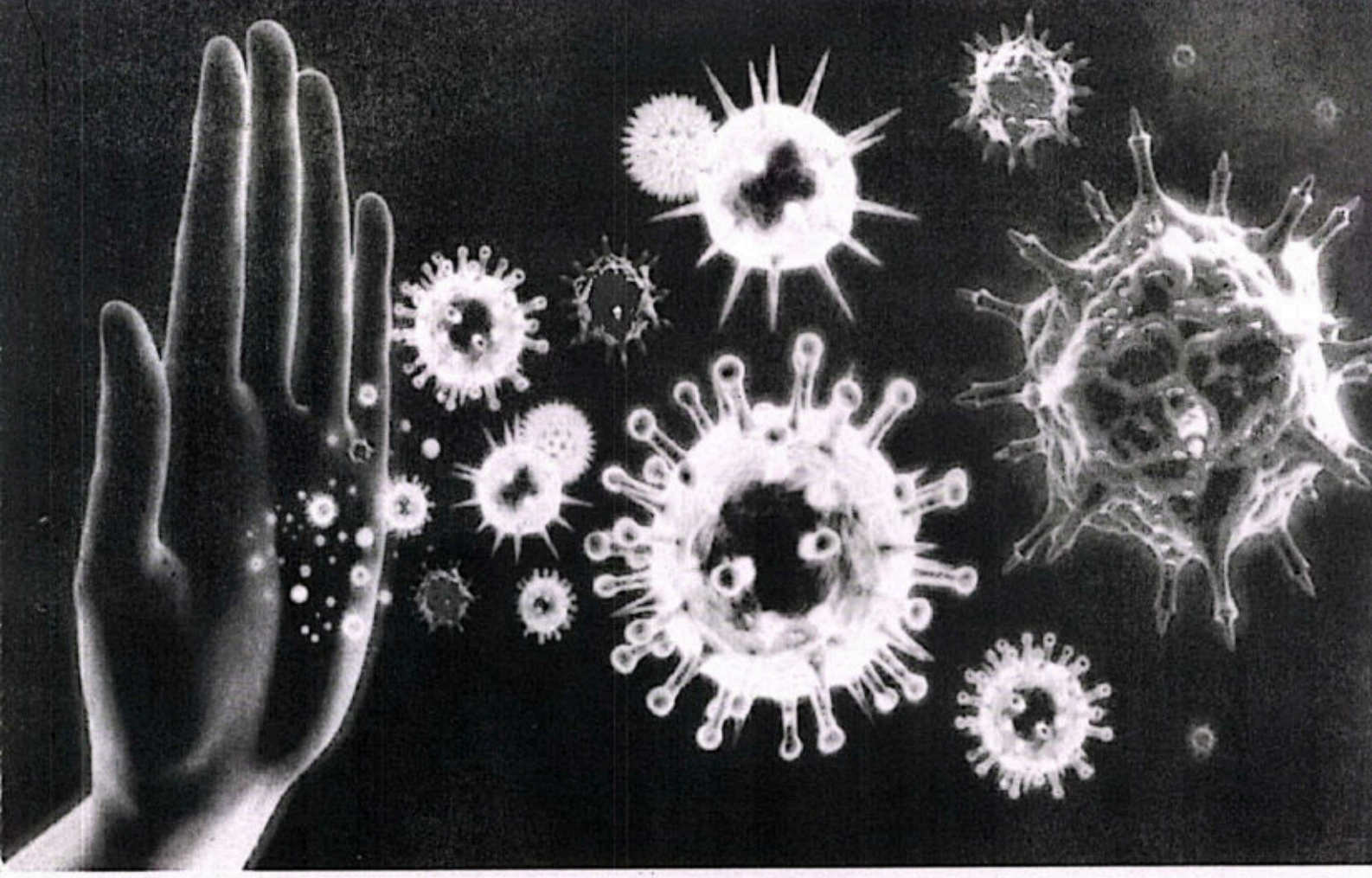

IMMUNITY

Students' learning outcomes
After studying this chapter, students will be able to:

1. [B-12-1-01] List the structural features of human skin that make it an impenetrable barrier against invasion by microbes. (1st line of defence).
2. [B-12-1-02] Explain how oil and sweat glands within the epidermis inhibit the growth and also kill microorganisms. (1st line of defence).
3. [B-12-1-03] Recognize the role of the acids of the digestive tract as killing bacteria present in food.
4. [B-12-1-04] State the role of the ciliated epithelium of the nasal cavity and the mucous of the bronchi and bronchioles in trapping airborne microorganisms.
5. [B-12-1-05] Describe the role of macrophages and neutrophils in killing bacteria.
6. [B-12-1-06] Explain how Natural Killer (NK) cells kill cells infected by microbes and cancer cells.
7. [B-12-1-07] State the way proteins of the complement system kill bacteria and that interferons inhibit viruses from infecting cells.
8. [B-12-1-08] State the events of the inflammatory response as a generalized, nonspecific defence.
9. [B-12-1-09] Outline the release of pyrogens by microbes and their effect on the hypothalamus to boost the body's temperature.
10. [B-12-1-10] List the ways that fever affects microbes.
11. [B-12-1-11] Define the specific immune system as providing specific defence and acting as the most powerful means of resisting infection.

12. [B-12-1-12] Identify monocytes, T cells, and B-cells as components of the immune system.
13. [B-12-1-13] State inborn and acquired immunity as the two basic types of immunity.
14. [B-12-1-14] Differentiate between active and passive immunity as the two types of acquired immunity.
15. [B-12-1-15] Describe the role of T-cells in cell-mediated immunity.
16. [B-12-I-16] Describe the role of B-cells in antibody-mediated immunity.
17. [B-12-1-17] Discuss the role of T-cells and B-cells in transplant rejections.
18. [B-12-1-18] Evaluate the discovery of monoclonal antibodies and justify how this accomplishment revolutionized many aspects of biological research.
19. [B-12-I-19] Identify the process of vaccination as a means to develop active acquired immunity.
20. [B-12-1-20] Draw the structural model of an antibody molecule.
21. [B-12-I-21] Explain the role of memory cells in long term immunity.
22. [B-12-1-22] Define allergies and correlate the symptoms of allergies with the release of histamines.
23. [B-12-1-23] Describe the autoimmune diseases with examples.

You have already learnt about immunity in previous classes. In this chapter we will learn about the body's defence and more emphasis would be on the immune system. The body's response to foreign particles, such as the production of antibodies directed against a specific antigen, is called an **immune response. 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 foreign particles that can affect the living body and the defence mechanisms, which are taken by the body to eliminate these particles. The human body has three lines of defence against microbial attack. First line of defence comprises **external barriers** that keep microbes out of the body. Second line of defence consists of **nonspecific internal defence** that combats all invading microbes. First line and second line of defence together make **innate immunity.** Third line of defence includes the **specific internal defence** also called **adaptive/ acquired immunity.**

9.1 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 external barriers to microbial invasion. Since these barriers inhibit generally all kind of microbial invasion thus, first line of defence is supposed to be a non-specific defence.

9.1.1 Skin: An Impenetrable Barrier Against Microbial Invasion

The skin is made up of two layers i.e., **epidermis** and **dermis.** Epidermis is outermost layer of the skin, composed of tightly packed cells that provide a physical barrier. Most cells of epidermis contain keratin protein that strengthens skin cells, making them resistant to abrasion and water loss. The outer surface of the skin also consists of dry dead cells. Consequently, most microbes that land on the skin cannot obtain the water and nutrients they need. The skin surface has a slightly **acidic pH (around 5.5),** which inhibits the growth of many pathogens. **Desquamation** is the process of shedding dead skin cells. This helps in removing attached microbes. Dermis is inner, comparatively thick layer containing glands, hair follicles, receptors, nerves and blood vessels. **Sebaceous glands** produce **sebum,** an oily substance. Sebum contains fatty acids that lower skin

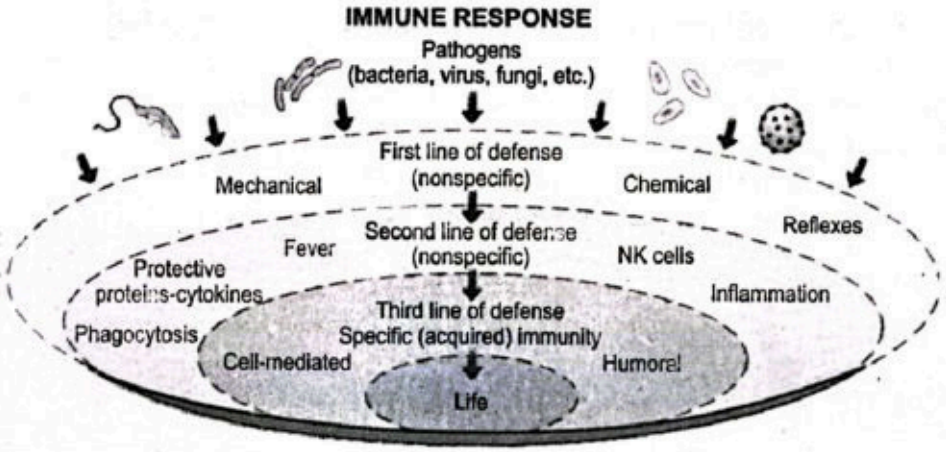

Fig. 9.1: The five drug development phases

pH and possess antimicrobial properties. Sweat glands secrete sweat, a salty fluid that generally provides cooling effect to the body. Sweat contains lysozyme, an enzyme that breaks down bacterial cell walls, and has a high salt concentration that can dehydrate bacteria. Secretion from sweat glands and sebaceous glands usually cover the skin. These secretions contain natural antibiotics such as lactic acid that inhibit the growth of bacteria and fungi. These multiple defences including chemical, physical and immune barriers make the unbroken skin an extremely effective block against microbial invasion.

