UNIT 4 LYMPHATIC AND IMMUNE SYSTEM

Structure

4.0 OBJECTIVES

In this unit students will learn about

- functions of lymphatic system;
- components of lymphatic system—Lymph nodes, Tonsils, Spleen, Thymus;
- functions of immune system; and
- major components of the immune system.

4.1 INTRODUCTION

The lymphatic system is a part of the immune system which is composed of a large network of lymphatic vessels that carry a clear fluid called lymph directionally towards the heart. In deference to the circulatory system, it is an open system.

4.2 FUNCTIONS OF LYMPHATIC SYSTEM

The lymphatic system has three primary functions. First of all, it returns excess interstitial fluid to the blood. Of the fluid that leaves the capillary, about 90 percent is returned. The 10 percent that does not return becomes part of the interstitial fluid that surrounds the tissue cells. Small protein molecules may "leak" through the capillary wall and increase the osmotic pressure of the interstitial fluid. This further inhibits the return of fluid into the capillaries, and fluid tends to accumulate in the tissue spaces. If this continues, blood volume and blood pressure decrease significantly and the volume of tissue fluid increases, which results in edema (swelling). Lymph capillaries pick up the excess interstitial fluid and proteins and return them to the venous blood. After the fluid enters the lymph capillaries, it is called lymph.

The second function of the lymphatic system is the absorption of fats and fat-soluble vitamins from the digestive system and the subsequent transport of these substances to the venous circulation. The mucosa that lines the small intestine is covered with fingerlike projections called villi. There are blood capillaries and special lymph capillaries, called lacteals, in the center of each villus. The blood capillaries absorb most nutrients, but the fats and fat-soluble vitamins are absorbed by the lacteals. The lymph in the lacteals has a milky appearance due to its high fat content and is called chyle. The third and probably most well known function of the lymphatic system is defense against invading microorganisms and disease. Lymph nodes and other lymphatic organs filter the lymph to remove microorganisms and other foreign particles. Lymphatic organs contain lymphocytes that destroy invading organisms.

4.3 COMPONENTS OF LYMPHATIC SYSTEM

The lymphatic system consists of a fluid (lymph), vessels that transport the lymph, and organs that contain lymphoid tissue.

4.3.1 Lymph

Lymph is a fluid similar in composition to blood plasma. It is derived from

blood plasma as fluids pass through capillary walls at the arterial end. As the interstitial fluid begins to accumulate, it is picked up and removed by tiny lymphatic vessels and returned to the blood. As soon as the interstitial fluid enters the lymph capillaries, it is called lymph. Returning the fluid to the blood prevents edema and helps to maintain normal blood volume and pressure.

4.3.2 Lymphatic Vessels

Lymphatic vessels, unlike blood vessels, only carry fluid away from the tissues. The smallest lymphatic vessels are the lymph capillaries, which begin in the tissue spaces as blind-ended sacs. Lymph capillaries are found in all regions of the body except the bone marrow, central nervous system, and tissues, such as the epidermis, that lack blood vessels. The wall of the lymph capillary is composed of endothelium in which the simple squamous cells overlap to form a simple one-way valve. This arrangement permits fluid to enter the capillary but prevents lymph from leaving the vessel.

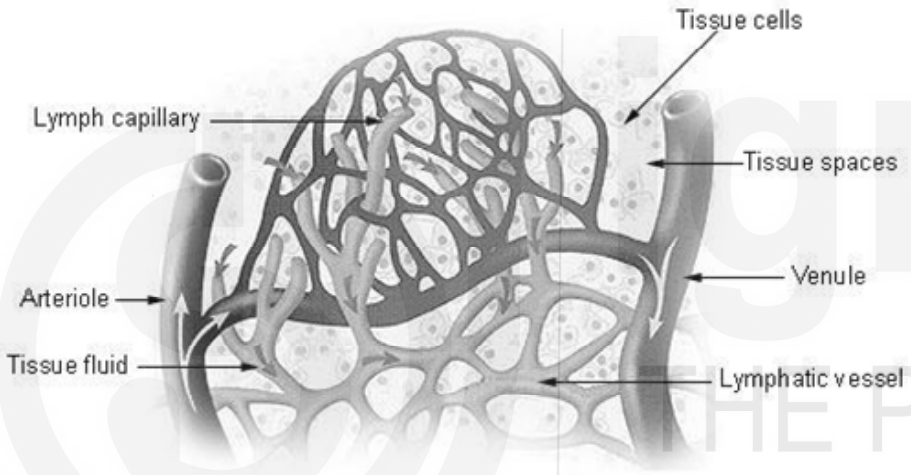

Fig. 4.1: Lymph capillaries in the Tissue Spaces

The microscopic lymph capillaries merge to form lymphatic vessels. Small lymphatic vessels join to form larger tributaries, called lymphatic trunks, which drain large regions. Lymphatic trunks merge until the lymph enters the two lymphatic ducts. The right lymphatic duct drains lymph from the upper right quadrant of the body. The thoracic duct drains all the rest.

Like veins, the lymphatic tributaries have thin walls and have valves to prevent backflow of blood. There is no pump in the lymphatic system like the heart in the cardiovascular system. The pressure gradients to move lymph through the vessels come from the skeletal muscle action, respiratory movement, and contraction of smooth muscle in vessel walls.

