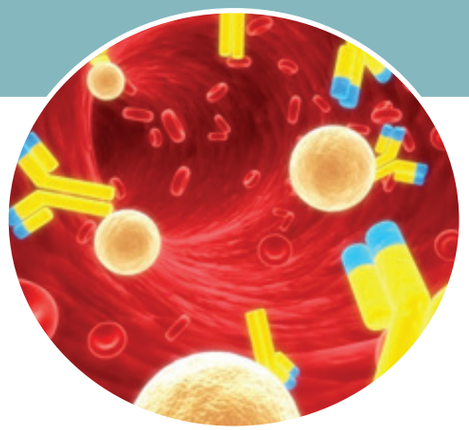
UNIT - III

8 CHAPTER

IMMUNOLOGY



Natural forces within us are the true healers of disease

- Hippocrates

Chapter outline

Learning objectives

- *Understands the basic concepts of immunology.*
- *Differentiates between innate immunity and acquired immunity, primary immune response and secondary immune response, active and passive immunity.*
- *Realizes the importance of immunization.*
- *Learns to comprehend the concept of hypersensitivity.*

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In the previous chapter, we have studied in detail the various infections which cause diseases in human beings. In this chapter, we shall discuss how our body protects us from these infections by the effective mechanism of the immune system.

8.1 Basic concepts of immunology

Immunology is the study of immune system. This system protects an indvidual from various infective agents. It refers to all the mechanisms used by the body for protection from environmental agents that are foreign to the body.

When the immune system does not function efficiently in an individual, it leads to infection causing disease. The overall ability of body to fight against the disease causing pathogen is called **immunity**. It is also called disease resistance and the lack of immunity is known as susceptibility. Immunity is highly specific.

Normally many of the responses of the immune system initiate the destruction and elimination of invading organisms and any toxic molecules produced by them. These immune reactions are destructive in nature and are made in response only to molecules

that are foreign to the host and not to those of host itself. This ability to distinguish foreign molecules from self is another fundamental feature of the immune system. However, occasionally, it fails to make its distinction and reacts destructively against the host's own molecules; such autoimmune diseases can be fatal to the organism.

Almost all the macromolecules e.g. proteins, polysaccharides, nucleic acids, etc., as long as they are foreign to recipient organism can induce immune response. Any substance capable of eliciting immune response is called an **ANTIGEN** (**ANTI**body **GEN**erator). There are two broad classes of immunity responses namely, innate immunity and acquired immunity **(Fig. 8.1)**.

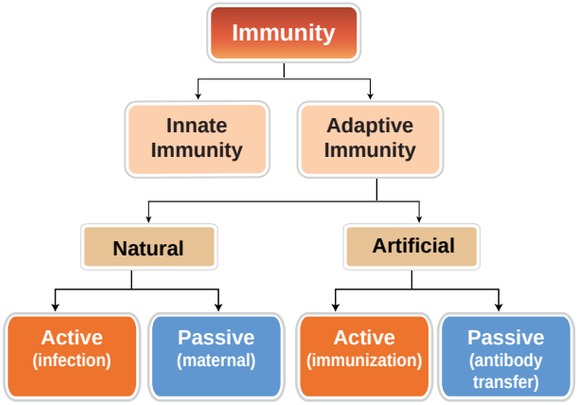


Fig. 8.1 Immune system

8.2 Innate immunity

Innate immunity is the natural phenomenon of resistance to infection which an individual possesses right from the birth.

Table 8.1 Innate immunity- types and mechanisms

Type of innate immunity	Mechanism
1. Anatomical barriers	
Skin	Prevents the entry of microbes. Its acidic environment (pH 3-5) retards the growth of microbes.
Mucus membrane	Mucus entraps foreign microorganisms and competes with microbes for attachment.
2. Physiological barriers	
Temperature	Normal body temperature inhibits the growth of pathogens. Fever also inhibits the growth of pathogens.
Low pH	Acidity of gastric secretions (HCl) kills most ingested microbes.
Chemical mediators	Lysozyme acts as antibacterial agent and cleaves the bacterial cell wall. Interferons induce antiviral state in the uninfected cells. Complementary substances produced from leucocytes lyse the pathogenic microbes or facilitate phagocytosis.
3. Phagocytic barriers	Specialized cells (Monocytes, neutrophils, tissue macrophages) phagocytose, and digest whole microorganisms.
4. Inflammatory barriers	Tissue damage and infection induce leakage of vascular fluid, containing chemotactic signals like serotonin, histamine and prostaglandins. They influx the phagocytic cells into the affected area. This phenomenon is called diapedesis.

The innate defense mechanisms are non-specific in the sense that they are effective against a wide range of potentially infectious agents. It is otherwise known as **non-specific immunity** or **natural immunity.**

A number of innate defense mechanisms are operative non-specifically against a large number of microorganisms as shown in the **Table 8.1** and **Fig. 8.2.**

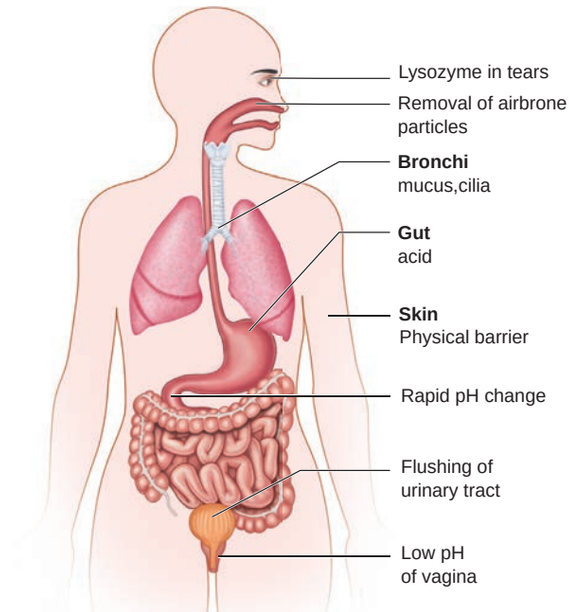


Fig. 8.2 Various anatomical and physiological barriers to microbial attack

8.3 Acquired immunity

The immunity that an individual acquires after birth is known as **acquired immunity**. It is the body's resistance to a specific pathogen.

The unique features of acquired immunity are antigenic specificity, diversity, recognition of self and non-self and immunological memory.

Components of acquired immunity

Acquired immunity has two components – **cell mediated immunity (CMI) and antibody mediated immunity or humoral immunity.**

1. Cell mediated immunity

When pathogens are destroyed by cells without producing antibodies, then it is known as cell mediated immune response or cell mediated immunity. This is brought about by T cells, macrophages and natural killer cells.

2. Antibody mediated immunity or humoral immunity

When pathogens are destroyed by the production of antibodies, then it is known as antibody mediated or humoral immunity. This is brought about by B cells with the help of antigen presenting cells and T helper cells. Antibody production is the characteristic feature of **vertebrates** only.

Types of acquired immunity

Acquired immunity may be **active immunity** or **passive immunity (Table 8.2)**.

The immunological resistance developed by the organisms through the production of antibodies in their body is called active immunity. Active immunity is acquired through the use of a person's immune responses, which lead to the development of memory cells. Active immunity results from an infection or an immunization.

Passive immunity does not require the body to produce antibodies to antigens. The antibodies are introduced from outside into the organism. Thus, passive immunity is acquired without the activation of a person's immune response, and therefore there is no memory.