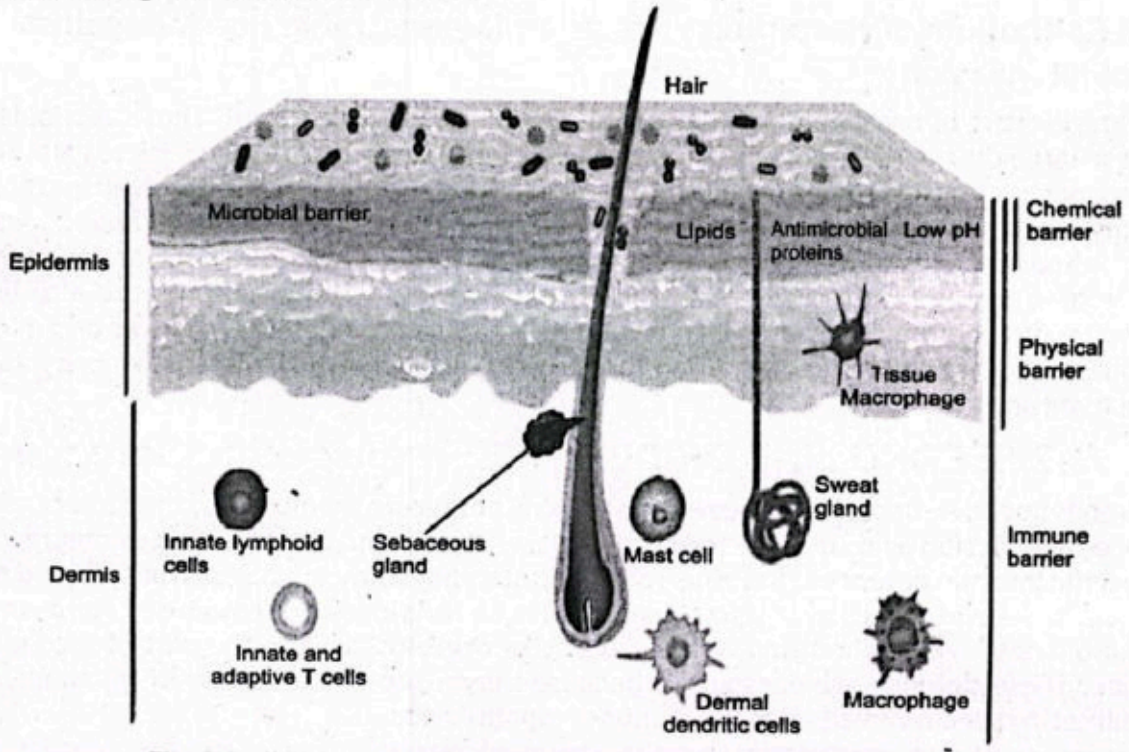

Fig. 9.2: Skin as an impenetrable barrier against microbial invasion

9.1.2 Epithelium of Digestive Tract: An Impenetrable Barrier Against Microbial Invasion

The gastrointestinal tract (GIT), is covered by mucous membrane, which protects the G1T against

microbial invasion by means of its various kind of secretions. Such as **hydrochloric acid** in the stomach is secreted by oxyntic or parietal cells that kills the bacteria present in food. In addition, various **digestive enzymes** present in gastric juice, intestinal juice and pancreatic juice also digest the bacteria present in food.

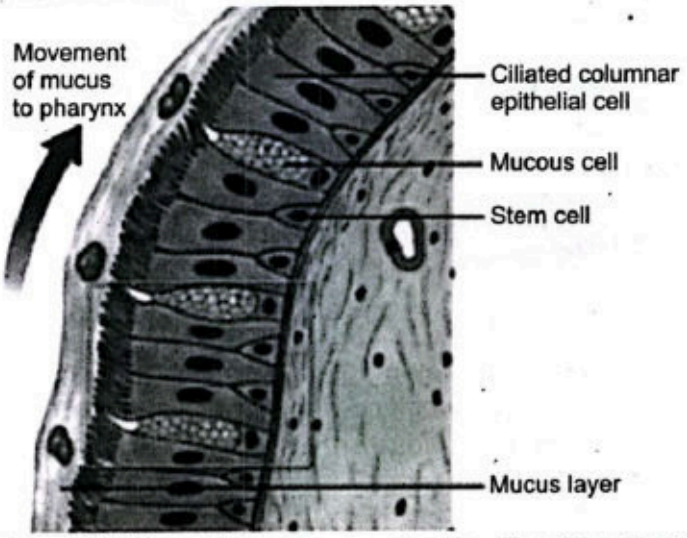

Fig. 9.3: Respiratory epithelium of trachea showing the direction of movement of mucous containing trapped particles towards pharynx

9.1.3 Epithelium of Respiratory Tract: an impenetrable barrier against microbial invasion

The anterior part of nasal cavities that contain hairs is called **vestibule**. These vestibular hairs filter the large dust particles of the inhaled air. The inner surface of nasal cavities is also lined by ciliated mucous epithelium. The mucus secreted by this epithelium is also involved in trapping of fine dust particles and microbes. The cilia of the epithelium sweep the trapped, fine dust particles and microbes posterior to the pharynx, where they are swallowed and are eliminated by the digestive system. The trachea and the air passageways within the lungs are also lined by ciliated mucous epithelium that is also involved in trapping of fine dust particles and microbes. The cilia in this region propel mucus and foreign particles towards the larynx, where they enter the pharynx and are swallowed.

9.2 SECOND LINE OF DEFENCE - Nonspecific Defence

If microbes become successful to penetrate the skin or mucous membranes, then a second line of defence takes action against these foreign invaders. The second line of defence comprises three nonspecific internal defence. First, the body has a standing army of **phagocytic cells** and **natural killer cells**. Second, invasion of microbes provokes an **inflammatory response**. Third, the body often produces **fever**. In addition, some **protective proteins** are also the part of second line of defence. These defence are nonspecific because they attack wide variety of microbes, rather than targeting specific invaders as the immune response does.

9.2.1 Killing Cells of Blood

There are white blood cells in the body called phagocytes. A phagocyte is a cell that destroys other abnormal body cells (cancerous cells) or invaded microorganisms by engulfing. This process is called phagocytosis. Main types of phagocytic white blood cells are: macrophages, dendritic cells, and neutrophils.

Macrophages and Dendritic cells

Monocytes are formed in bone marrow. From bone marrow. Monocytes typically circulate in the blood for 1-3 days before migrating into tissues, where they become macrophages or dendritic cells. Through blood, macrophages and dendritic cells are transported to the areas of the body where they are needed.

