UNIT V

NERVOUS SYSTEM, IMMUNE SYSTEM AND CELL SIGNALING

NERVOUS SYSTEM

- It is the network of nerve cells and fibres which transmits nerve impulses between parts of the body.

- The human brain is a network of billions of nerve cells.

- The nervous system contains a brain, a central cord (spinal cord) and nerves arising from the brain and central cord.

Nervous System

- Central Nervous System (CNS)
  - Brain + Spinal cord
  - evaluates the information and takes decision.
- Peripheral Nervous Sys. (PNS)
  - Cranial nerves + spinal nerves
  - Sends the information to CNS

- Nerves start at the brain and spinal cord and branch out to every part of the body.

UNIT IV

The nervous system has two types of cells -

① Glial cells
② Nerve cells / Neurons

Glial cells - (Greek word - Glue)

- They mainly support the nervous system.
- Do not transmit electrical impulse.
- They can be replaced.

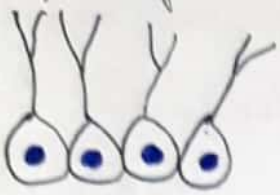
These are of four main types -

Ⓐ - Astrocytes - Star-shaped.

- They surround the neurons.
- They provide nourishment in the form of glucose.
- Control the Ca^+, K^+ ion concentration
- Synthesize and release growth factors.

Ⓑ Oligodendrocytes & Schwann cells -

- Oligodendrocytes are found in central nervous sys (CNS).
- Schwann cells are found in peripheral nervous sys (PNS).
- They form myelin sheaths around the axons.
- Schwann cells repair the damaged neurons of PNS.

© Ependymal cells - 

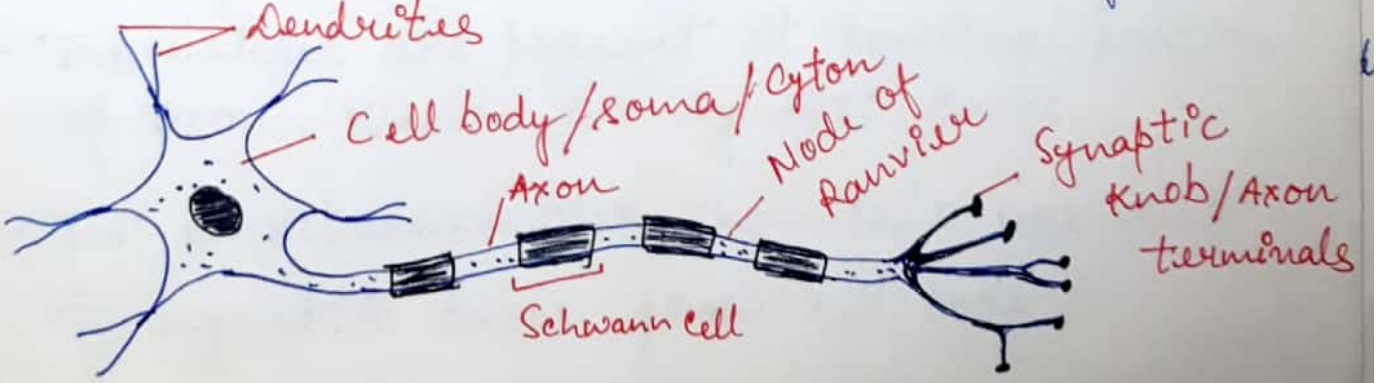
- They are found around the ventricles (grooves filled with cerebrospinal fluid CSF)
- They secrete CSF.
- CSF protects the brain from any shock.
- CSF eliminates waste products too.

(D) Microglia - 

- Small cells, least abundant
- They remove dead neurons, debris and microbes.
- They produce immune molecules and growth factors.

Nerve Cells - Neurons -

- Neuron is the basic structural unit of the nervous system.
- It transmits the signals to every area of the body.
- Neurons can not be replaced once they die.



- A Neuron -

A neuron consists of three parts -

① Cell body or soma

② Dendrites

③ Axon

① Cell body or Soma (or cyton) - It encloses cytoplasm containing nucleus.

- It has a plasma membrane.
- It synthesizes neurotransmitter chemicals.

② Dendrites - - Branch like outgrowths from cell body

- They receive messages from one neuron and transmits to the cell body.

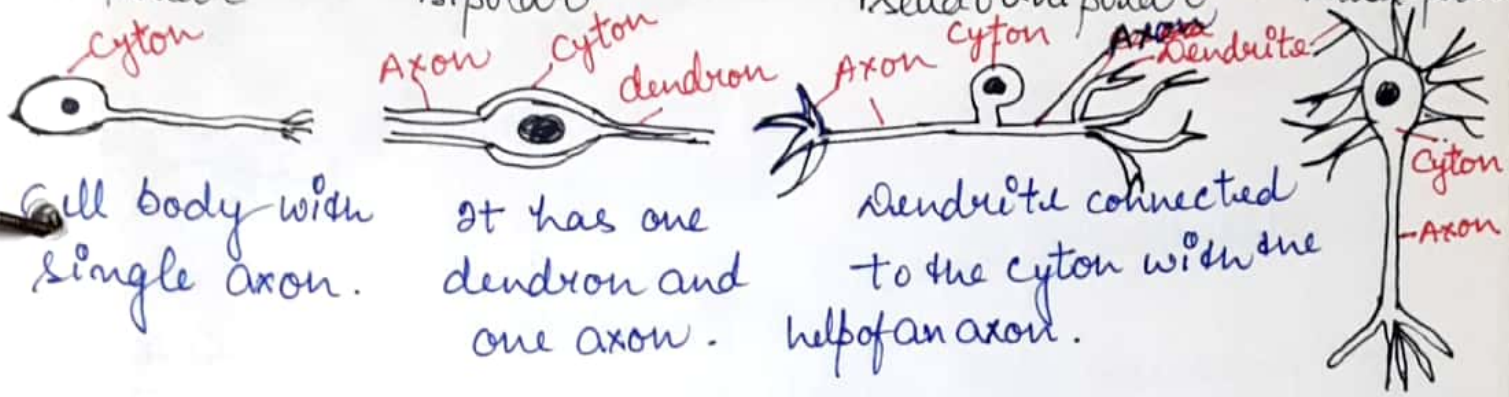
③ Axon - - It is a long extended structure.

- It carries the messages away from the cell body.
- Axons are covered with myelin sheath.
- The gap between myelin sheaths is called as "Node of Ranvier".
- The vesicles are present at terminal portion of axon, known as synaptic knobs.
- The neurotransmitter chemicals are sent to synaptic knobs from cell body.

On the basis of axons and dendrites the neurons are classified as -

Neurons

- Unipolar
- Bipolar
- Pseudounipolar
- Multipolar



Cell body with single axon.

It has one dendron and one axon.

Dendrite connected to the cyton with the help of an axon.

It possesses one axon and many dendrites.

On the basis of function they are classified as -

Neurons

- Sensory Neurons
- Motor Neurons
- Interneurons

Sensory Neurons: ~~receive~~ Produce the response to stimulus and sent to CNS.