The process of production of blood cells in the bone marrow is called **haematopoiesis**.

8.4 Immune responses

The immune responses may be **primary** or **secondary (Table 8.3)**.

Primary immune response

The primary immune response occurs when a pathogen comes in contact with the

Table 8.2 Differences between active and passive immunity

Sl.No	Active Immunity	Passive Immunity
1	Active immunity is produced actively by host's immune system.	Passive immunity is received passively and there is no active host participation.
2	It is produced due to contact with pathogen or by its antigen.	It is produced due to antibodies obtained from outside.
3	It is durable and effective in protection.	It is transient and less effective.
4	Immunological memory is present.	No memory.
5	Booster effect on subsequent dose is possible.	Subsequent dose is less effective.
6	Immunity is effective only after a short period.	Immunity develops immediately.

immune system for **the first time**. During this, the immune system has to learn to recognize the antigen, produce antibody against it and eventually produce memory lymphocytes. The primary immune response is slow and short-lived.

Secondary immune response

The secondary immune response occurs when a person is exposed to the same antigen again. During this time, immunological memory has been established and the immune system can start producing antibodies **immediately**. Within hours after recognition of the antigen, a new army of plasma cells are generated. Within 2 to 3 days, the antibody concentration in the blood **rises steeply** to reach much higher level than primary response. This is also called as "**booster response**".

8.5 Lymphoid organs

Immune system of an organism consists of several structurally and functionally different organs and tissues that are widely dispersed in the body. The organs involved in the origin, maturation and proliferation of lymphocytes are called **lymphoid organs (Fig. 8.3).**

Table 8.3 Differences between primary and secondary immune responses

Sl.No	Primary Immune Response	Secondary Immune Response
1	It occurs as a result of primary contact with an antigen.	It occurs as a result of second and subsequent contacts with the same antigen.
2	Antibody level reaches peak in 7 to 10 days.	Antibody level reaches peak in 3 to 5 days.
3	Prolonged period is required to establish immunity.	It establishes immunity in a short time.
4	There is rapid decline in antibody level.	Antibody level remains high for longer period.
5	It appears mainly in the lymph nodes and spleen.	It appears mainly in the bone marrow, followed by the spleen and lymph nodes.

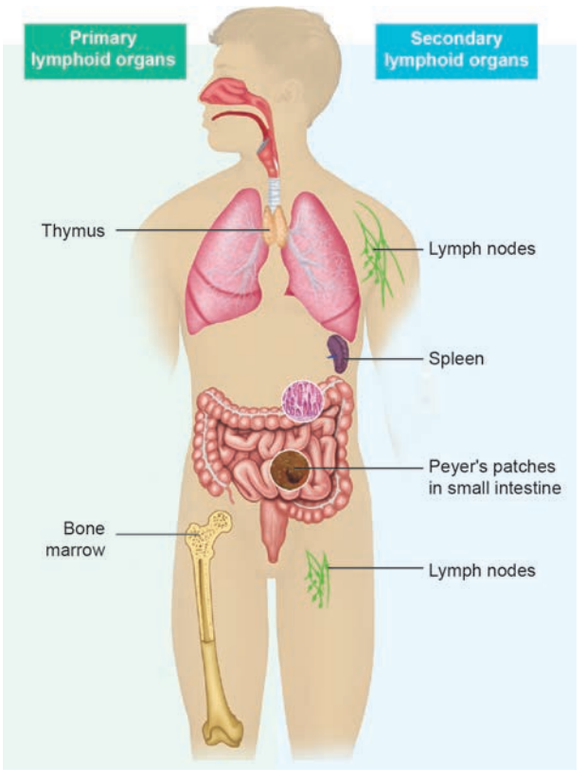
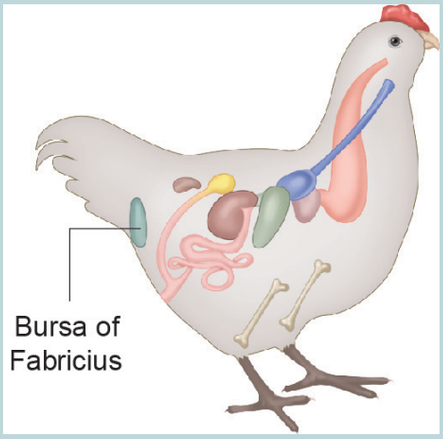


Fig. 8.3 Lymphoid organs in human body

Based on their functions, they are classified into **primary or central lymphoid organs** and **secondary or peripheral lymphoid organs**. The primary lymphoid organs provide appropriate environment for lymphocytic maturation. The secondary lymphoid organs trap antigens and make it available for mature lymphocytes, which can effectively fight against these antigens.



Bursa of Fabricius is a primary lymphoid organ of birds. It is attached to the dorsal side of the cloaca. B lymphocytes mature in the bursa and bring about humoral immunity.

Primary lymphoid organs

Bursa of Fabricius of birds, bone marrow and thymus gland of mammals constitute the primary lymphoid organs involved in the production and early selection of lymphocytes. These lymphocytes become dedicated to a particular **antigenic specificity**. Only when the lymphocytes mature in the primary lymphoidal organs, they become **immunocompetent cells**. In mammals, B cell maturation occurs in the bone marrow and T cells maturation occurs in the thymus.

Thymus

The thymus is a flat and bilobed organ located behind the sternun, above the heart. Each lobe of the thymus contains numerous lobules, separated from each other by connective tissue called septa. Each lobule is differentiated into two compartments, the outer compartment or **outer cortex,** is densely packed with immature T cells called thymocytes, whereas the inner compartment or medulla is sparsely populated with mature thymocytes. One of its main secretions is the hormone **thymosin**. It stimulates the T cell to become mature and **immunocompetent**. By the early teens, the thymus begins to atrophy and is replaced by adipose tissue **(Fig. 8.4).** Thus thymus is **most active** during the **neonatal and pre-adolescent periods**.

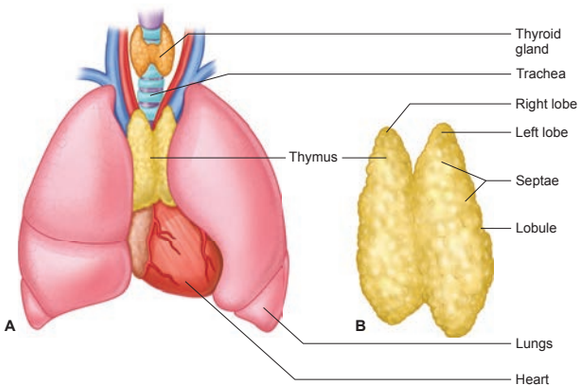


Fig. 8.4 Primary lymphoid organ - Thymus A) Location B) Structure

Bone marrow

Bone marrow is a lymphoid tissue found within the spongy portion of the bone. Bone marrow contains stem cells known as haematopoietic cells. These cells have the potential to multiply through cell division and either remain as stem cells or differentiate and mature into different kinds of blood cells.

Secondary or peripheral lymphoid organs

In secondary or peripheral lymphoid organs, antigen is localized so that it can be effectively exposed to mature lymphocytes. The best examples are lymph nodes, appendix, Peyer's patches of gastrointestinal tract, tonsils, adenoids, spleen, **MALT** (Mucosal-Associated Lymphoid Tissue), **GALT** (Gut-Associated Lymphoid Tissue), **BALT** (Bronchial/Tracheal-Associated Lymphoid Tissue).