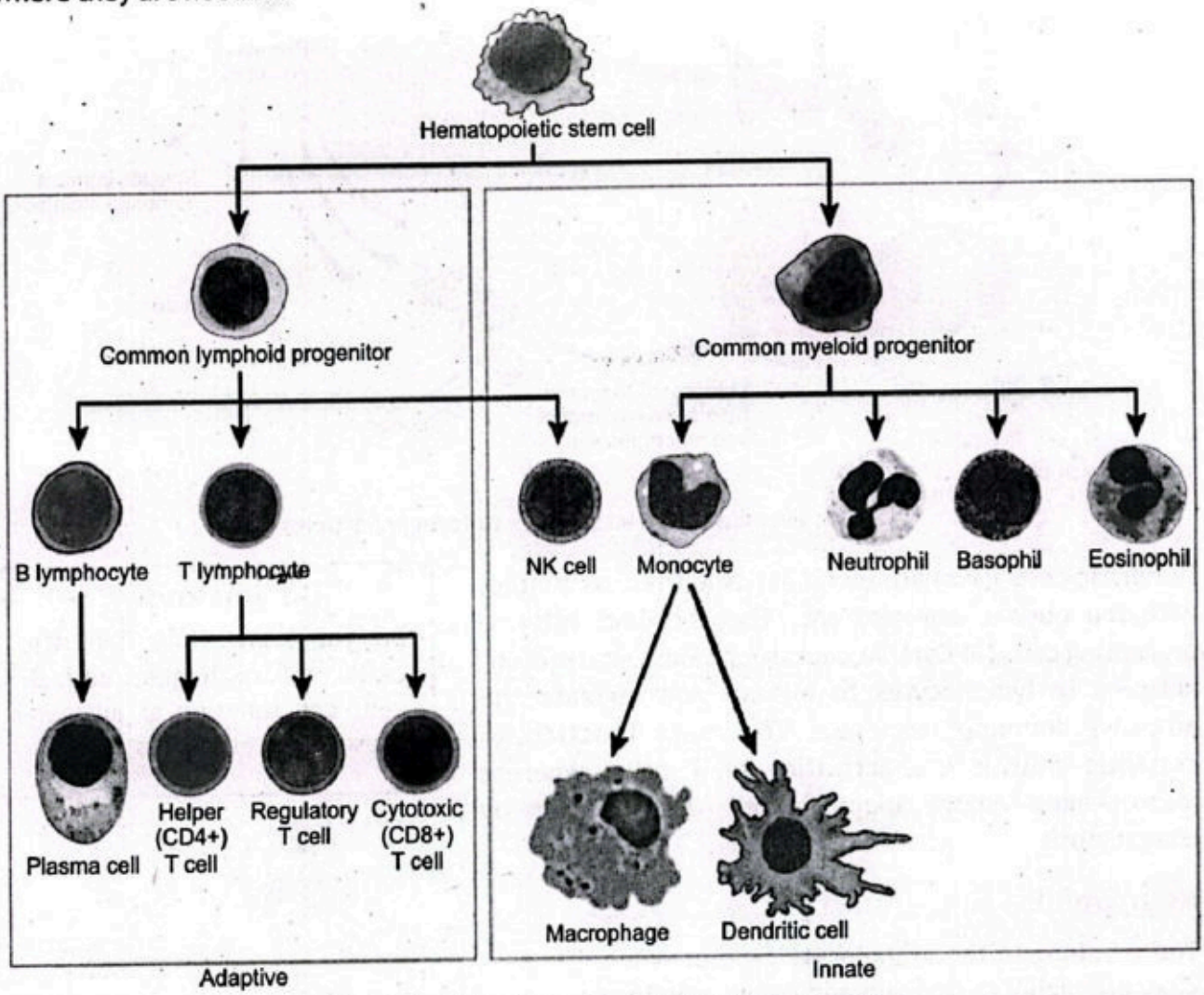

Fig. 9.4: Cells of Innate and Adaptive Immunity

Macrophages are generally found in the organs such as the lungs, liver, spleen, kidney and lymph nodes, rather than remaining in the blood. In these organs, they patrol within the free spaces among the cells and provide protection by trapping and destroying microorganisms entering the tissue. As macrophages interact with microbes, they not only engulf and destroy them; they also display some parts of microbes on their surface so that other body cells may also be informed. Such cells are called **Antigen Presenting Cells (APCs)**. The macrophages also secrete many different proteins when they perform phagocytosis of the microbes. Some of these proteins trigger the maturation of monocytes into macrophages, thereby increasing their numbers. Another protein interleukin-I signals the brain to raise the body temperature, producing fever. Some other proteins also stimulate the specific immune response. Macrophages also play an essential role in wound healing and tissue repair by removing dead cells and debris.

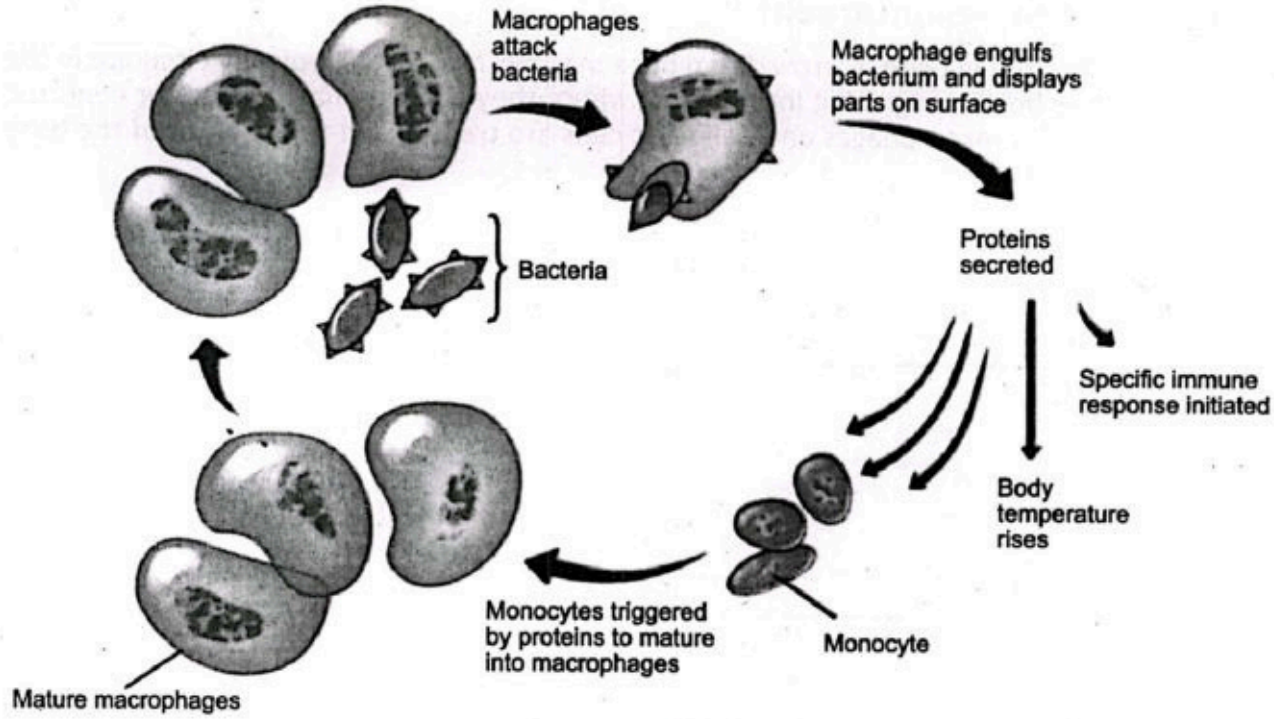

Fig. 9.5: Response of macrophages to foreign particles

Dendritic cells (DCs) are found in tissue that has contact with the outside environment. They become antigen-presenting cells (APCs) that capture, process, and present antigens to lymphocytes to initiate and regulate the adaptive immune response. The main function of dendritic cells is the activation of T cells, whereas macrophages remove apoptotic cells and microbes by phagocytosis

Do you know?

Do you know that Dendritic cells, macrophages, and B-cells can function as antigen-presenting cells (APCs)?

Neutrophils

These belong to the granulocyte type of WBCs. They are highly short-lived and highly mobile as they squeeze between cells of capillary walls and can enter parts of tissue where other cells would not be able to enter otherwise. They move like Amoeba forming pseudopodia. They proceed rapidly to infected area to perform their duty and they often die after a single phagocytic event. Neutrophils also release lysosomal enzymes by extracellular degranulation that kill microorganisms and cause inflammation. Neutrophils can release Neutrophil extracellular trap to kill microbes.

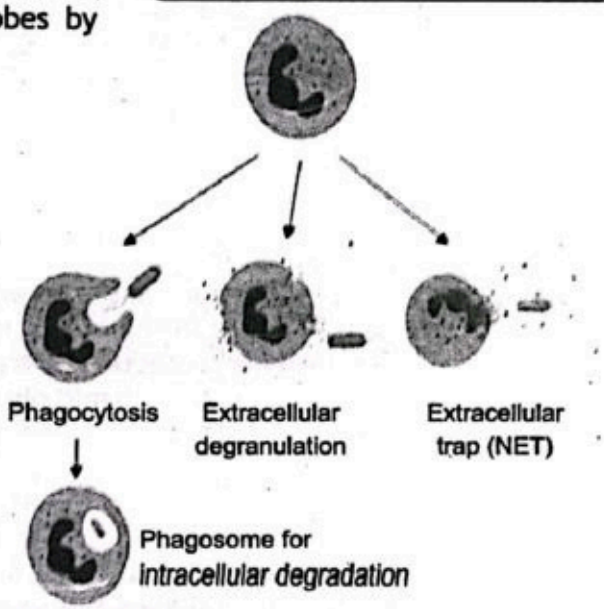

Fig. 9.6: Neutrophils immune response

Natural killer cells

Natural killer (NK) cells are a type of lymphocytes which provide innate immunity. In general, natural killer cells do not directly attack invading microbes. Instead, natural killer cells attack the cancerous cells or viruses infected body cells. NK cells kill their target by releasing proteins called **perforins**, which punch holes through the membranes of the infected cells. The pores formed by these proteins allow for the passive diffusion of certain apoptotic proteases, known as the **granzymes**, into the target cell. The cell dies by apoptosis. Macrophage engulfs and digests that dying cell.

