HUMAN HEALTH AND DISEASE

Health, for a long time, was considered as a state of body and mind where there was a balance of certain 'humors'. Health does not simply mean 'absence of disease' or 'physical fitness'. It could be defined as a state of complete **physical, mental** and **social well-being**. Balanced diet, personal hygiene and regular exercise are very important to maintain good health. Yoga has been practiced since time immemorial to achieve physical and mental health. Awareness about diseases and their effect on different bodily functions, vaccination (immunization) against infectious diseases, proper disposal of wastes, control of vectors and maintenance of hygienic food and water resources are necessary for achieving good health.

Health is affected by

I. **Genetic disorders** – Deficiencies with which a child is born and deficiencies/defects which the child inherits from parents from birth.
II. **Infections**
III. **Life style** including food and water we take, rest and exercise we give to our bodies, habits that we have or lack etc.

COMMON DISEASES IN HUMANS

Disease - Any change from the normal state causes discomfort or disability or impairs the health is called as disease. Disease can be broadly grouped into **infectious and non-infectious.**
Diseases which are easily transmitted from one person to another are called **infectious diseases**. Infectious diseases are very common and every one of us suffers from these at some time or other. Some of the infectious diseases like AIDS are fatal. Among **non-infectious** diseases, cancer is the major cause of death. Drug and alcohol abuse also affect our health adversely.

A wide range of organisms belonging to bacteria, viruses, fungi, protozoans, helminthes etc., could cause diseases in man. Such disease causing organisms are called **pathogens**. All parasites are therefore pathogens as they cause harm to the host by living in (or on) them. The pathogens can enter our body by various means, multiply and interfere with normal vital activities, resulting in morphological and functional damage.

Pathogens have to adapt to life within the environment of the host. For example, the pathogens that enter the gut must know a way of surviving in the stomach at low pH and resisting the various digestive enzymes. A few representative members from different groups of pathogenic organisms are discussed here along with the diseases caused by them. Preventive and control measures against these diseases in general, are also briefly described.

1. **Typhoid -** ***Salmonella typhi*** is a pathogenic bacterium which causes **typhoid** fever in human beings. These pathogens generally enter the small intestine through food and water contaminated with them and migrates to other organs through blood.

   Symptoms- Sustained high fever (39° to 40°C), weakness, stomach pain, constipation, headache and loss of appetite are some of the common symptoms of this disease. Intestinal perforation and death may occur in severe cases.
   Prevention and control- Typhoid fever could be confirmed by **Widal test**. A classic case in medicine, that of Mary Mallon nicknamed *Typhoid Mary*, is worth mentioning here. She was a cook by profession and was a typhoid carrier who continued to spread typhoid for several years through the food she prepared.

2. **Pneumonia-** Bacteria like ***Streptococcus pneumonia*** and ***Haemophilus influenzae*** are responsible for the disease **pneumonia** in humans which infects the alveoli (air filled sacs) of the lungs. As a result of the infection, the alveoli get filled with fluid leading to severe problems in respiration.

   Symptoms- Fever, chills, cough and headache. In severe cases, the lips and finger nails may turn gray to bluish in colour. A healthy person acquires the infection by inhaling the droplets/aerosols released by an infected person or even by sharing glasses and utensils with an infected person.
   Many **viruses** also cause diseases in human beings.

   Common cold- Rhino viruses is responsible for the disease **common cold**. They infect the nose and respiratory passage but not the lungs.

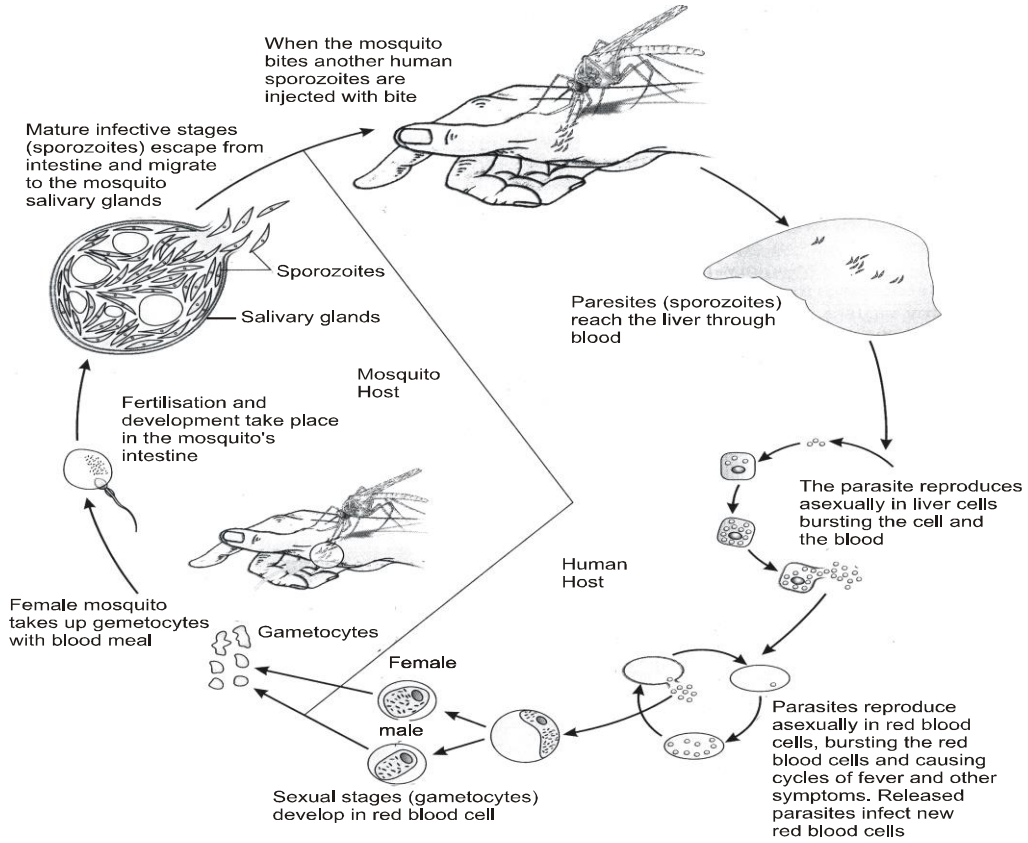
   Symptoms- The common cold is characterized by nasal congestion and discharge, sore throat, hoarseness, cough, headache, tiredness etc., which usually last for 3-7 days. Droplets resulting from cough or sneezes of an infected person are either inhaled directly or transmitted through contaminated objects such as pens, books, cups, doorknobs, computer keyboard or mouse, etc., and cause infection in a healthy person.

   Some of the human diseases are caused by **protozoans** too.

1. **Malaria -** A disease man has been fighting since many years. ***Plasmodium***, a tiny protozoan is responsible for this disease. Different species of *Plasmodium* (*P*. *vivax*, *P*. *malariae* and *P*. *falciparum*) are responsible for different types of malaria. Of these, malignant malaria caused by ***Plasmodium falciparum*** is the most serious one and can even be fatal.

   Life cycle of *Plasmodium*-*Plasmodium* enters the human body as sporozoites (infectious form) through the bite of infected **female *Anopheles*** mosquito. The parasites initially multiply within the liver cells and then attack the red blood cells (RBCs) resulting in their rupture. The rupture of RBCs is associated with release of a toxic substance, haemozoin, which is responsible for the chill and high fever recurring every three to four days.
   When a female *Anopheles* mosquito bites an infected person, these parasites enter the mosquito's body and undergo further development. The parasites multiply within them to form sporozoites that are stored in their salivary glands. When these mosquitoes bite a human, the sporozoites are introduced into his/ her body, thereby initiating the events mentioned above.

   It is interesting to note that the malarial parasite requires two hosts, human and mosquitoes to complete its life cycle.
   1. Human
   2. The female *Anopheles* mosquito is the vector (transmitting agent) too.



Stages in the life cycle of Plasmodium

2. **Amoebiasis (Amoebic dysentery) – *Entamoeba histolytica*** is a protozoan parasite in the large intestine of human which causes **amoebiasis (amoebic dysentery)**.

   Symptoms of this disease include constipation, abdominal pain and cramps, stools with excess mucous and blood clots.

   Houseflies act as mechanical carriers and serve to transmit the parasite from faeces of infected person to food and food products, thereby contaminating them.

Helminthic diseases

Drinking water and food contaminated by the faecal matter are the main source of infection. ***Ascaris*****,** the common round worm and ***Wuchereria*****,** the filarial worm, are some of the helminthes which are known to be pathogenic to man.

1. **Ascariasis**- ***Ascaris*****,** an intestinal parasite causes ascariasis.
   Symptoms of this disease include internal bleeding, muscular pain, fever, anemia and blockage of the intestinal passage. The eggs of the parasite are excreted along with the faeces of infected persons which contaminate soil, water, plants, etc. A healthy person acquires this infection through contaminated water, vegetables, fruits, etc.

2. **Elephantiasis** or **Filariasis- *Wuchereria*** *(W. bancrofti* and *W. malayi),* the filarial worms cause a slowly developing chronic inflammation of the organs in which they live for many years, usually the lymphatic vessels of the lower limbs and the disease is called **elephantiasis** or **filariasis**. The **genital organs** are also often affected, resulting in gross deformities. The pathogens are transmitted to a healthy person through the bite by the **female mosquito vectors**.

Ringworm- Many fungi belonging to the genera ***Microsporum*, *Trichophyton*** and ***Epidermophyton*** are responsible for ringworm which is one of the most common infectious diseases in man.

Symptoms- Appearance of dry, scaly lesions on various parts of the body such as skin, nails and scalp are the main symptoms of the disease. These lesions are accompanied by intense itching. Heat and moisture help these fungi to grow, which makes them thrive in skin folds such as those in the groin or between the toes. Ringworms are generally acquired from soil or by using towels, clothes or even the comb of infected individuals.

Maintenance of personal and public hygiene is very important for prevention and control of many infectious diseases. Measures for personal hygiene include keeping the body clean; consumption of clean drinking water, food, vegetables, fruits, etc. Public hygiene includes proper disposal of waste and excreta; periodic cleaning and disinfection of water reservoirs, pools, cesspools and tanks and observing standard practices of hygiene in public catering. These measures are particularly essential where the infectious agents are transmitted through food and water such as typhoid, amoebiasis and ascariasis. In cases of air-borne diseases such as pneumonia and common cold, in addition to the above measures, close contact with the infected persons or their belongings should be avoided.

For diseases such as malaria and filariasis that are transmitted through insect vectors, the most important measure is to control or eliminate the vectors and their breeding places. This can be achieved by avoiding stagnation of water in and around residential areas, regular cleaning of household coolers, use of mosquito nets, introducing fishes like ***Gambusia*** in ponds that feed on mosquito larvae, spraying of insecticides in ditches, drainage areas and swamps, etc. In addition, doors and windows should be provided with wire mesh to prevent the entry of mosquitoes. Such precautions have become all the more important especially in the light of recent widespread incidences of the vector-borne (*Aedes* mosquitoes) diseases like dengue and chikungunya in many parts of India.

The advancements made in biological science have armed us to effectively deal with many infectious diseases.

The uses of **vaccines and immunisation** programmes have enabled us to completely eradicate a deadly disease like smallpox. A large number of other infectious diseases like polio, diphtheria, pneumonia and tetanus have been controlled to a large extent by the use of vaccines. Biotechnology is at the verge of making available newer and safer vaccines. Discovery of antibiotics and various other drugs has also enabled us to effectively treat infectious diseases.

Sexually Transmitted Diseases (STD)

A sexually transmitted disease is one that is spread by sexual contact. In most developed countries of the world, such as those of Western Europe, Japan, Australia, and New Zealand, the incidence of STDs has declined markedly during the past 25 years.

1. **Chlamydia (Chlamydiasis) -**Chlamydiais a sexually transmitted disease caused by the bacterium ***Chlamydia trachomatis***. In most cases, initial infection is asymptomatic and thus difficult to recognize clinically. In males, urethritis is the principal result, causing a clear discharge, burning on urination, frequent urination, and painful urination. Without treatment, the epididymis may also become inflamed, leading to sterility. In 70% of females with chlamydia, symptoms are absent, but chlamydia is the leading cause of pelvic inflammatory disease. The uterine tubes may also become inflamed, which increases the risk of ectopic pregnancy (implantation of a fertilized ovum outside the uterus) and infertility due to the formation of scar tissue in the tubes.

2. **Gonorrhea-** Gonorrhea or "the clap**"** is caused by the bacterium ***Neisseria gonorrhoeae****.* Discharges from infected mucous membranes are the source of transmission of the bacteria either during sexual contact or during the passage of a newborn through the birth canal. The infection site can be in the mouth and throat after oral–genital contact, in the vagina and penis after genital intercourse, or in the rectum after recto-genital contact.
   Males usually experience urethritis with profuse pus drainage and painful urination. The prostate and epididymis may also become infected. In females, infection typically occurs in the vagina, often with a discharge of pus. Both infected males and females may harbor the disease without any symptoms, however, until it has progressed to a more advanced stage; about 5–10% of males and 50% of females are asymptomatic. In females, the infection and consequent inflammation can proceed from the vagina into the uterus, uterine tubes, and pelvic cavity. If bacteria in the birth canal are transmitted to the eyes of a newborn, blindness can result. Administration of a 1% silver nitrate solution in the infant's eyes prevents infection.

