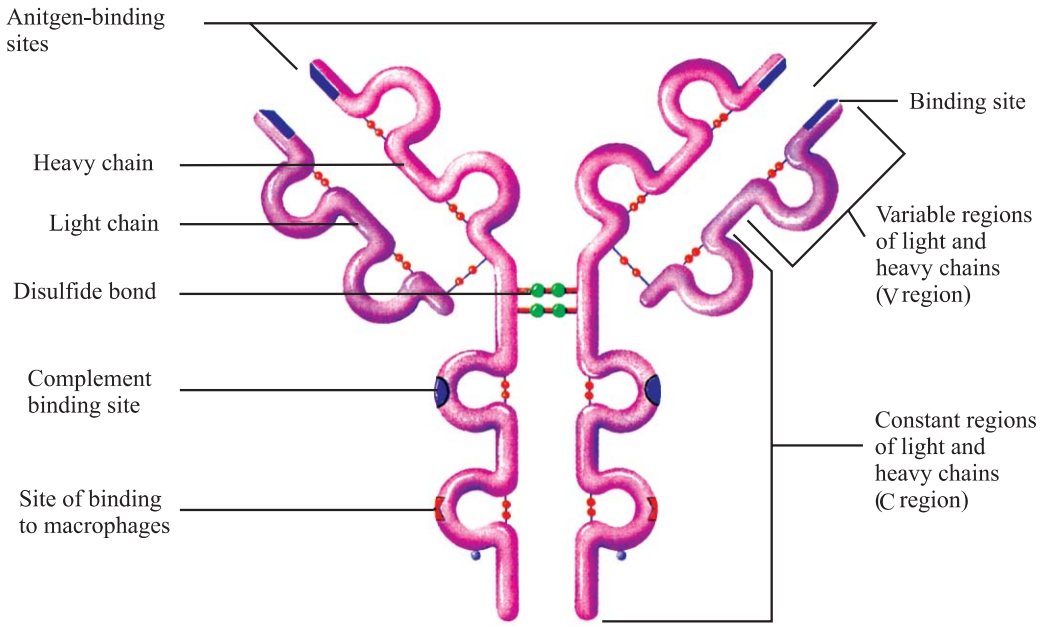


Fig: 13.10 Structure of the Antibody (IgG)

Monoclonal Antibodies

In 1970 **Cesar Milstein** and **Georges Kohler** working in Cambridge solve the problem of developing a technique for producing monoclonal antibodies, for which they were awarded Nobel Prize in 1984. Monoclonal means belonging to one clone. Each type of antibody is made by one type of B cells which cloned itself, in other words multiplies to make many identical copies of itself in response to a particular antigen. Milstein and Kohlar fused B cells with cancer cells, which are immortal to form **hybridoma cells**. The hybridoma cells continue to multiply and can be cloned so that large quantities of antibodies can be produced. Monoclonal antibodies are harvested from cell cultures rather than animals. The ability to make **monoclonal antibodies** has been spawned a new industry. A common area of application is **medical diagnosis**. Monoclonal antibodies are used for determining pregnancy and for diagnosing diseases (such as gonorrhea, syphilis), hepatitis, rabies, cancer, *Chlamydia*, streptococcal throat infections, herpes viruses, leukaemias (cancers of white blood cells), lymphomas. A monoclonal antibody has been developed which is very effective at preventing rejection of transplanted kidneys. Monoclonal antibodies can be used to find out the types of antigens present in the donor and increase the accuracy of matching.

Science, Technology and Society Connections

Describe the discovery of monoclonal antibodies and justify how this accomplishment revolution many aspects of biological research.

13.3.3 DISORDERS OF IMMUNE SYSTEM

Many people suffer from allergic reactions to substances that are not harmful in themselves and to which many other people do not respond. Common allergies include those to pollen, dust, mold spores, and bee stings.

Allergies are Inappropriately Directed Immure Responses

Allergies are actually a form of immune response. A foreign substance, such as a pollen grain, enters the bloodstream and is recognized as an antigen by a particular type of B cell. This B cell proliferates, producing **plasma cells** that pour out IgE antibodies attach to the plasma membranes of histamine-containing cells located in the respiratory and digestive tracts.