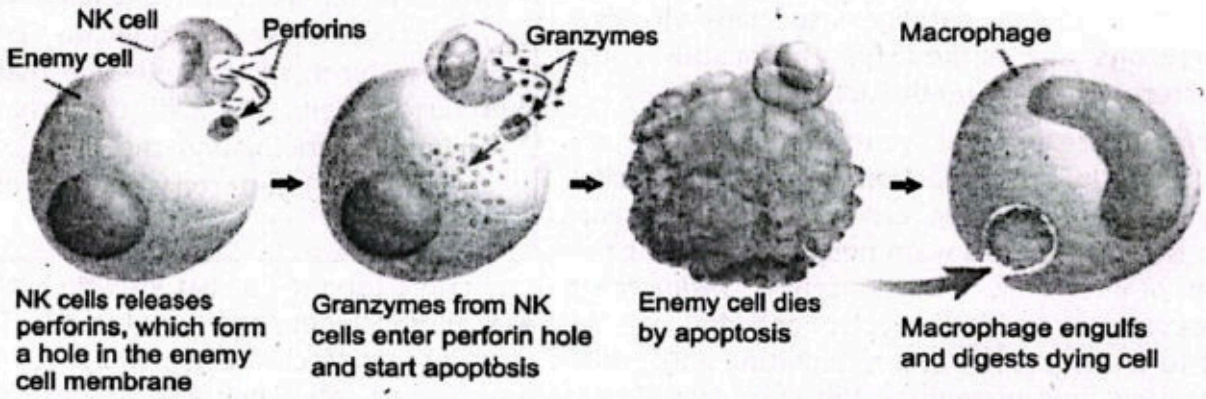

Fig. 9.7: NK cells attack on enemy cells (Cancerous cell/ Virus infected cell)

9.2.2 Protective Proteins of Complement System

The complement system consists over fifty types of small proteins found in the blood, synthesized by the liver, and normally circulating in inactive state. They are activated on the entry of foreign particles. Once a complement protein is activated, it activates another protein, which further activates other proteins of the system and so on. As a result, phagocytes clear foreign and damaged material. Development of inflammation to attract additional phagocytes at the site of infection. This activates cell killing membrane attack complexes. The complement system is an important supporter of the immune system that enhances (complements) the ability of antibodies and phagocytic cells to clear microbes and damaged cells from the body, promotes inflammation, and attacks the pathogen's plasma membrane.

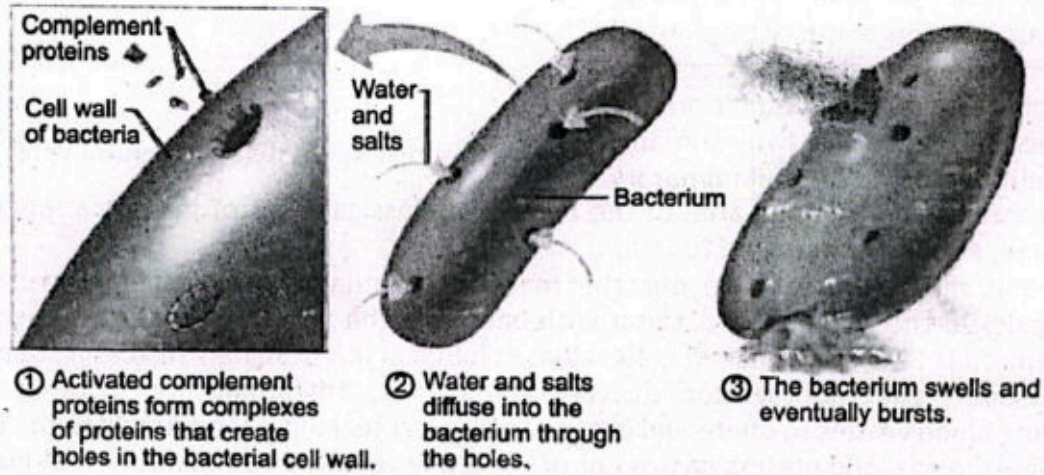

Fig. 9.8: Action of the complement system against a bacterium

An example of protective proteins of complement system is **membrane attack complex (MAC)** that produces holes in the bacterial cell walls and plasma membranes of pathogens. The holes allow fluids and salts to enter the bacterial cell, thus, bacterial cell swells and eventually burst.

Interferons

Interferons belong to the large class of proteins known as **cytokines**, molecules used for communication between cells during infection. They are released by host cells in response to the presence of several pathogens specially viruses. Interferons are named for their ability to "**interfere**" with viral replication.

> **Do you know?**
>
> A **cytokine** is a chemical messenger that regulates cell differentiation, production, and gene expression to affect immune responses. At least 40 types of cytokines exist in humans that differ in terms of the cell type that produces them, the cell type that responds to them, and the changes they produce. Interferon is one type of cytokine.

Interferons are antiviral agents produced by virus-infected cells. Upon infection, virus infected cells mount an innate immune response to protect them from the virus and to warn neighbouring cells by means of interferon. Interferons have a wide range of functions used to combat infection at all stages of a pathogen's life cycle. For a viral infection, examples include: signalling virus infected cells to undergo apoptosis, prohibiting entry of the virus into uninfected cells, stopping viral replication, and preventing the virus from leaving an infected cell. They also activate the immune cells to generate immune response.

The many forms of interferon are rapidly produced to defend against viruses. Interferons can also combat bacterial and parasitic infections, inhibit cell division, and promote or slow down the differentiation of cells.

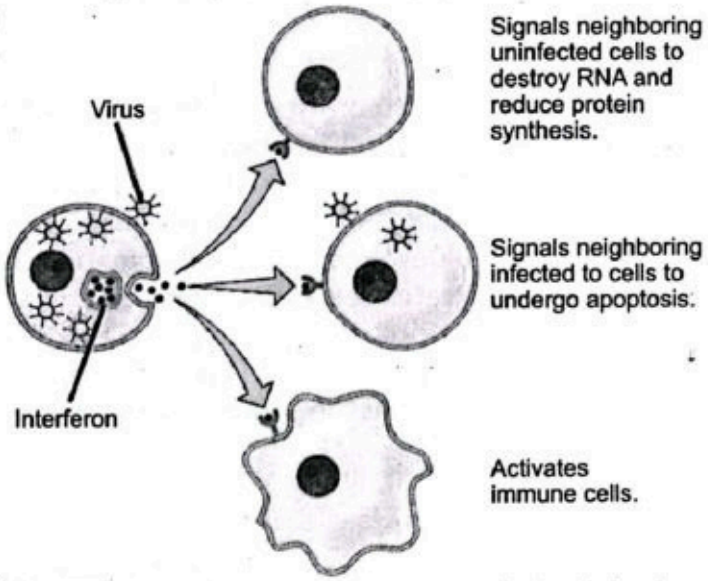

Fig. 9.9: Action of interferon to control virus infection

9.2.3 Inflammatory Response

The inflammatory response is a major component of the non-specific defence. Any damage to tissue, whether caused by an infectious microorganism or by physical injury, even just a scratch or an insect bite triggers this response. Inflammation can be localized or systemic (widespread). Local inflammation is an inflammatory response confined to a specific area of the body. The classical signs of inflammation are heat, pain, redness, swelling, and loss of function.

The figure 9.10 shows the chain of events that make up the inflammatory response, in case where a pin has pricked 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 defence. Histamine for instance induces neighbouring blood vessels to dilate and blood vessels start leaking. Blood supply to the damaged area increases, and blood plasma passes out of the leaky vessels into the interstitial fluid of the affected tissues causing inlammation.

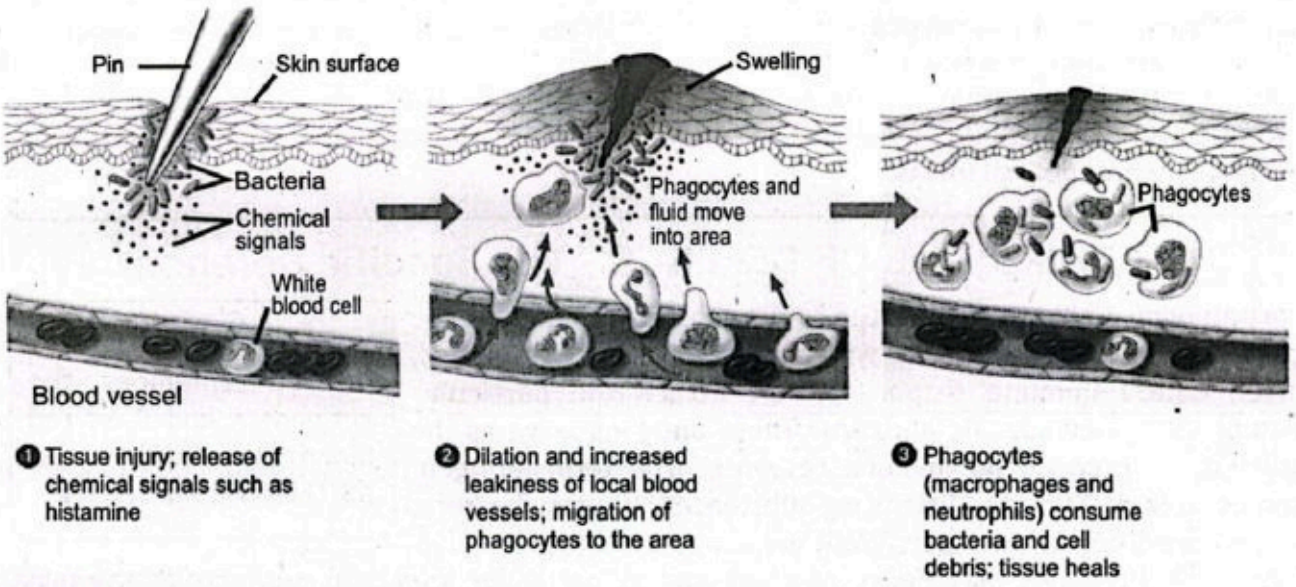

Fig. 9.10: The Inflammatory response

The function of inflammation is to eliminate the initial cause of cell injury, clear out necrotic cells and tissues damaged from the original insult (to attack physically) and the inflammatory process, and to initiate tissue repair. The inflammatory response also helps to prevent the spread of infection to the surrounding tissues.

