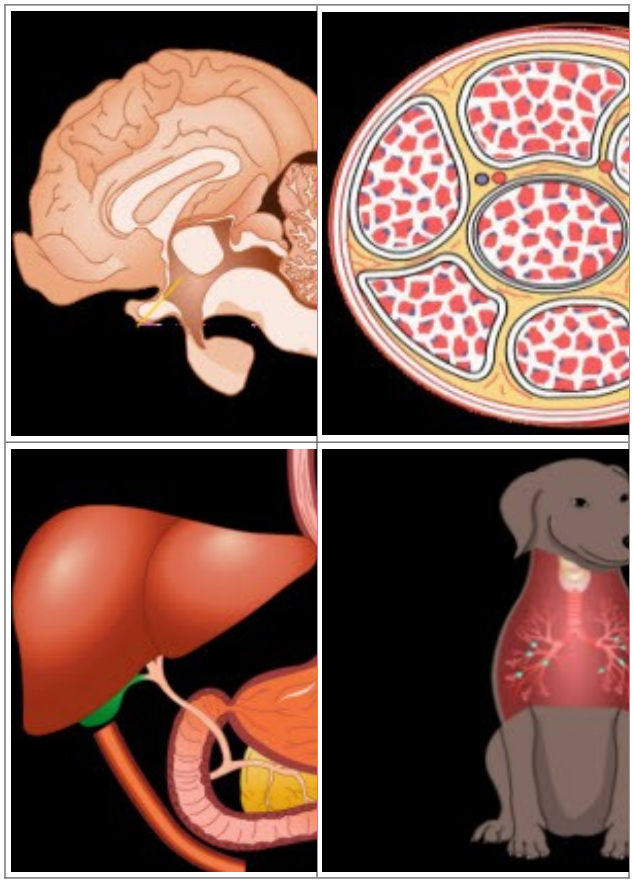
COURSE OVERVIEW

VPB 121: VETERINARY PHYSIOLOGY - II (2+1)

This course is the second course in the sequence designed to teach students the physiological mechanisms of animal body. Applied knowledge of this course with analytical thinking facilitates the understanding of the processes and how systems interact in the body with ultimate coordination by nervous system - HOMEOSTASIS , the basic motto of physiology. Learners appreciate the basic working of muscular, digestive and respiratory systems and their regulation by the nervous system.



The objectives of this course are,

To assist undergraduate students in understanding

- the complex dynamics of physiological process - thorough knowledge of this subject helps the student to develop the skill of understanding forthcoming subjects such as Pharmacology, Pathology, Clinical medicine, Anaesthesiology and Reproductive physiology.
- the coordination of various structures and functions in the animal body.
- the basic structural and functional charecteristics of muscular system and functions in different parts of the body.
- the sequential organization and functions of digestive system, the functional capabilities and differences exist in the physiological anatomy of alimentary system in different animals.
- the basic structural and capabilities of respiratory system in different animals

Overall knowledge gained from this course will help the learner to develop study skill ability and test taking skills.

TABLE OF CONTENTS - NERVOUS SYSTEM

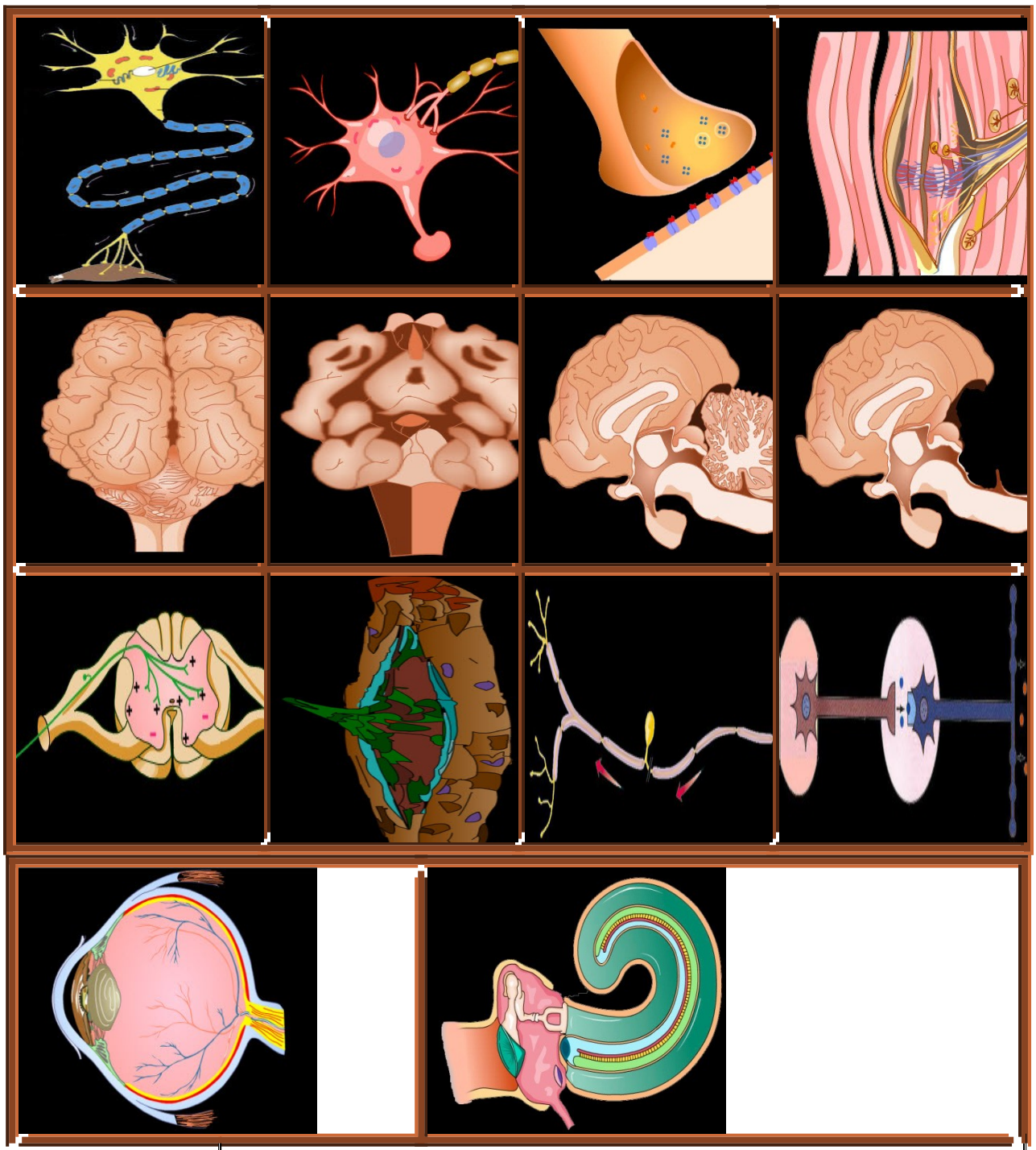


TABLE OF CONTENTS - MUSCULAR SYSTEM

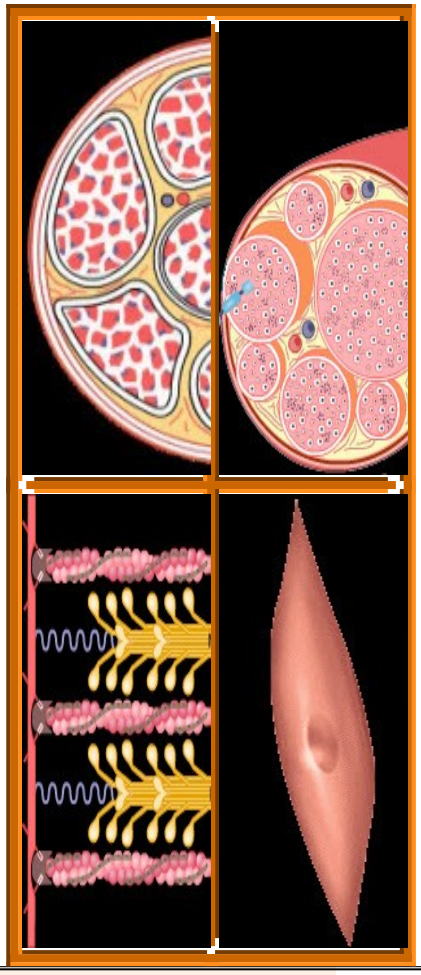
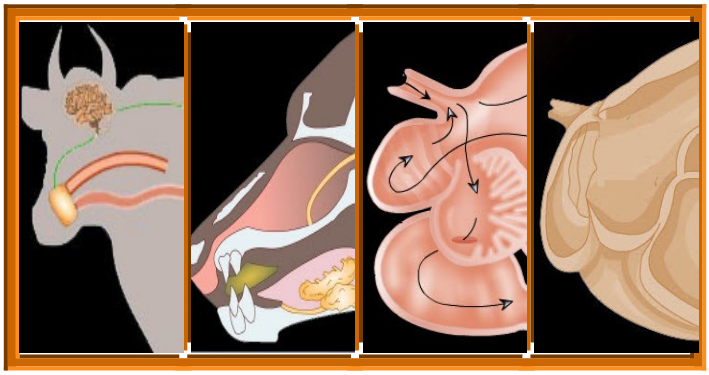
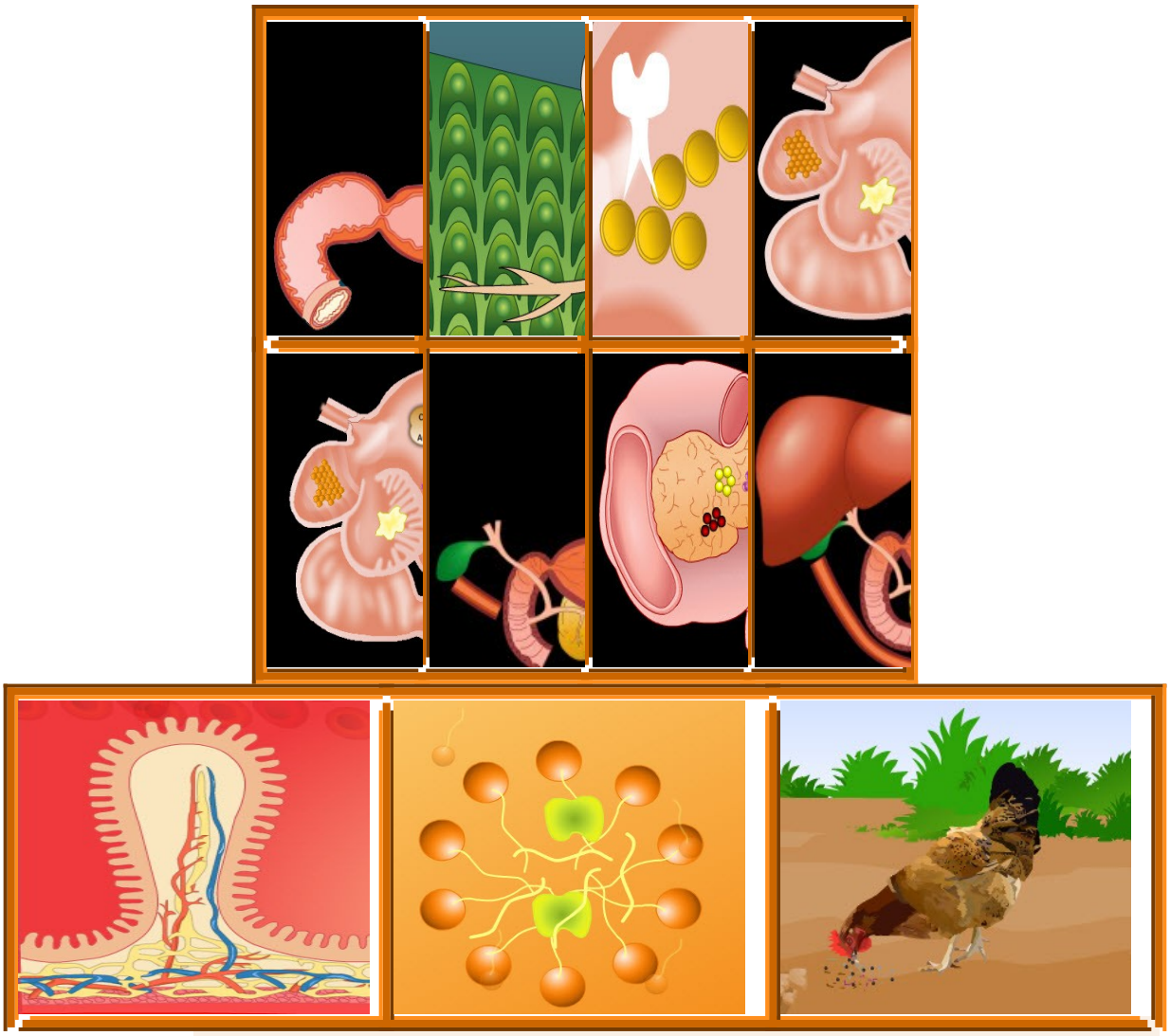
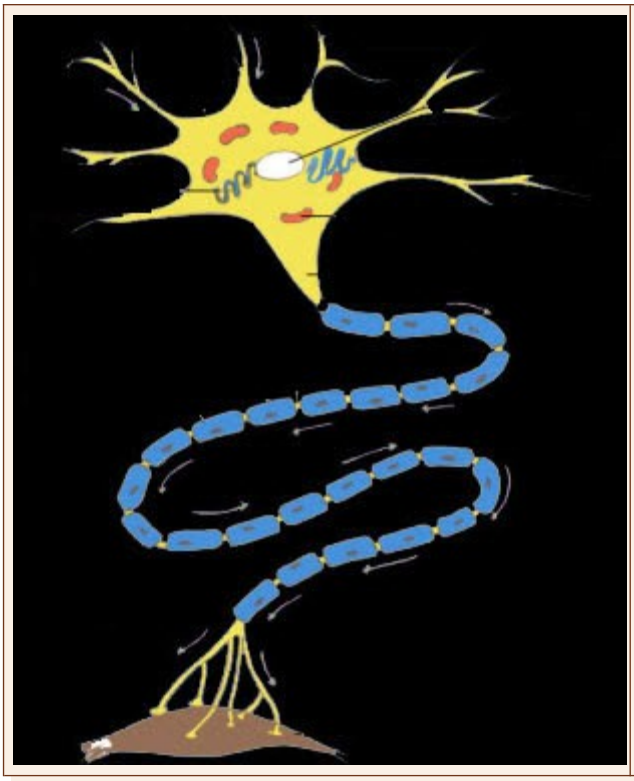


TABLE OF CONTENTS - DIGESTIVE SYSTEM





MODULE-1: ORGANISATION OF CNS NEURONS, NERVE FIBRES AND ITS CLASSIFICATION



LEARNING OBJECTIVES

This module deals with,

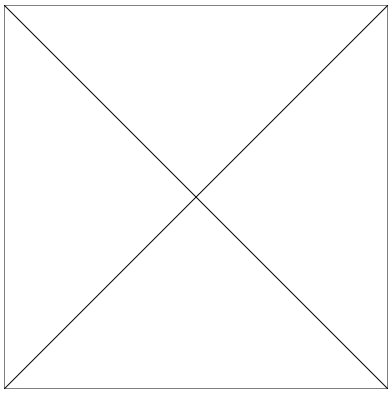
- the components of the nervous system,
- the structure of a neuron,
- Glial cells, its function and their basic types and
- the basic structure of nerve fibres.

NERVOUS SYSTEM - AN INTRODUCTION

- Pioneering discoveries of LUGI GALVANI'S explanation of animal electricity which he showed as a muscle twitch in a dead frog on application of electrical current led away to the modern study of neurophysiology.From his work, a clue was spread about the functions of nervous system, as a unit of control of activities of the body. Based on this revolutionary idea, nerves were thought to be similar to water carrying pipes. Much of such discussion on neuronal communications and cellular cross talk find its way for discoveries and updates theories in modern neurophysiology.
- Nervous system is a structural and functional mechanism involved in the co-ordination of an animal's response to internal and external environment.Nervous system collect information from outside and inside the body, as well as integrate the information. It comprises of collection of neurons to specialize to covey information with the great speed and accuracy. Nerve cells are designated to respond to stimuli and transmit information to various parts of the body. It provides effective responses to stimuli.Nervous system is composed of millions of discrete structural, functional and genetic unit called *neurons*.

Nervous system can be subdivided into different parts for the convenience of study but they function together.

- *Central nervous system(CNS):* brain & spinal cord
- *Peripheral nervous system(PNS):* cranial nerves and spinal nerves.
- *Autonomic nervous system (ANS):* sympathetic and parasympathetic divisions.



- Brain is the major area of central nervous system, is a large structure with the cluster of neurons viz SUPERGANGLION integrates and dictates other systems according to the external and internal stimuli.
- PNS is the communication network that connects CNS with the other parts of the body. Their neural tissue lie outside the CNS they have afferent division (towards) brings sensory information from receptor (centripetal) and efferent division (from/ exit) carries motor commands to effectors. Effectors can be skeletal muscles, smooth muscles or cardiac muscles. Efferent division includes somatic nervous system (skeletal muscle) and autonomic nervous system(smooth muscles, cardiac muscles, glands, brown fat and immune organs).
- Both central and peripheral nervous systems are made up of NEURONS and supporting tissues known as GLIAL CELLS.

EMBRYOLOGICAL DEVELOPMENT AND DIVISION

- Embryonic neural tube which is a hollow structure from epithelial origin, develop into brain and spinal cord.
- Brain is derived from anterior portion and spinal cord is divided from posterior portion of neural tube.
- Anterior portion develop into three swellings viz.
    - Rombencephalon (Hind brain)
    - Mesencephalon (Mid brain)
    - Prosencephalon (Fore brain)
- Cavity that develop in the centre is known as *ventricles* which are filled with cerebrosipinal fluid (CSF) and ependymal cells, a type of glial cell allow the circulation of CSF into ventricular and spinal cord due to their ciliary action.
- Hind brain controls reflex responses and regulate involuntary behaviour (breathing, equilibrium, maintenance of body position).
- Mid brain is predominantly involved in co-ordinating visual, auditory or sensory information from mechanoceptors (touch/pressure) from parts of the body. It acts as a routing centre.
- Fore brain is involved in processing olfactory information, integerates with other sensory information, regulates body vegetative functions. It is designated to perform complex tasks like memory processing etc.
- Size of the brain varies with body size individual structures type of activity pertaining to the environment of the animal.
- **Basal nuclei is the cluster of grey matter situated deep into the brain.**

Hind brain: (Pons , Medulla and cerebellum)

Location: Between spinal cord mid brain. Functions together to **support vital body functions such as respiration cardiac function and movement.**

- *Medulla*
  - Located at the top of the spinal cord
  - Has centres that **control reflex activities such as respiration, heart rate, vasodilation and blood pressure**.
  - Houses neural pathways that connects cerebral cortex and spinal cord seat of some of the cranial nerves (9th, 10th and 12th).
- *Pons*
  - Structures present above the medulla functions as bridging and communicating informations between medulla, cerebellum and fore brain structures.
  - **Has neurons that control rate of respiration.**
  - Concerned **control of alertness.**
- *Cerebellum*
  - Encased in cerebellar hemisphere and is located in the back of the brain.
  - Responsible for motor co ordination by integerating sensory inputs from receptors of muscle, eyes and ears with motor orders of the forebrain.
  - Maintain **Equilibrium and posture**.

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Mid brain

- Relay centre
- **Roof of midbrain is known as *tectum*** which has pair of brain centres namely optic lobes in non mammalian species.
- **Superior Colliculi is a similiar structure as optic lobes in mammals** functions as reflex optical response (orientation towards visual stimuli, focussing etc).
- **Tectum** has a pair of inferior colliculi which are neurons **concerned with hearing**.
- ***Tegmentum*** is the posterior part of midbrain that possess fine **control of muscles.**
- Brain stem is the grouping of midbrain with the pons and medulla.

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Fore brain

- Involved in processing and integrating sensory information and co ordinates behaviour.
- Structures of the fore brain consists of cerebrum , thalamus, epithalamus and hypothalamus.
- Cerebrum
  - Has outer layer known as cerebral cortex which is divided into two cerebral hemispheres.
  - Hemispheres excercise control over opposite side of the body.
  - Hemispheres functions independently of each other.
  - **Two hemispheres are connected by a mass of white matter known as *corpus collosum*** through which they communicate.
- Hypothalamus
  - Present in the base of the forebrain, below the thalamus.
  - Maintains homeostasis by controlling internal organs and interacts with autonomic nervous system.
  - Regulates endocrine system and links endocrine and neural systems.
  - Controls vegetative functions of the body.
  - **If forms the part of limbic system which influences emotion and behaviour.**

- *Limbic system* is a network of connected structures that lie between the cortex and reset of the brain.
- **Structures associated with limbic systems are hypothalamus, amygdala, hippocampus and olfactory bulbs.**
- *Structures of limbic system*
  - *Amygdala*
    - Concerns with emotional responses of **fear and aggressiveness.**
    - It is also involved in **maintenance of memories of the emotion.**
  - *Hippocampus*
    - Structures **convert short term memories to long term memories.**
  - *Olfactory bulb*
    - Organ of importance for **sensing the smell**. Behaviours are smell driven in animals. Sensory neurons from the olfactory epithelium are connected to the olfactory bulb.
    - Olfactory information reaches directly here without passing through thalamus.
    - Information are transmitted to cortex for processing .
    - It is connected to amygdala and hippocampus. Emotional behaviours are mediated through odours in animals and human beings.

- Thalamus
  - Act as relay centre, ***largest sensory ganglion of the brain***
  - Has group of grey matter located deep into the forebrain.
  - Receive all sensory information for upward transmission except olfaction.
  - Reticular formation is a set of neurons extend from thalamus to brain stem including pons, medulla and midbrain, that filters incoming sensory information.
- Epithalamus
  - Located above the thalamus **harbours pineal complex**, that establishes circadian rhythm and secretes melatonin.

NEURONS

- These are basic building blocks for communicating information using both chemical and electrical signals. Neurons are designed with specialized properties to receive process and transmit the information. Neurons like any cell have a cell membrane boundary, cellular organelles and extensions which perform conduction of information and reception.
- Cell membrane is electrically excitable. Neuronal shape and size vary depending upon the function. But they have common functions to change incoming information into electrical potential. This process is known as *impulse generation*.

Neuronal anatomy

- Soma (cell body) (perikaryon) responsive of metabolic maintenance of the cell.
- Processes to receive and conduct information. They are of two types
  - *Dendrites*
  - *Axons*
- Most of the neurons posses multiple dendrites and a single axon. These anatomical structures are arranged in specific zones and play a different role in neural signaling.

Neuronal soma

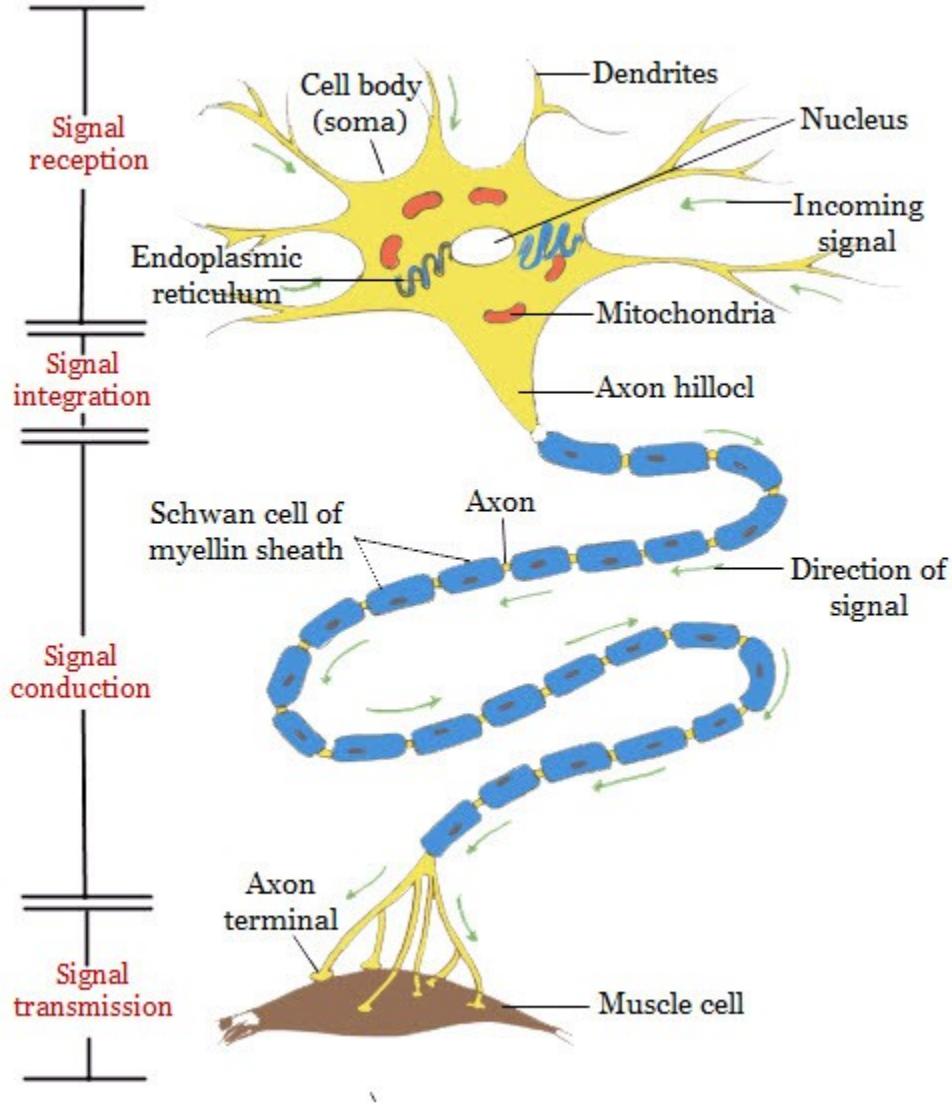
- Body of the neuron consists a nucleus surrounded by cytoplasm.
- It contains neurofibrils,nissil bodies (basophilic granules) or tigroid bodies, golgi apparatus and mitochondria. The nucleus is large, circular with large spherical nucleolus. Nucleolus has a ribonucleic acid (RNA) and no centrosome. Absence of this attributes to the failure of normal regeneration, it looses the cell division.

Neurofibrills

- Fine filamentous meshwork in cytoplasm connecting dendrites and axons.

Nissil granules

- Clumped basophilic granules in the cytoplasm concerned with the **protein synthesis & have the ribonucleic proteins.** These granules are not present in the areas of origin of axon. Their size, number and shape vary.



Dendrites

- They are fine branching extensions of the neuron originate from cell body and serve as the receptive surface.

- These show heavy branching and are responsible to sense and gather incoming signals. As they receive, are converted into an electrical signal. This in turn is propagated as change in membrane potential.
- The dendrite with extensive arborizatrion receives many inputs.

Axons

- This is otherwise known as nerve fibers. This is the long extension from soma to conduct information away from cell body. Nerves are general term referring bundles of axons running through the tissues. Axon has neurofibril and mitochondria. Axon arises from an area in the caudal soma known as **axon hillock** which is devoid of nissil granules. This area is said to be **trigger zone** where action potential are initiated. Axon terminates into numerous branches called TELODENDRIC or TERMINAL BUTTONS which allows the signals to pass on simultaneously to many structures. Telodendria contain vesicles to store synaptic transmitters.
- Both axon and dendrite are nourished by the cytoplasm of the cell. They transfer nutrients to the terminal axons. Cytoplasmic flow depicts ambeoid movement of the phagocytic cell. The flow in axon is popularly known as axoplasmic flow.

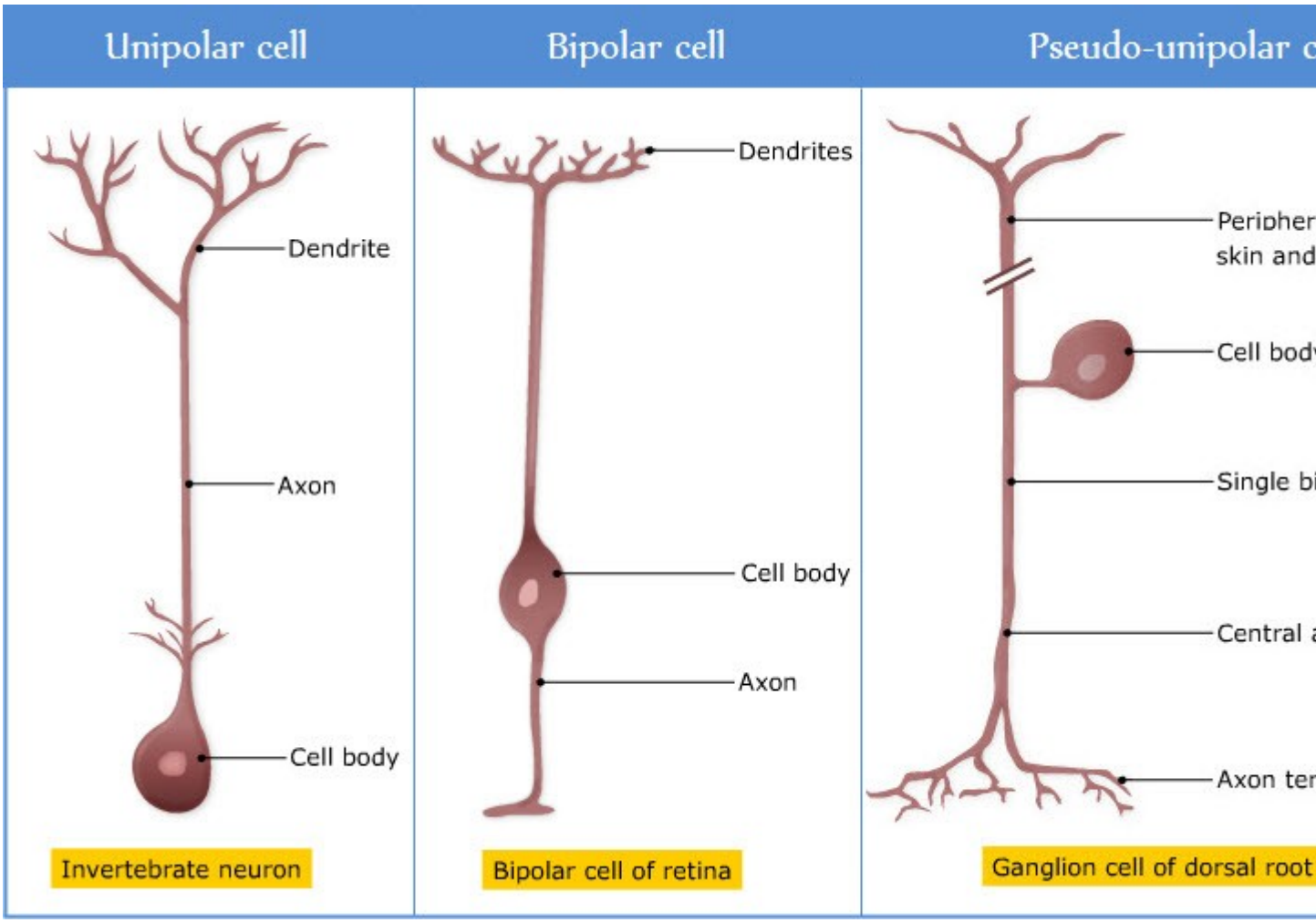
CLASSIFICATION OF NEURONS

Classification of Neurons

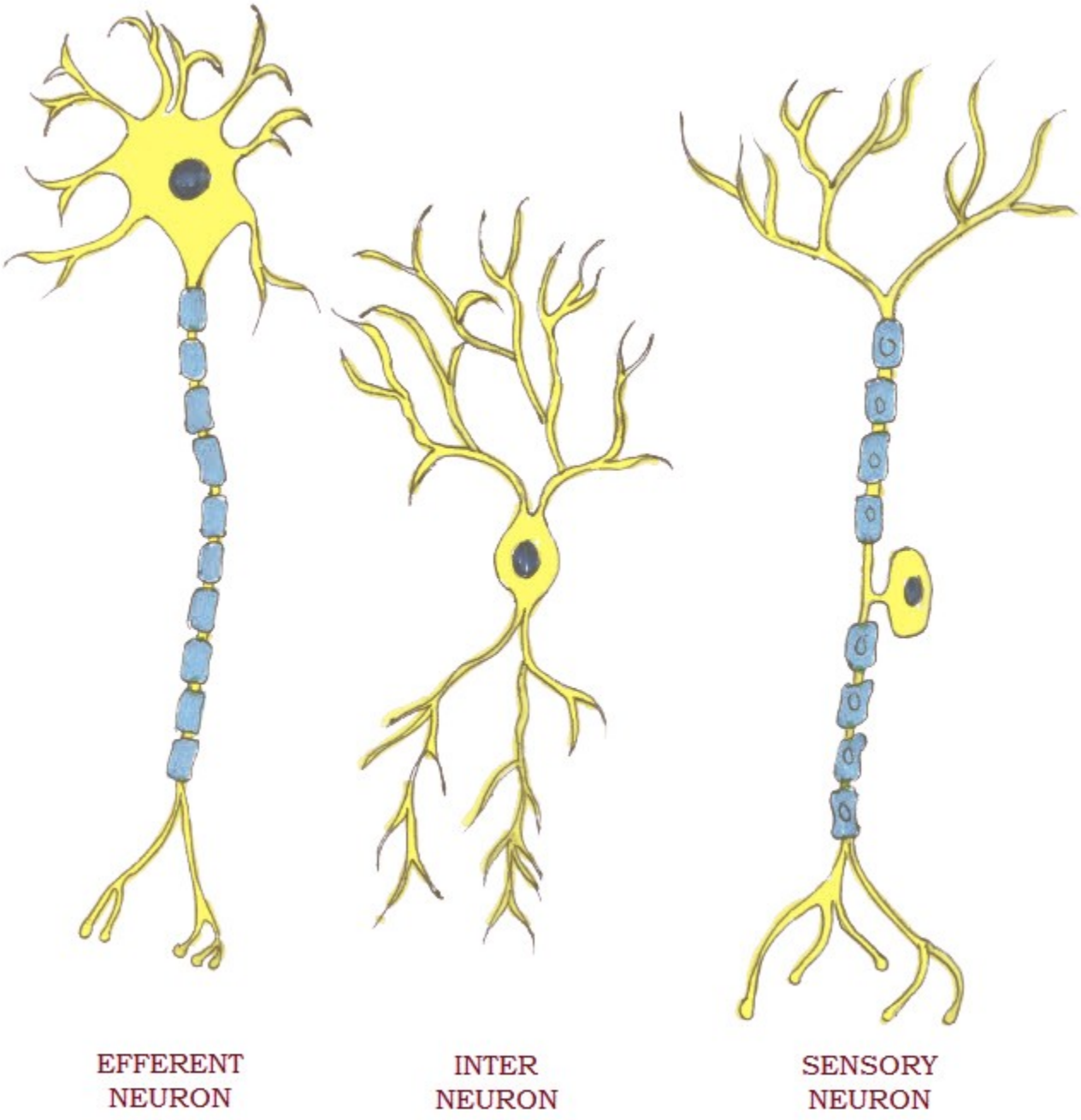
- Anatomical classification
- Functional classification

Anatomical classification

- According to the number of processes that arise during embryological development. All developing neuroblast pass the stages where processes are formed.

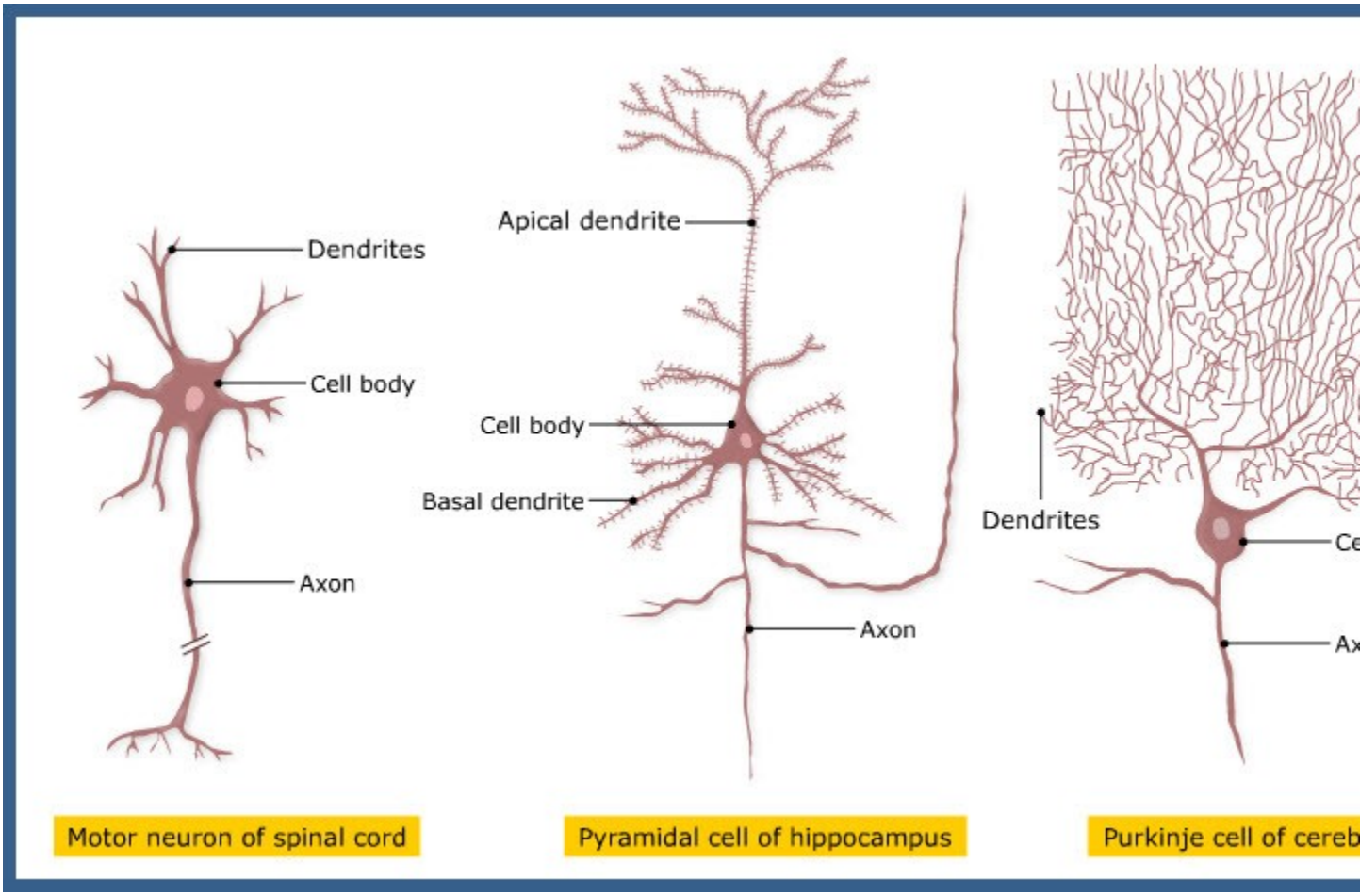


- *Apolar neuron:* There are no processes
- *Unipolar neuron:* They have a simple processes developing from soma. This process may split into two, one conveys towards the cell body and other conveys away from cell body. Hence they are referred to as pseudounipoloar neuron.
- *Pseudounipolar neuron:* A typical bipolar neuron. Develop as bipolar neuron but as it develops they fuse to form one process. Sensory in nature. Pseudo unipolar cells are "T" shaped cells whose peripheral branch is physiologically a dendrite but serve as axon to conduct nerve impulse centrally. Located in the ganglia outside the CNS.
- *Bipolar neuron:* These are the neurons are spindle shaped with axon at one pole and dendrite at the other pole. These are the neurons with the two processes emerging from opposite sides of the soma. Commonly seen in vertebrate retina to transmit light impulses to retinal ganglion cells, as well as olfactory neuroepitthelium. One of the two main processes extending from the cell body, is highly branched & conveys information to the cell body, similar to the function of dendrite.



- *Multipolar neuron:* These have many cellular processes extending from the cell body. One of these is an axon, and other constitutes highly branched dendrites. Most commonly seen in vertebrates, in cerebellar cortex (purkinje cells), motor coterx (pyramidal cells) and ventral horn of the spinal cord.
  There are two types of mutipolar neuron. Classified depending upon the length of the axon.
  - *Motor nerve cell:* cells with long axon. E.g. neurons in the ventral grey column of spinal cord. Axons of these cells arise from the CNS to become peripheral motor nerve fiber.

- *Type II Golgi cell:* cell with short axons. The axon divides into many branches in the area of cell body. Because of this arrangement sensory neurons are placed in contact with motor neurons. Hence they are known as interneurons or internuncial neurons. They lie within the CNS. They remain between afferent and efferent neurons. For more complicated actions more interneurons are involved.



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VIEW ANIMATION...

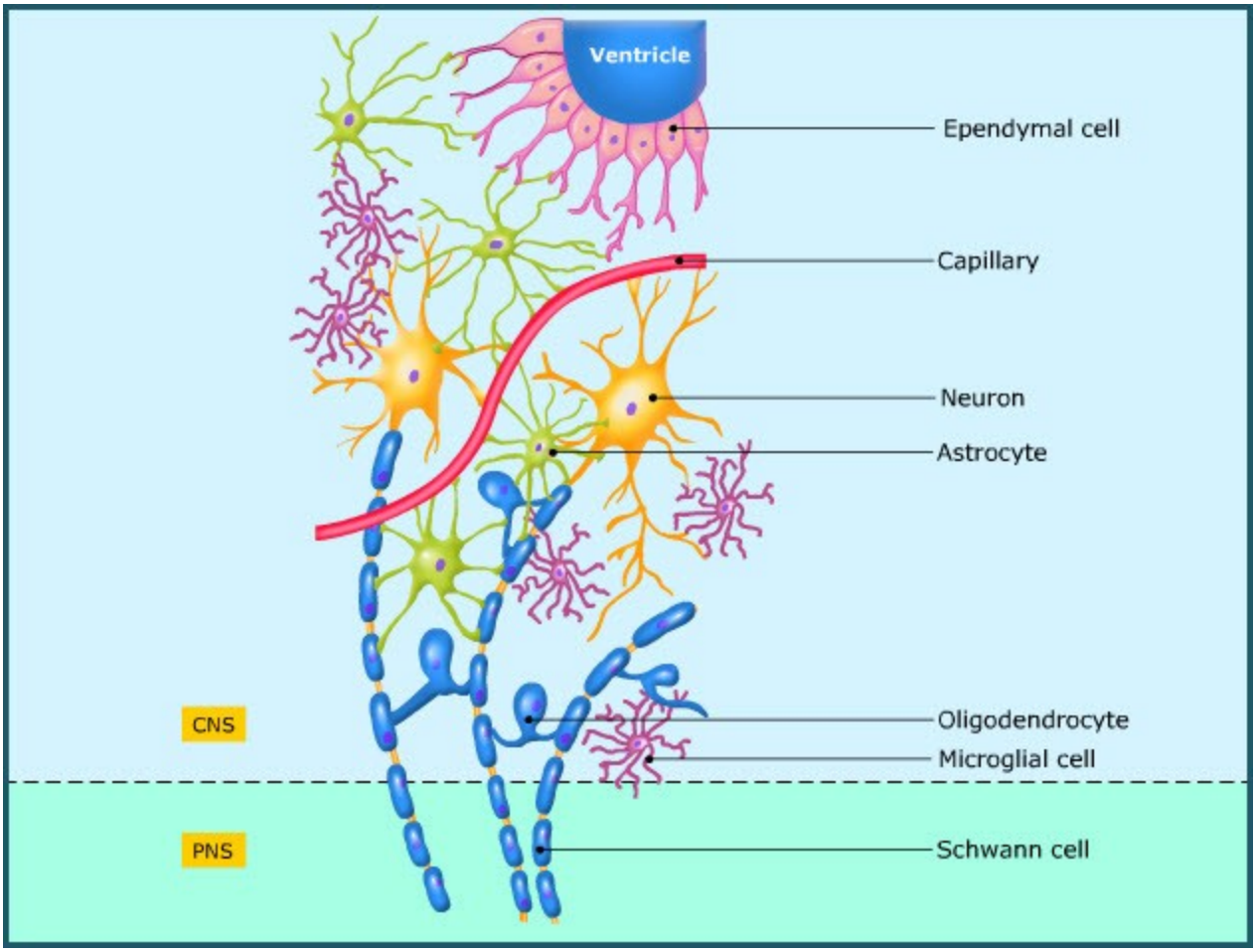
Functional classification

- *Sensory or afferent (towards/ carrying):* Information from sensors to CNS intimating CNS of external environment (sensory stimuli) and provides status reports on internal activities (visceral) that are regulated the nervous system.
- *Internuncial neurons:* remain in CNS act as a relay between two neurons.
- *Motor or efferent (from/ exit):* instructions from CNS to the effector organs to provide appropriate action.
- This outflow is by two means

- *Somatic nervous system* - to skeletal muscles. Fibers of motor neurons that supply skeletal muscles.
- *Autonomic nervous system* - using sympathetic and parasympathetic divisions control the effector organ such as smooth muscle, cardiac muscles and glands.

SUPPORTIVE CELLS

Supportive cells of *CNS are known as Glial cells or Neuroglia*. Neuroglia is a special type of interstitial tissue which provides nourishment to the neurons. Glial cells serve as a connective tissue of the CNS and provide support the neurons, both physiologically and metabolically. They constitute 90% of cellular population, and they do not branch as neurons. They don't participate in the initiation and conduction of nerve impulses. These cells homeostatically maintain composition of specialized environment surrounding the neuron.



They are classified according to shape, size and number of processes into three main types.

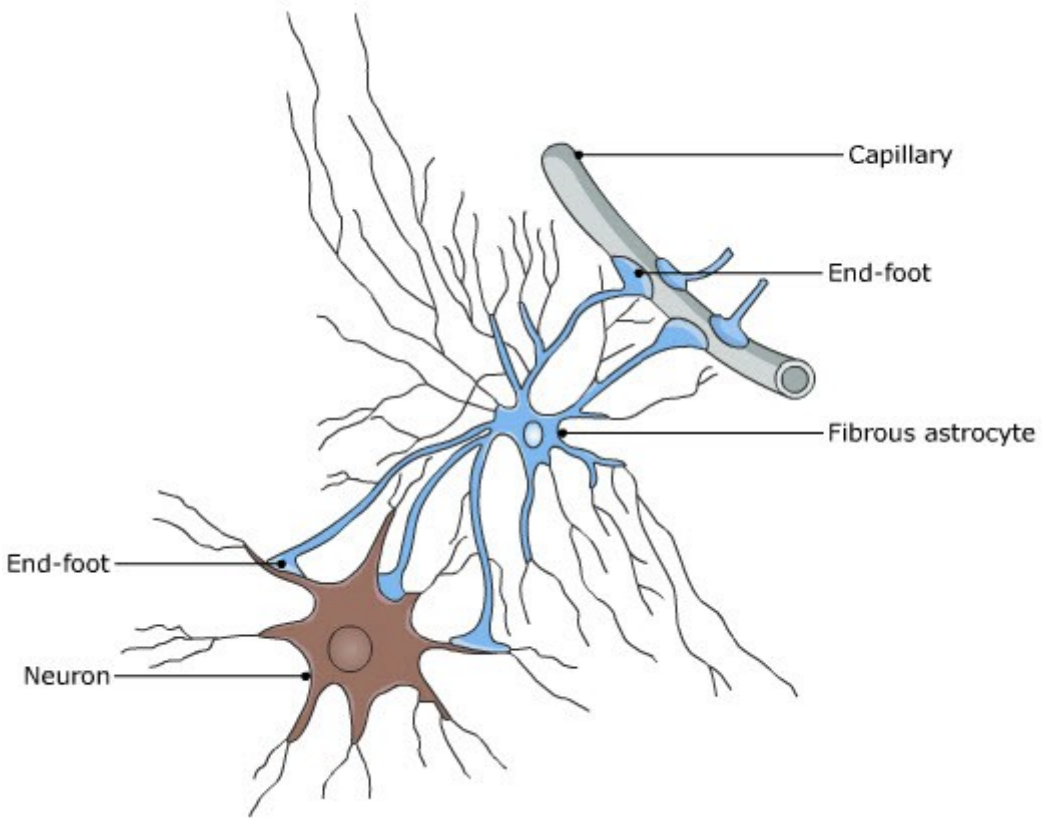
- Astrocytes (star shaped, ectodermal origin)
  - *Protoplasmic astrocyte- grey matter of brain and spinal cord. They have branching of protoplasmic processes.*
  - *Fibrous astrocyte- seen in white matter. They are long and have unbranched fibers.*
- Oligodendrites(ectodermal origin)
- **Microglia(smallest cells, mesodermal origin)**
- Ependymal cells.

General functions of neuroglia

- They provide support, insulation and phagocytosis. They support physically, metabolically and functionally. They provide biochemical and biophysical environment for proper functioning of neurons.

Astrocytes

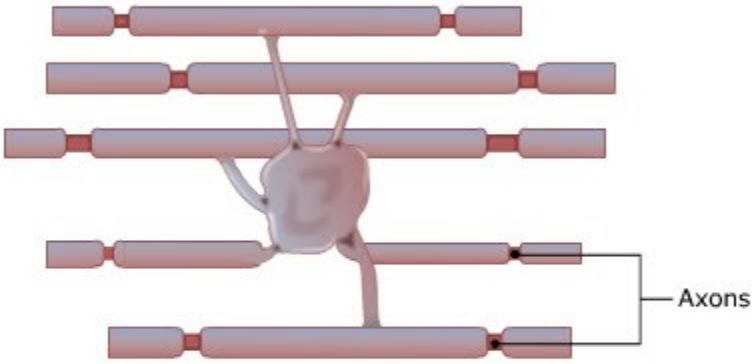
- Most abundant in number and they are star shaped. They posses number of critical functions.
    - During fetal development, they guide neurons for development.
    - These cells are responsible for **establishment for blood brain barrier.**
    - They act as a glue to hold the neurons together and confine their spatial relationship.
    - They regulate the neurotransmitter activity by degrading and reabsorbing the neurotransmitter.



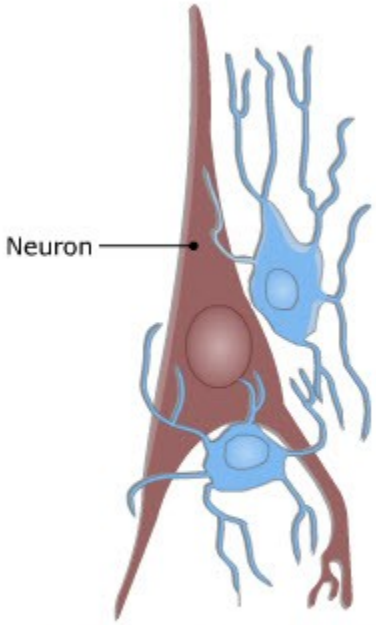
    - They absorb excess potassium ion by activating sodium–potassium pump and maintains ionic environment suitable for neural excitability.
    - They enhance synapse formation and potentiate synaptic transmission.
    - Astrocytes communicate via gap junctions between themselves and neurons.
    - Gap junctions are small tunnel like connecting units helping in signal communication.
    - Astrocytes have receptors for neurotransmitter and they release stored calcium ion prior to the release of neurotransmitter by the presynaptic neuron.
    - The release of calcium strengths the synaptic activity by accelerating the release of neurotransmitter.
    - They secrete neurotrophic factors that protect neurons against excitotoxicity and oxidative insult.

Oligodendrocytes

- They form the insulation by providing myelin sheath around the axons in the CNS.



Oligodendrocyte in white matter



Perineural oligodendrocytes

Microglia

- They are the immune defense cells of the CNS. They derived from the parent tissues of monocytes and they migrate to CNS during development. They are active when there is an infection in the CNS otherwise the resting microglia releases nerve growth factor that help neuron and other growth cells to survive.
- They have primary responsibility of phagocytosis in the CNS. These cells have long branches radiating outward during phagocytosis. They are getting activated. They retract the branches with their high motility and move towards the infective area to remove the invaders. Activated microglia releases degrading chemicals to neutralize the tissue debris.

Ependymal cells

- They line the internal cavities of vertebral CNS. They are of important as they contribute to the formation of CSF. Among the glial cells, they are ciliated and by the action of cilia the flow of CSF throughout the ventricles is regulated. An important characteristic of ependymal cells is that act as the stem cell which has the potential of forming glial cells and new neurons.

Supporting cells of PNS

- *Schwann's cell:* They are helpful in the formation of myelin sheath and provide insulation.

NERVE FIBRES

- Nerve fibres are *axons of neurons* which can be either insulated or naked. Insulation is provided by sheaths which may be either myelin sheath of lipoid layer or thin tubular covering of neurilemma or schwann sheath.

- The nerve fibres with myelin sheath are known as *myelinated* and those without myelin sheath are known as *unmyelinated fibres*. Myelinated fibres are seen in both CNS and PNS whereas fibres with schwann cell, sheathing core characteristically seen in fibres lie outside CNS.

Structure of Myelinated nerve fiber

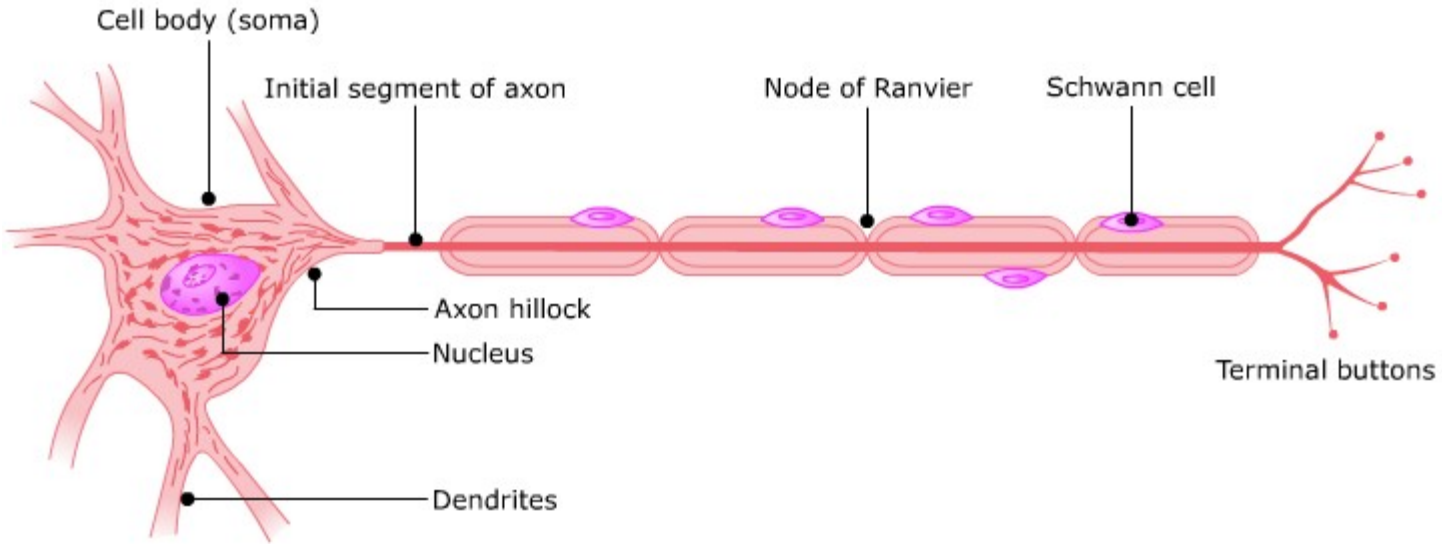
- Axon is composed of delicate neurofibrils embedded in an axoplasm along with mitochondria and endo plasmic reticulum. Axon has a cell membrane known as Axolemma separating the axon from the surrounding structures.
- Axolemma is surrounded by thick myelin sheath made-up of nucleated membranous Schwann cell sheath. This structure poses the axon to be highly refractive and provides white colour to the axon.
- **Myelin sheath consists of lipid-Sphingomyelin**. The myelin sheath is interrupted at regular intervals by constriction which appears to be a node and is known as Nodes of Ranvier. At each node, there is a constriction of neurilemmal sheath towards the axon. These sheath cells are absent in the myelinated fibers of CNS.