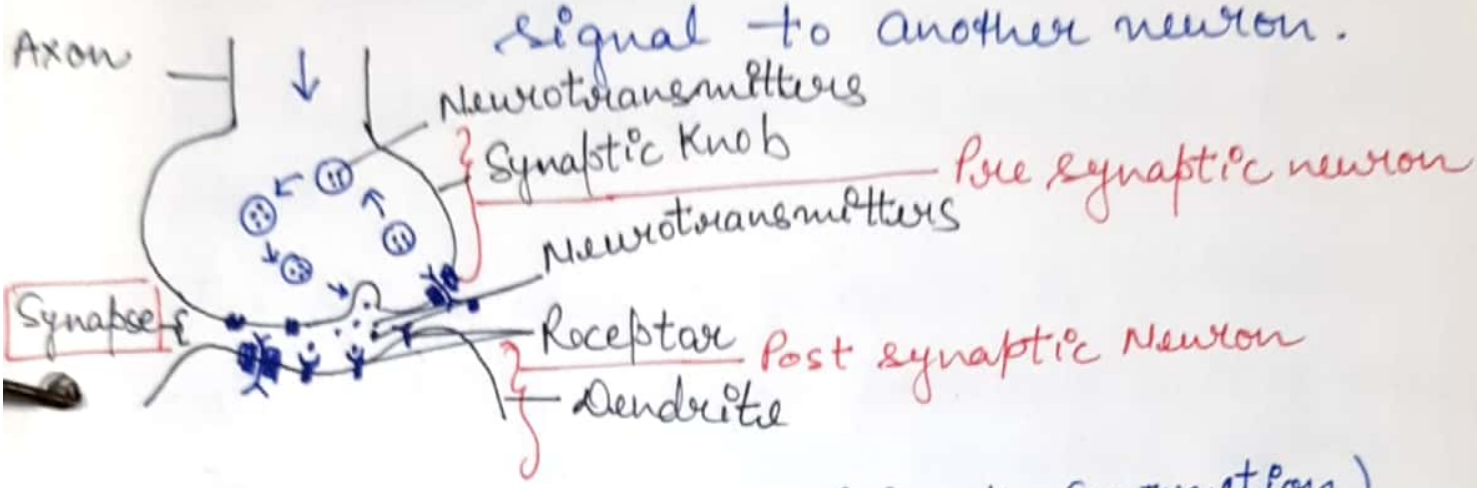
ex - A finger touches a hot plate.

Motor Neurons: convey the decisions of brain to the glands or muscles.

ex - withdrawal of finger from the hot plate.

Interneurons: Send the message to the brain and then convey the decisions of brain.

Synapse :- A synapse permits a neuron to pass an electrical or chemical signal to another neuron.



- A Synapse - — Synapse (Greek - conjunction)
- Synapse refers the gap between two neurons and the adjoining area of two neurons.
- The area which releases signal / chemicals/ neuro/electrotransmitters is called presynaptic and which receives these signals, called as postsynaptic.
- The presynaptic neuron sends message by releasing neurotransmitters in to synaptic gap.
- These chemicals are bound to the receptors of postsynaptic neuron
- For this transmission action potential is required.
- After this, neurotransmitters are taken back so that synapse could be ready to receive the next signal.

* - Neurotransmitters - Acetylcholine, Glutamic Acid

Central Nervous System :-

- It consists of two major structures : the brain and spinal cord.
- The brain is encased and protected by the skull.
- The spinal cord is protected by vertebra.
- The brain is a major functional unit of CNS, while the spinal cord processes reflexes.
- Major components of brain are -

① Cerebrum - Two hemispheres of brain are called as cerebrum.

- Many grooves (sulci) and ridges (gyri) tout.
- It is divided into four lobes :- temporal lobe, frontal lobe, parietal lobe and occipital lobe.
- Temporal lobe is associated with visual memory, hearing, language comprehension etc.
- Frontal lobe is involved in higher cognitive functions related to personality, behaviour and emotions.
- Parietal lobe functions in processing sensory infosmations i.e. taste, touch & temperature
- Occipital lobe is responsible for visual information of the eyes.

The regulation of memory, emotions, stress responses and body movement are associated with hippocampus, amygdala and basal ganglia.

(2) Diencephalon - It is associated with hypothalamus, that controls reproduction, body temp, growth, immune system, stress responses and metabolism.

(3) Cerebellum - It is situated below the occipital lobe. It performs motor skills i.e. coordination of movements, maintenance of posture, thinking, reasoning, memory, speech and emotions etc.

(4) Brain Stem - It has mainly two parts: pons, medulla. They control cardiovascular, respiratory, sleep, consciousness and alertness.

Another important part of CNS is spinal cord. It sends messages from PNS to Brain and transmits commands from brain to PNS.

The Peripheral Nervous System - The nerves arising from spinal cord and 10 pairs of cranial nerves constitute PNS. It is divided in to -

(1) Somatic Nervous System - Sensory neurons
- Sensory and motor nerves of muscles (voluntary)
- controls muscle movement (voluntary)

② ~~Parasympathetic~~ Autonomic Nervous System –

- Sympathetic Nervous System (SNS)
  It gives "flight or fight" response.
- Parasympathetic nervous System
  It controls SNS.

Diseases of the Nervous System –

Parkinson's disease – between the age of 50-60 cell bodies and neurons, producing dopamine, are destroyed.
Symptoms – tremors of hands, arms and head.

Dementia – common over the age of 60.
Brain tissues are deformed.
Symptoms – loss of memory, irritation, inability to learn a new task etc.

Alzheimer's disease – common in western countries.
Symptoms – loss of memory, mood swings, language problem, confusion, poor judgement, changes in personality.

IMMUNE SYSTEM

"Immune system is responsible for the maintenance of healthy status of an organism."

- The founder of immunology is called as Edward Jenner.
- He is given the credit for small pox-vaccination.
- Robert Koch proved that a particular disease is caused by a particular pathogen (microbe).
- Louis Pasteur developed a vaccine against cholera in chickens and rabies.

Comparison of innate & adaptive immunity

Property	Innate	Adaptive
Characteristics	Antigen nonspecific Rapid response (min) No memory.	Antigen specific Slow response (days) Memory
Immune components	Natural barriers (e.g. skin) Phagocytes Soluble mediators (e.g. complement) Pattern recognition molecules.	Lymphocytes Antigen-recognition molecules (B cell and T cell receptors) Secreted molecules (e.g. antibodies)

Immune system is responsible for the maintenance of healthy status of an organism. It protects the organism from various microbes such as bacteria, virus, protozoans etc.

or

The immune system is the body's defense against infectious organisms and other invaders.

To function properly, an immune system must be able to distinguish between foreign invaders (non-self) and body's own cells (self)

Disorders of the immune system can result in autoimmune diseases such as diabetes Type I, sclerosis, lupus, rheumatoid arthritis, inflammatory diseases and cancer.

Autoimmune diseases result from a hyper-active immune system attacking self tissues as if they were foreign organisms.