3. **Syphilis-** Syphilis, caused by the bacterium ***Treponema pallidum****,* is transmitted through sexual contact or exchange of blood, or through the placenta to a fetus. The disease progresses through several stages. During the *primary stage,* the chief sign is a painless open sore, called a **chancre,** at the point of contact. The chancre heals within 1 to 5 weeks. From 6 to 24 weeks later, signs and symptoms such as a skin rash, fever, and aches in the joints and muscles usher in the *secondary stage,* which is systemic. The infection spreads to all major body systems. When signs of organ degeneration appear, the disease is said to be in the *tertiary stage.* If the nervous system is involved, the tertiary stage is called **neurosyphilis.** As motor areas become damaged extensively, victims may be unable to control urine and bowel movements. Eventually they may become bedridden and unable even to feed themselves. In addition, damage to the cerebral cortex produces memory loss and personality changes that range from irritability to hallucinations.

4. **Genital Herpes-** Genital herpes is an incurable STD. Type II herpes simplex virus (HSV-2) causes genital infections, producing painful blisters on the prepuce, glans penis, and penile shaft in males and on the vulva or sometimes high up in the vagina in females. The blisters disappear and reappear in most patients, but the virus itself remains in the body. A related virus, type I herpes simplex virus (HSV-1), causes cold sores on the mouth and lips. Infected individuals typically experience recurrences of symptoms several times a year.

5. **Genital Warts-** Warts are an infectious disease caused by viruses. ***Human papillomavirus*** *(HPV)* causes **genital warts,** which is commonly transmitted sexually. Patients with a history of genital warts may be at increased risk for cancers of the cervix, vagina, anus, vulva, and penis. There is no cure for genital warts.

S.No.	Diseases	Pathogen	Symptoms
A. Bacterial diseases			
1	Tuberculosis	*Mycobacterium tuberculosis*	Chronic cough, fever, weakness, bloody sputum, breathlessness Treatment - DOTS (Direct observation treatment short course) Investigation - Mantoux test
2	Diphtheria	*Corynebacterium diphtheriae*	High grade fever, difficulty in breathing (Investigation-Schick test)
3	Whooping cough/Pertussis/100 days cough	*Bordetella pertussis*	Persistent large bouts of cough.
4	Cholera	*Vibrio cholerae*	Diarrhoea, dehydration, vomiting
5	Pneumonia	*Streptococcus pneumoniae*(Earlier *Diplococcuspneumoniae*) also caused by *Haemophilus influenza*)	Infection in lungs, difficulty in breathing, high fever, chill, cough, headache. In severe cases lips and finger nails may turn gray to bluish in colour.
6	Tetanus (Lock jaw)	*Clostridium tetani*	Sustained contraction of body muscles, spasms, lock jaw, unconsciousness, opisthotonus Risus Sardonicus - Stretching of facial muscles
7	Leprosy or Hanson's disease	*Mycobacterium leprae*	Patches on skin, ulcer and nodules formations in skin and nerves, deformities, ulceration and wasting of fingers and toes (Treatment-Multi drug therapy)
8	Typhoid fever	*Salmonella typhi* (Enters through contaminated foods and water)	Stomach pain, constipation, headache, sustain high fever (39° C to 40° C), loss of appetite, intestinal, ulcers, bradycardia and perforation, intestinal, Weakness, Detect by Widal test
9	Plague (Black death)	*Yersinia pestis* (Earlier name-*Pasteurella pestis*)	High fever, headache, enlargement of axillary lymph nodes unconsciousness

S.No.	Diseases	Pathogen	Symptoms
		(B) Viral diseases	
1	Polio or poliomyelities	Polio virus (Group-Picorna virus)	Fever, headache, paralysis
2	Influenza	Orthomyxovirus	Sudden fever after headache, nasal discharge
3	Measles	Paramyxovirus	High grade fever, white-brown patches on body and blisters
4	Chicken pox	pox virus (Varicella-herpes virus)	Rashes on body with fever (Dew drop like appearance rashes)
5	Mumps	Para myxovirus	Painful swelling in parotid gland
6	Dengue fever or Break bone fever	(Arbovirus (flavi)) Vector-***Aedes agypti***	Fever, pain in muscles and joints haemorrhagic condition in body (Torniquet test)
7	Chikungunya	Toga virus (flavi) Vector-***Aedes agypti***	Fever, joint pain, arthritis.
8	Rabies (hydrophobia)	Rhabdo virus or street virus (Vector-Rabbit, dog, cat and wild animals)	Affect CNS - Madness, hydrophobia due to laryngeal spasm and 100% death occur. For prevention - Human diploid cell culture vaccine.
9	Common cold	Rhinovirus **(Droplet infection)**	Infects nose and upper respiratory tract but not the lungs. Nasal congestion and discharge, sore throat, hoarseness, cough, headache, tiredness.
10	SARS (Severe Acute Respiratory Syndrome)	Corona virus **(Droplet infection)**	Pneumonia like symptoms.
11	Swine flu	H1 N1 virus **(Droplet infection)**	Pneumonia like symptoms. Treatment - Tamiflu
		(C) Protozoan diseases	
1	Malaria	*Plasmodium* spp. (*P. vivax, P. malarie, P. falciparum*)	High fever with chill of intermittent periodicity, pain in joints
2	Amoebiasis (Amoeboic dysentery)	*Entamoeba histolytica* (Parasite of large intestine of human). House flies act as mechanical carrier. Drinking water and food contaminated by faecal matter are the main source of infection.	Intestinal spasms, dysentery, stool with excess mucous and blood cell, constipation abdominal pain, cramps
3	Diarrhoea	*Giardia intestinalis*	Vomiting, loose motions
4	African sleeping sickness	*Trypanosoma gambiens*	Patient feels sleepy, nervous system impairment
5	Kala azar	*Leishmania donovani*	High fever associated with enlargement of spleen and liver

(D) Helminth diseases			
1	Ascariasis	*Ascaris lumbricoides* (Common round worm), eggs of the parasite are excreted along with faeces of infected persons which contaminate soil, water, plants	Abdominal spasm, insomnia, vomiting, loose motions, restlessness Internal bleeding, fever, anaemia, blockage of the intestinal passage.
2	Dracunculiasis	*Dracunculus medinensis*	Blisters on skin of arms, shoulders and legs
3	Elephantiasis or Filariasis	*Wuchereria bancrofti /W. malayi* (Filarial worm), Vector is female *Culex*.	Swelling of hands, scrotum, testis and breasts, it causes slowly developing chronic inflammation of lymphatic vessels of lower limbs. Genital organs are also affected resulting in gross deformities.

Some STDs, Their Pathogens and Symptoms		
Diseases	**Pathogen**	**Symptoms**
(A) Bacterial		
1.Syphilis or French pox (Incubation period Approx. 21 days**)**	*Treponema pallidum*	Round elevated ulcers on genital organs Investigation - **VDRL test** (Venereal disease research laboratory test)
2. Gonorrhea Incubation Period 2 to 5 days	*Neisseria gonorrhoeae*	Infection of urethra in male, discharge of white thick fluid from urethra, pain during urination In females - Infection in cervix, pain and burning during micturition
3. Vaginitis	*Gardnella vaginalis*	Grayish-white discharge from vagina
4. Chancroid	*Haemophilus ducreyi*	Foul smelling discharge and ulcers
5. Chlamydiasis	*Chlamydia trachomatis*	Recurrent pain and discharge
(B) Viral		
1. Herpes genitalis	HSV-2(DNA) Virus	In males-Painful rashes on prepuce, glans In females-Rashes on vulva and upper part of vagina
2. Condylomaacuminatum	Papova DNA Virus	Itching and fever
3. Molluscumcontagiosum	Pox DNA Virus	Pain
4. AIDS	Human Immuno deficiency Virus (HIV)	Immune system failure, fever, diarrhoea etc.
(C) Protozoan		
1.Trichomoniasis	*Trichomonas vaginalis*	Greenish-yellow vaginal discharge

Test your Resonance with concept

1. The disease caused by virus is

(1) Typhoid (2) Polio (3) Diptheria (4) Syphilis

2. Which one of the following contains bacterial diseases?

(1) Cholera, typhoid, pneumonia (2) Malaria, AIDS, cholera

(3) Typhoid, tuberculosis, influenza (4) Diabetes, malaria, syphilis

3. Metabolic waste responsible for malaria fever is called

(1) Haemozoin (2) Haematin (3) Melanin (4) Heparin

4. Filaria is transmitted by

(1) Male *Anopheles* (2) Male *Culex* (3) Female *Anopheles* (4) Female *Culex*

ANSWERS

1. (2) **2.** (1) **3.** (1) **4.** (4)

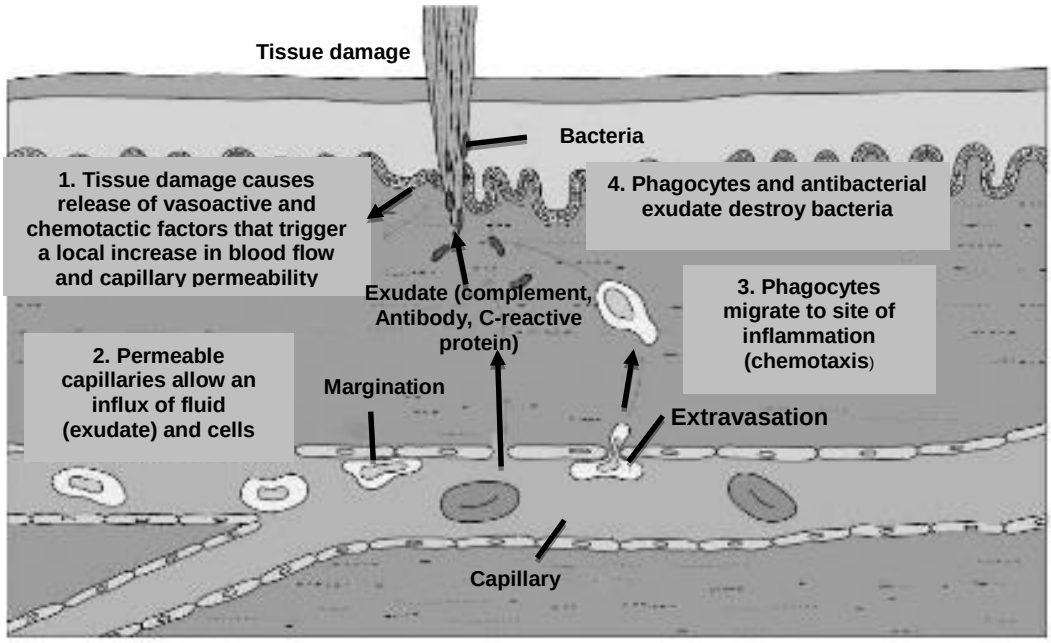
Immunity (Immune = Exempt or Freedom) **–**Every day we are exposed to large number of infectious agents. However, only a few of these exposures result in disease. This is due to the fact that the body is able to defend itself from most of these foreign agents. This overall ability of the host to fight the disease causing organisms, conferred by the immune system is called **immunity**. It is able to generate an enormous variety of cells and molecules capable of specifically recognizing and eliminating an apparently limitless variety of foreign invaders. It has both a less specific and more specific component.

Immunity is of two types

1. Innate immunity **2.** Acquired immunity

1. **Innate immunity - Innate** immunity is non-specific type of defense that is present at the time of birth. This is accomplished by providing different types of barriers to the entry of the foreign agents into our body. Innate immunity consists of four types of barriers. These are-
   - **i. Physical or Anatomical barriers:** Skin on our body is the main barrier which prevents entry of the micro-organisms. Mucus coating of the epithelium lining the respiratory, gastrointestinal and urinogenital tracts. It also help in trapping microbes entering our body.
   - **ii. Physiological barriers:** Acid in the stomach, saliva in the mouth, tears from eyes–all prevent microbial growth.
   - **iii. Cellular or Phagocytic barriers:** Certain types of **leukocytes** (WBC) of our body like polymorphonuclear leukocytes (PMNL-neutrophils) and **monocytes** and **natural killer cells** (type of lymphocytes) in the blood as well as **macrophages** in tissues can phagocytose and destroy microbes.
   - **iv. Cytokine barriers:** Virus-infected cells secrete proteins called **interferons** which protect non infected cells from further viral infection.

Resonate the Concept
Physical and Physiological barriers constitute the first line of defense, whereas cellular and cytokine barriers constitute the second line of defense of the body.



Innate and adaptive immunity operate in cooperative and interdependent ways. The activation of innate immune responses produces signals that stimulate and direct subsequent adaptive immune responses.