Myelinogenesis

- It is the process of myelin formation. It begins with crowding and excessive growth of Schwann cells completely encasing the whole length of the axon.
- The cell membrane of the Schwann cells surrounding the axons rotate in a manner to wrap around the axons and forms closely packed helically arranged layers of double membrane. Each membrane is composed of bilipid layer sand witched between the protein layer. Thickness of myelin sheath is determined by the number of membrane layers wrapped round the axon.
- Myelination of the sensory tract precedes the motor tract. Myelination is influenced by Vitamin B 12, Folic acid and Thyroxin hormone.

Stages of Myelination

- First stage begins with enclosure of axon with myelin forming cells. Mesoaxon is formed by the union of enveloping processes from outer surface.
- Elongation of mesoaxon in a spiral manner which coils around the axon occurs. Loss of cytoplasm of turns of mesoaxon tightens the spiral turns around the axon.



Conduction of impulse in myelinated fiber

- Nerve impulse travel at rapid rate in myelinated fibers. Electrical membrane has effective contact with the interstitial fluid only at the nodes of Ranvier.

- In myelinated fibers the local circuit flow is from one node to the other, known as Saltatory conduction.
- Due to this the conduction velocity in these fibers is greater as the conduction is restricted to patches of the membrane which are then depolarized. The conduction speed is 20 times greater than the unmyelinated fibers.

Unmyelinated nerve fiber

- Lacks myelin sheaths and are found in grey matter of spinal cord, some parts of brain and in ANS.
- Conduction velocity is about 1 meter and is dependant upon the diameter of the fiber.

CLASSIFICATION OF NERVE FIBRE

- Classified as *Type A, Type B* and *Type C fibers* based on the diameter, myelination and propagation speed. According to the diameter of the fiber, a physiological property of nerve fiber varies. **As diameter increases, the conduction velocity increases which requires lower threshold of excitation with greater magnitude of response**. **Time of conduction is shorter with shorter refractory period**.
- Based on the characteristics, nerve fibers are classified into 3 groups viz A, B and C fibres. Large fibers conduct impulses rapidly whereas small fibers are slow in conduction. The speed of conduction can be achieved by 2 nodes
    - By employing myelinated fibers
    - By increasing the diameter of the fibers.
- Group A consists of largest fibres (up to 30 microunit in dia) with conduction rates of 50-100m/sec. The fibres of this group are myelinated. This group is further typed into*alpha, beta, gamma and delta*.
    - Alpha is subtype is concerned with proprioception, to carry impulses from muscle spindle and golgi tendon organs.
    - Beta fibres are concerned with touch, pressure and other somatomotor impulses carrying from muscle spindle.
    - Gamma fibres are concerned with motor functions to muscle intrafusal fibers.
    - Delta fibres are similar to beta in function.Group B fibres are which are rich in preganglionic autonomic fibers and group C functions in post ganglionic sympathetic fibers.

PROPERTIES OF NERVE FIBRE

- Ability of nerve fibre to respond to stimulus.

Stimulus

- It is an external agent that brings about visual response. It can be also be from within and can elicit response which can not be visualized.
- Types of stimulus
    - *Electrical:* this is the most common stimulus to bring about neuronal response.
    - *Chemical:* osmotic also come under this. Hypo, hyperosmotic, acid or alkali.
    - *Mechanical:* touch, thermal, light, sound, pressure changes are included in this.

All or none law

- In a nerve fibre, action potential are equal in amplitude and velocity. Because amplitude and velocity are independent of intensity of the stimulus. This is the basis of all or none law. Nerve fibres obey all or none law.
- When adequate strength of stimulus is applied to a nerve, the action potential propagates in the same magnitude all along the nerve. If the stimulus is low in threshold, there is no action potential and if the stimulus is above the threshold the action potential is uniform, magnitude of action potential does not increase with the stronger stimuli. This is known as all or none principle. As the action potential travels along it triggers the subsequent axon to fibre.

Refractory period

- However, for a period following the passage of an impulse, there is un responsiveness , though a second stimulus is strong axons are incapable of generating new impulses. This interval known as **absolute refractory period**. This period varies wit the type of nerve and with species.
- In mammalian nerve it is about 1.04m sec. absolute refractory period is due to complete closure of sodium gates which resists the membrane to produce an action potential most of the axons exhibit 1 ms as their absolute refractory period.

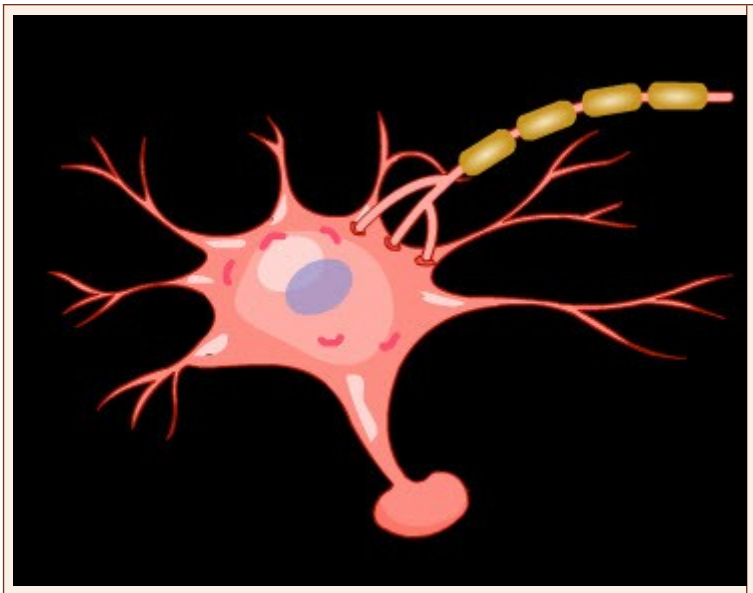
Relative refractory period

- It follows the absolute refractory period. In this, the response to second stimuli of threshold strength is absent but if the second stimuli is of higher strength than threshold response is appreciated.
- The excitability gradually rises to normal. Because of this the nerve fibre can be stimulated for hours without excitability fatigue.
- Relative refractory period is due to the opening ok K^+ gates with Na^+ gates resting their usual state. Due to free flow of K^+, stronger than usual stimulus is necessary to initiate action potential.
- Relative refractory period in axons experimented was 2-4 m s. The refractory period governs the rate at which a membrane can fire.

Accomodation

- Strength of the stimulus applied bears relationship with length of the time of its application to produce a response.
- Short duration, strong stimuli and long duration weak stimuli fail to produce a response.
- Rate of rise of stimuli when applied rapidly produces better response. But slow rise in stimuli for longer duration fail to provoke a response due to adaptation by nerves to weaker stimuli which is known as accommodation. This phenomenon is due to partial inactivation of sodium carrier by nerve cell.

MODULE-2: IMPULSE GENERATION AND PROPAGATION



LEARNING OBJECTIVES

This module deals with,

- generation of an action potential and impulse and
- the propagation of an impulse in myelinated and non-myelinated fibres and conduction velocities in them.

PRINCIPLES OF MEMBRANE POTENTIAL

Basic Physics

- In the tissue the fluid outside (interstitial fluid) and inside (intracellular fluid) are electrolytic solutions, containing 150 to 160 mEq / litre of positive ions (cations) and the same concentration of negative ions (anions).
- Generally a very small excess of negative ions accumulate immediately inside the cell membrane along it's inner surface, and an equal number of positive ions accumulate immediately outside the membrane, the effect of which is the establishment of membrane potential between the inside and outside of the cell membrane.
- Such a membrane whose inside is more negative than the outside is said to be a polarized membrane. The basic means by which membrane potentials develop are
    - Passive diffusion of ions i.e. diffusion along concentration gradient,
    - Active transport of ions against concentration gradient and creation of imbalance between negative and positive charges.

RESTING POTENTIAL

The resting potentials of nerve and muscle Fibers

- In the resting state of membrane i.e. the state under which the membrane of the nerve or muscle fibers is not transmitting signals, the fluid inside the nerve or muscle cells has greater concentration of K^+ and the fluid outside the Na^+.

- The potential across the membrane is a negative potential and is known as resting potential. The resting potential of the nerve as well as the muscle fiber is -75mV i.e. the potential inside the fiber is 75mV more negative than the potential outside.

Sodium - Potassium Pump mechanism

- The mechanism is present in all cells of the body. The negative resting membrane potential is established by this mechanism. It transports Na^+ from the cells to the exterior and K^+ from the exterior to the cell. Hence it is responsible for maintaining the normal Na^+-K^+ concentration difference across the cell membrane.
- The pump mechanism uses a carrier protein, which is a complex of two separate globular proteins, one of which is large with a molecular weight of about 100,000 and the other is small with a molecular weight of about 45,000. The function of the latter is not known. The large one has the following 3 specific features that confirm the pump function:
    - As the carrier protein complex exists across the cell membrane the large protein protrudes on either side of the membrane.
    - It has 2 receptor sites on the outside protrusion for K^+ and 3 on the inside protrusion for Na^+.
    - The site adjacent or close to the Na^+ receptors has ATPase activity.
- In the operation of the pump mechanism $3Na^+$ bind (each at a receptor) from interior of the cell and 2 K^+ (each at a receptor) from exterior of the cell. The binding of Na^+ at the receptors activates the ATPase. A molecule of ATP is cleaved and reduced to ADP. Energy is liberated from a high energy phosphate bond, cause conformational change in the carrier protein molecule and this change extrudes the Na^+ to the exterior and K^+ to the interior of the cell.
- Since all the while the concentration of Na^+ at the exterior and K^+ in the interior of the cell is high, both these ions are transported by the pump mechanism against very large concentration gradients.

Electrogenicity of the Na^+ - K^+ pump mechanism

- At each revolution of the pump 3 Na^+ are transported to exterior for every 2 K^+ to the interior of the cell. This amounts to a net of one positive change removed from the interior to the exterior.
- This obviously creates positivity outside the cell, leaving (owing to the deficit of positive ions inside the cell) negativity on the inside and thus an electrical potential is established across the cell membrane. Hence, the pump mechanism is said to be electrogenic.

ACTION POTENTIAL OF NERVE AND MUSCLE FIBERS

- The action potentials are the rapid changes in the resting membrane potential. Nerve signals are transmitted by action potentials.
- Each action potential begins with a sudden change from the normal resting negative potential to a positive potential, and ends with an equally rapid change back again to normal negative potential.
- The action potential initiated moves along the fiber until it comes to the end of the fiber and thus spreads the impulse or signal along the fiber.

THE STAGES OF ACTION POTENTIAL

Depolarization stage

- The resting membrane suddenly becomes very permeable to sodium ions (stimulus applied causes this permeability) allowing tremendous number of Na^+ to flow to the

interior of the fiber. *The normal resting state of -75mV* is lost with the potential rising or changing rapidly in the positive direction. This is called depolarization.

- In large fibers the potential over shoots beyond the zero level and becomes slightly positive (reversal potential). In some smaller fibers as well as in many CNS neurons the potential approaches the zero but does not overshoot or reverse.

Repolarization stage

- Within a fraction of a second (few 10,000 ^{ths} of a second) after the membrane becomes highly permeable for Na^+ the channels for the Na^+ close almost as rapidly as they had opened. Then rapid diffusion of K^+ to the exterior re-establishes the normal negative resting potential. This is called *repolarization of the membrane*.

THE VOLTAGE-GATED SODIUM CHANNEL

- *Depolarization Stage:* The resting membrane suddenly becomes very permeable to sodium ions (stimulus applied causes this permeability) allowing tremendous number of $Na^+$to flow to the interior of the fiber. *The normal resting state of -75mV* is lost with the potential rising or changing rapidly in the positive direction. This is called depolarization. In large fibers the potential over shoots beyond the zero level and becomes slightly positive (reversal potential). In some smaller fibers as well as in many CNS neurons the potential approaches the zero but does not overshoot or reverse.
- *Repolarization Stage:* Within a fraction of a second (few 10,000 ths of a second) after the membrane becomes highly permeable for Na^+ the channels for the Na^+ close almost as rapidly as they had opened. Then rapid diffusion of K^+ to the exterior re-establishes the normal negative resting potential. This is called *repolarization of the membrane*.

Voltage-gated channels of the Cell Membrane

- There are two separate and specific voltage-gated channels, one for Na^+ and the other for the $K^{+.}$
- The principle operator of the stages of action potential ie. causing the depolarization and repolarization of the membrane is the so called voltage-gated Sodium channel. However, the voltage-gated potassium channel also plays an important role in certain nerve fibers.

The Voltage-gated Sodium Channel

- The channel or the passage has two gates one at the exterior end (opening to the outside of the cell) and the other at the interior end (opening to the inside of the cell). These gates may be referred to as external or internal gates of the channel. **The external gate is known as 'Activation gate' and the internal as 'Inactivation gate'**. The potency of the gates at different stages of an action potential is explained as follows:
    - *Resting Stage:* The activation gate is closed and the inactivation gate is opened. The Na^+ cannot enter the channel.
    - *Activated stage (Depolarization stage):* Both the gates are opened and the Na^+ can freely pass through the channel from the exterior to the interior of the cell.

- *Inactivation Stage (Repolarization stage):* The inactivation gate is closed and the Na^+ cannot enter the channel from the interior of the cell.
  - When the activation gate is opened it is referred to as *"activation of the channel"* and when the inactivation gate is closed it is referred to as *"inactivation of the channel"*.

Activation

- Is effected when the resting membrane potential (-75mV) drops or becomes less negative and reaches a level between -60 to -50mV. Then sudden conformational change in the activation gate flipping it to the open position (Activated state). Then Na^+ literally pours into the cell through the channel. At that moment the depolarization process of the membrane begins. The movement of Na^+ through the membrane is referred to as Sodium permeability of the membrane and it is increased as much as 500 to 5000 fold during activation.

Inactivation

- The above said drop in negativity otherwise increase in voltage that opens the activation gate also closes the inactivation gate. However, the closure of the inactivation gate occurs a fraction of a second (few 100,000ths of a second) after activation gate opens ie. The conformational change that flips the inactivation gate to closed state is comparatively a slow process. Therefore, during the time lapse between the activation and inactivation of the channel which is also a fraction of a second (few 100,000ths of a second) there is passage of Na^+ to the interior of the cell and at the end the inactivation gate suddenly closes and the Na^+ no longer pour to the inside of the cell or membrane. At that moment the repolarization process begins.
- Important characteristics of the inactivation
  - *The inactivation gate will not reopen until the disturbed membrane potential returns either to or nearly to the original resting membrane potential level. Therefore, without the repolarization or nearing completion of repolarization of the fiber it is not possible for the Na^+ channel to open again.*

THE VOLTAGE-GATED POTASSIUM CHANNEL

- This channel has only one gate at the interior of the membrane and closes or opens to the interior of the cell. The opening of the gate is referred to as activation. The gate operates in two stages:
- *Resting stage:* During the stage the gate is closed and the K^+ is prevented from passing to the exterior of the cell through the channel.

During the stage of action potential manifestation

- When the membrane potential, rises from -80mV toward zero (becomes less negative). This voltage change causes conformational opening of the gate and allows K^+ diffusion outward. But, this process operates in a slow manner hence, it is timed, that **the opening of the K^+ channel is initiated at the same time that the Na^+channels are becoming inactivated (closing). The later decreases the Na^+ entry into the cells**.
- Thus the decreased Na^+ entry to the cell and concomitant increase in K^+ exit from the cell increases the intracellular negativity and greatly speeds the repolarization process.

Therefore, in a fraction of a second (few 10,000ths of a second) there is attainment of the resting membrane potential.

GENERATION OF THE ACTION POTENTIALS

- When a fiber is stimulated at a point the action potential is initiated at the point. A local current or EMF (Electromotive force) is produced at the point.
- A *"local circuit"* of current is established between the depolarized point and the adjacent resting point.
- Positive electric charges flow through the circuit into the fiber through the depolarized membrane and continue to flow along the core of the fiber. This kind of flow increases the voltage (to above threshold value) along the core through a distance of 1-3 mm. This strong impulse promptly activates the Na^+ channels present on the course and the explosive action potential spreads.

Spike potential

- **The initial very large action potential is called the spike potential**. In large myelinated nerve fibers the spike potential lasts for about 0.4 seconds. It is also called as ***nerve impulse.***

Negative after potential

- At the termination of the action potential the membrane potential sometimes fail to return to its resting level for an additional few milliseconds. Often instances will be there after a series of rapidly repeated action potentials. The situation is due to the build up of K^+ immediately outside the membrane and the side becomes more positive than normal and this increase the time for the potential to return to the normal resting level. This less negative membrane potential through the additional few milliseconds is called the negative after potential.

Positive after potential

- Once the resting value of the membrane potential is reached, it further becomes little more negative than the normal resting value. This excess negativity is from a fraction of an mV to a few volts than the normal resting level and this potential is known as **"Positive after potential".** The after potential state can last from 50 milliseconds to as long as many second. It is principally the recharging process (the electrogenic pumping of excess Na^+ outward).

PROPERTIES

All or nothing principle

- The principle operates in the membrane excitation of the fibers i.e. once an action potential has been elicited at any point on the membrane of a normal fiber, the depolarization process travels over the entire membrane. This is called the all or nothing principle of membrane excitation.
- It applies to all normal excitable tissues. However, when the fiber is in an abnormal state the action potential may reach a point in the membrane at which it does not generate sufficient voltage to stimulate the adjacent resting point of the membrane and therefore the spread of depolarization may stop.
- But under normal conditions, such stoppage will never occur and the impulse generated stops only when it reaches the fiber end.
- Therefore, for normal propagation of impulse, the ratio of action potential to the threshold for excitation of the fiber called "Safety factor" at all times be greater than one.

Conduction (Signal transmission) in nerve fibers

- A typical small nerve trunk is constituted by both the large nerve fibers and small nerve fibers.
- The large fibers are myelinated and the small fibers are unmyelinated.
- The ratio of distribution of these myelinated and unmyelinated fibers in such a trunk is 1:2 respectively.

STIMULUS

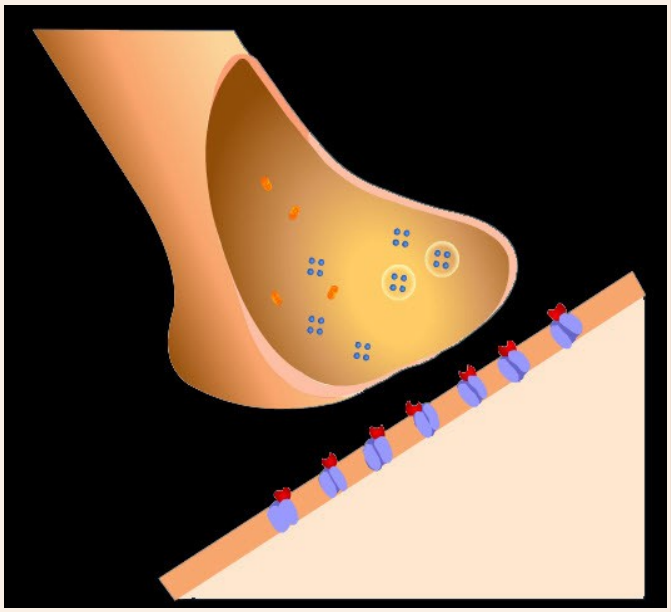
Classification of Qualitative stimulus

- *Chemical stimuli:* Strong acid or alkali or any chemical irritant inducing excitability.
- *Thermal stimuli:* Heat applied to the skin causing the excitability.
- *Mechanical stimuli:* Pinching, pin prick causing the excitability.
- *Osmotic stimuli:* Tissue when subjected to hypo or hypertonic solutions will be stimulated.
- *Electrical stimuli:* Exposed to shock.

The electrical stimulus is more or less similar to the natural stimulus present in the body. Moreover, the strength of the electrical stimulus can be regulated as required. So it is often preferred for conducting experiment. Based on the strength(Quantitative) of the electrical stimulus it is classified as follows

- Sub-minimal or sub-threshold strength
- Minimal or threshold strength
- Sub-maximal or above threshold strength
- Maximal strength
- Above maximal strength (destructible to the tissues)

MODULE-3: SYNAPSE AND ITS PROPERTIES



LEARNING OBJECTIVES

This module eloborates,

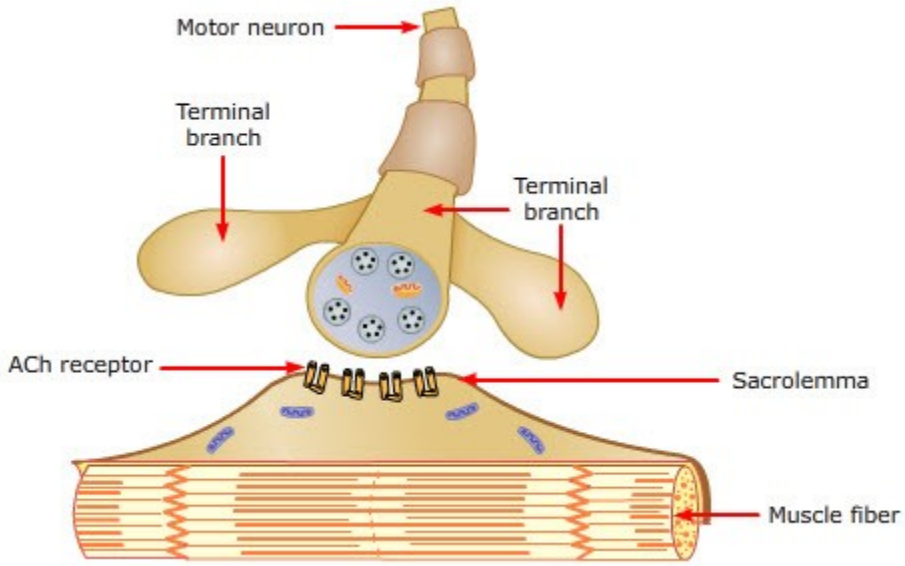
- the definition of a synapse and its types,
- the structure of a synapse, neurotransmitter release and synaptic transmission of impulse,
- the role of neurotransmitters on post synaptic

	membrane with special reference to chemically activated ion channels and second messenger activators and the fate of neurotransmitters, • the difference between chemical and electrical synapses and • the classification of neurotransmitters, its synthesis, effect and metabolism of a few common neurotransmitters.

SYNAPSE-ANATOMY

Functional anatomy of the synapse

- A typical motor neuron (efferent neuron) shown under electron microscope numerous (average about 6000) small knobs spread over the surface of the dentrites (80-90%) and soma (10-20%). These knobs are the ends of nerve fibrils that have their origin in many other neurons (usually not more than a few derived from any single previous neuron). The knobs are referred to as presynaptic terminals or terminal knobs, buttons, end feet and synaptic knobs.



- Neurons in other parts of the cord and brain differ markedly from the motor neuron in the following features :
    - Size of the soma
    - Size, length and number of dentrites (ranging in length as long as many centimeters)
    - Size and length of axon
    - The number of presynaptic terminals (range from few to more than one hundred thousand).
- These differences are responsible for the neurons of the different parts of the nervous system to react diversely to incoming signals in their functions.

TYPES OF SYNAPSES

Types of synapses

- Chemical synapse
- Electrical synapse

Chemical synapse

- **All the synapses present in the central nervous system are chemical synapses.**
- In these, the first neuron secretes a chemical substance called as a neurotransmitter at the synapse.
- The transmitter travels and acts on receptor (protein in nature) present in the membrane of the next neuron.
- According to the functional nature of the receptor there may be excitation or inhibition or modification of the sensitivity of the neuron.
- There are about 30 such different transmitter substances reported.
- The chemical synapses always transmit the signals in one direction (unidirectional transmission) that is from the presynaptic neuron to the post synaptic neuron.
- The unidirectional conduction allows signals to be directed toward specific goals, discrete and highly focused areas of the nervous system to perform its varied functions of sensation, motor control , memory and many others.

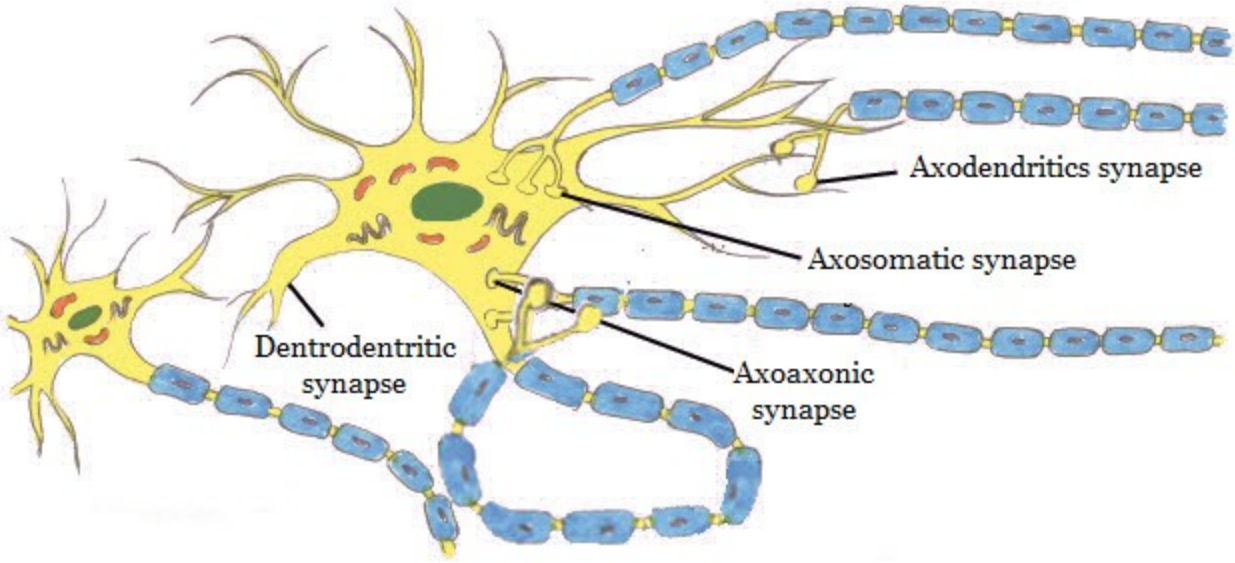
Electrical synapse

- Have channels directly connecting one neuron to the other and electricity is being conducted from one nerve cell to the other.

- **The channels are usually small tubular structures made up of protein and referred to as gap junctions.**
- The gap junctions allow free movement of ions from the interior of one cell to the other.
- Only few such synapses are found in the central nervous system.
- In smooth muscles the action potentials are transmitted from one fiber and in the cardiac muscle from one cell, to the next by way of the gap junctions.
- The conduction through electrical synapse is by-way or bi-directional i.e. the signals are transmitted in either direction.

Synaptic junctions of the nervous system

- *Axosomatic :* It is the synapse between the axon of one neuron and the soma of the next. Found in spinal cord and autonomic ganglia.
- *Axoaxonic :* It is a synapse between axons present in the (mammalian) spinal cord between axons of interneurons.
- *Axodentritics :* It is a synapse between axon of a neuron and dendrite of another neuron. Present in the dorsal horn of the spinal cord.
- *Dentrodentritic :* Synapse between the dentrites of different somas. Present in the cerebellum.



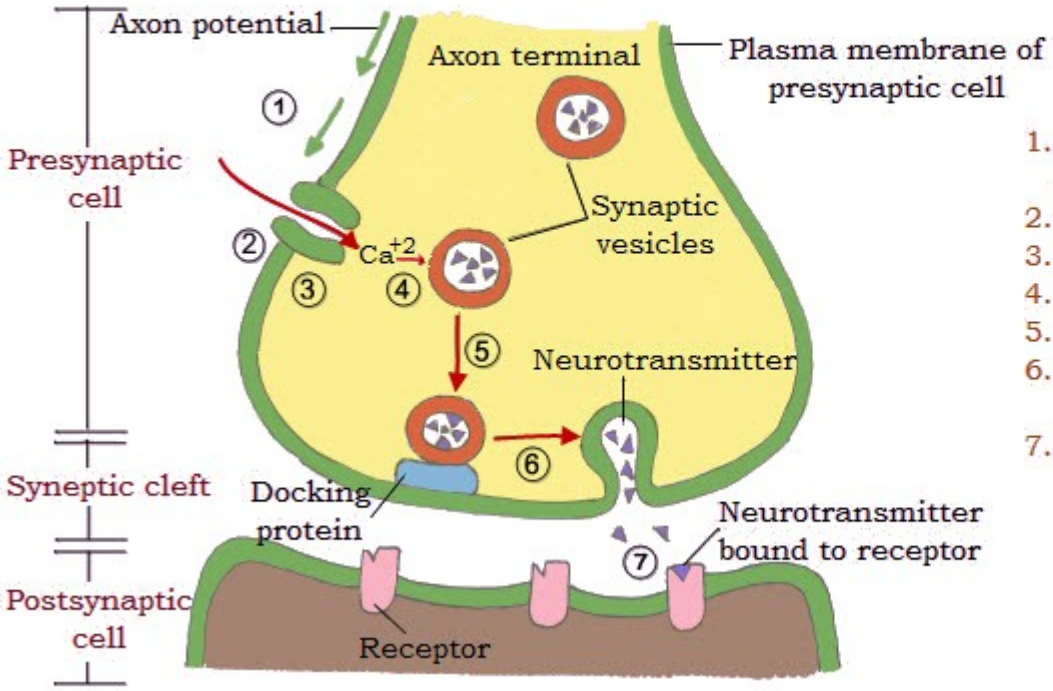
SYNAPTIC TRANSMISSION OF IMPULSE

Structural properties common to all synaptic functions

Presence of synaptic cleft

- There is no continuity of the cytoplasm across the synapse. There is a synaptic cleft (200-300 micron width) between the pre and post synaptic membranes.
- Thickened and modified portions both on the synaptic knob membrane and post synaptic membrane.
- Rich presence of mitochondria in the cytoplasm of the synaptic knob.
- Presence of synaptic vessicle (300-600 micron dia.) storing the chemical transmitter in the synaptic knob. The vessicles are absent in the post synaptic cell.

Mechanism of synaptic transmission



Transmitter release

- The membrane of the synaptic knob contains large number of voltage gated calcium channels (the other area of the nerve fiber has very few channels). The action potential travelling along the fiber depolarizes the terminal membrane. Large number of Ca^{++} along with Na^{+} from the extracellular fluid enter the synaptic knob. It is postulated that when the Ca^{++} enter the knob bind themselves with the protein receptors present on the inside of the knob membrane (synaptic membrane). The receptor sites are known as release sites. This Ca^{++} receptor combination causes the nearby vesicles to adhere and fuse with the synaptic membrane, and finally the vesicles to open to the exterior (into the cleft) by a process called exocytosis. A single action potential often opens several hundred vesicles and release their transmitter into the cleft.

Fate of the released transmitter

- It is accompanied by three ways
  - Reincorporation of the transmitter by or into the vesicles. The opened vesicle invaginates towards the inside of the knob and pinch off to reconstitute the vesicle. The appropriate transport proteins still present in the vesicle membrane shift into and concentrate the transmitter in the vesicle.
  - Resynthesis of the transmitter in the cytoplasm of the knob and their immediate absorption into the vesicles. This is a continuous process. By this mechanism, the exhaustion of the transmitter is minimised. As the vesicles by these methods of replenishing are used again this method is referred to as recycling of the vesicles.
  - But, when both the vesicle and the mitochondria are aged they disintegrate. Both, new vesicles and the mitochondria are continually transported from the

soma down the axon to the presynaptic knob. They move along the axon at a velocity from 1cm to 40 cm / day.

- Action of the transmitter on the post-synaptic membrane
  - The transmitter acts on the receptor proteins present on the post synaptic membrane. The receptor have two functional components
    - A binding component, which protrudes from the membrane to the exterior into the cleft and binds with the neurotransmitter released into the cleft.
    - An ionophore component which through the membrane protrudes to the interior of the post-synaptic membrane or neuron.

IONOPHORE COMPONENT

There are two types of ionophores

- Ion channels (chemically activated)
- Second messenger system (enzymatically activated internal metabolic system)

Chemically activated ion channels (ligand-activated channels) are of three types

- *Sodium channels:* Allow mainly Na^+ (Some K^+ as well)
- *Potassium channels:* Allow mainly K^+
- *Chloride channels:* Allow Cl^- and few other anions to pass through. The transmitter that selectively open the Na^+ channels excites the post synaptic neuron and called as excitatory transmitters. Those, open K^+ and Cl^- separately or both of these channels together inhibit the neuron, and referred to as inhibitory transmitters.

Enzymatically activated internal metabolic system

This type of receptor causes, in the post synaptic cell ,

- Activation of cellular genes and such genes cause manufacture of additional receptors for the post synaptic membrane
- Activation of protein kinases and effects disintegration of receptors and their reduction in number in the post synaptic membrane. These effects on the receptor number of the post synaptic membrane can alter the reactivity of the synapse for minutes, days, months or even years. The transmitters that act on the enzymatically activated system of the cell is called as modulators. The modulators are important in operating memory processes.

The duration of action and fate of the transmitters

- When either an excitatory or inhibitory transmitter is released into the synaptic cleft and excite or inhibit the post synaptic receptors by opening the specific chemically activated ion channels and these channels remained open for only 1 to 2 milliseconds. The reason for these channels be opened through a very short duration is that the transmitter agent is rapidly removed from the cleft in the following ways :
  - By diffusion of the transmitter out of the cleft, into the surrounding fluid.
  - By enzymatic destruction, within the cleft itself.
  - By transmitter re-uptake by the pre-synaptic knobs.
- The extent to which each of these methods of removal is operating is different for each type of transmitter.

SYNAPSE-NEUROTRANSMITTERS

- A transmitter cause excitation or inhibition is determined by
  - The transmitter released at the synaptic terminal
  - The nature of the receptor present in the post synaptic membrane
- A single neuron may either be excited or inhibited. When excited, a transmitter is released at the synaptic knob which acts on the post synaptic excitatory receptors of the

knob (eg. Acetyl choline). When inhibited, a transmitter is released at certain other knobs which acts on the post-synaptic inhibitory receptors of the knob (eg. glycine). Similarly, in the CNS norepinephrine released in the synaptic knob when acted on excitatory post synaptic receptors of the knob causes excitation and when the receptors are inhibitory causes inhibition.

- Usually, only **a single type of transmitter substance is released at the nerve terminal by each neuron and the concept is known as *"Dale's principle"*.** However, there are exceptions in which the same nerve terminal might secrete another transmitter which may be excitatory or inhibitory, and yet another that acts as a modulator.
- For example, the *excitatory* transmitter might be *glutamate* which causes immediate excitation as it secretes one of the *neuropeptides* might also be secreted as a *modulator*and increases the number of glutamate receptors and this increases the sensitivity of the synapse for days or weeks.

The transmitter substances

- More than 30 different biochemical substances have been identified. These substances are grouped as follows :
  - Class 1: Acetylcholine
  - Class 2: Several amines
  - Class 3: Several amino acids
  - Class 4: Neuroactive peptides.
- The following are the important transmitters :
- *Acetylcholine :* It is secreted by neurons of the following areas:
- Parts of the brain such as
  - large pyramidal cells of the motor cortex
  - neurons in the basal ganglia
  - motor neurons that innervate the skeletal muscles.
- Preganglionic neurons of the autonomic nervous system.
- Post ganglionic neurons of the parasympathetic nervous system
- Some of the post ganglionic neurons of the sympathetic nervous system.
- *Glycine:* Glycine mainly secreted at synapses in the *spinal cord* and probably always acts as an *inhibitor* transmitter.
- *Gamma-aminobutyric acid (GABA):* In addition to its secretion in the neurons of the *spinal cord*, it is secreted in the neurons of the cerebellum, basal ganglia and many areas of the cortex. It always causes inhibition.
- *Glutamate:* Glutamate is secreted by the presynaptic terminals in most of the *sensory pathways* and also in many areas of the *cortex*. It is an *excitatory transmitter***.**
- *Substance P:* ***It is released by pain fiber terminals present in the dorsal horn of the spinal cord. It is also found in the basal ganglia and hypothalamus. Generally it is a excitatory transmitter.***
- *Enkephalins:* Enkephalins are secreted by the nerve terminals, in the *spinal cord, brain, stem, thalamus and hypothalamus*. Act as *excitatory transmitters* to the *system* that ***inhibit the transmission of pain***.
- *Serotonin :* serotonin is secreted by the nuclei that present in the *median rapne of the brain stem* and the fibers of the nuclei project to many brain areas such as *hypothalamus*and *dorsal horn* of the *spinal cord***.** Serotonin **acts as an *inhibitor* of the pain pathways**.
- *The esterase:* Hydrolyses both, the noradrenaline and the adrenaline into the principal end product *3-Methoxy, 4-hydroxy mandalic acid* which is secreted along the urine. The esterase, is found in the adrenergic nerve ending.

- *Post-ganglionic:* The transferase is found predominantly in the adrenal medulla as the norepinephrine is the precursor of epinephrine in the medulla and the transferase-methylates the former to the later. On generalised sympathetic stimulation adrenal medulla releases 80% epinephrine and 20% norepinephrine into the circulation.
- In the nerve endings the enzymatic inactivation of the norepinephrine accounts only 15% of the total transmitter released on stimulation. The rest 85% is reincorporated into the storage vesicles of the nerve endings. The receptors bind the transmitter and prevents it's diffusion away from the nerve terminals, the later help the reincorporation of the transmitter.
- Examples of neurotransmitters are
    - Dopamine
    - Norepinephrine

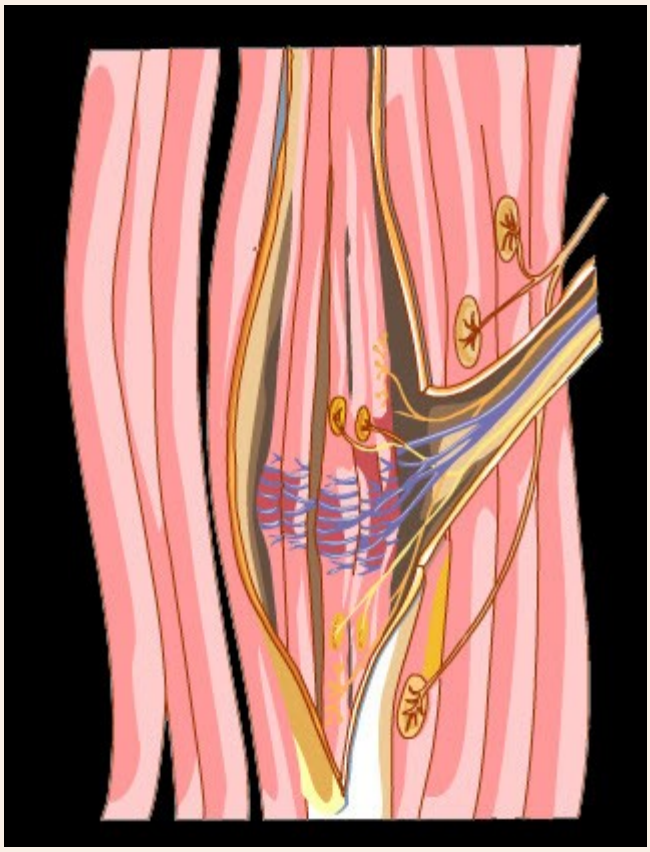
Dopamine

- It is secreted by the *neurons of* the *substantia nigra* and the *basal ganglia*. **The effect is usually *inhibition*.**
- There are about 3000 molecules of acetylcholine are present in each vesicle that store the transmitter. Enough number of such vesicles are present in the presynaptic terminal of a neuron to transmit few thousand impulses.
- Acetylcholine is synthesized from acetyl-CoA and choline with the help of the enzyme *choline acetyl transferase* which is present in abundance in the cytoplasm of the cholenergic type of presynaptic terminal. The released acetylcholine present in the cleft is rapidly split again to acetate and choline by the enzyme cholinesterase which is present in the proteoglycon reticulum filling the cleft. The choline is transported back into the knob and is reutilized for resynthesis of new ach. molecules.

Norepinephrine

- It is secreted by many neurons of the *brain stem, hypothalamus and pons*. The later sends nerve fibers to extensive areas of the brain and function in controlling the overall activity and mood of the mind. Mostly it causes excitation in the areas and however some inhibition too. Most of the post ganglionic nerve endings of the sympathetic system secrets norepinephrine and excite some organs and inhibits the others. The adrenaline acts on the other post ganglionic nerve endings.
- Catechol-O-methyl transferase and catechole-O-methyl esterase are the two enzymes that metabolise the noradrenaline and adrenaline respectively, in the cord and also helps to control the mood and cause sleep.
- Other substances such as *peptides*, other *amino acids, histamine, prostaglandins, cyclic AMP* and many others also act as neurotransmitters.

MODULE-4: RECEPTOR AND ITS TYPES



LEARNING OBJECTIVES

This module deals with,

- sensory function of skin and
- response, sensory transduction, generator potential, receptor adaptation and modality of sensation with reference to the somato-sensory nervous system.

DEFINITION OF A RECEPTOR

- Receptors are specialized as neuronal structures to detect diverse stimuli from the internal and external environment.

MECHANISM OF ACTION OF A RECEPTOR

- Incoming stimuli transduce the membrane potential into the receptor or generator potential.
- The protein structures within the sensory receptors absorb energy from stimuli to undergo conformational change which in turn activate signal transduction pathway.
- This allows change with appropriate voltage gated channel to induce the impulse generation through the proper neurotransmitters.
- Sensory reception include signal reception, signal transduction, signal amplification, signal transmission to higher centres and perception at the integrating centre.

Properties of Sensory Reception

- Primary afferent neuron is the cell whose axon carries the information to higher centres.
- Sensory receptor cells are present in the sense organs.

Generator potential vs Receptor potential

- If the potential developed by sensory receptor which also serve as primary afferent neuron, is termed as Generator Potential.
- If sensory receptor cell is different from primary afferent neuron the potential developed in the sensory receptor cell is termed as Receptor Potential.
- Mechanism of signal transduction varies in each of these situations.

Receptor characteristics

- Receptors have the ability to convert other form of energy in to electrical energy i.e. action potential, causes transduction if adequate stimuli is applied.
- They have differential sensitivities to different stimuli. The permeability of the receptor is modified and ends up in graded receptor potential.
- They show different adaptability to a stimulus and speed of adaption varies with receptors. Each receptor has specific acuity i.e. discriminative ability.

CLASSIFICATION OF SENSORY RECEPTORS

Sensory receptors are classified based on

- Function of the receptors
- Location of receptors
- Source of the stimulus
- Type of stimulus or modality
- Location of receptors

Function of the receptors

- *Phasic receptors:* Produce action potential during part of stimulation hence they initiate response. It does not provide clue for duration of stimulus.
- *Tonic receptors:* Generate action potential upon the application of stimulus and propagation of action potential goes on till the stimulus is removed. This gives information regarding the duration of stimulus. In this type, the possibility of weakening of the impulse irrespective of the maintenance of constant strength of stimulus due to prolonged exposure leading on to a phenomenon known as RECEPTOR ADAPTATION.

Location of receptors

Exteroceptors: Detect stimuli from outside the body in animals' micro or macro environment (change in temperature, air pressure). They can be divided into:

- *Superficial cutaneous sensations:* Touch, light superficial pressure, temperature, cold, warmth, and pain.
- *Deep sensations:* Receptors in the muscle tendon and joints together known as kinesthetic sensation mediated through the muscle spindle receptor and Golgi tendon organ to sense position and movement.
    - Special Sensory receptors
    - Skin receptors.
- *Interoceptors:* Detect stimuli within the body (Blood pressure, O2 uptake). They are,
    - *Proprioceptors:* Convey information from the muscles, tendons, and joints.
    - *Viscероceptors:* Carrying information from the viscera.
    - *Specialized receptors:* Baroceptors, osmoceptors, chemoceptors, and volume receptors.
    - *Baroceptors:* Present in carotid sinus and aortic arch to detect BP change.
    - *Osmoreceptors:* Present in hypothalamus to detect osmotic change.
    - *Chemoreceptors:* Sensitive to chemical change. Present in tongue to detect taste and in nose to detect smell. Hypothalamus central chemoreceptors detect pH change, blood glucose, and hormonal levels.

Source of the stimulus

- *Telereceptors:* Detect the stimuli at a distance (Photo and auditory receptors)

Stimulus or modality

- *Photoreceptors:* Detect change in intensity of light mediating sense of vision.
- *Thermoreceptors:* To detect change in temperature.
- *Electroceptors and Magnetoceptors:* (Mostly in insects and birds). They detect electrical and magnetic field respectively.

- *Mechanoreceptors:* Involved in sensing touch, pain, hearing, balance (equilibrium).
- *Chemoreceptors:* Detect chemical signals, sense of gustation, olfaction, blood O2, tension, and change in pH (internal environment).

Location of receptors

- *Superficial cutaneous sensations:* Touch, light superficial pressure, temperature, cold, warmth, and pain.
- *Deep sensations:* Receptors in the muscle tendon and joints together known as kinesthetic sensation mediated through the muscle spindle receptor and Golgi tendon organ to sense position and movement.

CUTANEOUS RECEPTORS

- These receptors mediate sensation of touch, light, pressure, heat, and cold.
- These consist of lamellated connective tissue capsule that surrounds soft core where the axon ends.
- Pain sensations are mediated through the fine free nerve ending.

			
Expanded tip receptor	Free nerve endings	Krause corpuscle	Meissners corpuscle
			
Pacinian	Ruffinis end	Tactile hair	Markel's disc

corpuscle	organ		

- Sensing light touch
  - Mediated by Meissner's corpuscles, Merkel's disc and basket arrangement of nerve fibers at the base of the hair follicle.
- Meissner's corpuscles
  - Located in the skin papillae beneath the epidermis. It has irregularly coiled nerve endings with capsules of connective tissue. The density of distribution is uneven.
- Merkel's discs
  - Associated with enlarged epidermal cell with small receptive field. It has group of 3 or more cup shaped discs. The discs have reticulated appearance. Nerve fibre branch out and supplies to each disc. They are found in the snout of pig and other mammals. They are used for fine tactile discrimination. They are slowly adaptive tonic receptors.
- Basket arrangement of nerve fibers or Root Hair Plexus
  - Most sensitive. They are located at the base of the hair follicle as wrappings and monitor movement across the body surface. It has short vertical nerve filaments that ends in bulged portions and gets stimulated by slight movement of hair. They adapt rapidly and are phasic receptors. Displacement of hair causes movement of hair follicle. This causes stretching of the sensory nerve ending and stimulates mechanoceptor protein stretch on the dendritic membrane.
- Touch receptors
  - Mediates through 3 qualities.
    - Tactile localization.
    - Tactile discrimination-Recognition of two different stimuli simultaneously
    - Stereognosis-Recognition of stimuli by touch without visual assistance.
- Pacinian corpuscles
  - Located in the deep layers of the skin, subcutaneous tissue, periosteum, muscle, tendon, joints, and blood vessels respond to stimuli of unequal firm, deep pressure. They have lamellated appearance similar to the cross section of an onion. They help out in recognizing the location of the stimulus with high degree of accuracy (Tactile localization). It mediates pressure sensation and they adapt quickly.

THERMOCEPTORS

- The hypothalamus of the animals has central thermoceptors to monitor their internal temperature.
- Two different receptors to mediate warmth and cold.
  - The *warmth receptors* are situated near deep blood vessels.
    - They are Ruffini end organ which can also serve to detect tactile sensation (Poly modal receptor).
    - Ruffini's corpuscles are located in the connective tissue of the skin in association with collagen fibers. Hence detect skin stretch and are involved in proprioception.
    - Warmth receptors detect change in temperature of 20° C to 47° C.
    - The frequency of action potential increases with increase in the temperature. Cold sensation is mediated by the end organ of Krause.

- The *Cold receptors* detect and are stimulated at the temperature between 10° C to 35° C.
  - These are extremely sensitive and can detect change in even 0.5° C.
  - There are also another thermoceptor which detect painful hot stimuli. The temperature ranges above 45° C.
  - The frequency of action potential generated is in accordance with the amount of pain sensation.

Mechanism of Action

- Free nerve ending of the thermoreceptor neurons have specific thermoreceptor proteins. They are known as Thermo TRPs. The thermo TRPs are many, variable to different temperature range, and some are to detect distinct temperature. They get stimulated and act through ion channels and gating mechanism by modifying the protein configuration.

NOCIOCEPTORS

Nocioceptors

- These detect pain sensation by naked nerve endings. This sensation does not have any special structure to mediate. These nociceptors are available in the superficial layers of dermis, which are represented by non-medullated fibers. They act as protective response to an injurious stimulus.

Vibratory sense

- It is mediated by tactile and pressure receptors namely Merkel's discs and Pacinian corpuscles.

Itching and tickling sense

- It is mediated by stimulation of both tactile and pain receptors.

PROPRIOCEPTORS

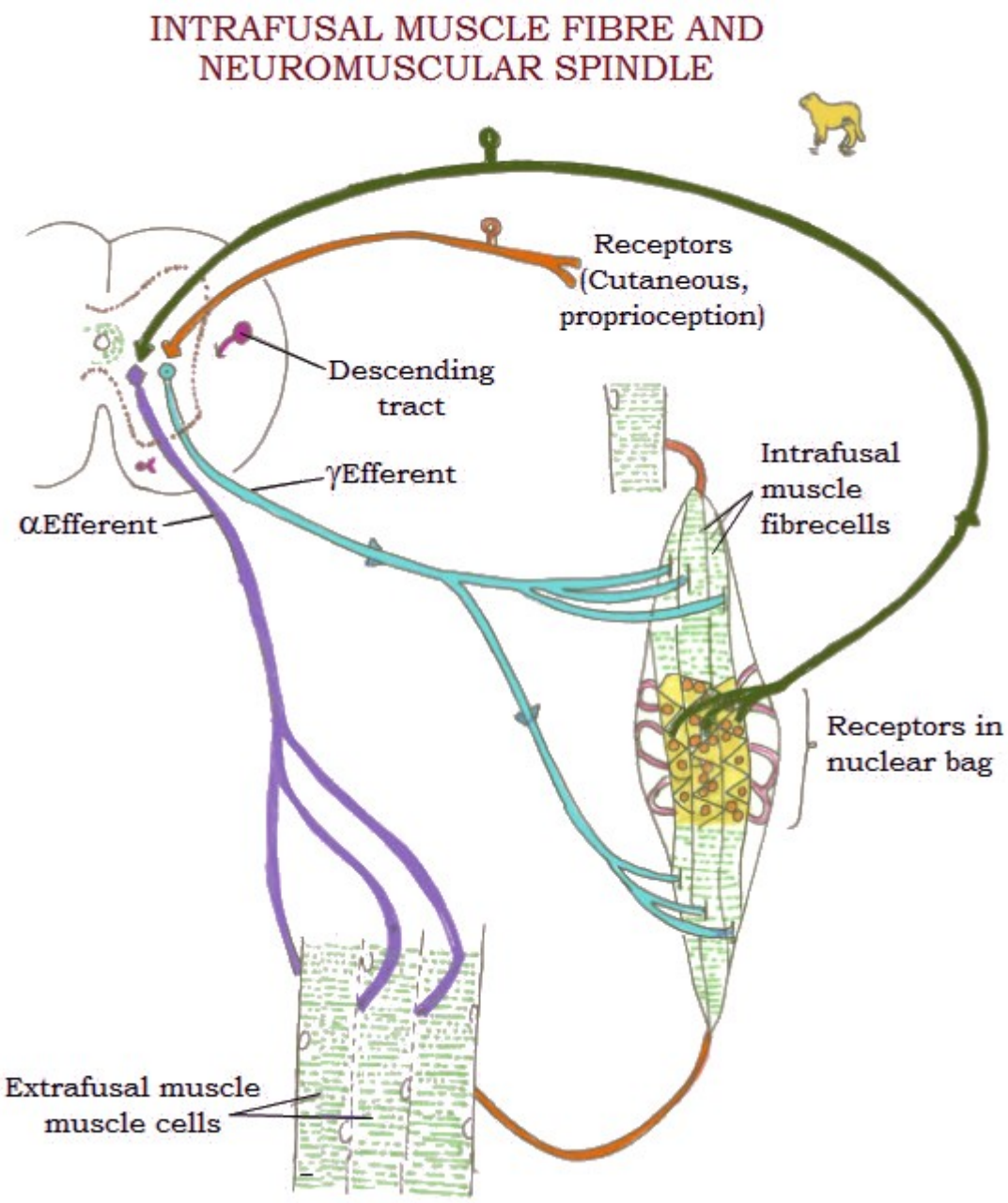
- Receptors are located in the skeletal muscle, tendons, and joints known as the kinesthetic receptors. These inform the CNS about the movement and position of the limbs to maintain posture and equilibrium.
- The joint sense includes sense of movement and sense of positions.
- The sense of movement is the ability to feel the movement with closed eyes. Sense of position is to feel the position of the body in relation to space. These two are mediated by receptors in and around the joint.
- Receptors involved are the Spray nerve endings, Pacinian corpuscles, touch receptors, and free nerve endings located in the synovial membrane, ligaments, and tissues near the joint.
- The impulses generated from these reach cerebral cortex through dorsal tracts, medial lemniscus, and thalamus to end in conscious perception of the position of the body in relation to space.
- The impulses from muscle spindle organ, Golgi tendon organ, and vestibular apparatus of the internal ear do not reach cerebral cortex.
- They are concerned with reflex adjustment of the muscle tone with the involvement of spinal cord to maintain posture and equilibrium. These are known as non-sensory proprioceptive impulses as they never bring out conscious sensations.

Proprioception and Respiration

- Some of these proprioceptors sends signals to the respiratory neurons about changes in the force exerted by the respiratory muscles and the movement of the ribcage.
- The functioning of diaphragm with respiratory control is also mediated by one of the tendon organs in the external costals which inhibit inspiration upon stimulation by small change in the force of contraction of these muscles.
- The stretching of diaphragm results in the inhibition of its contraction and inspiration acting through the tendon organs.
- The intercostal reflexes are significant due to the presence of numerous muscle spindle organs in the external intercostals.
- The muscle spindles help to coordinate breathing during changes in the posture and stabilize ribcage during reduction in lung compliance.

MUSCLE SPINDLE ORGAN

- These are located within the belly of the skeletal muscles.
- They are in the shape of a spindle and are made up of specialized striated muscle fibres which are known as Intrafusal fibers. These intrafusal fibers are placed within the connective tissue capsule attached to the perimysium of the skeletal muscle.
- The longitudinal axis of them are oriented parallel to that of skeletal muscle fibre which contains them.
- Structure of muscle spindles
    - There are two types of intrafusal fibers. One of them is known as *Nuclear bag* where their centre portion is interrupted and dilated which houses many nuclei. Nuclear bag region tapers towards the pole. Another intrafusal fibre is known as the *Nuclear chain*. They have uniform diameter throughout, but near the middle small, but appreciable increased diameter due to the increased number of cell nuclei.
- Nerve Supply
    - It is innervated by the Gamma motor neurons or Intrafusal fibers. The cell bodies of the Gamma motor neurons are located in the ventral horn of the grey matter of the corresponding spinal segment. The skeletal muscles are innervated by α-motor neurons. These are referred to Extrafusal fibers.



- The Gamma motor neurons are of two types,
  - Gamma plate neurons.
  - Gamma trail motor neurons.
- The Gamma plate neurons innervate nuclear bag intrafusal fibers and are tonic neurons generating sustained action potential.
- Gamma trail motor neurons supply nuclear chain intrafusal fibers. These are phasic neurons and produce action potential of short duration with high frequency.