When pollen grains encounter the attached IgE antibodies, they tigger the release of histamine, which causes increased mucus secretion, leaky capillaries, and other symptoms of inflammation. Because pollen grains most often enter the nose and throat, the major reactions occur in these locations, resulting in the runny nose, sneezing, and congestion typical of "heavy fever". Antihistamine drugs block some of the effects of histamine, relieving the symptoms of allergies. Food allergies cause equivalent symptoms, including cramps and diarrhea, in the digestive tract.

An Autoimmune Disease is an Immune Response against Some of the Body's own Molecules

A person's immune system does not normally respond to the antigens borne on the body's own cells. Occasionally, however something goes awry, and "anti-self" antibodies are produced. The result is an autoimmune disease, in which the immune system attacks some component of one's own body. Some types of anemias, for example, are caused by antibodies that destroy a person's red blood cells.

Many cases of insulin-dependent (juvenile-onset) diabetes occur because the insulin-secreting cells of the pancreas are the victims of a misdirected immune response. Unfortunately, at present there is no way to cure **autoimmune diseases**. The autoimmune response can be suppressed with drugs.

Role of T-cells and B-cells in Transplant Rejections

It is occasionally desirable to transplant some tissue or an organ such as the skin, kidney, heart, or liver, from one person to another to replace a non-functional damaged or lost body part. In such cases, there is a danger that the recipient cells may recognize the donor's organ or tissue as being foreign. This triggers the recipient's immune mechanisms, which may act to destroy the donor tissue. Such a response is called a tissue **rejection reaction**.

Role of T cells in Transplant Rejection

Although the mechanism of rejection probably varies with the nature of the tissue and the degree of incompatibility, all the mechanisms require that the host T_H cells (helper T cells) come into contact with the graft tissue's major histo compatibilty complex (MHC) antigens. This contact is probably mediated by the dendritic cells of the graft tissue itself.

At this point, three different possibilities exist. In the first, antigen-specific T_H cells stimulate the activation and proliferation of appropriate T cells, which then mount a focused attack on the transplant tissue. In the second, responsive antigen-specific T_H cells move to the graft site, where they release lymphokines. These recruit monocyte/macrophages and T cells to the graft site and maintain them at the scene while they destroy the tissue.

Role of B cells in Transplant Rejection

There is a third mechanism in which antibodies play a role. The responsive T_H cell interacts with the appropriate **B cell clone**, producing a shower of antibodies to the implanted tissue's MHC antigens. These can trigger either complement-mediated graft damage or antibodymediated cellular cytotoxicity. The latter is accomplished by K or killer cells.

Skills: Initiating and Planning

- **Justify why physician prescribe antihistamine therapy to the patients of runny nose or skin rashes.**

Runny nose or skin rashes are a type of hypersensitivity reaction in which histamine is released from the mast cells and basophils. Its release causes vasodilation, increased capillary permeability and smooth muscle contraction. Antihistamine drugs block histamine receptor sites so histamine action cannot take place. So in this way they are effective in allergic rhinitis i.e. runny nose and skin rashes.

Functions of B cells and T cells

Antibody-Mediated Immunity (B Cells)	Cell- Mediated Immunity (T Cells)
1. Host defence against infection (opsonize bacteria, neutralize toxins and viruses)	1. Host defence against infection (especially *M tuberculosis*, viruses, and fungi)
2. Allergy, e.g., hay fever	2. Allergy, e.g., poison oak
3. Autoimmunity	3. Graft and tumor rejection
	4. Regulation of anitbody response (help and suppression)

Skills: Initiating and Planning

- **Explain why a transplant recipient is given immune suppressant drugs and determine what implications does this have on his life.**

Organ transplantation has become a routine procedure due to improvement of surgical techniques, better tissue typing and the availability of drugs that more selectively inhibit rejection of transplanted tissues and prevent the patient from becoming immunologically compromised. Transplant rejection occurs as a delayed hypersensitivity reaction as a function of lymphocytes and not due to antibodies. Administration of immunosuppressive drugs enhances tolerance. People receiving immunosuppressive drugs have side effects like pain, diarrhoea, leukopenia, sepsis, lymphoma, thrombocytopenia, skin rashes, anaphylactic reaction, hypertension, hyperkalemia and neurotoxicity (tremors, seizures, hallucination). Hence, each system is affected, so the person starts to feel weakness and gets fatigue easily.