The immune system can be classified into -

① Innate immune system

② Adaptive immune system

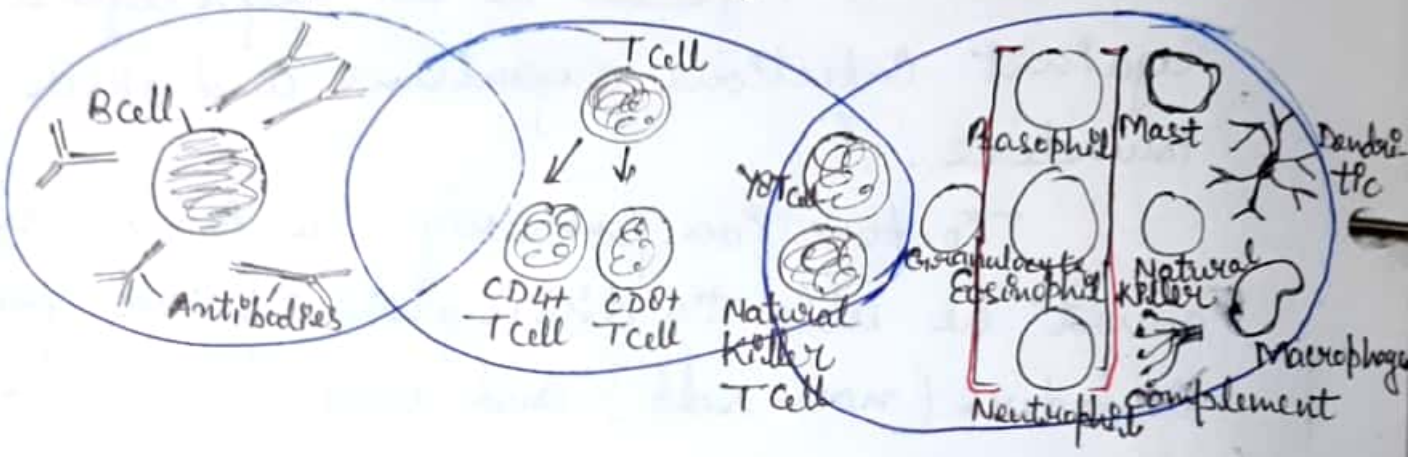
Any substance that is capable of generating antibody is called an antigen.

Adaptive Immunity

Innate Immunity

Humoral
(B-cell immunity)

Cellular
(T-cell immunity)



Immune System

- **Innate** (Non-specific)
  - immediate response within seconds
  - NO memory
  - Target - group of pathogens
- **Adaptive/Acquired** (Specific)
  - Gradual response (1-7 days)
  - Memory, target specific pathogen
  - Humoral (Antibody)
  - Cell-mediated (Cells)

Innate Immunity:- Innate immune system provides an immediate but non-specific response. It is inherited from mother and does not possess memory. The physical/chemical barriers and barriers of organism's body constitute the innate immunity such as:

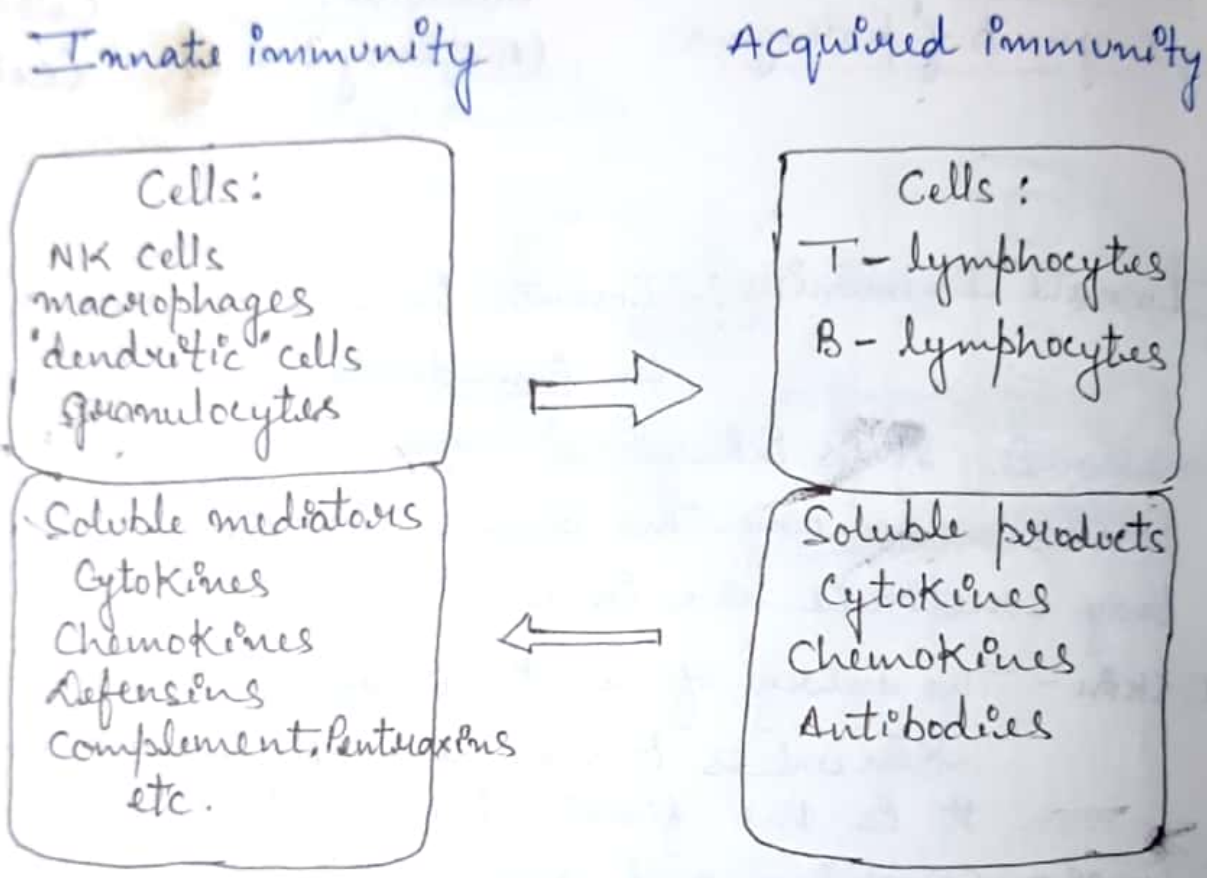
(1) Skin - The entry of most pathogens is prohibited by skin unless it has any opening ex- any cut. It is the first line of defense.

(2) Lungs - Coughing and sneezing mechanically eject pathogens out. Mucus traps the microbes.

(3) Tears, Saliva and Urine - The flushing action of tears, saliva and urine mechanically expels the pathogens.

(4) Enzymes - Some enzymes i.e. lysozyme and phospholipase A-2 are antibacterials.

(5) pH - Some skin secretions have acidic pH > 7.0 which inhibits the bacterial growth. Ex - Hair follicles secrete sebum that contains lactic and fatty acid, inhibits the fungi.