MECHANISM OF ACTION OF GAMMA MOTOR NEURONS

- Excitation of these neurons ends up in contraction of intrafusal muscles.
- This in turn stretches the nuclear bag fibers and nuclear chain fibers.
- Sensory receptor of the muscle spindle in limited to these areas and can detect the tension upon these receptors.
- Stretch initiates depolarization in the sensory receptor membrane.
- Intrafusal fibers have no control on the tension developed in the extrafusal fibers.
- The nuclear bag fibers are tonic and sarcolemma of these are not excitable.
- No appreciable action potential is generated, hence no muscle twitch occur.
- On contrary nuclear chain fibers respond to neural excitation and are phasic in nature. It is excitable when stimulated and generates action potential in response to gamma trail motor neurons.
- This end up in the twitch type of contraction.

Nature of Sensory fibers

- Afferent fibers from nuclear bag spiral around the intrafusal muscle and form *Annulospiral or Nuclear bag endings* of the muscle spindle. These fibers are large and myelinated, responsible for initiation of myotatic reflex.
- Sensory fibers associated with nuclear chain intrafusal fibers terminate in plaque like ending namely the *Floewer Spray ending*. These fibers are small and are myelinated and are responsible for flexor reflex. These system functions to maintain posture of an animal and muscle tone of the skeletal muscles.
- The effect exerted by Gamma plate motor neurons is referred to as Gamma loop mechanism.

GOLGI TENDON ORGAN

- It is located within the tendons of the skeletal muscles.
- It is present at the junction of muscle fiber and its collagenous tendon. As they are closely associated with the tendon, the stretch of the tendon causes depolarization of the receptor organ.
- Action potential is generated within the sensory fibers which are large myelinated fibers. Golgi tendon organ act as stretch receptor. These receptors are excited by muscle contraction that imposes tendon stretch.
- The stimulation of Golgi tendon initiates excitation of α-motor neurons supplying to antagonistic muscle of the contracted skeletal muscle. These receptors initiate reflex activity to reduce the tension in the tendons of the stretched muscles.

VISCERAL RECEPTORS

Mucosal receptors or Epithelial receptors

- Located immediately below the mucosal epithelium. These are well distributed in the stomach and small intestine. They are rapidly adapting mechanoceptors, but are slowly adapting to chemical stimuli.

Tension receptors

- Located within the stomach, small intestine of cats, sheep's rumen and urinary bladder. These are slowly adapting mechanoceptors and they monitor the distention of the above mentioned structures.

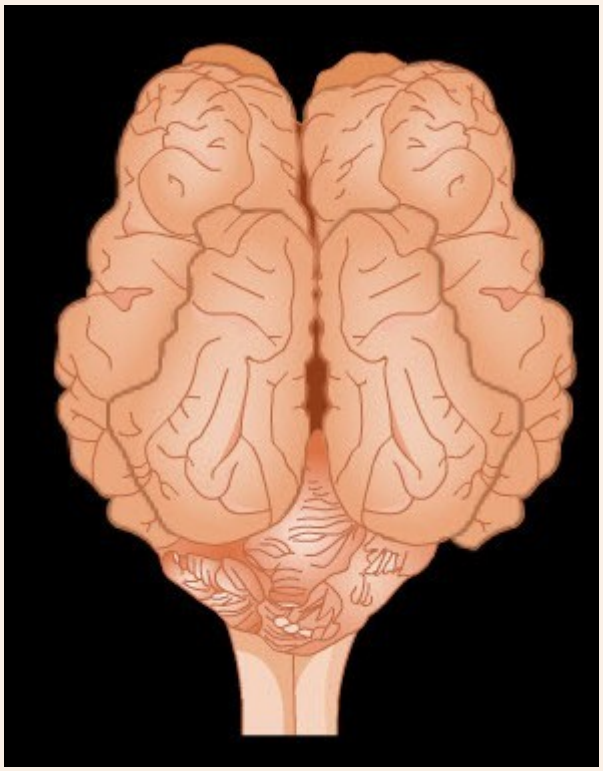
Serosal receptors

- Located under the serosa or in the mesentry. They are slowly adapting mechanoceptors. They monitor visceral filling and distortion in the shape.

RECEPTOR SPECIFICITY

- Adequate stimulus is preferred, if large magnitude of stimuli that can provoke response from many receptors.
- Some receptors are designated by nature to respond to different stimuli. Example: Nociceptors to detect pain which may be due to temperature, pressure, or chemicals. These are termed as Polymodal receptors.
- Receptive field : It is the region in the sensory surface of afferent neuron which detects the stimuli to generate response upon stimulation.

MODULE-5: CENTRAL NERVOUS SYSTEM - CEREBRAL CORTEX



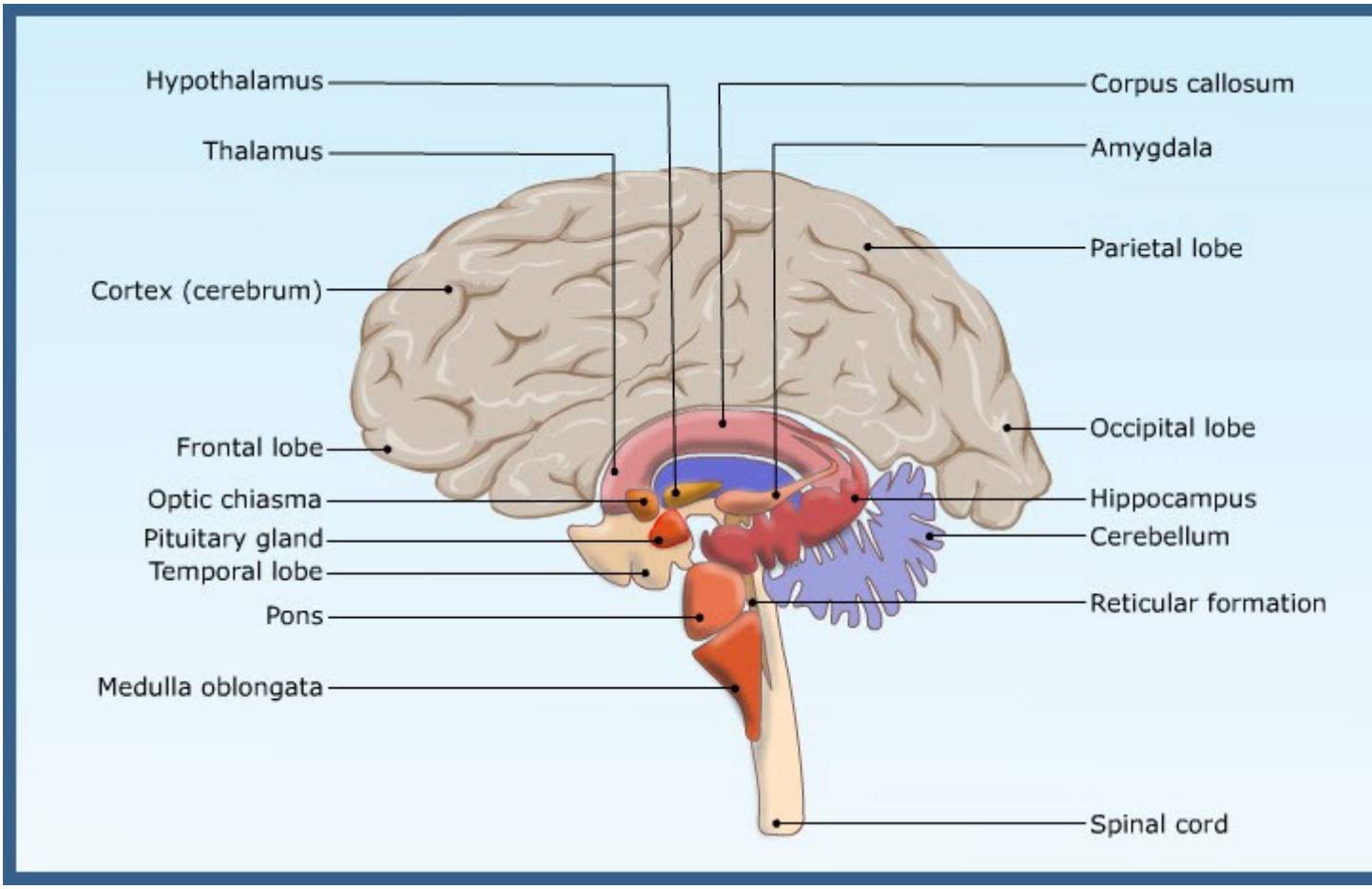
LEARNING OBJECTIVES

This module helps to understand conscious sensation voluntary movement of the animal by exploring,

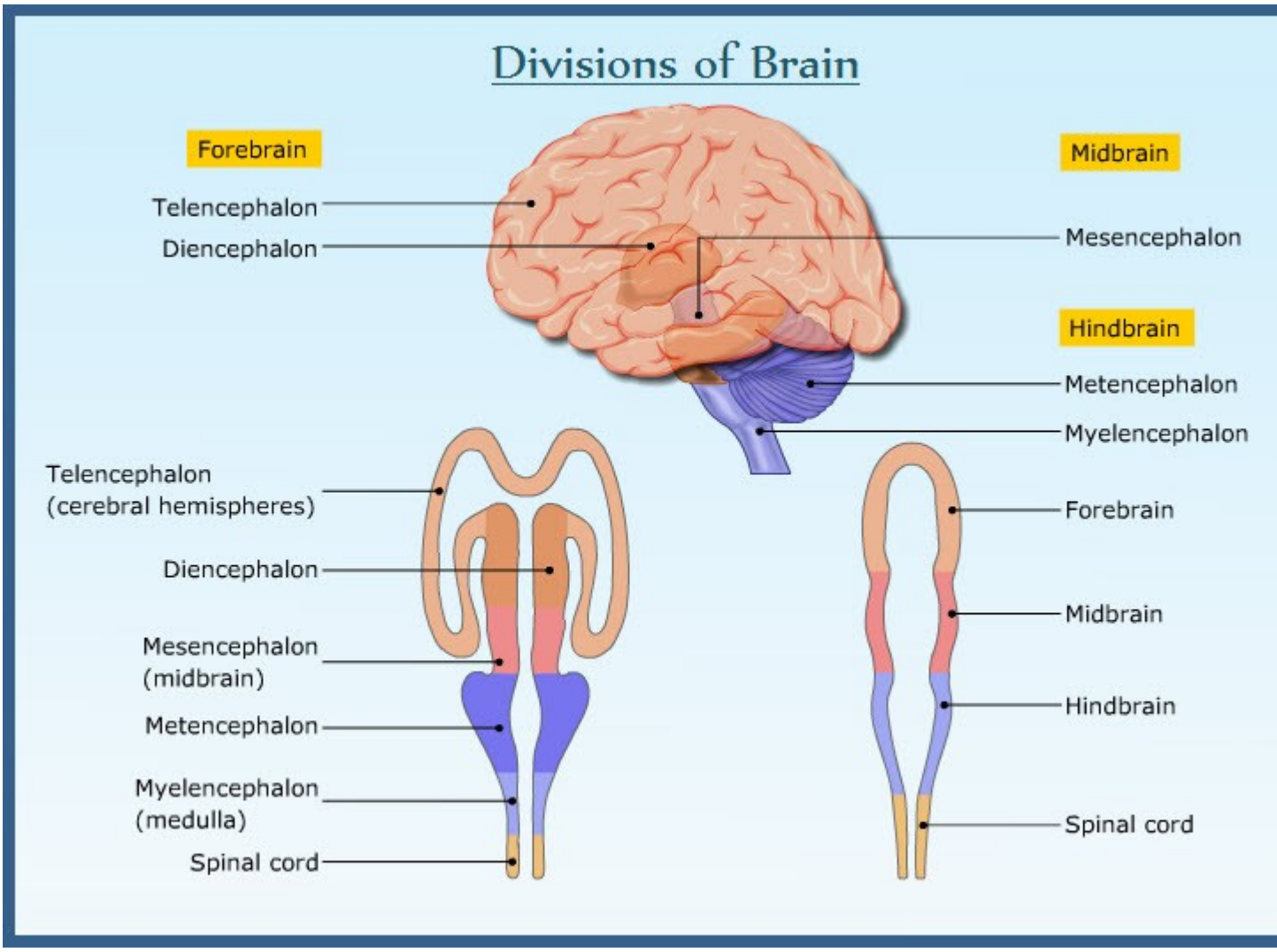
- the organization of the brain and basic anatomy of the cerebral cortex,
- different areas of cerebral cortex and
- the functions of the basal ganglia and its components namely the corpus striatum, globus pallidus and the amygdala.

CENTRAL NERVOUS SYSTEM

- The CNS comprise the brain and the spinal cord.
- The brain consists of structures situated intra cranially and includes cerebrum, mid brain, pons, medulla, and cerebellum.

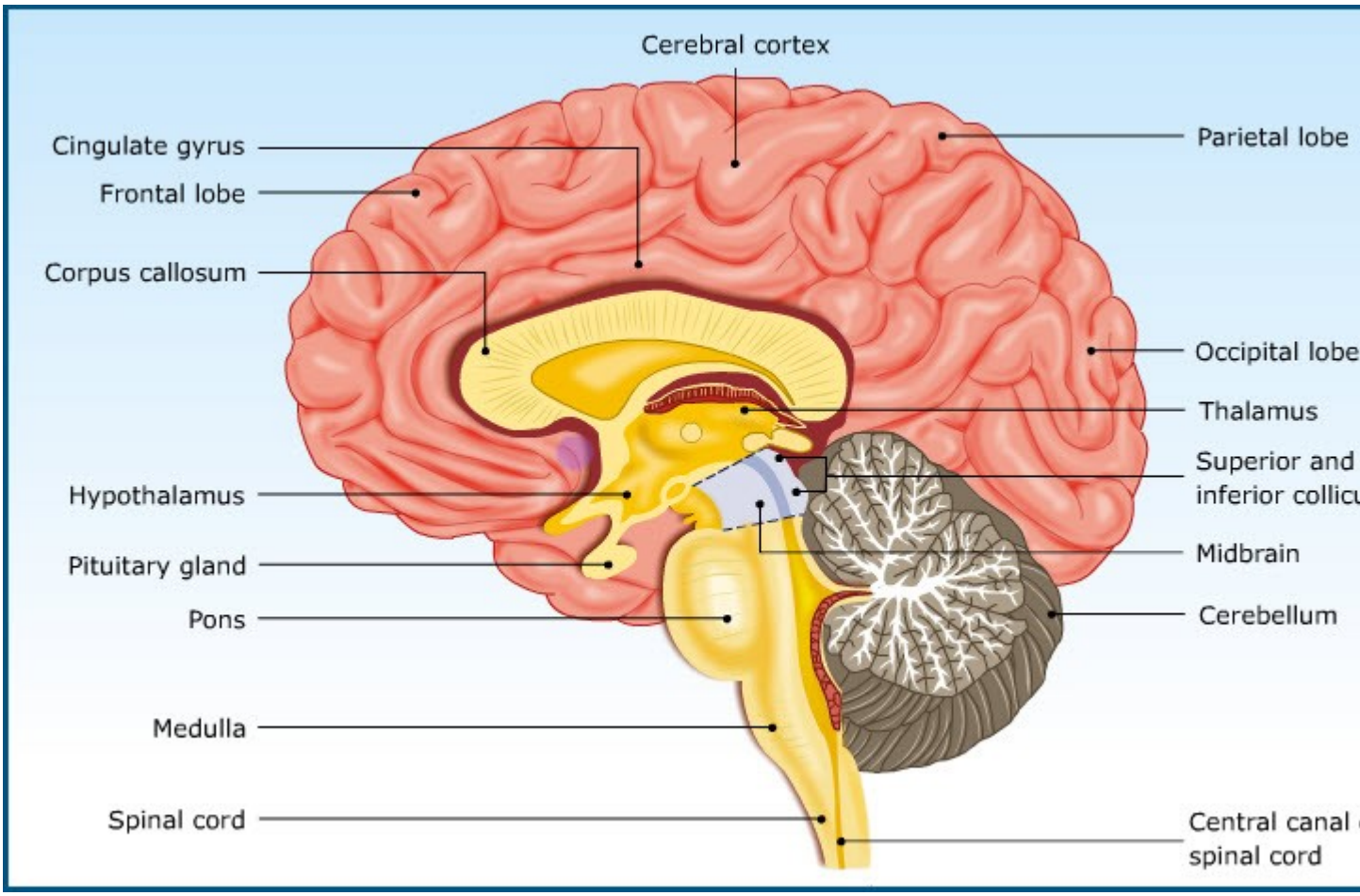


- Brain is divided into distinct regions,
    - The fore brain [prosencephalon] which is subdivide into telencephalon [two cerebral hemisphere] and diencephalon or inter brain [consists epithalamus, thalamus, subthalamus and hypothalamus, posterior pituitary and pineal glands]
    - The mid brain or mesencephalon
    - Hind brain or rhombencephalon comprising pons, medulla, and cerebellum.



CEREBRAL CORTEX

- Provides necessary neural connections and orders to skeletal muscles required for proper response based on emotion.
- As Ganglionic blanket covers the brain, has unexcelled structure function millions of nerve fibres are originated from here.
- The cerebral hemisphere is the predominant portion of the brain .
- Each cerebral hemisphere is composed of a covering of grey matter [cortex or pallium], a cerebral mass of white matter and the basal ganglia [mass of grey matter.
- The cortex is the highest integration centre in the somatic nervous system to regulate complex skeletal muscular movement and its functions are under voluntary control.
- It acts as a centre for consciousness, and storages of experience. The bilaterally situated cerebral cortex of telencephalon is divided into a primary olfactory portion called the allocortex and a non olfactory portion called the neocortex, in mammals the allocortex is often called as the limbic system



Isocortex

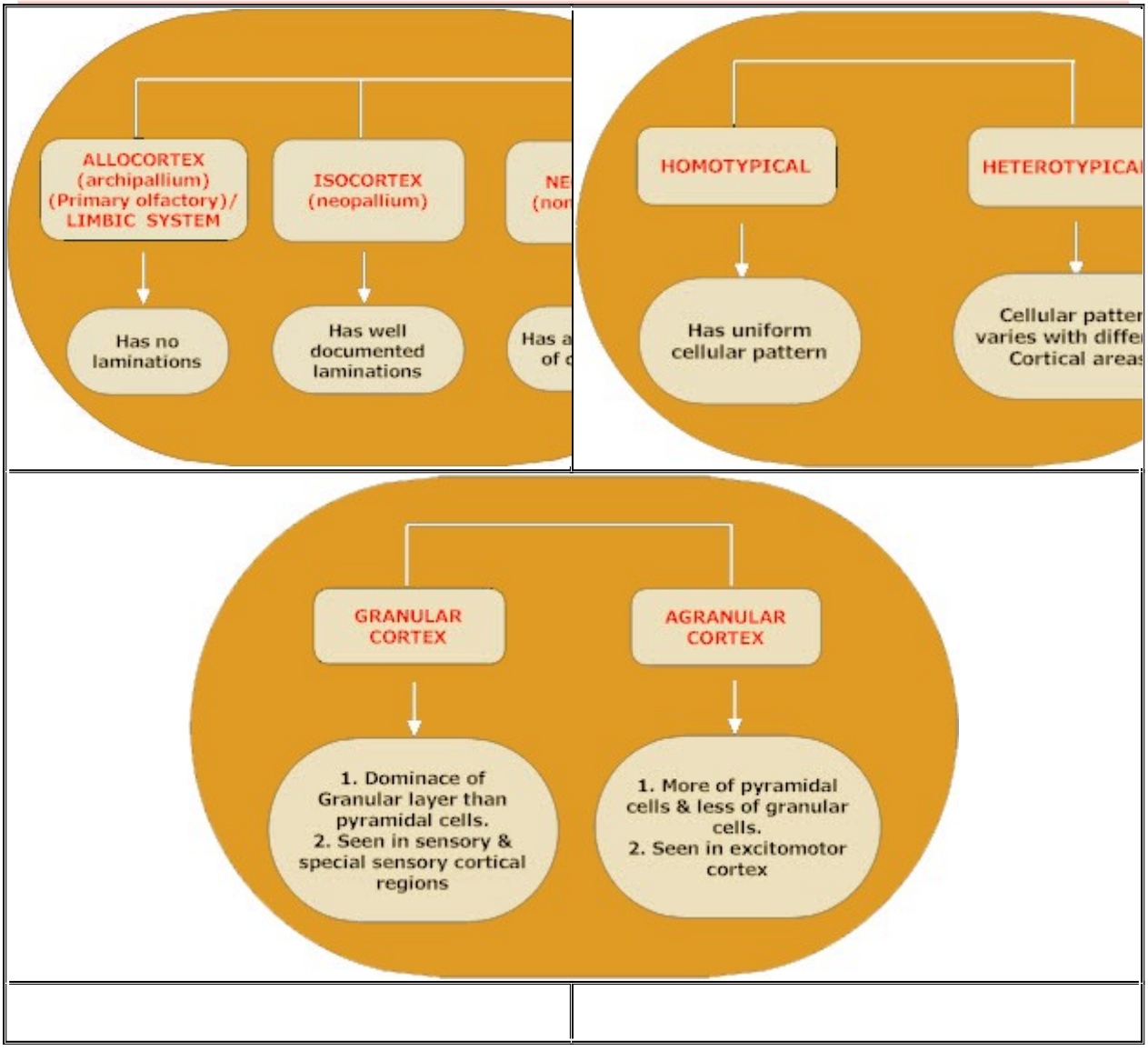
- It is the outer layer, that integrates and interprets sensory information to initiate voluntary movements.
- There are outer folds namely GYRI and grooves namely SULCI to increase the surface area of isocortex.
- Increase in surface area increases number of neurons, there inter connections enhance functional complexity.
- In other vertebrates like reptiles, birds and amphibians the neocortex is absent or poorly developed.
- Allocortex regulates emotions. Cortex has definite cellular architecture and divided into six layers.

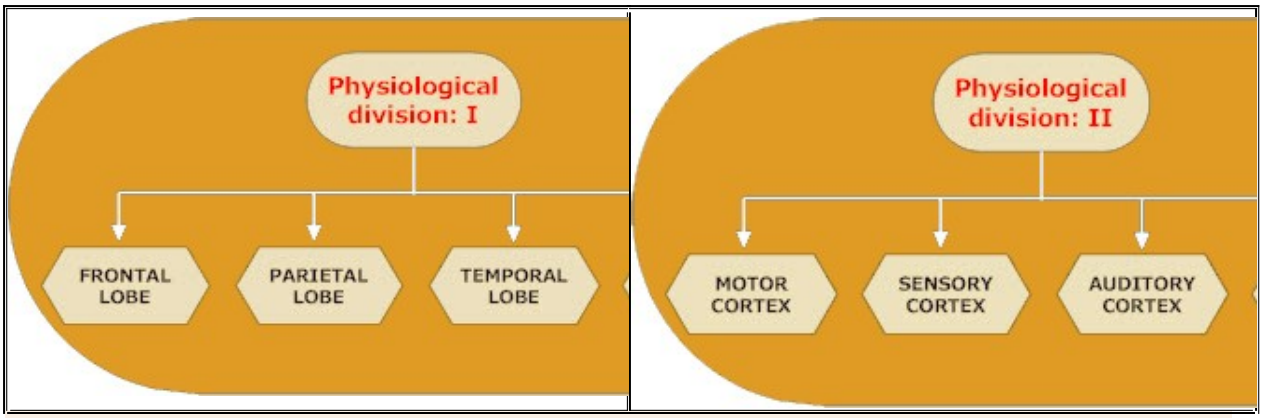
CYTO ARCHITECTURE OF CEREBRAL CORTEX

- Six functionally distinct layers have specific pattern of neuronal cell bodies.
- Variation exits between shape and density of neurons located in each layer.
    - *Molecular layer:* Most superficial layer has many dendritic, axons and glial cells from a felted mat like appearance. Few cell bodies and few connections among cells.
    - *External granular layer:* Has many different shaped [angular, polygonal, triangular, round cells] whose axon end in deep layers. Cells are many, fibers are less and integrates signals within in the cortex.
    - *External pyramidal layer:* Has pyramidal cells whose size increase gradually.

- *Internal pyramidal layer or ganglion layer:* Has graded sizes of pyramidalcells-giant pyramidal cells viz. BETZ cells are seen .This type of cellular architecture is evident is precentral cortex. Communication with other parts like thalamus, brain stem and spinal cord.
- *Internal granular layer:* Has number of small stellate cells.it has rich nerve fibres, horizontal crisscrossing fibres pose a white band like appearance.
- *Fusiform cells layer:* Has small spindle shaped cells that are matted perpendicular to the surface.

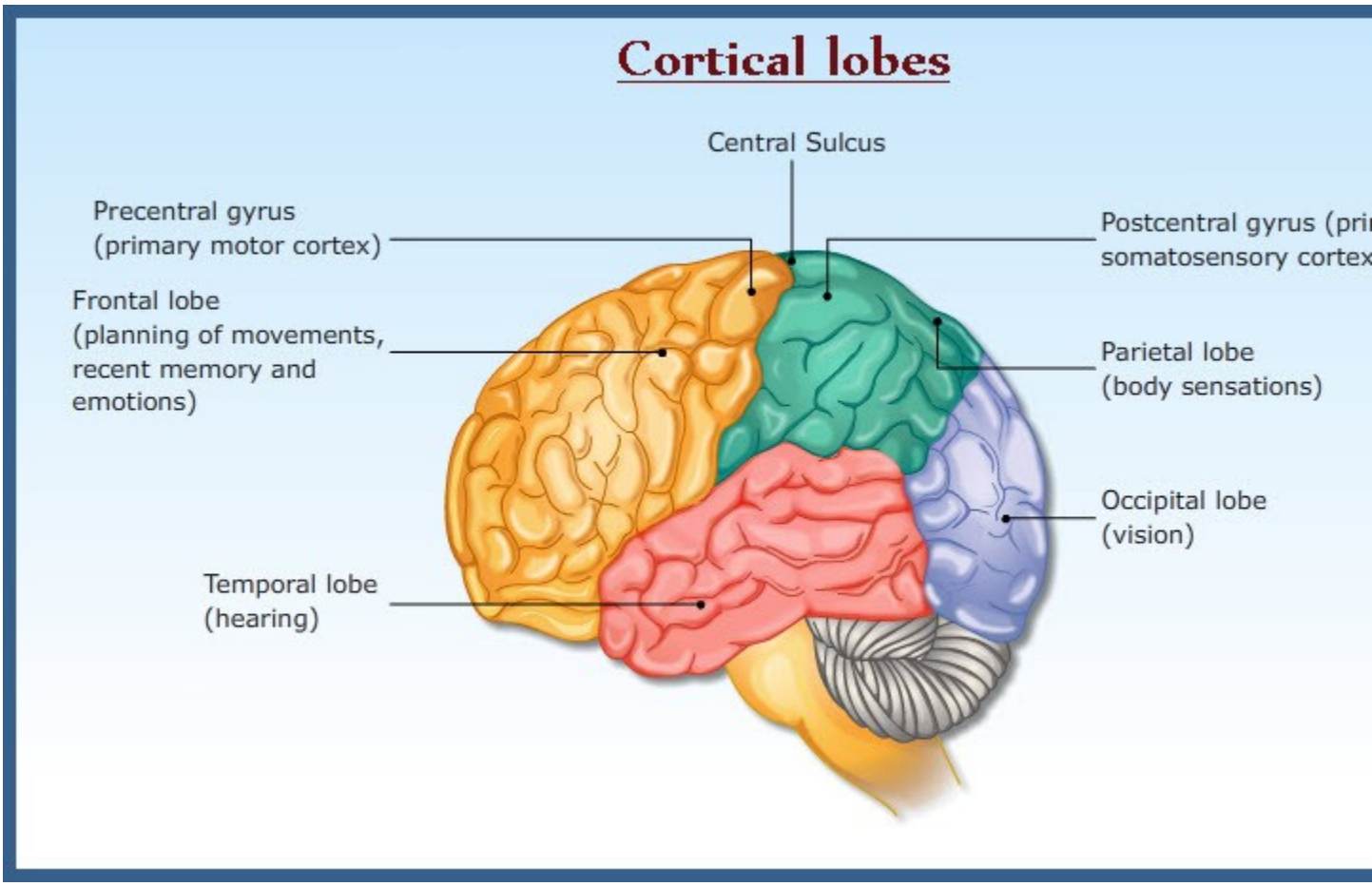
DIVISION OF CEREBRAL CORTEX





REGIONS OF CEREBRAL HEMISPHERE

- *Frontal lobe:* Voluntary motor activity, vocal ability and higher mental functions.
- *Parietal lobe:* Associated with movement, orientation, recognition, and perception of stimuli.
- *Occipital lobe:* Involved in visual processing
- *Temproal lobe:* Involved with perception and recognition of auditory stimuli.



Topographical organisation of cerebral cortex

- Visual cortex
- Auditory cortex
- Somatosensory cortex

- Motor cortex

Frontal lobe

Motor areas

- Primary motor cortex which is the exact motor cortex
    - Primary motor cortex is formed by precentral gyrus and has small narrow zone which posses BETZ cells. Primary motor cortex is a centre for voluntary movement, and initiates voluntary movement this is origin of corticospinal tract and project fibres to pons, corpus striatum red nucleus and subthalamus. Most of the skeletal movement are under the control of motor cortex.Stimulation of excitomotor cortex causes quick and phasic movement.
- Supplementary motor area
    - Present in the medial surface of the hemisphere,has greater threshold stimulation of this part causes show movement which causes some change in posture for brief period of time.There are other areas in primary motor cortex which includes secondary motor cortex which compensates loss function of primary motor cortex. Adjacent to this area is that, the one which control mainly postural and stretch reflex which on stimulation causes inhibition of reflex induced movement of cortically induced movement.It exerts such inhibitory influence.It has connection with caudate nucleus and reticular formation.
- Premotor cortex
    - Fibres of pyramidal and extra pyramidal tracts original from here, this area is concerned with
        - Excitatory effects
        - Complex coordinated movement of contra lateral side of the body.
            - Rotation of head and trunk to the opposite side simultaneous movement of flexion and extension of contra lateral limbs.
            - Adjacent to the premotor cortex is the area concerned with movement of eyes, pupillary dilation and secretion of lachrymal glands.

Prefrontal areas

- This area is concerned with socializing in animals. Stimulation of this area causes low frequency of autonomical, respiratory, circulatory renal and gastrointestinal responses.
- This area is principally connected to thalamus. Hypothalamus sub cortical and other cortical region.

Parietal lobe

- Parietal lobe have areas concerned with sensory function

Somesthetic area or primary sensory cortex

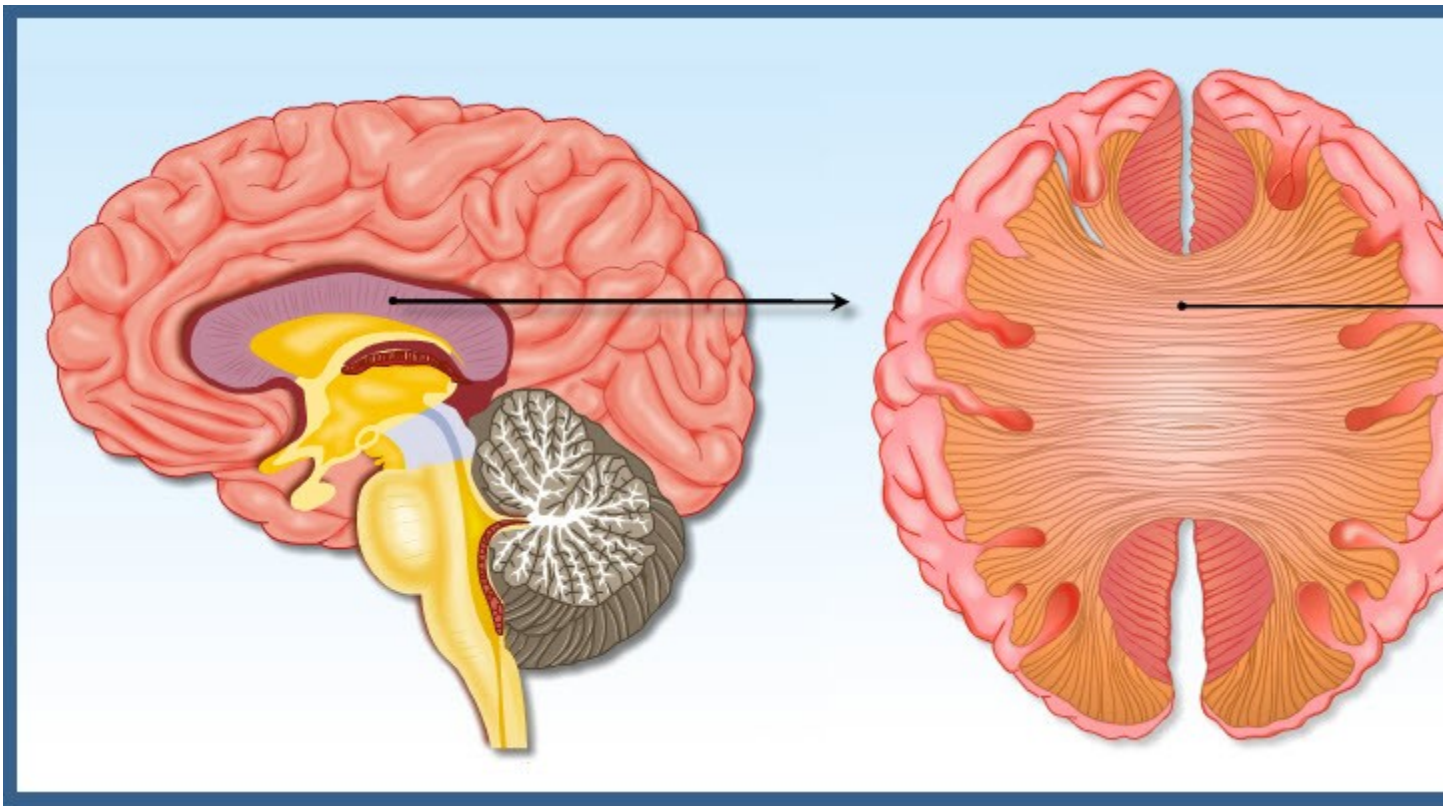
- All somesthetic sensation is perceived here except pain and crude temperature with are perceived at the thalamus.
- This is the area which helps in discriminating the qualities of external objects like size, shape, texture, weight and position of limbs in relation to space.
- Judging of the particular sensation and nature is done by this areas
- Its function includes
    - Discrimination and localisation of touch
    - Recognition and discrimination of different stimuli at different intensities
    - Spatial recognition –to relate the movement and position of limbs
    - Recognise the stimulation and dissimilarities [size, shape, weight]
    - Taste sensation –different taste in relation with different taste receptors. This area is adjacent to the motor cortex governing the masticatory muscles.

PHYSIOLOGICAL FUNCTIONS OF CEREBRAL CORTEX

- Centre for voluntary movements-exerted by primary motor cortex Viz. Excitomotor cortex and is also responsible for highly skilled movements.
- Centre for quick and phasic movements
- Centre for postural maintenance-exerted by supplementary motor area
- Centre for stretch and postural maintenance
- Centre for major motor control-mediated by pyramidal and extra pyramidal tracts
- Centre for complex co-ordinated movements
- Frontal eye field of cerebral cortex is concerned with eye movement, pupillary dilatation and tear secretion
- Centre for reflex vocalization
- Centre for learning, memory processing and memory storage-compares past experiances and interprets the present experience
- Centre for mood, emotions and behaviour-like socializing
- Centre to receive specific sensations-crude sensations have sub cortical destination(except pain and crude temperature perceptions at thalamus level itself) finer sensations of touch temperature joint and vibratory senses are relayed to cortex
- Centre for discriminative ability
- Centre for spatial recognition
- Centre for tactile discrimination and localization
- Centre to compare and recognise relative intensity of different stimuli
- Centre to recognise similarity and differences stereognosis
- Centre for gustation-lower end of somestheti c cortex, lie next to motor cortex governing muscles of mastication
- Centre for visual senses and visuo-psychic sensations
- Centre for auditory senses and audito-psychic sensations
- Centre for olfactory sensations

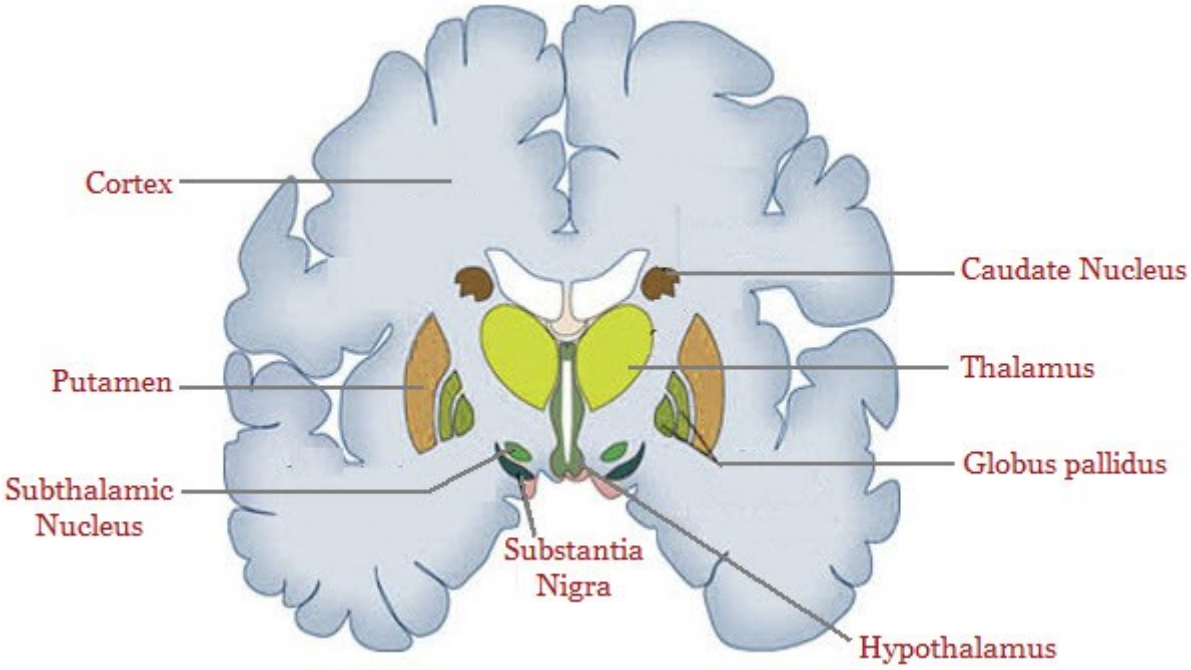
CORPUS CALLOSUM

- It is a thick band consist of million of neuronal axons transversing and helping communication between two hemispheres.
- They are myelinated fibres.



BASAL GANGLIA

- It is situated deep within the cerebral hemisphere as sub cortical gray matter with large masses of nerve cells.
- This acts as a part of the motor cortex in birds in which the motor cortex is poorly developed. It has *corpus striatum (striated body), globus pallidus (pallidum) and the amygdala*. It receives fibres from cortex to striatum, from striatum to pallidus, from pallidus to thalamus and from thalamus to all areas of cortex.



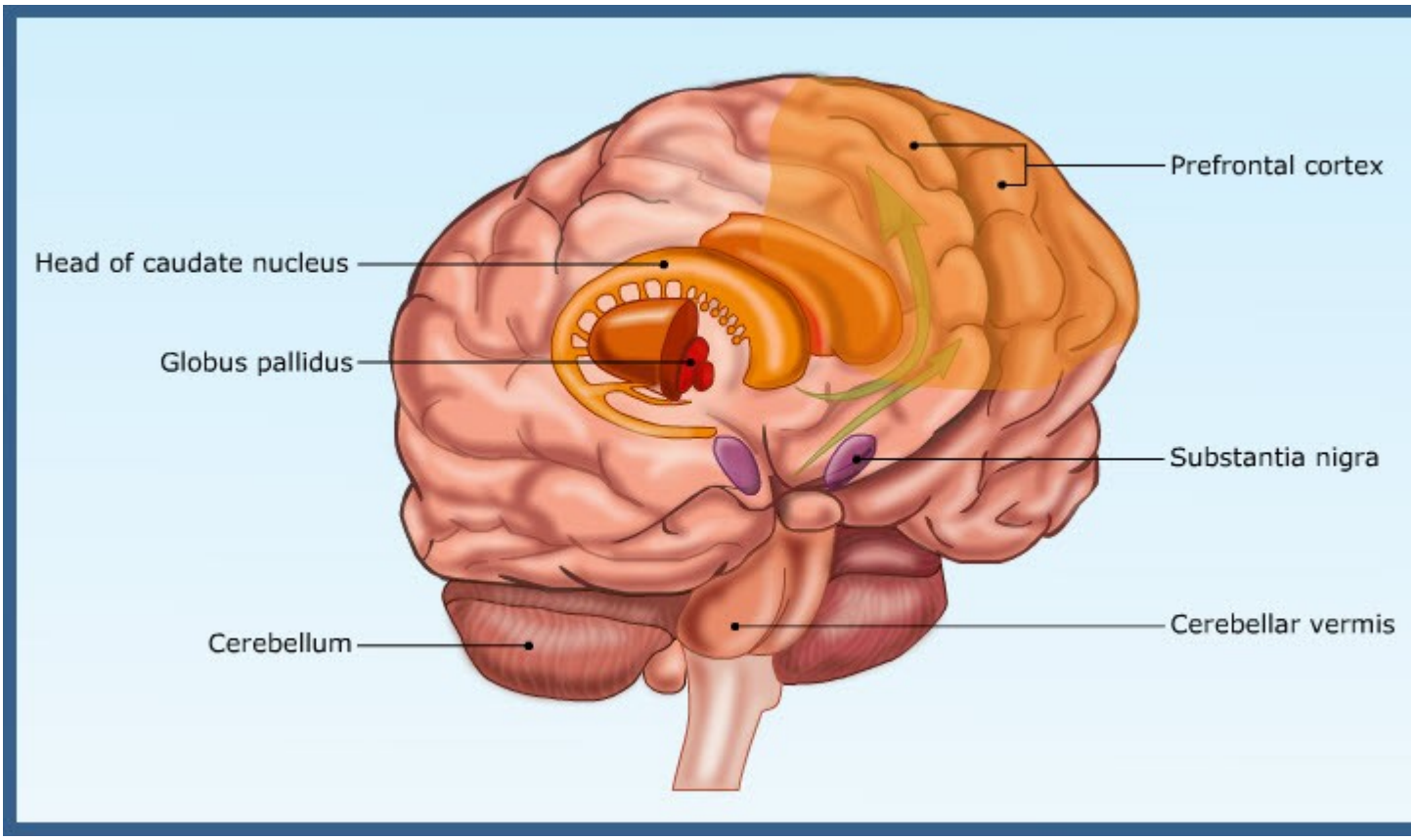
- The basal ganglia receives inputs from the sensory, motor and association areas of the cerebral cortex and cooperates in pre-programming of somatic muscle activity in voluntary motor activation.
- Integrates feeling and movement.
- Shifts and smooths a fine motor behaviour.
- Suppresses unwanted motor behaviours and forms over all control of voluntary movements to establish posture.
- Diseased structure causes involuntary jerky movements.
- In birds, the basal ganglia perform all the motor function, including the voluntary movements. In dog and cat, removal of cortex abolishes the discrete type of motor functions.

CORPUS STRIATUM

- It consists of CAUDATE NUCLEUS and PUTAMEN and initiate gross intentional movements of the body.
- It regulates the position of the body.It derives the name due to its straited appearance.

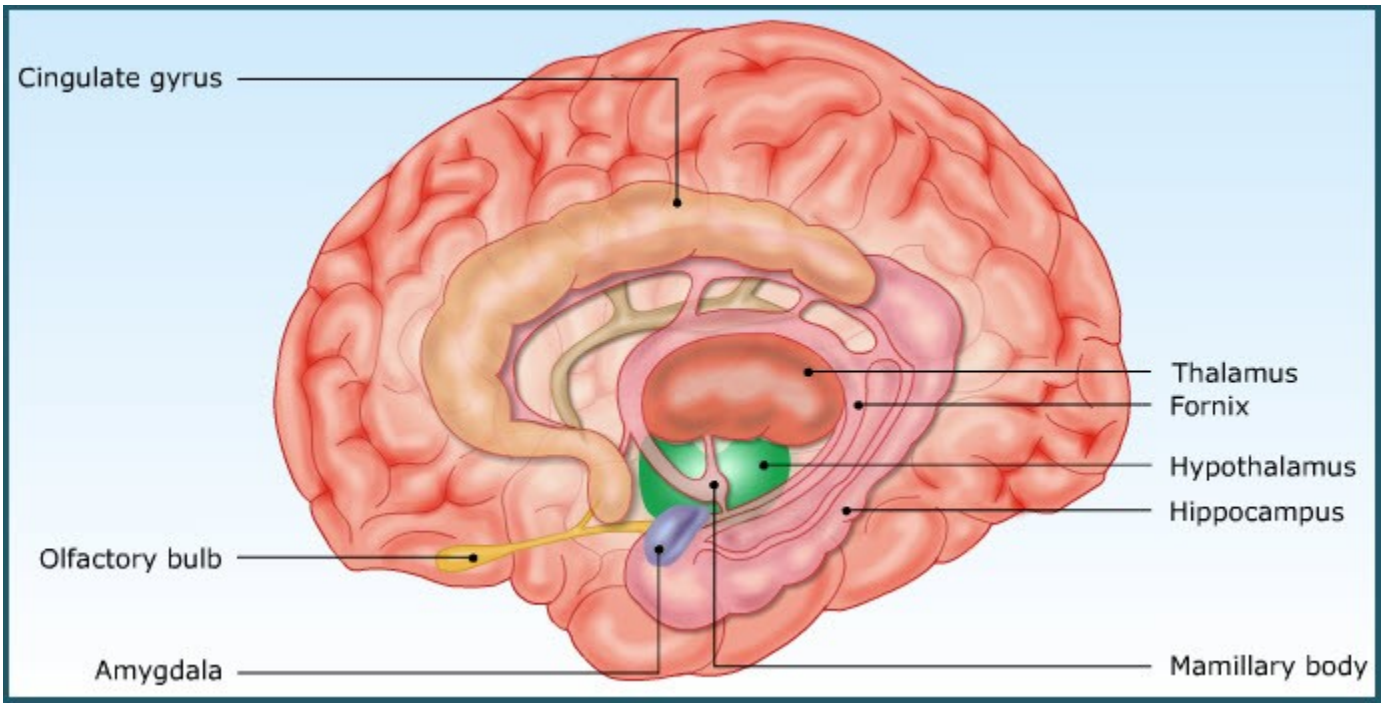
GLOBUS PALLIDUS

- Most of the outflow of signals from the basal ganglia is channelled through globus pallidus en route to cortex or lower brain centres.
- Its activity is associated with tonic contractions of voluntary movements to effect discrete activities. The Globus pallidus and the putamen collectively form a structure, theLenticular nucleus which resembles lens.



LIMBIC SYSTEM

- Consists of cortical and subcortical areas which are structurally and functionally related to forebrain. It forms a ring of forebrain structures that surround the brainstem and are interconnected by intricate neural pathways.
- The components of the limbic system are hippocampus, amygdala and cingulate gyrus.
- It is concerned with emotions and visceral functions viz. VISCERAL BRAIN. It helps out in basic survival and sociosexual behavioral pattern. The subcortical relay nuclei comprises of septal nuclei, mammillary bodies, medial and lateral hypothalamic nuclei associated with limbic system.
- Functionally, it includes lobes of cerebral cortex, basal nucleus, thalamus, and hypothalamus.
- Limbic system has certain areas designated as 'reward and punishment' centres which functions in the programmed way based on the previous experiences.
- Limbic system is not well defined in birds.

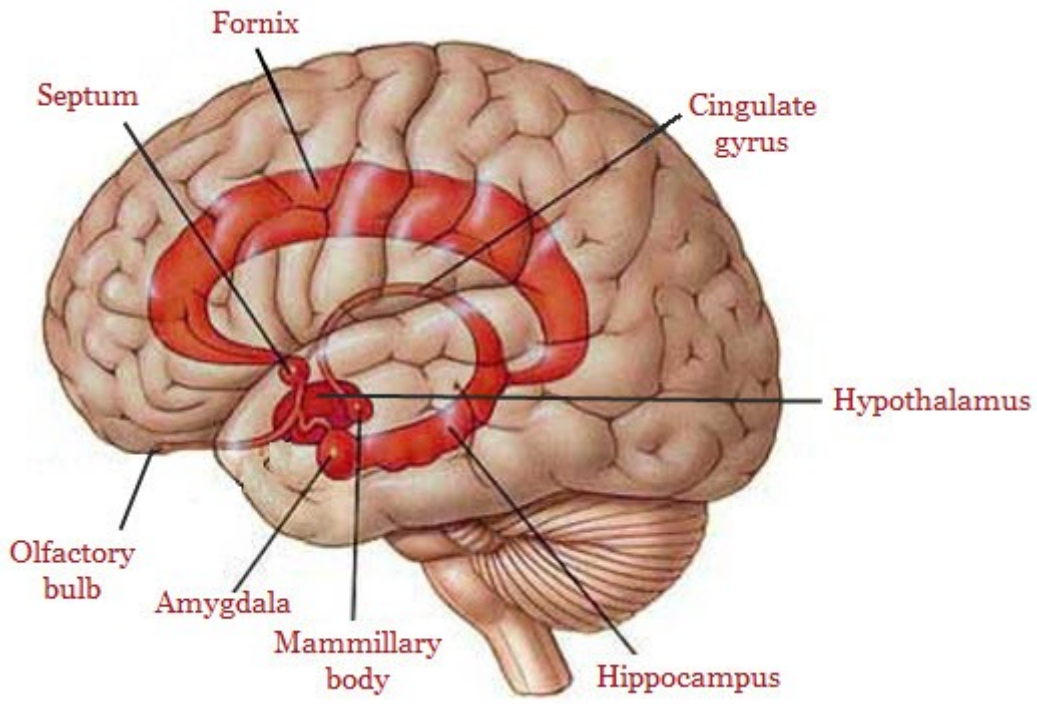


Functions of limbic system

- Limbic system is the neural substrate for emotional experience and expression through somatic and visceral changes.
- Limbic system is involved in 3 levels of behavior.
    - Drive
    - Emotions.
    - Goal directed behavior. (Motivation*:* It is the ability to direct behaviour towards specific goals and is called as goal direct behaviour.)
- Expression of drive is concerned with rhinal system comprising of amygdala, prepyriform cortex and septal nuclei. Emotional behavior is mediated via hippocampus. Goal directed behavior is mediated by cingulate gyrus, prefrontal cortex, and the hypothalamic structures.
- Visceral automatic control: Regulation of BP, respiratory and vasomotor mechanism.
- Olfactory processing.
- Neuro-endocrine control.
- Formation of memory process (Short-term-Long term memory by hippocampus)

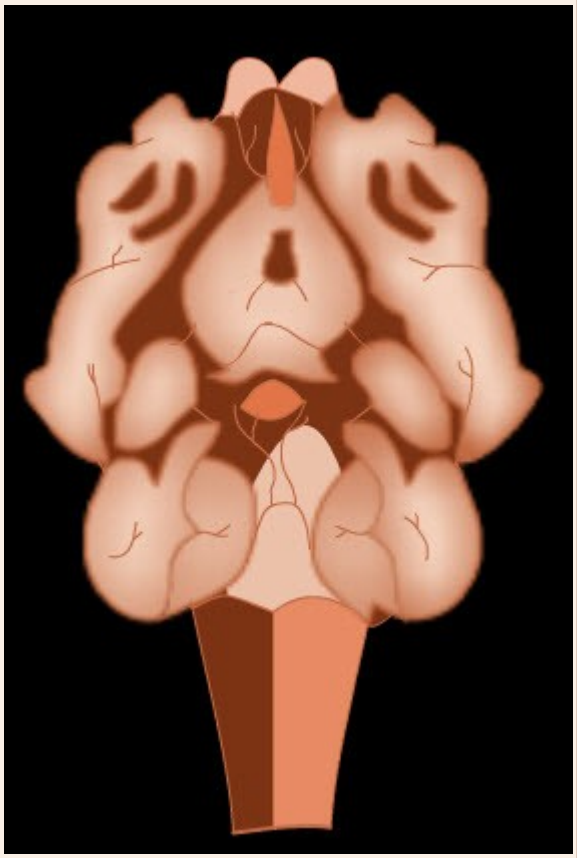
AMYGDALA

- It morphologically forms the part of the basal gangalia and has bi-directional connections with hypothalamus. Amygdala receives input signals from all the portions of the limbic cortex, the orbital surface of the frontal lobe, cingulate gyrus, hippocampal gyrus, neocortex of the temporal, parietal and occipital lobes especially from the auditory olfactory and visual associated areas. Hence it is referred to as window of the limbic system. This forms the behavioural awareness area that operates at a subconscious level. A portion of the amygdala has olfactory function.



- Amygdala in turn transmits signals back to the cortical area, hippocampus, septum, thalamus and hypothalamus.
- Septum functions in sexual and maternal behavioural pattern. Stimulation of amygdaloid nuclei causes a pattern of rage, escape, of being punished and reactions of reward and pleasure.
- Functions: It forms the part of the visceral control centre of the limbic system.
    - Located in the interior of the basal temporal bone.
    - Concerned to process inputs that generate fear response and to avoid danger.
    - Deals with emotional memories and prepare the animals to set the goal for fight-flight system.
    - The circuits of amygdala releases GABA, an inhibitory neurotransmitter, so as to initiate fight responses after receiving stronger stimuli.
    - Amygdala due to the presence of GABA filters unthreatening stimuli.