Science Titbits

Certain sites in the body are immunologically privileged. A few immunologically privileged locations exist in which foreign tissue is accepted by a host. The brain and corneas are examples. Corneal transplants are highly successful because the cornea has almost no blood or lymphatic vessels associated with it and so is out of reach of most lymphocytes. Furthermore, antigens in the cornea circulatory graft probably would not find their way into the circulatory system, and so would not stimulate an immune response.

Exercise

SECTION I : MULTIPLE CHOICE QUESTIONS

Select the correct answer

1. Plasma cells are
   A) the same as memory cells
   B) formed from blood plasma
   C) B cells that are actively secreting antibody
   D) inactive T cells carried in the plasma
2. Antibodies combine with antigens
   A) at variable regions B) at constant region
   C) only if macrophages are present D) both A and C are correct
3. Vaccines are
   A) the same as monoclonal antibodies
   B) treated bacteria or viruses or one of their proteins
   C) major histocompatibilty complex (MHC) proteins
   D) not destroyed by heating
4. In addition to the immune system, we are protected from disease by
   A) body temparature B) hormones
   C) antigens D) mucous membrane and cilia
5. Fevers
   A) decrease interferon production
   B) decrease the concentration of iron in the blood
   C) decrease the activity of phagocytes
   D) decrease the reproduction of invading bacteria

6. T and B cells are

A) lymphocytes B) macrophages

C) natural killer cells D) red blood cells

7. Foreign molecules that evoke an immune response are called

A) pathogens B) antibodies

C) lymphocytes D) histamines

8. When B-cells are presented with antigen they differentiate into

A) T-cells B) helper T-cells

C) plasma cells D) bursa cells

9. Memory cells are

A) modified T-cells B) B-cells

C) killer T-cells D) suppressor cells

10. When one receives a booster shot for polio which type of cell is most directly stimulated?

A) killer T-cells B) memory cells

C) phagocytes D) suppressor cells

SECTION II : SHORT QUESTIONS

1. List the ways of defence of the human body against invading microbes.
2. Define: immunity, immunology, microbes, monocyte, macrophages, allergy, T cells, B cells, cell mediated immunity, antigen, lymphocytes, antibody mediated immunity, autoimmune diseases, vaccine, vaccination.
3. What is the relationship between the lymphatic and immune system.
4. Write the level of defence against infection.
5. Name the parts of antibody molecule.
6. What are the memory cells?
7. How does an antibody differ from an antigen?
8. Name the disorders of immune system.
9. What is the difference between an antibody-mediated immune response and a cell-mediated immune response?

10. Why is passive immunity temporary?
11. List the benefits of fever.

SECTION III : EXTENSIVE QUESTIONS

1. Name the specific and non-specific line of defence of the human body against microbes. Explain your answer.
2. How do natural killer cells and cytotoxic T cells destroy their targets?
3. Describe humoral immunity and cell-mediated immunity.
4. How do immune system construct so many antibodies?
5. Draw and label the structure of an antibody. What parts bind only to antigens? Why does each antibody bind only to a specific antigen?
6. How do memory cells contribute to long lasting immunity to specific diseases?
7. How does vaccine confer immunity to a disease?
9. Explain the process by which a T cell is able to recognise an antigen.
10. How are active immunity and passive immunity achieved?

ANSWER MCQS

1. C 2. A 3. B 4. D 5. B 6. A 7. B 8. C 9. B 10. B

SUPPLEMENTARY READING MATERIAL

1. Campbell N.A. Mhchell, L.G. & Reece J.B., *Biology Concepts and connections*, 2nd edition Benjamin/Cummings Company California, 2003.
2. Madar, S.S., *Biology*, 6th edition, WCB, McGraw-Hill, USA, 1998.

USEFUL WEBSITES

1. en.wikipedia.org/wiki/Immunology
2. www.immunologylink.com/
3. www.biology.arizona.edu/immunology/immunology.html
4. www.whfreeman.com/kuby/