9.2.4 Temperature Response

Fever or **pyrexia** is the raised body temperature than normal. The invaded microorganisms often release certain chemicals, which are generally termed as **pyrogens**. These pyrogens cause the temperature set point of the **hypothalamic thermostat** of the body to rise; as a result, all the mechanisms for raising the body temperature are brought into play, such as heat conservation and increased heat production. Since, higher body temperature than normal facilitates the microbial growth in the body, this is the reason why invaded microorganisms want to increase the host's body temperature.

On the other hand, certain white blood cells in response to the infection, also release hormones collectively called **endogenous pyrogens** that further increase the temperature set point of hypothalamus because higher body temperature than normal increases the activity of phagocytic white blood cells that attack upon bacteria. The endogenous pyrogens also cause other cells to reduce the concentration of iron in the blood because many bacteria require more iron to reproduce at temperature of 38°C or 39°C than at 37°C, so fever and reduced iron in the blood combine to slow down their rate of reproduction. Fever also increases the production of interferons that travel to other cells and increase their resistance to viral attack. The higher body temperature may directly inactivate the virus particles, particularly enveloped viruses, which are more heat-sensitive than non-enveloped viruses. Replication of some viruses is reduced at higher temperatures, therefore fever may inhibit replication.

However, fever is nonspecific defence against microbial infections, but often, high degree fever becomes destructive for body's own metabolic system and ultimately body is collapsed. Therefore, physicians use to prescribe antipyretic drugs to the patients of high degree fever.

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

Antipyretic drugs 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.

9.3 THIRD LINE OF DEFENCE - The Specific Defences

Do you know?

Do you remember, the antigens A and B on red blood cells, you learned in ABO blood group system?

If a pathogen is able to get past the body's nonspecific defence, the third line of defence interferes with a series of defence responses, often called immune responses that attack the particular pathogens having specific antigens. These antigens serve as the stimulus to produce an immune response. The term "antigen" comes from **ANTI**-body **GEN**erating substances. Viruses, bacteria and other pathogen have specific antigens on their surface.

Since, the third line of defence respond against particular infections and acts as the most powerful means of resisting infections therefore, it is also called **specific defence**. Its response can be of two types: **Humoral immune response** and **cell-mediated immune response.** These immune responses are particularly carried out by two components: B-lymphocytes or B cells and T-lymphocytes or T cells. However, third line of defence also involves role of monocytes (macrophages) that participate in activation of these lymphocytes.

9.3.1 Role of Monocytes in Third Line of Defence

As already described in second line of defence that monocytes are kind of WBCs, which are produced by lymphoid tissues. The monocytes circulate in blood for one to three days and ultimately they leave the blood and come into the intercellular space of tissues. In the tissues, they swell and attain a larger size to become tissue **macrophages** or **dendritic cells** which are irregular in shape with many projections. When these cells perform phagocytosis of invaded microorganisms, after digesting them they not only display microbial antigens on their surfaces. Macrophages begin to secrete about 100 different compounds including various enzymes, interferons and a protein called **interleukin-1**. The interleukin-1 secreted by macrophages activates the T cells that in turn begin to secrete **interleukin-2**, which then activates the B cells. Interleukin-1 also promotes a general response to injury, causing fever and activating other mechanisms that defend the body against invasion. While dendritic cells after phagocytosis become antigen presenting cells for T cell activation.

9.3.2 Role of T Cells in Third Line of Defence (Cell mediated immune response)

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 thymus makes T cells immunocompetent that is capable of immunological response. The immune response provided by T cells is called **cell mediated immune response.**

Activations of T cells

In case of infection, macrophages perform phagocytosis of invaded microorganism and detect

particular **antigens (nonself molecules)** of the organism. Macrophages isolate and display these antigens on their surface with the help of their own proteins (self-protein) called **major histocompatibility complex (MHC)**. In this way, macrophages become **antigen-presenting cells (APCs)**. Macrophages also secrete **interleukin-1** that stimulates and attracts helper T cells towards the displayed antigen. Helper T cells have specific receptor on their surface called **T cell receptor (TCR)** by which they bind with a particular antigen displayed on APC. Interleukin-1 also stimulates the helper T cells to secrete another protein, the interleukin-2 that not only compel the helper T cells to divide but also causes the proliferation of certain cytotoxic T cells and B cells. The activation of T-cells by a specific antigen is called **cell-mediated immunity**. The body contains millions of different T-cells, each able to respond to one specific antigen.

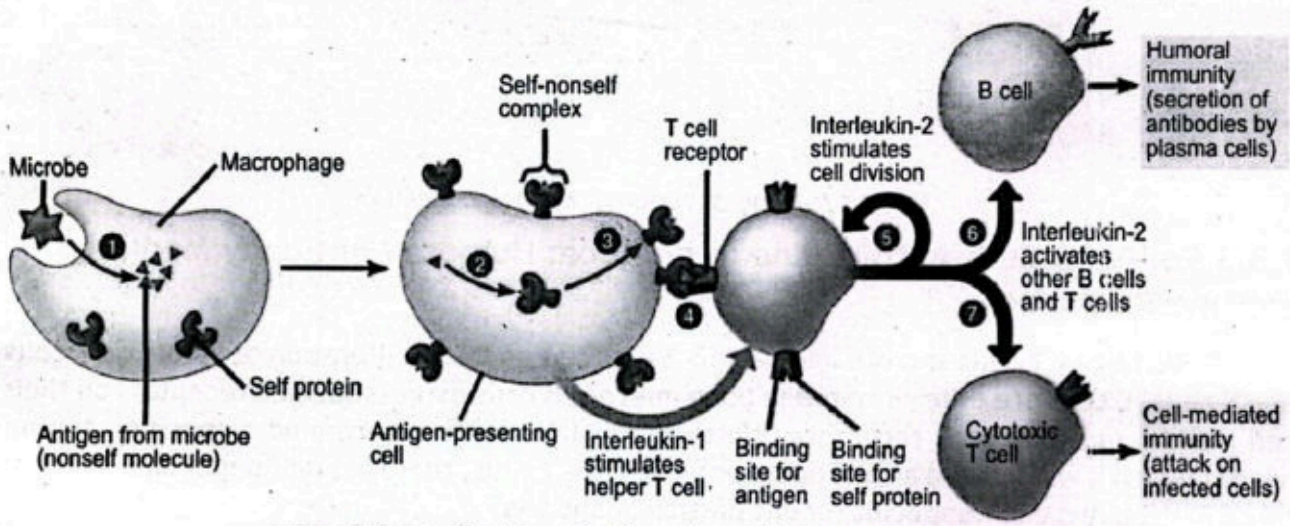

Fig. 9.11: Activation of cell mediated immune response

Types of T cells

Two main categories of T cells have been identified. The first group, known as **CD8** cells because they have surface marker designated **CD8**, include cytotoxic T cells and suppressor T cells. The second group i.e., **helper T cells** also known as **CD4** cells because they have a surface marker designated **CD4**.

When T cells are activated, they divide and produce four types of cells which have specific role in cell-mediated immune response.

(i) Cytotoxic T cells: These cells secrete cytotoxin which triggers destruction of the pathogen's DNA or perforin which is a protein that creates holes in the pathogens plasma membrane. The holes cause the pathogen to lyse (rupture).

(ii) Helper T cells: These cells secrete interleukin 2 which stimulates cell division of T cells and B cells. In other words, these cells recruit even more cells to help fight the pathogen.

(iii) Suppressor T cells: When infection is successfully removed, these cells begin to secrete certain proteins that inhibit further proliferation of T cell. Therefore, they shut down the immune response.

(iv) Memory T cells: These cells remain dormant after the initial exposure to an antigen. If the same antigen presents itself again, even if it is years later, the memory cells are stimulated to convert themselves into helper T cells and help fight the pathogen.