MODULE-6: INTERBRAIN, THALAMUS AND HYPOTHALAMUS



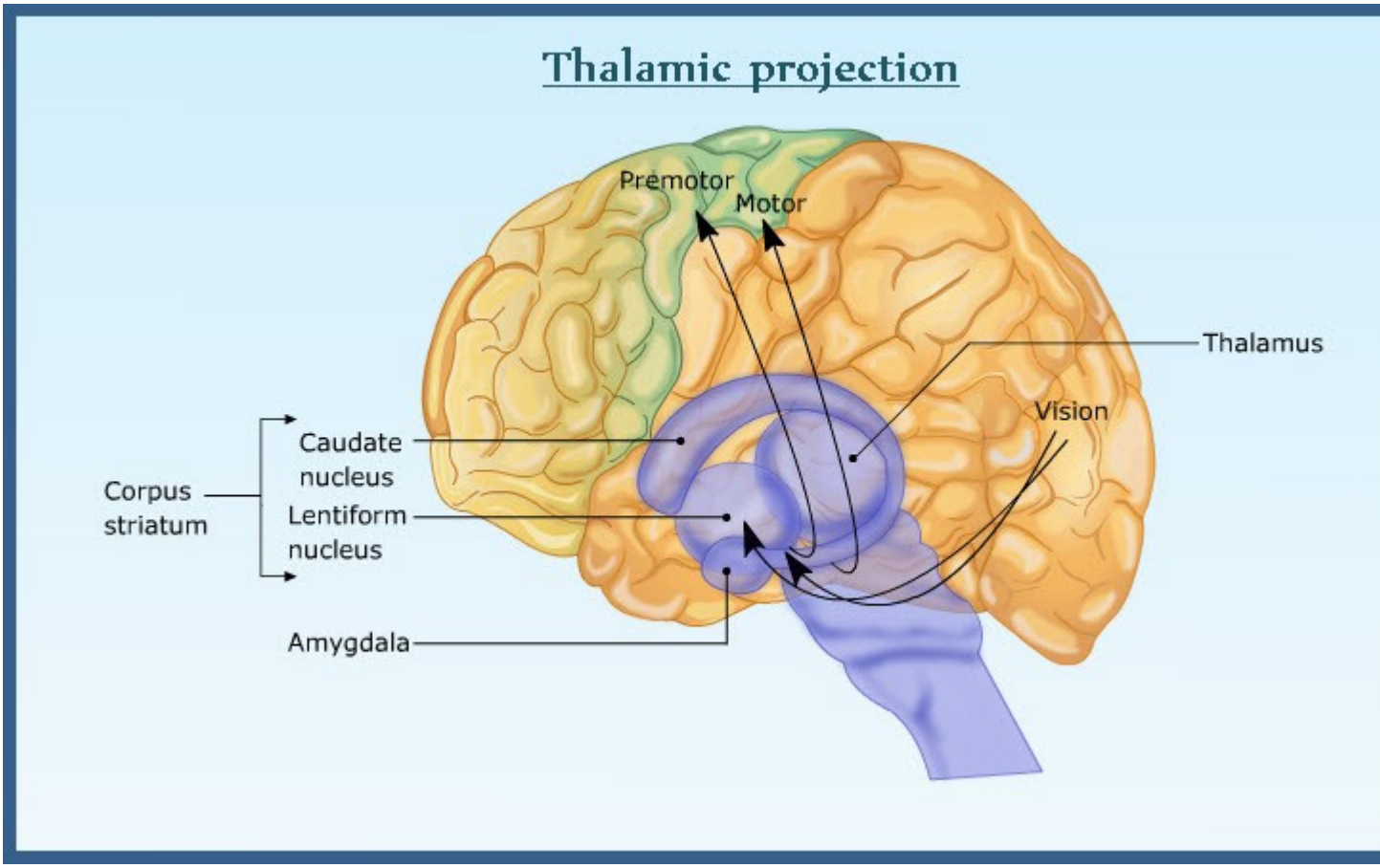
LEARNING OBJECTIVES

This module assists to equip the knowledge on,

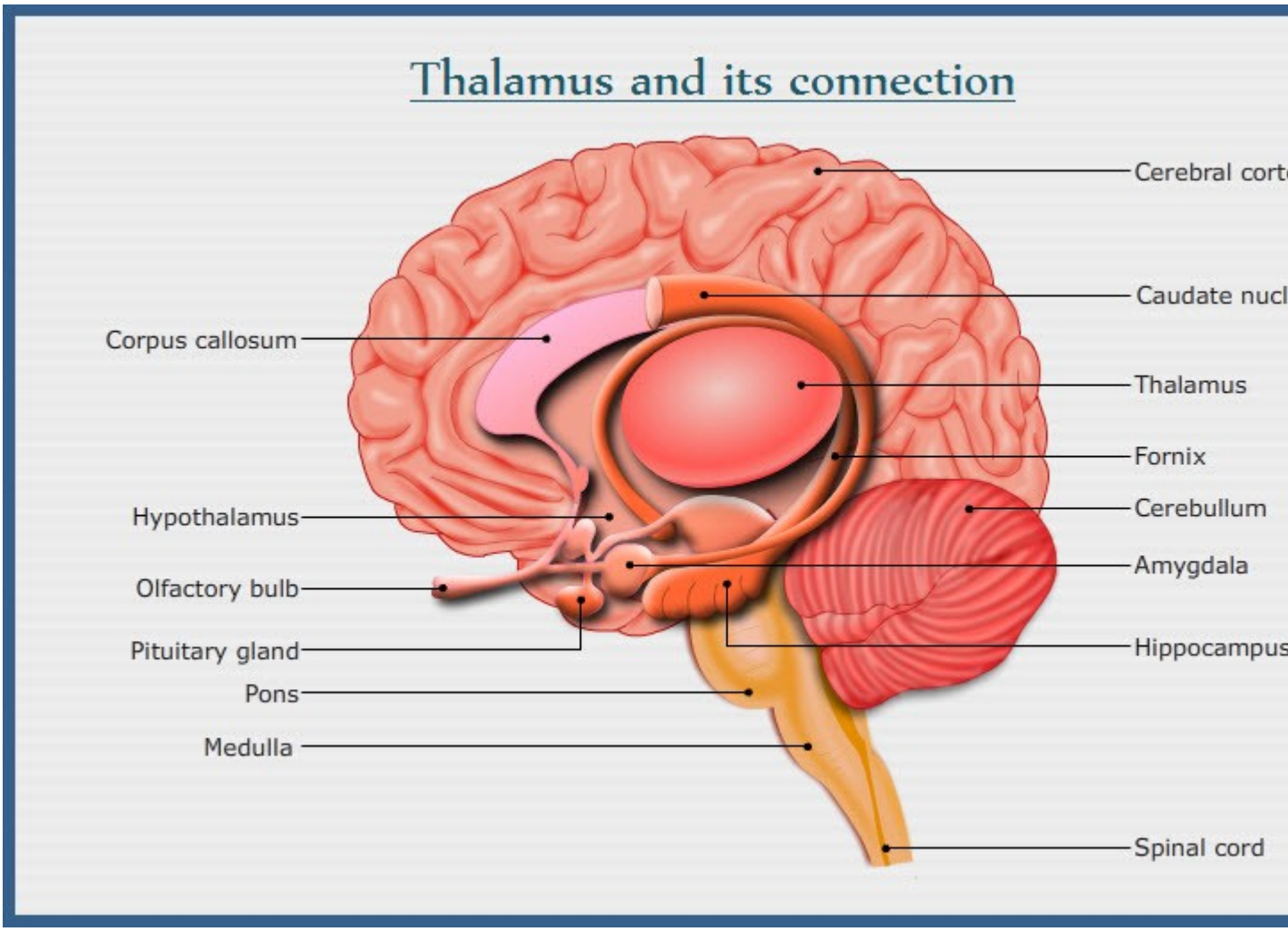
- the function and components of the interbrain,
- the projection systems and functions of the thalamus and the limbic system,
- the importance of hypothalamus and its control over the vegetative functions of the body and
- the function of the pineal gland in regulating photoperiod.

THALAMUS

- It is a sensory relay station and is important in motor control and play a major role in control of cerebral excitability.
- Located deep within the brain near the basal nuclei forms the part of diencephalon.
- Represented by large grey mass related medially to the third ventricle and at the base of lateral ventricle.
- It mediates connections between cerebral cortex, basal ganglia, hypothalamus, cerebellum, brainstem, reticular formation, and spinal cord. Physiologically thalamus can be considered to have three systems.
- Specific projection systems-transmits information to and from cortex.
- Nonspecific or diffused projection system-has widespread action on cortex.
- Acts as pacemaker that regulates the cortical activity.
- Nuclei with subcortical connections.



- *Specific projection system:* Receives specific afferents from the periphery, which are processed in the thalamus and relayed to specific areas of the cortex for conscious perception.
- *Lateral geniculate body:* Receives the visual signals through optic tract and projects the outputs to the visual or the striated area of the cortex.
- *Medial geniculate body:* Receives the auditory signals through the cochlear nerve and projects the efferents to the temporal lobe of the cortex.
- *Ventrobasal complex:* Receives sensory impulses through medial lemniscus, spinothalamic and trigeminaol nerve and projects its output signals to the somesthetic and gustatory areas of the cortex.
- *Posterior nuclear group:* Receives the pain sensations through medial lemniscus and spinothalamic tract and projects them to the cortex.
- *Ventrolateral nuclei:* Acts as a motor relay station that receives the input signals from the basal ganglia and cerebellum and projects the efferents to the motor cortex.
- *Anterior nuclei:* Receives input signals from the mammillary body of the hypothalamus and projects the efferents to limbic cortex and cingulate gyrus of the cortex.
- Non - specific projection system: It forms a widespread action on the cortex and thereby regulates cortical activity and consciousness.



Functions

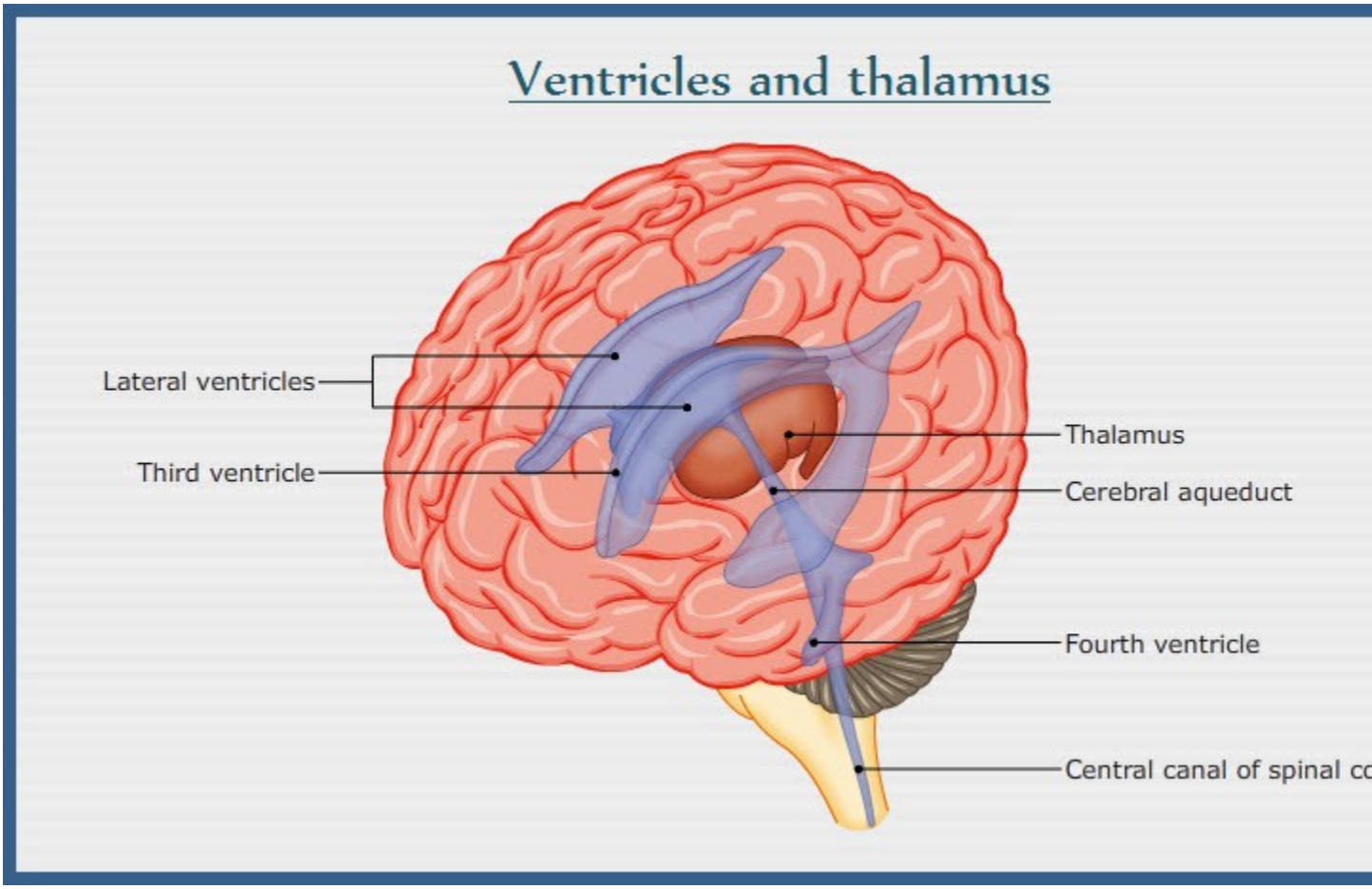
- It acts as a synaptic integrating centre for preprocessing of all sensory information to cortex except olfaction.
- It screens the sensory impulses to appropriate areas of the somatosensory cortex.
- It is capable of recognizing crude awareness of various sensations, but unable to identify and distinguish strength, location, and intensity.
- Somesthetic sensory impulses reach the thalamus through medial, spinal lemniscus to posteroventral nucleus of the thalamus.
- Taste fibers are relayed in arcuate nucleus.
- Arousal, alert, or wakefulness is maintained by part of the thalamus due to the fibers from forebrain and midbrain reticular formation and hypothalamus.
- Act as higher centre for crude sensation and of pain and temperature.

FUNCTIONS OF THALAMUS

Nonspecific nuclei

- Plays a dominant role in the control of cerebral excitability by antagonizing ascending reticular formation.
- Nonspecific thalamic nuclei are responsible for the production of α-rhythm in an awake, resting animal.
- These nuclei integrate the sensory inflow and elicit motor activity.

- These nuclei maintain relationship with hypothalamus and hence modify autonomic and endocrine functions.
- These nuclei functions in the crude conscious perception of sensory information.
- These nuclei represent the brainstem association centre and control many involuntary adjustments according to the environmental influences.



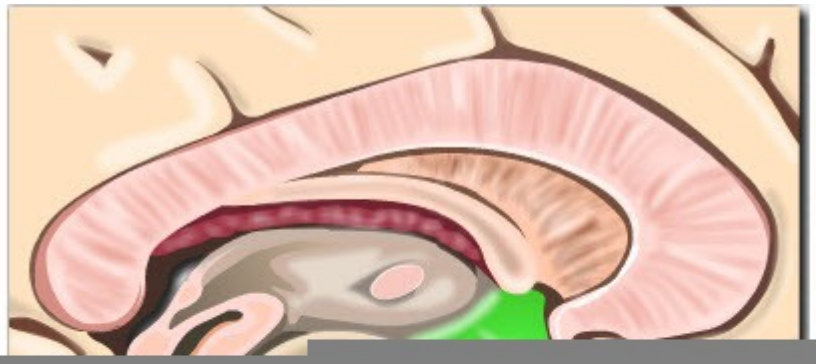
Specific nuclei

- Functions to relay sensory or motor information to and from the cerebral cortex, hypothalamus, and basal ganglia, and the reticular formation.
- Many sensory information reach here after converging through ascending systems like spinothalamic tract, lateral or medial lemniscus. Because of the convergence of mixed sensation, which lack specific receptor organ or neural pathway could be perceived.
- Specific sensation like from visual system project to lateral geniculate body and auditory system project to medial geniculate body of thalamus.
- Pain signals end in posterior group of nuclei.
- Tactile and gustatory pathways project to ventroposterior nuclei.
- Ventrolateral nucleus act as relay nucleus for sensory information from basal ganglia and cerebellum. They control voluntary motor activity.
- A largest nucleus of thalamus is dorsomedial nucleus functions to relay two way system of communicating information from prefrontal cerebral cortex and hypothalamus. They receive information from putamen, caudate nucleus, amygdaloid, and para-olfactory area of cortex.

HYPOTHALAMUS

- Responsible for involuntary internal response of body systems and prepares for appropriate action in a particular emotional state. It occupies the ventral portion of the brain stem.

- It serves as the major control of visceral motor activity namely CONSUMMATORY MOTOR BEHAVIOUR.
- The hypothalamus contribute to rage behaviour, affects emotions like fear response, arousal, exploration and orientation.
- The hypothalamus and its related structures control many internal conditions of the body such as body temperature, osmolality of the body fluids, the drive to eat and drink etc. known as "the vegetative functions of the body".
- It receives connection from amygdala, hippocampus, dorsomedial nucleus of thalamus septal area, ascending recticular formation, globus pallidus and cerebral cortex.

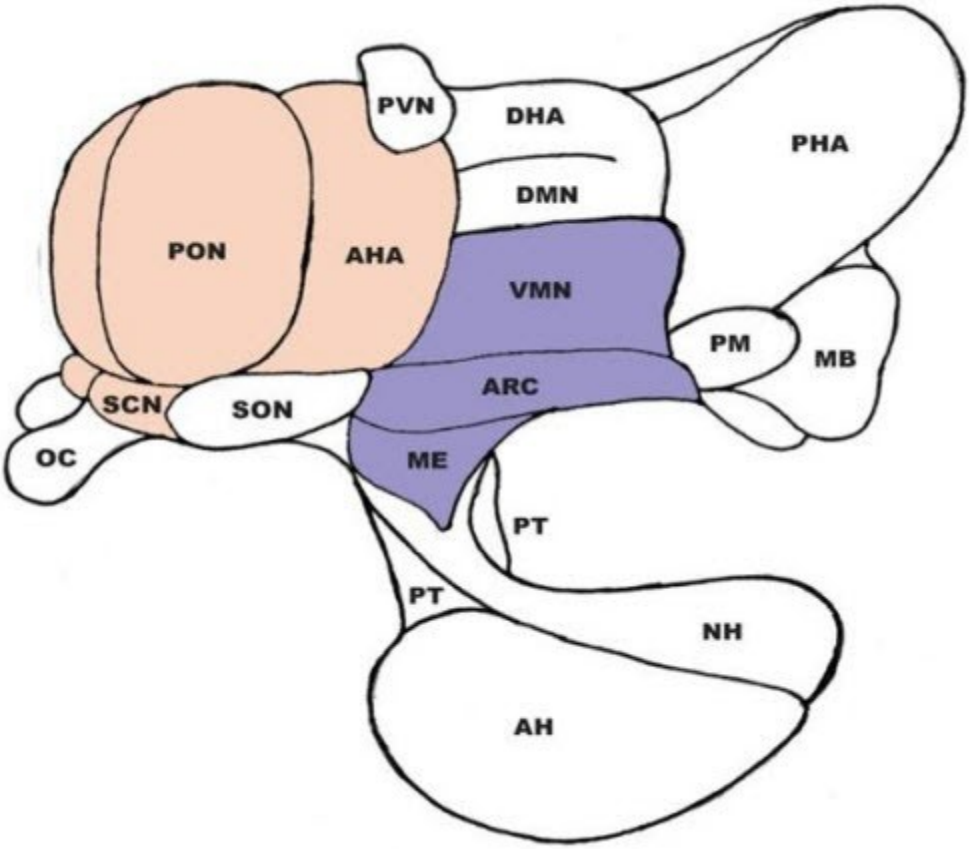


- Hypothalamus sends output signals downward through the brain stem reticular formation of mesencephalon, pons and the medulla as autonomic outflow and upward to the areas of the anterior thalamus and limbic cortex.
- It regulates emotional and visceral motor activity by passing efferent fibres to dorso medial nucleus of thalamus, anterior group of nuclei, superior colliculus and tegmentum (mid brain).
- The hypothalamus includes optic chiasma, tuber cinereum, mamilary bodies, median eminence, infundibulum and neurohypohysis.

It forms that portion of the rhinencephalon (limbic system) which are closely related to the behaviour.

VEGETATIVE FUNCTIONS OF HYPOTHALAMUS

- Cardio vascular regulation
  - Stimulation of the posterior and lateral hypothalamus increases the arterial pressure and the heart rate, but the stimulation of the preoptic, area depresses the blood pressure and heart rate.
- Regulation of body temperature
  - The preoptic and anterior hypo-thalamus is concerned with regulation of body temperature, panting and sweating. Temperature is monitored peripherally and centrally by thermosensitive neurons . Hypothalamic receptors sense both cold and warm and monitor core body temperature. These receptors are present in the preoptic area of the anterior hypothalamus . Posterior hypothalamus integrates peripheral and central thermal sense and modify the heat loss or heat generating mechanisms. Hypothalamus is more sensitive to central thermoceptors.



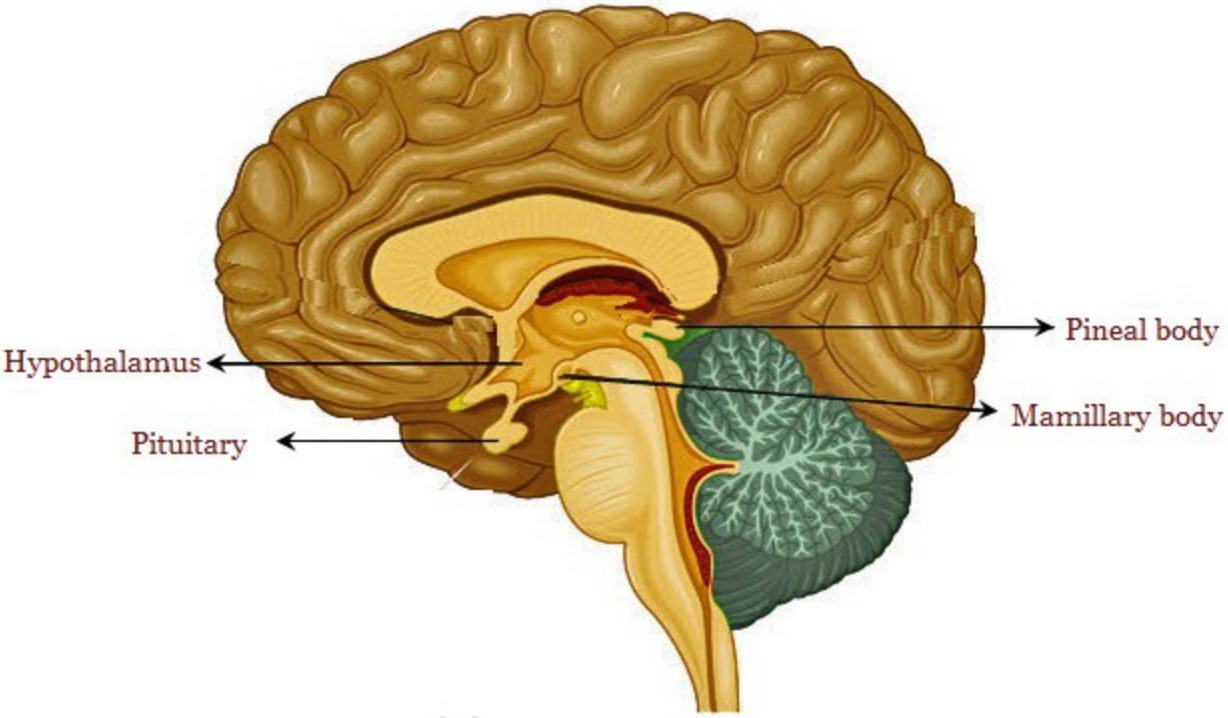
- Regulation of body water
  - Hyperosmolality of the body fluid stimulates the thirst centre in the lateral hypothalamus. The hyperosmolality (hemoconcentration) in turn stimulates the ADH secretion from the supraoptic nuclei, that aids in water reabsorption from the collecting tubules and ducts of the kidney.
- Regulation of thirst and water balance
  - Hypothalamus senses the external condition and control thirst. This region of the brain detects circulating hormones due to hyperosmolarity posed by Na+ as they lie in the zone of incomplete blood brain barrier system. Subfornical organ

(SFO) , Organum vasculosum of lamina terminalis (OVLT) in the median preoptic nucleus are collectively known as circumventricular organs that detect osmotic conditions. Detection is mediated by both osmotic and hormone receptors. Osmotic receptors monitor the osmolarity of CSF that cushions the hypothalamus. Hormone receptor to bind Angiotensin II in this area exerts renal water sparing action. Perception of osmolarity is mediated by above said mechanism. They send signals to the thirst center of dorsomedial hypothalamic nuclei and drives thirst behaviour.

- Regulation of uterine contraction and milk ejection
    - Neuroendocrine reflex stimulation of paraventricular nuclei, (entry of fetus into the birth canal stimulates sensory nerves, which passes via the spinal cord to hypothalamus and releases oxytocin) causes increased uterine contraction. Tactile stimulation of udder sends sensory impulses to hypothalamus causing release of oxytocin, which aids milk ejection by stimulating the contraction of the myoepithelial cells surrounding the alveoli of the mammary gland.
- Regulation of feed intake
    - The ventromedial region of the hypothalamus, is referred as feeding centre. Stimulation of this centre causes hyperphagia, whereas the lateral region of hypothalamus known as satiety centre, on stimulation reduces feeding behaviour. Stimulation of optic chiasma area of hypothalamus causes increased gastric secretions.
- Sleep and wakefulness
    - Stimulation of the anterior hypothalamus induces sleep, while the stimulation of mammillary body (caudal hypothalamus) activates the ascending reticular activating system (RAS) to produce wakefulness.
- Reproductive functions
    - Median eminence of the hypothalamus releases GnRH in a pulsatile manner, which regulates the FSH and LH release from the pituitary gland. Estrogen and progesterone acts on the hypothalamus and causes negative feed back effect on GnRH release; the estrogen also produces a positive feed back effect on GnRH release. Thus the functions of ovary and testes are regulated by the hypothalamus.In seasonal breeders and birds hypothalamus plays a key role to effect photoperiodism and thereby the breeding performance is regulated.
    - Melatonin released from the pineal gland regulates the duration of light, and activates/inhibits GnRH release from hypothalamus in short and long-day breeders. Until puberty, hypothalamic GnRH release is highly sensitive to oestrogen and is kept in check by the negative feed back effect of oestrogen. At the time of puberty, the sensitivity of hypothalamus to oestrogen is reduced resulting in pulsatile GnRH release and puberty occurs.
- Regulation of anterior pituitary functions
    - Hypothalamus controls the anterior pituitary gland secretions through neuro-secretory peptides and amines known as the releasing and inhibitory hormones. E.g. TRH, GHRH, GHIH, PIH, CRH, GnRH, PRH. The TRH and CRH are released from paraventricular nucleus, GnRH from preoptic area, GHIH from anterior hypothalamic area, GHRH and PIH from arcuate nucleus. These regulatory hormones pass from the hypothalamus to adenohypophysis through the hypothalamic-hypophyseal portal system.
- Regulation of emotional status
    - Hypothalamus controls both fear and aggressiveness. The posterior hypothalamus regulates sympathetic response of the emotional status via catecholamines.

PINEAL GLAND

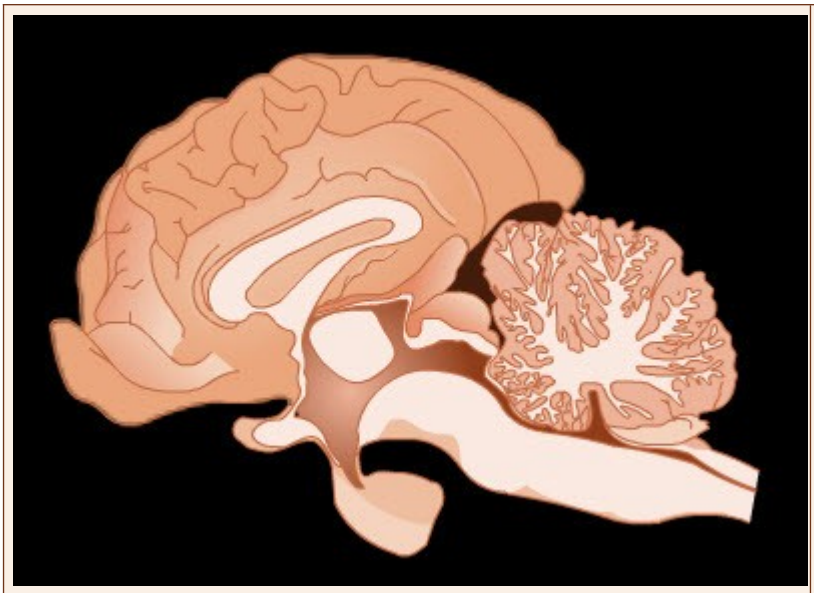
- It is the main translator of photoperiodic effect in animals.
- The pineal gland produces a hormone, melatonin in response to darkness. Light passes from the retina to supra chiasmatic nucleus of the hypothalamus, superior cervical ganglia and to pineal gland.
- The melatonin inhibits gonadal activity.
- Cat and horse are positively affected with increasing light period and goat and sheep are positively affected by decreasing photoperiod.
- The pineal gland acts to relay light-dark information to the hypothalamus and regulates seasonal breeding in animals.



INTERBRAIN (DIENCEPHALON)

- Structures including epithalamus, subthalamus (ventral area), thalamus (dorsal area), hypothalamus, pituitary gland and pineal gland constitute the interbrain.
- The epithalamus functions as olfactory centre. Subthalamus regulates motor activity through reticular nucleus.

MODULE-7: MID BRAIN AND CEREBELLUM



LEARNING OBJECTIVES

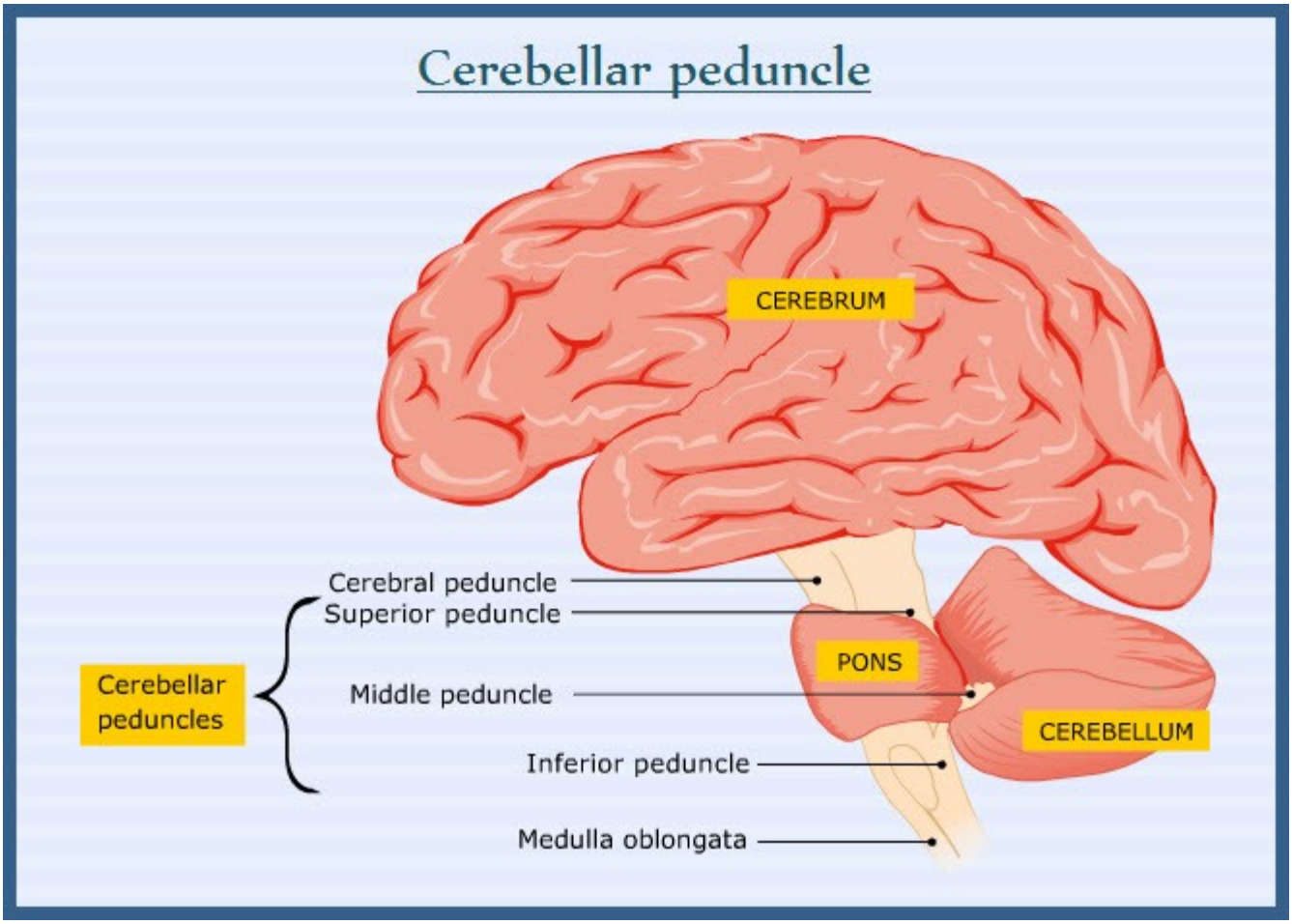
This module enables the learner to understand,

- the parts of the midbrain and the significance of the corpora quadrigemina and cerebral peduncle and
- the basic anatomical organization of the cerebellum and its functions.

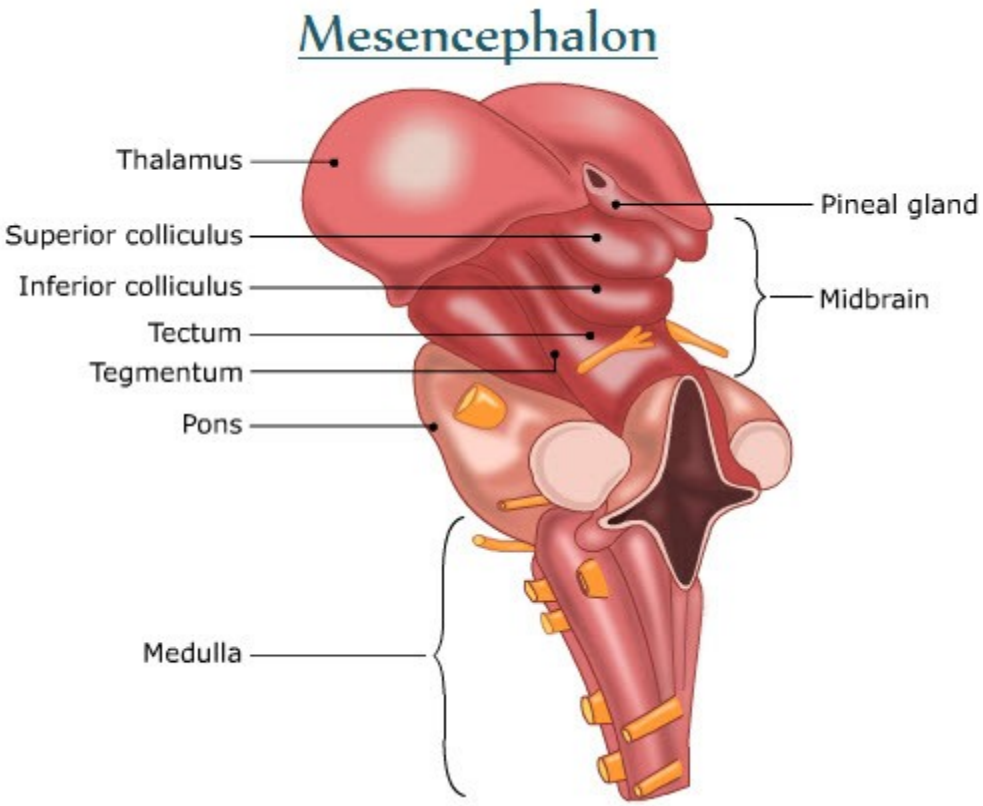
CEREBELLUM

- It is encased in cerebellar hemisphere and is located the back of the brain.
- Responsible for motor coordination by integrating sensory inputs from receptors located from muscles eyes and ears with motor orders of the fore brain.
- It maintains equilibrium and posture.
- Present in the anterior part of the brainstem, dorsal to the pons and medulla, and caudal to the cerebral cortex so called as little brain. It contains many neurons.
- It is present in all mammals. Jawless vertebrates lack cerebellum.
  It is concerned with proper positioning of the body in the space. It maintains subconscious coordination of the movement and coordinates fast phasic motor activity.

- Cerebellum is extensive in birds where they need to balance while flying.
- The anatomy of the cerebellum is as follow,
    - Made up of outer grey matter layer known as the CEREBELLAR CORTEX.
    - White matter of cerebellum is represented by stalks known as CEREBELLAR PEDUNCLE.



    - Three pairs of the cerebellar peduncle functions as sensory and motor fibers to and from cerebellum and through which it is attached to the brainstem.
        - Brachium conjunctivum-to thalamus and mesencephalon. It is the rostral cerebellar peduncle.
        - Brachium pontis-to pons. It is the middle cerebellar peduncle.
        - Restiform body-to medulla and spinal cord. It is the caudal cerebellar peduncle.



- Group of cerebellar nuclei known as subcortical nuclei is embedded in the cerebellar white matter, whose axons leave the cerebellum. They are dentate nucleus, globus emboliformis and fastigial nucleus.

CEREBELLAR HISTOLOGY

Cerebellar cortex shows 5 types of neuronal cells. They are similar to cerebral cortex in this region.

- Stellate
- Basket
- Golgi
- Granule
- Purkinje cells

They are arranged in 3 layers

- *Outermost layer:* *Molecular layer*. Made up of 2 types of cells. Outer stellate cells where axons confines to this layer. Basket cells whose dendrite remain in this layer and axons reaches Purkinje layer and make synaptic contact with cell bodies of Purkinje cells. Axons of the stellate cells synapse with primary and secondary dendrites of Purkinje. It has axons of granule cell (parallel fibers), neuronal dendrites of deep layers, few inhibitory neurons, stellate, and basket cells.
- *Middle layer:* *Purkinje cell layer*. It is composed of simple layer of ovoid/rounded cell bodies of Purkinje neurons. Uniqueness of those cells are extensive branching of their dendrites (multi polar neurons) which are oriented at right angles to parallel fibers. These cells are the output neurons, uses GABA as their neurotransmitter hence they are inhibitory in nature. Axons of Purkinje cells travel outside the cerebellar cortex to reach the cerebellar nuclei. Purkinje cell comprises of primary, secondary, tertiary, and

quaternary dendritic branches. The primary and secondary are smooth but tertiary and quaternary have numerous synaptic spines and are rough surfaced. They synapse with the neurons of the granular layer beneath this.

- *Inner layer: Granule cell layer*. It has cells which have darkly stained nucleus and little cytoplasm giving this layer granular appearance. It has many small granule cells with few Golgi neurons. The Golgi neurons are located at the junction between granular and Purkinje layers. Dendrites of granular cell limit within this layer and receive synaptic influence from sensory fibers to the cerebellar cortex (mossy fibers) and axons of Golgi neurons. Axons of granular cell project to the molecular layer through the tertiary and quaternary Purkinje branches and synapse their spines. Among the cells of the cerebellar cortex, only the granule cells have excitatory neuron.

Cerebellum consists of 3 functionally distinct parts in birds and mammals

Vestibulocerebellum/Archicerebellum

- The classification is based on the embryological basis. The archicerebellum is an initial evolutionary structure. It deals with control of tonic or postural reflexes of the spinal cord. Important for maintenance of balance and coordination with eye movement. It mediates coordination of vestibular reflexes.
- It is present in the flocculonodular lobe.
- It receives sensory information from vestibular system. It sends back orders to vestibular nuclei via cerebellar nuclei (fastigial nuclei), to coordinate the axial and proximal muscles controlling balance. These orders are mediated by vestibulospinal tracts which in turn help to coordinate head and eye movements.

Cerebrocerebellum/Neocerebellum

- It involves in planning and initiating voluntary activity.
- It provides input to motor cortex concerned with graceful, intricate, appropriately timed voluntary movements. It occupies most of the cerebellum representing in the lateral cerebellar hemisphere.
- It receives inputs predominantly from supplementary and premotor cortex via the corticopontine cerebellarly system. They have no clue of the sensory information from the peripheral receptors. Their output goes back to motor cortex from a communication loop for planning and preparation of movement ahead of actual execution and enhances appropriate timed transitions of a movement sequence.

Spinocerebellum/paleocerebellum

- This portion represents the medial portion of the cerebellum.
- It is concerned with maintenance of muscle tone, coordinates skilled voluntary movements. It controls the tonic or postural motor activity of the spinal cord. They are concerned with accurate timing of muscular contractions. It maintains coordination between muscles of different parts to complete an action, by receiving information from peripheral somatosensory system that constantly inform higher centres about the body movement.
- The cerebellum receives information from higher centres about the orders sent and at the same time they receive information from muscle spindle, vestibular, visual, and other sensory receptors about the movement the body is performing.
- It predicts the position of the body in next minute and to make adjustments needed. This mediates the intentions of the motor cortex to the execution of muscular movements happening. It is important to mediate the corrections on the intended movement. The general pathway is that it receives inputs from muscle and cutaneous receptors, spinal reflex circuits through the spinal cord. The information from corticospinal, descending brain stem pathway, primary motor cortex, and somatosensory cortex reaches this area.

The information from high centres encode the movement to be executed by the skeletal muscle and sensory inputs inform what exactly executed by the muscles.

- Output from these areas are mediated through deep cerebellar nuclei, reticular nuclei of brainstem that controls antigravity muscles, red nuclei of the brainstem which controls musculature of distal limbs, to adjust the timing and coordination of the movement and muscle tone. Inhibition of this area, activity of medullary lateral vestibular nuclei is enhanced by way of fastigial nucleus. This nucleus is one of the cerebellar nuclei that lie over the roof of the fourth ventricle. Enhanced activity of the medullary nucleus excites α-motor neurons of antigravity muscles of the limb and results in rigidity of the antigravity muscles.

The degree of tonic inhibition exerted on the fastigal neurons and medullary neurons is depended on orders from cerebral cortex (cortico-ponto cerebellar pathway), basal gangilia and from cutaneus and propioceptive systems of the body. Spinocerebellum exerts flexible controls over the skeletal muscle tone on the posture.

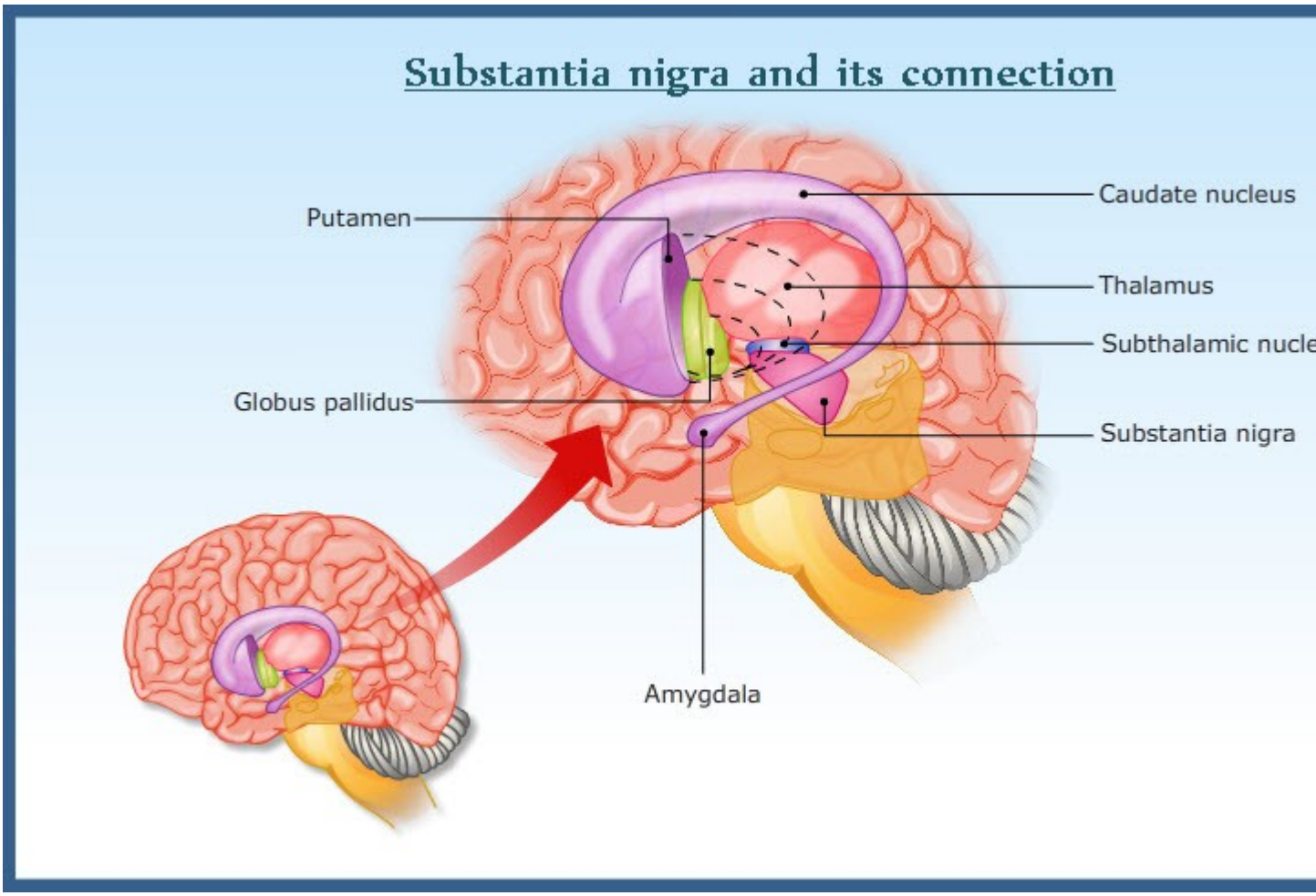
INPUT TO CEREBELLUM

- Represented by group of fibers namely Mossy fibers and Climbing fiber axons
- They use excitatory neurotransmitter to cause excitatory post synaptic potential in the subsequent cells of the cerebellar cortex. The climbing fiber axons exhibit one to one relationship with Purkinje cells.
- These fibers carry information from higher motor centres and peripheral sensory receptors.
- Both climbing and Mossy sensory fibers are excitatory. When peripheral receptor or CNS is stimulated, it causes activation of these two fibers. The CNS organization facilitates early excitation of Mossy fibers 5-10 millisecond prior to the excitation of climbing fibers. Hence rapid initiation of the cerebellar cortex activity is appreciated.
- Excitation of the granule cells and Golgi neurons of cerebellar cortex by Mossy fibers.
- Depolarization of dendrites of Purkinje cells, outer stellate, basket cells, and Golgi neurons through parallel fibers from excited granule cells.
- Mossy fibers influence the duration of discharge of impulse in the granule.
- Inhibition of Golgi neurons are potentiated by stellate and basket cells by way of parallel fibers.
- Degree of inhibition is inversely related to the excitation of climbing fibers that reaches the cerebellar cortex and efferents of the Purkinje cell reflect the cortical activity.
    - Cerebellar functions are mediated through disfacilitation of the structures of CNS.
    - α-RIGIDITY: It is the rigidity that results from hyper excitation of the α-motor neurons of the spinal cord.
    - γ-RIGIDITY: It is the result of the hyper excitation of the γ-motor neurons of the spinal cord.
- In birds, cerebellum is concerned with regulation of spinal cord and brain stem mechanism to help in flying and maintenance of equilibrium. Cerebellar pathology is associated with persistent rigidity of the antigravity muscles.

MIDBRAIN

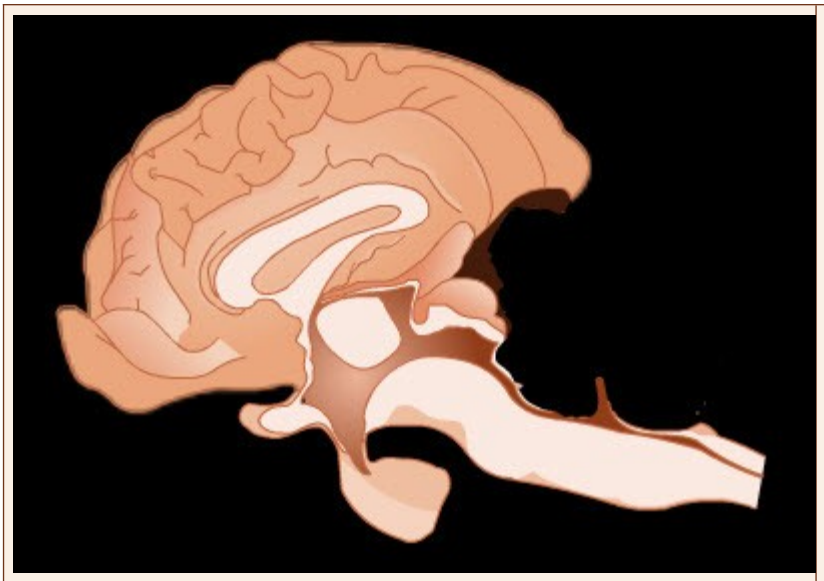
- It is a relay centre. Extends from pons to thalamus concerned mainly with auditory and visual relay system. It has dorsal portion namely the corpora quadrigemina which consists of two pairs of colliculi and ventral portion namely the cerebral peduncle. Roof of the midbrain is known as Tectum which has pair of brain centres vis namely optic lobes in non mammalian species. It has a pair of inferior colliculi.

- *Corpora quadrigemina:* Represented as paired colliculi, anterior pair concerned with visual relay is known as Superior colliculi and posterior pair concerned with auditory relay is known as Inferior colliculi.
- *Superior colliculi:* It is similar structure as optic lobes in mammals functions as reflex optical response (orientation towards visual stimuli, focusing etc.) Visual reflex centres houses many nuclei. Optic tract via lateral geniculate body of thalamus leaves collaterals to the suprachiasmatic nucleus of the hypothalamus, pretectal nucleus and superior colliculus. The pretectal region immediately anterior to superior colliculus receives inputs from retina, superior colliculus, lateral geniculate body and frontal eye field. Through these they modify pupillary light reflexes, accommodation, and ocular fixation reflexes. Through hypothalamic connections they modify the activities of limbic system and visual control. Through the connections with hypothalamus they also influence light-related endocrine secretions, circadian rhythm, sleeping cycle, and eating and drinking. Through connections with accessory optic system with flocculonodular lobe and inferior olivary nucleus, eyeball movements in relation to position and movements of head in space is integrated.Superior colliculi do receive collaterals through optic tract which connects visual and non-visual information via circuit. These neural circuits integrate visual information with non-visual information for coordinating head, eye, and body movements (postural reflexes).
- *Inferior colliculi:* It is concerned with hearing. It is an important relay station for the integration of ascending and descending auditory signals. These provide functional link between brainstem and telencephalic organization of auditory information. It receives the afferents from superior olivary nucleus which forms the major ascending auditory relay from cochlear nuclei. It involves lateral lemniscus to exhibit reflex vocalization and correlation of information of equilibrium.
- *Cerebral peduncle:* consists of tegmentum, substantia nigra, and basis peduncle.
- *Tegmentum:* It is a posterior part of midbrain that posses fine control of muscles. Act as a relay in integrating functions of sensory and motor functions. It forms the ascending reticular formation of the pons. It contains key structure of somatomotor neuron RED NUCLEUS along with the nuclei of trochlear and oculomotor nerves.
- *Red nucleus:* Located within the rostral portion of the midbrain and extend up to the posterior part of thalamus and hypothalamus. It is well connected with other structures of CNS via corticorubral (from cortex), pallidorubral (basal ganglia), and cerebellorubral (cerebellum-dendate nucleus) through the respective tracts and through axons to subthalamus. Motor fibers from red nucleus are projected to spinal cord via rubro-spinal tract, to reticular formation via rubro-thalamic tract, to olivary nucleus through rubro-olivary tract. They do send efferents via axons to III, IV, and VI cranial nerves.Red nucleus maintains muscle tone and equilibrium. It act as a centre for all righting reflexes except visual righting reflex. It integrates various impulses and transmits them to spinal cord to control somatic activity.
- *Substantia nigra:* Functions as integration centre for skilled muscular activity by receiving sensory information from the body surface, ear, eye, and nose. It inhibits extra-pyramidal motor movements.



- *Basis peduncle:* Forms the passage for corticospinal and corticopontile tracts.

MODULE-8: BRAIN STEM, RETICULAR FORMATION AND SLEEP



LEARNING OBJECTIVES

This module enables the learner to understand,

- the components that make up the brain stem,
- the medullary centers that control the body's functions, nerves that arise in the region and the nuclei present here,
- the function and reflex activities of the brain stem,
- the formation of the BSRF and its functions and

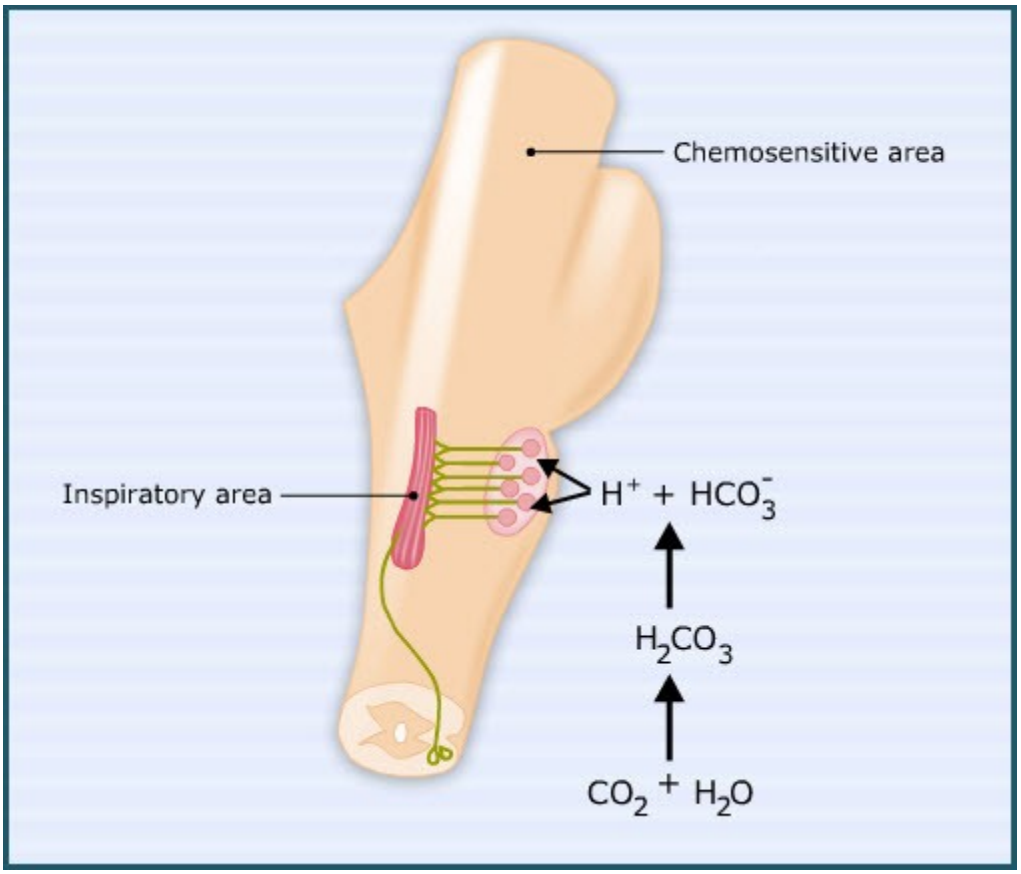
	• sleep, its types, theories and brain waves on the various stages of sleep.

BRAIN STEM

- It is the group of CNS structures continuous with the spinal cord. It forms a vital link between the spinal cord and higher centres of the brain. It comprises of medulla oblongata and pons that controls many of the life sustaining process and baseline activities of skeletal muscles. These comprise of caudal most portion of the brainstem. It maintains relationship with fourth ventricle.
- Difference exists in the distribution of the white and grey matter in the brainstem. Grey matter of brainstem is represented by nuclear group separated from each other by fiber system.
- Largest representation of the brainstem is the reticular structures namely the brainstem reticular formation. This extends from anterior end of the spinal cord to thalamus and hypothalamus. This system controls the consciousness and perception, motor and sensory activity of an animal.

NUCLEI OF BRAIN STEM

- These are associated with cranial nerves and are organized into columns, representing different functional types. They are three motor columns (somatic, visceral, and branchial motor columns) and two sensory motor columns (somatic and visceral sensory systems).
- Somatic motor column is placed in the dorsomedial position of the brainstem. It consists of α-motor neurons. These neurons supply the muscles of head, extrinsic muscles of eye, and muscles of tongue.
- Visceral motor column contains neurons similar to the intermediolateral cell column of the thoracic and lumbar spinal cord. They supply fibers to the intrinsic muscles of the eye, vagal fibers to the cervical, thoracic, and abdominal regions.