4.3.3 Lymphatic Organs

Lymphatic organs are characterized by clusters of lymphocytes and other cells, such as macrophages, enmeshed in a framework of short, branching connective tissue fibers. The lymphocytes originate in the red bone marrow with other types of blood cells and are carried in the blood from the bone marrow to the lymphatic organs. When the body is exposed to microorganisms and other foreign substances, the lymphocytes proliferate within the lymphatic organs and are sent in the blood to the site of the

invasion. This is part of the immune response that attempts to destroy the invading agent. To learn more about lymphatic organs, you have to learn about: Lymph Nodes, Tonsils, Spleen, Thymus

4.3.4 Lymph Nodes

Lymph nodes are small bean-shaped structures that are usually less than 2.5 cm in length. They are widely distributed throughout the body along the lymphatic pathways where they filter the lymph before it is returned to the blood. Lymph nodes are not present in the central nervous system. There are three superficial regions on each side of the body where lymph nodes tend to cluster. These areas are the inguinal nodes in the groin, the axillary nodes in the armpit, and the cervical nodes in the neck.

The typical lymph node is surrounded by a connective tissue capsule and divided into compartments called lymph nodules. The lymph nodules are dense masses of lymphocytes and macrophages and are separated by spaces called lymph sinuses. Several afferent lymphatic vessels, which carry lymph into the node, enter the node on the convex side. The lymph moves through the lymph sinuses and enters an efferent lymphatic vessel, which carries the lymph away from the node. Because there are more afferent vessels than efferent vessels, the passage of lymph through the sinuses is slowed down, which allows time for the cleansing process. The efferent vessel leaves the node at an indented region called the hilum.

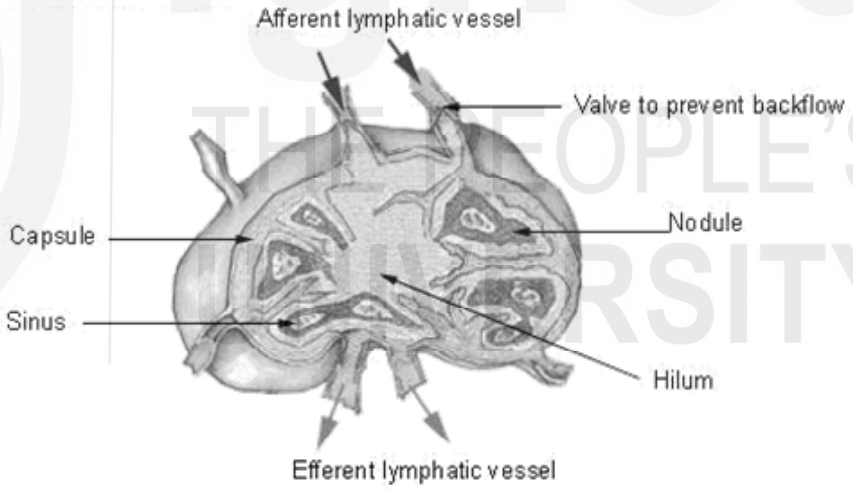

Fig. 4.2 : Lymph node structure

4.3.5 Tonsils

Tonsils are clusters of lymphatic tissue just under the mucous membranes that line the nose, mouth, and throat (pharynx). There are three groups of tonsils. The pharyngeal tonsils are located near the opening of the nasal cavity into the pharynx. When these tonsils become enlarged they may interfere with breathing and are called adenoids. The palatine tonsils are the ones that are located near the opening of the oral cavity into the pharynx. Lingual tonsils are located on the posterior surface of the tongue, which also places them near the opening of the oral cavity into the pharynx. Lymphocytes and macrophages in the tonsils provide protection against harmful substances and pathogens that may enter the body through the nose or mouth.

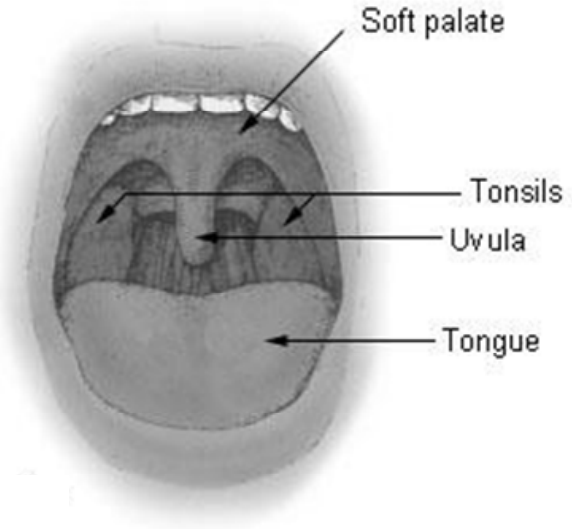

Fig. 4.3 : Tonsils

4.3.6 The Spleen

The spleen is located in the upper left abdominal cavity, just beneath the diaphragm, and posterior to the stomach. It is similar to a lymph node in shape and structure but it is much larger. The spleen is the largest lymphatic organ in the body. Surrounded by a connective tissue capsule, which extends inward to divide the organ into lobules, the spleen consists of two types of tissue called white pulp and red pulp. The white pulp is lymphatic tissue consisting mainly of lymphocytes around arteries. The red pulp consists of venous sinuses filled with blood and cords of lymphatic cells, such as lymphocytes and macrophages. Blood enters the spleen through the splenic artery, moves through the sinuses where it is filtered, then leaves through the spleenic vein.

