

UNIT 4

Human Diseases

Diabetes:

1)Definition: Diabetes is the condition in which the body does not properly process food for use as energy. Most of the food we eat is turned into glucose, or sugar, for our bodies to use for energy. The pancreas, an organ that lies near the stomach, makes a hormone called insulin to help glucose get into the cells of our bodies. When you have diabetes, your body either doesn't make enough insulin or can't use its own insulin as well as it should. This causes sugars to build up in your blood. This is why many people refer to diabetes as "sugar."

2) Causes: Type 1 diabetes causes

Type 1 diabetes is caused by the immune system destroying the cells in the pancreas that make insulin. This causes diabetes by leaving the body without enough insulin to function normally. There is no specific diabetes causes, but the following triggers may be involved:

- Viral or bacterial infection
- Chemical toxins within food
- Unidentified component causing autoimmune reaction

Underlying genetic disposition may also be a type 1 diabetes cause.

Type 2 diabetes causes are usually multifactorial – more than one diabetes cause is involved. There are a variety of risk factors for type 2 diabetes, any or all of which increase the chances of developing the condition. These include:

- Obesity
- Living a sedentary lifestyle
- Increasing age
- Bad diet

3)Symptoms:

- Frequent urination
- Excessive thirst
- Unexplained weight loss
- Extreme hunger 1
- Sudden vision changes
- Tingling or numbness in hands or feet
- Feeling very tired much of the time
- Very dry skin
- Sores that are slow to heal
- More infections than usual

Nausea, vomiting, or stomach pains may accompany some of these symptoms in the abrupt onset of insulin-dependent diabetes, now called Type 1 diabetes

- 4)Diagnosis:** 1. Fasting blood glucose level.
2. A1C.
3. Oral glucose tolerance test (OGTT).
4. Random blood glucose test.

5)Treatment and Prevention: Lifestyle changes, such as losing weight, eating healthy and increasing physical activity, can dramatically reduce the progression of Type 2 diabetes and may control Type 1 diabetes. These lifestyle changes can also help minimize other risk factors such as high blood pressure and blood cholesterol, which can have a negative impact on people with diabetes.

Cancer:

1)Definition: Cancer is a group of diseases involving abnormal cell growth with the potential to invade or spread to other parts of the body. These contrast with benign tumors, which do not spread. Possible signs and symptoms include a lump, abnormal bleeding, prolonged cough, unexplained weight loss, and a change in bowel movements.

2) Causes: Cancer is caused by changes (mutations) to the DNA within cells. The DNA inside a cell is packaged into a large number of individual genes, each of which contains a set of instructions telling the cell what functions to perform, as well as how to grow and divide.

3) Symptoms:

1. Fatigue
2. Lump or area of thickening that can be felt under the skin
3. Weight changes, including unintended loss or gain
4. Skin changes, such as yellowing, darkening or redness of the skin, sores that won't heal, or changes to existing moles
5. Changes in bowel or bladder habits
6. Persistent cough or trouble breathing
7. Difficulty swallowing
8. Hoarseness
9. Persistent indigestion or discomfort after eating
10. Persistent, unexplained muscle or joint pain
11. Persistent, unexplained fevers or night sweats
12. Unexplained bleeding or bruising

4) Diagnosis: Cancer diagnosis begins with a thorough physical exam and a complete medical history. Laboratory studies of blood, urine, and stool can detect abnormalities that may indicate cancer. When a tumor is suspected, imaging tests such as X-rays, computed tomography (CT), magnetic resonance imaging (MRI), ultrasound, and fiber-optic endoscopy examinations help doctors determine the cancer's location and size.

5) Treatment:

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1. [Surgery](#)
 2. [Radiation Therapy](#)
 3. [Chemotherapy](#)
 4. [Immunotherapy to Treat Cancer](#)
 5. [Targeted Therapy](#)
 6. [Hormone Therapy](#)
 7. [Stem Cell Transplant](#)
 8. [Precision Medicine](#)

6) Prevention:

1. Stop smoking.
2. Avoid excessive sun exposure.
3. Eat a healthy diet.
4. Exercise most days of the week.
5. Maintain a healthy weight..
6. Schedule cancer screening exams.
7. Ask your doctor about immunizations.

Hypertension:

1) Definition: Hypertension is high blood pressure. Blood pressure is the force of blood pushing against the walls of arteries as it flows through them. Arteries are the blood vessels that carry oxygenated blood from the heart to the body's tissues.

2) Causes:

1. age over 60
2. race
3. heredity
4. salt sensitivity

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- 5. obesity
 - 6. inactive lifestyle
 - 7. heavy alcohol consumption
 - 8. use of oral contraceptives

3) Symptoms:

Symptoms of complicated hypertension (high blood pressure) can include

- 1. dizziness,
- 2. shortness of breath,
- 3. headache, and
- 4. blurred vision.

Other possible symptoms and signs are

- 1. nosebleeds,
- 2. blood in the urine,
- 3. fatigue,
- 4. chest pain, and
- 5. a pounding sensation in the neck, chest, or ears.
- 6. nausea,
- 7. severe headache,
- 8. blurred vision, and
- 9. dizziness.

4) Diagnosis:

1. medical and family history
2. physical examination
3. ophthalmoscopy: Examination of the blood vessels in the eye
4. chest x ray
5. electrocardiograph (ECG)
6. blood and urine tests.

5)Treatment: To lower blood pressure to levels that will prevent heart disease and other complications of hypertension.

6)Prevention:

1. reducing salt intake
2. reducing fat intake
3. losing weight
4. getting regular exercise
5. quitting smoking
6. reducing alcohol consumption
7. managing stress

Influenza:

1)Definition: Influenza virus has three serotypes: Type A Type B & Type C .Influenza virus Type A and Type B are morphologically similar , but influenza virus Type C differs from them in certain respects, particularly in having only a single glycoprotein spike and RNA genome segmented into 7 pieces.

2)Causes: The flu is caused by influenza viruses that infect the nose, throat, and lungs. These viruses spread when people with flu cough, sneeze or talk, sending droplets with the virus into the air and potentially into the mouths or noses of people who are nearby. You can also get flu by touching a surface or object that has flu virus on it and then touching your own mouth, eyes or nose.