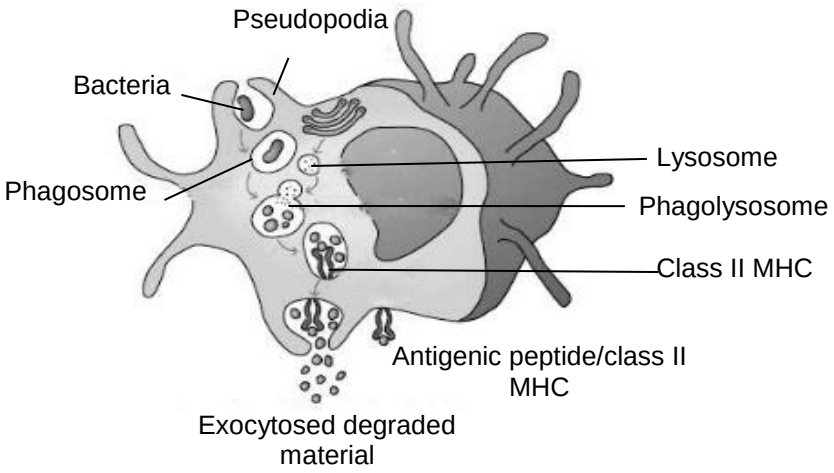
Natural Killer Cells and Phagocytes

When microbes penetrate the skin and mucous membranes or bypass the antimicrobial substances in blood, the next nonspecific defense consists of natural killer cells and phagocytes. About 5–10% of lymphocytes in the blood are **natural killer (NK) cells.** They are also present in the spleen, lymph nodes, and red bone marrow. NK cells lack the membrane molecules that identify B and T cells, but they have the ability to kill a wide variety of infected body cells and certain tumor cells. NK cells attack any body cells that display abnormal or unusual plasma membrane proteins.

The binding of NK cells to a target cell, such as an infected human cell, causes the release of granules containing toxic substances from NK cells. Some granules contain a protein called **perforin** that inserts into the plasma membrane of the target cell and creates channels (perforations) in the membrane. As a result, extracellular fluid flows into the target cell and the cell bursts, a process called **cytolysis**. Other granules of NK cells release **granzymes,** which are protein-digesting enzymes that induce the target cell to undergo apoptosis, or self-destruction. This type of attack kills infected cells, but not the microbes inside the cells; the released microbes, which may or may not be intact, can be destroyed by phagocytes.

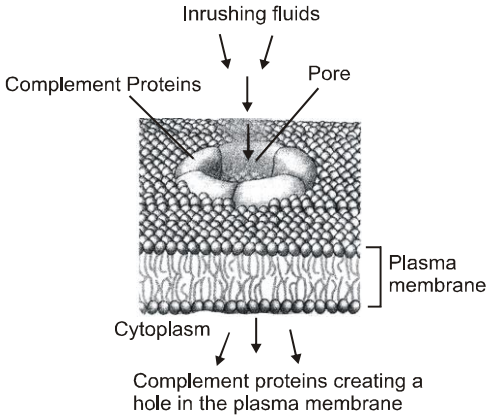
Phagocytes (phago- eat; cytes- cells) are specialized cells that perform **phagocytosis** (osis- process), the ingestion of microbes or other particles such as cellular debris. The two major types of phagocytes are **neutrophils** and **macrophages**. When an infection occurs, neutrophils and monocytes migrate to the infected area. During this migration, the monocytes enlarge and develop into actively phagocytic macrophages called **wandering macrophages.** Other macrophages, called **fixed macrophages,** stand guard in specific tissues. Among the fixed macrophages are histiocytes (connective tissue macrophages), stellate reticulo-endothelial cells (Kupffer cells) in the liver, alveolar macrophages in the lungs, microglia in the nervous system, and tissue macrophages in the spleen, lymph nodes, and redbone marrow. In addition to being an innate defense mechanism, phagocytosis plays a vital role in adaptive immunity. Phagocytosis occurs in five phases: **chemotaxis, adherence, ingestion, digestion,** and **killing.**

1. **Chemotaxis:** Phagocytosis begins with **chemotaxis,** a chemically stimulated movement of phagocytes to a site of damage. Chemicals that attract phagocytes might come from invading microbes, white blood cells, damaged tissue cells, or activated complement proteins.
2. **Adherence:** Attachment of the phagocyte to the microbe or other foreign material is termed **adherence.** The binding of complement proteins to the invading pathogen enhances adherence.
3. **Ingestion:** The plasma membrane of the phagocyte extends projections, called **pseudopods** that engulf the microbe in a process called **ingestion.** When the pseudopods meet, they fuse, surrounding the microorganism with a sac called a **phagosome.**
4. **Digestion:** The phagosome enters the cytoplasm and merges with lysosomes to form a single, larger structure called a **phagolysosome.** The lysosome contributes lysozyme, which breaks down microbial cell walls, and other digestive enzymes that degrade carbohydrates, proteins, lipids, and nucleic acids. The phagocyte also forms lethal oxidants, such as superoxide anion (O_2^-), hypochlorite anion OCl^-), and hydrogen peroxide (H_2O_2), in a process called an **oxidative burst.**
5. **Killing:** The chemical onslaught provided by lysozyme, digestive enzymes, and oxidants within a phagolysosome quickly kills many types of microbes. Any materials that cannot be degraded further remain in structures called **residual bodies.**



Complement system

The proteins and glycoproteins that compose the complement system are synthesized mainly by liver hepatocytes, although significant amounts are also produced by blood monocytes, tissue macrophages, and epithelial cells of the gastrointestinal and genitourinary tracts. These components constitute 5% (by weight) of the serum globulin fraction (**serum proteins**). Most circulate in the serum in functionally inactive forms as **proenzymes, or zymogens,** which are inactive until proteolytic cleavage, which removes an inhibitory fragment and exposes the active site.



The complement reaction sequence starts with an enzyme cascade. Complement activation occurs by the **classical, alternative, or lectin pathways**, each of which is initiated differently. The three pathways converge in a common sequence of events that leads to generation of a molecular complex that causes **cell lysis.**

In addition to its key role in cell lysis, the complement system mediates **opsonization** of bacteria, activation of **inflammation**, and **clearance of immune complexes**.

Interactions of complement proteins and protein fragments with receptors on cells of the immune system control both innate and acquired immune responses.

Summary of nonspecific host defenses	
Type	**Mechanism**
Anatomic barriers	
Skin	Mechanical barrier retards entry of microbes. Acidic environment (pH 3-5) retards growth of microbes.
Mucous membranes	Normal flora complete with microbes for attachment sites and numbers. Mucus entraps foreign microorganisms. Cilia propel microorganism out of body.
Physiologic barriers	
Temperature	Normal body temperature inhibits growth of some pathogens. Fever response inhibits growth of some pathogens.
Low pH	Acidity of stomach contents kills most ingested microorganisms.
Chemical mediators	Lysozyme cleaves bacterial cell wall. Interferon induces antiviral state uninfected cells. Complement lyses microorganisms or facilitates phagocytosis. Toll-like receptors recognize microbial molecules. Signal cell to secrete immunostimulatory cytokines. Collectins disrupt cell wall of pathogen.
Phagocytic / Endocytic barriers	Various cells internalize (endocytose) and break down foreign macromolecules. Specialized cells (blood monocytes. Neutrophils, tissue macrophages) internalize (phagocytose), kill, and digest whole microorganism.
Inflammatory barriers	Tissue damage and infection induce leakage of vascular fluid, containing serum proteins with antibacterial activity and influx of phagocytic cells into the affected area.

Acquired (Adaptive) Immunity

Adaptive immunity is capable of recognizing and selectively eliminating specific foreign microorganisms and molecules (*i.e.* foreign antigens). Unlike innate immune responses, adaptive immune responses are not the same in all members of a species but are reactions to specific antigenic challenges.

Adaptive immunity displays four characteristic attributes

1. **Antigenic specificity:** The antigenic specificity of the immune system permits it to distinguish subtle differences among antigens. Antibodies can distinguish between two protein molecules that differ in only a single amino acid.
2. **Diversity:** The immune system is capable of generating tremendous diversity in its recognition molecules, allowing it to recognize billions of unique structures on foreign antigens.
3. **Immunologic memory:** Once the immune system has recognized and responded to an antigen, it exhibits immunologic memory. This means that our body when it encounters a pathogen for the first time produces a response called **primary response** which is of low intensity. Subsequent encounter with the same pathogen elicits a highly intensified **secondary or anamnestic response**. This is ascribed to the fact that our body appears to have memory of the first encounter.
4. **Self / Nonself recognition:** Finally, the immune system normally responds only to foreign antigens, indicating that it is capable of self/nonself recognition**.** The ability of the immune system to distinguish self from nonself and respond only to nonself molecules is essential, for the outcome of an inappropriate response to self-molecules can be fatal.

Summary of Functions of Cells Participating in Immune Responses

CELLS	FUNCTIONS
ANTIGEN PRESENTING CELLS (APCs)	
Macrophage	Phagocytosis, processing and presentation of foreign antigen to T cells; secretion of interleukin-1, which stimulates secretion of interleukin-2 by helper T cells and induce proliferation of B cells; secretion of interferons that stimulate T cell growth.
Dendritic Cell	Processing and presenting antigen to T cells and B cells; found in mucous membranes, skin, and lymph nodes.
B cell	Processing and presenting antigen to helper T cells
LYMPHOCYTES	
Cytotoxic T- cell	Kills host target cells by release granzymes that induce apoptosis, perforin that forms channels to cause cytolysis, granulysin that destroys microbes, lymphotoxin that destroys target cell DNA. Gamma-interferon that attracts macrophages and increase their phagocytic activity, and macrophage migration inhibition factor that prevents macrophage migration from site of infection.
Helper T- cell	Cooperates with B cells to amplify antibody production by plasma cells and secretes interleukin-2, which stimulates proliferation of T cells and B cells. May secrete gamma-IFN and tumor necrosis factor (TNF), which stimulate inflammatory response.
Memory T- cell	Remains in lymphatic tissue and recognizes original invading antigen, even years after the first encounter.
B cell	Differentiates into antibody-producing plasma cell.
Plasma cell	Descendant of B cell that produces and secretes antibodies.
Memory B- cell	Descendant of B cell that remains after an immune response and is ready to respond rapidly and forcefully should the same antigen enter the body in the future.

The primary and secondary immune responses are carried out with the help of two special types of lymphocytes present in our blood, i.e., **B-lymphocytes** and **T-lymphocytes**.

1. **Humoral immune response -** The B-lymphocytes produce an army of proteins in response to pathogens into our blood to fight with them. These proteins are called antibodies. The T-cells themselves do not secrete antibodies but help B cells produce them. These antibodies are found in the blood, the response is also called as humoral immune response. This is one of the two types of our acquired immune response i.e. antibody mediated.

2. **Cell-mediated immune response -** The second type is called cell-mediated immune response or cell-mediated immunity (CMI). A cell-mediated immune response begins with activation of a small number of T cells by a specific antigen. Once a T cell has been activated, it undergoes clonal selection. Recall that **clonal selection** is the process by which a lymphocyte proliferates (divides several times) and differentiates (forms more highly specialized cells) in response to a specific antigen. The result of clonal selection is the formation of a **clone** of cells that can recognize the same antigen as the original lymphocyte. Some of the cells of a T cell clone become effector cells, while other cells of the clone become memory cells. The effector cells of a T cell clone carry out immune responses that ultimately result in elimination of the intruder.