HCl :- The mucus membrane of stomach secrete HCl which kills many pathogens.

Beside the physical and chemical barriers, cellular barriers of innate immunity system are as follows :-

① Polymorphonuclear (PMN) leukocytes (granulocytes)
ex :- basophils, mast cells, eosinophils and neutrophils (mitochondria absent)
- non-dividing, 1-4 day lifespan, segmented nucleus.
- lysosome enzyme is present which produces peroxide and superoxide radicals to cause destruction of the microbes.
- The neutrophils reach at first where the invasion is found and followed by macrophages.

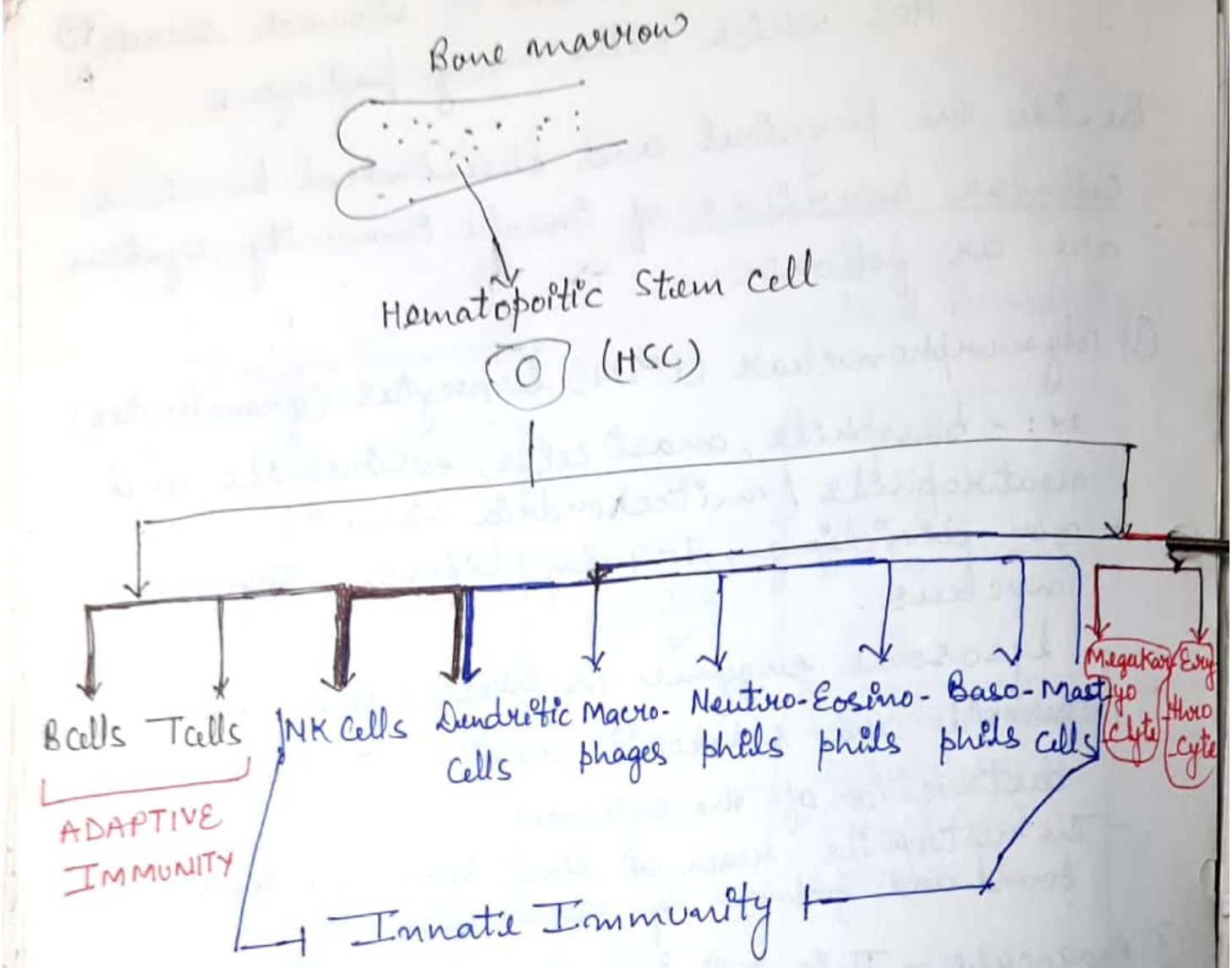
② Phagocyte - This cell ingests foreign bodies.

③ Macrophages - Promonocytes, made in the bone marrow and are released into the blood, finally get mature into macrophages (Big eaters).

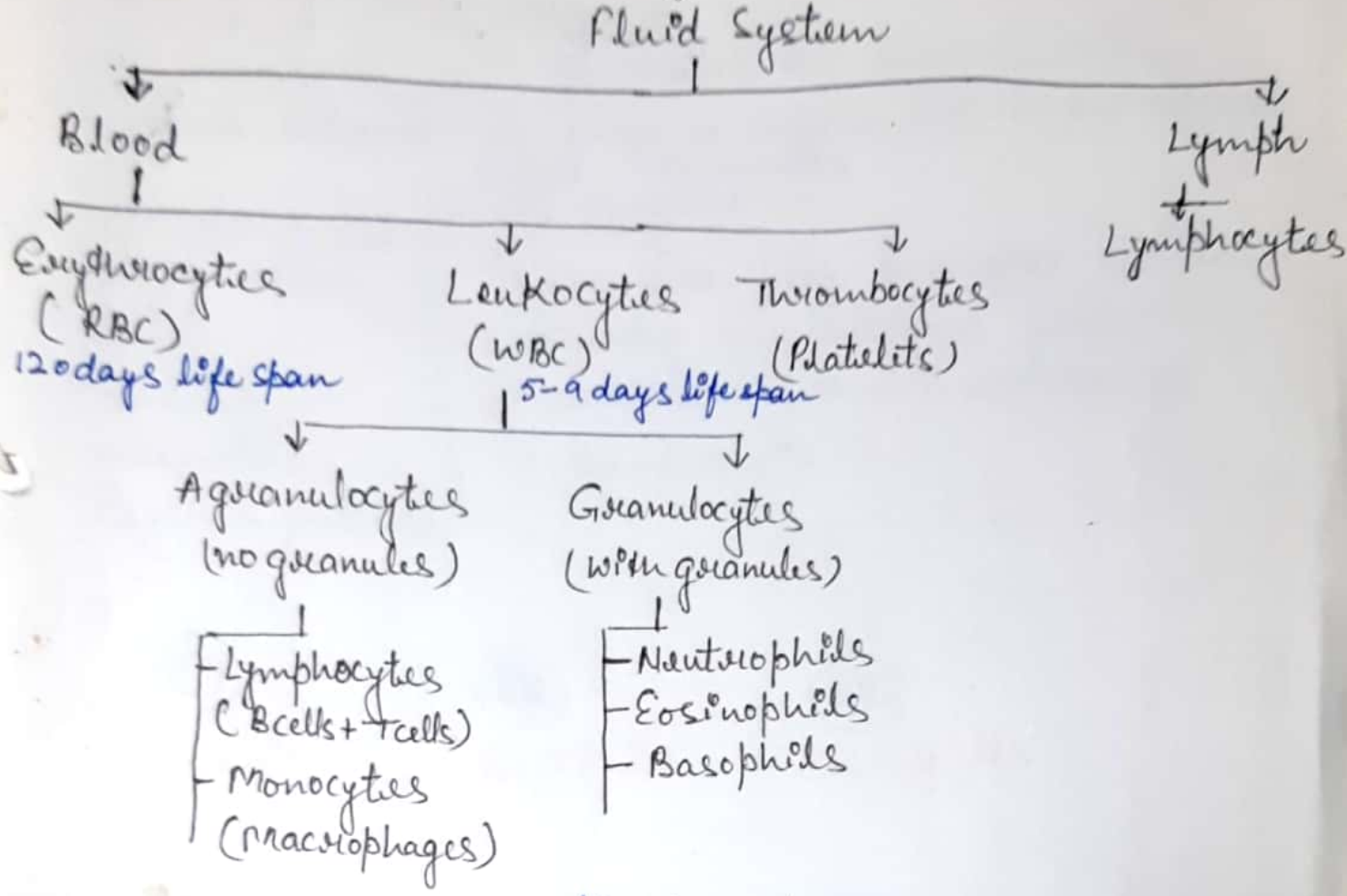
when a macrophage eats a pathogen, it places its proteins (epitopes) on its surface. These markers serve as signal to other immune cells. These are termed as antigen-presenting cells (APCs).