Peyer's patches are oval-shaped areas of thickened tissue that are embedded in the mucus-secreting lining of the small intestine of humans and other vertebrate animals. Peyer's patches contain a variety of immune cells, including macrophages, dendritic cells, T cells, and B cells.

The **tonsils** (palatine tonsils) are a pair of soft tissue masses located at the back of the throat (pharynx). The tonsils are part of the lymphatic system, which help to fight infections. They stop invading germs including bacteria and viruses.

Spleen is a secondary lymphoid organ located in the upper part of the abdominal cavity close to the diaphragm. Spleen contains B and T cells. It brings humoral and cell mediated immunity.

The **adenoids** are glands located in the roof of the mouth, behind the soft palate where the nose connects to the throat. The adenoids produce antibodies that help to fight infections. Typically, the adenoids shrink during adolescence and may disappear by adulthood.

Lymph node

Lymph node is a small bean-shaped structure and is part of the body's immune system. It is the **first one to encounter** the antigen that enters the tissue spaces. Lymph nodes filter and trap substances that travel through the lymphatic fluid. They are packed tightly with white blood cells, namely lymphocytes and macrophages. There are hundreds of lymph nodes found throughout the body. They are connected to one another by lymph vessels. **Lymph** is a clear, transparent, colourless, mobile and extracellular fluid connective tissue. As the lymph percolates through the lymph node, the particulate antigen brought in by the lymph will be **trapped** by the phagocytic cells, follicular and interdigitating dendritic cells.

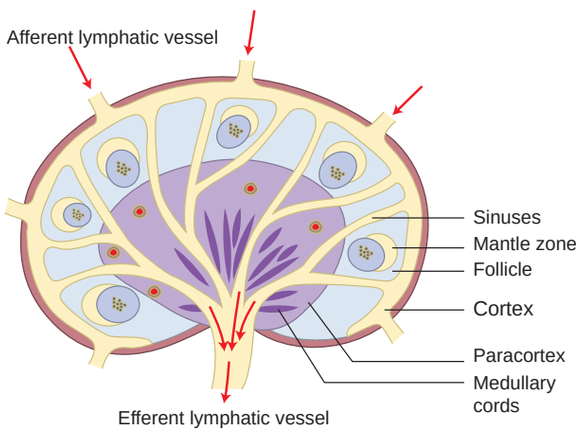


Fig. 8.5 Secondary lymphoid organ – Structure of lymph node

Lymph node has three zones **(Fig. 8.5).** They are the **cortex, paracortex and medulla**. The outer most layer of the lymph node is called cortex, which consists of B-lymphocytes, macrophages, and follicular dendritic cells. The **paracortex** zone is beneath the cortex, which is richly populated by T lymphocytes and interdigitating dendritic cells. The inner most zone is called the medulla which is sparsely populated by lymphocytes, but many of them are plasma cells, which actively secrete antibody molecules. As the lymph enters, it slowly percolates through the cortex, paracortex and medulla, giving sufficient chance for the phagocytic cells and dendritic cells to trap the antigen brought by the lymph. The lymph leaving a node carries enriched antibodies secreted by the medullary plasma cells against the antigens that enter the lymph node. Sometimes visible swelling of lymph nodes occurs due to active immune response and increased concentration of lymphocytes. Thus swollen lymph nodes may signal an infection. There are several groups of lymph nodes. The most frequently enlarged lymph nodes are found in the neck, under the chin, in the armpits and in the groin.

The mucosa-associated lymphoid tissue **(MALT)** is a diffuse system of small concentrations of lymphoid tissue in the alimentary, respiratory and urino-genital tracts. **MALT** is populated by lymphocytes such as T and B cells, as well as plasma cells and macrophages, each of which is well situated to encounter antigens passing through the mucosal epithelium. It also possesses IgA antibodies.

Gut-associated lymphoid tissue **(GALT)** is a component of the mucosa-associated lymphoid tissue **(MALT)** which works in the immune system to protect the body from invasion in the gut.

Bronchus Associated Lymphoid Tissues **(BALT)** also a component of MALT is made of lymphoid tissue (tonsils, lymph nodes, lymph follicles) is found in the respiratory mucosae from the nasal cavities to the lungs.

Cells of the immune system

The immune system is composed of many interdependent cells that protect the body from microbial infections and the growth of tumour cells. The cellular composition of adult human blood is given in **Table 8.4.**

Table 8.4 The cellular composition of adult human blood

Cell type	Number of cells per µl	Approximate percentage
Red blood cells	4200,000 - 6500,000	-
White blood cells		
Agranulocytes		
Lymphocytes	1500 - 4000	20-30
Monocytes	200 - 950	2-7
Granulocytes		
Neutrophils	2000-7000	50-70
Basophils	50-100	<1
Eosinophils	40-500	2-5
Platelets	150,000-500,000	-

All these cells are derived from pluripotent haematopoetic stem cells. Each stem cell has the capacity to produce RBC, WBC and platelets.

The only cells capable of specifically recognising and producing an immune response are the lymphocytes. The other types of white blood cells play an important role in non specific immune response, antigen presentation and cytokine production.

Lymphocytes

About 20-30% of the white blood cells are lymphocytes. They have a large nucleus filling most of the cell, surrounded by a little cytoplasm. The two main types of lymphocytes are B and T lymphocytes. Both these are produced in the bone marrow. B lymphocytes (B cells) stay in the bone marrow until they are mature. Then they circulate around the body. Some remain in the blood, while others accumulate in the lymph nodes and spleen. T lymphocytes leave the bone marrow and mature in the thymus gland. Once mature, T cells also accumulate in the same areas of the body as B cells. Lymphocytes have receptor proteins on their surface. When receptors on a B cell bind with an antigen, the B cell becomes activated and divides rapidly to produce plasma cells. The plasma cells produce antibodies. Some B cells do not produce antibodies but become memory cells. These cells are responsible for secondary immune response. T lymphocytes do not produce antibodies. They recognize antigen-presenting cells and destroy them. The two important types of T cells are Helper T cells and Killer T cells. Helper T cells release a chemical called cytokine which activates B cells. Killer cells move around the body and destroy cells which are damaged or infected **(Fig. 8.6)**.

Apart from these cells neutrophils and monocytes destroy foreign cells by phagocytosis. Monocytes when they mature into large cells, they are called macrophages which perform phagocytosis on any foreign organism.