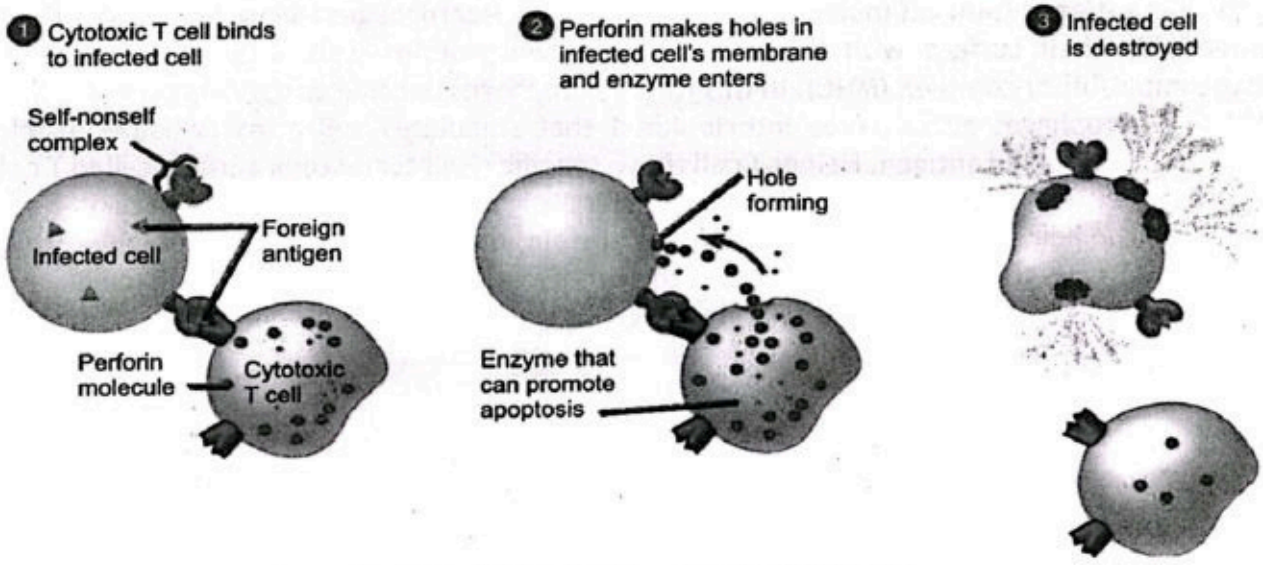

Fig. 9.12: Mode of action of cytotoxic T cells

9.3.3 Role of B Cells in third line of defence: Humoral/ Antibody Mediated Immune Response

Stimulated helper T cells secrete interleukin-2 that causes the proliferation of cytotoxic T cells and B cells. B cells are differentiated in bone marrow. B cells express specific receptors on their cell membrane, the B cell receptors (BCRs). BCRs allow the B cell to bind a specific antigen, against which it will initiate an antibody response. Like T cells, there are millions of B cells types, found in the body; each is specific for one particular antigen.

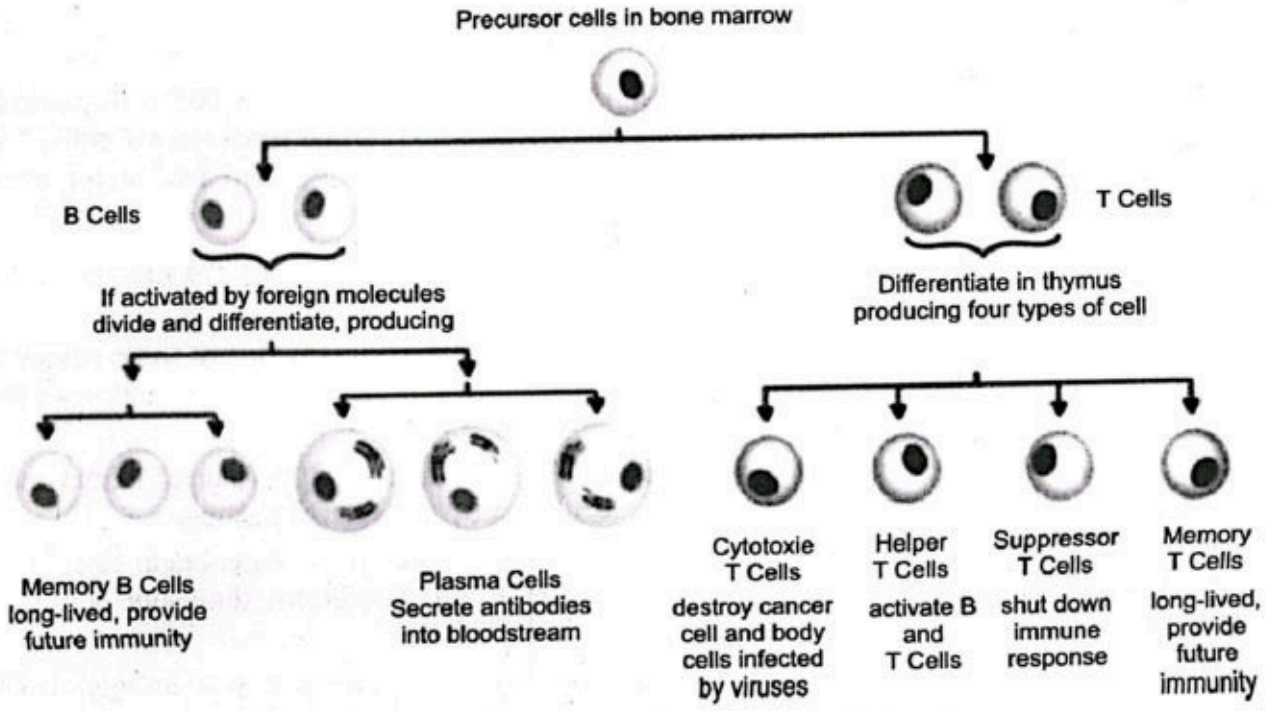

Fig. 9.13: The major cells of Adaptive Immunity and their roles in the immune system

Activation of B cells

B cell activation begins when the B cell binds to an antigen via its BCR. Actually, B cells are stimulated to bind with specific antigen by interleukin-2 proteins, which are secreted by helper T cells. After binding with specific type of antigen the B cells divide to produce two type of cells: **plasma clone cells** and **memory B cells**. The plasma clone cells are specialized to secrete bulk quantity of antibodies. After B cells become plasma cells they live only for a few days but secrete a great deal of antibody during the time. A **plasma cell** can produce more than 10 million molecules of antibody per hour. If the same antigen enters the body later, the **memory B cells** divide to make more plasma cells and memory cells that can protect against future attacks by the same antigen. The stimulation of B cells to divide into plasma clone cells and memory B cells and the secretion of antibodies by plasma clone cells is called **humoral mediated immune response.**

Structure of an antibody

Antibodies (also called immunoglobulins or Ig's) are Y-shaped proteins that circulate through the blood stream and bind to specific antigens, thereby attacking microbes. The antibodies are transported through the blood and the lymph to the pathogen invasion site.

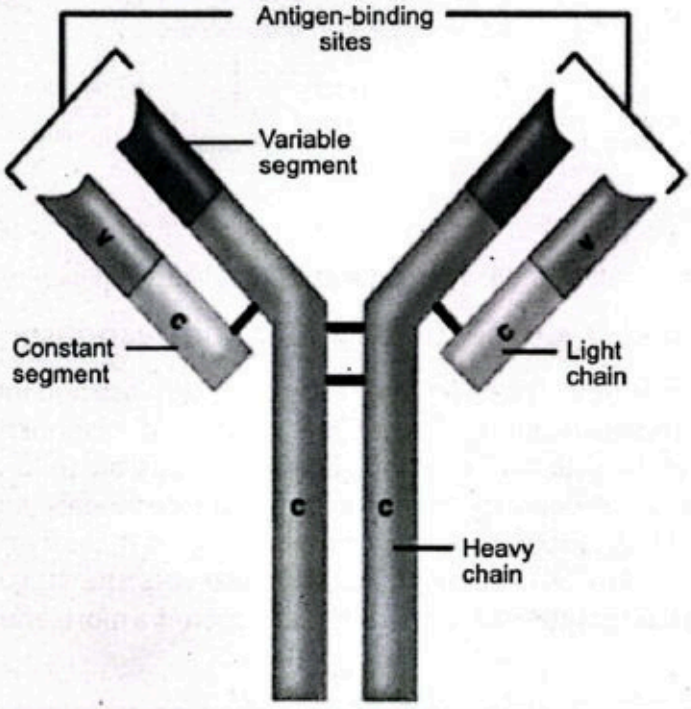

Fig. 9.14: Structure of an antibody

A typical antibody is a Y-shaped molecule, which 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, (C) of the heavy chains, the amino acid sequence is constant within a particular immunoglobulin class. On the other hand, the variable segments (V) consist of different amino acid sequences in every antibody. Therefore, they act as antigen-binding site. Each antibody has two antigen-binding sites.

Mode of action of an antibody

Antibodies work in different ways:

1. Antibodies can combine with virus and toxins to neutralize them. This prevents binding o pathogens with host cells.
2. The antibody can bind to an antigen, forming an antigen-antibody complex thus promote phagocytosis by macrophages. This mode of action is called **opsonization.**
3. They can activate complement system to form **membrane attack complex.** As a result, target *cell either bursts* or undergoes phagocytosis.
4. Antibodies can attach with virus infected cells or tumour cells to start **antibody dependent cell mediated cytotoxicity.** NK cells attach with target cell and induce apoptosis to kill that cell.