3)Symptoms:

1. runny or blocked nose
2. a sore throat
3. a cough

4. high temperature
5. cold sweats and shivers
6. headache
7. aching joints and limbs
8. fatigue, feeling exhausted

There may also be gastrointestinal symptoms, such as nausea, vomiting, and diarrhea. These are more common in children than in adults.

4)Diagnosis:

1. Antigen Detection
2. Isolation of the virus
3. Polymerase chain reaction (PCR)
4. Serology

5)Treatment: Amantadine and the Remantadine are useful in the treatment of Influenza. They cause symptomatic improvement but viral shedding and antibody response are not affected.

Zanamivir and Oseltamivir (Tamiflu),new drugs that have blocked viral Neuraminidase have been found effective in the treatment and prevention of Influenza . Zanamivir is taken by inhalation .In contrast , Oseltamivir is well observed when administered orally.

6)Prevention: Vaccination is a primary means of prevention of Influenza but the major difficulty in immunoprophylaxis is the frequent change in the antigenic structure of Influenza virus .Vaccines cannot be made in bulk and stockpiled, as the appearance of a new variant strain will make the old vaccine useless. The most important indication for immunoprophylaxis access is when a pandemic is threatened by a new virus Vaccines are of two types:

1. Inactivated Vaccines
2. Live Attenuated Vaccines

Aids:

1)Definition: HIV is a spherical enveloped virus about 90-120 nm in diameter. It contains two identical copies of single stranded, positive sense RNA genome .In Association with viral RNA is the reverse transcriptase enzyme .The virus core is surrounded by a nucleocapsid composed of protein. The virus contains in lipoprotein envelope ,which consists of liquid derived from the host cell membrane and glycoproteins which are virus coded.

2)Causes:

1. Sexual Contact
2. Parental Transmission
3. Perinatal Transmission

3)Symptoms:

- rapid weight loss.
- severe night sweats.
- continual fevers.
- extreme fatigue.
- unexplained tiredness.
- prolonged swelling of lymph glands in the groin, neck, or armpits.
- bouts of diarrhea lasting longer than a week.
- sores located near the mouth, genitals

4)Diagnosis: Blood tests are the most common way to **diagnose** the human immunodeficiency virus (**HIV**), the virus that causes acquired immunodeficiency syndrome (**AIDS**). These tests look for antibodies to the virus that are present in the blood of infected individuals. People exposed to the virus should get tested immediately.

5)Treatment: There's no cure for **HIV/AIDS**, but many different drugs are available to control the virus. Such **treatment** is called antiretroviral therapy, or ART. Each class of drug blocks the virus in

different ways. ART is now recommended for everyone, regardless of CD4 T cell counts.

6)Prevention: There's no vaccine to prevent **HIV** infection and no cure for **AIDS**.

Hepatitis

1)Definition:

i)Hepatitis A Virus: HAV is 27 nm non-enveloped single stranded RNA virus with an isosahedral symmetry. It belongs to the picornavirus family. It is originally designed as 'enterovirus 72'.It is now recognized as the prototype of a genus Hepatovirus. Only one serotype of the virus exists.

ii)Hepatitis B Virus : HBV belongs to the family Hepadnaviridae which also includes certain viruses causing infection to animals. It differs from Hepatitis A in various aspects. It is a complex 42 nm double shelled particle. The outer surface or envelope of virus contains hepatitis B surface antigens.

iii)Hepatitis C virus : HCV belongs to the family Flaviviridae. It is 50-60nm virus with a linear single stranded RNA of positive polarity, enclosed within a core and surrounded by an envelope, carrying glycoprotein spikes.

2)Causes:

i) Hepatitis A is a liver **disease caused** by the **hepatitis A virus (HAV)**. The **virus** is primarily spread when an uninfected (and unvaccinated) person ingests food or water that is contaminated with the faeces of an infected person.

ii) Hepatitis B infection is **caused** by the **hepatitis B** virus (**HBV**). The virus is passed from person to person through blood, semen or other body fluids.

iii)Hepatitis C is an inflammation of the liver due to a viral infection. A person contracts the **hepatitis C** virus by coming into contact with infectious fluids and secretions from someone else who is already infected with **hepatitis C** virus.

3)Symptoms:

i)Symptoms By Hepatitis A

-
1. Fatigue.
 2. Sudden nausea and vomiting.
 3. Abdominal pain or discomfort, especially on the upper right side beneath your lower ribs (by your liver)
 4. Clay-colored bowel movements.
 5. Loss of appetite.
 6. Low-grade fever.
 7. Dark urine.
 8. Joint pain.

ii) Symptoms By Hepatitis B

1. Jaundice.- Your skin or the whites of the eyes turn yellow, and your pee turns brown or orange.)
2. Light-colored poop.
3. Fever.
4. Fatigue that persists for weeks or months.
5. Stomach trouble like loss of appetite, nausea, and vomiting.
6. Belly pain.

iii) Symptoms By Hepatitis C

1. Feeling very tired.
2. Sore muscles.
3. Joint pain.
4. Fever.
5. Nausea or poor appetite.
6. Stomach pain.
7. Itchy skin.
8. Dark urine.

4) Diagnosis:

i) For Hepatitis A:

1. Demonstration of Virus
2. Detection of Antibody

3. Biochemical tests

ii)For Hepatitis B: Tests that can help **diagnose hepatitis B** or its complications are: Blood tests. Blood tests can detect signs of the **hepatitis B** virus in your body and tell your doctor whether it's acute or chronic. A simple blood test can also determine if you're immune to the condition.

iii)For Hepatitis C: HCV Antibody Testing: Diagnosing **hepatitis C** begins with an antibody test. Antibodies to **HCV** can be detected in the blood, usually within two or three months after the virus enters the body. If a person is positive for **HCV** antibodies, he or she has been exposed to the virus in the past.

5)Treatment:

i) For Hepatitis A: Treatment is symptomatic. No specific antiviral therapy is available.

ii)For Hepatitis B: No specific antiviral treatment is available . Interferon- α aloneor in combination with other antiviral agents (e.g. lamivudine,telvudine and entecavir) has been beneficial in some chronic hepatitis cases.

iii)For Hepatitis C: Treatment with Interferon- α , either alone or in combination with antiviral agents such as ribavirin has been found to be useful in some cases.