Dendritic cells are called so because its covered with long, thin membrane extensions that resemble dendrites of nerve cells. These cells present the antigen to T-helper cells. Four types of dendritic cells are known. They are langerhans, interstitial cells, myeloid and lymphoid cells

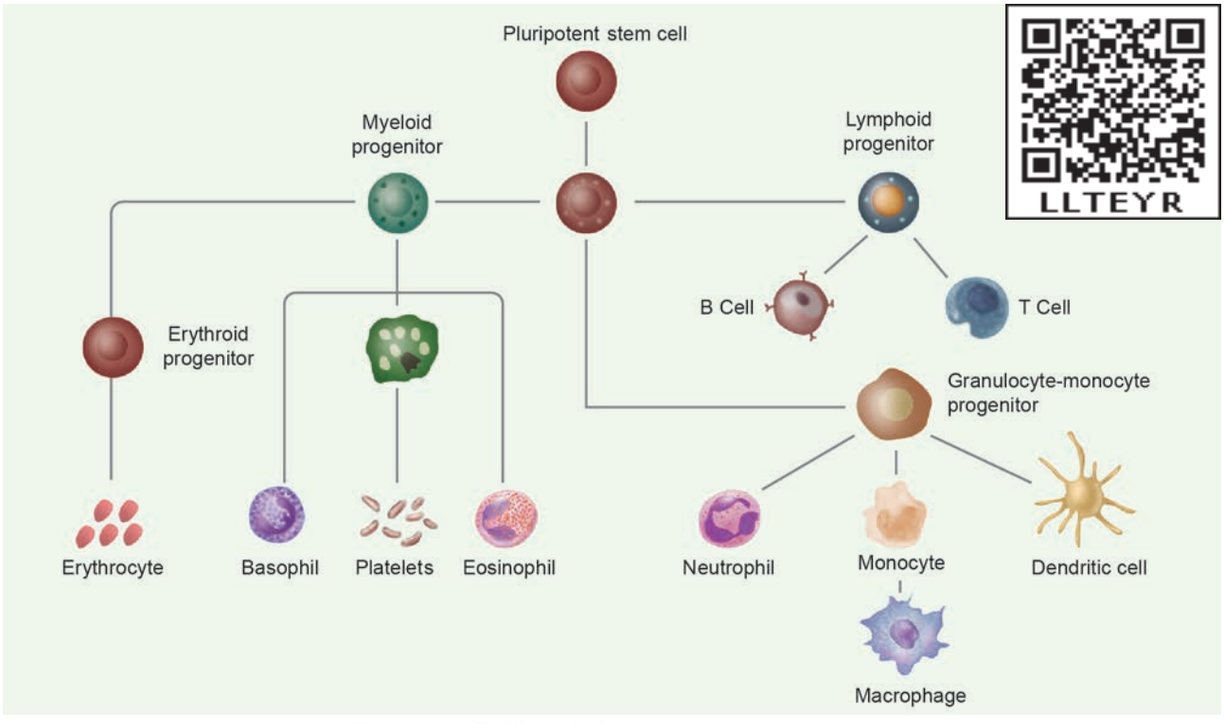


Fig. 8.6 Cells of the immune system

8.6 Antigens

The term **antigen** (Ag) is used in two senses, the first to describe a molecule which generates an immune response and the second, a molecule which reacts with antibodies. In general antigens are large, complex molecular substances that can induce a detectable immune response. Thus an antigen is a substance that is specific to an antibody or a T-cell receptor and is often used as a synonym for immunogen.

The histocompatibility antigens are cell surface antigens that induce an immune response leading to rejection of allografts.

An **immunogen** is a substance capable of initiating an immune response. **Haptens** are substance that are non-immunogenic but can react with the products of a specific immune response. Substances that can **enhance the immune response** to an antigen are called **adjuvants**. **Epitope** is an antigenic determinant and is the active part of an antigen. A **paratope** is the antigen – binding site and is a part of an antibody which recognizes and binds to an antigen.

Antigenicity is the property of a substance (antigen) that allows it to react with the products of the specific immune response.

Types of antigens

On the basis of origin, antigens are classified into **exogenous antigens** and **endogenous antigens**.

The antigens which enter the host from the outside in the form of microorganisms, pollens, drugs, or pollutants are called **exogenous antigens**. The antigens which are formed within the individual are **endogenous antigens**. The best examples are blood group antigens.

8.7 Antibodies

Antibodies are immunoglobulin (Ig) protein molecules synthesized on exposure to antigen that can combine specifically with the antigen. Whenever pathogens enter our body, the B-lymphocytes produce an army of proteins called antibodies to fight with them. Thus, they are secreted in response to an antigen (Ag) by the effect of B cells called plasma cells. The antibodies are classified into five major categories, based on their physiological and biochemical properties. They are **IgG** (gamma), **IgM** (mu), **IgA** (alpha), **IgD** (delta) and **IgE** (epsilon).

In the 1950s, experiments by **Porter and Edelman** revealed the basic structure of the immunoglobulin. An antibody molecule is **Y** shaped structure that comprises of four polypeptide chains, two identical light chains **(L)** of molecular weight 25,000 Da (approximately 214 amino acids) and two identical heavy chains **(H)** of molecular weight 50,000 Da (approximately 450 amino acids). The polypeptide chains are linked together by di-sulphide (S-S) bonds. One light chain is attached to each heavy chain and two heavy chains are attached to each other to form a Y shaped **(Fig. 8.7)** structure. Hence, an antibody is represented by H_2 L_2. The heavy chains have a flexible hinge region at their approximate middles.

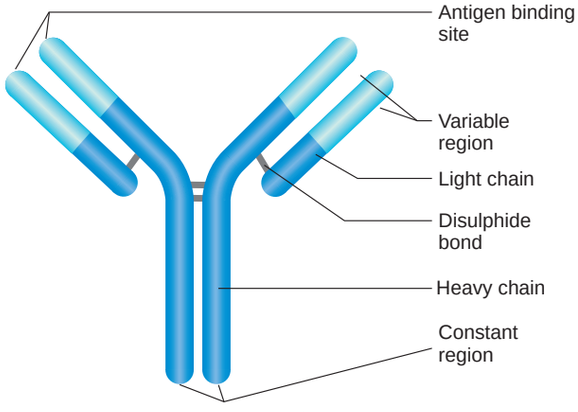


Fig. 8.7 Structure of immunoglobulin

Each chain (**L** and **H**) has two terminals. They are C - terminal (Carboxyl) and amino or N-terminal. Each chain (**L** and **H**) has two regions. They have variable (**V**) region at one end and a much larger constant (**C**) region at the other end. Antibodies responding to different antigens have very different (V) regions but their (C) regions are the same in all antibodies. In each arm of the monomer antibody, the (V) regions of the heavy and light chains combines to form an antigen – binding site shaped to 'fit' a specific antigenic determinant. Consequently each antibody monomer has two such antigen – binding regions. The (C) regions that forms the stem of the antibody monomer determine the antibody class and serve common functions in all antibodies.

The functions of immunoglobulin are agglutination, precipitation, opsonisation, neutralization etc.,

8.8 Antigen -antibody interaction

The reaction between an antigen and antibody is the basis for humoral immunity or antibody mediated immunity. The reaction between antigen and antibody occurs in three stages. During the first stage, the reaction involves the formation of antigen - antibody complex. The next stage leads to visible events like precipitation, agglutination, etc., The final stage includes destruction of antigen or its neutralization **(Fig. 8.8).**

Binding force of antigen - antibody reaction

The binding force between antigen and antibody is due to **three factors**. They are closeness between antigen and antibody, non-covalent bonds or intermolecular forces and affinity of antibody.

When antigen and antibody are closely fitted, the strength of binding is great. When they are apart binding strength is low. The bonds that hold the antigen to the antibody combining site are all **non-covalent** in nature. These include **hydrogen bonds, electrostatic bonds, Van der Waals forces and hydrophobic bonds**. Antibody affinity is the strength of the reaction between a single antigenic determinant and a single combining site on the antibody.

The chief **application** of antigen - antibody reactions are to determine blood groups for transfusion, to study serological ascertainment of exposure to infectious agents, to develop immunoassays for the quantification of various substances, to detect the presence or absence of protein in serum and to determine the characteristics of certain immunodeficiency diseases.