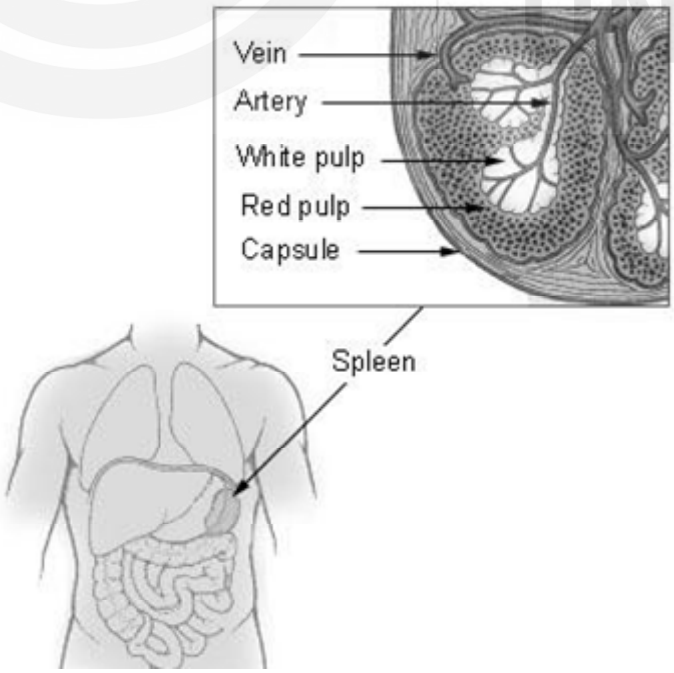

Fig. 4.4: Spleen

The spleen filters blood in the same way as the lymph nodes filter lymph. Lymphocytes in the spleen react to pathogens in the blood and attempt to destroy them. Macrophages then engulf the resulting debris, the damaged cells, and the other large particles. The spleen, along with the liver, removes old and damaged erythrocytes from the circulating blood. Like other lymphatic tissue, it produces lymphocytes, especially in response to invading pathogens.

The sinuses in the spleen are a reservoir for blood. In emergencies such as hemorrhage, smooth muscle in the vessel walls and in the capsule of the spleen contracts. This squeezes the blood out of the spleen into the general circulation.

4.3.7 Thymus

The thymus is a soft organ with two lobes that is located anterior to the ascending aorta and posterior to the sternum. It is relatively large in infants and children but after puberty it begins to decrease in size so that in older adults it is quite small.

The primary function of the thymus is the processing and maturation of special lymphocytes called T-lymphocytes or T-cells. While in the thymus, the lymphocytes do not respond to pathogens and foreign agents. After the lymphocytes have matured, they enter the blood and go to other lymphatic organs where they help provide defense against disease. The thymus also produces a hormone, thymosin, which stimulates the maturation of lymphocytes in other lymphatic organs.

Check Your Progress-1

1. Fill in the blanks.

(i) Of the fluid that leaves the capillary, about _____ percent is returned. The _____ percent that does not return becomes part of the interstitial fluid that surrounds the tissue cells.

A. 50, 50

B. 40, 60

C. 90, 10

D. 20, 80

(ii) One of the functions that the lymphatic system performs is to return excess _____ fluid to the blood.

A. clear

B. interstitial

C. red-colored

D. thoracic

(iii) Lymph nodes are widely distributed throughout the body along the lymphatic pathways where they filter the _____ before it is returned to the _____.

A. lymph, blood

B. lymph, heart

C. blood, heart

D. blood, lymph

(iv) Lymph enters a lymph node through _____, filters through the _____, and leaves through _____. efferent vessels, afferent vessels, sinuses

A. sinuses, afferent vessels, efferent vessels

B. afferent vessels, sinuses, efferent vessels

C. . afferent vessels, efferent vessels, sinuses

(v) The _____ tonsils are the ones that are located near the opening of the oral cavity into the pharynx.

A. lingual

B. pharyngeal

C. palatine

D. oral

(vi) The spleen is a lymph organ that filters blood and also acts as a reservoir for _____.

A. water

B. fat

C. interstitial fluid

D. blood

(vii) The thymus is a soft organ with _____lobes that is located anterior to the ascending aorta and posterior to the sternum.

A. one

B. two

C. three

D. four

(viii) The thymus also produces a hormone, _____, that stimulates the maturation of lymphocytes in other lymphatic organs.

A. oxytocin

B. thymosin

C. calcitonin

D. estrogen

2. Write a brief note on :

A. Functions of Lymphatic system.

B. Lymphatic organs

4.4 THE IMMUNE SYSTEM

The **immune system** is a host defense system comprising many biological structures and processes within an organism that protects against disease. To function properly, an immune system must detect a wide variety of agents,

known as pathogens, from viruses to parasitic worms, and distinguish them from the organism's own healthy tissue. In many species, the immune system can be classified into subsystems, such as the innate immune system versus the adaptive immune system, or humoral immunity versus cell-mediated immunity. In humans, the blood–brain barrier, blood–cerebrospinal fluid barrier, and similar fluid–brain barriers separate the peripheral immune system from the neuroimmune system, which protects the brain.