- Branchial motor column is located ventrolateral to the somatic sensory column and are similar to the α-motor neurons of the somatic motor column. They supply motor fibers to the skeletal muscles of mastication, facial muscles, and muscles of larynx, pharynx, and trapezius.
- Somatic sensory column consists of neurons of sensory fibers of trigeminal nerve supplying to head and face. As they function to innervate muscle spindle of the cheek muscles, they are responsible for control of muscle tone of masticatory muscles and reflex control of chewing. These neurons are responsible for perception of delicate tactile sensation, pain, and temperature in the areas of head and face are processed via the nucleus gracilis and nucleus cuneatus.
- Visceral sensory column is represented by a single nuclear structure at the medulla and is known as nucleus of fasciculus solitarius. Sensory information from mouth, pharynx, larynx, thoracic, and abdominal viscera are received by this via visceral afferents of vagus and glossopharyngeal. This nucleus relays taste afferents within the facial, glossopharyngeal, and vagus nerves.

Other nuclei of brainstem

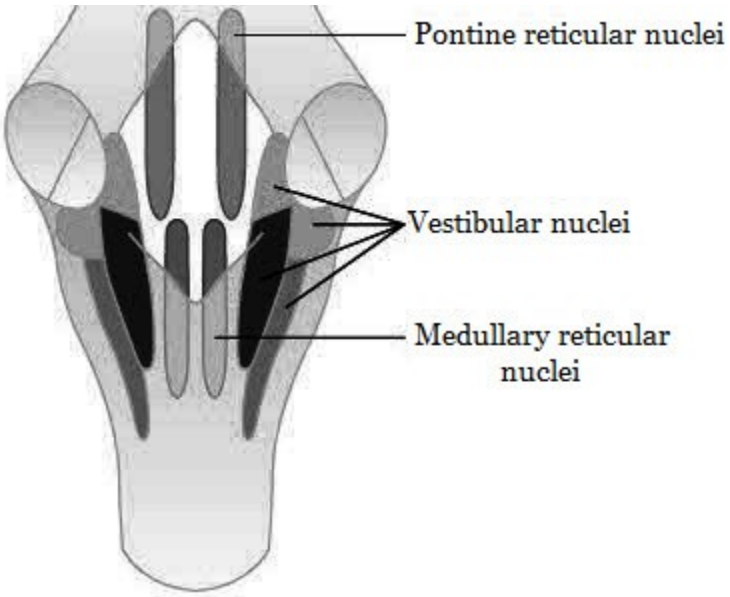
- These nuclei serve as relay of sensory or motor functions. and cerebral cortex are also received by these nuclei as a part of messaging system of CNS to the cerebellum for the control of somatic motor activity.
- Nucleus gracilis and nucleus cuneatus lie within the medulla and relay sensory information of tactile and kinesthetic sense of joint to higher centres of the

brainstem. Fibers of this nucleus at the medullary level form medial lemniscus by arching and decussating to the opposite side and terminate within thalamus.

- Accessory cuneate nucleus forms relay nuclei for tactile, joint angle, and muscle stretch of areas of neck via the spinocerebellar tract. These nuclei lie lateral to nucleus gracilis and cuneatus.
- Caudal olivary nuclear complex is similar to the accessory cuneate. They receive neural information from spinal cord and project them to the cerebellum. Fibers from basal ganglia
- Pontine grey matter lies within pons and serve to relay information for pontocerebellar fiber system to control somatic motor activity. Nerve fibers of this decussate to form Brachium Pontis, third peduncle in the cerebellum.
- Red nucleus is a prominent somatic motor nucleus of midbrain. Midbrain comprises of structures concerning auditory and visual relay system. This nucleus receives sensory fibers from cerebellum, motor cortex, globus pallidus, thalamus, vestibular nuclei, and brainstem reticular nucleus and give rise to RUBROSPINAL TRACT to control somatic motor activity by ending in the internuncial neurons to excite somatic and visceral motor neurons of the spinal cord.
- *Nuclear mass*
- Pre cerebellar reticular nuclei projects to cerebellum.
- Non-cerebellar reticular nuclei: Raphe nuclei: Inhibits the reticular activation system (RAS) and induces sleep.
- Central group of nuclei and Lateral group of nuclei -These two nuclei contain respiratory and cardiac centres.

MEDULLA OBLONGATA

- Located in the top of the spinal cord.
- Has centres that control reflectes activities such as respiration, heart rate, vaso dilation and blood pressure.
- Houses neural part ways that connect cerebral cortex and spinal cord
- The cranial nerves glosso-pharyngeal (IX), vagus (x), spinal accessory (xi) and the hypoglossal (xii) originate from the medulla.
- The nuclei gracilis, and cuneatus transmit the informations of the spinal cord to the somato sensory regions of the cerebral cortex through the thalamus.
- The nucleus gracilis and cuneatus give rise to fibres, which pass to the contralateral side and form the medial lemniscus; this medial lemniscus ascends to thalamus.
- The inferior olivary nucleus input signals to cerebellum. Within medulla there are centres for cardiac, respiratory (inspiratory and expiratory), vasomotor, swallowing, vomiting, cough and sneezing activities.
- Most of the tracts between the spinal cord and the higher levels of the brain pass through medulla.



- Ascending tracts: A portion of dorsal funiculus of the spinal cord terminates in accessory cuneate nucleus from which fibres project to cerebellum as external arcuate fibres. Other ascending fibre tracts of the medulla are spinothalamic, dorsal and ventral spinocerebellar, spino-olivary, spino-tectal tracts.
- Descending tracts: includes Vestibulo spinal, rubro spinal, tecto spinal tracts.

PONS

- Structures present above the medulla function as bridging and communicating information between medulla cerebellum and forebrain structures.
- Pons contain pontine nuclei.
- It also includes superior olivary nucleus of auditory system and nuclei of visceral centres to regulates respiratory and cardio vascular system.
- It is concerned with control of alertness and initiates sleep.
- It serves as integration centre and relay motor centres.
- It also houses cranial nerves 5,6,7 and 8.
- It has two paired respiratory centres known as pneumotaxic centre and apneustic centre that control respiratory rate and rhythm.

FUNCTIONS OF BSRF

- It is a neuronal network extending the length of the medulla, pons, midbrain and then projects into thalamus and hypothalamus.
- Caudally it is continuous with the internuncial neurons of the spinal cord.
- The efferent fibres of the reticular formation are organised into ascending and descending reticular formation.
- The ascending reticular formation projects into other areas of brain, including brain stem, cerebrum and cerebellum; the descending reticular formation projects into the spinal cord.
- The BSRF regulates the sensory, motor and the endocrine functions.
  It is constituted by very small to very large sized sensory and motor neurons.
- The small neurons form multiple connections within the reticular formation.
- The large size neurons are motor in function which bifurcate with one division extending upward to the thalamus or the basal regions of the diencephalon or the cerebrum.
    - Nuclear mass

- Pre cerebellar reticular nuclei ------> projects to cerebellum.
- Non-cerebellar reticular nuclei:
  - Raphe nuclei: Inhibits the reticular activation system (RAS) and induces sleep.
  - Central group of nuclei and
  - Lateral group of nuclei -These two nuclei contain respiratory and cardiac centres.
- The brainstem reticular formation receives sensory input signals from all sensory systems–somesthetic, vestibular, visual, auditory, gustatory and olfactory sensory systems, through spino- reticular tract and also from the vestibular nuclei, cerebellum, and basal ganglia and motor area of the cerebral cortex.
- It integrates the sensory information within the CNS and controls the activities of both the motor neurons of skeletal muscles and the autonomic neurons (cardiovascular, respiratory and the G. I. tracts). The BSRF plays a key role in somatic and visceral motor control.
- The BSRF may either causes consciousness (wakefulness) by providing continuous stimulatory signals to the cortex or it may induce sleep by its inhibitory signals through raphe nucleus to the ascending reticular activation system (ARAS).

Ascending reticular formation

- It alters the consciousness through the sensory inputs from the auditory, visual, olfactory, tactile, pain and proprioceptive sensory systems. It regulates the neuronal activity within the brain and contributes to wakefulness. It controls the activity of the cerebral cortex, hippocampus, basal ganglia and cerebellum and it is referred to as behavioral arousal.
- Ascending Reticular Activating System (ARAS) of the BSRF is involved in alertness/ wakefulness of the animal. They receive sensory information from all sensory receptors and also have inputs from the brainstem, cerebellum and cerebral cortex. These sensory inputs activate the RAS neurons and this in turn activates wide areas of the cerebral cortex. Reduction in the activity of the RAS can lead to sedation, sleep and coma.

Descending reticular formation

- It influences the motor activities such as flexor and extensor reflexes and decerebrated rigidity. It alters the activity of the alpha and gamma motor systems through reticulospinal tract. It also contains centres that inhibit spinal motor neurons.
- The reticular formation contains the centres that promote wakefulness (midbrain RAS). Through pontine raphe nuclei it promotes sleep.

Other functions of BSRF are - Respiratory control, cardiovascular, micturition, emesis, rumination, deglutition, mastication control etc.

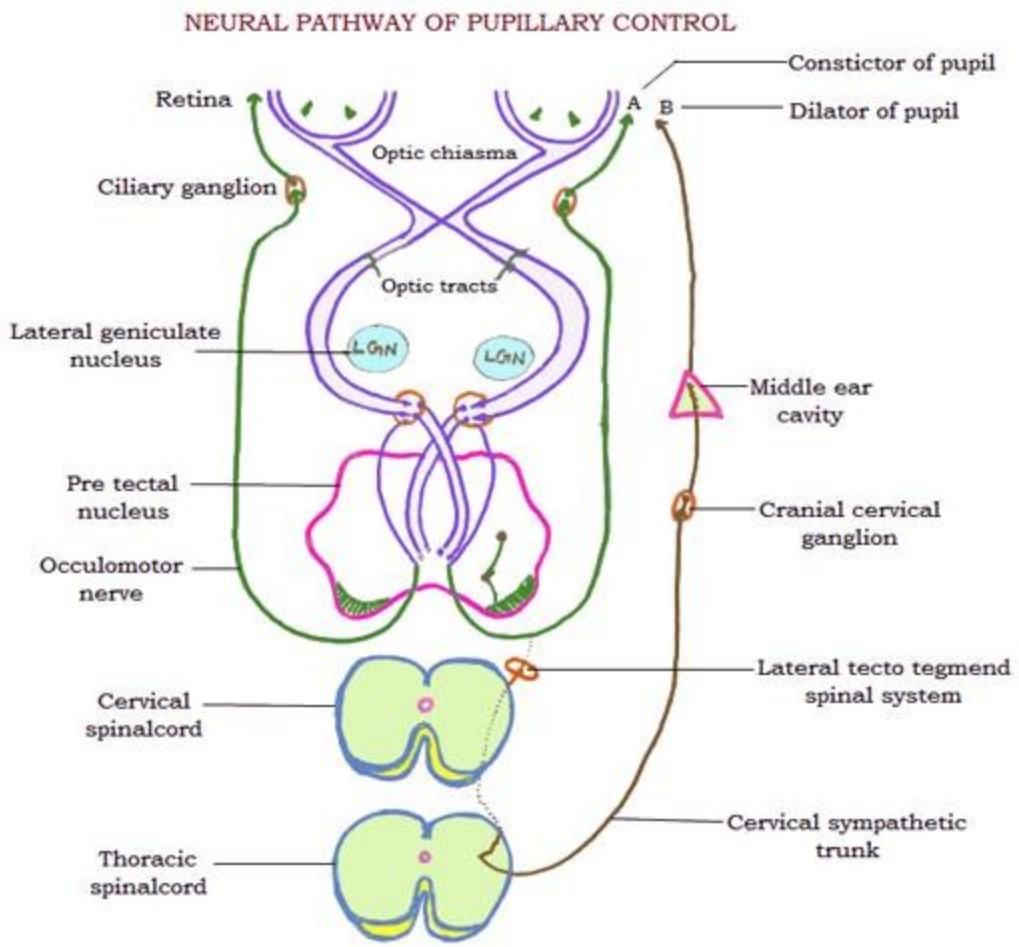
REFLEX ACTIVITIES OF BRAIN STEM

- Brain stem exhibits reflex activities.

Light reflexes - Pupillary light reflex

- When light strikes the retina of either eye both the pupils constrict to reduce the amount of light passing through the pupil.
- Receptor organ is retina
- Sensory fibres pass via optic nerve that terminate in the pre tectal nucleus.
- This nucleus lie between the mid brain and thalamus.
- The fibre synapse with internuncial neurons of the pre tectal nucleus from here the fibre project to occulomotor nuclei to cause excitatory post synaptic potential.

- The induced stimulus on occulomotor nerve causes generation of action potential in the circular smooth muscles of the iris-effector organ.
- Pupillary construction is the effect produces by this reflex.



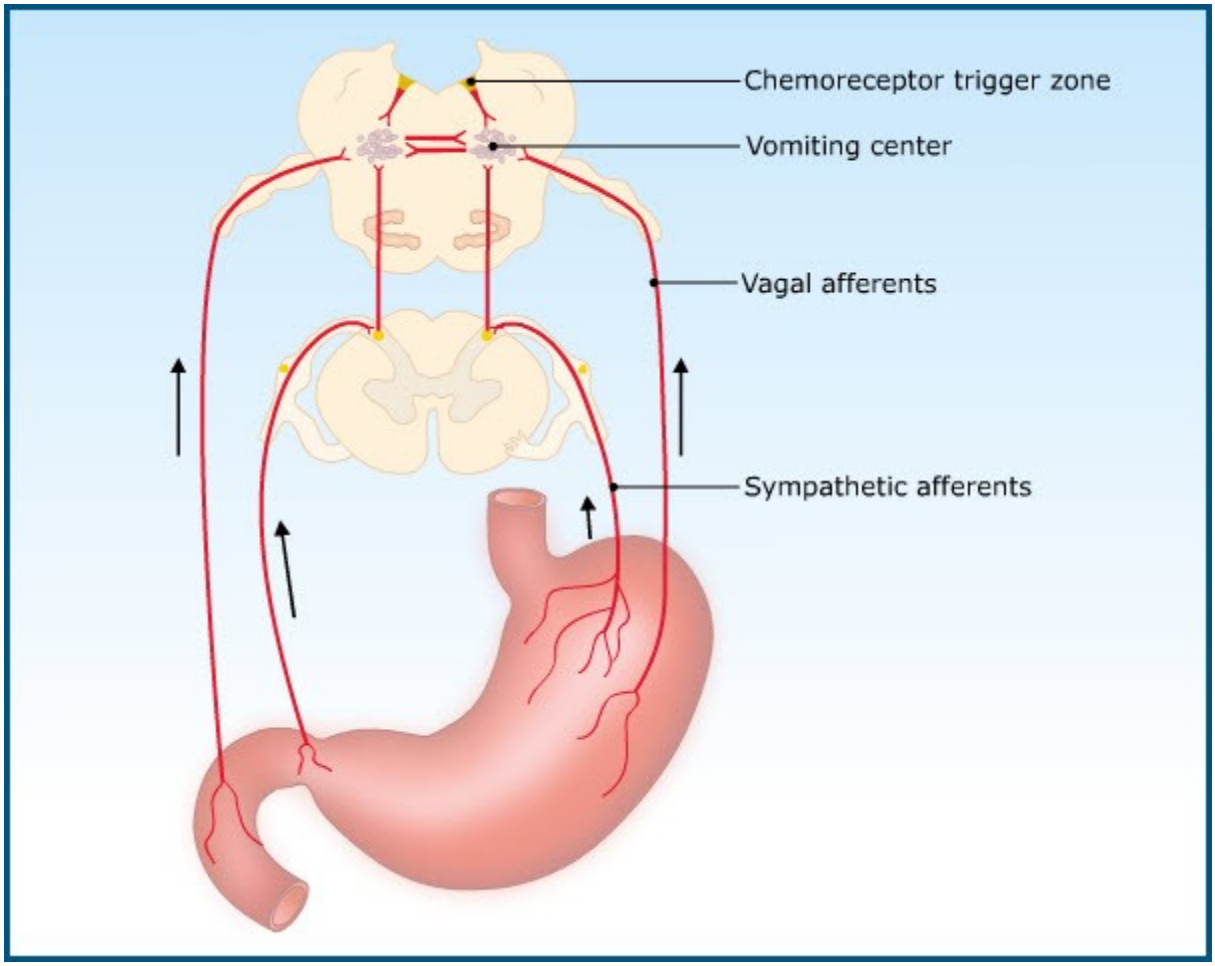
Corneal reflexes

- Corneal blink reflex
  - It is a protective reflex preserving cornea from injurious foreign material.
  - Receptor organ is the cornea.
  - Sensory fibres passes via opthalmic division of trigeminal nerve.
  - It involves internuncial neurons located within the BSRF.
  - Motor neurons are the alpha motor neurons of the facial nucleus that supply muscles of orbicularis oculi, that cause closure of the eyelid.
  - In most occasion blink reflex is acccompanied with lacrimation reflex.
  - If not associated with lacrimation it is known as palpebral blink reflex.
- Lacrimation reflex
  - It is a protective reflex preserving cornea from drying and preserves vision.
  - Afferent fibres or through opthalmic division of trigeminal nerve.
  - Internuncial neurons are involved.
  - Cell bodies are located within the reticular formation of the brain stem.
  - The efferent neurons comprise a portion of rostral salivatiry nucleus.
  - These neurons are parasympathetic pre ganglionic fibres to the lacrimnal gland.
  - The efferent fibres pass via facial nerve from BSRF joint to the petrosal nerve.

- At this point the synapse with pterygopalantine ganglian.
- From here fibres are projected to lacrimnal gland
- This reflex modify the rate of lacrimal flow and aids the removal of foreign material from the surface of the cornea.

EMETIC REFLEX

Emesis is the regurgitation of materials from stomach and upper intestine through oesophagus to oral cavity.



- This reflex is initiated by irritating stimuli from vicera.(pharynx, stomach, duodenum, heart, uterus) or from external auditory canal.
- Protective mechanism to remove the irritating stimuli.
- Motion sickness results due to irritation of the vestibular receptor organs. This particular event involves the participation of flocculonodular lobe of cerebellum.
- This reflex is preceded by salivation & swallowing.
- The nerves of afferent limbs are glossopharyngeal, vagus or vestibular and visceral afferent of the spinal cord (for abdominal/pelvic visceral).
- Emetic center is located in the caudal medulla.
- Cells present in chemo receptor triggerzone of medulla can also initiate emesis on stimulation by specific chemical (apomorphine, ergot alkolids morphine, glycosides or metobolites of systemic acidosis, alkolosis, uremia)
- The central neural mechanism of efferent limb includes nerves supplying to
  - Smooth muscles of G.I tract.

    - Skeletal muscle of larynx, pharynx, thorax, abdominal wall.
- Effernt nerve of emeticreflex causes closure of glottis with inhibition of inspiration; These together produce negative pressure in the intrathoracic and oesophagus.
- Relaxation of cardia, fundus, body of the stomach and oesophagogastric cardiac sphincter prior to act of vomiting.
- Followed by forceful contraction of the abdominal muscle.
- This result in movement of content of stomach to oesophagus.
- Closure of nasopharynx prevents the entry of contents to respiratory organs.
- Powerful antiperistalsis with negative I/oesophageal pressure expels the content to oral cavity.
- Creation of negative pressure by forceful inspiration against closed glottis and strong abdominal muscle contraction is important than antiperistalsis.
- Relaxation of pyloris allow contents from duodenum to oesophagus and then to oral cavity.
- Efferent fibers also reaches salivatory nucleus to initiate salivation before emesis to prevent oral mucosa from acid contents.
- Fibers project to respiratory and cardiac centre to modify appropriately the B.P and the rate of respiration.

SUCKLING REFLEX

- More prominant in newborn animals to fecilitate withdrawal of milk from teat canal and mammary gland while feeding.
- Suckling is a physiological process involving coordinated synchronus movement of tongue and buccal musculature.
- It is termed as a reflex since it involves set pattern of neuronal inputs to complete this action.
- Afferent fibers pass through trigeminal and facial nerve.
- Involves internuncial neurons located within the brain stem reticular formation.
- Motor fibres with orders to the specific muscles reach via hypoglassol, facial and branch of trigeminal that is involved in mastication.
- This reflex is initiated by creating a vaccum which is assisted by withdrawal of tounge from the heart palate.
- The creation of partial vaccum within the oral cavity help to withdraw milk from the mammary gland.
- This reflex is always associated with reflex closure of reticular groove of the young animal to direct the flow of milk into the omasum and abomasum.

SALIVATORY REFLEX

- Protective reflex preventing oral mucosa from drying.
- Elicited when oral and lingual mucosa is stimulated by foreign substances.
- Afferent fibres pass via trigeminal, facial, glossopharyngeal and vagus.
- These fibres end in brain stem reticular formation by synapsing with intenuncial neurons.
- Efferent fibres reach salivary glands depend upon primary stimuli via different routes.
- They arise from neurons of rostral and caudal salivatory nuclei.
- Fibres via facial nerve reaches mandibular and lingual salivary gland.
- Parotid secretion is increased by way of glossopharyngeal motor fibres.
- Feeding and presence of food in the oral cavity influences through this reflex mechanism ends in production of mucinous saliva from sublingual, sub maxillary, pharyngeal and labial glands to facilitate swallowing.

- Noxius when consumed end up in copious flow of serous saliva so as to wash away them without being injested or they are diluted by the saliva from parotid, inferior molar, buccal and phalangial gland as a protective mechanism.
- Salivatory reflexes is initiated by many difference stimuli ans is potentiated by olfactory, gustatory, auditory and visual mechanism.

SWALLOWING REFLEX

- Swallowing centre is located in the brain stem (medulla oblongata)
- Stimulation of the receptors in the soft palate, pharynx (posterior wall) and epiglottis (dorsal surface) by food material initiate this reflex.
- It is a complex multi synaptic reflex involving pharyngeal and oesophageal stage.
- Sensory fibres pass through trigeminal, glossopharyngeal and vagus nerve.
- This reflex involves internuncial neurons.
- Efferent fibres emerge through glossopharyngeal, vagus and hypoglossal nerves which supply to the muscles of myohyoid and hypoglossal.
- The muscles press the tounge against hard palate.
- This causes the tounge to draw backward with the elevation of soft palate.
- Now the tounge forces the bolus into opened oesophagus.
- Opening of the oesophagus is by the pulling action of hyoid bone and layrnx.
- As it happens the epiglottis closes so as to shut the layrnx.
- Swallowing centre also activate through its efferent limb the neighbouring neurons that control respiration.
- This interupts respiration during swallowing as a preventive measure to avoid aspiration of food particles into respiratory passage.

MASTICATION REFLEX

- Reflex activity under the control of brain stem.
- Mastication is basically voluntary but usually takes place involuntarily.
- Mastication reflex or chewing reflex is by the rhythmic movement of the mandible.
- Lowering of the mandible due to the extension of the tongue is known as linguo mandibular reflex.
- Stimuli for masticatory reflex is the presence of food in the oral cavity
- Receptors in the tongue and oral mucosa initiate mastication by the sense of food.
- Sensory impulses are carried via trigeminal, facial and glossopharyngeal nerves to brain stem.
- Motor orders reach masticatory muscles via trigeminal nerve
- This inturn causes rhythmic movement of mandible in relation to the maxilla.
- This results in shearing and crushing a food.
- The main masticatory muscles supplied by trigeminal nerve include Temporalis with assistants from Massetor muscle for shearing and Massetor with assistants from Pterygoid muscles for grinding.

COUGH REFLEX

- It is a protective reflex to remove thr irritant from the respiratory tract.
- Receptor for this reflex is from respiratory tract.
- Irritation of any part of the respiratory tract serve as sensory impulse.
- Vagus is the sensory nerve to endup in BSRF via Fasciculus solitarius nucleus.
- Efferent nerve via vagus project to respiratory centre and laryngeal muscle to effect cough.

SNEEZE REFLEX

- It is a protective reflex to remove the irritant stimuli.
- Receptors are present in the upper respiratory pathway.
- Sensory information passes via trigeminal to the BSRF.
- The efferent via vagus, trigeminal and facial effect sneezing.

MICTURITION REFLEX

- Micturition is the complex phenomenon involves initiation from stretch receptors in the bladder wall.
- Axons have their cell bodies located in the sacral spinal ganglia and dorsal grey column of the spinal sacral segments.
- Stretching of the bladder stimulate the sensory fibres which in turn causes the generation of action potential that passes via spinal nerves to the spinal cord.
- They may employ sacral inter neurons prior to terminate in the higher centre or travel straight to end in the higher centre.
- If sacral inter neurons are involved, spinal cord completes the reflex arc by synapsing with pre ganglionic parasympathetic neurons.
- These parasympathetic system causes contraction of smooth muscles of urinary bladder.
- There is involvement of sympathetic system and is evident in the early stages of filling of the bladder by activating beta adrenergic preganglionic sympathetic neurons by the synapsing of interneurons. These fibres inhibit smooth muscle contraction allowing still more stretching to hold the urine.
- Spino thalamic tract from spinal segments at the level of bladder can also serve as a afferent fibers to end in fasciculus gracilis of medulla where they synapse in the nucleus gracilis. These fibers pass via thalamus and reach somesthetic cortex to cause conscious perception of bladder sensation.
- Stimulation of cell bodies in pelvic plexus especially in bladder wall via axons of post ganglionic para sympathetic system causes contraction of detrusor muscle and relaxes the striated sphincter of the bladder.
- This in turn causes evacuation of urine from bladder and allows the flow via urethra.
- Sympathetic activation via alpha receptor system potentiate contraction and smooth muscle tone of the bladder allows urine output.
- Involvement of brain stem via tecto spinal and reticulo spinal tract results in voluntary micturition.

ROLE OF RETICULAR FORMATION

- Ascending projections to the BSRF to cortex involves in maintenance of cortical excitability and consciousness.
- Wakefulness depend on an adequate impulse from BSRF through the *Ascending Reticular Activating System(ARAS) and Diffuse Thalamo Cortical Projection System(DTPS)*
- Neuro humoral theory suggests the involvement of noradrenaline and serotonin in sleep-wakefulness rhythm.
- Noradrenaline from nerve endings of medullary cells have positive influence on ARAS and maintain wakefulness. It also responsive for phasic events of sleep like rapid eye movement(REM).
- Serotonin produced by the midbrain raphe nucleus is a depressant acting on the BSRF and diminishes the ascending reticular drive, ultimately end up in sleep.
- Acetyl choline balances the action of NE and serotonin in sleep – wakefulness rhythm.
- Melatonin- pineal hormone causes sleep and act as a trigger switching the reticular system to act through other neurotransmitter .

SLEEP

- It is a state of reversible unconsciousness and relative immobility of an animal.
- It is due to temporary inhibition of the reticular activation system of the ascending reticular formation, which in turn reduces the normal excitability of the cortex.
- Sleep centres are located in the pons and medulla known as raphe nuclei. The nerve fibres of this area secrete serotonin. These nuclei send fibres to reticular formation, upward to thalamus, neocortex, hypothalamus and many areas of the limbic cortex. Fibres extend downward to spinal cord where they inhibit the incoming pain signals. The raphe nuclei provide inhibitory signals to the ascending reticular activation system (ARAS) and thereby induce sleep.
- Diffused Thalamic Projection System, (DTPS), the sleep-inducing centre is present in the thalamic reticular area, projects its ascending fibres to cortex and descending fibres to reticular formation. DTPS regulates cortical activity and is antagonistic to ARAS.
  Based upon the period of rest and activity, the animals may be classified as
  - *Monophasic animals:* Have prolonged period of rest during night and are active during daytime (Man, birds).
  - *Polyphasic animals:* Show several alternate periods of rest and activity (wild animals)
  - *Intermediate type:* Has alternate periods of rest and activity during daytime followed by brief period of rest at night (domestic animals).

Changes during sleep

- Decrease in sensitivity and responsiveness of the individual to environmental stimuli.
- Reduction in metabolic processes.
- Fall in body temperature and BMR.
- Decrease in heart rate, B.P and respiratory rate.
- Decrease in alimentary secretions and motility.
- Pupillary constriction
- Decrease in muscle tone.

Endocrine secretions

- Decrease in corticoids
- Episodic increase in GH, melatonin and testosterone.

Theories of sleep

- Sleep is due to depression of the cortical centre by acid metabolites accumulated during active periods.
- Increased physical efforts during active hours demand increased skeletal blood flow and relative cerebral ischemia which inhibits brain function.
- Sleep producing substance in the brain is stimulated follwing ischemia.
- Cortical excitation and cortical inhibition rhythmically alternate with each other, conditioned to an environmental cue (day, light/ darkness) internal signals. This rhythm brings about the sleep wakefulness cycle.
- Hence sleep is defined as rhythmic phenomenon which involves the entire cortical excitability.
- **Sleep centre- anterior hypothalamus - trop hotrophic area**
- **Waking centre- posterior hypothalamus - ergotrophic area**

PHASES OF SLEEP

- Two distinct phases alternates with each other.
  - Slow wave sleep or orthodox or NREM sleep: 70% of sleep period

    - REM sleep or paradoxical sleep- interprets the slow wave sleep given by RES
- During **slow wave sleep, EEG records characteristically slow, synchronized theta waves and delta waves**. Muscle tone and responsiveness to stimuli are decreased.

ELECTRO ENCEPHALO GRAM

- It is the graphic record of electrical activity of the brain recorded from the surface.
- Technique is known as Electro Encephalography
- It is the recording of the potential difference as rhythm (frequency) and magnitude.
- Rhythm of the EEG are designated as alpha, beta, theta and delta rhythm

Alpha rhythm

Frequency	Amplitude	Characteristics
8-13 cycles/sec	50-100 mv	Seen in subject when awake relaxed state and closed eyes.

- Replaced by faster wave <---- alpha blocking <----> when respond to stimuli and wave disappear (Not responding to any stimuli)
- Alpha rhythm represents state of relaxed wakefulness of reflex the optimal state of brain excitability namely synchronized rhythm.

Beta rhythm

Frequency	Amplitude	Characteristics
More than 20-30 cycles/sec	25-50mv	Seen in alert cortex wakefulness and responding to a stimulus knowns as desynchronized rhythm.

Theta rhythm (slow rhythm)

Frequency	Amplitude	Characteristics
37 cycles/sec	50-100 mv	dominant in wakefuness is young subjects.

		seen in early stages of slow wave sleep from hippocampus.

Delta rhythm

Frequency	Amplitude	Characteristics
Less than 3 cycles/sec	High amplitude < 100 mv	stages of slow wave sleep

- Lamda wave - have high amplitude (from fronto-temporal regions)
- Mu waves - from motor cortical areas
- Spike and wave pattern: indicates abnormal electrical activty of neurons seen in epileptic cases.

Mechanism of EEG

- Wave pattern is due to the Oscillation of alternating excitatory and inhibitory post synaptic potentials produced by impulses of non-specific thalamic nuclei.
- Frequency of the rhythm is by the activity of non-specific thalamic nuclei.
- At low intrinsic frequencies (8-13 cycles/sec) the EPSP's are summated & give rise to low frequency synchronised EEG rhythm (alpha).
- When thalamic neurons are driven by the reticular activating system, the frequency becomes too high for summation and becomes desynchronized to become fast EEG rhythm – beta rhythm results.
- Normal ECG
    - 8-13 cycles/sec - alpha wave
    - 20-30 cycles/sec - beta wave
    - 3-7cycles/sec - theta wave
    - Less than 3 cycles/sec - delta wave

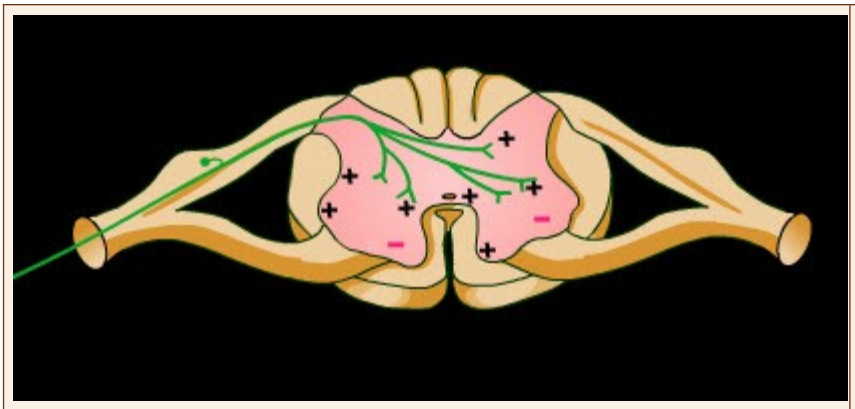
EEG and sleep stages

- EEG studies help in understanding the different stages of sleep Each stage of sleep manifest different wave pattern in EEG. 4 stages of slow wave sleep can be distinguished with different wave pattern, frequency and amplitude.

Drowsiness

- In the relaxed awake state alpha waves predominant 1st stage of slow wave sleep is characterised by fluctuations between alpha wave and low amplitude wave (3-7 cycles/sec) .
- As sleep deepens into stage 2 wave pattern changes.
- In stage 3 and 4 EEG shows gamma waves (less than 3 cycles/sec) .
- In REM sleep low voltage fast waves are seen.

MODULE-9: SPINAL CORD



LEARNING OBJECTIVES

This module explores,

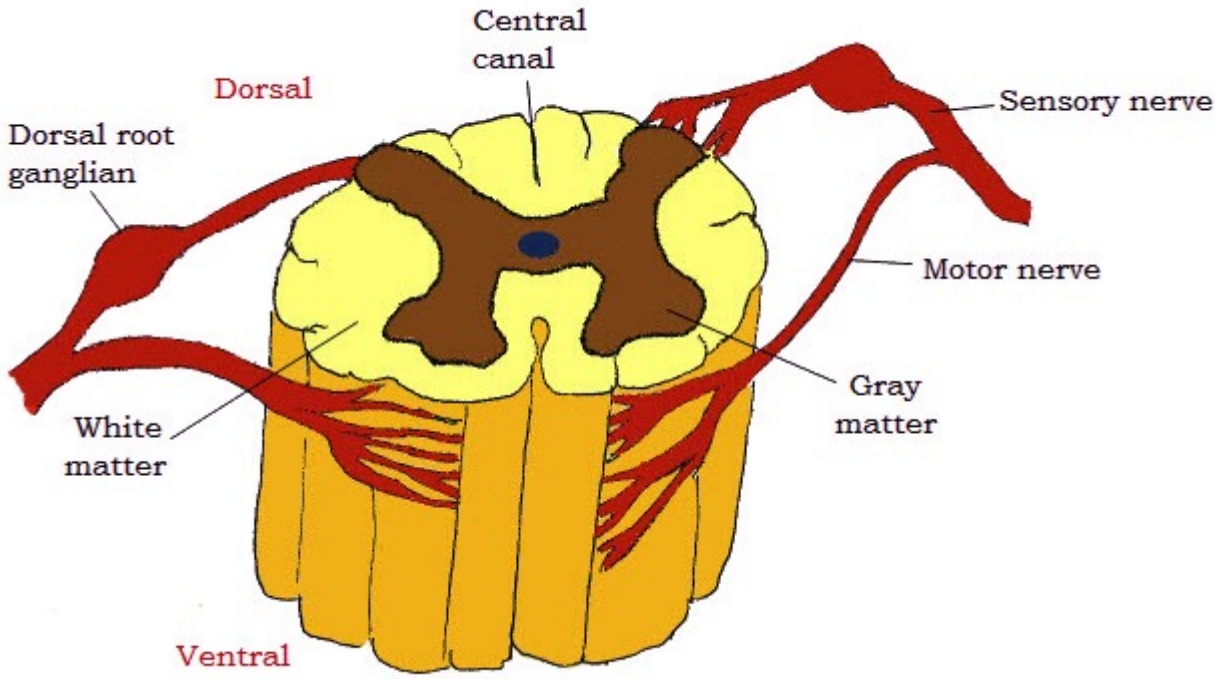
- the structure and organization of the spinal cord,its nuclei ,tracts and their functions and
- the understanding of involvement of higher nervous system to complete the prescribed action.

SPINAL CORD - AN INTRODUCTION

- It is a caudal extension of the medulla oblongata present throughout the length of the vertebral canal. Each spinal segment provides a pair of spinal nerves that are formed by the fusion of dorsal root (sensory) fibres and the ventral root (motor) fibres.

STRUCTURE OF SPINAL CORD

- Cylindrical
- Extends from medulla oblongata at level of atlas for varying distances down the spinal cord



- Divided into many parts : Sensory fibers enter the spinal cord by dorsal roots of spinal nerves along the dorsolateral sulcus and motor fibers leave the spinal cord by way of the ventral roots of spinal nerves along the ventrolateral sulcus
- This arrangement divides the spinal cord into 4 compartments
- Cellular components are distributed primarily within the center of the cord where they form an H shaped column of cells called Gray matter.
    - The grey matter has two types of multipolar neurons called the root cells, and the tract cells.
    - The motor neurons are the principle component of the root cells, whereas the interneurons or the fusiform neurons form the tract cells.
- Nerve fibers are found predominantly outside of the gray matter where they form the white matter of the cord.
- The white matter is divided into components : paired dorsal funiculi (funiculus = a bundle of nerve fibers) , two lateral funiculi and paired ventral funiculi
- The paired dorsal fasciculi are separated by a dorsal median septum and the ventral fasciculi are separated by a ventral median fissure
- Size and shape of the spinal cord vary at different lengths
- Two distinct spinal cord enlargements are seen in domestic animals : a cervical enlargement which serve the pectoral limbs and a lumbar enlargement which serve the pelvic limbs
- Spinal cord and the vertebral column grow at the same rate during fetal life but the vertebral column grows faster in the post natal life
- This causes the spinal cord to be pulled forwards in the vertebral column.
- Spinal cord extends for different lengths along the vertebral column in different species

- Stretching out of spinal nerves arising from the caudal portion of the spinal cord forms the cauda equina
- Spinal cord is organized into segments each of which is associated with a single spinal nerve
- There are as many spinal cord segments as there are spinal nerves, But the spinal nerves and spinal cord segments do not actually correspond in adults due to differential growth. The relationship however is necessary in determining the locations of pathological processes in the spinal cord.

GRAY MATTER

Two types of cells

- Motor neurons
- Internuncial neurons

Motor neurons

- It project their axons into the PNS
- They are of 3 types
    - *Somatic or Alpha motor neurons* – supplying skeletal muscles
    - *Autonomic neurons* – supplying visceral organs
    - *Intrafusal or Gamma motor neurons* – supplying special receptors called muscle spindles
        - Somatic or Alpha motor neurons show Nissel substance in their cytoplasm
        - Internuncial neuron processes remain within the confines of the CNS
        - They vary considerably in their shape, size , organization
        - Two classes according to the course of their projection of their fibers within the nervous system
        - Commissural Internuncial neurons whose fibers cross the midline
        - Non Commissural Internuncial neurons or association neurons whose fibers do not cross the mid line
        - Association neurons are called so because by their connections they correlate activities within various portions of the nervous system
        - Gray matter of the spinal cord is divided into many nuclei on anatomical basis
        - Many portions of the CNS are said to composed of cell laminae which are groups of similar cells arranged together in a particular order

INTERNUNCIAL NEURONS

- Classified into 2 types based on their synaptic capacity :
    - *Excitatory Internuncial Neurons* – exert a depolarizing influence on the postsynaptic with which they have contact
    - *Inhibitory Internuncial Neurons* – exert hyper polarizing influence on the neurons with which they have contact

- With the production of presynaptic inhibition, Internuncial Neuron produces inhibition by depolarizing the presynaptic terminals of other neurons.
- The presence of two types of Internuncial neurons ensure that activity and signaling inside the spinal cord remain flexible
- Reciprocal innervation
    - A phenomenon exhibited by afferent nerves to the spinal cord on somatic efferent nerve activities
    - When motor neurons supplying a skeletal muscle are depolarized by excitatory interneurons or by dorsal root afferents, the motor neurons supplying muscles that are antagonistic to this muscle are hyperpolarized by inhibitory interneurons.
    - All voluntary motor activity is made meaningful because of this integration by inhibitory and excitatory interneurons
- Interneurons are classified based on their pattern of convergence into 5 basic groups
- They can have one or two or three muscle groups projecting muscle spindle fibers to them
- One synergistic muscle group :
- Some of these are excited by exteroceptive afferent sources especially from the foot pads or hair in between the toes
- Two different muscle groups : Usually antagonists acting on the same joint
- Or they may be synergists acting at neighboring

joints
- Or antagonists acting at neighboring joints
- Few are influenced by sensory information from the skin (cutaneous afferents)
- Three muscle groups are also seen
- Interneurons form the system that is within the spinal cord
- Interneurons are capable of prolonged rapid discharge of action potentials following afferent stimulation
- Interneurons play an important role as convergence systems for sensory (afferent) fibers of sensory modalities
- The convergence systems are not necessarily anatomical but rather are ones that are active at that time
- Spinal reflexes usually involve interneurons except some autonomic reflex arcs through the spinal cord and the myotatic reflex
- The corticospinal, rubrospinal, vestibulospinal, tectospinal, interstitiospinal and reticulospinal motor pathways for somatic and autonomous controls exert their influence through these interneurons
- Many interneurons are organized to perform specific functions
- Alpha motor neurons give rise to large fibers which innervate skeletal muscle
- These fibers also give rise to collateral branches which reenter spinal gray matter to synapse upon inhibitory interneurons
- These Internuncial neurons are called Renshaw cells

- They control the duration, intensity and distribution for motor neuron discharge
- Thus they function in localization of reflex motor activity
- Disinhibition : The above neurons in certain cases increase the firing of motor neurons inhibitory to the alpha motor neuron
- Discharge of Renshaw cells is inhibited by stimulation of the cutaneous and muscle afferents
- A group of neurons within the nucleus intermedialis and nucleus proprius give rise to the ascending fiber system
- These neurons give rise to ventral and rostral spino cerebellar tracts , the spino cervical tracts, the spino olivary tract and spino reticular tracts

NUCLEI OF SPINAL CORD - SENSORY NUCLEI

- Spinal cord has 9 laminae - sensory nuclei

Nucleus Dorsomarginalis

- Corresponds to lamina I
- Extends the length of the spinal cord
- Covers the dorsal and lateral surfaces of the dorsal horn of the spinal cord
- Cells are spindle shaped
- Neurons receive afferent fibers from the dorsal root fibers and project their axons into dorsal and lateral funiculus from which they may ascend or descend to form inter segmental pathways for intraspinal integration of neural activity
- These fibers form the dorsolateral fasciculus of the propriospinal fiber system.
- It receives the pain and thermal sensation .
- It act as a low threshold mechanoceptors.

Nucleus Substantia Gelatinosa

- Corresponds to laminae II and III of the spinal gray matter
- Cells have small , spheroid or spindle shaped nucleus and little cytoplasm
- They also have a rich dendritic tree
- Axons of these cells turn either dorsally into dorsolateral fasciculus or ventrally. Some turn ventromedially and thereby reach the Substantia Gelatinosa of the other side
- Substantia Gelatinosa is a closed neuronal system because all of its axons turn back and terminate within the nucleus of origin
- Long range connections between different regions a re established over the lateral part and the dorsal part of the lateral propriospinal tract
- These connections may bridge 5 to 7 segments of the spinal cord

- Ipsilateral (same side) short range connections of 2 to 3mm distances are also seen
- Axons originating in the Substantia Gelatinosa are always traced back to the Substantia Gelatinosa of the ipsilateral or contralateral side
- The Substantia Gelatinosa has its outlet in the large cells that occupy the underlying lamina IV and project dendrites into the nucleus Substantia Gelatinosa.
- It forms a chief association centre for pain, thermal, tactile sensory perception mediatory reflexes.

Nucleus Proprius

- Forms the nuclear column that extends the length of the spinal cord and comprises lamina IV and lamina V
- This nucleus serves as a origin of both crossed and uncrossed ascending tracts
- The lateral portion of nucleus proprius is referred to as the reticular formation of the spinal cord.
- It acts as a sensory pathway for light cutaneous mechanical stimulations (tactile, pain and thermal perception) and also from the Golgi tendon organ.

Nucleus dorsalis

- Extension is limited to the thoracic and upper lumbar levels of the spinal cord
- Occupies a medial portion of lamina VII
- In cat the nucleus begins at the most cranial thoracic segments of the spinal cord
- Cells of dorsal nucleus gives rise to ipsilateral dorsal spinocerebellar tract which terminates in the vermis of the cerebellum
- This system has proprioceptive functions related to Golgi tendon organ and muscle spindle activity
- The system also has two sub divisions activated exclusively by afferents from cutaneous receptors :
- One informs the CNS about pressure on foot pads
- The other has neurons activated by light touch , pressure and pinching of cutaneous areas
- An additional dorsal spinocerebellar tract subdivision which is neither exteroceptive nor proprioceptive is seen. These are activated by the flexor reflex afferents
- Proprioceptive cells of the nucleus dorsalis receive afferent information from the class Ia fibers from the muscle spindles and from class Ib of the Golgi tendon organs of skeletal muscles
- A given neuron receives inhibitory influences mediated by group I afferents from both synergistic and antagonistic muscles
- Synapses upon the cells of the dorsal nucleus by group Ia afferent fibers from muscle spindles are large compared to the synapses of group Ia fibers with alpha motor neurons
- Though these synapses use the same neurotransmitter according to Dale's principle , they have widely varied effects
- Synaptic activity upon the dorsal nucleus requires less summation to discharge to discharge action potential
- One bouton gives rise to a small series of action potential because of larger amount of transmitter agent released per action potential in the pre synaptic fiber or less diffusion of transmitter agent away from the reactive site
- Both alpha motor neurons and neurons of dorsal nucleus exhibit long positive after-potentials
- Discharge rate of alpha motor neurons as about 200 impulses per second and that of the dorsal nucleus neurons about 700 impulses per second
- Action potential is brief – about 0.5 to 0.75 msec
- Repetitive firing of neurons of the nucleus dorsalis is important in CNS function.

- In primates it extends from the upper lumbar to lower cervical spinal cord, while in other animals it extends from upper lumbar to lower thoracic levels.
- It receives the input signals from the muscle spindle through the dorsal root ganglion of the spinal cord, caudal to T1 spinal segment.

Nucleus Intermedialis and Nucleus intermediolateralis

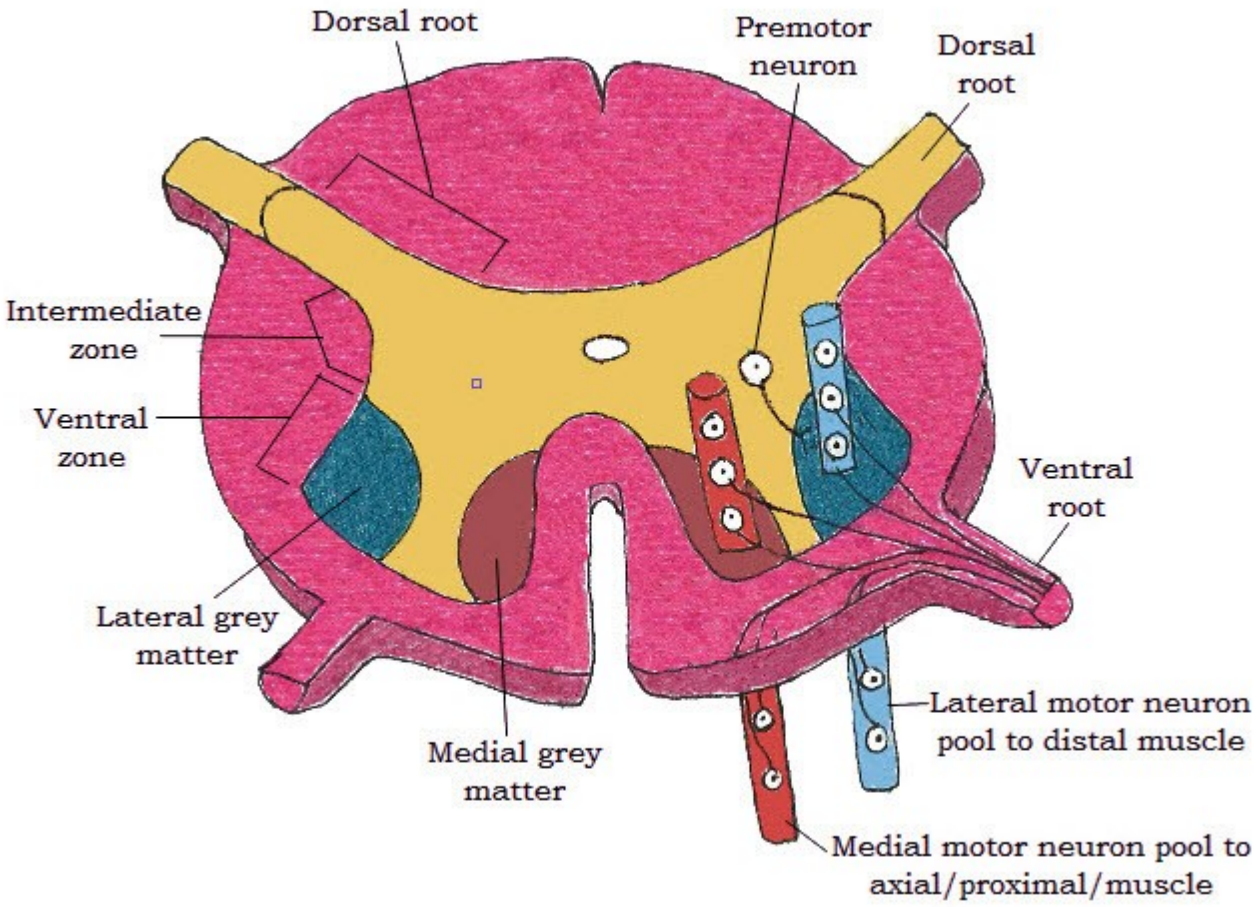
- It receives the sensory signals from Golgi tendon organs up to cervical level in primates and up to thoracic level in other animals.
- It also senses tactile, thermal and pain sensations along with nucleus proprius.

NUCLEI OF SPINAL CORD - MOTOR NUCLEI

These nuclei are placed in the medial, lateral and intermediolateral columns of the spinal grey matter and controls somatic and visceral motor activities. They include

- Medial motor nuclei
  - Extend throughout the length in the medial motor column of the spinal grey matter and controls the motor functions of skeletal muscles.
- Lateral motor nuclei
  - This group of nuclei is placed in lateral motor column of the spinal grey matter and they extend the entire length of the spinal cord. They control the motor functions of the muscles in forearm, hind limb, shoulder, hip and lateral portions of the trunk.
- Intermediolateral nuclei
  - They are located in the inter-mediolateral column of the spinal grey matter from first thoracic to third lumbar spinal segments that form the pre ganglionic sympathetic fibres which control the motor activities in the visceral organs.

SPINAL CORD - MOTOR NEURONS



- Large motor neurons (alpha motor neurons) supply extrafusal muscles and small motor neurons (gamma motor neurons) supply either extrafusal or intrafusal muscle spindles
- Motor nuclei are placed somatotropically – laterally located cells supply distal extremity muscles and medially placed ones supply muscles of upper limb and trunk
- The cells of the motor neurons are excited monosynaptically by group Ia afferent fibers from muscle spindle receptors
- Multisynaptic activation or inhibition occurs by means of internuncial neurons of gray matter.

WHITE MATTER

- It forms the tract systems of the spinal cord containing myelinated nerves, and they transmit sensory impulses through ascending tracts and the motor impulses through the descending tracts between the spinal cord and the higher centres of the brain.
- The white matter is divided into paired dorsal funiculi, ventral funiculi and two lateral funiculi
    - Ascending (Sensory) tracts of spinal cord
    - Dorsal funiculus
        - Is composed of two ascending fiber tracts

- These terminate in the medulla oblongata
- The fasciculus gracilis terminates on the nucleus gracilis of the medulla
- The fasciculus cuneatus terminates on the nucleus cuneatus and nucleus cuneatus lateralis of the medulla
- But many of the fibers of the Dorsal funiculus terminate in the gray matter of the spinal cord before the rest enter the medulla
- These fibers support intersegmental reflex activity and a portion them terminate on the cells of the nucleus proprius , nucleus dorsalis and nucleus intermedialis, and these further give rise to another system that ascends like the spinocerebellar, spinobulbar and spinothalamic tracts
- The fasciculus gracilis and fasciculus cuneatus are also arranged somatotropically
- Ascending fibers from the coccygeal, sacral, lumbar and thoracic levels comprise the fasciculus gracilis
- Fibers from the cervical and upper cervical (T1) comprise the fasciculus cuneatus
- As these fibers represent sensory information , the ipsilateral surface of the body is represented topographically within the dorsal funiculus
- The fibers of the Dorsal funiculus convey impulses from joint receptors, muscle spindle and golgi tendon organ, cutaneous receptors for tactile and pressure sensations and so relay sensations related to joint movement and position.
- Fibers from joint afferents and skin afferents terminate in the spinal cord for reflex mechanisms or within the nucleus gracilis and nucleus cuneatus of medulla for relay to thalamus and then cortex.

LATERAL FUNICULUS OF SPINAL CORD

- Ascending fiber tracts of lateral and ventral funiculi.
- These are not as clearly seen as that of the dorsal funiculus.
- It contains the following spinal tracts
  - Dorsal spino cerebellar tract
  - Ventral spino cerebellar tract
  - Rostral spino cerebellar tract
  - Spino cervical tract
  - Spinothalamic tract (Ventral and Lateral)
  - Spino-olivary tract
  - Spino reticular tract
  - Spino vestibular tract
  - Spino tectal tract

DORSAL SPINOCEREBELLAR TRACT

- Occupies a portion of the lateral funiculus between the lumbar vertebrae and medulla
- This fiber tract originates from the ipsilateral dorsal nucleus and ends within the ipsilateral cerebellar cortex
- The fibers terminate in two regions of the cerebellar cortex.
- Conduction velocity of these fibers range from 30 to 110 m /sec.
- It carries afferent impulses from muscle spindle through dorsal root ganglion of the spinal cord and project to cerebellar cortex.

VENTRAL SPINOCEREBELLAR TRACT

- Arises from the cells occupying the lateral part of nucleus proprius and nucleus intermedialis
- This tract is not excited by afferents from the forelimbs
- The axons are mostly contralateral
- The tract reaches the cerebellum exclusively by brachium conjunctivum
- Most terminate contralaterally which make them ipsilateral to their origin
- Conduction velocity of these fibers range from 70 to 120 m /sec
- The tract contains afferent fibers of both exteroceptive and proprioceptive systems (Golgi tendon mostly) .

ROSTRAL SPINOCEREBELLAR TRACT

- Forearm equivalent of Ventral spinocerebellar tract
- Activated from ipsilateral forelimb nerves and uncrossed
- The tract reaches the cerebellum through the restiform body and the bracium conjunctivum
- The tract is activated monosynaptically by Golgi tendon organ afferents and polysynaptically by flexor reflex afferents

SPINOCERVICAL TRACT

- The tract arises from the nucleus intermedialis
- The tract terminates in the lateral cervical nucleus from where it is relayed to the ventero – postero-lateral nucleus of the thalamus
- Mostly involved with tactile afferents.

SPINOTHALAMIC TRACT

- The lateral and ventral Spinothalamic tracts which are present in primates, are absent in domestic animals.
- Instead these exist as a single tract concerned with tactile , thermal and pain sensations.
- The fibers project through the lateral lemniscus of the brain stem to the ventro – postero-lateral nucleus of the thalamus.
- The fibers also project through the reticular formation and central tegmental fasciculus to the intralaminar nuclei and the nucleus medialis dorsalis of the thalamus.
- In primates, the fiber system is very important for the relay of pain sensations but in domestic animals transection of this tract does not affect pin perception because pain perception continues due to the diffuseness of the propriospinal fiber which crosses and re crosses.
- Hence unilateral hemisection of the spinal cord in primate alleviates pain from contralateral lower extremity. This is not seen in domestic animals.
- Spinothalamic tracts arise from cells located in the dorsal horn in the region of the nucleus proprius of the spinal cord.