Different types of antigen and antibody reactions

The reaction between **soluble antigen** and antibody leads to visible precipitate formation, which is called **precipitin reaction**. Antibodies that bring about precipitate formation on reacting with antigens are called as **precipitins**.

Whenever a **particulate antigen** interacts with its antibody, it would result in **clumping or agglutination** of the particulate antigen, which is called **agglutination reaction**. The antibody involved in bringing about agglutination reaction is called **agglutinin**.

Opsonisation or enhanced attachment is the process by which a pathogen is marked of ingestion and destruction by a phagocyte. Opsonisation involves the binding of an **opsonin** i.e., antibody, to a receptor on the pathogen's cell membrane. After opsonin binds to the membrane, phagocytes are attracted to the pathogen. So, opsonisation is a process in which **pathogens are coated with**

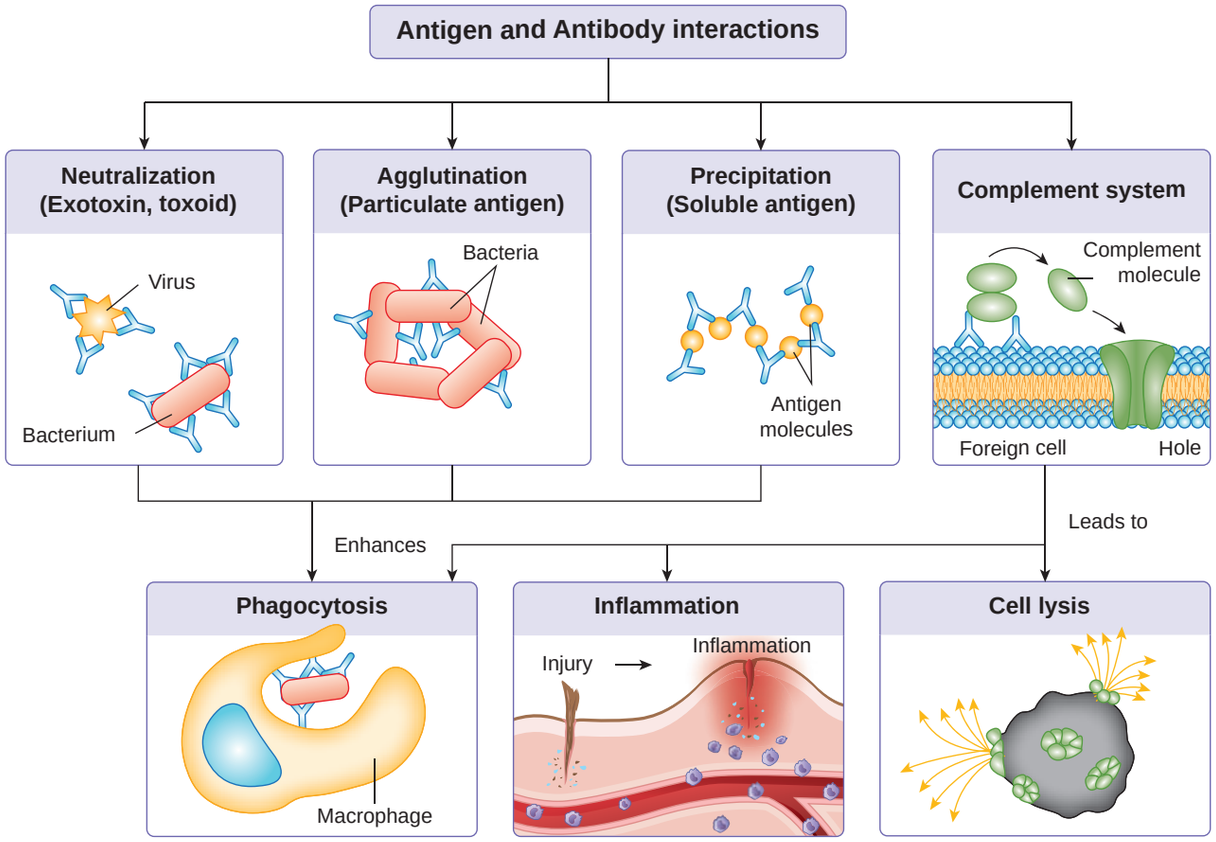


Fig. 8.8 Antigen and antibody reaction

a substance called an opsonin, marking the pathogen out for destruction by the immune system. This results in a much more **efficient phagocytosis**.

The **neutralization** reactions are the reactions of antigen-antibody that involve the **elimination of harmful effects** of bacterial exotoxins or a virus by specific antibodies. These neutralizing substances i.e., antibodies are known as **antitoxins**. This specific antibody is produced by a host cell in response to a bacterial exotoxin or corresponding toxoid (inactivated toxin).

8. 9 Vaccines

A vaccine **is a biological preparation that provides active acquired immunity** to a particular disease and resembles a

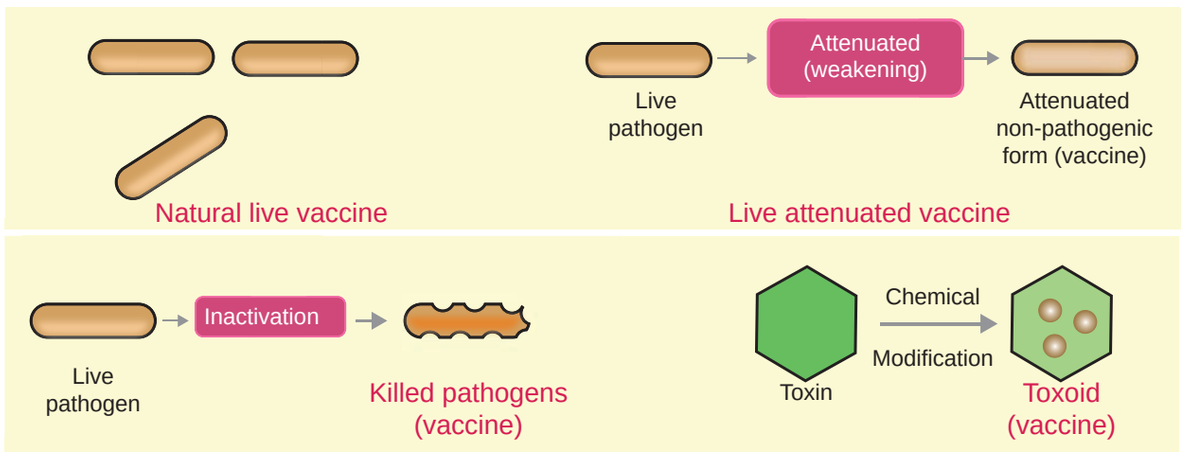


Fig. 8.9 Types of vaccines

disease-causing microorganism and is often made from weakened or attenuated or killed forms of the microbes, their toxins, or one of its surface proteins. Vaccines **"teach"** our body how to defend itself when viruses or bacteria, invade it. Vaccines deliver only very little amounts of inactivated or weakened viruses or bacteria, or parts of them. This allows the immune system to recognize the organism **without actually experiencing the disease**. Some vaccines need to be given more than once (i.e., a 'booster' vaccination) to make sure the immune system can overcome a real infection in the future.

Vaccine initiates the immunization process. The vaccines are classified as first, second and third generation vaccines.