Pathogens can rapidly evolve and adapt, and thereby avoid detection and neutralization by the immune system; however, multiple defense mechanisms have also evolved to recognize and neutralize pathogens. Even simple unicellular organisms such as bacteria possess a rudimentary immune system in the form of enzymes that protect against bacteriophage infections. Other basic immune mechanisms evolved in ancient eukaryotes and remain in their modern descendants, such as plants and invertebrates. These mechanisms include phagocytosis, antimicrobial peptides called defensins, and the complement system. Jawed vertebrates, including humans, have even more sophisticated defense mechanisms, including the ability to adapt over time to recognize specific pathogens more efficiently. Adaptive (or acquired) immunity creates immunological memory after an initial response to a specific pathogen, leading to an enhanced response to subsequent encounters with that same pathogen. This process of acquired immunity is the basis of vaccination.

Disorders of the immune system can result in autoimmune diseases, inflammatory diseases and cancer. Immunodeficiency occurs when the immune system is less active than normal, resulting in recurring and life-threatening infections. In humans, immunodeficiency can either be the result of a genetic disease such as severe combined immunodeficiency, acquired conditions such as HIV/AIDS, or the use of immunosuppressive medication. In contrast, autoimmunity results from a hyperactive immune system attacking normal tissues as if they were foreign organisms. Common autoimmune diseases include Hashimoto's thyroiditis, rheumatoid arthritis, diabetes mellitus type 1, and systemic lupus erythematosus. Immunology covers the study of all aspects of the immune system.

Table 4.1:Types of immune system

Innate immune system	Adaptive immune system
1. Response is non-specific	Pathogen and antigen specific response
2. Exposure leads to immediate maximal response	Lag time between exposure and maximal response
3. Cell-mediated and humoral components	Cell-mediated and humoral components
4. No immunological memory	Exposure leads to immunological memory
5. Found in nearly all forms of life	Found only in jawed vertebrates

Both innate and adaptive immunity depend on the ability of the immune system to distinguish between self and non-self molecules. In immunology, *self* molecules are those components of an organism's body that can be distinguished from foreign substances by the immune system.[6] Conversely, *non-self* molecules are those recognized as foreign molecules. One class of non-self molecules are called antigens (short for *anti*body *gen*erators) and are defined as substances that bind to specific immune receptors and elicit an immune response.

Newborn infants have no prior exposure to microbes and are particularly vulnerable to infection. Several layers of passive protection are provided by the mother. During pregnancy, a particular type of antibody, called IgG, is transported from mother to baby directly through the placenta, so human babies have high levels of antibodies even at birth, with the same range of antigen specificities as their mother. Breast milk or colostrum also contains antibodies that are transferred to the gut of the infant and protect against bacterial infections until the newborn can synthesize its own antibodies. This is passive immunity because the fetus does not actually make any memory cells or antibodies—it only borrows them. This passive immunity is usually short-term, lasting from a few days up to several months. In medicine, protective passive immunity can also be transferred artificially from one individual to another via antibody-rich serum.

4.4.1 Innate Immune System

Microorganisms or toxins that successfully enter an organism encounter the cells and mechanisms of the innate immune system. The innate response is usually triggered when microbes are identified by pattern recognition receptors, which recognize components that are conserved among broad groups of microorganisms, or when damaged, injured or stressed cells send out alarm signals, many of which (but not all) are recognized by the same receptors as those that recognize pathogens. Innate immune defenses are non-specific, meaning these systems respond to pathogens in a generic way. This system does not confer long-lasting immunity against a pathogen. The innate immune system is the dominant system of host defense in most organisms.

4.4.2 Surface Barriers

Several barriers protect organisms from infection, including mechanical, chemical, and biological barriers. The waxy cuticle of most leaves, the exoskeleton of insects, the shells and membranes of externally deposited eggs, and skin are examples of mechanical barriers that are the first line of defense against infection. However, as organisms cannot be completely sealed from their environments, other systems act to protect body openings such as the lungs, intestines, and the genitourinary tract. In the lungs, coughing and sneezing mechanically eject pathogens and other irritants from the respiratory tract. The flushing action of tears and urine also mechanically expels pathogens, while mucus secreted by the respiratory and gastrointestinal tract serves to trap and entangle microorganisms.

Chemical barriers also protect against infection. The skin and respiratory tract secrete antimicrobial peptides such as the β-defensins. Enzymes such as lysozyme and phospholipase A2 in saliva, tears, and breast milk are also antibacterials. Vaginal secretions serve as a chemical barrier following

menarche, when they become slightly acidic, while semen contains defensins and zinc to kill pathogens. In the stomach, gastric acid serves as a powerful chemical defense against ingested pathogens.

Within the genitourinary and gastrointestinal tracts, commensal flora serve as biological barriers by competing with pathogenic bacteria for food and space and, in some cases, by changing the conditions in their environment, such as pH or available iron. As a result of the symbiotic relationship between commensals and the immune system, the probability that pathogens will reach sufficient numbers to cause illness is reduced. However, since most antibiotics non-specifically target bacteria and do not affect fungi, oral antibiotics can lead to an "overgrowth" of fungi and cause conditions such as a vaginal candidiasis (a yeast infection). There is good evidence that re-introduction of probiotic flora, such as pure cultures of the lactobacilli normally found in unpasteurized yogurt, helps restore a healthy balance of microbial populations in intestinal infections in children and encouraging preliminary data in studies on bacterial gastroenteritis, inflammatory bowel diseases, urinary tract infection and post-surgical infections.