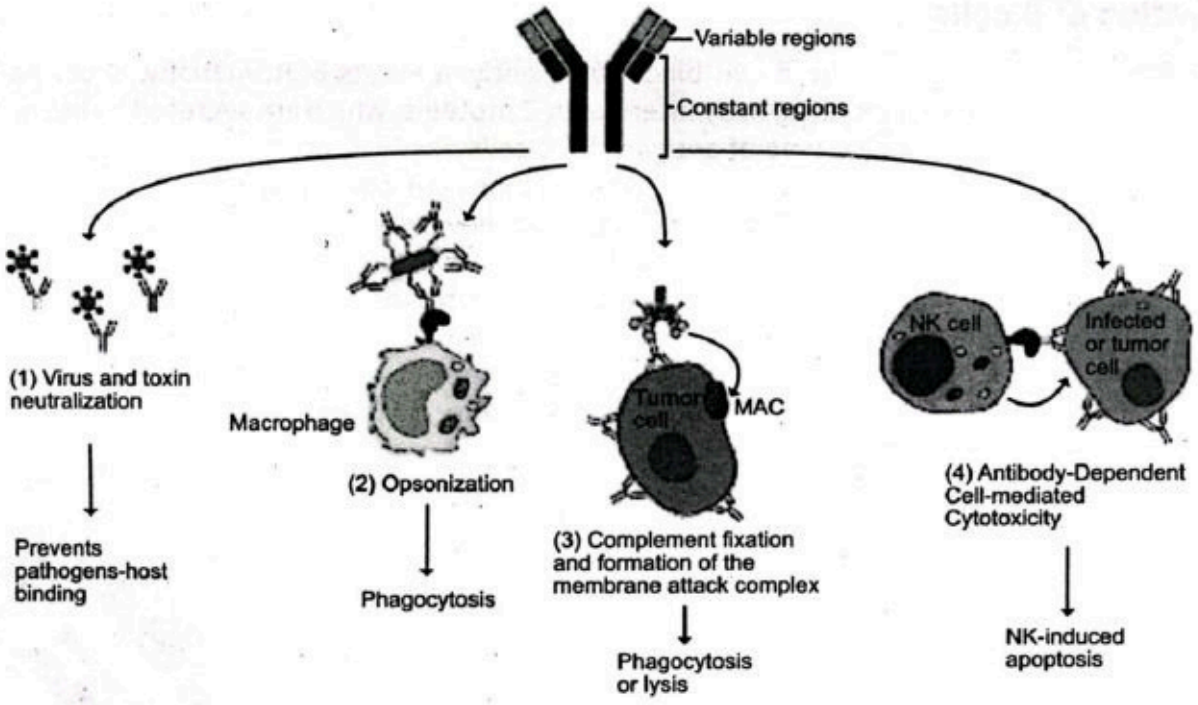

Fig. 9.15: The major cells of Adaptive Immunity and their roles in the immune system

Primary and secondary immune response

The action of the immune system can be classified into two parts: the primary and the secondary immune response. The **primary immune response** displays the first contact of the immune system with an infectious agent whereas all following contacts with the same pathogen are named **secondary immune response**. Secondary immune response is faster and stronger than primary response. Primary response forms memory cells, while secondary response uses existing memory cells. The primary response sets the stage for the secondary response, allowing the immune system to "remember" and mount a more effective defence against future infections.

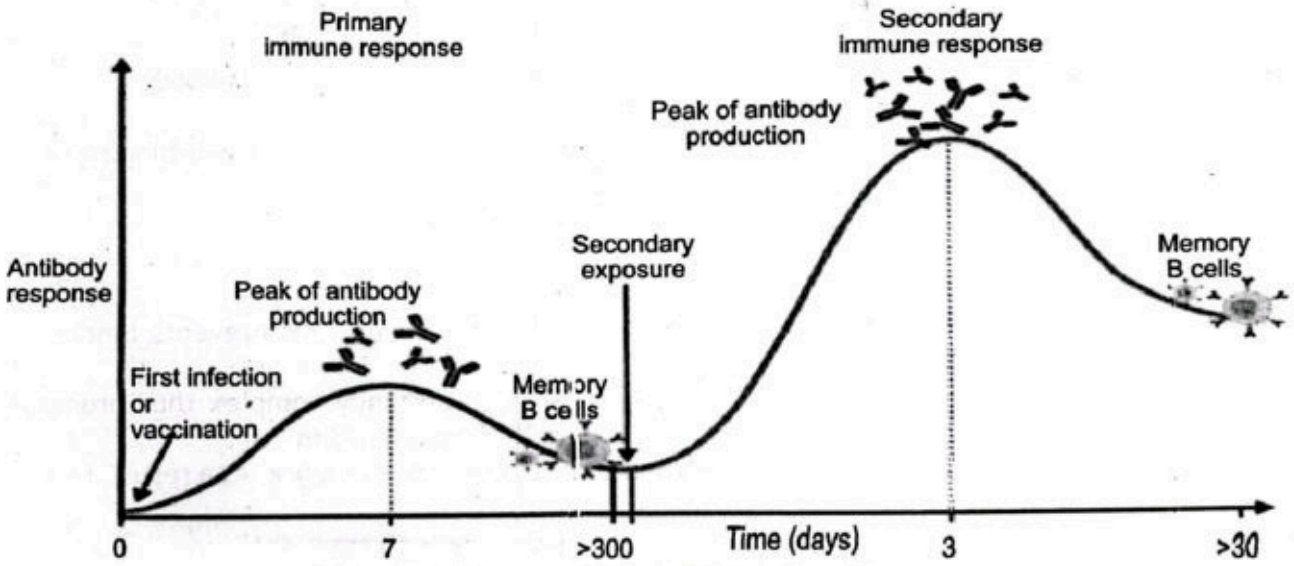

Fig. 9.16: Primary vs Secondary immune response

Monoclonal antibody

Whenever a person falls ill, the body responds by producing antibodies to counteract the antigens of pathogens. These antibodies are specific to a particular antigen. Scientists can replicate these antibodies and help in the treatment of a disease. Monoclonal antibodies (mAbs) are artificially engineered in laboratories by scientists as a form of medication.

This is because they are characterized by their ability to help human body combat diseases better. These can target only one specific type of antigen.

The discovery of mAbs by Köhler and Milstein in 1975 revolutionized various aspects of biological research, diagnostics, and therapy. mAbs are a single type of antibody that are produced by identical immune cells (clones). These mAbs specifically bind to a particular antigen. This uniqueness allows for precise targeting and recognition of specific molecules.

Impact on biological research

1. **Specificity and sensitivity:** mAbs enabled researchers to detect and quantify specific molecules with precision. This helped in the study of complex biological processes.
2. **Immunological research:** mAbs helped explain immune responses, cell signaling, and antigen-antibody interactions.
3. **Cancer research:** mAbs aided in understanding cancer cell biology. As a result, targeted therapies and diagnostic tools are developed.
4. **Protein analysis:** mAbs facilitated the detection and characterization of specific proteins. It increased our understanding of protein function and expression.
5. **Drug development:** mAbs are responsible for the creation of new targeted therapies of cancer and autoimmune diseases.

Impact on diagnostics

1. **ELISA (Enzyme Linked Immunosorbent Assay) and Western blot:** mAbs enabled the development of sensitive and specific diagnostic tests, like ELISA and Western blot.
2. **Imaging agents:** mAbs combined with radioactive or fluorescent labels help imaging techniques like PET and fluorescence microscopy. Positron Emission Tomography (PET) is a medical imaging technique that uses radioactive tracers to creat 3D images of metabolic and physiological processes in the body.PET helps doctors diagnose and monitor various diseases, such as cancer, neurological disorders, and cardiovascular conditions

Impact on therapy

1. **Targeted therapies:** mAbs have revolutionized disease treatment. It is used to treat cancer, COVID-19, cardiovascular disease and autoimmune diseases.
2. **Immunotherapy:** mAbs can make use of immune system to combat cancer.

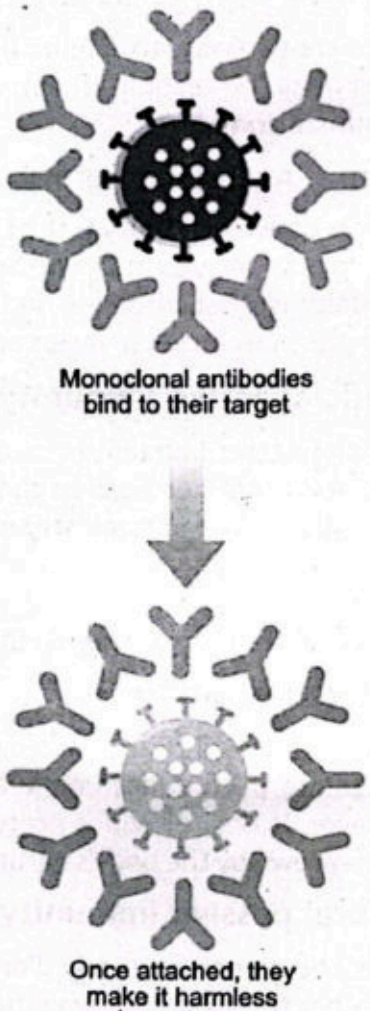

Fig. 9.17: Action of mAbs onCOVID-19 virus to control the disease

9.3.4 Inborn and Acquired Immunity

The two basic types of immunity are (a) inborn or innate immunity (b) acquired immunity. The ability of the innate immune system to kill microorganisms is not specific. First and second line of defence that you have already studied in this chapter are the part of **innate or inborn immunity.** 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.**

Adaptive immunity is unique to vertebrates, while innate immunity is found in all multicellular organisms.