First generation vaccine is further subdivided into live attenuated vaccine, killed vaccine and toxoids **(Fig. 8.9). Live attenuated vaccines** use the **weakened (attenuated), aged, less virulent** form of the virus. E.g. Measles, mumps and rubella (MMR) vaccine and the Varicella (chickenpox) vaccine, **Killed (inactivated) vaccines** are killed or inactivated by heat and other methods. E.g. Salk's polio vaccine. **Toxoid vaccines** contain a **toxin or chemical** secreted by the bacteria or virus. They make us immune to the harmful effects of the infection, instead of to the infection itself. E.g. DPT vaccine (Diphtheria, Pertussis and Tetanus).

Second generation vaccine contains the pure surface antigen of the pathogen. E.g.Hepatitis-B vaccine. **Third generation vaccine** contains the purest and the highest potency vaccines which are synthetic in generation. The latest revolution in vaccine is **DNA vaccine** or **recombinant vaccine** (Refer Chapter- 10 for details).

Vaccino therapy is the method of use of vaccine for treatment of disease. Dr. Edward Jenner prepared first vaccine for small pox in 1796. Polio vaccine was developed by Dr. Jonas Salk (vaccine consists of inactivated microorganism) and Dr. Albert Sabin (live attenuated oral polio vaccine). Louis Pasteur (1885) discovered vaccine against rabies, anthrax and cholera. BCG vaccine was developed by Calmette and Guerin against tuberculosis in France in the year 1908.

8. 10 Vaccination and immunization

"**Vaccination** is the process of administrating a vaccine into the body or the act of introducing a vaccine into the body to produce immunity to a specific disease." **Immunization** is the process of the body building up immunity to a particular disease. Immunization describes the actual changes in the body after receiving a vaccine. Vaccines work by fighting the pathogen and then recording it in their **memory system** to ensure that the next time this pathogen enters the body, it is eliminated far quickly. Once, the body is able to fight against the disease, it is believed to have built the immunity for it, also known as the body being immunized against the disease.

8.11 Hypersensitivity

Some of the individuals are very sensitive to some particles present in the environment. The exaggerated response of the immune system to certain antigens present in the environment is called **allergy (allo-altered, erg-reaction)**. The substances to which such an immune response is produced are called **allergens**. An allergen is an antigen that causes an allergic

reaction. Allergic reactions begin within few seconds after the contact with the allergen and last about half an hour. The common examples of allergens are mites in dust, pollens and some proteins in insect venom. Hay fever and asthma are some common examples of allergy. **Symptoms** of allergic reactions include sneezing, watery eyes, running nose and difficulty in breathing. Allergy is a form of over active immune response mediated by **IgE** and **mast cells.** It can also be due to the release of chemicals like histamine and serotonin from the mast cells.

Anaphylaxis is the classical immediate hypersensitivity reaction. It is a sudden, systematic, severe and immediate hypersensitivity reaction occurring as a result of rapid generalized mast-cell degranulation.

8.12 Immunodeficiency diseases

Immunodeficiency results from the failure of one or more components of the immune system. Primary immune deficiencies are caused by genetic developmental defects. Secondary immune deficiencies arise due to various reasons like radiation, use of cytolytic and immunosuppressive drugs and infections. **AIDS** is an acronym for Acquired Immuno Deficiency Syndrome. It is the deficiency of immune system, acquired during the life time of an individual indicating that it is not a congenital disease. AIDS is caused by Human Immuno Deficiency Virus **(HIV)**. It selectively infects helper T cells. The infected helper T cells will not stimulate antibody production by B-cells resulting in loss of natural defence against viral infection. On the basis of genetic characteristics and differences in the viral antigens, HIV is classified into the types 1 and 2 **(HIV-1, HIV-2)**.

Structure of HIV

The human immunodeficiency virus belongs to the genus **Lentivirus**. When observed under the electron microscope, HIV is seen as a spherical virus, **100-120 nm** in diameter, containing a dense core surrounded by a lipoprotein envelope. The envelope has **glycoprotein (gp)** spikes termed gp 41 and gp 120. At the core, there are two large **single stranded RNA**. Attached to the RNA are molecules of reverse transcriptase. It also contains enzymes like protease and ribonuclease. The core is covered by a capsid made of proteins. This is followed by another layer of **matrix proteins** as shown in the **Fig 8.10.**

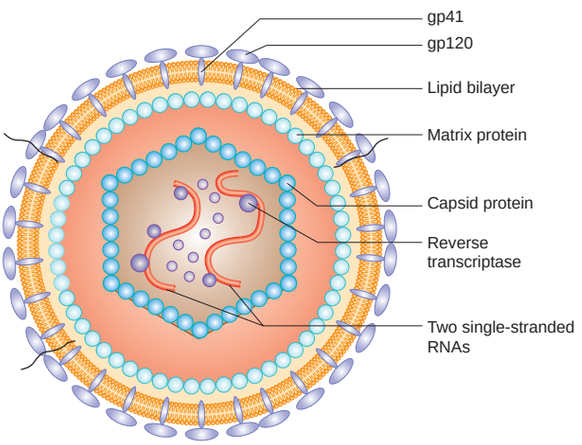


Fig. 8. 10 Structure of HIV

HIV Transmission

The HIV is often located within the cells especially in macrophages. HIV can survive for 1.5 days inside a cell but only about 6 hours outside a cell. Routes of HIV transmission include unsafe sexual contact, blood-contaminated needles, organ transplants, blood transfusion and vertical transmission from HIV infected mother to child. HIV is not transmitted by insects or by casual contact.

After getting into the body of the person, the virus enters into macrophages where **RNA genome** of the virus replicates to form **viral DNA** with the help of the enzyme **reverse transcriptase**. This viral DNA gets incorporated into the DNA of host cells and directs the infected cells to produce viral particles. The macrophages continue to produce virus and in this way acts like a HIV factory. Simultaneously, HIV enters into helper T-lymphocytes, replicates and produces progeny viruses. The progeny viruses released in the blood attack other helper T-lymphocytes. This is repeated, leading to a progressive decrease in the number of helper T lymphocytes in the body of the infected person. During this period, the person suffers from bouts of fever, diarrhoea and weight loss. Due to decrease in the number of helper T lymphocytes, the person starts suffering from infections and becomes immune deficient and unable to protect against any infection.

A simple blood test is available that can determine whether the person has been infected with HIV. The **ELISA** test (Enzyme Linked ImmunoSorbent Assay) detects the presence of HIV antibodies. It is a preliminary test. **Western blot** test is more reliable and a confirmatory test. It detects the viral core proteins. If both tests detect the presence of the antibodies, the person is considered to be HIV positive.

AIDS has no cure. **Prevention** of AIDS is the best option. Advocating safe sex and promoting regular check-up, safe blood for transfusion, use of disposable needles, use of condoms during sexual contact, prevention of drug abuse, AIDS awareness programme by **NACO** (National AIDS Control Organisation), **NGO**s (Non-Governmental Organisations) and **WHO** are to prevent the spreading of AIDS.

8.13 Autoimmune diseases

Autoimmunity is due to an abnormal immune response in which the immune system fails to properly distinguish between self and non-self and attacks its own body. Our body produces antibodies **(auto antibodies)** and **cytotoxic T cells** that destroy our own tissues. If a disease-state results, it is referred to as auto-immune disease. Thus, autoimmunity is a misdirected immune response. Autoimmunity is evidenced by the presence of **auto antibodies and T cells** that are reactive with host antigens. When the cells act as antigens in the same body, they are called autoantigens.