6)Prevention:

i) For Hepatitis A: wash your hands thoroughly after using the restroom and when you come in contact with an infected person's blood, stools, or other bodily fluid. Avoid unclean food and water.

ii)For Hepatitis B: **Hepatitis B** infection can be **prevented** by getting vaccine and HBIG (**hepatitis B** immune globulin) soon after coming into contact with the virus.

iii)For Hepatitis C: Unfortunately, there is no vaccine to prevent **hepatitis C**. To reduce your risk of getting **hepatitis C**: Injection drug use is the most common way people get **hepatitis C**. Avoid injecting drugs to reduce your risk. If you do inject drugs, use sterile injection equipment. Avoid reusing or sharing.

IMMUNITY

The term 'immunity' is defined as resistance exhibited by the host against any foreign antigen including microorganisms. This resistance plays a major role in prevention of infectious diseases. Immunity may be *innate or acquired.*

I. INNATE IMMUNITY

It is the resistance which individual possesses by birth. It is by virtue of his genetic and constitutional make-up. It does not depend on prior contact with foreign antigen. It may be nonspecific, when there is resistance to infections in general, or specific when resistance to a particular pathogen is concerned.

A. Types of Innate Immunity

1. Species Immunity

It refers to the resistance to a pathogen, shown by all members of a particular species e.g. *B. anthracis* infects human beings but not chickens. The mechanism of such type of immunity is not clearly understood. The physiological and biochemical differences between tissues of different host species may be responsible for species specific resistance.

2. Racial Immunity

Within one species, different races may exhibit differences in susceptibility or resistance to infections. This is termed as *racial immunity*. Algerian sheep is highly resistant to

II. ACQUIRED IMMUNITY

The resistance acquired by an individual during life is known as acquired immunity. It is of two types, *active* and *passive*.

A. Active Immunity

Active immunity is subdivided into two types : Natural and Artificial.

Natural—Through clinical or subclinical infection

Artificial—Induced by vaccination

It is the resistance developed by an individual as a result of contact with an antigen. This contact may be in the form of natural infection or by vaccination. It leads to stimulate the immune apparatus to form antibodies and/or the production of immunologically active cells.

Active immunity develops after a latent period which is required for immune system to act but once developed, the active immunity is long lasting.

Types

(i) Natural active immunity

It is acquired by natural subclinical or clinical infections. Such immunity is long lasting. Persons recovering from smallpox infection develop natural active immunity.

(ii) Artificial active immunity

It is produced by vaccination. The vaccines are prepared from live, attenuated or killed microorganisms, or their antigens or toxoids. In killed vaccines the organisms are killed by heat, formalin, phenol and alcohol. These are preserved in phenol, N-merthiolate and alcohol. Toxoids are prepared from bacterial exotoxins inactivated by formalin (formol toxoid) or by alum (alum precipitated toxoid-APT). Toxoids are immunogenic but not toxigenic.

B. Passive Immunity

Passive immunity is subdivided into two types : Natural and Artificial.

Natural—Through transplacental maternal IgG antibodies.

Artificial—Through antiserum injection.

Passive immunity is induced in an individual by preformed antibodies (generally in the form of antiserum) against infective agent or toxin. This antiserum is prepared by injecting infective agent or toxin in another host. The immune system has no active role in passive immunity. Protection starts immediately after transfer of immune serum. There is no latent period as present in active immunity (Table 11.1). Passive immunity is short lasting but is useful when immunity is required immediately.

Natural

It is transferred from the mother to foetus or infant. Transfer of maternal antibodies to foetus transplacentally and to infant through milk (colostrum) protects them till their own immune system matures to function.

Artificial

It is through parenteral administration of antibodies. The agents used for artificial passive immunity are hyperimmune sera of animal or human origin, convalescent sera and pooled human gammaglobulin. The oldest method is to employ horse hyperimmune sera. Antitetanus serum (ATS) is prepared by injecting a

Ch 11: Immunity

series of doses of tetanus toxoid to horses, and bleeding them to separate the serum. As ATS is a foreign protein, it is liable to cause hypersensitivity reactions. To eliminate these complications, human ATS is employed. This is prepared by hyperimmunisation of human volunteers with tetanus toxoid. Protection with human ATS lasts longer as there is no immune elimination of the human globulins.

Convalescent sera (sera of patients recovering from infectious diseases) contain high levels of specific antibody and therefore is employed for passive immunisation against measles and rubella. Sera of healthy adults can be pooled and is used for passive immunisation against common infectious diseases prevalent in the region. Pooled human gammaglobulin are used for passive immunisation against some viral infections e.g. hepatitis A. It has to be ensured that all preparations from human sera should be free from the risk of infections with hepatitis B, hepatitis C, hepatitis D, HIV and other viruses.

I. Antigen Antibody Immune Response

The specific reactivity induced in a host following an antigen stimulus is known as the immune response. It is of two types:

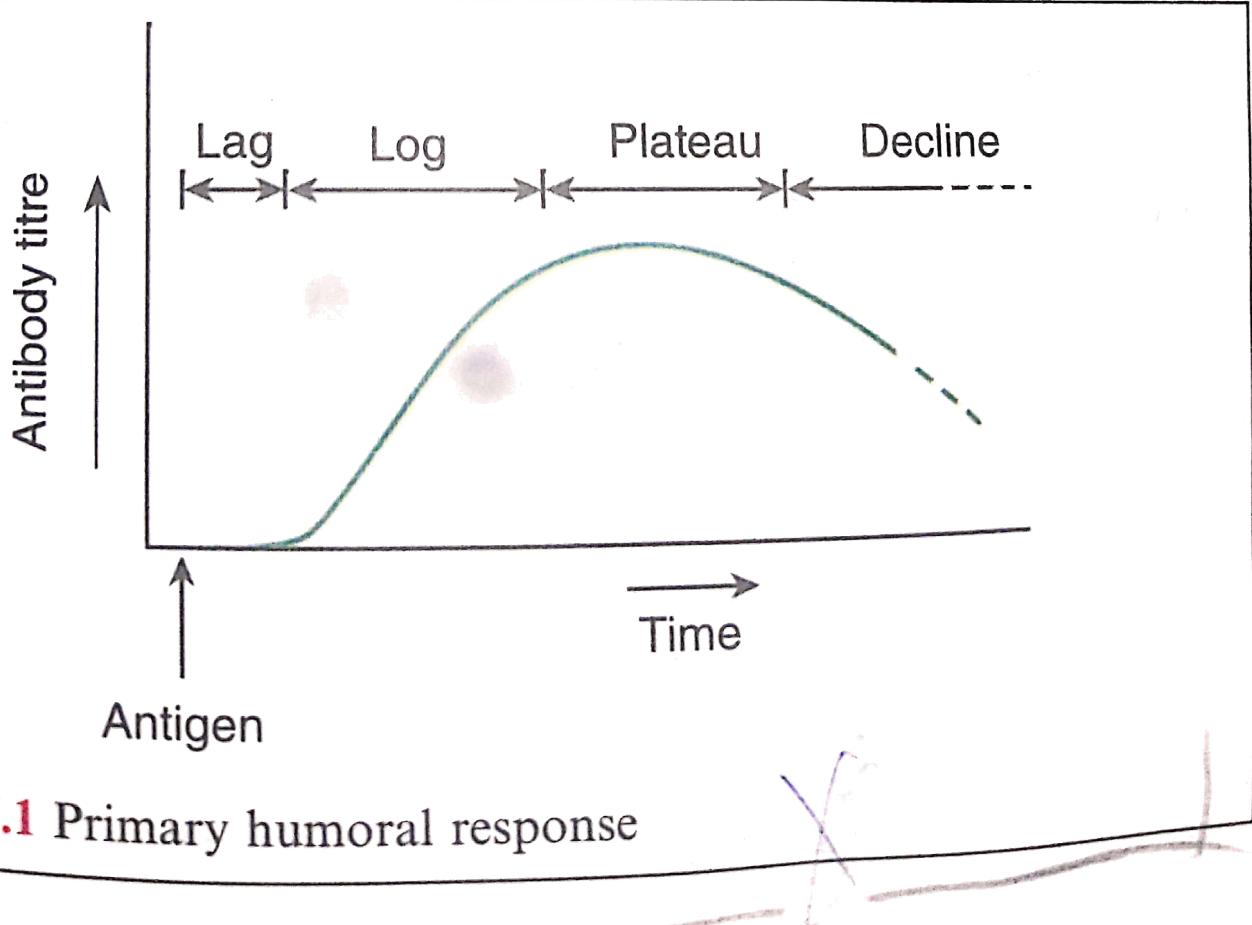
1. Humoral or antibody mediated immunity
2. Cell-mediated Immunity

~~Humoral~~ Antibody mediated immunity (AMI) provides primary defence against most extracellular bacteria and helps in defence against viruses those infect through respiratory or intestinal tracts. AMI also participates in the pathogenesis of immediate (type I, II and III) hypersensitivity and certain autoimmune diseases. Cell mediated immunity (CMI) protects against fungi, viruses and intracellular bacteria like *M. tuberculosis*, *M. leprae* and parasites such as *Leishmania* and trypanosomes. It plays an important role in allograft rejection, graft-versus-host reaction (GVH), and mediates the pathogenesis of delayed (type IV) hypersensitivity and certain autoimmune diseases. It also provides immunological surveillance and immunity against cancer. Both AMI and CMI usually develop together, though at times one or other may be the predominant type.

II. HUMORAL IMMUNE RESPONSE

Antibody production follows a characteristic pattern (Fig. 17.1) which consists of:

1. *a lag phase*—The immediate stage following antigenic stimulation when no antibody is detectable in circulation.
2. *a log phase*—There is steady rise in titre of antibodies.
3. *a plateau*—There is an equilibrium between antibody synthesis and catabolism.



III. CELL MEDIATED IMMUNE RESPONSES

The term cell mediated immunity refers to specific acquired immune responses mediated by sensitised T cells. This form of immunity can be transferred from donor to recipient with intact lymphocytes, but not with antisera, hence it is called *cell mediated immune reaction*. Cell mediated immunity (CMI) plays an important role in the following immunological functions:

1. delayed hypersensitivity (type IV hypersensitivity)
2. immunity in infectious diseases caused by intracellular organisms
3. transplantation immunity and graft-versus-host (GVH) reaction
4. immunological surveillance and immunity against cancer
5. pathogenesis of certain autoimmune diseases e.g. thyroiditis.

A. Induction of CMI

Foreign antigen is presented by antigen presenting cells (APCs) to T-lymphocytes. T-lymphocytes possess antigen recognition receptors known as T cell receptors (TCRs) that recognise foreign antigen and a self MHC molecule on the surface of the APC. These sensitised T-lymphocytes undergo blast transformation, clonal proliferation and differentiation into memory cells and effector cells (Th, Tc, Td and Ts). The activated lymphocytes release biologically active products (lymphokines) which are responsible for various manifestations of CMI.

T cells recognise antigens only when presented with MHC molecules. CD8 + cells can recognise the combination of foreign antigen and Class I MHC antigen and differentiate into Tc and Ts lymphocytes whereas CD4 + cells can recognise the combination of foreign antigen with Class II MHC antigen and differentiate into Th and Td cells. Tc lymphocytes recognise foreign antigen and Class I MHC antigen and gets attached to the target cell. This stimulates Tc lymphocytes to release cytolsins which leads to lysis of the target cell. Subsequently, the Tc cell may detach from the target cell and repeat the same process with another. Tc lymphocytes also synthesise and secrete interferon- γ and thus they probably also contribute to some extent to macrophage activation.

B. Cytokines

These are biologically active substances secreted by monocytes, lymphocytes and other cells. They are named lymphokines if they are derived from lymphocytes and monokines if they are derived from monocytes and macrophages. Interleukins are chemical substances that function primarily as growth and differentiating factors. They exert a regulatory influence on other cells. All these biologically active substances (lymphokines, monokines, interleukins) are collectively known as cytokines. They are not specific for antigens. Various cytokines are shown in Table 17.1.