Cellular Components

Human blood, as you are aware contains red blood cells, several knobby white blood cells including lymphocytes, a monocyte, a neutrophil, and many small disc-shaped platelets.

Leukocytes (white blood cells) act like independent, single-celled organisms and are the second arm of the innate immune system. The innate leukocytes include the phagocytes (macrophages, neutrophils, and dendritic cells), innate lymphoid cells, mast cells, eosinophils, basophils, and natural killer cells. These cells identify and eliminate pathogens, either by attacking larger pathogens through contact or by engulfing and then killing microorganisms. Innate cells are also important mediators in lymphoid organ development and the activation of the adaptive immune system.

Phagocytosis is an important feature of cellular innate immunity performed by cells called phagocytes that engulf, or eat, pathogens or particles. Phagocytes generally patrol the body searching for pathogens, but can be called to specific locations by cytokines. Once a pathogen has been engulfed by a phagocyte, it becomes trapped in an intracellular vesicle called a phagosome, which subsequently fuses with another vesicle called a lysosome to form a phagolysosome. The pathogen is killed by the activity of digestive enzymes or following a respiratory burst that releases free radicals into the phagolysosome. Phagocytosis evolved as a means of acquiring nutrients, but this role was extended in phagocytes to include engulfment of pathogens as a defense mechanism. Phagocytosis probably represents the oldest form of host defense, as phagocytes have been identified in both vertebrate and invertebrate animals.

Phagocytes

Neutrophils and macrophages are phagocytes that travel throughout the body in pursuit of invading pathogens. Neutrophils are normally found in the bloodstream and are the most abundant type of phagocyte, normally representing 50% to 60% of the total circulating leukocytes, and consisting of neutrophil-killer and neutrophil-cager subpopulations. During the acute phase

of inflammation, particularly as a result of bacterial infection, neutrophils migrate toward the site of inflammation in a process called chemotaxis, and are usually the first cells to arrive at the scene of infection. Macrophages are versatile cells that reside within tissues and produce a wide array of chemicals including enzymes, complement proteins, and cytokines, while they can also act as scavengers that rid the body of worn-out cells and other debris, and as antigen-presenting cells that activate the adaptive immune system.

Dendritic Cell

Dendritic cells (DC) are phagocytes in tissues that are in contact with the external environment; therefore, they are located mainly in the skin, nose, lungs, stomach, and intestines. They are named for their resemblance to neuronal dendrites, as both have many spine-like projections, but dendritic cells are in no way connected to the nervous system. Dendritic cells serve as a link between the bodily tissues and the innate and adaptive immune systems, as they present antigens to T cells, one of the key cell types of the adaptive immune system.

Granulocytes

Mast cells reside in connective tissues and mucous membranes, and regulate the inflammatory response. They are most often associated with allergy and anaphylaxis. Basophils and eosinophils are related to neutrophils. They secrete chemical mediators that are involved in defending against parasites and play a role in allergic reactions, such as asthma.

Innate Lymphoid Cells

Innate lymphoid cells (ILCs) are a group of innate immune cells that are derived from common lymphoid progenitor (CLP) and belong to the lymphoid lineage. These cells are defined by absence of antigen specific B or T cell receptor because of the lack of recombination activating gene (RAG). ILCs do not express myeloid or dendritic cell markers.

Natural killer cells, one of member ILCs, are lymphocytes and a component of the innate immune system which does not directly attack invading microbes. Rather, NK cells destroy compromised host cells, such as tumor cells or virus-infected cells, recognizing such cells by a condition known as “missing self.” This term describes cells with low levels of a cell-surface marker called MHC I (major histocompatibility complex)—a situation that can arise in viral infections of host cells. They were named “natural killer” because of the initial notion that they do not require activation in order to kill cells that are “missing self.” For many years it was unclear how NK cells recognize tumor cells and infected cells. It is now known that the MHC makeup on the surface of those cells is altered and the NK cells become activated through recognition of “missing self”. Normal body cells are not recognized and attacked by NK cells because they express intact self MHC antigens. Those MHC antigens are recognized by killer cell immunoglobulin receptors (KIR) which essentially put the brakes on NK cells.

4.4.3 Inflammation

Inflammation is one of the first responses of the immune system to infection. The symptoms of inflammation are redness, swelling, heat, and pain, which are caused by increased blood flow into tissue. Inflammation is produced by

eicosanoids and cytokines, which are released by injured or infected cells. Eicosanoids include prostaglandins that produce fever and the dilation of blood vessels associated with inflammation, and leukotrienes that attract certain white blood cells (leukocytes). Common cytokines include interleukins that are responsible for communication between white blood cells; chemokines that promote chemotaxis; and interferons that have anti-viral effects, such as shutting down protein synthesis in the host cell. Growth factors and cytotoxic factors may also be released. These cytokines and other chemicals recruit immune cells to the site of infection and promote healing of any damaged tissue following the removal of pathogens.