Autoimmune diseases in human can be divided into two broad categories, namely organ-specific and non-organ-specific (systemic) autoimmune diseases. In organ-specific disease, the autoimmune process is directed mostly against one organ. The autoantibodies may block the functions performed by the organs. Examples include Hashimoto's thyroiditis, Graves' disease (thyroid gland) and Addison's disease (adrenal glands).

In non-organ specific (systemic) disorders, autoimmune activity is widely spread throughout the body. Rheumatoid arthritis and multiple sclerosis are example for systemic disorder.

8.14 Tumour immunology

A **tumour** or **neoplasm** is a group of cells whose growth has gone unchecked. When a tumour continues to grow and invades healthy tissue, it is called cancer. They spread to other parts of the body from the tumour and give rise to secondary tumour. This is known as **metastasis**. Tumour may be benign or malignant depending on its characteristics. Benign or non-cancerous tissues are capable of indefinite growth and do not invade other body parts. In the malignant tumour, the cells grow indefinitely, detach and migrate into healthy surrounding tissues.

In normal cells, cell growth and differentiation is highly controlled and regulated. But in cancer cells, there is breakdown of this regulatory

mechanism. Normal cells show a property called **contact inhibition**, which inhibits uncontrolled growth. Cancer cells do not have this property. As a result, cancerous cells divide continuously giving rise to mass of tissues called tumours **(Table 8.5).**

When a cell undergoes malignant transformation, it acquires new surface antigen and may also lose some normal antigens. These antigens are present on the membranes of malignant cells and they induce an immune response. Both humoral and cellular responses can be observed in malignancy. Cancer cells can avoid immune detection as they are not foreign bodies but are abnormally functioning body cells. This makes them difficult to treat.

The concept of immunological surveillance postulates that the primary function of the immune system is to "**seek and destroy**" malignant cells that arise by somatic mutation. The efficiency of the surveillance mechanism reduces either as a result of ageing or due to congenital or acquired immunodeficiencies, leads to increased incidence of cancer. Thus, if immunological surveillance is effective, cancer should not occur. The development of tumour represents a lapse in surveillance.

Immunotherapy of cancer

Immunotherapy also called biological therapy uses substances made by the body or in a laboratory (monoclonal antibodies) to improve or to resist the immune system function. Different approaches have been attempted in the immunotherapy of cancer. Immunotherapy appears to be important in getting rid of the residual malignant cells after the gross tumour has been removed. The best results in the treatment of cancer is to follow an integrated approach to therapy, combining surgery, radiotherapy, chemotherapy and immunotherapy.

Scope of Immunology

The younger graduates in this field can find number of employment opportunities in Government as well as private hospitals. The scope of the immunology is immunotherapy, microbial immunology, clinical immunology, cellular immunology, allergy and immunology, translational immunology, transplantation immunology, neuro-inflammatory disorders, tumour immunology, vaccine immunology, inflammatory disorders, ocular immunology and inflammation.

Table 8.5. Differences between normal cell and cancer cell

Normal Cells	Cancer cells
Small, uniformly shaped nuclei Relatively large cytoplasmic volume	Large, variable shaped nuclei Relatively small cytoplasmic volume
Conformity in cell size and shape Cells arranged into discrete tissues	Variation in cell size and shape Disorganised arrangement of cells
May possess differentiated cell structures Normal presentation of cell surface markers	Loss of normal specialised features Elevated expression of certain cell markers
Lower levels of dividing cells Cell tissues clearly demarcated	Large number of dividing cells Poorly defined tumor boundaries

Summary

Immunology deals with a study of the immune system. The immune system recognises and eliminates the invaders, and the ability of the body to overcome the pathogen is called immunity. Immunity is classified into innate immunity and acquired immunity. Acquired immunity is further classified into cell mediated immunity and antibody mediated immunity as its components. Acquired immunity may be active or passive immunity. Immune response is the body's response to pathogens and it may be primary or secondary. The organs involved in the origin, maturation and proliferation of lymphocytes are called lymphoid organs. Thymus, bone marrow are primary lymphoid organs. The secondary lymphoid organs are lymph node, MALT, GALT and BALT.

An antigen is a substance that is specific to an antibody. An immunogen is a substance capable of initiating an immune response. Haptens are substance that are non-immunogenic but can react with the product of a specific immune response. Substances that can enhance the immune response to an antigen are called adjuvants. An epitope is also known as antigenic determinant and is the active part of the antigen. A paratope is the part of antibody. Precipitation, agglutination, neutralization, opsonisation etc., are the different types of antigen and antibody reaction. A vaccine is biological preparation that provides active acquired immunity. The malfunctioning of immune system leads to hypersensitivity, immunodeficiency or autoimmune diseases. A tumour or neoplasm is a group of cells whose growth has gone unchecked. The best results in the treatment of cancer is achieved by an integrated approach to therapy, surgery, radiotherapy, chemotherapy and immunotherapy.

Evaluation

NBMY3E

1. Colostrum provides
   a) Naturally acquired active immunity
   b) **Naturally acquired passive immunity**
   c) Artificially acquired active immunity
   d) Artificially acquired passive immunity

2. Paratope is an
   (A) Antibody binding site on variable regions
   (B) Antibody binding site on heavy regions
   (C) Antigen binding site on variable regions
   (D) Antigen binding site on heavy regions

3. Allergy involves
   a) IgE b) IgG
   c) lgA d) IgM

4. Anaphylactic shock is due to
   (A) Allergic reaction
   (B) Secretion of toxins
   (C) Secretion of histamines
   (D) All the above

5. Spread of cancerous cells to distant sites is termed as
   (A) Metastasis
   (B) Oncogenes
   (C) Proto-oncogenes
   (D) Malignant neoplasm

6. AIDS virus has
   (A) Single stranded RNA
   (B) Double stranded RNA
   (C) Single stranded DNA
   (D) Double stranded DNA

7. All are peripheral lymphoid organs except
   (A) Lymph nodes
   (B) Spleen
   (C) Mucosa associated lymphoid tissue
   (D) Thymus

8. Which is not a macrophage?
   (A) Monocyte (B) Microglia
   (C) Kupffer cell **(D) Lymphocyte**

9. True about interferon is that
   (A) It is synthetic antiviral agent
   (B) It inhibits viral replication in cells
   (C) It is specific for a particular virus
   (D) It causes infection

10. Cell mediated immunity is carried out by…….. while humoral immunity is mainly carried out by
   (A) B cells/T cells
   (B) Epitopes/antigens
   (C) T cells/B cells
   (D) antibodies/antigens

11. B Cells are activated by
   (A) Complement
   (B) Antibody
   (C) Interferon
   (D) Antigen

12. In agglutination and precipitation reactions, the antigen is a _____ and _____ respectively
   (A) Whole cell/soluble molecule
   (B) Soluble molecule/whole cell
   (C) Bacterium/virus
   (D) Protein/Antibody

13. B cells that produce and release large amounts of antibody are called
   (A) Memory cells (B) Basophils
   (C) Plasma cells (D) killer cells

14. Raja is injured and got swelling. The swelling is due to the infection of tissue is an example of
   (A) Mechanical barrier
   (B) Physiological barrier
   (C) Phagocytosis
   (D) Inflammation

15. Given below are some human organs. Identify one primary and one secondary lymphoid organ. Explain its role.
   Liver, thymus, stomach, thyroid, tonsils

16. How does saliva act in body defence?

17. How does immune system work?

18. Name and explain the type of barriers which involve macrophages.

19. What are interferons? Mention their role.

20. List out chemical alarm signals produced during inflammation.

21. Differentiate between
   (A) Innate immunity and acquired immunity
   (B) Primary and secondary immune responses
   (C) Active and passive immunity
   (D) Humoral and CMI immunity
   (E) Autoimmune disease and Immunodeficiency disease

22. Where are B-cells and T-cells produced in the human body? How do they differ from each other? Mention any two differences.