④ Dendritic cells - Long-lived cells, APCs (langerhans cells, interstitial dendritic cells etc)

They are important for both innate and adaptive immunity.



Fluid System of the body:



There are two main fluid systems -

① Blood ② Lymph (RBC, WBC, Platelets)

Blood - The blood cells are made in the bone marrow by a process called hematopoiesis.

2,400,000 RBCs are produced each second and they die in the spleen.

WBCs are present 5000-10,000/mm³. They mainly form cells of Immune System. Lymph consists of various cells of WBCs.

Lymph - alkaline pH > 7.0 fluid, clear, transparent and colourless.

The blood and lymph systems are connected with each other throughout the body and transport

The major organs of human lymphoid organs include:

① Primary Lymphoid Organs :-

Bone marrow – it generates the immune cells.

Thymus Gland – it plays a major role in the cell mediated immunity.

② Secondary Lymphoid Organs :-

Lymph nodes
Spleen
Tonsils
Adenoids
Peyer's patches

These play a major role in capturing the antigens, production of antibodies and induction of T. lymphocyte.

Lymphocyte

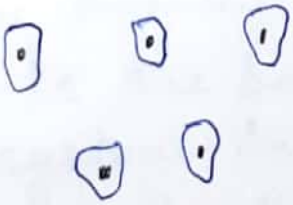
Basophils

Eosinophils

Monocytes

Neutrophils

RBC



Platelets

(5) NK cells (Natural Killer cells) - are found in the blood and lymph.
They KILL cancer cells and viruses - infected body cells by releasing cytotoxic molecules.

(6) Eosinophils - release MBP major basic protein, cationic protein, perforins, O_2 metabolites. They burn holes in cells and helminths. The lifespan is 8-12 days.

(7) Complement system - It coats microbes with molecules that those are susceptible for phagocytosis (eating). They encourage PMN to adhere to the walls of capillaries.

(8) Pattern-recognition receptors - These receptors help in binding the immune cells to antigens.

ADAPTIVE OR ACQUIRED IMMUNITY - It is also known as the specific immune system. Adaptive immunity creates the immunological memory. This is the basis of vaccination. The adaptive system includes both humoral immunity components and cell-mediated immunity components.

- Adaptive immune system is highly specific to a particular pathogen.
- It can provide long-lasting protection.

(B)

Humoral immunity - It is associated with circulating antibodies (i.e. immunoglobulins Ig)

Antibodies are proteins secreted by the B-lymphocytes. The humoral response involves B cells that recognise antigens or pathogens that are circulating in the lymph or blood.

- Antigens bind to B cells and make to produce antibodies
- Antibodies clear the pathogens. These are secreted by B-lymphocytes.
- T helper cell sensitizes or primes the B cell for clonal selection.
- The B-cells produce highly specific antibodies. Remaining B-cells become memory cells

Antibodies are also called as immunoglobulins (Igs)

- Igs constitute the gamma globulin part of blood.
- Igs are soluble proteins, secreted by B-cells.
- Igs work on antigens in following ways:

(A) Complement fixation - proteins attach to antigen surface and cause holes i.e. cell lysis.

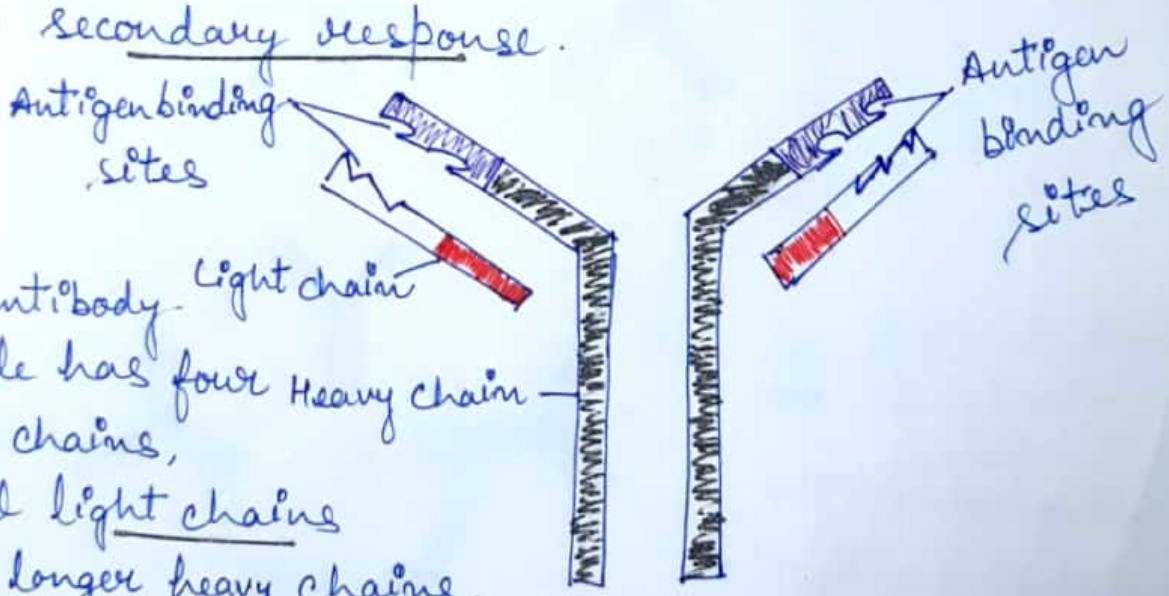
(B) Neutralization - prevent antigens to attach through binding the specific sites.