4.4.4 Complement System

The complement system is a biochemical cascade that attacks the surfaces of foreign cells. It contains over 20 different proteins and is named for its ability to "complement" the killing of pathogens by antibodies. Complement is the major humoral component of the innate immune response. In humans, this response is activated by complement binding to antibodies that have attached to these microbes or the binding of complement proteins to carbohydrates on the surfaces of microbes. This recognition signal triggers a rapid killing response. The speed of the response is a result of signal amplification that occurs after sequential proteolytic activation of complement molecules, which are also proteases. After complement proteins initially bind to the microbe, they activate their protease activity, which in turn activates other complement proteases, and so on. This produces a catalytic cascade that amplifies the initial signal by controlled positive feedback. The cascade results in the production of peptides that attract immune cells, increase vascular permeability, and opsonize (coat) the surface of a pathogen, marking it for destruction. This deposition of complement can also kill cells directly by disrupting their plasma membrane.

4.4.5 Adaptive Immune System

The adaptive immune response is antigen-specific and requires the recognition of specific "non-self" antigens during a process called antigen presentation. Antigen specificity allows for the generation of responses that are tailored to specific pathogens or pathogen-infected cells. The ability to mount these tailored responses is maintained in the body by "memory cells". If a pathogen infects the body more than once, these specific memory cells are used to quickly eliminate it.

4.4.6 The Recognition of Antigen

The cells of the adaptive immune system are special types of leukocytes, called lymphocytes. B cells and T cells are the major types of lymphocytes and are derived from hematopoietic stem cells in the bone marrow. B cells are involved in the humoral immune response, whereas T cells are involved in cell-mediated immune response.

Killer T cells only recognize antigens coupled to Class I MHC molecules, while helper T cells and regulatory T cells only recognize antigens coupled to Class II MHC molecules. These two mechanisms of antigen presentation reflect the different roles of the two types of T cell. A third, minor subtype are the γδ T cells that recognize intact antigens that are not bound to MHC receptors. The double-positive T cells are exposed to a wide variety of self-antigens in the thymus, in which iodine is necessary for its thymus development and activity.

In contrast, the B cell antigen-specific receptor is an antibody molecule on the B cell surface, and recognizes whole pathogens without any need for antigen processing. Each lineage of B cell expresses a different antibody, so the complete set of B cell antigen receptors represent all the antibodies that the body can manufacture.

4.4.7 Antigen Presentation to T-lymphocytes

Both B cells and T cells carry receptor molecules that recognize specific targets. T cells recognize a "non-self" target, such as a pathogen, only after antigens (small fragments of the pathogen) have been processed and presented in combination with a "self" receptor called a major histocompatibility complex (MHC) molecule.

4.5 CELL MEDIATED IMMUNITY

There are two major subtypes of T cells: the killer T cell and the helper T cell. In addition there are regulatory T cells which have a role in modulating immune response.

Killer T Cells

Killer T cells are a sub-group of T cells that kill cells that are infected with viruses (and other pathogens), or are otherwise damaged or dysfunctional. As with B cells, each type of T cell recognizes a different antigen. Killer T cells are activated when their T-cell receptor (TCR) binds to this specific antigen in a complex with the MHC Class I receptor of another cell. Recognition of this MHC:antigen complex is aided by a co-receptor on the T cell, called CD8. The T cell then travels throughout the body in search of cells where the MHC I receptors bear this antigen. When an activated T cell contacts such cells, it releases cytotoxins, such as perforin, which form pores in the target cell's plasma membrane, allowing ions, water and toxins to enter. The entry of another toxin called granulysin (a protease) induces the target cell to undergo apoptosis. T cell killing of host cells is particularly important in preventing the replication of viruses. T cell activation is tightly controlled and generally requires a very strong MHC/antigen activation signal, or additional activation signals provided by "helper" T cells.

Helper T Cells

Antigen-presenting cells (APCs) present antigen on their Class II MHC molecules (MHC2). Helper T cells recognize these, with the help of their expression of CD4 co-receptor (CD4+). The activation of a resting helper T cell causes it to release cytokines and other stimulatory signals that stimulate the activity of macrophages, killer T cells and B cells, the latter producing antibodies. The stimulation of B cells and macrophages succeeds a proliferation of T helper cells.

Helper T cells regulate both the innate and adaptive immune responses and help determine which immune responses the body makes to a particular pathogen. These cells have no cytotoxic activity and do not kill infected cells or clear pathogens directly. They instead control the immune response by directing other cells to perform these tasks.

Helper T cells express T cell receptors (TCR) that recognize antigen bound to Class II MHC molecules. The MHC:antigen complex is also recognized by the helper cell's CD4 co-receptor, which recruits molecules inside the T

cell (e.g., Lck) that are responsible for the T cell's activation. Helper T cells have a weaker association with the MHC:antigen complex than observed for killer T cells, meaning many receptors (around 200–300) on the helper T cell must be bound by an MHC:antigen in order to activate the helper cell, while killer T cells can be activated by engagement of a single MHC:antigen molecule. Helper T cell activation also requires longer duration of engagement with an antigen-presenting cell. The activation of a resting helper T cell causes it to release cytokines that influence the activity of many cell types. Cytokine signals produced by helper T cells enhance the microbicidal function of macrophages and the activity of killer T cells. In addition, helper T cell activation causes an upregulation of molecules expressed on the T cell's surface, such as CD40 ligand (also called CD154), which provide extra stimulatory signals typically required to activate antibody-producing B cells.