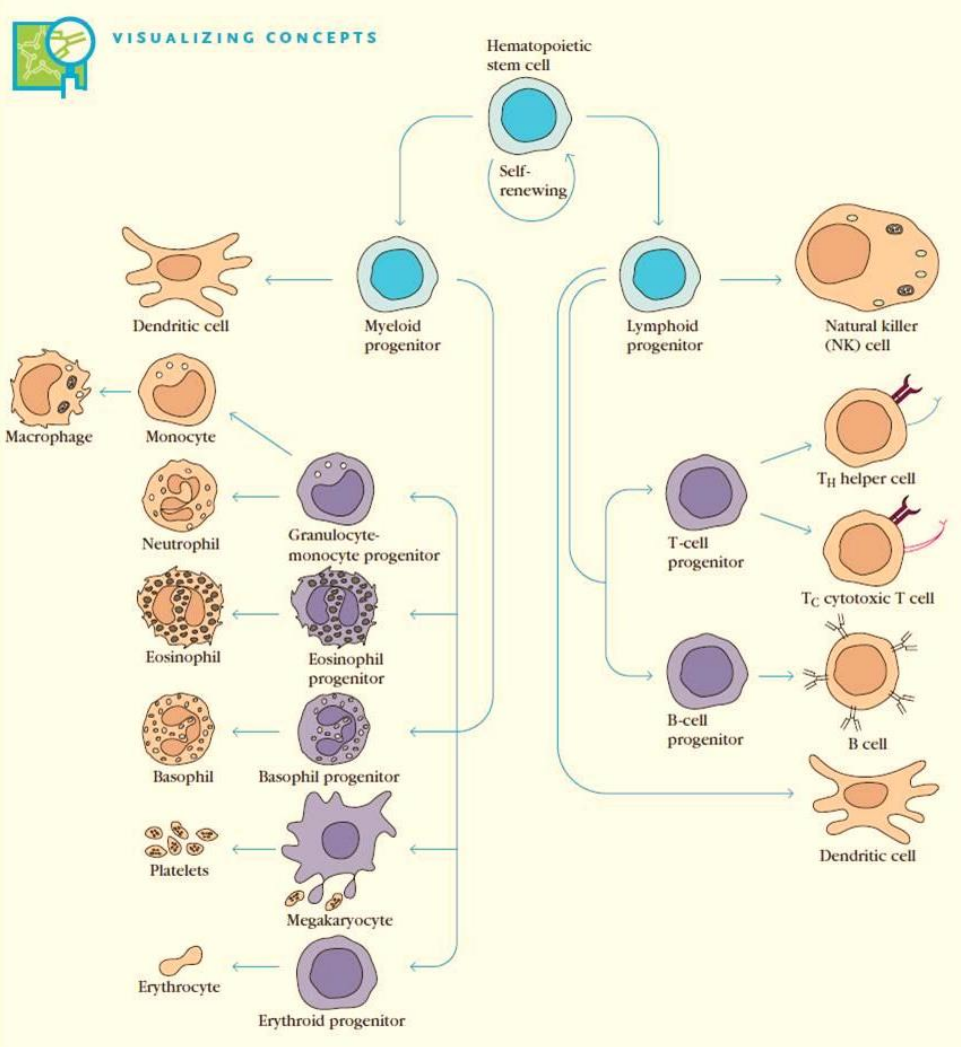


Fig. Function of different types of WBCs

Resonate the Concept
Transplantation: Very often, when some human organs like heart, eye, liver and kidney fail to function satisfactorily. Transplantation is the only remedy to enable the patient to live a normal life. Then a search begins to find a suitable donor. Grafts from just any source an animal, another primate, or any human beings cannot be made since the grafts would be rejected sooner or later. Tissue matching, blood group matching are essential before undertaking any graft/transplant and even after this the patient has to take immuno–suppressants all his/her life. The body is able to differentiate 'self' and 'nonself' and the cell-mediated immune response is responsible for the graft rejection.

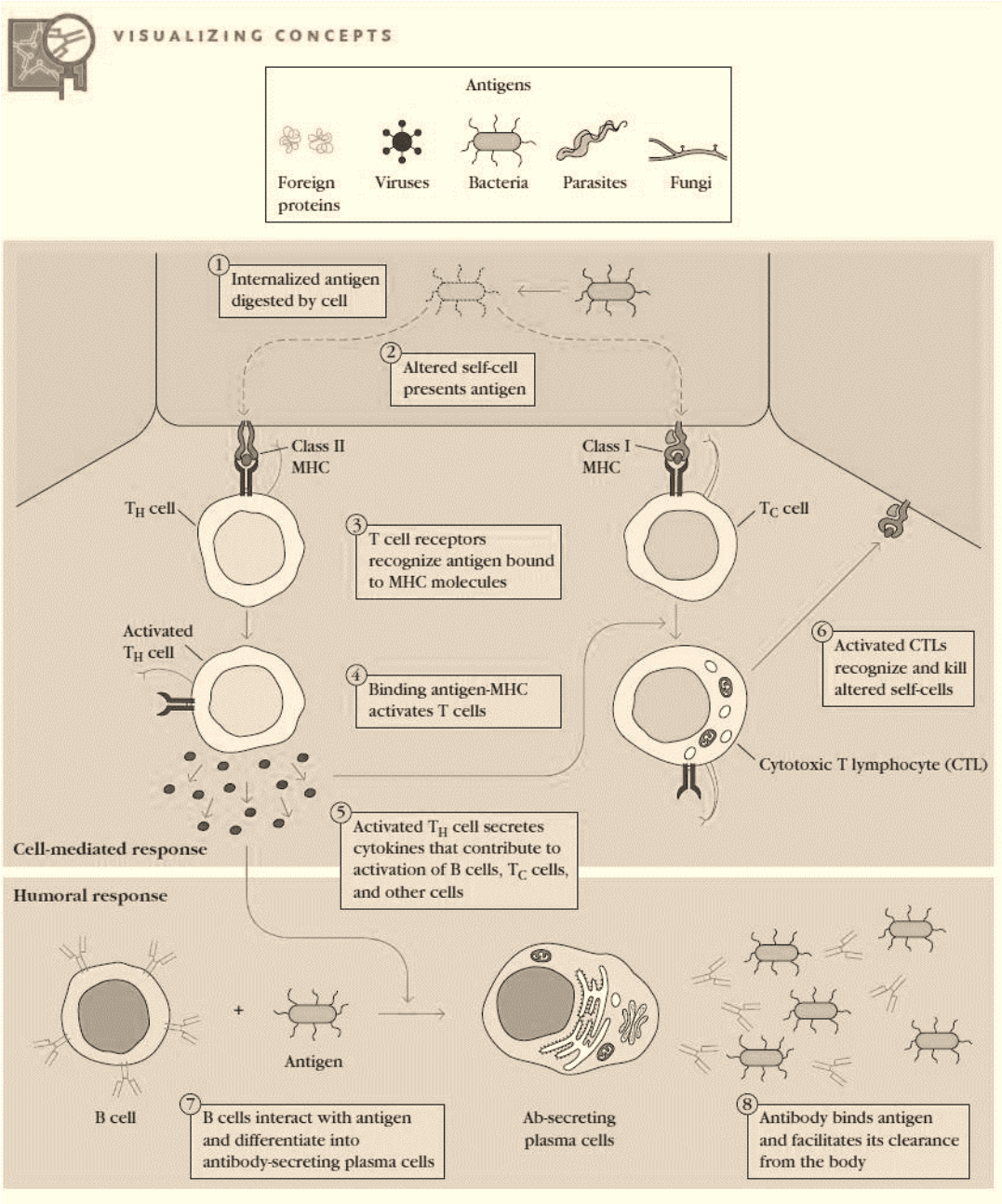
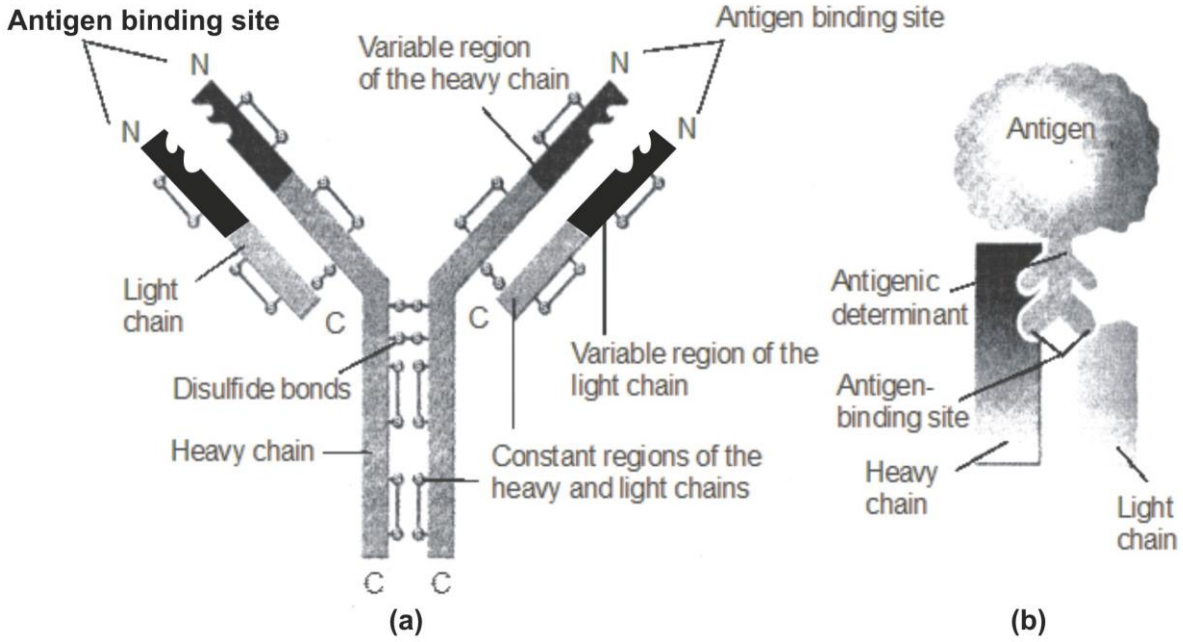


Fig. Mechanism of Acquired Immunity

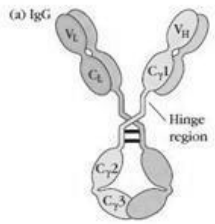
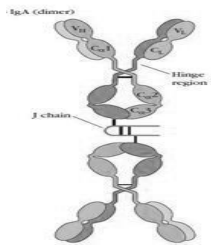
Structure of Antibody

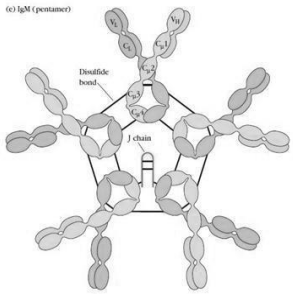
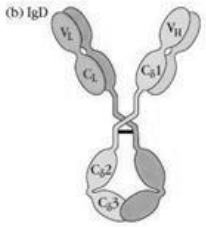
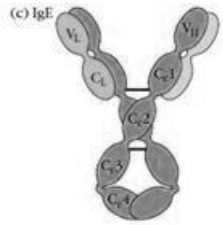
Each antibody molecule has four peptide chains, two small called **light chains or L-chains** and two longer called **heavy chains or H-chains**. Hence, an antibody is represented as H_2L_2. These four polypeptides chains are held together to form a Y- shaped molecule. The top two tips of this Y-shaped molecule bind to the specific antigens in a **lock and key fashion** forming an antigen antibody complex. Antibody molecule may be bound to a cell membrane or they may remain free.



Immunoglobulins (a) Structure (b) Antigen binding site

Classes of immunoglobulins- Different types of antibodies are produced in our body**. IgG, IgA, IgM, IgD**, **IgE** are some of them.

NAME	STRUCTURE	FUNCTIONS
IgG		Most abundant, about 80% of all antibodies in the blood; found in blood, lymph, and the intestines; monomer (one-unit) structure. It is smallest with least molecular weight. Protects against bacteria and viruses by enhancing phagocytosis, neutralizing toxins, and triggering the complement system. It is the only class of antibody to cross the placenta from mother to fetus, conferring considerable immune protection in newborns.
IgA		Found mainly in **sweat, tears, saliva, mucus, breast milk, and gastrointestinal secretions**. Smaller quantities are present in blood and lymph. It is also called secretory antibody. Makes up **10–15%** of all antibodies in the blood; occurs as monomers and dimers (two units). Levels decrease during stress, lowering resistance to infection. Provides localized protection of mucous membranes against bacteria and viruses.

IgM		About **5–10%** of all antibodies in the blood; also found in lymph. Occurs as **pentamers** (five units); **first antibody** class to be secreted by plasma cells after an initial exposure to any antigen. It is largest antibody with maximum molecular weight. Activates **complement and causes agglutination** and lysis of microbes. Also present **as monomers on the surfaces of B cells**, where they serve as antigen receptors. In blood plasma, the anti-A and anti-B antibodies of the ABO blood group, which bind to A and B antigens during incompatible blood transfusions are also IgM. It is first antibody to be formed in foetus.
IgD		Mainly found on the surfaces of B cells as antigen receptors, where it occurs as monomers; involved in activation of B cells. About **0.2%** of all antibodies in the blood.
IgE		Less than **0.1%** of all antibodies in the blood; occurs as monomers; located on **mast cells and basophils**. Involved in **allergic and hypersensitivity** reactions; provides protection against parasitic worms.

Types of acquired immunity

1. **Active immunity -** When a host is exposed to antigens, which may be in the form of living or dead microbes or other proteins, antibodies are produced in the host body. This type of immunity is called **active immunity.** Active immunity is slow and takes time to give its full effective response. Injecting the microbes deliberately during immunization or infectious organisms gaining access into body during natural infection induce active immunity.
   - **Natural active immunity:** Follows clinical or subclinical infections.
   - **Artificial active immunity:** induced by vaccination.
2. **Passive immunity -**When ready-made antibodies are directly given to protect the body against foreign agents, it is called **passive immunity**.
   - **Natural passive immunity: The** yellowish fluid **colostrum** secreted by mother during the initial days of lactation has abundant antibodies (IgA) to protect the infant. The foetus also receives some antibodies from their mother, through the **placenta during pregnancy**.
   - **Artificial passive immunity:** Injection of preformed antibodies (e.g. ATS).