(c) Agglutination – clumping
(d) Precipitation – Insolubility

Constituents of gamma globulins are –
IgG – 76%, IgA – 15%, IgM – 8%, IgD – 1% and IgE – .002%

IgG is inherited by foetus from mother through placenta. It gives protection to new-born for 3–6 months.
IgG is produced during secondary immune responses.
IgM is produced during primary immune responses.

When our body encounters a pathogen for the first time produces a response called primary response.
Subsequent encounter with the same pathogen elicits secondary response.



Each antibody molecule has four peptide chains, 2 small light chains and 2 longer heavy chains.

– Structure of an antibody –
An antibody has flexible upper part to bind the antigen.

IMMUNE SYSTEM.

This is known as fab portion. Antibody attaches to specific proteins on the antigen. The specific proteins on antigen are known as epitopes.

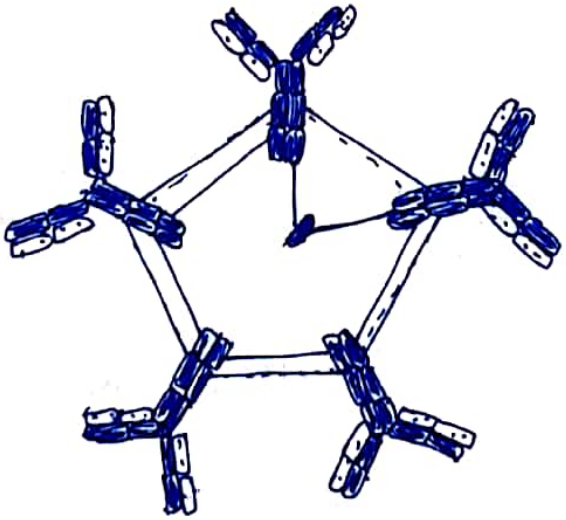
Antibody recognizes only epitopes not the entire antigen.

Because these antibodies are found in the blood, the response is called as humoral immune response.

Ig G, Ig D

Ig E

Ig A

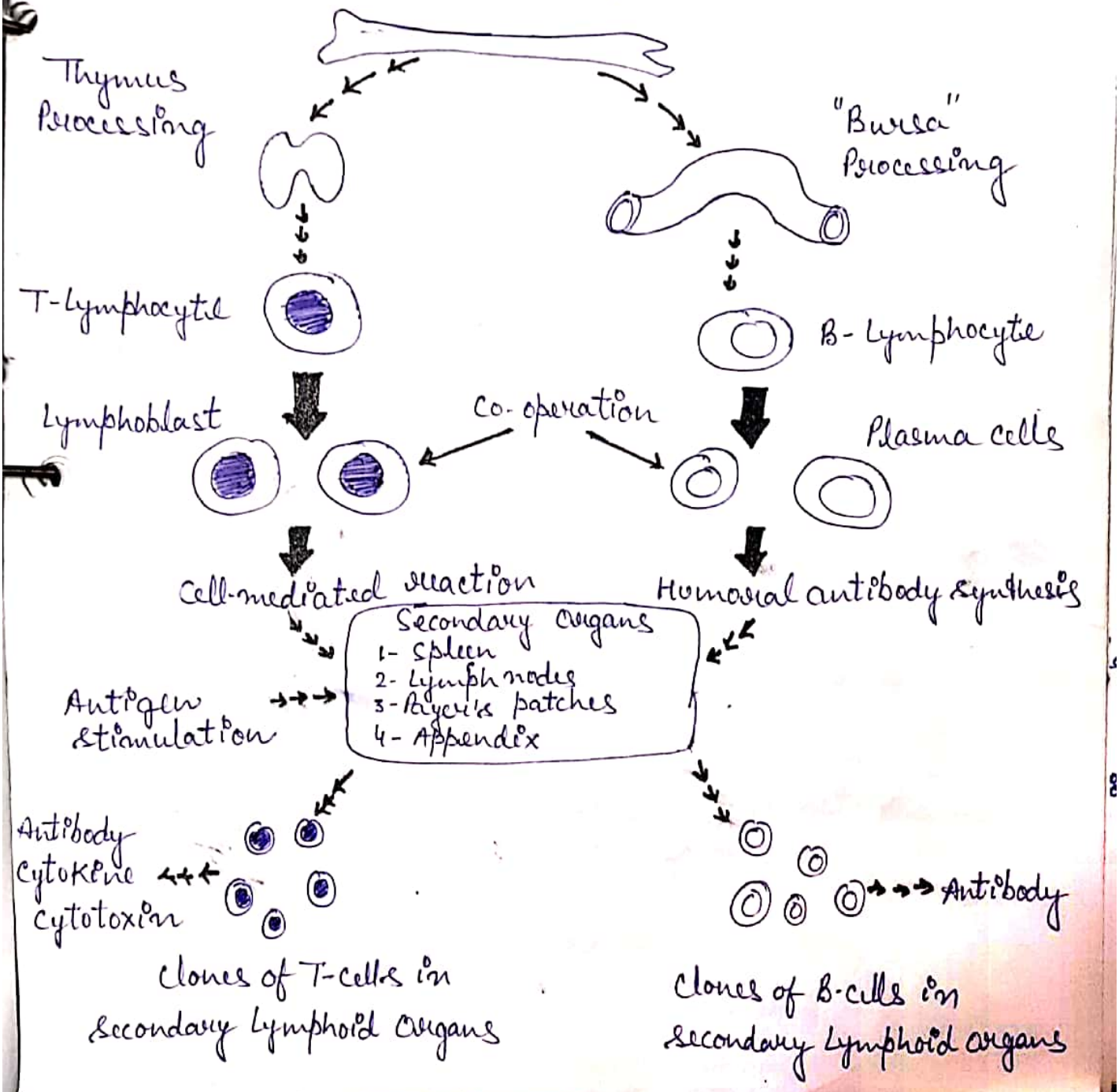


Ig M

- Light chain domain
- heavy chain domain
- Joining domains
- Disulphide bridge

5- different types of antibodies of humoral immunity

Cell mediated immunity - This is related to T cells. T-cells are non-antibody producing lymphocytes which are also produced with B-cells in the bone marrow. In thymus, T-cells are made able to recognize or sensitize the specific pathogen. This is the basis of cell mediated immunity.



- Macrophages engulf antigens, process them internally, then attach some proteins on them.
- This helps the T cells to recognize these antigens.
- There are various coating substances which form 160 clusters.
- CD stands for cluster of differentiation.
- CD8+ is read as "CD8 positive".
- Every B and T cell is coated about 10^5 molecules.
- B-cells are coated with CD21, CD35, CD40 and CD45 in addition to other non-CD molecules.
- T-cells have CD2, CD3, CD4, CD28, CD45R and other non-CD molecules on their surfaces.
- These molecules serve as receptors (approx. 10^{18}) and provide a near-perfect fit to the antigen with B or T-cell (lymphocyte).
- Two types of T cells are processed in Thymus:

① those can recognize MHC (major histocompatibility complex) molecules for self recognition.