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.

9.4 TYPES OF ACQUIRED 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

Natural active Immunity 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. This type of immunity is most effective and generally persists for a long time, sometimes even for life. For example, you can get measles only once in your life, as it gives lifelong natural active immunity.

Artificial active immunity

Artificial Active Immunity (vaccination) is achieved by injecting (or 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 other antigen. Often a second, booster 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.

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

It 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

> **Do you know?**
> The first antibody-based therapies were used to treat snake bites and were called antivenoms!

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.

9.3.5 Disorders of Immune System

Some conditions that stimulate a defective immune response or destroy immune system are called disorders of immune system.

Allergies

Allergies are defective immune responses leading to chronic health conditions like Hay fever, eczema, asthma and food allergy. The immune system of allergy patients overreacts when allergens (like pollen, dust or mold) are inhaled or ingested or enter through skin. The body starts producing large quantity of special antibodies IgE (Immunoglobulin E). This IgE binds with basophils to release inflammatory chemicals like histamine. Histamine increases capillary leakiness, swelling, mucus secretion, inflammation and other allergic responses. Antihistamine drugs block some of the effects of histamine, relieving the symptoms of allergies. Vaccination can be effective treatment of allergy specially for asthma.

Autoimmune disease

In autoimmune disease, the immune system attacks the healthy cells of body's organs and tissues by mistake. The antibodies are produced against body's own components and begin to destroy them. There are more than 80 types of autoimmune diseases. They can affect almost any part of your body. For example:

a. Some types of anaemias are caused by antibodies that destroy a person's red blood cells.
b. 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.
c. Vitiligo is a chronic autoimmune disorder that causes patches of skin to lose pigment or colour.

Unfortunately, at present there is no way to cure autoimmune diseases. The autoimmune response can be suppressed with drugs.

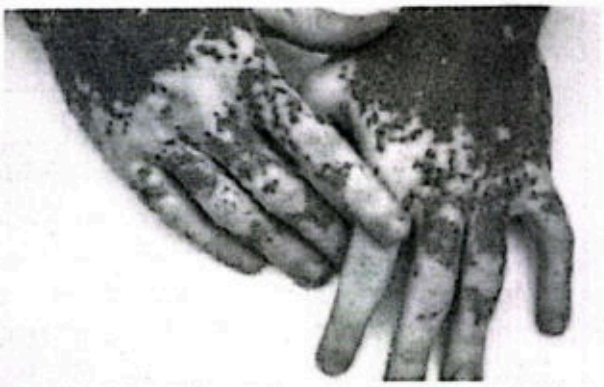

Fig. 9.18: Vitiligo causes pigment-less patches on skin

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 **transplant rejection.**

Do you know?

The first successful kidney transplant was performed in 1954 between identical twins.

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 helper T cells come into contact with the graft tissue's major histocompatibility 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 TH cells** stimulate the activation and proliferation of appropriate T cells, which then enhance a focused attack on the transplant tissue. In the second, **responsive** antigen-specific TH 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.

Lymphokines are signaling molecules released by immune cells (like lymphocytes) that help communicate with other immune cells to fight infections. They act like messengers, coordinating the immune response to eliminate pathogens.

Role of B cells in transplant rejection

There is a third mechanism in which antibodies plays a role. The responsive helper T 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 facilitating the phagocytosis of the grafted tissue by macrophages.
The immune system is a highly complex and dynamic network of organs, cells, and molecules that work in concert to defend the body against a wide array of threats. The interplay between innate and adaptive immunity ensures a robust and efficient response to both common and novel pathogens. Understanding the mechanisms of immunity not only helps in appreciating how our body protects us but also underscores the importance of vaccinations and the impact of allergies.

Explain why a transplant recipient is given immune suppressant drugs and determine what implications does this has 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.

STEAM ACTIVITY 9.1

Recognizing phagocytes and lymphocytes while observing prepared slides

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. In addition to the immune system, we are protected from disease by
   A. normal body temperature
   B. hormones
   C. antigens
   D. mucous membrane and cilia

4. Fever decrease the
   A. interferon production
   B. concentration of iron in the blood
   C. activity of phagocytes
   D. inflammation

5. T and B cells are
   A. lymphocytes B. macrophages C. natural killer cells D. red blood cells

6. When B-cells are presented with antigen they differentiate into
   A. T-cells B. helper T-cells C. plasma cells D. bursa cells

7. 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

8. Natural killer cells kill virus infected and cancerous cells by:
   A. phagocytosis B. complement proteins C. perforins and granzymes D. antibodies

9. Colostrum provides
   A. natural active immunity
   B. artificial active immunity
   C. natural passive immunity
   D. artificial passive immunity

10. mAbs can help to combat diseases like:
    A. measles B. cancer C. anorexia D. haemophilia

11. A patient has a severe burn injury, compromising their skin barrier. Which of the following is most likely to occur?
    A. Increased risk of infection due to loss of chemical and physical barriers
    B. Decreased risk of infection due to increased immune response
    C. No change in infection risk
    D. Increased risk of autoimmune disease

12. Dendritic cells are crucial for initiating an adaptive immune response. What would happen if dendritic cells were unable to present antigens?
    A. The adaptive immune response would be enhanced
    B. The innate immune response would be impaired
    C. The adaptive immune response would be impaired
    D. There would be no impact on the immune response

13. Neutrophils use extracellular traps to kill pathogens. What is the primary advantage of this mechanism?
    A. Targeted killing of specific pathogens
    B. Ability to phagocytose large pathogens
    C. Immobilization of pathogens in a localized area
    D. Activation of complement system

14. NK cells play a crucial role in controlling viral infections and cancer. What would happen if NK cell function was impaired?
    A. Increased risk of bacterial infections
    B. Increased risk of viral infections and cancer
    C. Decreased risk of autoimmune disease
    D. No impact on immune function

15. Interferons released by virus-infected cells trigger a response in neighboring cells. What is the primary purpose of this response?
    A. To induce apoptosis in uninfected cells
    B. To destroy RNA in infected cells
    C. To activate the adaptive immune response
    D. To prevent viral replication in neighboring cells

16. Antibodies can bind to an antigen, forming an antigen-antibody complex. What would be the most likely outcome if antibodies were unable to opsonize bacteria?
    A. Increased phagocytosis of bacteria
    B. Decreased phagocytosis of bacteria
    C. Increased activation of complement system
    D. Decreased activation of NK cells

17. Monoclonal antibodies have revolutionized the field of immunotherapy. What is a potential benefit of using monoclonal antibodies in cancer treatment?
    A. Increased killing of virus infected cells
    B. Targeted killing of cancer cells
    C. Enhanced tumor growth
    D. Increased risk of infection

18. Vitiligo is an autoimmune disease characterized by skin depigmentation. What would be a potential consequence of vitiligo, in majority of patients, if left untreated?
    A. Increased risk of skin cancer
    B. Decreased risk of autoimmune disease
    C. Increased risk of infection
    D. Emotional distress due to cosmetic impact
19. Transplant rejection occurs due to the immune system's ability to recognize foreign antigens. What would happen if a patient received a transplant from an identical twin?
    A. Increased risk of graft-versus-host disease
    B. Decreased risk of transplant rejection
    C. Increased risk of autoimmune disease
    D. No impact on immune function
20. Lymphokines, such as interleukins, play a crucial role in coordinating the immune response. What would be the consequence of impaired lymphokine production?
    A. Enhanced activation of cytotoxic T-cells
    B. Reduced activation of immune cells
    C. Increased production of antibodies
    D. Enhanced phagocytic activity of neutrophils

Section II: Short Answer Questions

1. What is immune response?
2. Name the three lines of defence against microbial attack.
3. How oil and sweat glands take part in defence against microorganisms?
4. Name the parts of antibody molecule.
5. How interferons control spread of virus in the body?
6. How do antibodies kill pathogens?
7. Why does each antibody bind only to a specific antigen?
8. Why is passive immunity temporary?
9. Name the disorders of immune system.
10. What are the autoimmune diseases?
11. Write the differences between:
    a. sebaceous gland and sweat gland
    b. macrophages and neutrophils
    c. antibody-mediated immune response and a cell-mediated immune response.
    d. cytotoxic T cells and suppressor T cell
    e. plasma cells and memory cells
    f. antibody and antigen
    g. inborn immunity and acquired immunity
    h. primary and secondary immune response

Section III: Extensive Answer Questions

1. Describe the human skin as an impenetrable barrier against invasion by microbes.
2. What is the role of macrophages and neutrophils in killing bacteria?
3. Explain the protective proteins of complementary system with diagram.
4. Explain in detail inflammatory response with diagram.
5. Explain temperature response against infection.
6. What are the ways fever kills microbes?
7. Describe the role of monocytes in immune system.
8. What is the role of T cells in cell mediated response.
9. Describe the role of B cells in humoral antibody mediated immune response.
10. Describe the types of acquired immunity.
11. Describe the role of T cells and B cells in transplant rejection.
12. Explain why a transplant recipient is given immune suppressant drugs and determine what implications this has on his life.
13. Evaluate the discovery of monoclonal antibodies and justify how this accomplishment revolutionized many aspects of biological research.