Some of the important cytokines are described below:

1. *Interleukin-1*: Interleukin-1(IL-1) is principally secreted by macrophages and monocytes. It occurs in two forms IL-1 alpha and beta. Its production is stimulated by antigens, toxins, inflammatory processes and inhibited by corticosteroids and cyclosporin A. It is a stable polypeptide.

Immunological effects of IL-1

1. Stimulation of T cells for the production of IL-2 and other lymphokines
2. B cell proliferation and antibody synthesis
3. Neutrophil chemotaxis and phagocytosis

Immunization:

Definition of Immunization:

Immunization is the ability of your body to eradicate a malicious "invader" in the body. By having immunization to a virus or disease, your body already contains the memory cells or the virus fighters to immediately destroy the virus without it taking hold of your body and making you sick.

Advantages of Immunization:

- Protects individuals against disease
- Prevents epidemics and pandemics
- Prevents you spreading the disease to others
- Prevents the potential greater cost treating the infected patients
- Suffering, Disability and Death are avoided.
- Immune system is aware of the virus and produces antibodies to help protect.
- Early control of Infection.
- Effective control of non-invasive Infections
- Obviates the need of Injection

For Infants				
BCG	At birth or as early as possible till one year of age	0.1ml (0.05ml until 1 month age)	Intra-dermal	Left Upper Arm
Hepatitis B - Birth dose	At birth or as early as possible within 24 hours	0.5 ml	Intra-muscular	Antero-lateral side of mid-thigh
OPV-0	At birth or as early as possible within the first 15 days	2 drops	Oral	Oral
OPV 1, 2 & 3	At 6 weeks, 10 weeks & 14 weeks (OPV can be given till 5 years of age)	2 drops	Oral	Oral
Pentavalent 1, 2 & 3	At 6 weeks, 10 weeks & 14 weeks (can be given till one year of age)	0.5 ml	Intra-muscular	Antero-lateral side of mid-thigh
Rotavirus#	At 6 weeks, 10 weeks & 14 weeks (can be given till one year of age)	5 drops	Oral	Oral
IPV	Two fractional dose at 6 and 14 weeks of age	0.1 ml	Intra dermal two fractional dose	Intra-dermal: Right upper arm
Measles /MR 1st Dose\$	9 completed months-12 months. (can be given till 5 years of age)	0.5 ml	Sub-cutaneous	Right upper Arm
JE - 1**	9 completed months-12 months.	0.5 ml	Sub-cutaneous	Left upper Arm
Vitamin A (1st dose)	At 9 completed months with measles-Rubella	1 ml (1 lakh IU)	Oral	Oral
For Children				
DPT booster-1	16-24 months	0.5 ml	Intra-muscular	Antero-lateral side of mid-thigh
Measles/ MR 2nd dose \$	16-24 months	0.5 ml	Sub-cutaneous	Right upper Arm
OPV Booster	16-24 months	2 drops	Oral	Oral
JE-2	16-24 months	0.5 ml	Sub-cutaneous	Left Upper Arm
Vitamin A*** (2nd to 9th dose)	16-18 months. Then one dose every 6 months up to the age of 5 years.	2 ml (2 lakh IU)	Oral	Oral
DPT Booster-2	5-6 years	0.5 ml.	Intra-muscular	Upper Arm
TT	10 years & 16 years	0.5 ml	Intra-muscular	Upper Arm

KEY POINTS

1. The *Immunity* is defined as resistance exhibited by the host against any foreign antigen including microorganisms.
2. Immunity may be *innate* or *acquired*.
3. Acquired immunity is of two types, *active* and *passive*.
4. Active immunity is subdivided into two types, *natural* and *artificial*.
5. Artificial active immunity may be produced by vaccination.
6. Passive immunity is also subdivided into two types, *natural* and *artificial*.
7. Artificial passive immunity is through parenteral administration of *antibodies* (antisera).
8. *Herd immunity* refers to the overall resistance in the community.

KEY POINTS

1. The specific reactivity induced in a host following an antigen stimulus is known as the *immune response*.
2. Immune response is of two types: *humoral immunity* and *cell mediated immunity*.
3. Humoral immunity is due to *antibody* production while cell immunity is because of sensitised T cells.
4. There are many theories of antibody formation but the *clonal selection theory* is widely accepted.
5. Antibodies that are usually produced in response to a single antigen are *polyclonal*, i.e., synthesised by several different clone of cells.
6. A single antibody forming cell or clone produces antibodies directed against a single antigen or antigenic determinant only and such antibodies are called *monoclonal antibodies*.
7. *Hybridoma* technique is used to produce monoclonal antibodies.
8. Many commercial diagnostic systems use monoclonal antibodies for identification of bacterial, viral and other antigens. *Direct fluorescence* and *enzyme-linked assays* utilise monoclonal antibody conjugates.
9. Cell mediated immunity (CMI) plays an important role in *delayed hypersensitivity* (*type IV hypersensitivity*), *transplantation immunity*, immunity in infectious diseases caused by *intracellular organisms*, *immunity against cancer* and pathogenesis of certain *autoimmune diseases*.
10. The biologically active substances are responsible for various manifestation of CMI. These are named *cytokines*. These include *lymphokines*, *monokines* and *interleukins*.
11. *Immunological tolerance* is defined as a state in which contact with an antigen specifically abolishes the capacity to mount an immune response against that particular antigen when it is administered subsequently, the immune reactivity to other antigens being unaffected.

TRANSGENIC ANIMALS

①

- A transgenic animal contains in its genome; a genes or DNA segment introduced by one of the other technique of transfection.
- The gene introduced is called "transgene".
- Transgenic animals are formed by rDNA technology.

Main Objectives:-

- To improve their milk, meat, wool etc production.
- Large scale production of proteins encoded by these genes in milk, urine or blood of such animals. Such animals are also called Bioreactor.
- It also help in eliminating diseases through gene therapy.
- Used for research and experimental use.

* Transgenics have been produced in a variety of animal species e.g., mice, rabbits, swine, sheep, goat, cattle, poultry, fish, insects, amphibians, and nematodes.