Vaccination and Immunization

Definition: -The principle of immunization or vaccination is based on the property of 'memory' of the immune system.

History

1. **Edward Jenner (1796):** He noticed that milkmaid did not suffer from small pox but they had scabs of cow pox. He transport the material parasite from sore of milkmaid who was suffering from cow pox to the young body of 8 year old. After sometime he injected live small pox material into that boy. But symptoms of disease did not appear. He tried this procedure on other person and got success. He gave the term vaccination for this process.

2. **Louis Pasteur:** Louis Pasteur, a French scientist, found that ageing cultures of cholera bacteria were too weak to cause disease when injected into chickens. But chickens injected with these cultures becomes immune to fowl- cholera. Using this method, Pasteur developed a vaccine (Latin, vacca, meaning: cow) against rabies in 1885. It was later discovered that animals injected with small amounts of the tetanus toxin became immune to the disease. By the end of 1920s, vaccines for diphtheria, tetanus, pertussis (whooping cough) and tuberculosis were available.

Types of vaccines

1. **First generation vaccines:** These vaccines are prepared by inactivating the **whole pathogen,** but they have many side effects. e.g.
   - **i.** Live attenuated– (OPV, Sabin polio, BCG, Small pox, Influenza etc.)
   - **ii.** Killed– (Typhoid, Salk polio, Cholera, Rabies, Plague etc.)
   - **iii.** Toxoid– (Diphtheria, Tetanus)
   - **iv.** Combination– (DPT, MMR)
2. **Second generation vaccines:** Recombinant DNA technology has allowed the production of antigenic polypeptides of pathogen in transgenic organisms. These are made by multiplication of surface antigen by genetic engineering. e.g., Hepatitis B vaccine produced from transgenic yeast, meningococcal, pneumococcal vaccines, etc.
3. **Third generation vaccines:** These are highly potent, synthetic in nature &prepared by genes**.** They are also called **DNA vaccine.** e.g., Leukemia virus vaccine.

Types of immunization

1. **Passive immunization** involves giving **pre-formed antibodies** to a person (or animal). These antibodies are gradually broken down by the normal processes of protein catabolism, so this form of immunity is temporary. Passive immunization can be natural or artificial.
   - **A. Natural passive immunization** includes the passage of **maternal IgG across the human placenta**. In regions with a high incidence of tetanus, immunization of pregnant women with tetanus toxoid results in them makes antitetanus IgG which is transmitted across the placenta to the fetus, and can protect the newborn from tetanus. In humans, I**gA** is transmitted to the baby's gut via colostrum and milk.
   - **B. Artificial passive immunization** is effected when immunodeficient patients are given doses of antibodies from a donor; travelers to the tropics may be given 'pooled γ-globulins' (antibodies) from donors who live in the visited areas, hopefully, the cocktail of donated antibodies may protect them from endemic diseases. There is a danger that recipients will mount immune reactions to the antibodies themselves (which they will 'see' as 'nonself' proteins), resulting in immune complexes depositing themselves on the glomerular membranes of the kidneys (this is an example of type III complex-mediated hypersensitivity). Genetic engineering techniques are being pursued to develop high-affinity antibodies against rubella (German measles virus), etc.

2. **Active immunization (vaccination)** works on the principle of stimulating the individual's own immune system to make antibodies, effector cells and memory T and/or B cells in response to the infectious agent, usually delivered in a dead or less virulent form. The aim is to provide effective immunity by establishing adequate levels of antibody and a population of memory lymphocytes which can expand rapidly on renewed contact with antigen. For poliomyelitis protection, high levels of blood antibody are desirable. In mycobacterial diseases such as tuberculosis, a macrophage-activating cell-mediated immunity is sought, cytotoxic T cells are most effective with influenza infection. The site of the response may be important – for cholera the response must be in the gut cavity to present adherence to and colonization of the gut wall. Immunizing antigens need to be cheap, safe (not injuring the recipient) and stable.

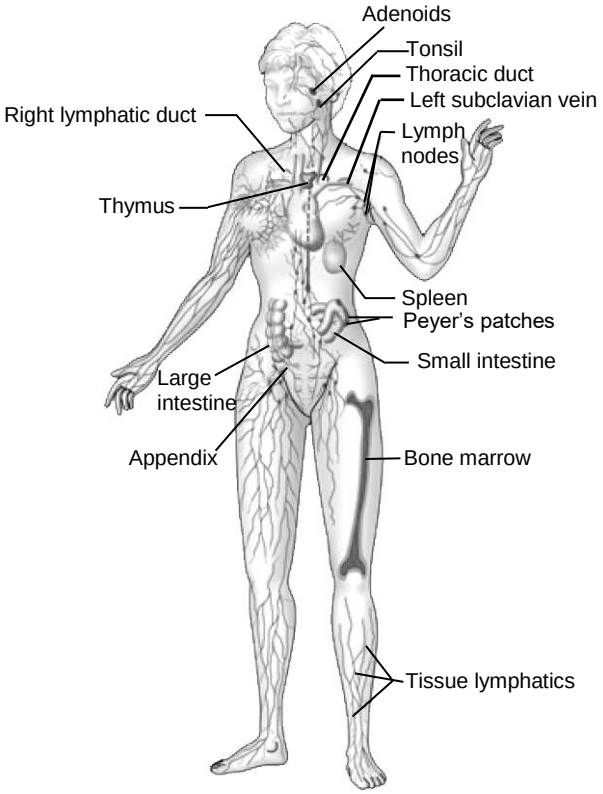
Immune system in the body

The human immune system consists of lymphoid organs, tissues, cells and soluble molecules like antibodies. As you have read, immune system is unique in the sense that it recognises foreign antigens, responds to these and remembers them. The immune system also plays an important role in allergic reactions, auto-immune diseases and organ transplantation.

Lymphoid organs: These are the organs where origin and/or maturation and proliferation of lymphocytes occur. Blood vessels and lymphatic systems connect these organs, uniting them into a functional whole.

1. **Primary lymphoid organs-**These are **bone marrow** and **thymus** where immature lymphocytes differentiate into antigen-sensitive lymphocytes.
   - **A. Bone marrow- I**t is the main lymphoid organ where all blood cells including lymphocytes are produced. In humans and mice, bone marrow is the site of B-cell origin and development. Arising from lymphoid progenitors, immature B cells proliferate and differentiate within the bone marrow, and stromal cells within the bone marrow interact directly with the B cells and secrete various cytokines that are required for development.
   - **B. Thymus**- It is a lobed organ located near the heart and beneath the breastbone. The thymus is quite large at the time of birth but keeps reducing in size with age and by the time puberty is attained it reduces to a very small size. Both bone-marrow and thymus provide micro-environments for the development and maturation of T-lymphocytes.

2. **Secondary lymphoid organs- These** are **spleen, lymph nodes, tonsils, Peyer's patches of small intestine and appendix**. The secondary lymphoid organs provide the sites for interaction of lymphocytes with the antigen, which then proliferate to become effector cells. The location of various lymphoid organs in the human body is shown in figure.
   - **A. Spleen-** It is a large bean shaped organ. It mainly contains lymphocytes and phagocytes. It acts as a filter of the blood by trapping blood-borne microorganisms. Spleen also has a large reservoir of erythrocytes.



B. Lymph node- These are small solid structures located at different points along the lymphatic system. Lymph nodes serve to trap the micro-organisms or other antigens, which happen to get into the lymph and tissue fluid. Antigens trapped in the lymph nodes are responsible for the activation of lymphocytes present there and cause the immune response.

C. Tonsils- These are found in three locations: **lingual** at the base of the tongue; **palatine** at the sides of the back of the mouth; and **pharyngeal** (adenoids) in the roof of the nasopharynx. All three tonsil groups are nodular structures consisting of a meshwork of reticular cells and fibers interspersed with lymphocytes, macrophages, granulocytes, and mast cells.

D. Peyer's patches of small intestine- The sub-mucosal layer beneath the lamina propria contains **Peyer's patches,** nodules of 30–40 lymphoid follicles. Like lymphoid follicles in other sites, those that compose Peyer's patches can develop into secondary follicles with germinal centers.

E. Mucosal Associated Lymphoid Tissue (MALT)- The mucous membranes lining the digestive, respiratory, and urogenital systems have a combined surface area of about 400 m^2 (nearly the size of a basketball court) and are the major sites of entry for most pathogens. These vulnerable membrane surfaces are defended by a group of organized lymphoid tissues mentioned earlier and known collectively as mucosal-associated lymphoid tissue (MALT).It constitutes about 50 per cent of the lymphoid tissue in human body.

Immune dysfunction and its consequences

Sometimes the immune system fails to protect the host adequately or misdirects its activities to cause discomfort, debilitating disease, or even death. There are several common manifestations of immune dysfunction.

1. Allergy and asthma
2. Autoimmune disease
3. Immunodeficiency

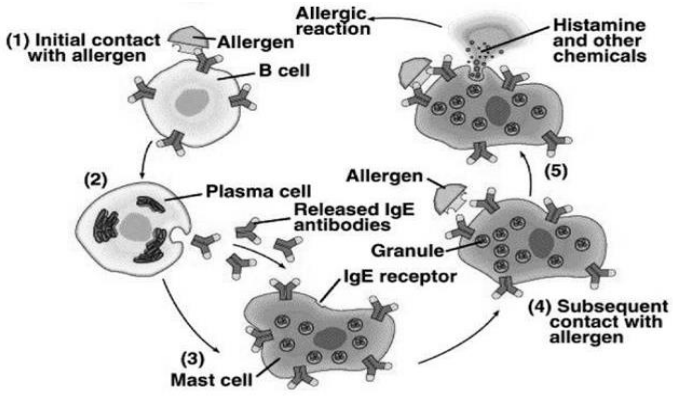
1. Allergy and asthma

The exaggerated response (**inappropriate immune responses**) of the immune system to certain antigens present in the environment is called **allergy**. The substances to which such an immune response is produced are called allergens. The antibodies produced to these are of IgE type. Common examples of allergens are mites in dust, pollens, animal dander, etc. **Symptoms** may

include sneezing, wheezing, and difficulty in breathing (asthma), dermatitis or skin eruptions (hives) and, in more extreme cases, strangulation due to blockage of airways by inflammation.

Allergy is due to the release of chemicals like **histamine** and **serotonin** from the mast cells. For determining the cause of allergy, the patient is exposed to or injected with very small doses of possible allergens, and the reactions studied.

The use of drugs like **anti-histamine**, **adrenalin** and **steroids** quickly reduce the symptoms of allergy. Somehow, modern-day life style has resulted in lowering of immunity and more sensitivity to allergens – more and more children in metro cities of India suffer from allergies and asthma due to sensitivity to the environment. This could be because of the protected environment provided early in life.



2. Auto Immunity

Memory based acquired immunity evolved in higher vertebrates based on the ability to differentiate foreign organisms (e.g., pathogens) from self-cells. While we still do not understand the basis of this, two corollaries of this ability have to be understood.

A. Higher vertebrates can distinguish foreign molecules as well as foreign organisms. Most of the experimental immunology deals with this aspect.

B. Due to influence of unknown environmental triggers and certain genes that make some people more susceptible, self-tolerance breaks down, leading to activation of self-reactive clones of T cells and B cells. These cells then generate cell-mediated or antibody-mediated immune responses against self-antigens. This results in damage to the body and is called **auto-immune** disease. **For example,**

i. **Multiple sclerosis** is due to an **autoimmune attack on the brain and central nervous** system. Antibodies are formed against the myelin sheath of nerve cells. Destruction of myelin sheath causes neurological dysfunction.

ii. **Crohn's disease** is an attack on the **tissues in the gut**.

iii. **Rheumatoid arthritis** is an attack on joints of the **arms and legs**. It is due to presence of rheumatoid factor (a type of immunoglobulin IgM). It is the primary symptom of inflammation of synovial membrane. If it is left untreated, then the membrane thickens and synovial fluid increases, exerting pressure that causes pain. The membrane then starts secreting abnormal granules, called pannus, which after accumulating on the surface of the cartilage, cause its erosion. As a result, the fibrous tissues are attached with the bones and become ossified, making the joints immovable.

Treatment: Pain and inflammation by heat treatment and physiotherapy. Joint replacement surgery will be done in extreme cases.

iv. **Hashimoto disease:** Antibodies are formed **against the thyroid.** These antibodies destroy the thyroid gland and deficiency of thyroid hormone is called **hypothyroidism.**

v. **Myasthenia gravis:** In this disorder, antibodies are formed against **acetylcholine receptors** so these receptors are destroyed. It causes depressed nerve conduction at neuromuscular junction and decrease movement of muscles. Muscle becomes degenerate after some time.

vi. **Pernicious (Destructive) anemia:** In this disorder, antibodies are formed against castle intrinsic factor (stomach) so the vitamin B_{12} is not absorbed in intestine and blood formation is decreased. This deficiency of blood is called pernicious anemia

The genetic and environmental factors that trigger and sustain autoimmune disease are very active areas of immunologic research, as is the search for improved treatments.