SPINO OLIVARY TRACT

- Arise from cells of the nucleus proprius of the spinal cord.
- The tract terminates in the caudal olivary complex of the medulla (medial and dorsal accessory olivary nuclei).
- This forms another pathway to the cerebellum for exteroceptive and proprioceptive afferents.
- Action potentials reach the cerebellar cortex ipsilateral to their origin within the peripheral nerves.

- This tract is important in informing the cerebellum of the position of the limbs and the external environment.

SPINO RETICULAR TRACT

- Arise bilaterally from all levels of the spinal cord.
- Terminate within many portions of the nuclei of the Brain stem reticular formation. These nuclei all receive afferents from the spinal cord.
- *Nucleus lateralis reticularis:* Projects fibers ipsilateral to cerebellar cortex
- *Nucleus reticularis paramedianus:* Projects fibers both ipsilateral and contralateral to cerebellar cortex. This forms another spino reticular cerebellar pathway
- *Roller nucleus and Nucleus intrafascicularis:* Project fibers ipsilateral to cerebellar cortex and forms a third spino reticular cerebellar pathway
- *Nucleus reticularis tegmenti pontis:* Forms a fourth spino reticular cerebellar pathway

Functions

- Important in many facets of normal activity.
- Carry sensory information from the skin and deep tissues and play an important role in the regulation of somatic and visceral motor activity.
- In maintenance of consciousness and perception .
- Accommodation of motor activities occur if this is transected bilaterally in domestic animals.
- Relay ascending activity to higher centers of the brain.
- Significant in pain perception.
- Modify respiration by terminating some of the fibers on nucleus of the pneumotaxic center.
- Control micturition.
- The tract terminates on neurons of the BSRFand serves as a feedback system for control of spinal cord activities.

SPINO VESTIBULAR TRACT

- Fibers ascend ipsilaterally
- Serve as part of a feedback system for the control of activity within the lateral vestibular nucleus and modifies activities within the spinal cord
- Plays an important role in regulating muscle tone

SPINO TECTAL TRACT

- Arise from cells located within the nuclei proprius and nuclei intermedialis of the gray matter.
- They decussate to the contralateral side and project to the cerebellum through rostral colliculi.
- *Function:* Convey tactile and thermal information and the sensation of pain.
- Also modifies activity within the descending tectospinal tract which is important in the control of motor activities of neck muscles.
- Also functions as a part of a multisynaptic pain pathway.
- Descending fiber tracts of the lateral and ventral funiculi.

PYRAMIDAL AND EXTRA PYRAMIDAL SYSTEM

Descending (Motor) tracts of spinal cord

It consist of pyramidal and extra pyramidal system

- Pyramidal system

    - This system controls the voluntary and fine motor movements in association with pyramidal motor cortex.
    - This tract is well developed in primates and carnivores, but absent in birds and reptiles.
    - It consist of cortico spinal tract
- Extra pyramidal system
    - It is a complex network consisting of three important motor nuclei, red nucleus, vestibular nucleus and reticular formation and the inter-connecting tracts passing the motor signals from the motor cortex to the motor neurons of the spinal cord. This system generates *gross involuntary movements* by providing muscle tone of the extensor muscle and thereby regulates posture and locomotion.
    - Cortical activity descending in the extra-pyramidal pathways to the *lateral vestibular nuclei* of the brain stem (strong excitatory for spinal alpha -motor neurons) is primarily inhibitory.
    - This system is constituted by four major descending tracts - the reticulospinal, vestibulospinal, and rubrospinal and tectospinal tracts that leave the brain stem to influence the spinal motor neurons.

CORTICO SPINAL TRACT

- It originates from the pyramidal (Betz) cells of the motor cortex, (60% from primary motor cortex and 40% from somasthetic motor cortex).
- Enter the internal capsule, pass through the cerebral peduncles, form the pyramids at he base of the medulla and then enter the spinal cord.
- In the medullary region, it divides into two unequal portions.It partially decussates before entering the spinal cord so the crossed ventral, uncrossed lateral, uncrossed ventral tracts are also formed.
- 80% of this tract decussate to the opposite side (contralateral) and descends as lateral corticospinal tract, in the lateral funiculus of the spinal cord.
- It extends throughout the length of the spinal cord in primates and carnivores and regulates fine motor control both in the fore and hind limbs by its direct synapse with the spinal alpha motor neurons. While in other animals it synapses with the internuncial neurons, which in turn control, the motor activities of the alpha and the gamma neurons.
- The remaining 20% of the tract descend from the medulla as uncrossed (ipsilateral), forming the ventral corticospinal tract in the ventral funiculus of the spinal cord and descend up to caudal cervical and cranial thoracic spinal segments.
- At this point, it decussates to the opposite side of the spinal cord and synapse with the alpha motor neurons, ventral corticospinal tract is totally absent in dogs.
- Four in number in domestic animals :
    - Crossed lateral
    - Uncrossed lateral
    - Crossed ventral

    - Uncrossed ventral
- All four tracts degenerate in the cervical and thoracic portions of the spinal cord
- The differential termination make them important in various function that can be grouped as :
    - Involving components from the sensory cortex : function primarily to alter activities of ascending sensory systems such as spinocerebellar, spinothalamic, spinotectal and spinoreticular tracts
    - Involving components from the motor cortex: function primarily to alter somatic and sensory motor activities
- There is always one Internuncial neuron between the corticospinal tract fibers and spinal alpha motor neurons
- Thus a high frequency discharge is necessary to overcome synaptic resistance and produce a motor activity
- In ungulates (horse, cow, pig, sheep and goat) the Corticospinal tract terminates upon the Internuncial neurons of the spinal cord. From here it is carried to the thoracic and lumbo sacral levels of through propriospinal systems.
- Primary function is the control of spinal cord reflexes for the elicitation of motor mechanisms in animals
- Produces excitation of alpha motor neurons supplying flexor muscles and inhibition of alpha motor neurons supplying extensor muscles of the limbs
- Also exerts control over the ANS.
- The pyramidal tract is involved in the voluntary motor control of the skeletal muscles.
- The pyramidal system is important in maintaining muscle tone.

RETICULO SPINAL TRACT

- Originate from Pontine and medullary reticular formations.
- Pontine reticular fibres are ipsilateral.
- Medullary reticular fibres descend bilaterally.
- They exert an influence upon the motor neurons (alpha and gamma) of the spinal cord without the involvement of interneurons.
- But the majority use interneurons for their influence upon somatic motor activity
- Visceral functions are mediated by this tract include the control of respiration , micturition, defecaton,cardiovascular alterations and gastrointestinal activity.
- This tract is tonically active and influences lower gamma motor neurons, the gamma loop mechanism mediated by this tract causes reflex contraction in the anti gravity muscle to maintain postural muscle tone

VESTIBULO SPINAL TRACT

- Consists of two descending fiber tracts :
    - Vestibulospinal tract and
    - Medial longitudinal fasciculus.
- Oringinates from the lateral vestibular nucleus and descends ipsilaterally through th length of the spinal cord.
- Medial longitudinal fasciculus fibres terminate monosynaptically upon alpha motor neurons.
- The tract ipsilaterally exerts an excitatory influence upon extensor muscle tone and an inhibitory influence upon flexor muscle tone and contralaterally exerts an inhibitory influence upon extensor muscle tone and an inhibitory influence on flexor muscle tone.

- Also alters the tonus of the muscles of neck and forelimb.
- Exert considerable influence upon the ANS by the production of motion sickness involving the constant acceleration and deceleration of the head.

RUBRO SPINAL TRACT

- This is the more important motor tract in domestic animals.
- Arises from the red nucleus of the midbrain
- Decussates near its origin and enters the spinal cord contralateral to its origin
- Descends in the lateral funiculus throughout the entire length of the spinal cord
- There is always involvement of Internuncial neuron between the rubrospinal tract fibers and spinal alpha motor neurons
- They are rapidly conducting.
- This controls semi skilled movements.
- It functions to stimulate the flexor motor activity and inhibit the extensor and motor neuron activity.

TECTO SPINAL TRACT

- Arises from the deep layers of rostral colliculus.
- It deccussates within the dorsal tegmentum.
- Descends caudally in the brain stem.
- In cat it descends contralaterally.
- Terminates in the rostral region of cervical spinal cord.
- Plays a major role in mediation of auditory and visual reflexes and modifies neck reflexes.
- There is always involvement of Internuncial neuron between the tectospinal tract fibers and spinal alpha motor neurons.

MAJOR MOTOR CONTROL

- Many fibres connect adjoining and distant segments of the spinal cord with each other and do not project outside the spinal cord , called the Propriospinal fiber systems.
- They make up a major mass of the white matter of the spinal cord.
- They originate from the spinal gray matter except the motor nuclei.
- They are important in the interrelation of neural activities within the spinal cord.
- Reflex ats and complex reflexes involve several such relays.
- During walking or running, they are responsible for coordination of motor activity required to maintain equilibrium and allow the proper sequence of limb movement for propelling the animal forward.
- In spinal animals after a period of weeks , if assisted in maintaining balance , exhibit stepping movements similar to those observed in normal locomotion.
- The central motor control system includes the *motor cortex*, *basal ganglia* and the *cerebellum*. The motor cortex transmits its signals through caudate nucleus, putamen, globus pallidus, subthalamic nucleus, substantia nigra and reticular nuclei of the brain stem into the spinal cord.
- The motor cortex controls *pyramidal* and *extra pyramidal systems*. The motor cortex-pyramidal system is associated with voluntary performance of fine skilled movements. Gross involuntary movements are generated by the motor cortex-extra pyramidal system.
- The primary motor cortex controls the contraction of individual muscles and evokes discrete movements. The secondary cortex regulates complex movements of head, neck,

trunk and limbs. The premotor cortex controls fine movements of hands, fingers, mouth and tongue, co-ordinated movements of eyes and head.

- Both the basal ganglia and the cerebellum are concerned with co-ordinated movements with pyramidal and extra-pyramidal systems. Co-ordination of *slow or ramp movements* is associated with basal ganglia. The cerebellum co-ordinates the *fast or ballistic movements.*

MOTOR CONTROL OF THE BRAIN

Demonstration of the motor control of the brain

- Motor control system of the brain is studied by removal of a particular portion and observing the alterations in the somatic motor activity.

Decorticate preparation

- Demonstrated in cat or dog.
- In such preparations cerebral cortex with underlined white matter will be removed.
- Such animal will exhibit normal standing posture.
- When the animals are suspended in space they extend their limbs.
- This extension disappears when they contact the supporting surface.
- In such preparations tactile placing and visual placing reflexes are absent.
- Vestibular placing, tonic reflexes and body righting reflexes are present.
- Righting reflex
    - To perform righting reflex and progressive movement certain brain structures are necessary.
    - They are sub thalamic nucleus, Red nucleus, substantia nigra with inter connecting fiber tracts, basal ganglia, reticular formation and cerebellum.
    - These enters responsible for righting reflexes are located within the rostral mid brain. This can be demonstrated in amphibians/animals when it is put on its back it immediately rights itself.
    - When it is placed in water it swims. Frog response to various stimuli by jumping and crawling.

Decerebrate preparation

- This preparation emphasis the importance of the motor activity of structures or parts of the brain anterior to the pons and lower mid brain.
- This preparation is done by transection of the brain stem at the level of mid brain.
- Such animal exhibit pronounced antigravity rigidity that is depended on hyper excitability of the segmental myotatic reflex.
- This is known as “Decerebrate rigidity”.
- This is primarily due to hyper excitability of gamma motor neurons. Hence, otherwise known as “GAMMA RIGIDITY”.
- Transecting the dorsal root supply to the particular limb will be abolished by this rigidity.
- The higher centre responsible for the development of rigidity is located within pontine reticular formation.
- During this preparation pontine reticular formation is relieved from inhibitory influences of cerebral cortex.
- Other portion of brain stem reticular formation is also renowned of inhibitory influences from brain stem.
- These causes increase in reticulo spinal excitation on gamma motor neurons supplying intra fusal fibres.
- To maintain the decerebrate rigidily cerebellum and verticular system play a major role.
- In the decerebrate preparation, tonic labyrinth and tonic neck reflexes are elicited.

- Vestibulo spinal tracts are major system contributed to decerebrate rigidly.
- Righting reflexes like vertibular lighting reflexes are absent in these preparation. They stand when placed in a standing position but they cannot be moved.
- Decrebrated animal will have increase in muscle tone of both flexors and extensors of the fore limbs.
- The limbs become pillars while standing and tail become erect and horizontal.
- Head is extended and body shows hyper extension (hobby/cortoon/caricature animal)
- Increase in muscle tone is due to intact vestibulo spinal tract but, removal of inhibitory reticulo spinal tract.
- Normal standing posture is exaggerated.
- Stretching postural reflexes like stretch reflex, supporting reactions, tonic reflexes labyrinth reflexes are present.

GAMMA LOOP MECHANISM

- To initiate all somatic motor actions the influence of motor system upon gamma motor neuron is significant.
- The motor pathways depolarized dominantly gamma motor neurons which in turn initiate the contraction of intrafusal fibres of muscle spindle organ. These results in activation of group Ia afferent fibres.
- These fibres monosynaptically connect with alpha motor neurons and causes extra fiscal muscle contraction. This is known as "*Gamma loop mechanism*"
- Cutting across the dorsal root blocks this mechanism and causes immobility and uncoordinated somatic motor activity.
- Excitability of gamma motor neurons in proportion to alpha motor neurons is determined by particular spinal afferent under the influences of BSRF.
- BSRF is under the influences of basal ganglia and cerebral cortex.
- This indicates cerebellum and basal ganglia alter the motor activity directly through the involvement of red nucleus primary motor cortex and vestibular nucleus and indirectly through BSRF.

SPINAL ANIMAL (FROG)

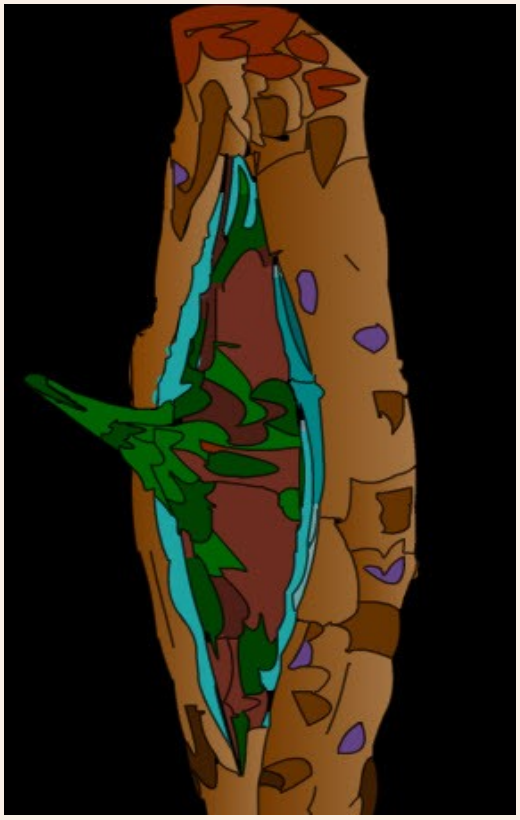
- Spinal animal is prepared either transecting at the spinomedullary junction or by ligating both carotid arteries and the mid-vertebral artery to arrest the brain activities.
- Frog's head behind the tympanic membrane is transected to separate spinal cord from the brain. Transection is to be done below the foramen magnum.
- In these preparation when frog is palced on its back there is no spontaneous movement due to complete paralysis of the movement.
- When a portion of a skin is pricked with the needle no withdrawal reflex is noticed.
- This is known as "Spinal shock depression of the spinal function and is reversible.
- Spinal shock is removed in few minutes in a frog and few hours in a dog.
- Regaining from the spinal shock certain reflex activity are seen.
- When one of the limb is pulled down it is quickly drawn up.
- Withdrawal of the limb is noticed on pinching. (flexor reflex)
- If one of the limb is stimulated with the greater force all the limbs are flexed.
- However, respiratory movement voluntary movement righting reflexes are absent (they can't swim when they place in the water).

- Except basic stretch reflex and supporting reactions all the other reflexes are absent.

Thalamic animal

- Cerebral cortex, white matter some portion of the basal ganglia are removed.
- Thalamus and hypothalamus with the caudal portion of the basal ganglia remain intact.
- These animals show righting reflexes and temperature regulation.
- Reflexes associated with emotional states fight and anger are present .
- Tonic labyrinth and tonic neck reflexes and other righting reflexes are present.
- Propriokinesthetic, righting reflexes placing reactions and hopping reflexes are absent.

MODULE-10: REFLEXES OF SPINAL CORD



LEARNING OBJECTIVES

- The outcome of this module help to,
  - understand basic operation of reflexes,
  - components involved,
  - participation of various levels of system,
  - spinal reflexes with an indepth analysis of its importance to animal,
  - properties of reflex arcs and study the classification of reflex arcs and
  - conditioned reflexes and their mechanism.

POSTURAL REFLEXES

- This is also known as postural reactions.
- It is defined as the position or arrangement of the body and its limbs.
- It is controlled by the activity of the skeletal muscles of the neck and limbs.

- Control of posture involves mechanisms that alter the excitable activity of α-motor neurons of the spinal cord.
- Structures concerned for maintenance of posture are located at all levels of brainstem, medulla and pons.
- It is divided into
    - Supporting reflexes
    - Attitudinal reflexes

Supporting reflexes

- These reflexes involve activity that initiates co-ordinated skeletal muscle activity to cause the limbs to be fixed into supporting columns against the pull of gravity.
- The supporting reflexes are further classified as local supporting reflexes and segmental supporting reflexes.
- Local supporting reflexes
    - These reflexes of the limbs produce a fixed standing posture, which prevents collapse under the force of gravity.
    - They involve only a few segments of the spinal cord for reflex actions.
    - Local supporting reflexes include the myotatic reflex, and extensor thrust reflex. These reflexes are initiated by the stimulation of muscle spindle or cutaneous receptors of the limbs involved or by stimulation of the opposite limbs with noxious stimulus.
- Extensor thrust reflex
    - When pressure is applied to the footpads of a dog, that limb is extended into a supporting column by the extensor muscles of the elbow, which are initiated by myotatic reflex.

Segmental supporting reflex

- These reflexes use many segments of the spinal cord. Segmental supporting reflex arcs are not solely limited to the spinal cord, but also involve the brain stem.
- The reflex is represented by crossed extensor reflex. These reflexes involve sensory input to a local area and produce reflex activity over a wide region of the spinal cord.

- The same reflex occurs in the opposite limb. When a hind limb is extended, the opposite forelimb also is extended.

ATTITUDINAL REFLEXES

Attitudinal reflexes

- It involves modification of posture as a result of varying positions of the head.
- Displacement of one part of the body is followed by postural changes in other parts so that a new posture is assumed.
- This is classified into two types,
    - Cortical reflexes
    - Extra cortical reflexes.

Cortical reflexes

- It is mediated through cerebral cortex and can be divided into
    - Placing reflex
    - Hopping reflex
    - Vestibular placing reflex

CORTICAL REFLEXES - VESTIBULAR PLACING REFLEXES

Vestibular placing reflex

- Blind folded animal if dropped head down position towards the ground; the animal assumes specific supporting postures.
- The forelimbs are greatly extended.
- Toes are spread apart.
- Tries to get support against an expected contact with the ground.
- Here, direction of acceleration within the field of gravity is not a deciding factor to initiate this reflex.

CORTICAL REFLEXES - HOPPING REFLEX

Hopping reflex

- If the animal is made to stand on one limb and if simultaneously is moved horizontally the supporting limb will hop to maintain support for the body.
- This is supported by spinal reflex, myotactic reflex and tactile placing reflex.
- This reflex is temporarily abolished by transecting the corticospinal motor pathways. But due to involvement of myotactic reflex of the limbs, there will be weak exhibition of this reflex.

CORTICAL REFLEXES - PLACING REFLEX

Tactile placing reflex

- Blind folded animal if held in space in a dropping position near a supporting surface to facilitate either of the parts of the body like feet, ventral surface of the body, neck or chin in contact with the surface, the animal quickly assumes a posture to place either of the limbs with the supporting surface.
- This reflex requires involvement of both spinal and cerebral cortex by way of corticospinal motor system.
- Decorticate animals or animals wherein descending motor pathways are abolished are not in a position to exhibit this reflex.

Visual placing reflex

- Similar to tactile placing reflex in a normal animal which is mediated through visual integrity system to reach the supporting surface prior to involvement of the cutaneous contact.
- Descending corticospinal motor system do participate in this surface.

EXTRACORTICAL REFLEXES

- It is mediated through spinal cord, medulla and pons. It is of two types - the tonic neck reflexes and tonic labyrinthine reflexes.

Tonic neck reflex

- Neck receptors include muscle stretch receptors and receptor organs that sense the position of joints between cortical vertebrae related to head position.
- Extension of the head to dorsal position causes flexion of the hind limbs, but extension of the forelimbs occurs when the head is moved downwards.
- Turning of head to right side causes the extension of both the right limbs and the flexion of both the left limbs to support the body against gravity; this helps to prevent falling.

- If the turning is on the left side, it results in the extension of the left limbs and the flexion of the right limbs.

EXTRACORTICAL REFLEXES - TONIC LABYRINTHINE REFLEXES

Phasic labyrinth reflex

- These reflexes are initiated by receptor organs of the semicircular canal.
- Rotational acceleration of the head stimulates vestibular semicircular canal.
- Maintenance of upright posture on rotation if kept on rotating platform and altering the position of head and body to the opposite of the rotation.
- On stoppage of the rotation, the animal's head will be turned and animal lean towards the opposite direction.
- Semicircular canals help to maintain the animal's balance on sudden change in the head's direction.

Righting reflex(RR)

- This is the involvement of tonic labyrinthic reflex to maintain the position of the head upon the neck.
- If the animal is maintained in a supine position. Further due to the involvement of tonic neck reflex to later the body's position to an upright position.
- This reflex response to body position is known as righting reflex.
- If a cat is dropped in a space from a supine position, as in the process of dropping, the position of the head is immediately altered to an upright position due to tonic labyrinth reflex. Due to this, other parts of the body of the body position so as to support which is due to tonic neck reflex and assist the animal to land

in upright position.

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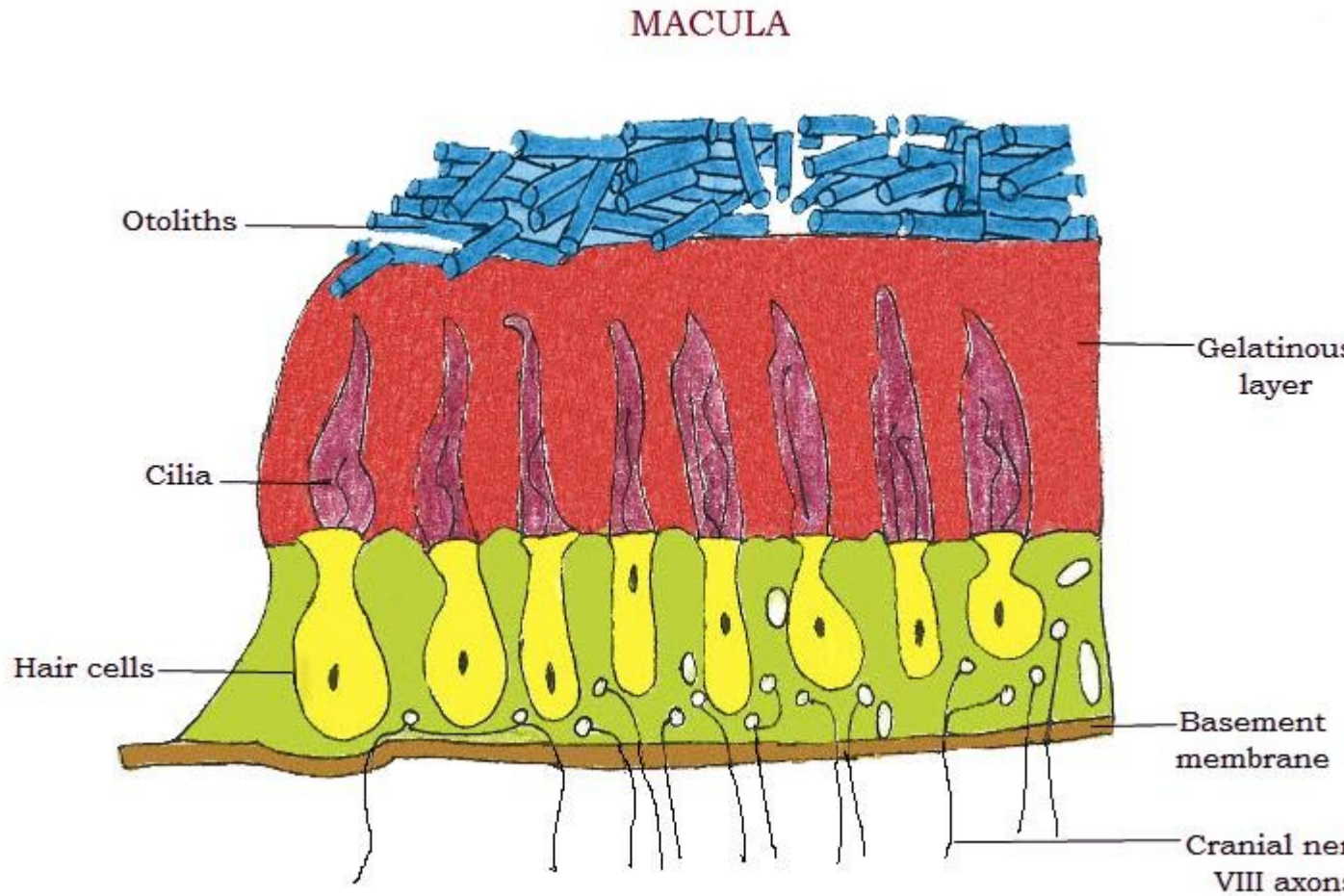
VESTIBULAR APPARATUS

- The vestibular apparatus located in internal ear that detects sensation related to equillibrium (linear accelaration of head).
- Popularly known as OTOLITHIC organ.
- It consist of bony labyrinth (semicircular canal with utricule and saccule) and membranous labryinth. This is the functional part of the vestibular apparatus and is composed of cochlear duct, three semicircular canals, the utricle and saccule.
- Membranous labryinth with an enlargement at one end called as is filled with endolymph and surrounded by perilymph.
- The ampulla is the enlargement of the semicircular canals at it base and is filled with endolymph.
- The bag-like structures (vestibular sacs) the utricle and saccule have sensory area known as *maculae*. This detects the orientation of the head according to the direction of gravitational pull.

VIEW ANIMATION...



- Utricule and saccule are located within the petrous portion of the temporal bone.
- The maculae is covered by a gelatinous layered and has otoconia or statoconia which are small crystals of calcium carbonate.
- The gelatinous layer has numerous hair cells projecting with their cilia with synapse with the sensory axons of vestibular nerve.
- Change in the orientation of head alter the bending of the celia due to the weight of otoconia accordingly signals are transmitted to cerebellum.
- Maculare detect linear acceleration of the head and act as the receptor for righting reflex.
- The ampullae of the semicircular canals do not have otoliths, but has the cristae which contains hair cells inside the cup shaped gelatinous mass called as cupula. This houses a sensory organ called crista ampullaris that will be excited by the flow of endolymph.
- Hair cells do project their cilia into cupula and the base of these hair cells are connected to axons of vestibular nerve.
- Bending of cupula with the flow of endolymph alters the position of the head.
- The cristae detect angular/rotary acceleration of the head, while the ampullae of the vestibular sacs detect linear acceleration. Most of the vestibular nerve fibres from the macula and semicircular canals end in vestibular nuclei present at the junction of medulla and pons; some fibres pass directly to cerebellum.
- The fibres that end in the vestibular nuclei send second order neurons to the cerebellum, cerebellar cortex, vestibulospinal tract and other areas of the BSRF.

Process of equilibrium maintenance

- When the head is tiled to one side, the otoliths and gelatinous mass of the ampullae of the vestibular sacs induce a bend in the hair cells. This excites or stimulates the hair cells.
- Change in head movements causes movement of otoliths and inertia cost subsequently induces generation of action potential and through vestibular nerve cerebellum receives the information relating the position of head in space.
- The macula of the utricle is placed horizontally in the ear and therefore can detect movement in the horizontal plane.
- The macula of the saccule is placed in vertical position and therefore detects vertical movement of the head.
- But within these maculae, the hair cells are oriented in opposite direction and thereby detect movements of forward, backward, and side to side directions.
- Since the hair cells placed in one plane are stimulated to tilt of the head in one particular directfion, the brain can perceive the direction of the movement, which sends motor signals to maintain the body in posture to maintain the position of the body.
- The semicircular canals are located at right angles to each other and therefore the ampulla in these canals detects angular movement of the head. Each semicircular canal detects the acceleration in one single plane pertaining to it.
- If the head is turned in one particular plane of one particular canal, then there is fluid motion inside the canals causing push on the ampulla and stimulating the hair cells.
- Since each canal is placed in one plane, the degree of movement is sensed by the stimulation of the hair cells in the canals.
- The whole body position is maintained by inputs from visual, auditory and proprioceptive systems.

VIEW ANIMATION...

NYSTAGMUS

- It is the movement of the eye in relation to the movement in the head of the animal.
- It consists of rhythmic movements of the eyes in a dorsoventral, lateromedial, or oblique directions.
- It is characterized by the slow movement of the eye in one direction and then quick return to its original starting position.
- These movements are continued till the rotatory acceleration is maintained.
- The receptor organs of the nystagmus are the cristae of the semicircular canals.
- The afferent neurons for the nystagmus are present within the VIII cranial nerve.
- These fibers synapse with internuncial neurons within the vestibular nuclear complex of the medulla and pons.
- The motor activity is relayed to the extrinsic muscles ot the eye via the brainstem reticular formation.

REFLEXES

- A reflex is a specific, stereotyped, involuntary response to peripheral stimulation.
- The spinal cord is a reflex neural system and its activity is modified by influences transmitted from the brain via descending fiber system

- The regulating system of the brain are informed of the reflex activity initiated within the spinal cord and is able to initiate descending influences to modify this reflex activity so that it is of maximum economy to the animal
- Reflexes involve several components of CNS and PNS connected in series
- Skeletal motor system and visceral motor system (ANS) are closely related to spinal cord reflexes.
- The components of a reflex arc are,
    - Receptor organ
    - Afferent neuron
    - Efferent neuron
    - Effector organ
- Sometimes one or more internuncial neurons
- Only the reflex arcs utilized by the muscle spindle stretch receptor afferents do not contain internuncial neurons Eg : The myotatic reflex arc in which fibers terminate directly on the efferent neurons . Such an reflex arc is known as an monosynaptic reflex arc because only one synapse is involved
- All other reflexes are referred to as polysynaptic reflex arcs indicating that more than one synapse is involved
- Reflex arcs that do not involve a synapse either in the PNS or CNS involve in reflexes referred to as axonal reflexes
- Many autonomic reflexes take place within peripheral ganglia without spinal cord component and are known as ganglionic reflexes which are mostly monosynaptic
- All autonomous reflex arcs that pass through the spinal cord are polysynaptic or atlest bisynaptic in nature.
- Alpha motor neurons are the final common pathway to skeletal muscle.
- Alpha motor neurons possess large cell bodies which are filled with well-developed, granular endoplasmic reticulum called Nissel substance.
- Before emerging out of the spinal cord , the axon gives rise to form one to six branches which terminate within the confines of the spinal cord called the recurrent collaterals of Alpha motor neuron axons.
- They terminate upon neurons that exert an inhibitory effect on Alpha motor neurons called the Renshaw cells.
- According to Dale's principle, a given neuron can produce only one type of transmitter agent at all its terminal synapses. The Alpha motor neurons produce acetylcholine at all its neuro effector junction.
- Prolonged discharges of action potentials upto 50 msec at high frequencies of 500 to 1000 per sec are possible at these synapses.

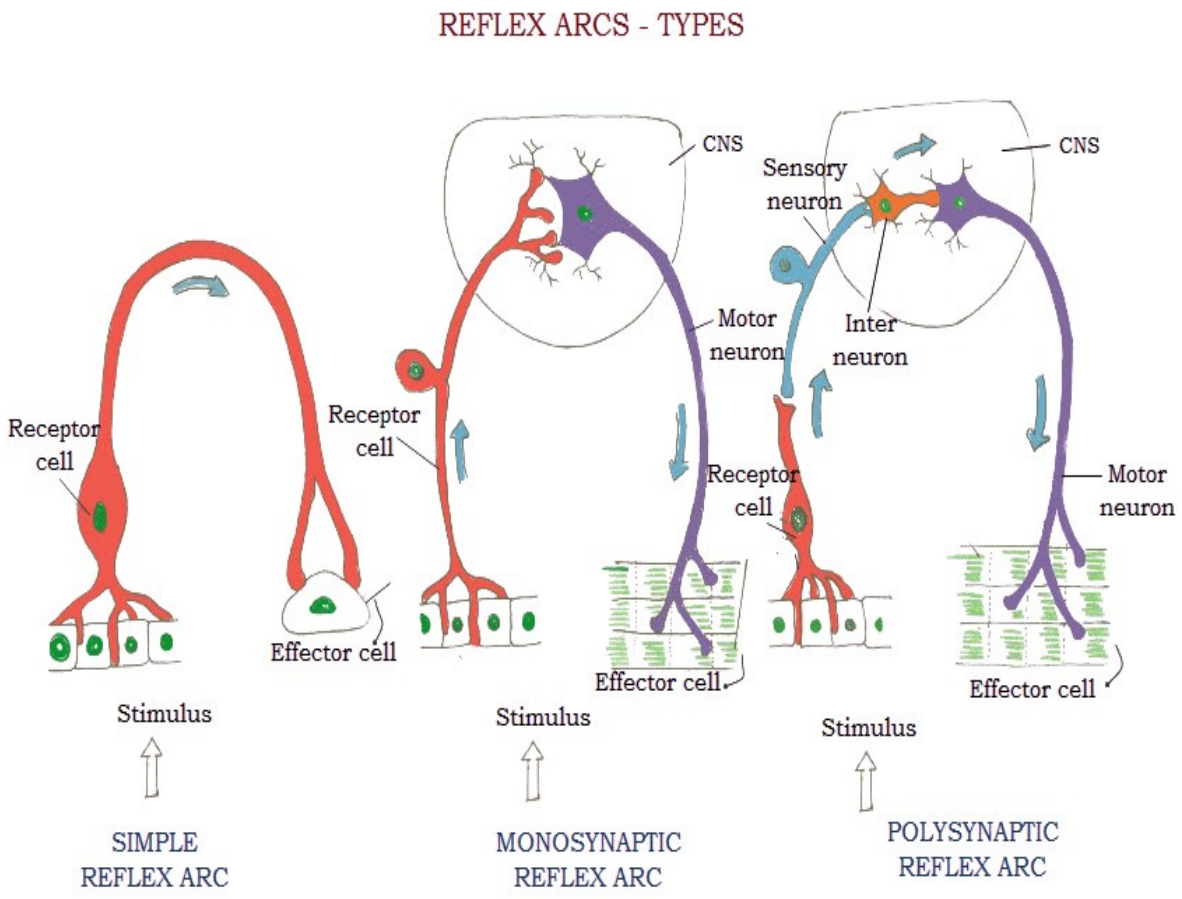
CLASSIFICATION OF REFLEX ARCS

Components of reflex arc

- The neural circuit for reflex is referred to as reflex arc. Five components commonly make up a reflex arc. They are the receptor organ, sensory (afferent) neurons, interneurons in spinal cord or brain, motor neurons (efferent) and an effector organ (muscle or glands).

Classification of reflex arcs

- Neurons may combine to give at least five types of reflex arcs.



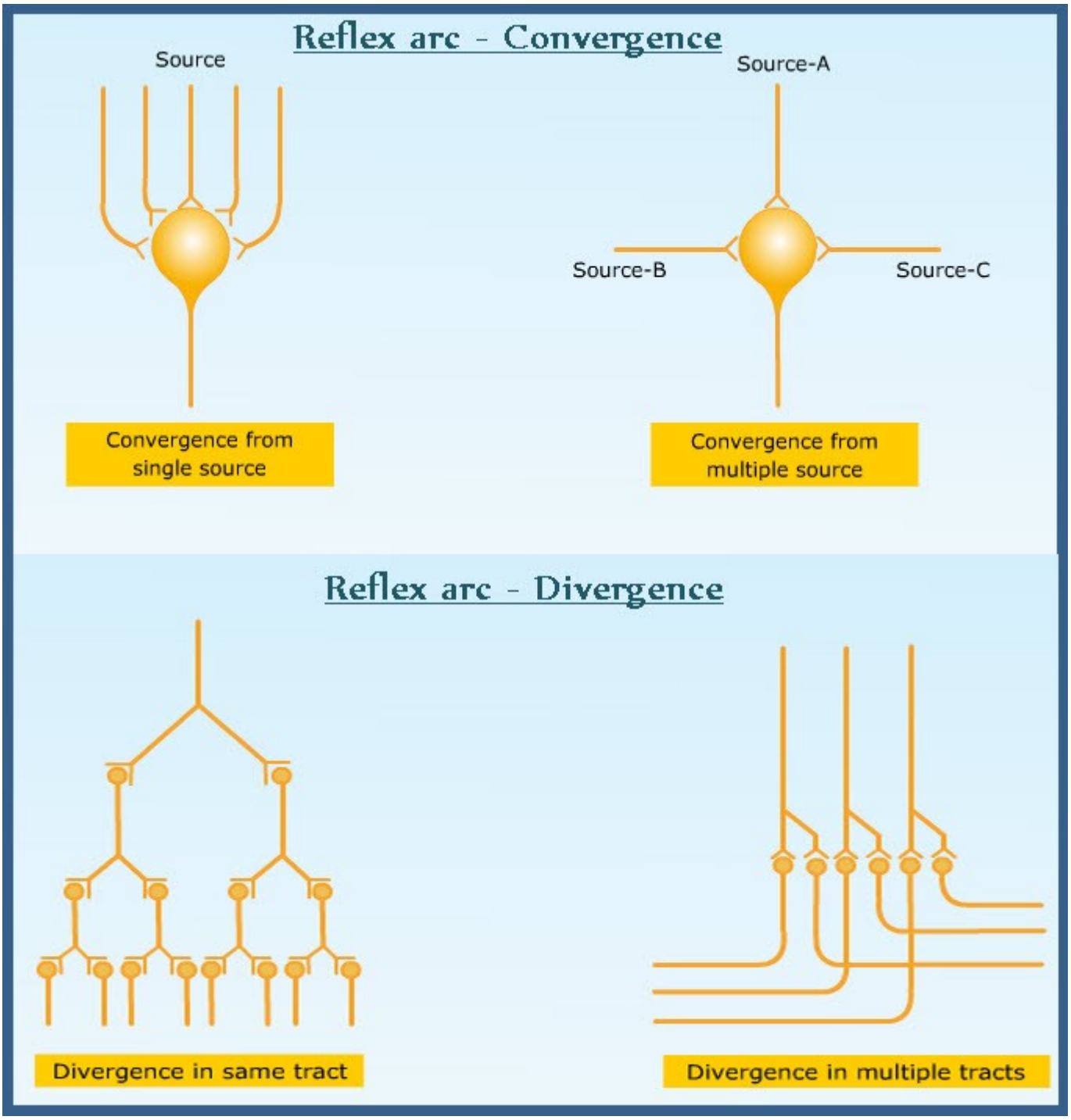
Monosynaptic reflex arc

- There is a single synapse between sensory and motor neurons of the spinal cord (without interneuron) e.g Myotatic reflex

Polysynaptic arcs

PROPERTIES OF POLYSYNAPTIC ARCS

- *Series synaptic reflex arcs:* Several simple reflex arcs are united in series to give a chain of reflex arcs, e.g. flexor and extensor responses related to muscle tone.
- *Convergent effector reflex arcs:* Two or more afferent neurons are in synaptic relation with only one efferent neuron. Hence, stimulation of many receptors converges to excite a single effector.
- *Divergent effector reflex arc:* One afferent neuron is synaptic connection with two or more efferent neuron. Stimulation of a single receptor diverge through many neurons to excite more than one effector
- *Internuncial reflex arcs:* Two or more afferent neurons are connected with two or more effectors. Stimulation of either of the two receptors causes reflex response in one or both effectors. The connections are established through interneuonrs. It provides reciprocal excitation and inhibition for smooth co-ordinated activity.



PROPERTIES OF REFLEX ARC

One way conduction (Bell and Magendie law)

- The dorsal root fibres of the spinal cord are afferent (sensory), while the ventral root fibres are efferent (motor).
- The sensory impulses are centripetal (towards the CNS) and motor impulses are centrifugal (away from the CNS).

Slow speed of conduction

- Slow build up of EPSP to threshold stimulus causes the synaptic delay, thus slows the speed of conduction.
- *Fatigue:* Due to exhaustion of the neurotransmitter substance at the synapse.
- *Refractory period:* Show both absolute and relative refractory periods.
- *Reinforcement:* (Successive induction): By discharging signals from many neurons. It is of two types,
    - *Positive successive induction:* Irritation at a point of the skin by a tick leads to scratch reflex
    - *Negative successive induction:* Reciprocal stimulation and inhibition; e.g., biting reflex, reflex flexion and extension of the limbs.
- *Rebound:* Increased reflex response following the withdrawal of inhibitory stimulus.
- *After discharge:* Continuous impulse discharge from the centre, even after the cessation of the original stimulation.
- *Summation:* Subminimal stimuli at rapid succession develop effective EPSP, the temporal summation.
- *Recruitment:* Prolonged and altered intensity of stimulus progressively activates more number of motor neurons.
- *Irradiation:* Gradual increase in the intensity of stimulus excites the additional neurons, and the effectors.

MYOTATIC REFLEX

- Sudden stretch of a muscle causes its reflex contraction.
- Commonly known as "KNEE-JERK" reflex.
- It forms the basis of the maintanence of *"Muscletone"*
- Receptor organ concerned with this reflex is *Muscle –spindle organ.*
- These receptors are encapsulated in the belly of skeletal muscle.
- CNS receives sensation from these receptors and coordinates *Posture and Locomotoin* .

MUSCLE-SPINDLE ORGAN

Muscle-spindle organ -Complex receptor organs

- Made up of specialized striated muscle called *intra fusal muscle fibres*, present within a connective tissue capsule and are attached to the skeletal musclel.

Extra-fusal-fibres

- These are the muscle fibres which produces physical shortening of the muscle.
- Alpha motor neurons innervates them.

Speciality of intra fusal muscle fibres

- Have contractile proteins at their polar ends only and not in the centre.i.e. polar ends can contract without the contraction of centre portion.
- Centre portion is known as equatorial region from where sensory nerve arises and carries information to CNS from muscle spindle via peripheral nerves.
- The contractile ends of intra fusal fibres are innervated by gamma motor neurons (ventral horn of spinal cord).

IMPORTANCE OF EQUTORIAL REGION

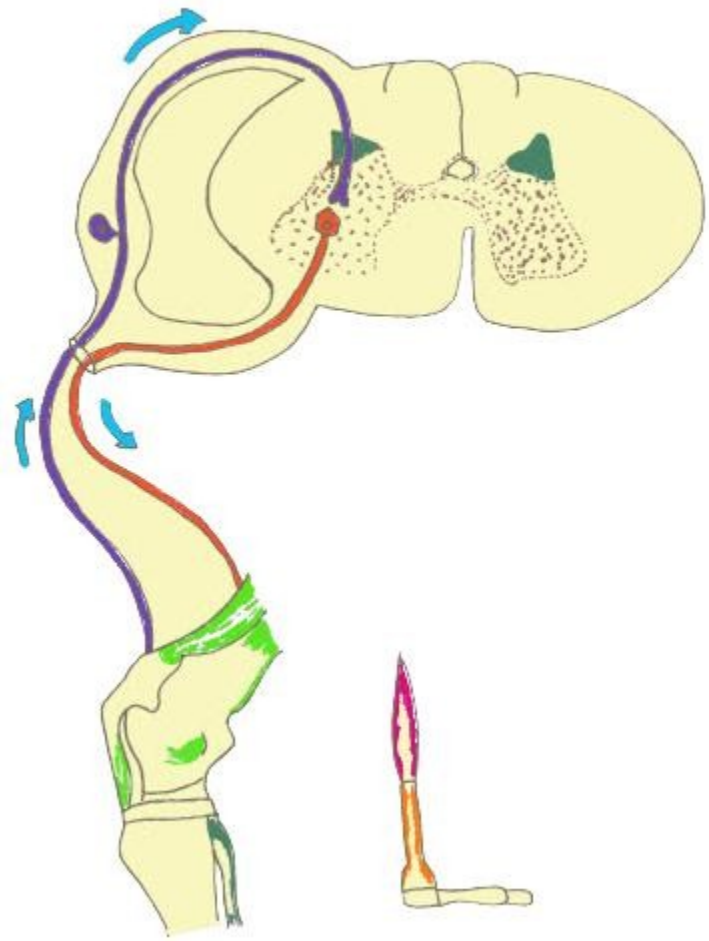
- Action potential are generated from this region by stretching
- Muscle spindle receptors lie parallel to the extra fusal fibres.
- Functionally these receptors are connected to the origin and insertion of the tendon i.e. lengthening of the whole muscle will stretch the equatorial region.

- Contraction of polar ends also generate action potential, which passes in the sensory nerve, in proportion to lengthening of the equatorial region.
- Sensory fibres are capable of detecting the changes in length during the dynamic phase of muscle lengthening and during resting stage.
- When CNS receives the sensory inception, it causes excitatory mono-synaptic connection with alpha-motor neurons (that supplies extra fusal fibres of the same muscle)
- This leads to contraction of the whole muscle which results in shortening of the muscle spindle (especially the equatorial region)
- This shuts-off the action potential from spindle receptor and muscle contraction is stopped.

KNEE-JERK REFLEX

- Strech of quadriceps muscle results when patellar tendon is struck with a blunt object. (the muscle spindle is stretched).
- Action potential from muscle spindle go to lumbar spinal cord and causes excitation of alpha motor neurons of quadriceps which causes contraction of the muscle and extension of knee joint.(muscle stretch reflex).
- Action potential passing on the gamma motor neurons causes shortening of polar region of intra fusal fibres and not the equatorial region.Hence the equatorial region stretches and initiates contraction.
- CNS initiates contraction of extra fusal fibres reflexely by gamma motor neurons viz gamma-loop. Gamma-loop has gamma motor neurons, intra fusal fibres (including middle receptor), sensory nerve of the spindle which forms excitatory mono synaptic synapse and alpha-motor neurons back to the same muscle and extra fusal fibres

KNEE JERK REFLEX



Co-activation

- Each time when CNS transmits signals to alpha-motor neurons, the Gamma-motor neurons are also stimulated.This causes the contraction of both extra fusal and intra fusal fibres around the same time.
- This mechanism of simultaneous contraction check the length of the muscle spindle receptor and to maintain proper body movements without jerks.

GOLGI TENDON REFLEX

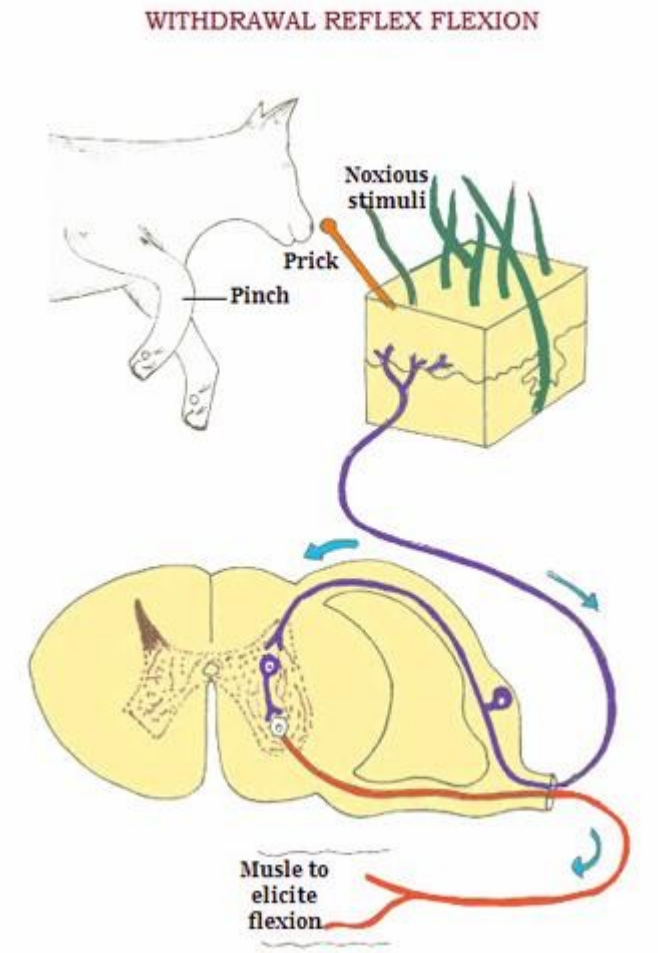
GOLGI tendon REFLEX/ inverse myotatic reflex / clasp-knife reflex

- Sensory receptor organ : golgi tendon organ
- Present in tendons of somatic skeletal muscle
- Present in pheripheral terminal and large of mylinated, class I_b nerve fibres.
- These receptors are excited during muscle contraction as contraction causes stretch of the tendon.
- These recptors are sensitive to change in the muscle tension.
- Class Ib fibres terminate in the internuncial neurons of spinal cord after forming a mono synaptic reflex arc.
- When muscle contracts, muscle tension increases which also causes increased tension of muscle tendons which in turn ends in the stimulation of golgi tendons.

- Sensory fibres from this receptor transmit signals to spinal cord to inhibit muscle contraction.
- It is a protective reflex to prevent over stretching and tear of muscle fibres and coordinate skeletal muscle activity.

WITHDRAWAL REFLEX

- Protective reflex, helps to avoid noxious stimuli by flexion, hence known as flexion reflex. Ex. Withdrawal of limb if noxious stimuli is applied to the limb. This reflex is poly synaptic
- Withdrawal is achieved by contraction of flexors (the muscle should be excited) and inhibition of extensors (occurs simultaneously).



CROSSED EXTENSOR REFLEX

- To avoid noxious stimuli there will be withdrawal of limb and is associated with alteration of posture involving extensors of unaffected limbs to support the body.
- Neurons involved are same as that of withdrawal reflex and also include neurons that control the extension of opposite limbs.

EXTENSOR THRUST REFLEX

- When pressure is applied to the footpad it causes simultaneous contractions of flexors of the digits and the extensors of elbow which extend the limb into a supporting column which are initiated by myotatic reflex.

SCRATCH REFLEX / MULTISYNAPTIC REFLEX

- Initiated by combination of tactile and pain receptor organ.
- Afferent enters the spinal cord and end in internuncial neurons.
- Preventive reflex helps to remove the irritating stimuli from skin (dorsal lateral surface of the thorax and neck) with one rear limb and out affecting the posture of the animal.

CONDITIONED REFLEXES

Conditioned reflexes (Conditioned responses)

- These reflexes are acquired or reflexes that are gained naturally or artificially by the individual during the course of their lifetime.
- Salivary and the gastric secretions produced in response to food is a natural and inborn reflex. The sight or the smell of the food forms the natural stimulus, which causes the natural conditioned response in the form of salivary or gastric secretions.
- If the animal is fed in association with the bell sound or music (neutral stimuli) and this practice is frequently repeated, it causes conditioned salivary secretion to the bell sound or music even in the absence of food. This type of response is referred to as artificial conditioned reflexes. Pavlov, a Russian Scientist proved this reflex mechanism in the dogs.
- Conditioned responses develop in relation to an already existing mechanism, which can be an inborn reflex or another conditioned mechanism. These reflexes have been developed in relation to cardiovascular, alimentary, pupillary and secretary reflexes.
- Visual, olfactory, auditory, gustatory, tactile and proprioceptive stimuli have been used to evoke conditioned responses. The afferent side of the conditioned mechanism of conditioned stimuli becomes attached to an already functional efferent side of the reflex.
- Cerebral cortex plays an important role in the formation and maintenance of conditioned responses.

REQUIREMENTS OF CONDITIONED REFLEXES

- The natural stimulus and the conditioned stimulus (neutral stimulus) must be in coincidence with each other. E.g. Food supplies (natural stimuli) along with a bell sound (neutral stimuli). The animal exhibits simultaneous conditioned response only for the bell sound even in the absence of food. But if the application of the neutral stimulus (sound) precedes the natural stimulus (food) the animal develops delayed conditioned response.

PROPERTIES OF CONDITIONED RESPONSES

Reinforcement

- If two neutral stimuli (e.g. sound and light) are applied simultaneously, the conditioned response will be greater than by a single stimulus.

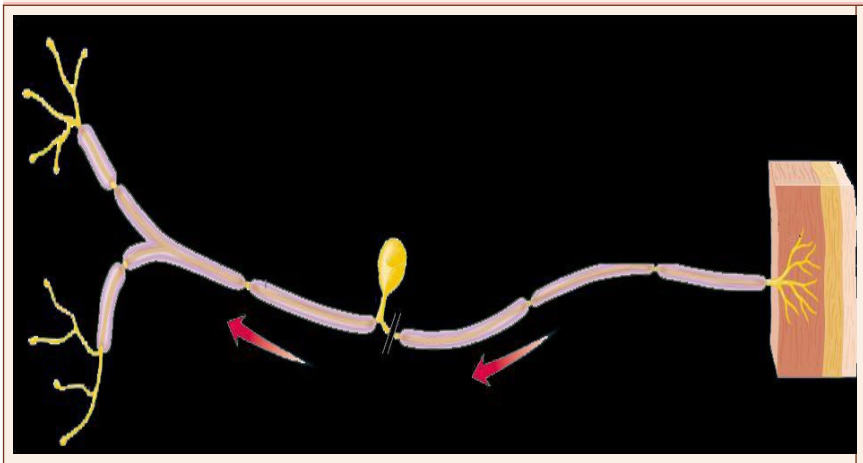
Abolition

- The neutral or the conditioned stimuli must be applied at a constant strength and duration to produce a conditioned response. Otherwise, this may gradually weakens and finally disappears.
- Frequent rapid succession of the conditioned stimulus (neutral) without the natural stimulus (e.g. food) the developed conditioned response will gradually weaken and finally disappears completely.

Differentiation

- Animal that has the ability to differentiate two independent neutral stimuli (sound and the flashes of light), develops two types of conditioned responses which are very specific. Hence, the other neutral stimuli cannot produce the same conditioned response.