An antibody is made up of two heavy chains and two light chains. The unique variable region allows an antibody to recognize its matching antigen.

4.6 THE HUMORAL IMMUNE RESPONSE

A B cell identifies pathogens when antibodies on its surface bind to a specific foreign antigen. This antigen/antibody complex is taken up by the B cell and processed by proteolysis into peptides. The B cell then displays these antigenic peptides on its surface MHC class II molecules. This combination of MHC and antigen attracts a matching helper T cell, which releases lymphokines and activates the B cell. As the activated B cell then begins to divide, its offspring (plasma cells) secrete millions of copies of the antibody that recognizes this antigen. These antibodies circulate in blood plasma and lymph, bind to pathogens expressing the antigen and mark them for destruction by complement activation or for uptake and destruction by phagocytes. Antibodies can also neutralize challenges directly, by binding to bacterial toxins or by interfering with the receptors that viruses and bacteria use to infect cells.

4.7 IMMUNOLOGICAL MEMORY

When B cells and T cells are activated and begin to replicate, some of their offspring become long-lived memory cells. Throughout the lifetime of an animal, these memory cells remember each specific pathogen encountered and can mount a strong response if the pathogen is detected again. This is "adaptive" because it occurs during the lifetime of an individual as an adaptation to infection with that pathogen and prepares the immune system for future challenges. Immunological memory can be in the form of either passive short-term memory or active long-term memory.

The time-course of an immune response begins with the initial pathogen encounter, (or initial vaccination) and leads to the formation and maintenance of active immunological memory.

4.8 PHYSIOLOGICAL REGULATION

The immune system is involved in many aspects of physiological regulation in the body. The immune system interacts intimately with other systems, such as the endocrine and the nervous systems. The immune system also plays a crucial role in embryogenesis (development of the embryo), as well as in tissue repair and regeneration.

Check Your Progress-2

1. Distinguish between adaptive and innate immunity.
2. Write a short note on
   (a) humoral immune response
   (b) immunological memory
   (c) Cell mediated immunity
3. List important surface barriers which protect organisms from antigens/ foreign agents.

4.9 LET US SUM UP

The lymphatic system returns excess interstitial fluid to the blood, absorbs fats and fat-soluble vitamins, and provides defense against disease.

Lymph is the fluid in the lymphatic vessels. It is picked up from the interstitial fluid and returned to the blood plasma.

Lymphatic vessels carry fluid away from the tissues.

The right lymphatic duct drains lymph from the upper right quadrant of the body and the thoracic duct drains all the rest.

Pressure gradients that move fluid through the lymphatic vessels come from the skeletal muscle action, respiratory movements, and contraction of smooth muscle in vessel walls.

Lymph enters a lymph node through afferent vessels, filters through the sinuses, and leaves through efferent vessels.

Tonsils are clusters of lymphatic tissue associated with openings into the pharynx and provide protection against pathogens that may enter through the nose and mouth.

The spleen is a lymph organ that filters blood and also acts as a reservoir for blood.

The thymus is large in the infant and atrophies after puberty.

The immune system is a host defense system comprising many biological structures and processes within an organism that protects against disease. The innate immune system is the dominant system of host defense in most organisms.

In humans, the blood–brain barrier, blood–cerebrospinal fluid barrier, and similar fluid–brain barriers separate the peripheral immune system from the neuroimmune system, which protects the brain.

Disorders of the immune system can result in autoimmune diseases, inflammatory diseases and cancer. Immunodeficiency occurs when the immune system is less active than normal, resulting in recurring and life-threatening infections. In humans, immunodeficiency can either be the result of a genetic disease such as severe combined immunodeficiency, acquired conditions such as HIV/AIDS, or the use of immunosuppressive medication.

Several barriers protect organisms from infection, including mechanical, chemical, and biological barriers. These include skin, flushing action of tears, mucus, enzymes.

Inflammation is the first immune response.

The cells of the adaptive immune system are special types of leukocytes, called lymphocytes. B cells and T cells are the major types of lymphocytes and are derived from hematopoietic stem cells in the bone marrow. B cells are involved in the humoral immune response, whereas T cells are involved in cell-mediated immune response.

4.10 ANSWERS TO CHECK YOUR PROGRESS

Check Your Progress-1

1. (i) A (ii) C (iii) A (iv) A (v) C (vi) A (vii) B (viii) C

a) The lymphatic system has three major functions.

i) It returns excess interstitial fluid to the blood.

ii) The second function performed by lymphatic system is the absorption of fats and fat-soluble vitamins from the digestive system and the subsequent transport of these substances to the venous circulation.

iii) The third and most important function of the lymphatic system is providing defense against invading microorganisms and disease.

b) Lymphatic organs are characterized by presence of clusters of lymphocytes and other cells, such as macrophages, enmeshed in a framework of short, branching connective tissue fibers. The lymphocytes originate in the red bone marrow with other types of blood cells and are carried in the blood from the bone marrow to the lymphatic organs. When the body is exposed to microorganisms and other foreign substances, the lymphocytes proliferate within the lymphatic organs and are delivered through the blood to the site of the invasion. This is part of the immune response that attempts to destroy the invading agent. The other important lymphatic organs are lymph nodes, tonsils, spleen and thymus.

Check Your Progress-2

1.