3. Immunodeficiency

If any of the many components of innate or specific immunity is defective because of genetic abnormality or if any immune function is lost because of damage by **chemical, physical, or biological agents**, the host suffers from **immunodeficiency.**

i. **Severe Combined Immuno Deficiency (SCID): A** rarer immunodeficiency called severe combined immunodeficiency (SCID), which affects both B and T cells, if untreated, results in death from infection at an early age. This disorder is due to gene mutation or gene deficiency of enzyme **adenosine deaminase**. This enzyme involved in formation of T and B lymphocytes. SCID is characterized by very low number of circulating thymocytes. The affected individuals die at an early age. Treatment can be done by gene therapy.

ii. **AIDS (Acquired Immune-Deficiency Syndrome):** Since the 1980s, the most common form of immunodeficiency has been acquired immune deficiency syndrome, or AIDS, which results from infection with the retrovirus Human Immunodeficiency Virus, or HIV. In AIDS, helper T cells are infected and destroyed by HIV, causing a collapse of the immune system. This cause the decrease count of helper T-cells from normal 950/mm^3 to less than 200 /mm^3.

iii. **De-George's syndrome or Thymic-aplasia:** In this syndrome deficiency of T-cell occurs due to inactive thymus gland.

iv. **Bruton's agammaglobulinemia:** Deficiency of gamma antibodies occurs due to deficient formation of B-cells.

Immunotherapy

Immunotherapy is a treatment procedure that involves suppression or augmentation of immune response, to achieve therapeutic effects. Manipulation of the immune response can be carried out by modulating various components involve in it. Cytokines are natural Immunomodulators secreted by one type of immune cell that elicits response in another type of immune cell; these include interleukins, interferons and tumour necrosis factors.

Immunomodulators: - These are drugs that modulate the activity of a patient's immune response, either up or down, until a desired level of therapeutic effects are reached. There are two general clinical approaches of immunomodulation.

i. **Immuno potentiation therapies:** This includes administration of immune potentiating agent like preformed antibodies or immune potentiating drugs. This strategy augments the immune response.

ii. **Immuno suppressive therapies:** When the patient's immune system becomes activated against his or her own body, in situations such as autoimmune diseases, the response is suppressed by using specific therapies. These include inhibitors of cell division, cytokine production, etc.

Test your Resonance with concept

1. Colostrum provides
(1) Auto immunity (2) Passive immunity
(3) Active immunity (4) Innate immunity

2. Immune deficiency syndrome in human could develop as consequence of
(1) AIDS virus infection (2) Defective liver
(3) Defective thymus (4) Weak immune system

3. T-cells are lymphocytes which produce the cellular immunity. These are developed from
(1) Thymus (2) Liver
(3) Spleen (4) Endothelium of blood vessels

4. Characters of acquired immunity are
(1) Specificity of antigen (2) Recognition between self & non-self
(3) Retains memory (4) All of these

Answers

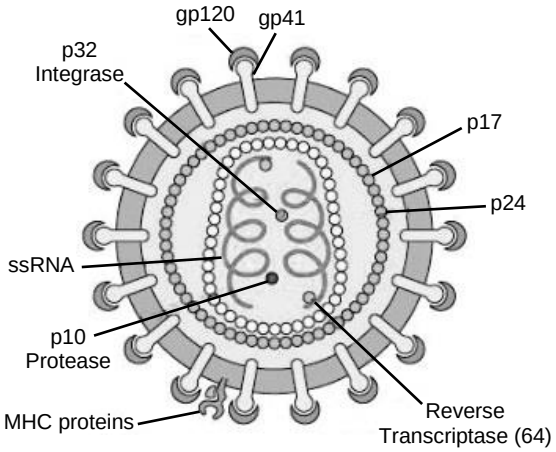
1. (2) **2.** (1) **3.** (1) **4.** (4)

AIDS

The word AIDS stands for **Acquired Immuno Deficiency Syndrome**. This means deficiency of immune system, acquired during the lifetime of an individual indicating that it is not a congenital disease. '**Syndrome**' means a group of symptoms. AIDS was first reported in 1981 and in the last twenty-five years or so, it has spread all over the world killing more than 25 million persons. AIDS is caused by the Human Immuno deficiency Virus (HIV). The HIV virus infects and eliminates key cells of the immune system, destroying the body's ability to defend itself from cancer and infection. Study of HIV revealed it to be closely related to a chimpanzee virus, suggesting a recent host expansion to humans in central Africa from chimpanzees.

A. Structure of HIV

HIV consists of an inner core of ribonucleic acid (RNA) covered by a protein coat (capsid). HIV is classified as a retrovirus since its genetic information is carried in RNA instead of DNA. Retrovirus has RNA genome and enzymes e.g., reverse transcriptase, integrase and protease. Core of virus has inner protein coat (P-24), outer protein coat (P-17) and lipoproteins (GP-120 and GP-41). GP-120 has complementary sequence to CD-4 receptors present on macrophages (HIV factory), helper T-cells etc.



B. Transmission of HIV

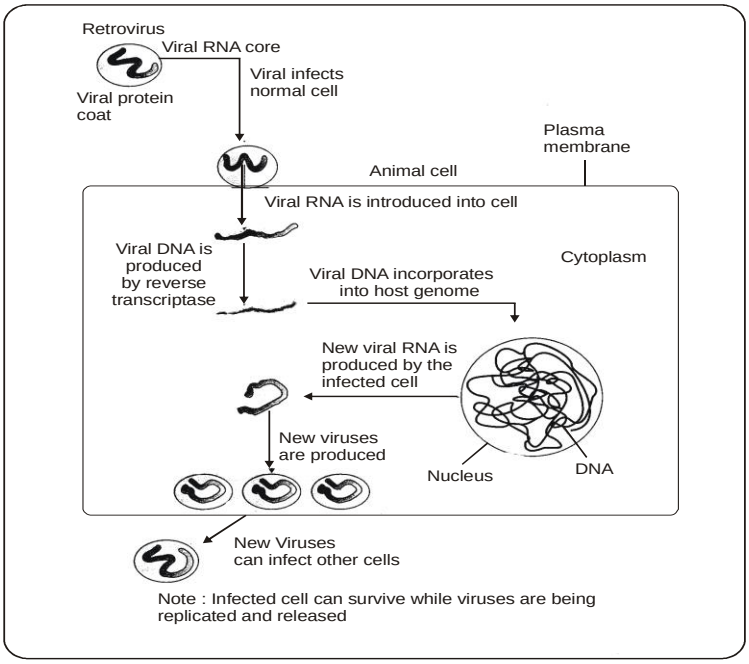
(a) Sexual contact with infected person,
(b) By transfusion of contaminated blood and blood products,
(c) By sharing infected needles as in the case of intravenous drug abusers and
(d) From infected mother to her child through placenta.

So, people who are at high risk of getting this infection includes - individuals who have multiple sexual partners, drug addicts who take drugs intravenously, individuals who require repeated blood transfusions and children born to an HIV infected mother.

It is important to note that HIV/AIDS is not spread by mere touch or physical contact; it spreads only through body fluids. It is, hence, imperative, for the physical and psychological well-being, that the HIV/AIDS infected persons are not isolated from family and society. There is always a time-lag between the infection and appearance of AIDS symptoms. This period may vary from a few months to many years (usually 5-10 years).

C. Mechanism of infection

1. 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.
2. This viral DNA gets incorporated into host cell's DNA and directs the infected cells to produce virus particles.
3. The macrophages continue to produce virus and in this way acts like a HIV factory. Simultaneously, HIV enters into helper T-lymphocytes (T_H), replicates and produce progeny viruses.
4. 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.
5. 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 that could have been otherwise overcome such as those due to bacteria especially *Mycobacterium*, viruses, fungi and even parasites like *Toxoplasma.* The patient becomes so immune deficient that he/she is unable to protect himself/herself against these infections.



Replication of retrovirus

Resonate the Concept

1. **Asymptomatic phase**
   There is a time lag between the infection and appearance of AIDS symptoms this period may vary from a few months to many years (usually 5 to 10 years) this is called asymptomatic phase. There is no antibody production in initial (2-12 weeks) so AIDS cannot be detected in this period by ELISA test. This period is called as **window period.**
   But infectivity of patient or activeness of virus is maximum in this period and as the number of helper T-cells start decreasing in human blood, the body of host passes through different phases.
2. **AIDS related complex (ARC)**
   Second stage in development of AIDS characterised by swollen lymph nodes, bouts of fever, repeated episodes of diarrhoea, weight loss (more than 10 % of body weight), prolonged cough etc.
   Patient's immune system starts deteriorating and when T-lymphocytes or CD_4cell count becomes less than "200×10^6/ litre" (normal CD_4 count > 900×10^6 / litre) then this condition leads to full blown AIDS.
3. **Full blown AIDS**
   Due to very low level of immunity patient acquires those opportunistic infections that could have been otherwise overcome by normal defense mechanism of body. Some of the opportunistic infections are tuberculosis by *Mycobacterium avium,* candidiasis of mouth and oesophagus by *Candida albicans,* pneumonia by fungus *Pnemocystiscarinii,* sores by Herpes simplex virus-II, cancer of skin and lymphnodes (Kaposi' sarcoma), HIV acts as an oncovirus, dysentery by cryptosporidium, AIDS dementia (memory loss) by Herpes Zoster Virus, encephalitis by *Toxoplasma gondii.*

D. Investigation:

1. **Screening test:** A widely used diagnostic test for AIDS is **enzyme linked immuno-sorbent assay** (ELISA).
2. **Confirmatory test:** Western blot test which detects antibodies, in patient's serum.

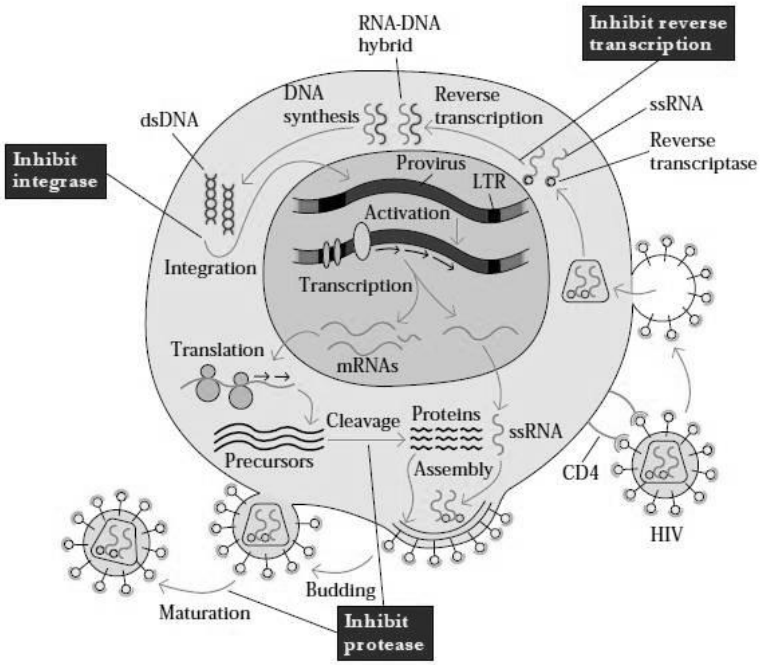
E. Treatment

Treatment of AIDS with anti-retroviral drugs is only partially effective. They can only prolong the life of the patient but cannot prevent death, which is inevitable.

i. Reverse transcriptase inhibitor = Zidovudine (previously called AZT- a nucleoside analog), Stavudine, Trizivir, DDI (Didexymidine), Foscarnet, etc.

ii. Protease inhibitor - Ritonavir, Nelfinavir, SequinaviretcIntegrase inhibitor

iii. HAART (highly active anti-retroviral therapy) - Protease inhibitors has proven effective when used in conjunction with AZT and/or other nucleoside analogs. Current treatment for AIDS is a combination therapy; using regimens designated HAART (highly active anti-retroviral therapy). In most cases, this combines the use of two nucleoside analogs and one protease inhibitor. The combination strategy appears to overcome the ability of the virus to rapidly produce mutants that are drug resistant.



F. Prevention of AIDS

As AIDS has no cure, prevention is the best option. Moreover, HIV infection, more often, spreads due to conscious behavior patterns and is not something that happens inadvertently, like pneumonia or typhoid. Of course, infection in blood transfusion patients, new-born (from mother) etc., may take place due to poor monitoring. The only excuse may be ignorance and it has been rightly said – “don’t die of ignorance”.

In our country the National AIDS Control Organization (NACO) and other non-governmental organization (NGOs) are doing a lot to educate people about AIDS. WHO has started a number of programmes to prevent the spreading of HIV infection? Making blood (from blood banks) safe from HIV, ensuring the use of only disposable needles and syringes in public and private hospitals and clinics, free distribution of condoms, controlling drug abuse, advocating safe sex and promoting regular check-ups for HIV in susceptible populations, are some such steps taken up.