MODULE-11: PERIPHERAL NERVOUS SYSTEM



LEARNING OBJECTIVES

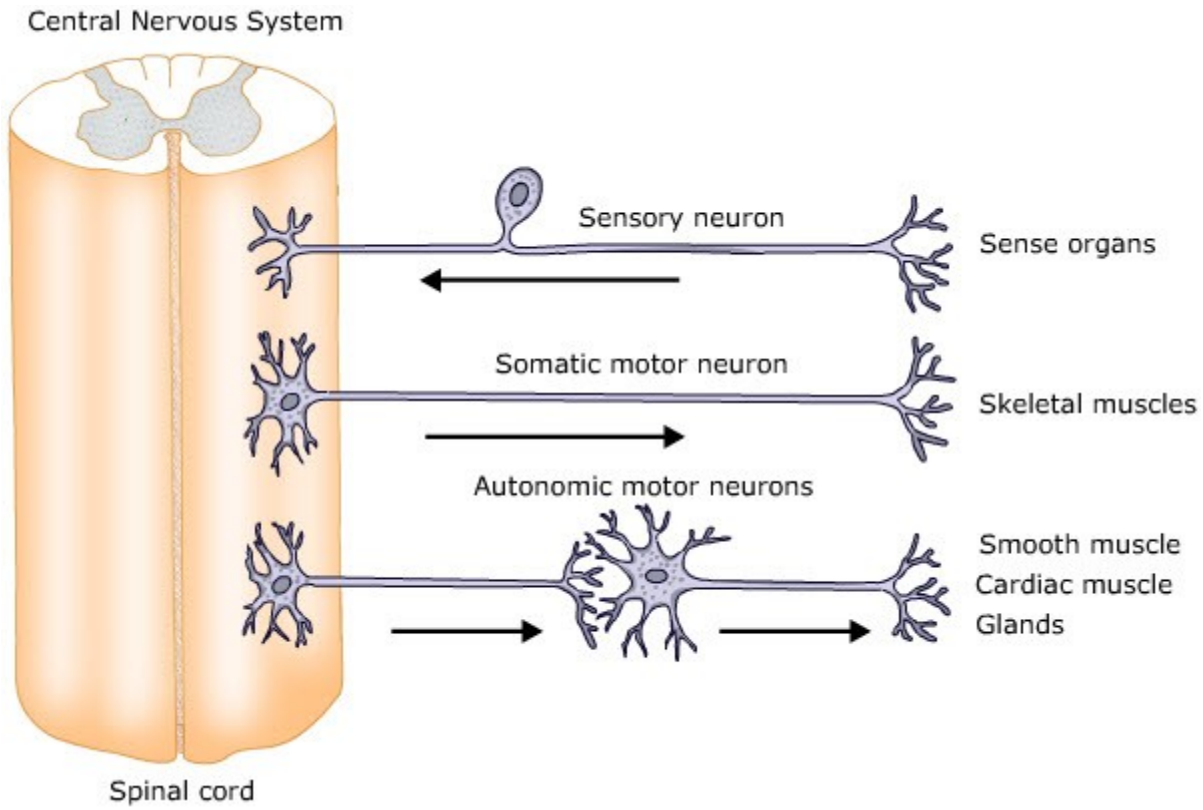
Learning this module fulfills,

- the understanding of the nervous system and the learner will appreciate how an animal reacts instantaneously to an external stimulus with the linking of

	peripheral nervous system to central nervous system.

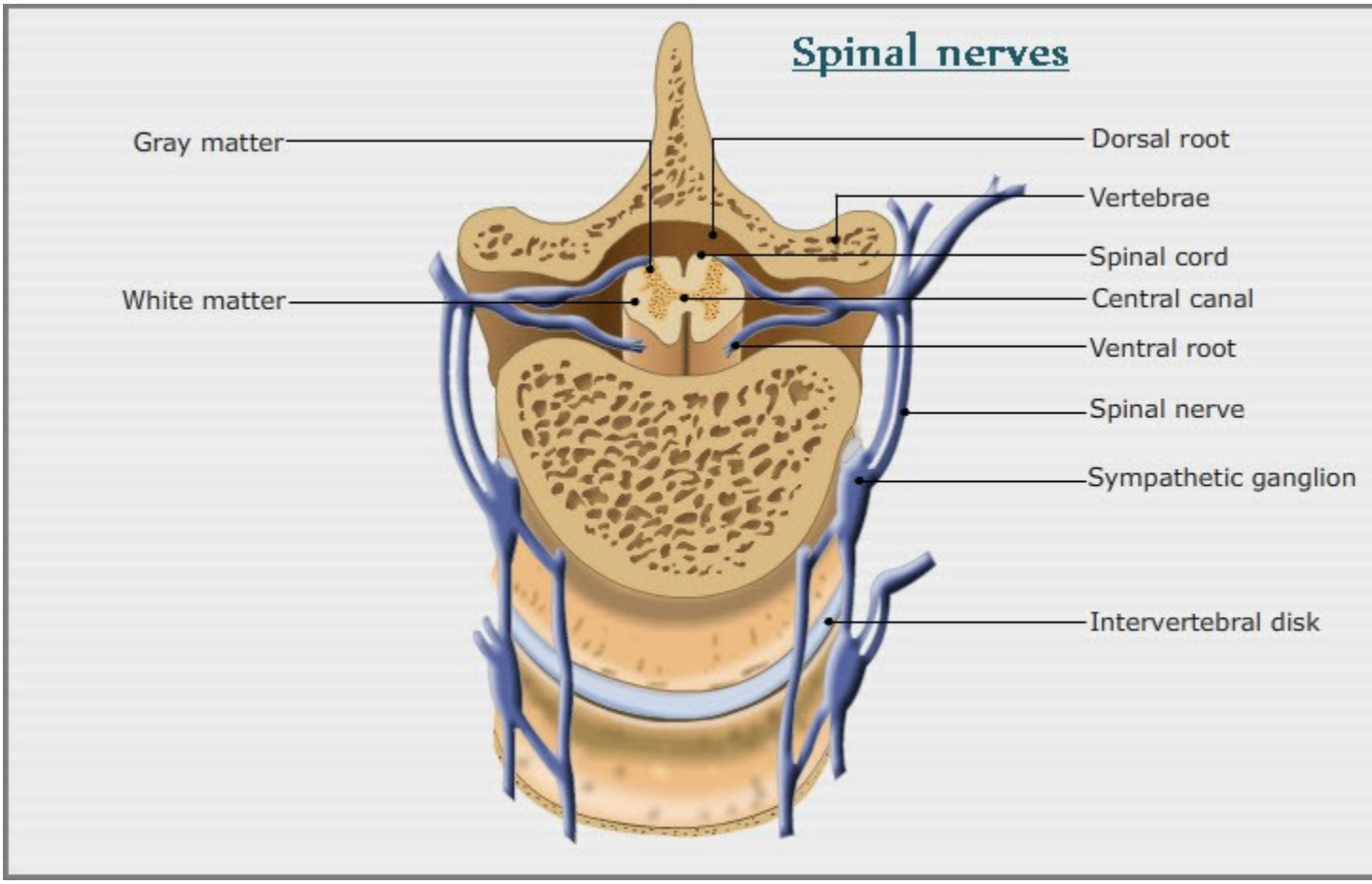
INTRODUCTION TO PERIPHERAL NERVOUS SYSTEM

- This includes all nervous structures, the peripheral ganglia, spinal nerves, cranial nerves and the autonomic nerves, located out of the brain and the spinal cord.
- It functions to provide communication between the receptor organ and the CNS (sensory), from the CNS and the effector organs (motor).
- Peripheral nerves are myelinated.
- It is divided into motor (efferent) and sensory (afferent) subsystems.
- The motor peripheral nerves that supply to skeletal muscles are referred to as somatic motor nerves and those that supply the cardiac and smooth muscles and exocrine glands are referred to as autonomic nerves.
- The afferent (sensory) system is of two types: Somatic and visceral.
  Somatic sensory nerves carry impulses from the photoreceptors (eye), auditory receptors (ear) and stretch receptors (skeletal muscles), whereas the visceral sensory nerves carry visceral sensations from the chest and abdomen.



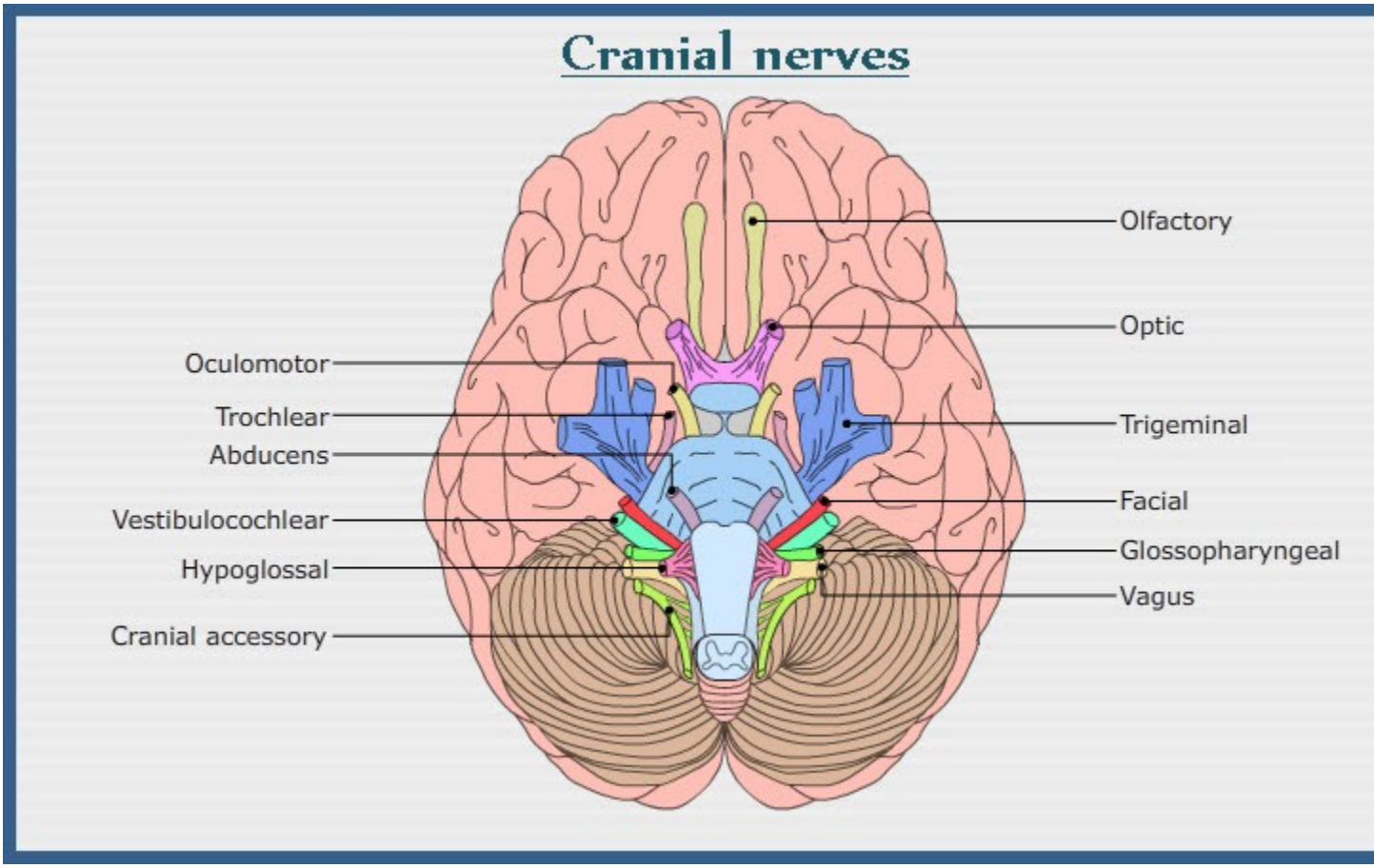
SOMATIC COMPONENTS

- The spinal nerves emerge as a pair of nerves from each spinal segment through the inter-vertebral foramina, which lies between the two adjoining vertebrae.
- Thus, the number of pairs of thoracic, lumbar and sacral nerves is similar to the respective vertebrae.
- Although the cranial portion has seven cervical vertebrae, eight pairs of cranial nerves emerges, while the caudal vertebrae have fewer pairs of coccygeal nerves.
- The terminal portion of the spinal cord, the meninges and the nerves are collectively referred to as cauda equinae.

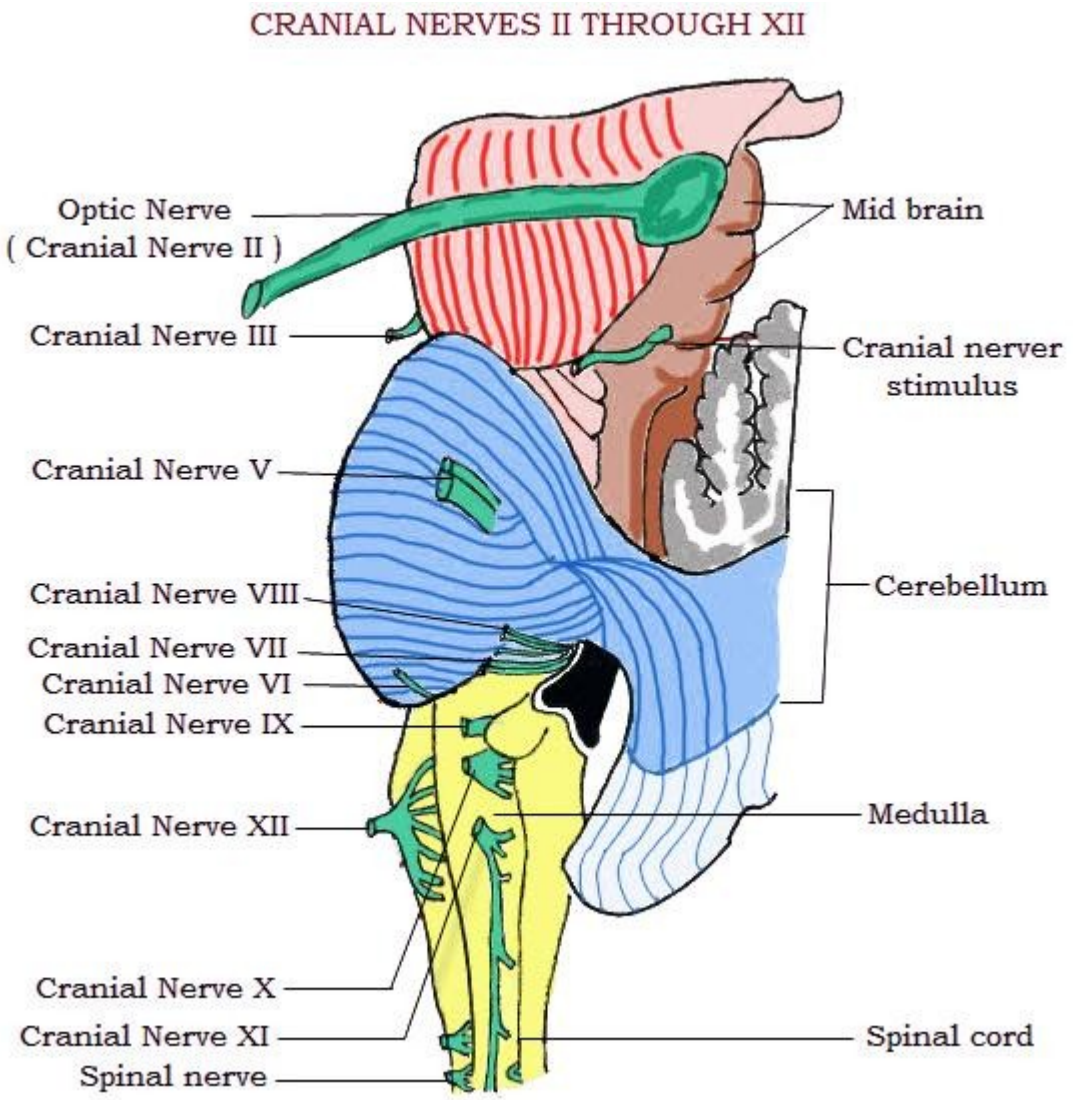


- The dorsal spinal root is the afferent neuron and it propagate sensory impulses from the periphery towards spinal cord and the cell bodies of these neurons are located in the dorsal root ganglion.
- The somatic motor nerves or the efferent nerves emerge from the cell bodies of ventral roots, located in the ventral horn of the spinal cord. Both the dorsal and ventral roots unite to form the spinal nerves that emerge through the inter-vertebral foramen.
- Thus, the spinal nerves are mixed nerves, containing both sensory and motor fibres. However, outside the vertebral canal it divides into dorsal and ventral branches.
- The nerves from the last three cervical and the first one or two thoracic nerves form a net work, the left and the right brachial plexus, supply to the respective fore limbs.
- The ventral branches of the last 3 to 5 lumbar and first 2 to 3 sacral nerves unite to form the right and left lumbo-sacral plexus, supplying to the respective hind limbs.

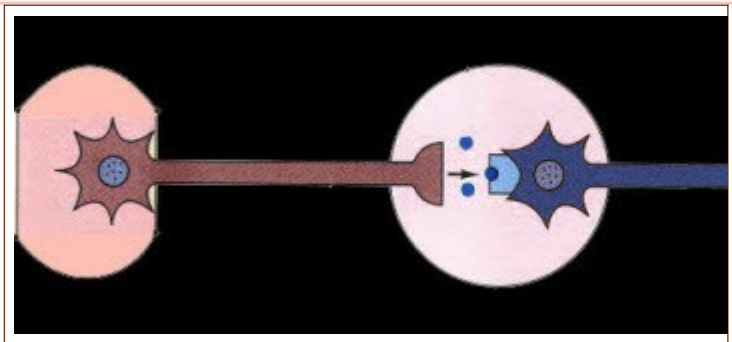
CRANIAL NERVES



- Twelve pairs of cranial nerves emerge through the foramina of the skull; hence they do not have dorsal and ventral roots.
- Some of the cranial nerves are purely sensory and some are strictly motor in function, while some nerves are mixed in functions.



MODULE-12: AUTONOMIC NERVOUS SYSTEM



LEARNING OBJECTIVES

This module explains,

- the overall effects of

autonomic motor functions, their divisions and its control over visceral activity.

- the functions of the ANS and the importance of the ANS in stress and emergency reactions.

AUTONOMIC NERVOUS SYSTEM

- Described as visceral efferent system by Langley in 1898.
- All efferent axons leaving the CNS other than those of skeletal muscle belong to ANS.
- ANS supplies efferent information to smooth muscle, glands & cardiac muscle.
- ANS modifies motor activities that have been initiated with in the involved effector organs.
- Neural activity of ANS may either be excitatory or inhibitory.
- It has two divisions
    - Sympathetic (thorocolumular)
    - Parasympathetic (craniosacral divisions)
- ANS as the name implies is not under the control of structures of other nervous systems.
- Unique difference from somatic nervous system is the presence of ganglia along their nerve trunks or in the wall of the effector organ. Ganglia are clusters of neurons of peripheral autonomic neurons which form swelling on the nerve trunk.
- It provides mechanism of synapsing for efferent fibre prior to innervating effector organs.

CLASSIFICATION OF GANGLIA

Vertebral ganglia

- Located along vertebral column and are associated with sympathetic trunk.

Collateral ganglia

- Located in between CNS and viscera, associated with visceral blood vessels. eg. celiac ,pelvic and cranial & caudal mesentric

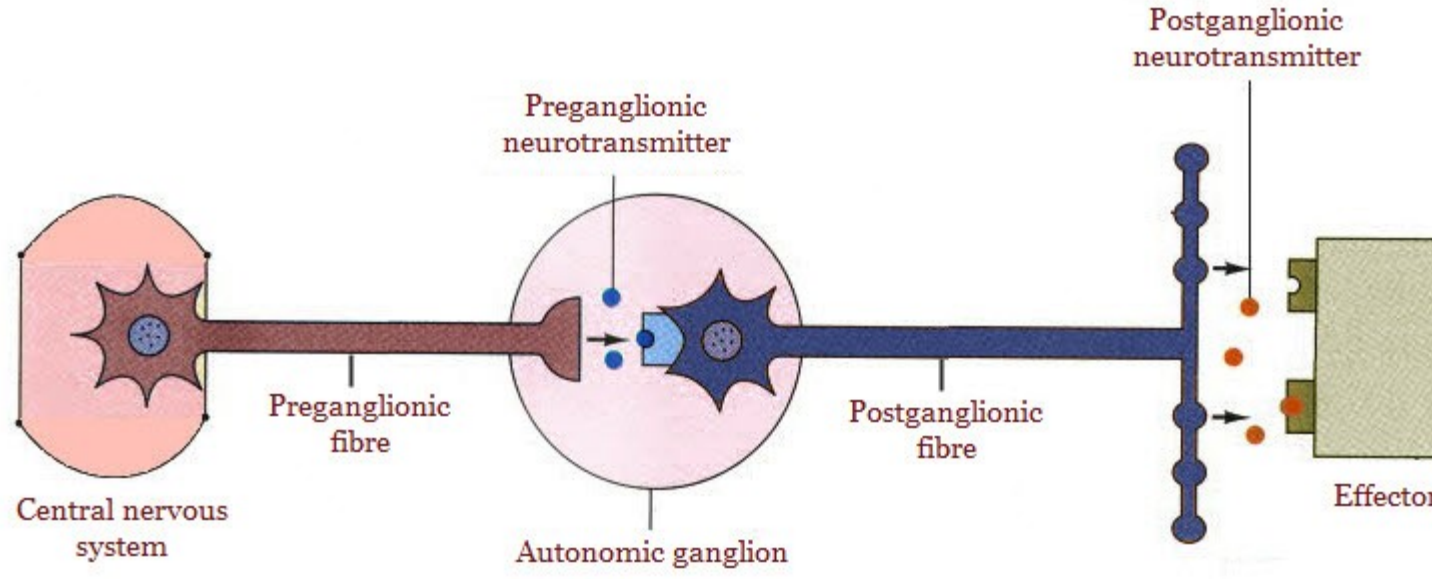
Terminal ganglia

- Located in the wall of the visceral organ eg. Cardiac, pulmonary & enteric ganglia.

NERVE FIBRES

- Ganglia possess two types of nerve fibres
    - Pre ganglionic nerve fibre
        - Nerve fiber from CNS to cells of ganglia for synapse.
        - They are small, myelinated with conduction velocity of 3-15 m/sec, representing class B fibre.
    - Post ganglionic nerve fibre

- Nerve fibre from ganglia to effector organ.
- These fibres are non-myelinated, small , class C fibers with conduction velocity of 0.7-2.3 m/sec.



SEGMENTS OF ANS

- The ANS is divided into small segments after its origin from CNS.
- Three segments are evident:
  - Cranial segment
    - From brain stem with nerve fibers of oculomotor, facial, Glossopharyngeal & Vagus
  - Thoraco lumbar segment
    - From spinal cord with ventral root of spinal nerves from T_1 or L_{5or6} segments.
  - Sacral segment
    - From spinal cord and the ventral root of S_1-S_3 Sacral nerves.
    - Preganglonic axons of the parasympathetic division originate in the cell bodies of the brain stem (cranial out flow) and in the terminal segment of (sacral out flow) of the spinal cord .

NEURO TRANSMITTER OF ANS

Acetyl choline (Ach)

- This is the neuro transmitter produced by *preganglionic* fibers of both sympathetic & parasympathetic systems.
- Post ganglionic fiber of parasympathetic system produce Ach at their neuro effector site in visceral organ

Adrenaline/Nor-adrenaline

- Post ganglionic fibers of sympathetic system produce noradrenaline or adrenaline at their neuro effector site on the effector organs.
- Exception
  - Isolated preparation of sympathetic neuro effector junctions of cat's sweat gland secrete Ach.

    - HYPOGASTRIC sympathetic supply to the uterus of bitch receives Ach as post ganglionic sympathetic neuro transmitter.
    - Stellate ganglionic sympathetic fibers at their post ganglionic end secretes Ach in corony supply of cat and dog.
- Other
    - Sympathetic vasodilators secreting Ach is seen in the buccofacial region of dog, hind limb muscles of cat, coronary arteries of dog and cat, and penis in dog.

PERIPHERAL DISTRIBUTION OF NERVE FIBERS

	Sympathetic	Parasympathetic
Preganglionic	Short fibers and ganglia are close to spinal cord or brainstem with in the vertebral or collateral ganglia	CNS to collateral or terminal ganglia
Post ganglionic	Long fibers	Short fibers

SYMPATHETIC NERVOUS SYSTEM

- Cell bodies of preganlionic sympathetic fibers are located on the intermedia lateral column of thoracic & upper lumbar spinal cord
- Fibers from these nucleus emerge out through respective spinal nerves from ventral root of the spinal cord.
- Short fibres of pre ganglionic system synapse with autonomic ganglia.

SYMPATHETIC TRUNK

- Composed of chain ganglia viz vertebral ganglia.
- This extends from upper cervical to coccygeal vertebrae.
- Sympathetic trunk is represented as a paired structure having a ganglion for each thoracic, lumbar, sacral & upper coccygeal nerve.
- Segmental ganglia in the cervical region is fused into three large ganglia (cranial cervical, middle cervical & caudal vertical ganglia)
- Stellate ganglion is the fusion of caudal cervical ganglia with upper two thoracic ganglia.
- Fibres from trunk composed of pre ganglionic & post ganglionic system.
- Sympathetic pre ganglionic fibers in thoracic cavity, neck , head, blood vessel and sweat glands synapse with vertebral ganglia.
- Those supplying abdominal and pelvic organs do not synapse within the vertebral ganglia
- But collateral ganglia are formed by the synapse formed by these pre ganglionic fibers with post ganglionic neurons.

FUNCTIONS OF SYMPATHETIC AND

PRASYMPATHETIC DIVISIONS

Effector organ	Sympathetic	Receptor	Parasympathetic
Heart S A node	Increased in heart rate	β_1	Decrease in heart rate
Atria	Increase contractility and conduction velocity	β_1	↓ contractility & conduction velocity
AV node and Conduction system	conduction velocity	β_1	↓ conduction velocity
Ventricles	contractility & conduction velocity	β_2	---
Arterioles Coronary, skeletal, Pulmonary, renal, Abdominal & skin	Vasoconstriction Dilatation	α β_2	Dilatation
Systemic veins	Constriction or Dilatation	α / β_2	---
Respiratory tract Bronchial muscles	Relaxation	β_2	Contraction
Bronchial	Inhibition?		Stimulation

glands			
Smooth muscles G. I. Tract	Decreased motility Sphincter constriction Inhibits secretion?	α, β_2 α	Increased motility Sphincter relaxation Stimulates secretion
Gall Bladder	Relaxation		Contraction
Urinary bladder Muscle Sphincter	Relaxation Contraction	β α	Constriction Relaxation
Ureters	Increase motility	α	Increase?
Uterus	Variable Contraction	α, β_2	Variable
Male Sex organs	Ejaculation	α	Erection
Sweat glands	Localised secretion		Generalised secretion
Secretions Salivary	Vasoconstriction Thick, viscous secretion	α	Copious and watery
Pancreatic	Decreased secretion $\downarrow$ insulin & glucagon secretion	α β	Increased secretion insulin & glucagon Secretion
Gastric	viscous		secretion

	secretion		
Juxtaglomerular cells	Increased renin secretion	β	--
Pineal gland	Increased melatonin secretion	β	--
Milk letdown	Inhibition		--
Ciliary muscle	Relaxation (far vision)	β	Constriction (near vision)
Pupillary muscle	Dilatation (dim light)		Constriction (bright light)
BMR	Increased		---

FUNCTIONS OF ANS

- Preserves cellular environment of animal to maintain homeostasis
- Sympathetic and para sympathetic system makes fine adjustments to rectify the effect of minor internal and external stress in a resting
- It involves specific reflex activities of an organ or a part of the organ.
- In stress, sympathetic systemic activity is modified. They involve accelerated response in whole of the visceral motor system
- Referred by Cannon as FIGHT OR FLIGHT RESPONSE
- This ends up in the immobilization of energy and reroute the circulation to vital organs for nutrients.
- Psychological modification evident in fight/flight response are due to sympathetic activity are
    - Increased Heart rate
    - Increased B.P
    - Vasocostrictor of blood vessels of skin and viscera
    - Vasodilatation and increase in blood supply to skeletal muscles
    - Spleenic contraction to increased oxygen carrying capacity of blood
    - Increased bronchodilation and vasodilatation of lung facilitate increased oxygen uptake and used up Carbondioxide release
    - Pupillary dilation to widen the visual receptivity
    - Piloerection to conserve body heat (calorigenic and glycogenic effect)
    - Muscle glycogenolysis and hepatic glycogenolysis (to some extent) to mobilze glucose to skeletal muscle for energy need.
    - Increased activity of many receptor organs to sense changes in homeostasis like mechanoceptors of skin and mesentery, muscle spindle response, gustatory and olfactory activity are evident.

    - Potentiated by adrenal medullary involvement as an autonomical counterpart - sympathetic adrenal system
- Parasympathetic system plays an important role in co-coordinating specific functions of digestive tract.

REFLEX ACTIVITIES OF AUTONOMIC NERVOUS SYSTEM

Autonomic reflexes

- These reflexes arc, similar to somatic reflex arc have
    - Sensory part
    - Motor part.
- Visceral sensory fibers enter the dorsal horn of spinal cord, branching into spinal sensory column.
- They employ interneurons.
- Interneurons transmit impulses to the preganglionic neurons in the spinal cord or to the brain stem.
- <liEfferent part represented by preganglionic axon to carry the visceral motor stimuli to ganglionic cell.</li
- Post ganglionic axons innervate visceral effectors.
- Examples of Autonomic reflexes are
    - Peristaltic reflex and
    - Micturition reflex.

Peristaltic reflex

- Peristalsis is the motor activity of the intestinal musculature to cause onward propulsion of the contents.
    - Sensory information by way of stretching of the wall.
    - This intum stimulates intra mural sensory neurons.
    - Sensory neuron either directly or through interneuron synapse with Post ganglionic parasympathetic neuron.
    - This reflex is unique, that it can be seen in isolated preparatious also and is known as a type of Extra spinal reflex.
    - In normal animals, this reflex has an additional influence from brain stem.
    - Control is mediated through preganglionic vagal, pelvic nerves.

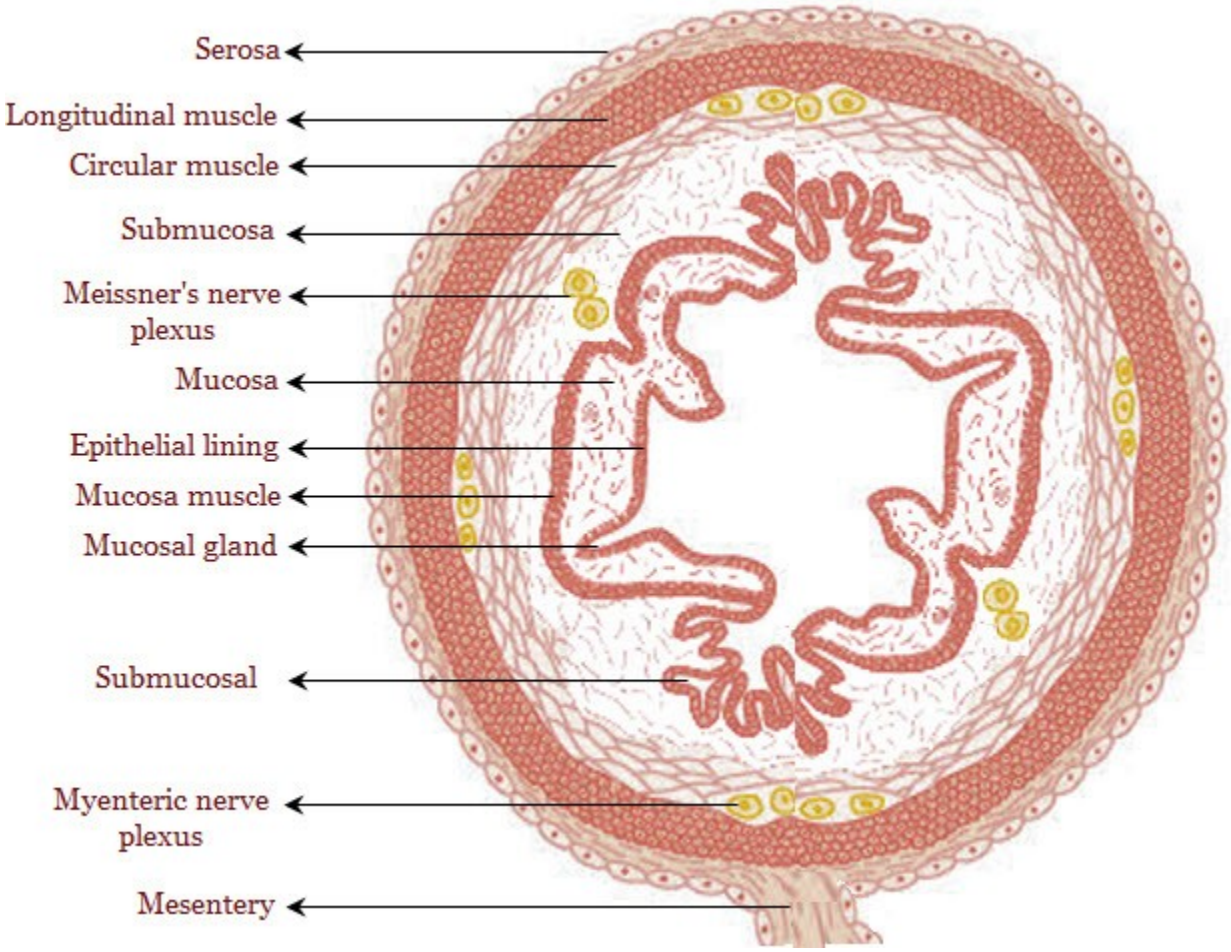
Micturition Reflex

- Act of voiding urine is known as micturition.
- It is a reflex act, under the control of higher centres.
- But the uniqueness is that this reflex persist even after the transection of the spinal cord.
- This reflex involves stretch receptors of the bladder wall, primary axons of cell bodies in the sacral spinal segment and dorsal grey column of sacral segments.
- The urinary bladder is the storage component and allows urine to be accumulated.
- Contractions of the smooth muscles in the walls of renal pelvis and ureter by way of action potentials move down towards urinary bladder. The contractions are initiated by stretch and distension as a result of continued production of urine.
- This peristaltic activity is autonomous and myogenic.
- Junction of uretar and urinary bladder is not provided with any anatomical sphincter.
- There is a functional sphincter developed by the bladder muscle viz Detrusor muscle.
- The functional sphincter act as a valve to prevent reflux of urine into ureter.

- The smooth muscle fibers of Detrusor muscle interlaces and converge at the urethral ori face.
- It allows the bladder as a leak proof compartment while it is filling, that is as the bladder expands , the neck of the bladder at the level of urethra constricts due to the convergence of smooth muscle fibers and vice versa as it relaxes.
- Detrusor muscle is controlled primarily by parasympathetic and sympathetic innervation.
- Activity of Detrusor muscle in expulsion of urine is a reflex mechanism.
- This micturition reflex centre is located within the sacral spinal card and this centre is intum controlled by the brain stem and cerebral cortex.
- Filling of urinary bladder activate stretch receptors.
- Sensory neuron via pelvic nerve which has its cell bodies in the dorsal root ganglia of sacral spinal nerves.
- They employ inter neurons.
- Fibers take two routes from here, one is for local reflex and other passes to fasciculus gracilius to the nucleus gracilius of medulla.
- Some fibers through another set of interneurons synapse with spinothalamic tract.
- Thus, information about the stretch reaches medulla / brainstem and also to cerebral cortex for conscious perception and voluntary emptying of the bladder.
- Motor pathway is mediated via pelvic nerves, whose cell bodies are in intermediate mucleus of the sacral spinal segment.
- When motor activity is initiated to contract the bladder Detrusor muscle, the neck of the bladder relaxes simultaneously with contracting of bladder wall allowing the urine to flow down.
- Pudental nerve serve as motor nerve to external urethral sphincter which is a skeletal muscle.
- As micturition reflex is in progress, the external urethral sphincter relaxes allowing voiding of urine.

ENTERIC NERVOUS SYSTEM

- Innervations are from sympathetic and parasympathetic divisions of ANS, which control on intramural plexus (myenteric/auerbach plexus and meissner's plexus)
- Intramural plexus made up of 10^8 neurons which is almost equal to number of neurons in spinal cord.
- Sympathetic division made of thoracolumbar outflow has got preganglionic cholinergic nerve fibres.
- They end upon coeliac ganglia , superior and inferior mesenteric ganglia or hypogastric plexus.
- From these ganglia, post ganglionic adrenergic nerve fibres arise these nerves end up on intramural plexus and bring about inhibitory action (secretion & motility reduced). Some branches of post sympathetic nerves end upon sphincters and when sympathetic is stimulated it will inhibit the myenteric plexus in sphincters. As a result sphincters relax-defaecation occurs.
- Inhibitory action includes reduced glandular secretion, reduced blood supply (constricted blood vessel), reduced motility, (when there is sympathetic dominance).
- Parasympathetic outflow is from cranio sacral division (3,7,9,10 cranial nerves and sacral) has got preganglionic cholinergic nerves which are long enough to reach intramural plexus (ganglia).

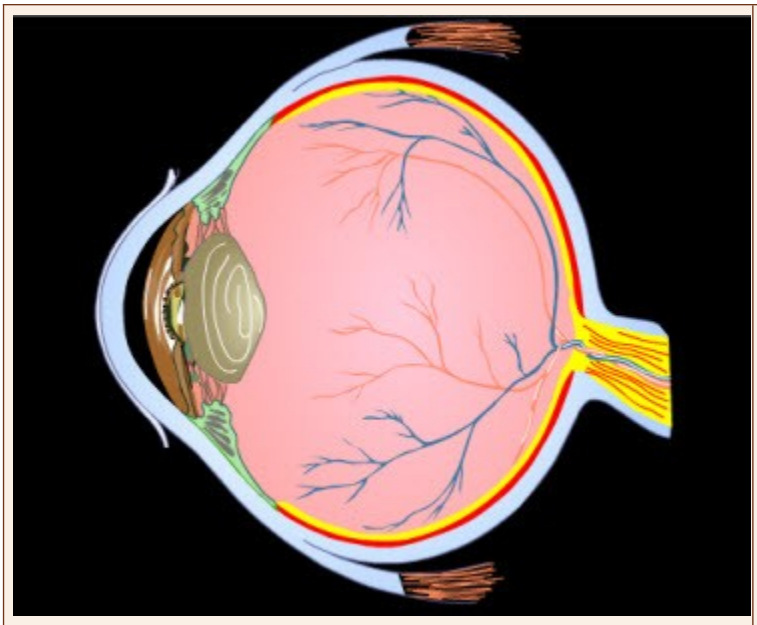


- The post ganglonic parasympathetic nervous system arise from these ganglia and thus are present within the structure or organ.
- Post ganglionic PSNS use Acetyl choline as neurotransmitter .
- Post ganglonic SNS use Nor epinenephrine as neurotransmitter.
- Sympathetic stimulation decreases GI function and Parasympathetic stimulation increases GI function.
- Organo phosphorous compounds are parasympathomimetics.
- In case of Organophosphorous poisoning in animals, there will be excess salivation, shooting of diarrhoea, body temperature is reduced.
- Sympathetic post ganglonic nerves act on neural circuits in the intra mural plexus that provide signals to smooth muscles of GI tract.
- Intramural (intrinsic) plexus can control much of the coordinated activity in the absence of extrinsic innervation of GI tract.
- Parasympathetic nervous division (Vagus and Sacral spinalcord outflow) with their cholinergic preganglionic fibres act up on intramural plexus (i.e. Intramural plexus act as ganglia for preganglionic PSNS).
- From intramural plexus, postganglionic nerves arise which are seen within the structure of innervation. On stimulation motor and sensory activities are improved.
- There are local and central reflex pathways that affect the functioning of GI tract organs.
- Meissners plexus contains neurons with are intimately attached with circular muscles and glands and blood vessels of GI tract (Synaptic cleft is very much shortened). The neurons of their synaptic cleft is widened. So it takes more time for axon potential to reach post synaptic structure. The circular muscles of GI tract contract ahead of

longitudinal muscles as a result gut becomes longer and thinner. When longitudinal muscles contract, gut becomes shorter and wider. Preganglionic parasympathetic nerves sometimes get innervations from post ganglionic sym nerves and adrenoreceptors are present on both pre or post ganglionic sympathetic nerves and α_1 adrenoceptors are present on both pre and post ganglionic PSNS. In such cases Ach (acetyl choline) will not be discharged thereby Parasympathetic activity getting reduced. NE (norepinephrine) inhibits Ach release through its interference via α_1 adrenoceptors on axon terminals of PSNS.

- Atropine is the cheapest and effective antidote for OP (Organo phosphorous) poisoning. (Atropin- from Atropa belladonna)
- In OP poisoning -excess PSNS dominance.
- Atropine inhibits Ach to occupy post synaptic membrane receptors. In these two ways (ie NEP and Atropine) the vagal refex can be controlled.
- The Vagovagal reflex (generally is stimulating in nature (i.e. Increase motility, secretory and vasodilatory) carries both afferent and efferent through vagus, whereas only ENS is independent of CNS generally inhibitory involving only ENS and is intestine intestinal reflex is generally inhibitory involving only ENS and is independent of CNS.
- Central reflex pathway eg. Vagovagal reflex.
- Local reflex pathway eg. intestino intestinal reflex.
- Most of the reflexes are mediated by Ach and NE There are other neuromodulatory substances/neuro transmittors which include enkephalins, 5-hydrooxytryptophan (5HT), cholecystokinin (CCK), glycine, motilin, angiotensin, secretin, galanin, somatostatin, VIP (vasoactive intestinal polypeptide), substance-P, GABA, bombesin, gastrin, histamine, GRP (Gastrin releasing polypeptide) PG (Prostaglandin), GIP (Gastrin inhibitory polypeptide), enteroglucagon etc. Out of these, 7 are produced from enteroendocrine cells whereas others are produced from gut cells as well as from nerve endings, so called brain gut peptides.
- The chief neurotransmitters of ENS are Ach , NEP, enkaphalin (or opioid compounds) and VIP (Vasoactive intestinal peptide).
- Enkephalins decreases gastro intestinal motility by inhibiting release of Ach.
- VIP acts directly on smooth muscles to cause muscle relaxation. It is localised with cholinergic nerves in vagus.
- VIP is in local neurons (ENS) and is released when vagal fibres excite these inhibitory neurons to cause relaxation.
- Enkephalins, VIP, nitric oxide (NO-only gaseous neuro transmitter) serotonin are all neurotransmitters produced by specialised neurons which are localized along with Ach or NEP secreting neurons in ANS.
- Depending on the nerve, whenever Ach or NEP are released, these neurons release their neurotransmitters.

MODULE-13: PHYSIOLOGY OF VISION



LEARNING OBJECTIVES

At the end of this module, the learner will be able to understand,

- the structure of the eye,
- the visual cycle and photoreceptor functions,
- the theory of vision and types of vision and
- the Accommodation of eye and problems in vision.

PHYSIOLOGICAL ANATOMY OF EYE

SCLERA	Covering of the eye – Protective in function, Tough in nature.
CORNEA (stratified squamous)	Transparent Structure, anterior modification of sclera.
CHOROID	Vascular and Pigmented area of sclera in its posterior part.

RETINA	Innerside of choroid, has PHOTORECEPTORS.
DARK PIGMENT	Animal with day light vision, to absorb light which has to pass receptor without stimulating, present between CHOROID and PHOTORECEPTORS.
TAPETUM	Causes nightshine in nocturnal animal by reflecting the light viz REFLECTING PIGMENT. (allows use of optimum light by retina)
LENS	Causes accomadation, made up of elastic capsule filled with jelly like substance, suspended by suspensory ligament.
SUSPENSORY LIGAMENT	Muscular structure connecting lens and ciliary body.
CILIARY BODY	Convexity of the lens is altered to focus the images of varying distance and is achieved by ciliary muscles and its contraction increases convexity and focusses near objects.
ANTERIOR CHAMBER	Between CORNEA and LENS
POSTERIOR CHAMBER	Between IRIS and Suspensory Ligament
AQUEOUS HUMOR	clear watery fluid, from ciliary processes of ciliary body in the posterior chamber, flows through PUPIL to anterior chamber. Absorbed into veins, passes through CORNEA and IRIS. Accumulation of aqueous humor due to obstruction in absorption causes increased intraoccular pressure viz GLAUCOMA.

IRIS	Diaphragm separating Anterior and Posterior chambers. Pigmented structure has dilator and constrictor muscles (smooth)
PUPIL	Hole in the Iris, whose diameter can be modified by smooth muscles and allows the varying intensity of light to strike retina
VITREOUS HUMOR	HYDROGEL with mucopolysaccharide, hyaluronic acid and collagen fibers filling the chamber behind IRIS, nourishes retina.
NEURAL RETINA	Present behind vitreous humour.
OPTIC DISK	Area where axons of retinal ganglia passes to brain. Has optic nerve (cranial nerve), arteries and veins. Nutrition of retina is taken care by CHOROID VESSELS.
LACRIMAL GLANDS	Production of tears from this, near lateral canthus. Parasympathetic stimulation ends in tears and are drained into nose by NASO-LACRIMAL DUCT.
NICTITATING MEMBRANE	3 EYE LID, Present in medial carithus, protects eye and also produce tears.
HARDERIAN GLANDS	Lacrimal gland, absent in carnivores, found in birds and mammals.

RETINA

RETINA	Has 5 cell types,

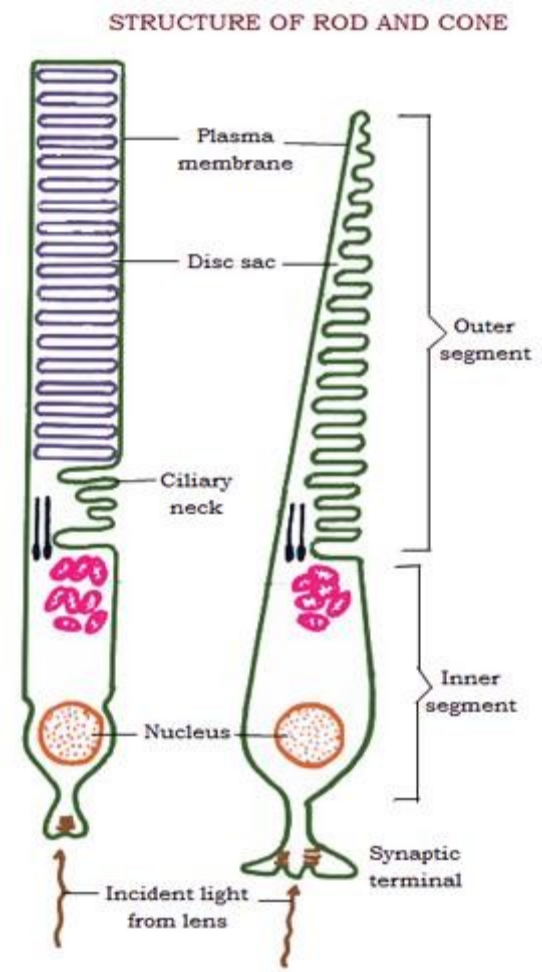
(part of CNS)	• Photoreceptor cells has two types RODS, CONES. • BIPOLAR CELLS with INTERNEURONS – Connects rods and cones with ganglion cells by synapsing. • GANGLION CELLS : Ganglion cell layer-single layer of multipolar ganglion cells with scattered neuroglia cells with some blood vessels. ◦ Transparent and Unmyelinated carry impulses to brain via optic nerve. • AMACRINE CELLS and HORIZONTAL CELLS : are interneurons lie between the bipolar and the ganglion cells. • The light has to pass all the other layers like the nerve fibre layer, ganglion cell layer, etc., to reach the layer of rods and cones.
FOVEA	• Area present in the back of the retina – Light rays are not distorted in this area, devoid of ganglion and bipolar cells. • Light rays directly fall on retinal photoreceptors. Provides sharp visual image. • FOVEA IS ABSENT IN DOMESTIC ANIMALS.
CONES	• They are present in dense in the central portion of the retina - (in primates) cones are best in day light – PHOTOPIC VISION. • They are color sensitive. • Similarly to fovea more no. of cones are present in MACULA or CENTRALIS in other animals.
RODS	• Extremly sensitive to light, present in the periphery of retina.

	• Responsible for NIGHT/SCOTOPIC vision, Sensitive to blue – green light.
BLIND SPOT	• No photoreceptors at the origin of optic disk which is viz Blind spot.(Free from Rods and cones).

STRUCTURE OF RODS AND CONES

Rods and cones have 3 parts

- *Outer segment* – Photoreceptor part, has stacked membrane discs with VISUAL PHOTOPIGMENTS.
- *Inner segment* – Has nucleus, mitochondria and cytoplasm.
- *Synaptic Termial* – Synapse with bipolar cells.



BIOCHEMISTRY OF RODS AND CONES

- Photosensitive pigment – *rhodopsin / visual purple :* Present in rods
- Made up of proteins viz *opsins*

- In Rods it is called *scotopsin* which consist of an aldehyde of vitamin A called *retinal*.
- As light strikes, Rhodopsin is transformend from CIS to TRANS and by hydrolysis, gets splits into scotopsin and retinal.
- Retinal is enzymatically changed into retinol (alcholic form) and is stored as retinyl ester in the pigment cell
- Stability of rhodopsin and its functions depends on the presence of CIS form of vitamin A. Formation of Rhodopsin is continuous, in the presence of Isomerase, retinal joins with scotopsin to form rhodopsin.
- During night/darkness- rhodopsin accumulates in rods, and have maximum sensitivity to light, this is known as *dark adaptation*. When exposed to light concentration of Rhodopsin decreases in rods and so rods become insensitive to light and the vision is caused by cone stimulation known as *light adaptation*. A vitaminosis causes night blindness viz nictalopia.
- *Cones:* Colour sensitive photoreceptor responsive for day vision photopigment in cones are IODOPSIN consists of opsin and RETINAL IODOPSIN varies from SCOTOSIN, in their protein part.
- Cone opsins are of 3 types
    - Blue cone (430 nm)
    - Green cone (535 nm)
    - Red cone (575 nm)
- Difference cones respond to different wavelength. The primary colours are specific with cone. Various colour sensation are made possible by the combination of different cones. Colour blindness endup is due to lack of different cones.
- Domestic animals has more rods and birds have more cones.
- *ELECTRO RETINOGRAM – ERG :* Recording of electrical changes in the retina by flashing the light. Has 3 waves a,b and c;
- a wave : originates from rods and cones.
- b wave: from glial cells, Amacrine and bipolar cells.
- c wave: from Pigment epithelium.

PHOTO TRANSDUCTION

- The light falls on the retina by the adjusting the refractive media of the eye.
- As the light falls on the retina, the rods and cones absorb energy and convert it into electrical signal.
- The rods and cones are located at the back of the retina synapse with bipolar cells which in turn synapse with the ganglion cells.
- Many rods cells synapse with single bipolar cell and many bipolar cells synapse with single ganglion cell.
- The rods provide hazy images, but the visual field is much larger.
- Each cone synapse with single bipolar cell and single bipolar cell synapse with single ganglion cell. Thus cone provide very fine detailed image of the object, but the receptive field of a cone photoreceptor is very small.
- The receptive fields of ganglion cells contain both ‘on’ and ‘off’ regions. In both regions, the 11-cis retinal is converted to all-trans retinal when the light activates the photoreceptors.
- The all-trans retinal in turn activates transducin, a G-protein which decreases the cGMP found inside the photoreceptor cell. As the cGMP is decreased it closes the Na+ channel, thereby hyperpolarizing the cell.
- The hyperpolarized cell releases neurotransmitter, the glutamate. The activity of the glutamate determines the ‘on’ and ‘off’ region of the receptive field.

- The glutamate depolarizes the bipolar cells, which synapse with the 'on' region photoreceptor and increases neurotransmitter release from the bipolar cell which in turn depolarizes the ganglionic cell.
- The glutamate hyperpolarizes the bipolar cells, which synapse with 'off' region photoreceptor, and decreases the neurotransmitter release from bipolar cell, which causes hyperpolarization in the ganglion cell.
- The complex receptive fields of ganglion cells improve the ability to detect the difference between light and dark. When both the receptive fields of the ganglion cell are exposed to light, both 'on' and 'off' regions are activated and result in weak stimulation.
- The horizontal cells enhance the contrast through lateral inhibition of the bipolar cells. The lateral inhibition increases contrast, sharpen borders and edges as it is excited strongly when the light is focussed on the 'on' region photoreceptors. Another step in increasing the integration of the image is by the synapsing of the bipolar cells with amacrine cells via gap junctions.
- It modifies the inputs from many bipolar cells and alters the neurotransmitter release in to the ganglion cell.

MECHANISM OF PHOTORECEPTION

- As the light strikes the photoreceptors, transformation of photo pigment occurs with the resultant HYPERPOLARIZATION of receptor cells.
- During darkness, the Na^+ channel are opened / remain open on rod and cone cell membrane.
- Na^+ leak into rods and lower the membrane potential. As light strikes the rods retinal is released from rhodopsin and causes closure of many Na^+ channels.
- This causes HYPERPOLARIZATION of the receptor cell membrane and a decrese in the transmitter released at the synapse with the bipolar cells.
- Breakage of rhodopsin to RETINAL + OPSIN by light is temporary and Rhodopsin is resynthesized afterwork.

Activity of photoreceptors

In dark

- The cell membrane of the photoreceptors contains chemical messenger-gated Na^+ channels. They respond to the second messenger cGMP.
- The Na^+ channels are open when the cGMP is bound to them. In absence of light, the concentration of cGMP is high; therefore it is bound with the Na^+ channels, keeping them open.
- The inward leak of the Na^+ ions depolarizes the photoreceptors. This in turn keeps the Ca^{2+} channels opened, which triggers the release of the neurotransmitter from synaptic terminal.

In Light

- There are other biochemical cascades that take place in the light. The concentration of the cGMP is reduced.
- The reduction in cGMP is by the cascades as follows: The retinene absorbs light and changes the conformation and activates the photopigment.
- The rods and cones contain G-protein called transducin, activates the enzyme phosphodiesterase. which degrades the cGMP causes the closure of Na^+ channels. As the Na^+channels closes, the photoreceptor cell gets hyperpolarized which in turn reduced the release of neurotransmitter.

VISUAL PATHWAY

- Hyperpolarization of rods and cones alter the activity of bipolar cells.
- Impulse frequency of ganglion cells too get altered.
- Horizontal cells influence Bipolar cells, Amacrine cells influence ganglion cells to detect contrast and contour.
- Axons of ganglion cells project as OPTIC NERVE to the lateral geniculate nucleus of THALAMUS (visual relay area) and the cells of this area project to VISUAL CORTEX (The Occipital Lobe)
- Axons of ganglion cell travel with optic nerve to optic Chiasma where crossing of right and left optic nerve occurs. So they travel to the respective side of lateral geniculate body. Images from left field is perceived at right visual cortex and right field is perceived at left visual cortex.
- Few fibers of optic nerve ends in the Superior Colliculi of mid brain and pretectal nucleus of the brainstem for Reflex activity.

TYPES OF VISION

Monocular or periscopic

- Laterally placed eyes (frog and reptiles) viewing the object independently due to wide visual angle between optic axis and mid line of the eye.

Binocular vision

- Anterio laterally placed eyes (primates, carnivores, birds), both the eyes view the same object simultaneously, overlap of field of vision due to parallel optic axis and mid line of the eye.

Stereo vision

- Anteriorly placed eyes (cats) Dissimilarity in viewing the object by left and right eyes, three dimensional view due to very small angle between optic axis and mid line of the eye, fusion of the image by the visual centre.

ACCOMMODATION OF THE EYE

- Ability of the eye lens to change its focal length by changing its radius of curvature.
- In near vision contraction of ciliary muscels causes decreased tension to the suspensory ligament and causes bulging of the anterior curvature of the eye.
- To cause distant vision ciliary muscles are relaxed and causes increased tension of the suspensory ligament which flattens the anterior curvature of the eye.
- *Presbopia :* It is the gradual loss in the power of accommodation of eye lens due to aging.
- *Refraction errors :* Inability of the eye lens to adjust its focal length.

- *Myopia (short sight) :* Due to abnormal increase in the anterior – posterior diameter, image fall just before the retina
- *Hypermetropia (long sight) :* Due to reduction in the anterior-posterior diameter, image fall just behind the retina

- *Astigmatism :* No common point of focus due to difference in the radius of curvature of cornea, overlapping of images.