Innate immune system	Adaptive immune system
1. Response is non-specific	Pathogen and antigen specific response
2. Exposure leads to immediate maximal response	Lag time between exposure and maximal response
3. Cell-mediated and humoral components	Cell-mediated and humoral components
4. No immunological memory	Exposure leads to immunological memory
5. Found in nearly all forms of life	Found only in jawed vertebrates including humans

2. (i) The humoral immune response

B cell identifies pathogens when antibodies on its surface bind to a specific foreign antigen. This antigen/antibody complex is taken up by the B cell and processed by proteolysis into peptides. The B cell then displays these antigenic peptides on its surface MHC class II

molecules. This combination of MHC and antigen attracts a matching helper T cell, which releases lymphokines and activates the B cell. As the activated B cell then begins to divide, its offspring (plasma cells) secrete millions of copies of the antibody that recognizes this antigen. These antibodies circulate in blood plasma and lymph, bind to pathogens expressing the antigen and mark them for destruction by complement activation or for uptake and destruction by phagocytes. Antibodies can also neutralize challenges directly, by binding to bacterial toxins or by interfering with the receptors that viruses and bacteria use to infect cells.

(ii) Cell mediated immunity

There are two major subtypes of T cells: the killer T cell and the helper T cell. In addition there are regulatory T cells which have a role in modulating immune response.

Killer T cells

Killer T cells are a sub-group of T cells that kill cells that are infected with viruses (and other pathogens), or are otherwise damaged or dysfunctional. As with B cells, each type of T cell recognizes a different antigen. Killer T cells are activated when their T-cell receptor (TCR) binds to this specific antigen in a complex with the MHC Class I receptor of another cell. Recognition of this MHC:antigen complex is aided by a co-receptor on the T cell, called CD8. The T cell then travels throughout the body in search of cells where the MHC I receptors bear this antigen. When an activated T cell contacts such cells, it releases cytotoxins, such as perforin, which form pores in the target cell's plasma membrane, allowing ions, water and toxins to enter. The entry of another toxin called granulysin (a protease) induces the target cell to undergo apoptosis. T cell killing of host cells is particularly important in preventing the replication of viruses. T cell activation is tightly controlled and generally requires a very strong MHC/antigen activation signal, or additional activation signals provided by "helper" T cells.

Helper T cells

Function of T helper cells: Antigen-presenting cells (APCs) present antigen on their Class II MHC molecules (MHC2). Helper T cells recognize these, with the help of their expression of CD4 co-receptor (CD4+). The activation of a resting helper T cell causes it to release cytokines and other stimulatory signals that stimulate the activity of macrophages, killer T cells and B cells, the latter producing antibodies. The stimulation of B cells and macrophages succeeds a proliferation of T helper cells. Helper T cells regulate both the innate and adaptive immune responses and help determine which immune responses the body makes to a particular pathogen. These cells have no cytotoxic activity and do not kill infected cells or clear pathogens directly. They instead control the immune response by directing other cells to perform these tasks. Helper T cells express T cell receptors (TCR) that recognize antigen bound to Class II MHC molecules.

An antibody is made up of two heavy chains and two light chains. The unique variable region allows an antibody to recognize its matching antigen

(iii) Immunological memory

When B cells and T cells are activated and begin to replicate, some of their offspring become long-lived memory cells. Throughout the lifetime of an animal, these memory cells remember each specific pathogen encountered and can mount a strong response if the pathogen is detected again. This is "adaptive" because it occurs during the lifetime of an individual as an adaptation to infection with that pathogen and prepares the immune system for future challenges. Immunological memory can be in the form of either passive short-term memory or active long-term memory.

3. The important surface barriers are :

Several barriers protect organisms from infection, including mechanical, chemical, and biological barriers. Skin is an example of a mechanical barrier that forms the first line of defense against infection. However, as human beings cannot be completely sealed from their environments, other systems are brought into play to protect body openings such as the lungs, intestines, and the genitourinary tract. In the lungs, coughing and sneezing mechanically eject pathogens and other irritants from the respiratory tract. The flushing action of tears and urine also mechanically expels pathogens, while mucus secreted by the respiratory and gastrointestinal tract serves to trap and entangle microorganisms.

Chemical barriers also protect against infection. The skin and respiratory tract secrete antimicrobial peptides such as the ²-defensins. Enzymes such as lysozyme and phospholipase A2 in saliva, tears, and breast milk are also antibacterials. Vaginal secretions serve as a chemical barrier following menarche, when they become slightly acidic, while semen contains defensins and zinc to kill pathogens. In the stomach, gastric acid serves as a powerful chemical defense against ingested pathogens.

Within the genitourinary and gastrointestinal tracts, commensal flora serve as biological barriers by competing with pathogenic bacteria for food and space and, in some cases, by changing the conditions in their environment, such as pH or available iron. As a result of the symbiotic relationship between commensals and the immune system, the probability that pathogens will reach sufficient numbers to cause illness is reduced. However, since most of the antibiotics non-specifically target bacteria without causing any damage to fungi, oral antibiotics can result in an "overgrowth" of fungi and cause conditions such as a vaginal candidiasis (an infection caused by a yeast like fungus). There is good evidence that re-introduction of probiotic flora, such as pure cultures of the *Lactobacilli* normally found in unpasteurized yogurt, helps restore a healthy balance of microbial populations in intestinal infections in children