ANIMALS IN WHICH GENES ARE TRANSFERRED	NAME OF THE GENE	OBJECTIVE	ACHIEVEMENT
1) Cattle, Goat, Sheep and Swine	Protein Gene	Gene farming	Genes expressed in mammary tissues, protein secreted in milk.
2) Sheep	genes concerned with cysteine biosynthesis	Improved wool production	Genes expressed in t. animal

Mice / Swine	Genes for haemoglobin & antibodies	Proteins from blood serum for blood transfusion & disease diagnosis	Genes encoding proteins released in blood serum
Swine / sheep	Increased and desirable body growth	Human growth hormone.	Improved body weight gain, fat lean meat/fat ratio etc
Rabbits	Human genes of proteins	Molecular farming	Proteins harvested from milk.
Fish	Growth hormone	Increased body growth	Up to 60% increase in size.

TRANSGENIC PLANTS

The plants obtained through genetic engineering contain a gene or genes from an unrelated organisms, such genes are called transgene and the plants are called transgenic plants.

→ The first transgenic animal was produced in 1983 when a tobacco line expressing kanamycin (antibiotic) resistance was produced.

→ Soon transgenic crop variety resistant to herbicides, viruses, insects, delayed ripening or slow fruit softening were developed.

→ "Flavr Savr" tomato was the first transgenic variety to reach the market, this variety remained fresh for prolonged period.

- ## APPLICATION OF TRANSGENIC PLANTS.
- ② ③
 - 1) Valuable tool in studies on plant molecular biology
 - 2) To improve plants' agronomic & other features.
 - 3) To produce plant resistant to insects & viruses etc.
 - 4) To improve the product quality, e.g. protein or lipid quality etc. of plants.
 - 5) To produce biochemicals like infections, insulin, antibodies etc.
 - 6) It is also used as vaccination.

EXAMPLES

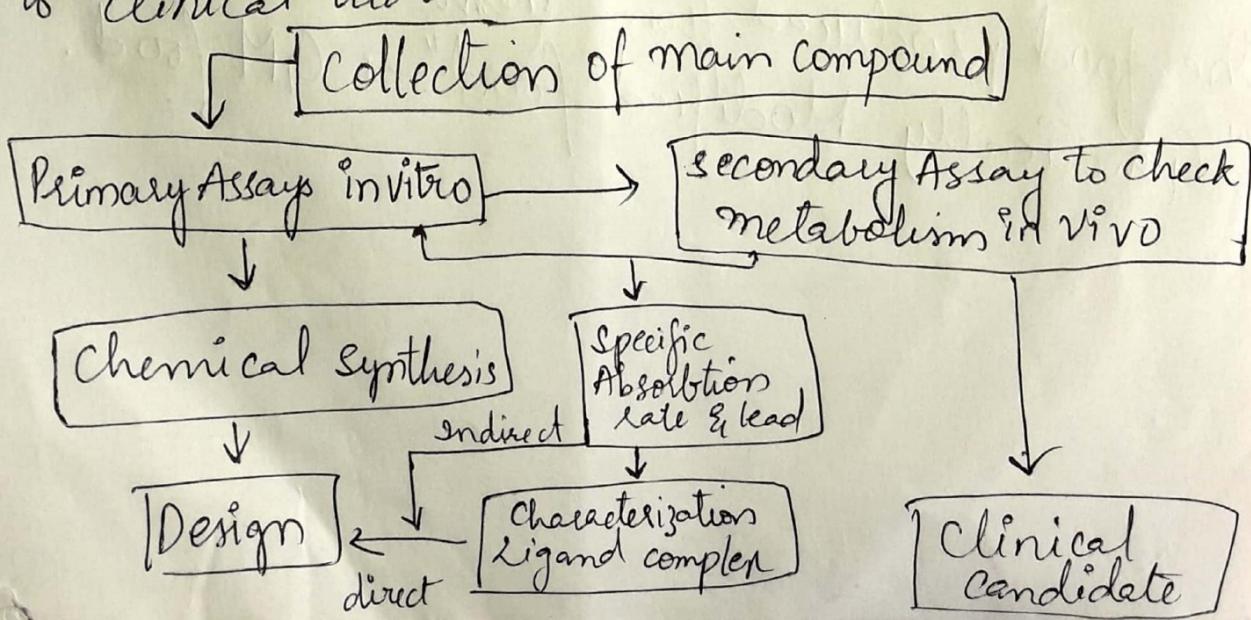
Slow Fruit Softening Tomato - enhanced shelf life
Biochemicals production (Protein, enzymes, reagents)
- Reduced cost.

Herbicide resistance plant.

Insect resistance plants - contain gene from bacteria
The food produced from them are called
"Genetically Modified food" or GM food.

DRUG DISCOVERY

- In medicine, biotechnology and pharmacology drug discovery is the process by which drugs are discovered and/or designed.
- In past most drugs have been discovered either by identifying the active ingredient from traditional remedies or by serendipitous discovery [Enr Insulin]
- A new approach has been to understand how disease and infection are controlled at the molecular and physiological level and to target specific entities based on this knowledge.
- * The process of drug discovery involves the identification of candidates, synthesis, characterization, screening and assays for therapeutic efficacy.
- * Once a compound has shown its value in these tests, it will begin the process of drug development prior to clinical trials.



TISSUE ENGINEERING

(4) ②

- The embryonic stem cells can be cultured *in vitro* where they proliferate. They can be selectively induced to differentiate into cardiac cells, blood cells, skin cells, etc.
- Cell culture technique has been used to produce ^{stem cells,} tissues for implantation in patients, this is often called "^{stem cell} tissue engineering".
- The ultimate objective of tissue engineering are to reconstitute body parts *in vitro*.
- 1) For use as grafts or transplants and
- 2) To be used as models for studies on drug delivery and action.
- It is a combination use of cells, engineering and materials methods and suitable biochemical and physicochemical factors to improve or replace biological tissues.
- STEPS involved in formation of 3D functional tissue to help repair, replace and regenerate a tissue or an organ in the body are given below.

 - a) Cell selection (especially stem cells)
 - b) Cell Isolation
 - c) Cells Cultivation
 - d) Transferring the cell to SCAFFOLDS
 - e) IMPLANTATION OF TISSUE INTO LIVING BODY
 - f) DETECTION.