② those can recognize MHC molecules with foreign peptides.

- Cytotoxic or Killer T cells (CD8+) functions by releasing porphyrins and granzymes, which cause cell lysis.
- Helper T cells (CD4+) serve as managers, directing the immune response by secreting

Cytokines.

- Cytokines stimulate cytotoxic B cells and T cells to grow and divide, attract neutrophils and enhance the ability of macrophages to engulf and destroy microbes.
- If the purpose of cytotoxic T cells is fulfilled, Suppressor T cells inhibit their production, so that other healthy cells could not be damaged.
- Memory T cells are produced during the immune response and stored for future recognition and elimination of that pathogen.

Principles of Cell Signaling

DR. KAMAKSHI SAXENA

Cell signaling can be defined as the communication between the cells to regulate cell activities and maintain basic functions of the cells.

Unicellular organisms (ex Yeast) communicate by using small peptides.

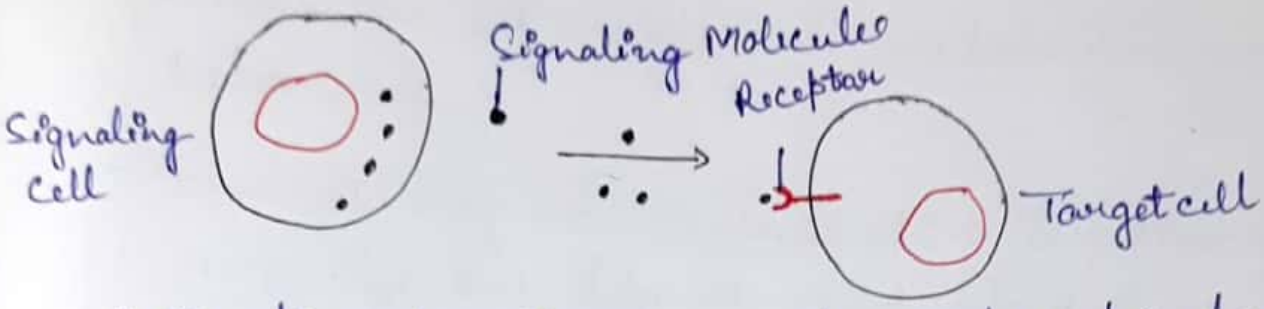
Multicellular organisms communicate with the help of proteins, small peptides, amino acids, nucleotides, fatty acid derivatives, steroids, gases as nitric oxide and co, cytokines etc.

Unicellular
ex - Yeast
Signal molecules =
few small peptides

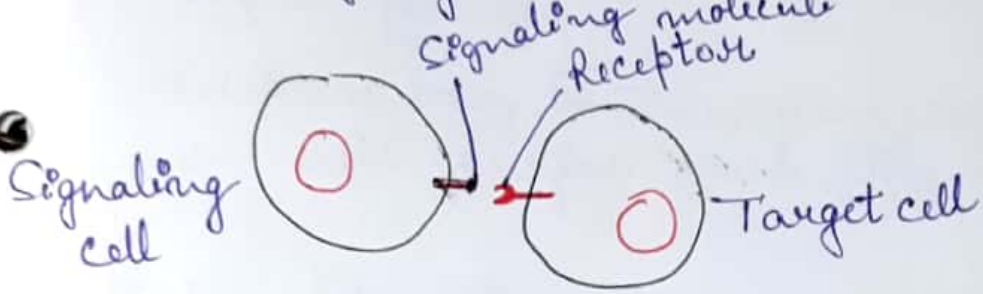
Multicellular
ex - animals, plants etc
Signal molecules =
proteins, small peptides
amino acids, nucleotides
fatty acids
steroids, cytokines.
Gases -
nitric oxide, CO

Every target cell has a special structure to receive the signal molecule. The special structure is known as receptor and signal molecule as ligand.

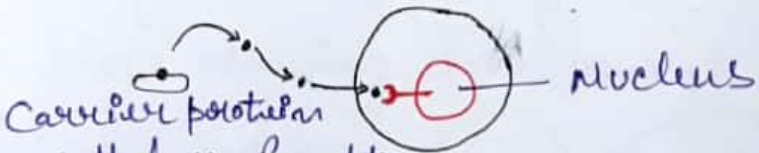
1) Signaling by Secreted molecules



2) Signaling by Plasma-membrane-bound molecule



3) Cell-Surface Receptors



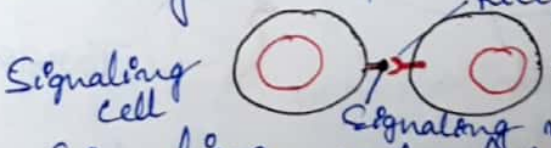
4) Intra cellular Receptors

- Intracellular Signaling in animals -

- The signal molecule binds to the receptor which alters the cell's internal metabolism and behaviour.
- Even at very low concentration receptor molecules recognize the ligand and bind them with high affinity.
- Receptors may be transmembrane proteins present on cell's surface or inside the target cell.

Types of Signaling - Type of signaling is determined by signaling molecules.

① Contact-dependent - This signaling involves influencing the cell that contacts the signaling molecule bound to the surface of the signaling cell. This process takes place during development and immune responses.



② Paracrine Signaling - Molecules are secreted and transported to short distance.

③ Synaptic Signaling - Long distance communication is effectively facilitated with the help of neurons. The

signaling molecules ex- neurotransmitters, initiating action potential, transmits the electrical impulses.

④ Endocrine Signaling - Endocrine cells secrete hormones that are carried through the blood to the target cells.

⑤ Autocrine Signaling - when the signals are sent to other cells. ex - development, immune response etc. During the immune response, a cell produces cytokines which facilitates the production of same type of cells to eliminate the microbes.

Response of cell to multiple extracellular signaling molecules -

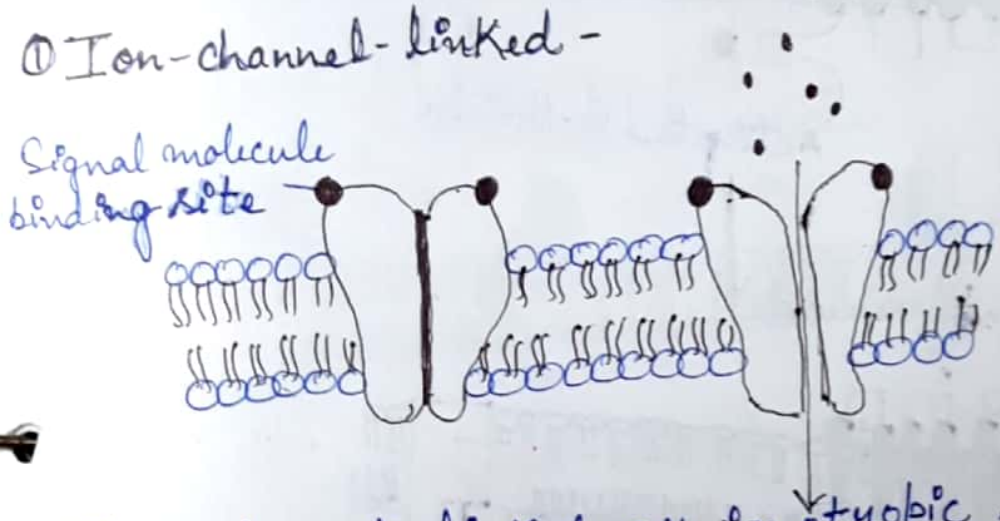
- Each cell is programmed to respond to a set of signals for a specific function.
- If the cells donot get appropriate signals, they tend to have programmed cell death or apoptosis (suicide).
- The response of the cell to a signal depends on the type of receptor it possesses.
- The single signal molecule can produce different responses in the presence of different receptors.