Infection with HIV or having AIDS is something that should not be hidden – since then, the infection may spread to many more people. HIV/AIDS-infected people need help and sympathy instead of being shunned by society. Unless society recognises it as a problem to be dealt with in a collective manner – the chances of wider spread of the disease increase manifold. It is a malady that can only be tackled, by the society and medical fraternity acting together, to prevent the spread of the disease.

CANCER

- **Cancer** is one of the most dreaded diseases of human beings and is a major cause of death all over the globe. More than a million Indians suffer from cancer and a large number of them die from it annually. The mechanisms that underlie development of cancer or oncogenic transformation of cells, its treatment and control have been some of the most intense areas of research in biology and medicine.
- **Types of Tumors-**
  - **(A) Benign Tumor-** A benign tumor, such as a common skin wart, remains confined to its original location, neither invading surrounding normal tissue nor spreading to distant body sites, so it is not so harmful. Benign tumors can usually be removed surgically.
  - **(B) Malignant Tumor-** A malignant tumor is capable of both invading surrounding normal tissue and spreading throughout the body via the circulatory or lymphatic systems (**metastasis**). **Only malignant tumors are properly referred to as cancers**, and it is their ability to invade and metastasize that makes cancer so dangerous. The cancerous cells continue to divide and form new masses of cells called **neoplasm**. The spread of malignant tumors to distant body sites frequently makes the surgical treatment inefficient.
- **Types of Cancer-**
  - **(A) Carcinomas**, which include **approximately 90% of human cancers**, are malignancies of **epithelial cells**. Eg. Breast cancer (most common cancer in women), lung cancer (most common cancer in men) and cancer of stomach.
  - **(B) Sarcomas**, which are **rare in humans**, are solid tumors of **connective tissues**, such as muscle, bone, cartilage, and fibrous tissue.
  - **(C) Leukemias and lymphomas**, which account for approximately 7% of human malignancies, arise from **the blood-forming cells** and from **cells of the immune system**, respectively.
- **Differences between Normal and Cancerous cells-**
  - **(A)** A primary distinction between cancer cells and normal cells in culture is that normal cells display **density-dependent inhibition of cell proliferation**. Normal cells proliferate until they reach a finite cell density, which is determined in part by the availability of growth factors added to the culture medium (usually in the form of serum). They then cease proliferating and become quiescent (arrested in the G_0 stage of the cell cycle). The proliferation of most cancer cells, however, is not sensitive to density-dependent inhibition (**Contact inhibition**). Rather than responding to the signals that cause normal cells to cease proliferation and enter G_0, tumor cells generally continue growing to high cell densities in culture, mimicking their uncontrolled proliferation in vivo.
  - **(B)** Cancerous cells have **reduced requirements for extracellular growth factors**.
  - **(C) Most cancer cells are less adhesive than normal cells**, often as a result of reduced expression of cell surface adhesion molecules. For example, loss of E-cadherin, the principal adhesion molecule of epithelial cells, is important in the development of carcinomas (epithelial carcinomas).
  - **(D)** Cancerous cells generally secrete **proteases that digest extracellular matrix components, allowing the cancer cells to invade adjacent normal tissues**. Secretion of collagenase, for

example, appears to be an important determinant of the ability of carcinomas to digest and penetrate through basal lamina to invade underlying connective tissue.

(E) Cancerous cells secrete **angiogenesis factors** that promote the formation of new blood vessels.

(F) Another general characteristic of most cancer cells is that they **fail to differentiate normally**. Such defective differentiation is closely coupled to abnormal proliferation since, most fully differentiated cells cease cell division. Rather than carrying out their normal differentiation program, cancer cells are usually blocked at an early stage of differentiation, consistent with their continued active proliferation.

(G) Programmed cell death (apoptosis) is an integral part of the differentiation program of many cell types, including blood cells. Many cancer cells fail to undergo apoptosis and therefore exhibit increased life spans compared to their normal counterparts.

(H) Normal Somatic cells divide by mitosis, while **cancerous cells divide by amitosis.**

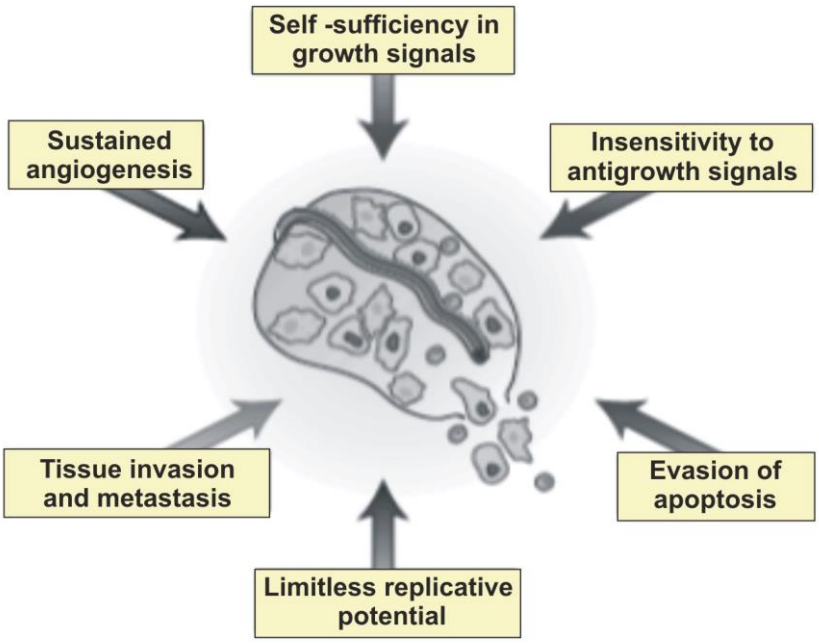
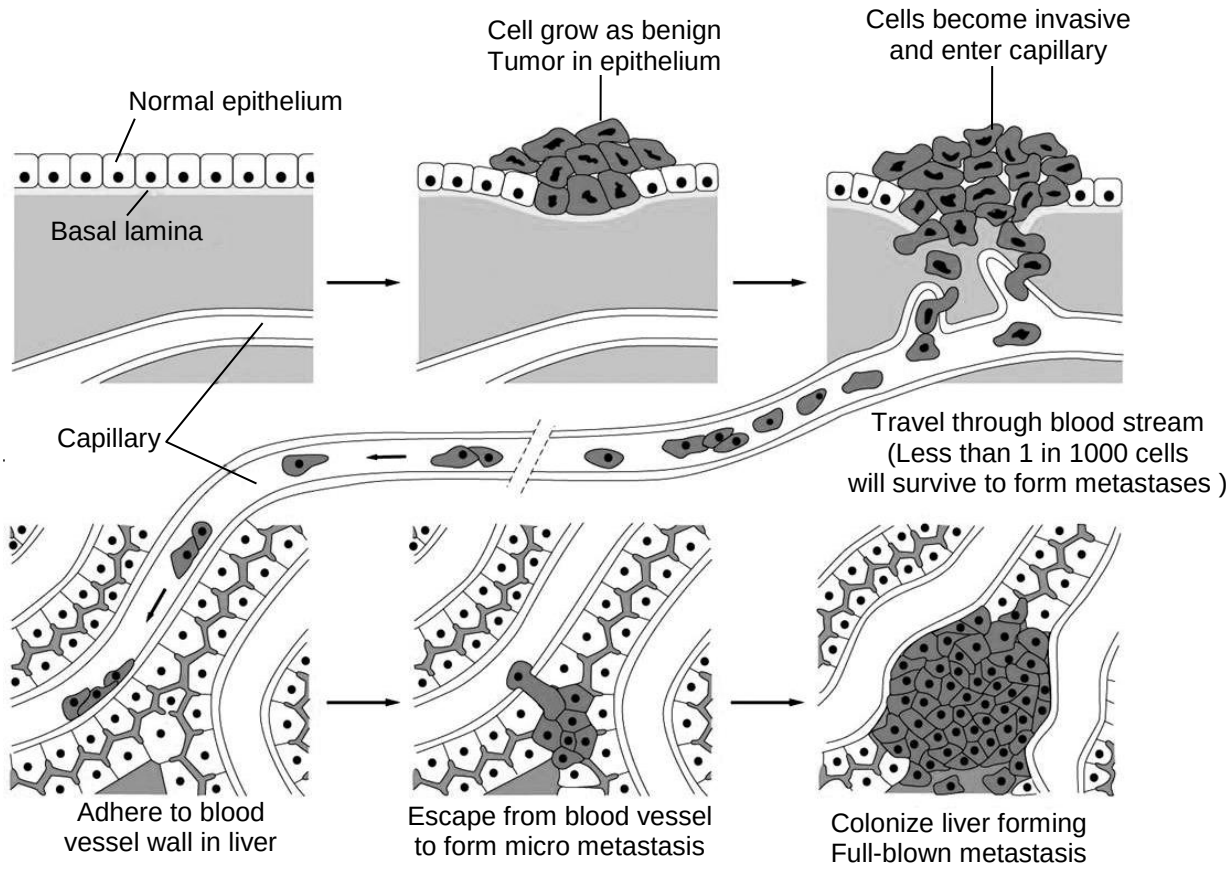


Figure- Overview of changes in cells that cause cancer- During carcinogenesis, six fundamental cellular properties are altered, as shown here, to give rise to the complete, most destructive cancer phenotype. Less dangerous tumors arise when only some of these changes occur. In this chapter we examine the genetic changes that result in these altered cellular properties.



- **Causes of Cancer-**

(A) Physical Agents-

Ionizing radiations- X rays and gamma rays.

Non-ionizing radiations- UV radiations.

These radiations cause damage to DNA, which result in cancer.

(B) Chemical Agents-

Carcinogen	Target tissue
Soot	Lungs and Skin
Coal tar (3-4- benzopyrene)	Lungs and Skin
Cigarette smoke (N-nitrosyldimethylene)	Lungs
Cadmium oxide	Prostate gland
Aflatoxin (mould metabolite)	Liver
Mustard gas	Lungs
Vinyl Chloride	Liver
Asbestos	Lungs
Di-ethyl stiboesterol (DES)	Vagina

The **Ames test** is a widely employed method that uses bacteria to test whether a given chemical can cause mutations in the DNA of the test organism. More formally, it is a biological assay to assess the mutagenic potential of chemical compounds.

(C) Biological Agents- Cancer causing viruses are called oncogenic viruses, which have viral oncogene which can cause cancer. **Viral oncogenes were first discovered in RSV (Rous Sarcoma Virus)**, which transforms chicken embryo fibroblasts in culture and induces large sarcomas within 1 to 2 weeks after inoculation into chickens.

Virus	Cancer
hepatitis B and C viruses	liver cancer
Papillomaviruses	cervical cancers
Epstein-Barr virus	Burkitt's lymphoma and nasopharyngeal carcinoma
HIV	Kaposi's sarcoma
human T-cell lymphotropic virus	adult T-cell leukemia

More than 40 different highly oncogenic retroviruses have been isolated from a variety of animals, including chickens, turkeys, mice, rats, cats, and monkeys. All of these viruses, like RSV, contain at least one oncogene (in some cases two) that is not required for virus replication but is responsible for cell transformation.

Now the question arises that why viruses did evolved oncogenes? One hypothesis to the answer the question is that the **retroviral oncogenes are derived from genes of the host cell**, and that occasionally such a host cell gene becomes incorporated into a viral genome, yielding a new, highly oncogenic virus as the product of a virus-host recombination event. The critical prediction of this hypothesis was that normal cells contain genes that are closely related to the retroviral oncogenes. This was definitively demonstrated in **1976 by Harold Varmus, J. Michael Bishop**, and their colleagues, who showed that a cDNA probe for the src oncogene of RSV hybridized to closely related sequences in the DNA of normal chicken cells.

Cellular Oncogene (c-onc) and Tumor Suppressor gene-

Proto-oncogenes are normal cellular genes that become oncogenes when mutated. Some proto-oncogenes encode receptors for growth factors, and others encode proteins involved in signal transduction that act after growth factor receptors. If a receptor for a growth factor becomes mutated such that it is permanently “on,” the cell is no longer dependent on the presence of the growth factor for cell division. **Genes coding for PDGF (platelet derived growth factor) and EGF (epidermal growth factor) receptors both fall into the category of proto-oncogenes**. Only one copy of a proto-oncogene needs to undergo this mutation for uncontrolled division to take place; thus, this change acts like a dominant mutation. The number of proto-oncogenes identified has grown to more than 50 over the years.

In contrast to proto-oncogene and oncogene proteins, the proteins encoded by most **tumor suppressor genes** inhibit cell proliferation or survival. **The first tumor suppressor gene (Rb gene)** was identified by studies of retinoblastoma, a rare childhood eye tumor.

Provided that the disease is detected early, retinoblastoma can be successfully treated and many patients survive to have families. Consequently, it was recognized that some cases of retinoblastoma are inherited. In these cases, approximately 50% of the children of an affected parent develop retinoblastoma, consistent with Mendelian transmission of a single dominant gene that confers susceptibility to tumor development. The **second tumor suppressor gene to have been identified is p53**, which is frequently inactivated in a wide variety of human cancers.