Process: Tissues collected from patient cells are being separated apart using enzymes that digest material that holds cells together.

- As cells need structure, nutrients and oxygen to grow it is provided by scaffold.
- SCAFFOLD gives cells structure on which they need to grow, without them cells are free floating, cannot connect with each other, communicate & form tissue.
- These are biocompatible & biodegradable; it gets dissolve once the ^{tissue} structure is formed.
- Scaffold provide a structure that cells needs for a certain period of time until they have formed enough tissues to have their own structure.
- Once the tissue is formed it is implanted to the patients, along with scaffolds.

PROS :-

- Help a person to conquer a disease/illness
- No chance of rejection
- People would not have to wait for donor
- People would not have to donate their organ after death
- Permanent Solution

CONS

- Difficulty in construction of suitable scaffold
- lot of research & understanding each organ and tissues.
- cells dont stay alive inside the body in some cases

Bioreactors: A bioreactor refers to any manu-^(a)
factured device or system that support a biologically
active environment.

Bioreactor is a vessel in which a
chemical process is carried out which involves
organism or biologically active substances derived
from such organism. This process can either be
aerobic or anaerobic. These bioreactors are
commonly called cylindrical and made of stainless
steel.

It may also refer to a device or
system designed to grow cell or tissues in the
context of cell culture.
These devices are being used
for developing tissue engineering or biochemical
engineering.
Organism growing in bioreactors may
be submerged in liquid medium or may be attached
to the surface of a solid medium.

There are six types of bioreactors.

- ① Continuous Stirred Tanked Bioreactor
- ② Bubble column Bioreactor
- ③ Airlift "
- ④ Fluidized Bed "
- ⑤ Packed Bed or
- ⑥ Photo - Bioreactor

A bioreactor is a device which support a biologically active environment. It used for chemical process which involves organisms or biochemically active substance derived from such organisms.

Bioreactors ensure cell survival through adequate delivery of essential nutrients throughout the three dimensional tissue engineered construct. Bioreactors are also used for the large scale production of biotechnology products from raw material. They provide optimal condition to obtain the desired product by providing the optimum temperature, pH, Vitamin, or etc.

Uses: Bioreactors are used for fermentation chamber for growing organisms such as bacteria or yeast under controlled condition, biotechnological production of substance such as pharmaceutical, antibodies or vaccines or for the bio conversion of organic waste.

Bio pharming

Bio pharming is the production and use of transgenic plants and animals genetically engineered to produce pharmaceutical substance for use in human or animals. It often involves the insertion of gene constructs derived from humans.

Biopharming in plants (1)

Biopharming in plants is use to cultivate crops for pharmaceutical purpose, giving them the ability to produce desire therapeutic proteins that are then extracted, purified & used by the pharmaceutical industry to produce large molecule, protein-based drugs.

Biopharming in animals :

Gene pharming is a technology that scientists use to alter an animal's own DNA or to splice in new DNA, called transgene from another species.

In Biopharming, there genetically modified (transgenic) animals are used mostly to make human protein that have medicinal value.

Biological neural control networks

Bioenergy :-

Bioenergy is renewable energy made available from material derived from biological sources. Biomass is any organic which has stored sunlight in the form of chemical energy. Eg. Wood as fuel, crop residues, sugar cane ~~byproduct~~ byproduct from a variety of agricultural processes.

Bioenergy is a synonym to biofuel.

Biofuel derived from biological sources). Biomass, the biological material used as a biofuel, as well as the social, economic benefits & technical fields associated with any

biological sources for energy.

One of the advantages of biomass ^{fuels} is that it is often a by-product residue new or waste product of other processes, such as ^{fuels} ^{of} farming, animal husbandry & forestry.

Biomass is the material derived from recently living organisms, which include plants, animals & their by-products.

Manure & garden waste & crop residues are all sources of biomass. It is a renewable energy source based on the carbon cycle. Animal waste is also used as biomass (gobar gas).

There are also agricultural products specifically being grown for biofuel production e.g. Corn, soybeans, wheat sugar etc. Bio-degradable output from industry, agriculture, forestry & household can be used for biofuel production. e.g. anaerobic digestion to produce biogas, gasification to produce syngas.

Biomass can be converted to other usable forms of energy like methan gas or transport fuel like ethanol and biodiesel. Rotting garbage, agriculture & human waste release methane gas or biogas. Corn & sugarcane can be fermented to produce the transport fuel. Transport fuel also produced from left over food products (vegetable & animal fat).

Biomass The use of municipal and household waste as a new source for Biomass is largely discarded resource on which new research is being conducted for use of energy (6)

Biomaterials A biomaterial is any substance that has been engineered to interact with biological systems for a medical purpose - either a therapeutic (treat, augment, repair or replace a tissue further of the body) or diagnostic one. Biomaterial is different material such as bone.

Biomaterials can be derived either from nature or synthesized in the laboratory using a variety of chemical approaches utilizing metallic component polymers, ceramics or composite materials. (Pace maker) Biomaterials are also used every day in dental application, surgery & drug delivery. For example, a constituent with impregnated pharmaceutical products can be placed into the body, which permits the prolonged release of a drug over an extended period of time.

Uses Biomaterials are used in:-

- ① Joint replacements
- ② Bone plates
- ③ Bone cement
- ④ Lenses
- ⑤ Artificial ligament & tendons.
- ⑥ Dental implants
- ⑦ Pace Makers

Bio polymers & Biopolymers are polymers produced by living organisms. Cellulose, starch, proteins and peptides & DNA & RNA are all examples of biopolymers, in which the monomeric units respectively are sugars, amino acids & nucleotides.

⇒ ~~Bio~~ Bio polymers as material : Some naturally occurring polymers such as Poly - 3-hydroxy butyrate can be used as Poly ethylene based plastics.

⇒ Some plastics are now referred to as being degradable. Oxy-degradable or UV degradable.

⇒ Bio polymers can be sustainable carbon neutral & are always renewable, because they are made from plant materials which can be grown indefinitely. These plant materials come from agricultural non food crops. Therefore the use of biopolymers would create a sustainable industry.