23. Explain the process of replication of retrovirus after it gains entry into the human body.

24. Why is an antibody molecule represented as $H_2 L_2$?

25. Explain the structure of immunoglobulin with suitable diagram.

26. What are the cells involved innate immune system?

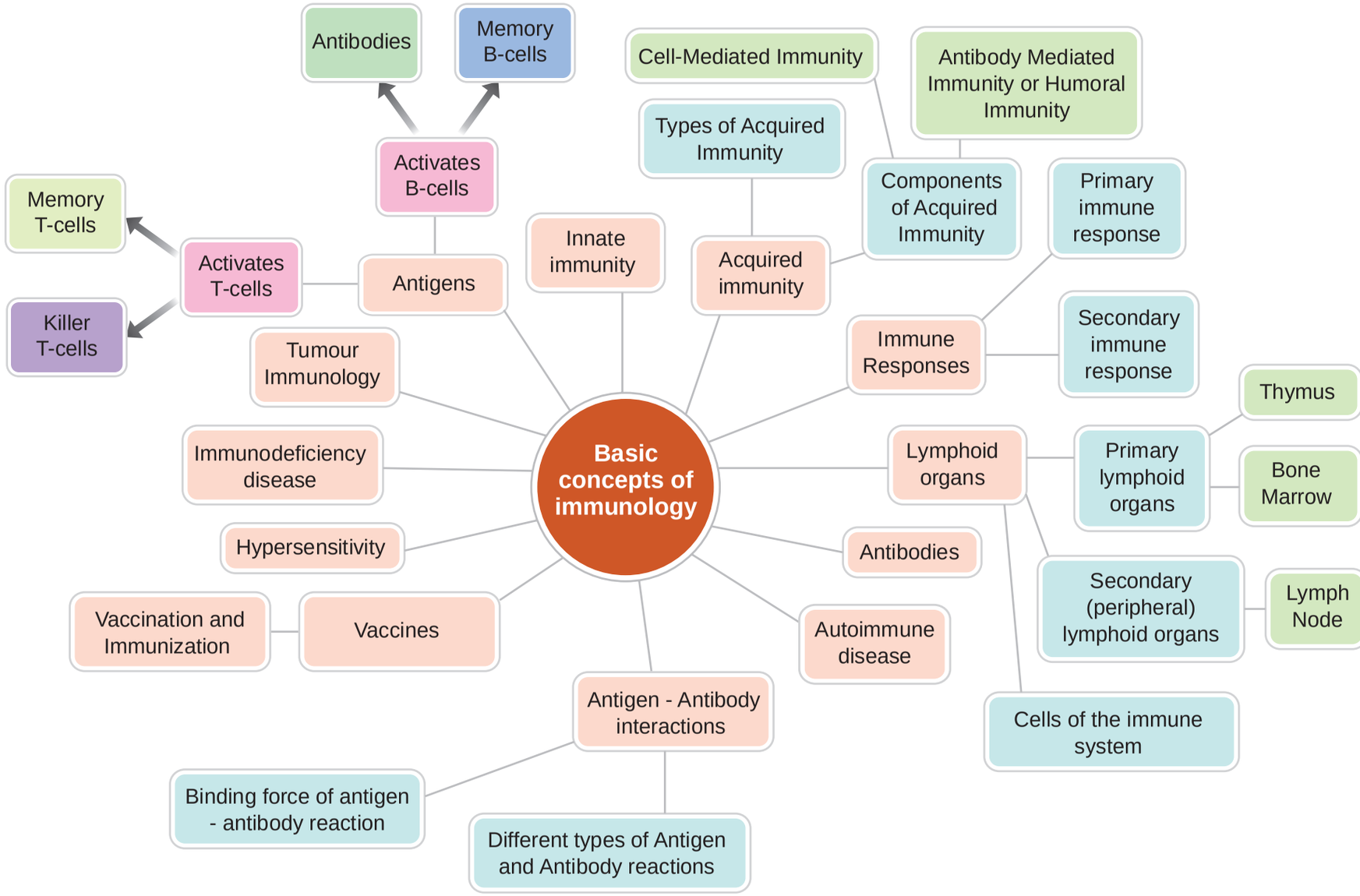
27. Why is opsonisation efficient in phagocytosis?

28. What is vaccine? What are its types?

29. A person is infected by HIV. How will you diagnose for AIDS?

30. Autoimmunity is a misdirected immune response. Justify.

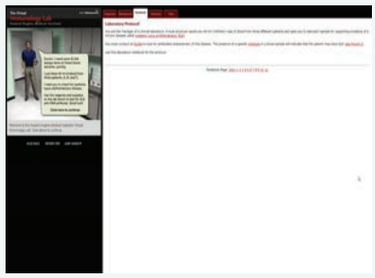
Concept Map



ICT CORNER

IMMUNOLOGY

Let us do examine to know the chronic disease - systemic lupus erythematosus (SLE)



Procedure :

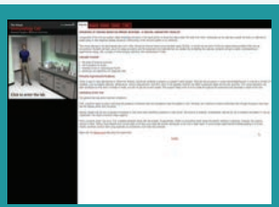
Step -1 : Type the **URL** or scan the **QR** code to open the activity page. Click **"To enter the lab"** to start the test.

Step -2 : Follow the interactive steps guided by the virtual lab starting from centrifugation and to **ELISA**.

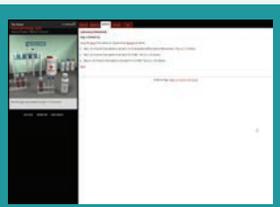
Step -3 : On the right, Find the different headers such as **"Diagnosis, Background, Notebook**, Glossary and **Help"** and **click** to know the virtual procedure happening aside on the left.

Step – 4 : Find **"Launch Gene Body"** on the right bottom of the window, and Click it to analyse and understand about the cloning.

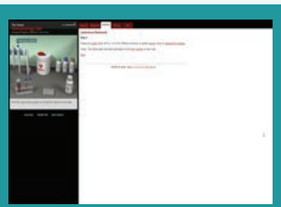
Step -5: Complete this **ELISA** to know a patient acquired the disease or not.



Step 1



Step 2



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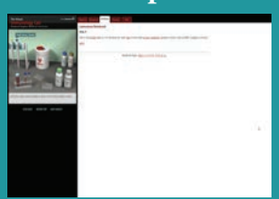

Step 4

IMMUNOLOGY URL:

http://media.hhmi.org/biointeractive/vlabs/immunology/index.html?_ga=2.219254809.1253796128.1545143882-264360672.1545143882

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*Pictures are indicative only

*Allow flash player