The p53 protein coded by p53 gene acts as G_1 checkpoint if cell division. It checks DNA for any abnormality, if detected then cell is not allowed to divide, firstly repair in DNA is attempted, if no repair is possible then apoptosis factors are activated which cause cell death. In order to ensure survival of a cell with faulty DNA, p53 has to be deactivated.

Tumor suppressor genes represent the opposite side of cell growth control, normally acting to inhibit cell proliferation and tumor development. In all tumors, these genes are lost or inactivated, thereby removing negative regulators of cell proliferation and contributing to the abnormal proliferation of tumor cells.

Tumor Promoters-

They increase cell division and so they induce the outgrowth of a proliferative cell population during early stages of tumor development. Hormones, particularly **estrogens**, are important as tumor promoters in the development of some human cancers. The proliferation of cells of the uterine endometrium, for example, is stimulated by estrogen, and exposure to excess estrogen significantly increases the likelihood that a woman will develop endometrial cancer. The risk of endometrial cancer is therefore substantially increased by long-term postmenopausal estrogen replacement therapy with high doses of estrogen alone.

Cancer detection and Diagnosis-

Biopsy and histopathological studies of suspected tissue.
Blood cell count and bone marrow tests for leukemia.
CT scan (X-ray is used), MRI (strong magnetic field is used).
Antibody against specific cancers

Treatment of cancer-

1. **Surgery**
2. **Radiotherapy**- Radiation therapy uses high-energy particles or waves, such as x-rays, gamma rays, electron beams, or protons, to destroy or damage cancer cells. Other names for radiation therapy are radiotherapy, irradiation, or x-ray therapy. Radiation therapy is one of the most common treatments for cancer. Cancerous cells are destroyed as they are rapidly dividing and immature.
3. **Chemotherapy- Vincristine and vinblastine** obtained from ***Catharanthus roseus*** are used for treatment of leukaemia.
4. Combined therapy
5. Immunotherapy- biological response modifiers as **α-interferon** and monoclonal antibodies as **Herceptin** for breast cancer and stomach cancer.

Test your Resonance with concept

1. AIDS is a
(1) Cancer (2) Viral disease (3) Bacterial disease (4) Deficiency disease

2. AIDS day is
(1) June 1 (2) May 1 (3) December 1 (4) December 20

3. Choose the wrong statement regarding AIDS
(1) AIDS is an immunodeficiency disease
(2) It is caused by a retrovirus, HIV
(3) HIV selectively infects and kill B-lymphocytes
(4) Retroviruses have RNA genomes that replicate via DNA intermediate

4. Which disease is caused by activation of oncogenes?
(1) Cholera (2) Cancer (3) T.B. (4) Viral flu

5. Identify the wrong statement/s
A. The tumor of haematopoietic cells is called leukemia
B. Cancer arising from the epithelial tissues of internal organs and glands is referred as melanoma
C. Sarcoma is a type of cancer where bone and cartilages are involved
D. Only benign tumors are called as true cancer or neoplasm
(1) A and B only (2) B and Conly (3) B and D only (4) A and C only

ANSWERS

1. (2) **2.** (3) **3.** (3) **4.** (2) **5.** (3)

DRUGS AND ALCOHOL ABUSE

It has been observed that the use of drugs has increased especially among youth. This is a matter of concern as it could cause many harmful effects. Proper education and guidance would enable youth to safeguard themselves against dangerous behavioural patterns and follow healthy life styles.

Major Categories of Psychoactive Drugs, their Effects and Clinical Uses

Type of Drug	Examples	Effects	Clinical Uses
Sedatives and tranquillisers (depressants)	Barbiturates Benzodiazepines *(e.g.,* Valium)	Depress brain activity and produce feelings of calmness, relaxation, drowsiness and deep sleep (high doses)	Hypnotic, antianxiety
Opiate narcotics	Opium, morphine, heroin, pethidine, methadone	Suppress brain function, relieve intense pain (physical and mental), produce temporary euphoria	Analgesic
Stimulants	Caffeine (very mild), amphetamines (including dexamphetamine), cocaine and its derivative Novacaine	Stimulate the nervous system; make a person more wakeful, increase alertness and activity, produce excitement	Attention deficit, Narcolepsy, weight control
Hallucinogens	LSD, mescaline, psilocybin, charas, hashish, marijuana (bhang)	Alter thoughts; feelings and perceptions; hallucinations	None

The drugs, which are commonly abused are **opioids, cannabinoids and coca alkaloids.**

(i) Opioids:

These drugs bind to specific receptors present in our central nervous system and gastrointestinal tract and relieve pain, so they are also called as analgesic (pain killers).

Morphine is extracted from the latex of poppy plant *Papaver somniferum.* It is very effective sedative and painkiller and is very useful for patients who have undergone surgery.

Heroine is obtained by acetylation of morphine (diacetyl morphine) commonly called as **smack** which is white, odourless and bitter crystalline compound. Generally, it is taken by snorting or injection. It is a depressant and slows down body functions.

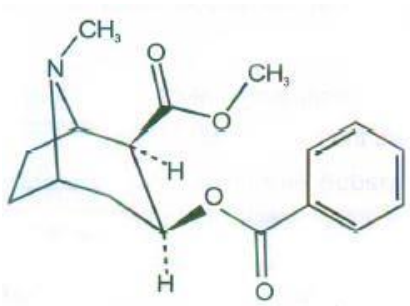


Fig. : Chemical structure of Morphine

Fig. : *Opium poppy*

(ii) Cannabinoids:

These are a group of chemicals, which interact with cannabinoid receptors present principally in brain.

- Natural cannabinoids are obtained from the inflorescences of the plant *Cannabis sativa.*
- The flower tops, leaves and the resin of *Cannabis* plant are used in various combinations to produce marijuana, hashish, charas and ganja.
- Generally taken by inhalation and oral ingestion and are known for their effects on cardiovascular system of body.
- These days cannabinoids are also being abused by some sports persons.

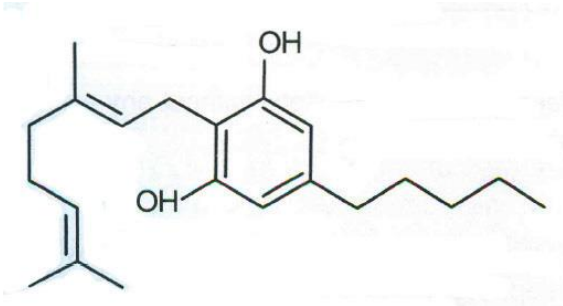


Fig. : Skeletal structure of cannabinoid molecule

Fig. : Leaves of *Cannabis sativa*

(iii) Cocaine:

Coca alkaloid or cocaine is obtained from coca plant, *Erythroxylum coca,* a native to South America.

- Cocaine, commonly called **coke or crack** is usually snorted.
- It interferes with the transport of the neuro-transmitter **dopamine.**
- It has a potent stimulating action on central nervous system, producing a sense of euphoria (feeling of well being) and increased energy.
- Excessive dosage of cocaine causes hallucinations.

(iv) Seeds of *Datura* and aerial parts of *Atropa beladona* are misused for their hallucinogenic properties.

Fig. : Flowering branch of *Datura*

(v) Tobacco addiction:

Tobacco has been used by human being for more than 400 years

- It is smoked, chewed or snuffed.
- Tobacco contains large number of chemical substances including **nicotine** (an alkaloid).
- Nicotine stimulates adrenal gland to release **adrenaline** and **non-adrenaline** into blood circulation both of which increase blood pressure and heart rate.
- **Tobacco chewing** is associated with increased risk of oral cavity cancer.
- Smoking increases **carbon monoxide (CO)** content in blood and reduces the concentration haembound oxygen so it causes oxygen deficiency in body and is associated with increase incidence of cancer of lungs, urinary bladder and throat, bronchitis, emphysema, coronary heart diseases, gastric ulcer etc.

  Smoking is very prevalent in society, both among youth and the old. There is a need to spread awareness about its addictive nature and addicts must be given proper medical help an counseling. The cigarette packing also carriers a warning "Smoking is injurious to health".

Resonate the Concept

Hallucinogens / Psychedelic drugs

These drugs change one's behaviour, thoughts, feelings and perceptions without any actual sensory stimulus. **e.g.** LSD (Lysergic acid and diethyl amides) cannabinoids etc.

Sedatives

These are drugs that reduces excitement by depressing the CNS activity and lowers the physiological or functional activity leading to drowsiness or sleep. **e.g. barbiturates, benzodiazepines** etc. These drugs are normally used as medicine to help patients cope with mental mental illnesses like depression, insomnia etc. and are often abused by drug addicts.

Stimulant

These drugs stimulate the nervous system, make a person more wakeful, alert active and cause excitement. **e.g.** Caffine, cocaine, amphetamines.

Majority of drugs are obtained from flowering plants. Some drugs like **LSD** (Lysergic acid diethyl amides) is an extract of fruiting body of fungus *Claviceps purpurea,* ergot that is a parasite on rye plant.

Several plants, fruits and seeds having hallucinogenic properties have been used for hundreds of years in folk medicine, religious ceremonies and rituals all over the world.

Adolescence and Drug/ Alcohol Abuse

Adolescence is the period of rapid growth (physical, mental and psychological development) and is a bridge linking childhood with adulthood (the period between 12-18 years). It is also marked by several biological and behavioural changes.

Curiosity, excitement, need for adventure and experimentation are common causes which motivates youngsters towards drug and alcohol. The first use of drugs or alcohol may be due to curiosity or experimentation but later on child starts using it to escape facing problems such as academics or examinations etc. The thought amongst youngsters that it is 'cool' or progressive to smoke, use drugs or alcohol is also a major cause for youth to start these habits. Television, movies, newspapers, internet etc.

Also promote this perception. Unstable or unsupportive family structures have been seen to be associated with drug and alcohol abuse among adolescents.

Alcohol Abuse

The use of alcohol during adolescence may also have long term effects. It could lead to heavy drinking in adulthood. The chronic use of alcohol damages the nervous system and liver (Liver cirrhosis).

Interaction of Alcohol and other Substances of Abuse with some Common Drugs

Drugs	Effects
Alcohol and other depressants, e.g., *Barbiturates*	Dramatically increased depressant effect
Alcohol + Antihistamines	Marked drowsiness (normally little or no sedative effect)
Alcohol + Benzodiazepines	Rapid increase in sedative effect; often dramatic
Alcohol + Marijuana or Hashish	Decreased coordination, increased reaction time, impaired judgement
Alcohol + Aspirin	Increased risk of damage to gastric mucosa
Benzodiazopines + Barbiturates	Increased sedation
Amphetamine + Insulin	Decreased insulin effect
Nicotine + Cocaine	Increased cardiovascular effects
Cocaine + Antidepressants	Hypertension

Addiction and Dependence

The drugs are normally used as medicines to help the patients cope with illnesses. But when these drugs are taken for purpose other than their normal clinical use, it is called drug abuse / addiction. Addiction is a habitual, physiological and psychological dependence on a substance or practice which is beyond voluntary control. A person who is habituated to a substance/drug is called an addict. Repeated use of drugs increases the tolerance level of the receptors present in our body, consequently the receptors respond only to higher doses of drugs or alcohol leading to greater intake. So addiction is a psychological attachment to certain effects such as euphoria and a temporary feeling of well being associated with drugs and alcohol. In the absence of any guidance or counselling, the person gets addicted and becomes dependent on drug use.

WHO (1964) has introduced the term drug dependence in place of drug addiction.

Dependence is the tendency of the drug addict's body to manifest a characteristic and unpleasant withdrawal syndrome symptoms, if regular dose of drugs/alcohol is discontinued. This is characterised by anxiety, shakiness, nausea and sweating, which may be relieved when drug use is resumed.

In some cases, withdrawal symptoms can be severe and even life threatening and the person may need medical supervision.

Test your Resonance with concept

1. Smoking addiction is harmful because it produces polycyclic aromatic hydrocarbons, which cause

(1) Reduction in oxygen transport (2) Increase in blood pressure

(3) Cancer (4) Retardation of growth of foetus

2. A person who is addict of alcohol gets his liver destroyed because

(1) Liver stores excess of glycogen (2) Liver stores excess of starch

(3) Liver stores excess of protein (4) Liver stores excess of fat

3. Which of following is/are hallucinogen/s?

(1) Lysergic acid diethylamide (2) Psilocybin

(3) Mescaline (4) All of these

4. 'Marijuana' is extracted from

(1) Dried leaves and flowers of hemp plant (2) Ergot fungus

(3) Hemp plant (*Cannabis sativa*) (4) Cocoa plant

5. Amnesia is

(1) loss of memory (2) loss of filtration capacity of kidney

(3) loss of appetite (4) loss of blood

ANSWERS

1. (3) **2.** (4) **3.** (4) **4.** (3) **5.** (1)