Bio polymers are bio degradable and some are also compostable.
Biomass → fermentation → Biobenzene → ethyl ester
Rubber sheet & all types of rubbers are also good examples of Bio-polymers.

RECOMBINANT VACCINES

(5) ①

Recombinant vaccine contains either a protein or a gene encoding a protein of pathogen that is immunogenic and critical to pathogen function; the vaccine is produced using recombinant DNA technology.

- These are also called "subunit vaccines".
 - In simple terms Proteins are generally immunogenic and many of them are specific for pathogen.
 - The genes encoding such proteins can be identified and isolated from pathogens and expressed in E. coli or some other suitable host for mass production of the proteins.
 - The concerned proteins are then purified and mixed with stabilizers and used for immunization.
- The different steps involved in the development of a recombinant vaccine are as follows.
- i) identify a protein that is both immunogenic and specific for pathogen.
 - ii) The gene encoding this protein is then identified and isolated
 - iii) The gene is integrated (inserted) into suitable vector (~~host~~) (plasmid) and introduced into a suitable host where proteins are produced in large quantities.

- iv) The proteins is then isolated and purified from the host cells and
- v) is used for the preparation of vaccine.

The host organisms used for expression of immunogenic proteins are following

- a) Yeast
- b) Animal cell culture
- c) Transgenic plants
- d) Insect larvae

PROS:-

- No risk of pathogenicity
- Defined composition
- Various delivery systems
- Large scale production

CONS:-

Multiple doses needed.

Adjuvants needed.

CLONING

r = recombinant

A clone consists of asexual progeny of a single individual or cell while the process of producing a clone is called 'cloning'.

→ The term recombinant DNA technology or genetic engineering is used as a synonym for DNA or gene cloning.

→ A recombinant DNA molecule is produced by joining together two or more DNA segments usually originating from different organisms.

→ More specifically a rDNA molecule is a vector (e.g. plasmid or virus) into which desired DNA fragment has been inserted to enable its cloning in an appropriate host.

→ The above process is achieved by using gene cloning tools or genetic engineering tools.

→ rDNA molecules are produced with one of the following 3 objectives:

① To obtain a large number of copies of specific DNA fragments.

② To recover large quantities of proteins produced by concerned gene.

③ To integrate the gene in question into the organism where it express itself.

All these steps concerned with piecing together DNA segments of diverse origin and placing them into suitable vector together constitute rDNA technology.

STEP IN GENE CLONING / rDNA TECHNOLOGY.

1. Production and isolation of DNA fragment to be
2. Insertion of isolated gene in a suitable vector ^(the) to obtain rDNA.
3. Introduction of the rDNA into a suitable organism ^(co.) (E.coli) called "host" ^(III) (transformation).
- 4) Selection of transformed host cells and identification of the clone containing the desired gene.
- 5) Multiplication/ expression of the successful introduced gene in the host.
- 6) Where needed, transfer and expression of gene into another organism.

The above steps concerned with transformation of a suitable host with rDNA and cloning of the transformed cells is called gene cloning-

TOOLS INVOLVED ARE

Following 4 different types of enzymes are used

- i) Nucleases. Ex- Restriction endonucleases, exonucleases, S1 nucleases,
- ii) DNA ligases
- iii) Polymerases. Ex- DNA Pol I, Reverse transcriptase
- iv) DNA modifying enzyme. Ex Phosphatases, Kinases, transpherase.

Other tools are DNA insect (Vector + desired DNA)
host.

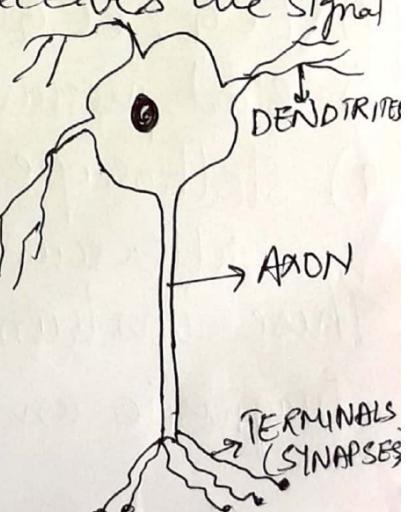
BIOLOGICAL NEURAL NETWORKS - 9

The neural system of human body consists of three stages: i) receptors ii) neural network and iii) effectors.

- The receptor receive the stimuli either internally or from the external world, then pass the information into the neurons in a form of electrical impulses.
- The neural network then ^{processes} ~~makes~~ the inputs then makes proper decision of outputs.
- Finally EFFECTORS translate electrical impulse from neural network into response to the outside environment.



- * The fundamental element of the neural network is called a NEURON.
- * A neuron mainly consists of three parts: Dendrites, axon, and Terminals (synapses).
- * DENDRITES are tree like structure that receives the signal from surrounding neurons.
- * Axon is a thin cylinder the signal from one neuron to another.
- * At the end of axon, terminal is present that is connected to dendrites of other neurons, through a synapse.
- * A neuron fires a electrical signal when conditions are met.



BASICS BIOMEDICAL INSTRUMENTS

Bioinstrumentation is an application of biomedical engineering which focuses on the device and mechanics used to measure, evaluate and treat biological systems.

- It focuses on the use of multiple sensors to monitor physiological characteristics of a human/animal.
- Bioinstrumentation is a new and upcoming field, concentrating on treating diseases and bridging together the engineering and medical worlds.
- These instruments has revolutionized the medical field and has made treating patients much easier.
- Some of the fields of biomedical instruments are genetic testing, drug delivery, biosensors, etc.

Ex:- Sensors present in smartphones capable of measuring heart rate, O₂ saturation, Step count etc

- 2) Lasik eye surgery i.e through LASER.
- 3) Genetic testing through gel electrophoresis
- 4) Hearing aid / Pacemaker for heart
- 5) Soil sampling as well as measuring plant growth
- 6) Dialysis instruments
- 7) ECG, EEG (brain)
- 8) Blood pressure meter, Blood cell counter
- 9) Stethoscope, Diagnostic instruments like X-rays, ultrasound etc

These instruments are mainly used for Monitoring Diagnostic and therapy-