Types of cell surface receptor proteins - (5)

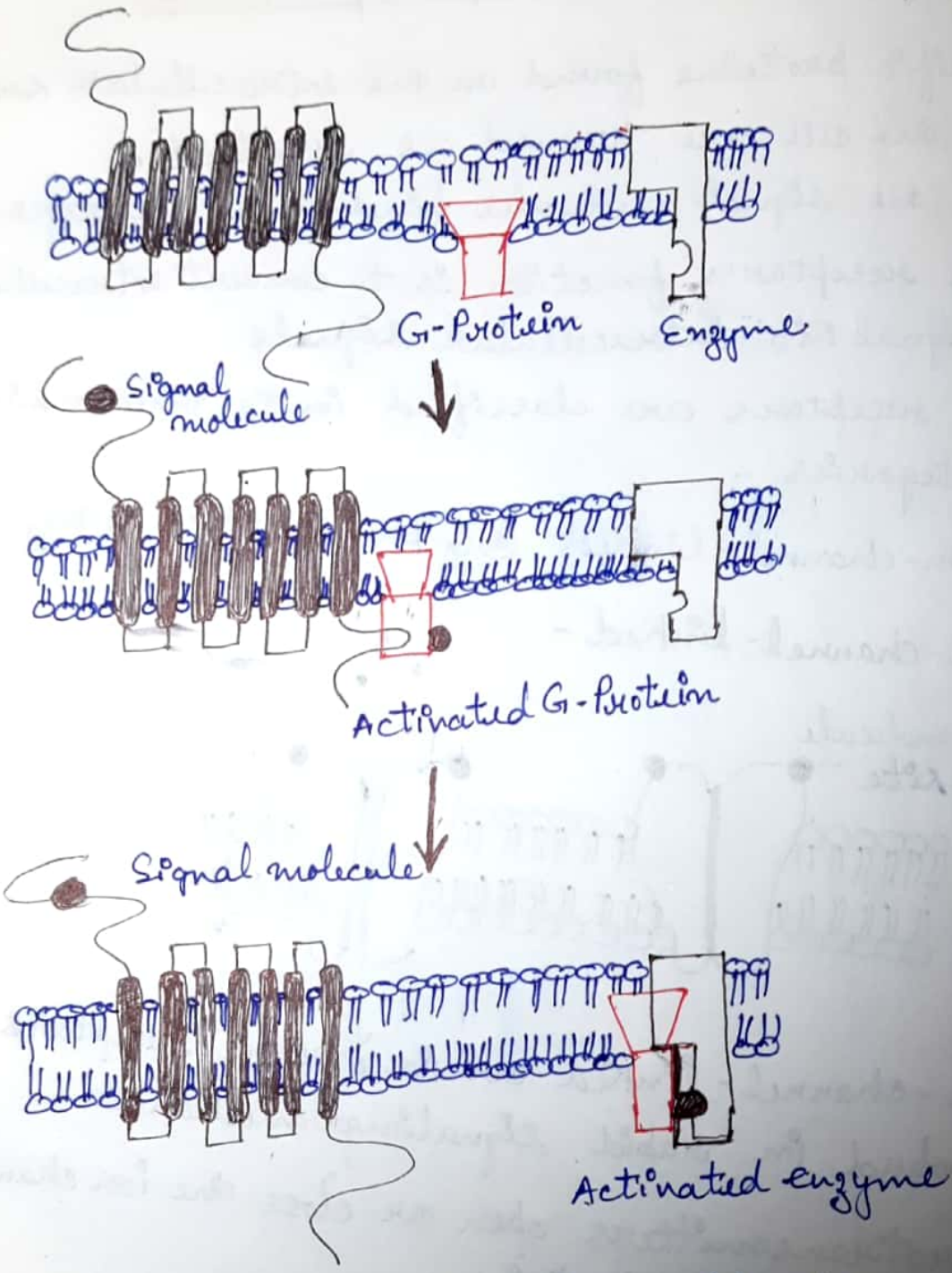
- Specific proteins found on the extracellular surface of the cell are termed as receptors.
- All the signal molecules bind to the receptors.
- The receptor's function is to convert extracellular signal into intracellular signals.
- All receptors are classified in to three main categories -

① Ion-channel-linked ② G-protein linked ③ Enzyme linked

① Ion-channel-linked -



- Ion-channel-linked or ionotropic receptors are involved in rapid signaling mechanism.
- Neurotransmitters open or close the ion channel formed by the protein.
- These bind with the protein and enhance the permeability of plasma membrane.
- Ex - muscle movement

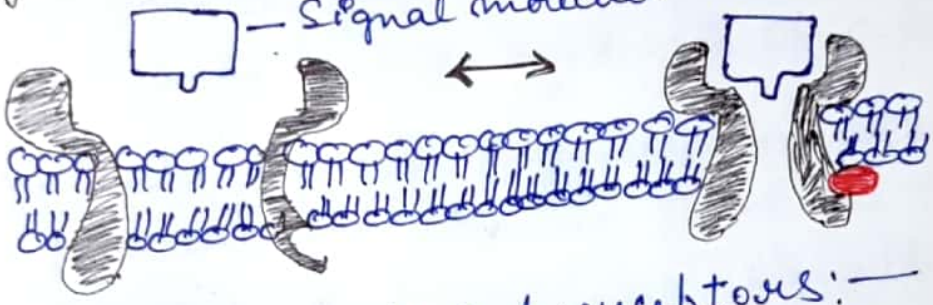


- G-protein-linked receptors -

) G-protein-linked -

- Binding of a signal molecule (ligand) to G-protein-coupled receptors modify the functions of proteins (ex- enzymes or ion channels) which are found in plasma membrane.
- These receptors are known as GPCR (G-protein-coupled receptors).
- The binding between GPCR and ligand is facilitated by GTP-binding proteins.
- GPCR are basically homologous, seven-trans-membrane domain proteins.

(3) Enzyme-linked receptors -



—: enzyme-linked-receptors:—

- Enzyme-linked receptors function as enzymes or activate enzymes.
- Their ligand-binding site face towards extracellular site and catalytic site in the cytoplasm.
- Binding of ligands to receptors leads phosphorylation, which facilitates intracellular events.