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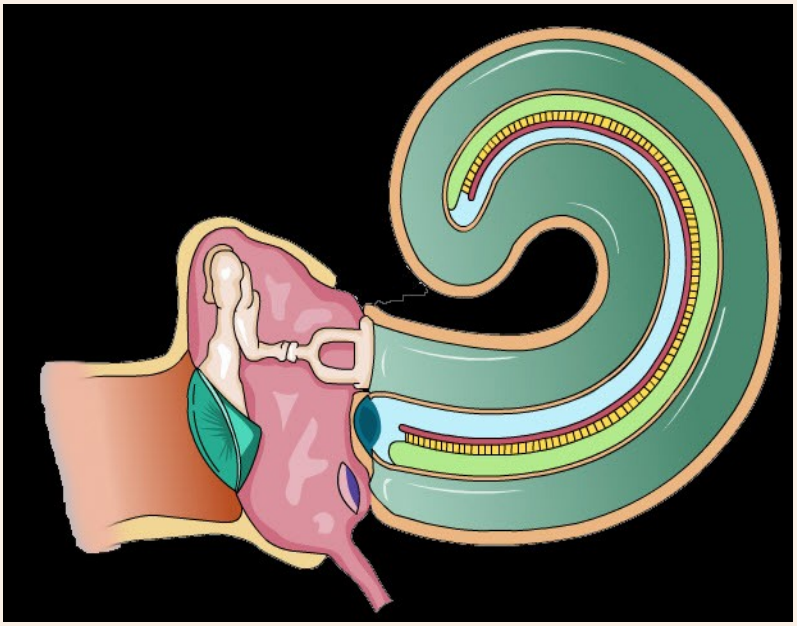
MODULE-14: PHYSIOLOGY OF HEARING, OLFACTION AND TASTE



LEARNING OBJECTIVES

This module enable the learner to appreciate,

- the structure of the ear,
- the mechanism of hearing and the auditory pathway,
- the major component of olfactory system and basic mechanism of the sense of smell and
- the basic structure of taste buds and the gustatory pathway.

HEARING

Auditory apparatus

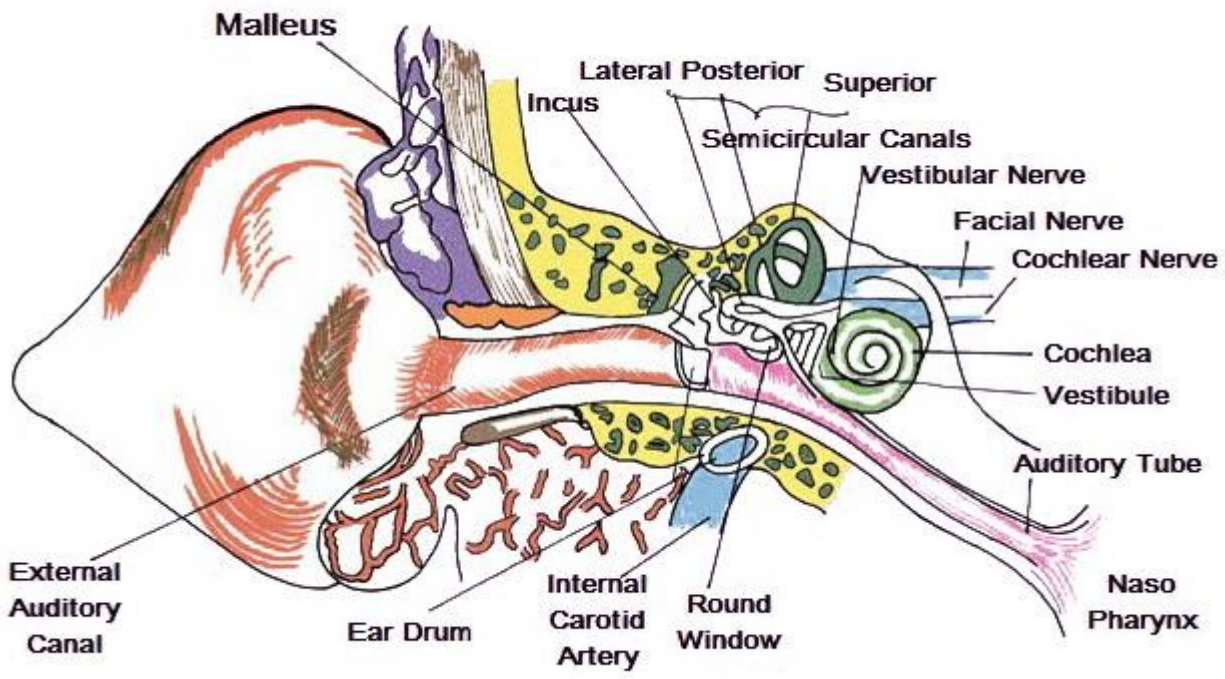
- The sense of hearing is the process of detecting and interpretation of sound waves.
- It is done by the organ called as the ears.
- The ear consists of three parts: The outer ear, middle ear, and inner ear.
- The outer ear is of the external pinna and the auditory canal.

- The pinna is of different shape and sizes in various species of animals and helps in focussing the sound waves to the auditory canal.
- The auditory canal conducts the sound waves into the middle ear. It is lined by waxy secretion called as cerumen. This filters the air entering the ear to avoid infections.
- There is a separation between the outer ear and the middle ear called as the tympanic membrane or commonly called as the ear drum.
- The ear drum transfers the sound waves to the vibrations which are conducted towards the inner ear by the middle ear.
- The middle ear consists of the ear ossicles. The ear ossicles are bony structures namely malleus (hammer), incus (anvil), and stapes (stirrup). They conduct the vibrations toward the inner ear.

VIEW ANIMATION...

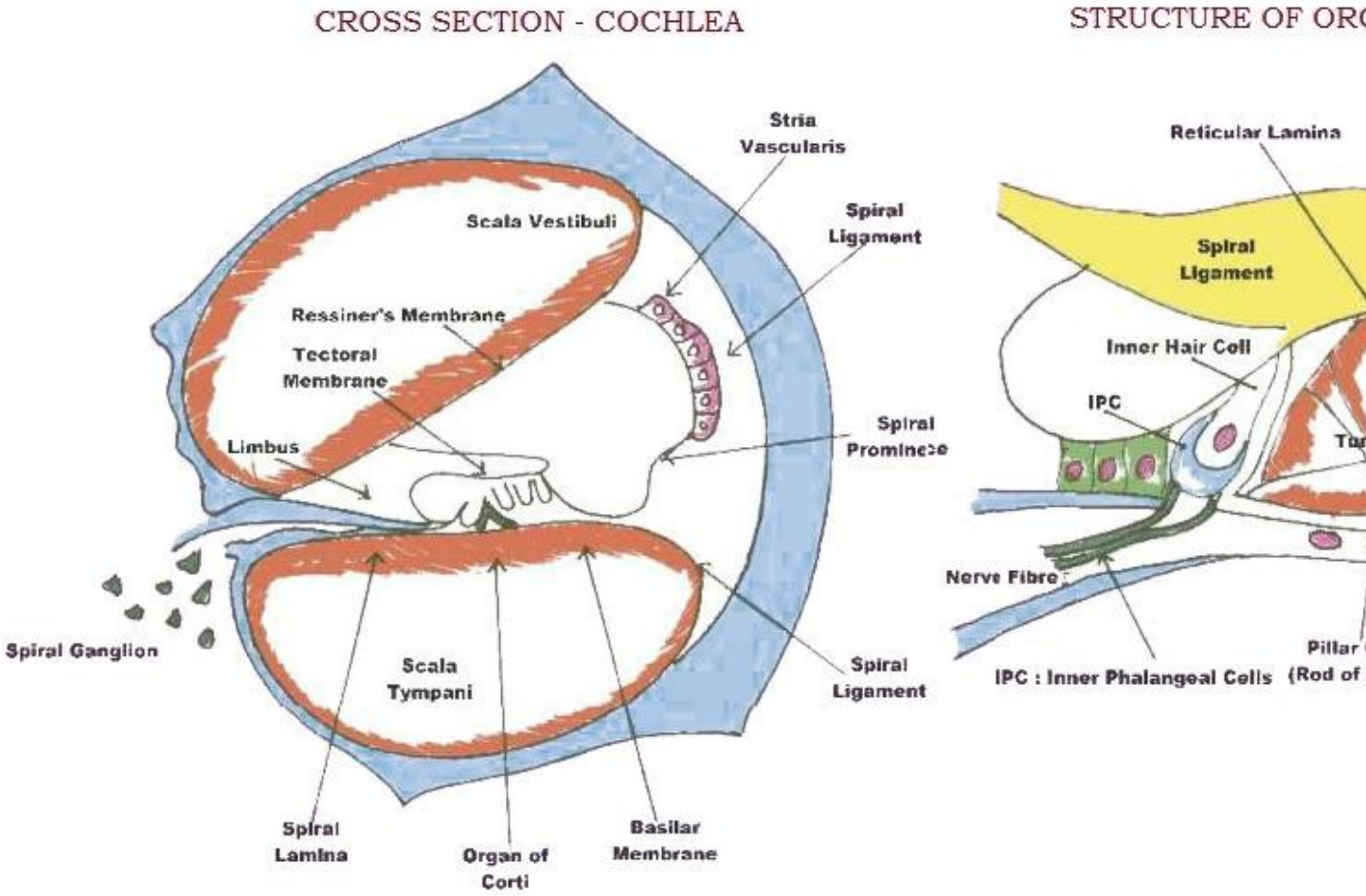
- These ear ossicles are connected in a way to amplify the sound waves to evoke or stimulate the hair cells of the inner ear.

STRUCTURE OF EAR



- The middle ear and the inner ear is separated by the oval window
- The inner ear consists of fluid filled membranous sacs and canals.
- The whole inner ear is covered by a fluid perilymph.
- The inner ear has both vestibular apparatus, which is the organ of equilibrium and hearing apparatus.

- The hearing apparatus is the coiled tubular structure called as the cochlea.
- The cochlea is replaced by cochlear duct in birds, which is the hearing apparatus and it is small in size.
- The cochlea is filled with a fluid known as endolymph, which has high K+ concentration than the Na+ concentration.
- The cochlea is formed by the coiling of three fluid-filled tubes known as *scala vestibuli*, *scala media* (cochlear duct), and *scala tympani*.

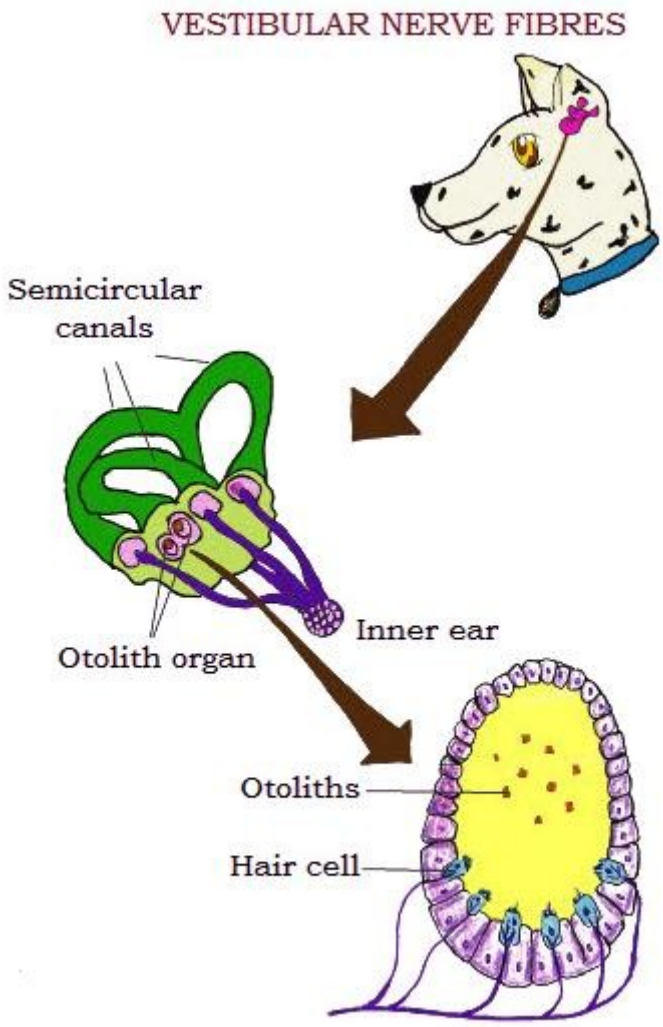


- The scala media is separated from the scala vestibubi by the *Ressiner's membrane* or *vestibular membrane*, while the scala media is separated from the scala tympani by the*basilar membrane*.
- Along the floor of the scala media, on the basilar membrane lies the *hair cell* receptor system, the *Organ of Corti*.
- The basilar membrane of the cochlea consists of the real organ of hearing called as the Organ of Corti. It contains hair cells.
- The hair cells mainly are of two types: The inner hair cells and outer hair cells.
- The inner hair cells detect sounds and outer cells amplify the sound waves.
- The cochlea contains two fluid systems *perilymph* (similar in composition to extracellular fluid) is the fluid in the scala tympani and scala vestibuli and *endolymph* (similar to intracellular fluid) is the fluid in the scala media.
- The oval window is located at the proximal end of the scala vestibuli, and the round window is located at the proximal end of the scala tympani.
- The hair cells are modified epithelial cells and they synapse with the sensory neurons.

- The hair cells contain projections called as cilia. Among these, one cilium is much longer than the other and is present in one side and is named as kinocilium. The shorter cilia are called as stereocilia. These stereocilia are arranged in increasing order of size gradually till they reach the kinocilium.
- The stereocilia and kinocilium are interconnected with tip-links and acts as one unit.
- The hair cells present within a cupula, a gelatinous mass covering over the hair cells with the synapsing the sensory neurons are known as neuromast.
- These hair cells are present both for hearing as well as maintaining equilibrium.
- The hair cells, tectorial membrane and basilar membranes with *cochlear nerve* terminals form the *organ of Corti*.
- *Stereocilia* that project into the endolymph filled scala media. The tectorial membrane, the specialised flap of the basilar membrane, over hangs the cilia of the hair cells. The terminals of the cochlear nerve fibres synapse with the basal ends of each hair cell. The auditory impulses are transmitted through *vestibulo - cochlear nerve, (cranial nerve VIII)* to higher brain centres.

PROCESS OF HEARING

- The pinna concentrates the sound waves to the auditory canal which conducts the sound waves to the ear drum.
- The sound waves strike the ear drum causing it to vibrate. These vibrations are conducted by the ear ossicles to the inner ear through the oval window.
- The vibrations cause the perilymph to vibrate causing waves of that fluid. These waves push on the basilar membrane of the cochlea causing it to vibrate.
- The vibrations are transferred to the organ of Corti. Thereby the inner hair cells bend in response to the vibrations.
- The bending of the stereocilia causes opening of the ion channels and depolarize.
- The inner hair cells release glutamate as neurotransmitter, which excites the synapsing sensory neurons.
- This action potential is propagated via the auditory nerve.
- The neurons from each part of the basilar membrane synapse with neurons in particular area of the brain's auditory cortex. Since the tension of the basilar membrane differs from the centre and the periphery of the membrane, which in turn differs in frequency of the vibrations, the specific areas of the auditory cortex respond to particular frequencies. This phenomenon is known as place coding.
- The round window of the ear bulges outward in response to the increasing pressure in the inner ear thus avoiding backflow of the fluid and increasing the sound clarity.
- The outer hair cells change in shape in response to the sound waves.
- The outer hair cells depolarize just like the inner hair cells, but sends signal to voltage-sensitive motor protein unlike neurotransmitter release of the inner hair cells. This protein changes the shape of the outer hair cells.
- Due to the change in shape, the outer hair cells pull the basilar membrane and ending in increasing tension which in turn results in increased basilar membrane movement.
- Since basilar movement is related to the sound loudness, increased basilar membrane movement causes increase in the stimulus for the inner hair cells.
- The ears can also detect the location of the sound by perception of the brain about the time lag and sound intensity. In mammals, outer ear also helps to localize the sounds. But this is not efficient, so the animals move their head to localize the direction of the sound.



AUDITORY PATHWAY

View animation...

- The vestibulo cochlear nerve endup in the cochlear nucleus of the medulla.
- The impulses from here are transmitted to superior olivary nuclei, inferior colliculus and median geniculate body of thalamus.
- From thalamus it endsup in temporal lobe of cerebral cortex (auditory cortex)
- Temporal lobe sends efferent to limbic system for behavioural modification and to muscles of larynx for reflex vocalization.

OLFACTION

- It is defined as the detection of chemicals that are carried in the air. It is the sense of smell.
- The vertebrates have greater capacity in distinguishing the variety of odorants (chemicals detected by the olfactory system).

Olfactory system

- It comprises of the olfactory receptors, supporting cells, and basal cells.
- The supporting layer, Bowman' glands secrete mucus which covers the nasal passage.

- The basal cells are precursors for new olfactory receptors, which are replaced once in every two months.
- The olfactory receptors found in dogs are about 50 million in number.

Process

The olfactory system of the vertebrates is located in the roof of the nasal cavity.

- Olfaction starts when the odorant enters the nasal cavity and comes into contact with the mucus layer that lines the olfactory epithelium of the nose.
- These mucus contain odorant binding proteins which allow lipophilic odorants to dissolve in the aqueous mucus layer.
- The olfactory receptor cells are bipolar neurons where one end of the neuron ends in the olfactory epithelium and the other ends as a synaptic terminal with the neurons of the olfactory bulb of the brain.
- The olfactory receptor cells are covered by cilia which project into the nasal passage. These are non-motile, and contain odorant receptor proteins.
- The odorant receptor proteins are G-proteins. These proteins are of multigene family and contain many numbers of genes coding for odorant receptors. In mouse about 1000 potential odorant receptor genes have been identified.
- Each receptor expresses single receptor protein. Thereby the ability to distinguish even the slightest change in the odorants.
- As the odorant molecules bind with the receptor, the receptor undergoes conformational change that sends signals to the G-protein associated with it. The activated protein act through the adenylate cylase pathway and cause generator potential. There are also other mechanism of causing action potential like the IP3 pathway.
- If the depolarization is large enough, then the action potential is triggered which travel to the bipolar neuron. In this, the action potential moves toward the cell body and not away from it as in other motor neurons.
- The action potential is transmitted from the bipolar neuron to the synaptic terminal with the neurons of the olfactory bulb and they carry the information to the olfactory bulb.
- The olfactory bulb is a complex neural structure. It has a lining of ball-like neural junction known as glomeruli. Each glomerulus receives signals only from a single type of receptor cell. Thereby, these glomeruli act as smell files to sort out the type of smell of the odorant.
- The fibers leaving the olfactory bulb pass through two routes.
    - *Subcortical route:* It goes to the regions of the limbic system mainly to the medial sides of the temporal lobe which is concerned with olfaction and known as primary olfactory cortex. It includes hypothalamic involvement and coordinates smell with behavioral reactions.
    - *Thalamic-cortical route:* This route is important for conscious perception and fine discrimination of smell.
        - The odorants are cleared from the nasal passage very quickly and the olfactory system adapts quickly, so the sensitivity to the smell of a particular odorant diminishes after a short exposure to the smell. The odorants are cleared by enzymes named as odorant-clearing enzymes. They resemble the detoxification enzymes in liver.

Pheromone

- It is a chemical that causes a natural behavioral response from the another member of the same species (especially reproductive behaviour).
- These pheromones are detected by separate organ known as Vomeronasal organ. It is also known as Jacobson's organ. It is found on each side of the base of the nasal cavity near the nasal septum. A narrow tube is found between the vomeronasal organ and the

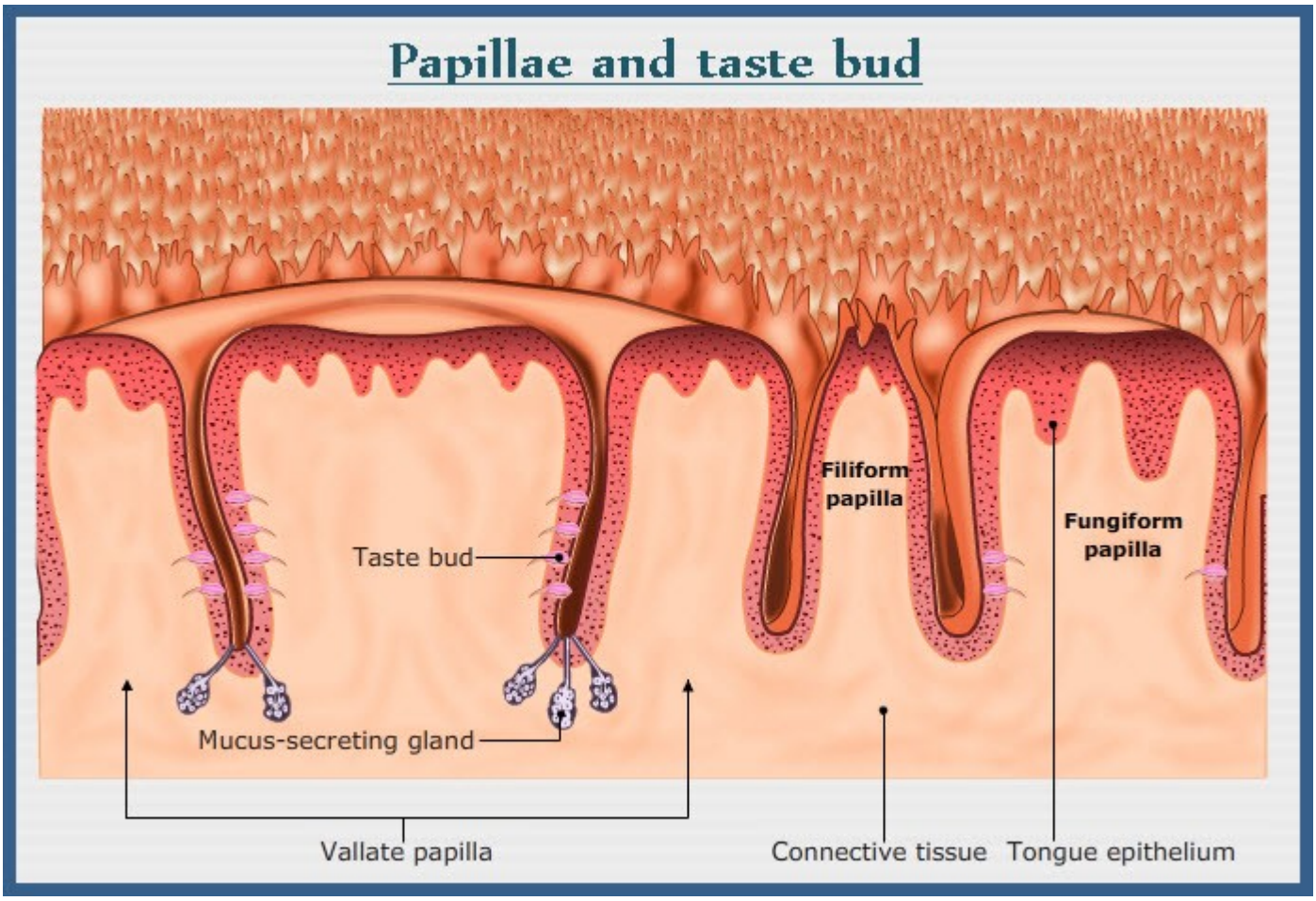
nasal cavity. The vomeronasal organ has receptors that act via the phospholipase C-based signal transduction.

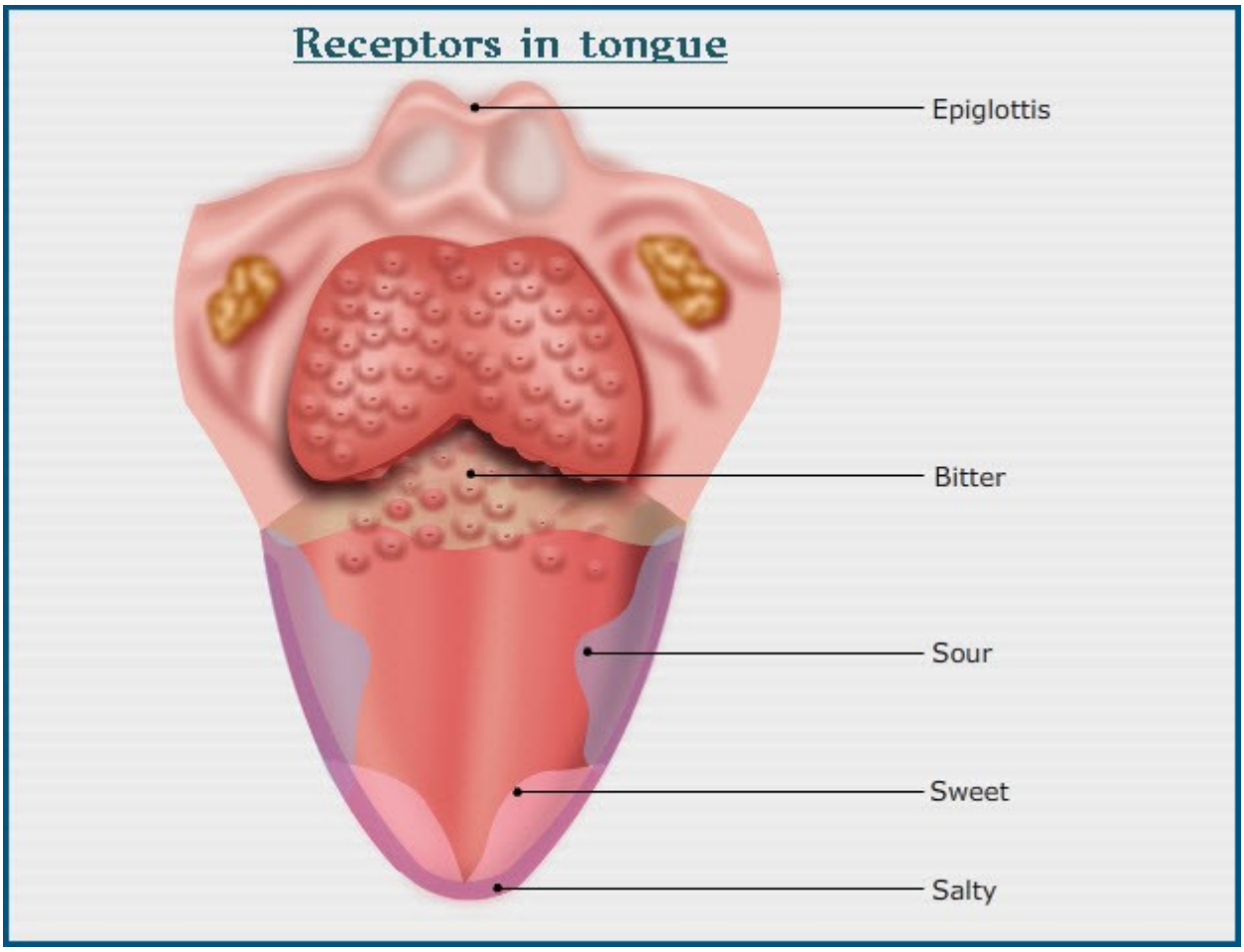
Variation in olfaction

- Animals differ in their ability to detect odours. Animals like dogs, are very sensitive in detection of odour and are called as macrosmatic; those that can detect odour but with less sensitivity like birds are termed microsmatic; those that lack olfactory apparatus like dolphins and whales are termed anosmic.
- Ungulates and rhesus monkeys detect the female in heat by the odour of the vaginal secretions. The olfactory system involved in maternal recognition, regulation of reproduction, mother-young interaction, establishment of dominance.

GUSTATION

- It is the process of detecting dissolved chemicals emitted from the ingested food. It is the sense of taste.
- This is carried out by receptor known as taste buds. There are almost 15,000 taste buds in the porcine oral cavity and throat, while 1 550 in the lizards, but only 24 in chickens.
- The taste buds are not able to discriminate between different molecules as olfactory system.
- Taste buds are onion shaped structure that contains numerous taste receptor cells. It has a pore that opens onto the surface where the tastants (chemicals from the food) enter and contact the receptors.
- On its apical surface, the taste bud has number of microvilli, which also contain receptors and ions channels to mediate taste signal.


Papillae and taste bud
Filiform papilla
Fungiform papilla
Taste bud
Mucus-secreting gland
Vallate papilla
Connective tissue
Tongue epithelium



TRANSDUCTION OF TASTE

- There are primarily five tastes like salty, sour, sweet, bitter, and umami. The salt taste is mainly due to the Na^+ ions. So the salty food causes opening of the Na^+ channels. The substance namely Amiloride inhibits the receptor channels and diminishes the salt sensation of the receptors.
- The sour taste is due to the H^+ ions in the food. The sour perception is done via the Na^+ channels, which are permeable to H^+ ions, but compete with them and so, it is done only in species which have less Na^+ ions in their saliva. In other animals, it is by acid-sensing ion channels. It causes opening of the Na^+ channels in response to the change in pH.
- The sweet perception is by the binding of the sweet substance to the G-protein which activates G-protein gustducin, which signals the adenylate cyclase pathway. High sweet containing substances also use IP3-mediated signal transduction.
- The umami is caused by L-glutamate and other amino acids present in the food. There are two different types of receptors. One resembles that of the glutamate receptor in the brain. When glutamate binds to the G-protein, it changes it conformation and releases phosphodiesterase enzyme that degrades cAMP to AMP and that causes increase in neurotransmitter release. The other receptor resembles that of the sweet perception.

- The bitter perception is complex and it is estimated that at least 25 genes code for bitter-taste receptors in human beings.
- Each taste receptor cell expresses more than one taste receptor protein. The taste receptors are not neurons instead they are epithelial cells which secrete neurotransmitter onto a primary afferent neuron. Single taste neurons synapse with more than one taste receptor cells. Olfaction and gustation work together closely and that is the reason why the taste perception is dependent on smell perception of an item.

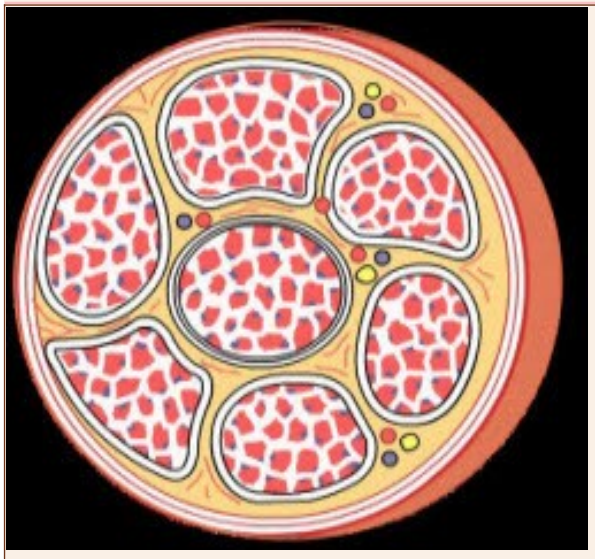
GUSTATORY PATHWAY

- Taste impulses from the anterior two third of the tongue pass through chorda tympani branch of the facial nerve, thence to nuclei tractus solitarius of the brain stem, while the posterior one-third sends the taste sensations through the glossopharyngeal nerve to nuclei tractus solitarius. Vagus receives the sensory inputs from the base of the tongue and other parts of the pharyngeal region.
- Thalamic area adjacent to ventrobasal complex receives the second order neurons from the nuclei tractus solitarius. The third order neurons originate from the thalamus to the lower tip of the post central gyrus in the parietal cortex, the gustatory cortex. Some of the third order neurons also project to the nearby opercular - insular area, located deep in the sylvian fissure.

Taste reflex

- Tractus solitarius transmits impulses to the superior, and the inferior salivatory nuclei, thus reflexly regulates the secretions of the submandibular, sublingual and the parotid glands.

MODULE-15: STRUCTURE OF MUSCLE, TYPES AND EXCITABILITY



LEARNING OBJECTIVES

- This module helps to,
  - explore the structure and types of muscles,
  - appreciate the ionic basis of muscle membrane potentials and
  - know about inner

	capabilities of muscle fibres and their compositions.

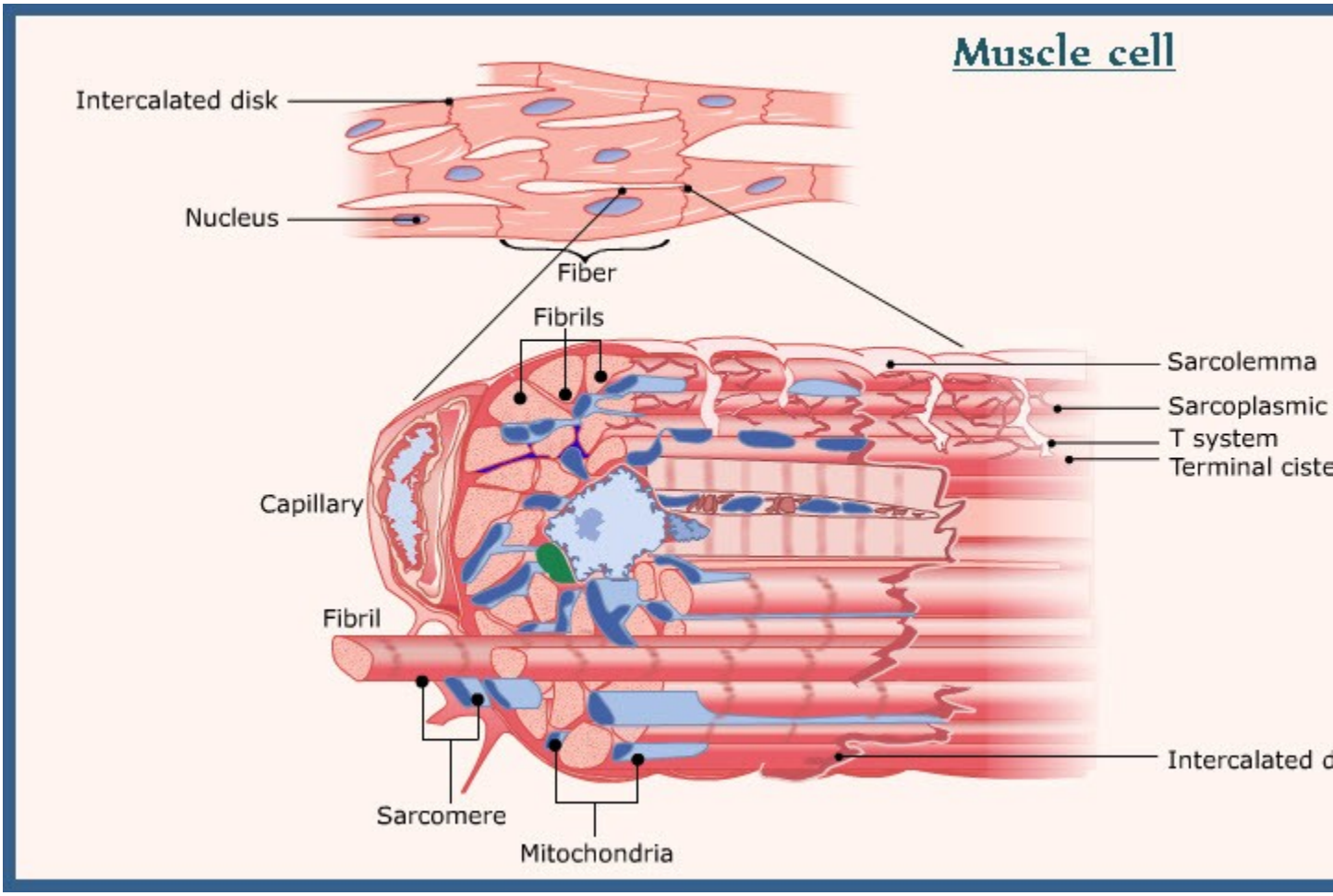
ELECTRON MICROSCOPIC STRUCTURE OF MUSCLE FIBRES

- *Myofibril*
  - Muscle fibres are made up of several hundred to several thousand of parallely arranged myofibrils having the special function of *contraction*. Each myofibril posses the contractile proteins *myosin (thick)* and *actin (thin) myofilaments* results in regular repetition of dark and light bands in the skeletal and cardiac muscles. Each muscle fibre contains about 1500 molecules of myosin and 3000 molecules of actin.
- *Myosin* is a large protein molecule composed of 6 polypeptide chains 2 of which are 100% α - helically exist. Well distinct Head with binding site for Actin and is equipped with ATPase system.They have Hinges to alter the position of the head. The twisted end show the tail.
- Properties of myosin molecular are
  - It has enzymatic ability to split ATP and release energy. Enzyme is myosin ATPase. **Actin and Mg^{2+} are required for activating these enzymes.**
  - Myosin binds with actin and the actin myosin complex is specifically dissociated by ATP.
  - Myosin spontaneously aggregates to form dimers which can aggregate again to form native thick filaments.
    - The active sites for the myosin ATPase are activity and the sites on myosin that bind to actin are both located in the heads of the myosin molecule and each of the myosin molecule has two such sites.
- *Actin:* much smaller molecule than myosin and contains only one polypeptide chain per molecule. Actins are found in aggregations which form a double stranded helical filament. It has been calculated that one thick filament contains around 500 myosin molecules and each thin filament contains 340-380 actin monomers.
- *Tropomyosin:* molecules are rod shaped they lie in the 2 grooves of the double stranded actin filament and aggregate end to end to produce two strands of tropomyosin running enter length of this filament.
- *Troponin:* More ellipsoidal or globular molecule, binds to a particular site on the tropomyosin molecule. Troponin has an important role as switch for muscle contraction. It has got 3 sub unit polypeptide chains called,
  - *Troponin – T* (This chain has site for attachment with tropomyosin)
  - *Troponin – I* (Inhibits the actin activated myosin ATP ase)
  - *Troponin – C* (binding sites (4 numbers) for Ca^{2+}).
    - Troponin – I attach not only with troponin C and T and but also with actin in the absence of Ca^{2+}. Troponin C attaches itself to Troponin T and I but not with actin.
    - The electron microscopic view of light bands indicates actin filaments represented as *"I" bands* because they are isotropic to polarised light.

- The dark bands of myosin is represented by "*A" Band*, which are anisotropic to polarised light. "H" zone represents partial overlapping the myosin filaments with actin filament. Small projections of myosin filaments called *cross-bridges* protrude out of the myosin filaments along the entire length except the very centre of the myosin filament.
- The centre of I bands contain a dark line called the "*z line*" or "z disc" where the ends of the actin filaments are attached. The z-discs are filamentous proteins, located in a vertical position in the myofibril. That portion of the myofibril between two successive z-discs is called as *"sarcomere"*. The sarcomere is the physiological contractile unit of muscle.
- *`H' Band* of the myofibril is a dark line seen at the centre of "A" band is rarely seen in normally functioning muscle. It is well marked only during relaxation beyond physiological limit.

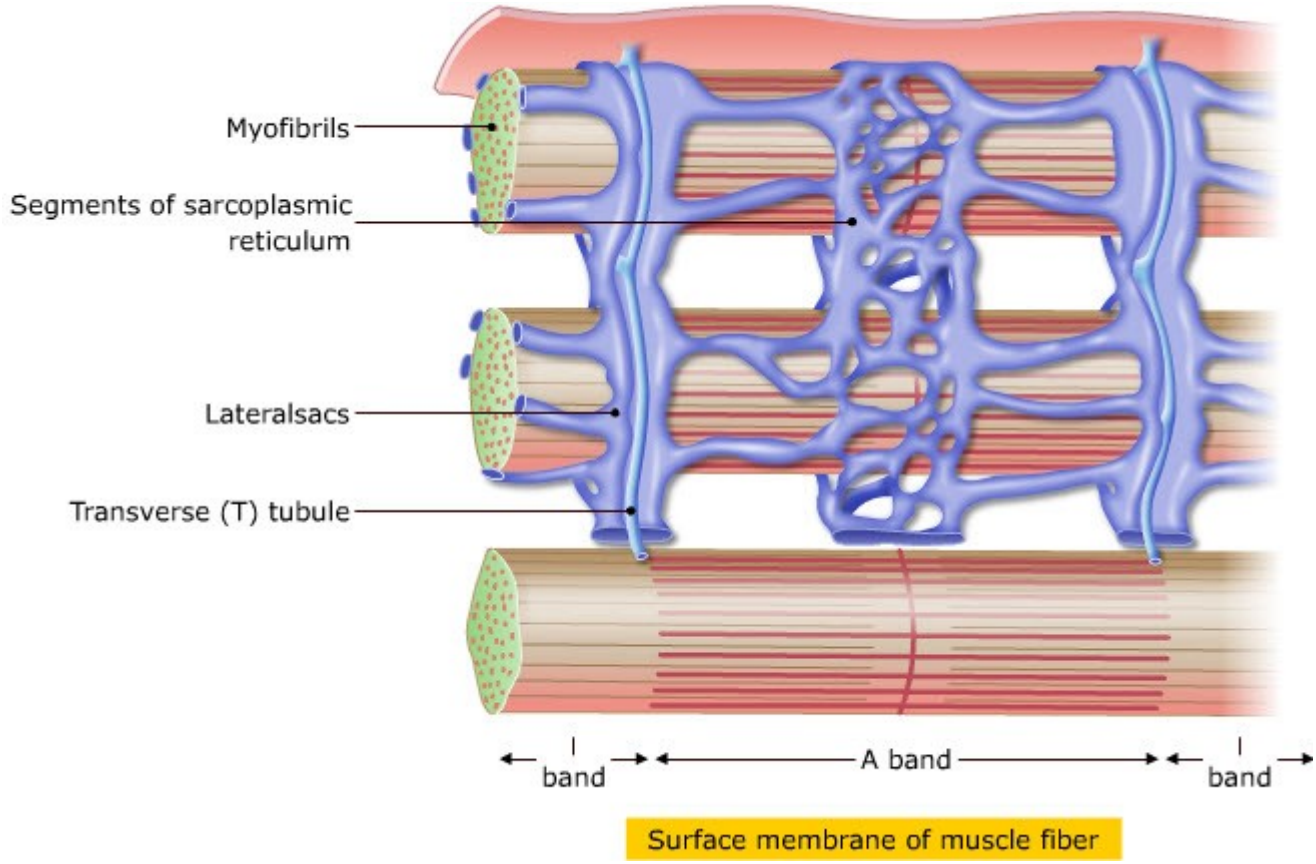
TYPES OF MUSCLES

- In mammal three kinds of muscles tissue are found
  - Skeletal muscles
    - Cross striated and attached to skeleton
    - 40% of the total body weight
    - Voluntary neural control.
  - Cardiac muscle
    - Cross striated
    - Involuntary in function
    - Under autonomic nervous system control.
    - Myofibrils are similar to skeletal muscle except at the point of "Z" line cardiac muscle forms Intercalated Disc which forms the muscular network of "Syncytium".
    - T tubular system is present at the level of Z line and not at the level of A and I bands.
    - Triads are simple due to ill developed sarco plasmic reticulum.
    - cardiac muscles have rich mitochondrial supply and many Ca-Na exchangers.
  - Smooth muscle
    - No cross striations found, poorly organized Actin and Myosin filaments.Ratio of Actin and Myosin is 15:1
    - Absence of Troponin complex.
    - Involuntary under ANS control
    - 10% of the total body weight
    - Found in the walls of blood vessels, lymph vessels, urinary tract, digestive, respiratory, reproductive organs and gizzard of chickens and turkey.
    - Exist as Multi unit and single unit muscle fibres.
    - Muscles cells, like neurons can be excited chemically, electrically and mechanically to produce an action potential that is transmitted along their cell membrane Sarcolemma. They contain contractile proteins which are activated by action potential.



STRUCTURE OF MUSCLE

- A muscle has an origin (less movable), belly and the insertion (highly movable) parts.Muscles are surrounded by a sheet of connective tissue called *epimysium* (site for fat deposition).
- From epimysium smaller sheets of connective tissue called *perimysium* arise and divide muscle into several small bundles. This perimysium contains blood vessels, nerves and muscles spindles. Perimysium envelopes a bundle of 50 to 200 fibres. At the end of each fibre, the sarcolemmal sheath fuses to form tendon fibre. Bundle of tendon fibres in turn forms the muscle tendon, which aids the attachment of the muscle into the bones. Each muscle fiber is enclosed by *endomycium* which is a fine sheet of connective tissue arising from perimysium.
- A muscles fiber is termed as a muscle cell- which is elongated tubular structure with tapering ends. Muscle cell is covered by the plasma membrane called *sarcolemma* (Gk: Sarkos – flesh). Each muscle cell is around 20-30 mm in length with a diameter of 10-100 µm. Length and diameter varies with exercise, plane of nutrition and maturity. In a muscle, the muscle fibers are arranged as number of muscle bundles known as "*fasciculus*".



Muscle cells can be grouped into 3 categories as per its metabolism

- *FG* cells (fast twitch glycolytic cells) – Type IIIb (white) – absent in canines
- *FOG* cells (fast twitch oxidative glycolytic cells) – Type IIa
- *SO* cells (slow twitch oxidative cells) – Type I (red)

Sub cellular components

- Muscle cell contains organelles like sarcolemma, nucleus, Golgi apparatus, lysosomes, mitochondria or sarcosomes, endoplasmic or sarcoplasmic reticulum, perioxisomes and ribosomes and myofibrils.
- *Sarcolemma* is about 70 – 100 nm in thickness composed of 60% proteins, 20% phospholipids, 15% cholesterol and 5% collagen fibrils, can propagate an action potential.
- Skeletal muscle cells are *multinucleated* and an average of 100 - 200 nuclei per cell. Because skeletal muscle cell in a mature muscle originates form fusion of 100 – 200 different embryonic muscle cells called myoblasts, with each myoblast contributing one nucleus. They lie peripherally just under sarcolemma in mature vertebrates skeletal muscle. Nuclei of skeletal muscle lack mitotic ability where as smooth and cardiac muscle cell contains only one nucleus, located in the interior of the cell.
- Cardiac muscles cells and FOG and SO types of skeletal muscle cells contains numerous mitochondria and they are concerned with aerobic metabolism for energy and are capable of prolonged and sustained contractions. FG skeletal muscle cells contain a low no of sarcosomes.
- Muscle cells contain small spherical glycogen granules which are numerous in cells of well fed rested animals than in muscle cells of starved or exhausted animals (1% of the muscle mass).

SARCOPLASM AND MYOFIBRIL

Sarcoplasm

- It is the fluid present inside each fibre in which the organelles like *sarcosomes* (mitochondria), sarcoplasmic reticulum and myofibril are suspended.
- Large number of sarcosomes is placed in between the myofibrils, indicates the large quantity of energy (ATP) requirement for the contraction of fibrils.
- Cytoplasm of the muscle cell is called sarcoplasm which contains myoglobin. It is an O_2 storage protein and has a higher affinity for O_2 than haemoglobin. Myoglobin binds with O_2 from oxygenated hemoglobin in the blood stream. This O_2 is used by mitochondria for aerobic metabolism. Oxygenated myoglobin is red in colour and myoglobin concentration varies from 1-4 mg/g in mammals.

Myofibrils

- *Myofibrils* which are elongated protein threads are the contractile organelles.
- They lie parallel with the long axis of the muscle cell. Myofibrils occasionally branch and this branching is a growth mechanism.
- Not covered by any membrane and are insoluble at the ionic strength of the sarcoplasm. 12 to 14 proteins have been identified in the myofibrils: Actin (15% by wt), Myosin(45%), Tropomyosin (4%), Troponin (4%), C- Protien (2.5%), Actinin (3%), M-Protein (3%), Creatine kinase(1%), Desmin (1%), Filamim (1%), Titin (10%), Nebulin (3%), Gelsolin (1%) and Para myosin (6.5%).
- Myofibrils are cross striated, i.e they consist of alternating light and dark bands – transversely striated.
- The dark band is anisotropic or birefringent called 'A' band. The light band is isotropic called 'I' band. The I band is bisected by a dark disc called 'Z' disc or 'Z' line. (The distance from 'Z' disc to next is called sarcomere and is 2.5 to 2.8 µm in resting mammalian muscle.
- During contraction the sarcomere length reduced to 2 or even to a maximum of 1.8m). A contractile unit of the myofibril is the sarcomere. In the middle of the dark A band there seen H zone or Hensons band.
- Myofibrils consist of two kinds of filaments – thick and thin in an interdigitating fashion. Thick filaments got double the thickness over thin filaments (14-16nm) and have a length of 1.5 µm. Thin filament got 1 µm length anchored to the Z disc.
- Thick filaments got cross bridge or protrusions projecting outside. Thick filament – myosin and thin filament – actin, tropomyosin and troponin. Z disc composed of actinin, actin and tropomyosin. 'M' line is present which is a transverse structure connecting thick filaments at their centre is made up of M protein and creatine kinase.

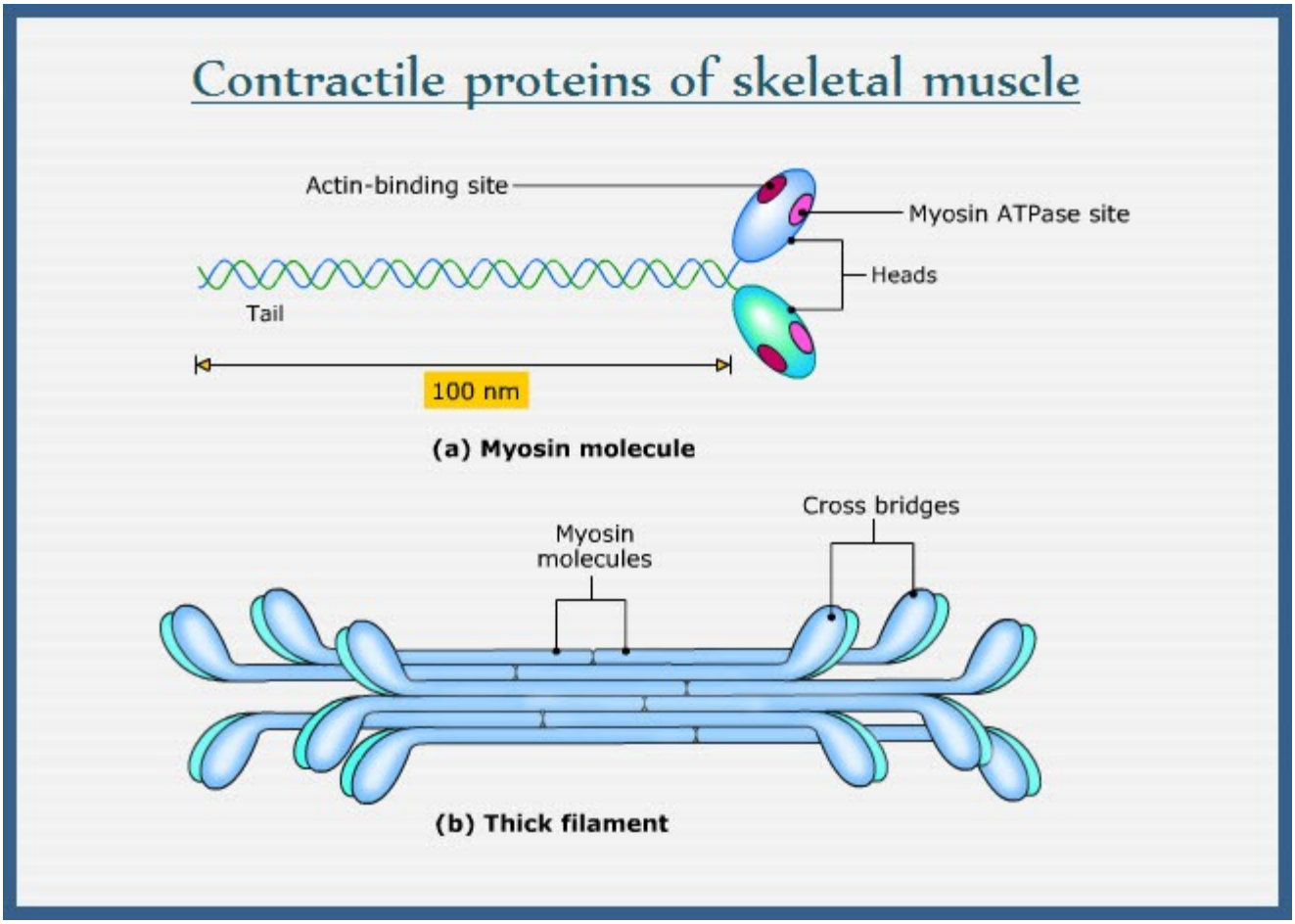
MYOSIN AND ACTIN FILAMENT

Myosin Filament (View animation)

- It is composed of multiple myosin molecules, each molecule having a molecular weight of 480,000. It has two polymerized portions, *Heavy meromyosin* and *Light meromyosin* . Heavy meromyosin is formed by HMM – S_1 and HMM – S_2 molecules.
- The myosin molecule is made up of six polypeptide chains: *2 heavy chains* and *4 light chains*. The two heavy chains wrap spirally around each other forming a double helix. At one end of these chains get folded into a globular structure called *myosin head*. Thus each myosin molecule has two free heads lying side by side at one end of the myosin molecule. Myosin head is made up of HMM – S_1 molecule, has ATPase activity and readily binds with the "G" actin. The elongated coiled portion of the myosin molecule is called*tail* formed by HMM – S_2 molecule has no ATPase activity and binding property

with "G" actin. Out of the 4 light chains, outer two are folded and form part of the myosin heads whereas the inner two form the tail and body.

- The heads of the myosin molecules hang outward to the sides of the body. Along with the head, *"arm"* extends outward from the body of the myosin filament. The flexible points of the arm are *hinges* which allow the head to be extended outward or brought closer to the body of myosin filament. The protruding arms and heads together are called *"cross-bridges"*. There are no cross-bridges at the centre of the myosin filament.
- The myosin head possess ATPase enzyme, which helps to cleave the ATP to release energy for the contraction process. The binding ability of the myosin head with the binding site *G actin* is regulates by ATPase. Only in the presence of actin, Mg^{++} ions enhance the ATPase activity of the myosin head.



Actin Filament

- It is composed of three proteins; actin, tropomyosin and troponin
- Actin
  - It is a double helix structure formed by the basic unit "*F" actin* molecule. Each strand of F-actin helix has hundreds of "*G" actin* molecules which have ADP molecule. G-actin provides the active binding site to myosin head. *Tropomyosin* and *Troponin* are the polymer of actin.
  - Tropomyosin
    - During resting stage, it covers "G" actin and prevents the binding of myosin head with the binding site.
- Troponin

- It is a complex made up of 3 proteins namely Troponin "T", *Troponin "I", and Troponin "C".*
  - *Troponin "T"* has high affinity to tropomyosin and binds the troponin complex with tropomyosin.
  - *Troponin "I"* readily binds with actin and tropomyosin. In resting muscles, they inhibit ATPase activity in myosin head.
  - *Troponin "C"* has a very high affinity for calcium ions. Each molecule can bind up to 4 Ca^{++} ions. The combination of Ca^{++} ions with troponin is the triggering factor to initiate muscular contraction.
- The presence of *troponin and tropomyosin (tt-complex)* in actin filament inhibits the binding reaction of actin with myosin. In a relaxed muscle fibre, the tt - complex physically covers the "G" actin for binding with myosin.

- When a muscle is stimulated, a high concentration of Ca^{++} ions is released from the cisternae into the sarcoplasm. The Ca^{++} ions readily combine with the troponin `C' of the TT – complex causes conformational change in the troponin complex and moves the tropomyosin molecule deeper into the groove between two actin strands. This exposes the "G" actin filament to myosin to initiate the contractions of the myofibrils. Only the skeletal muscle and cardiac muscle require troponin and tropomyosin, for execution of contraction coupling.
- In cardiac muscle during excitation-contraction coupling, Ca^{++} ion is released not only from the cisterna of 'L' tubules, but also from ECF through "T" tubules and the strength of cardiac fibre contraction depends to a great extent on the ECF Ca^{++} concentration.
- In smooth muscle instead of troponin another regulatory protein "*calmodulin*" reacts with four Ca^{++} ions. The calmodulin-Ca^{++} complex activates myosin kinase and Ca^{++}dependent phosphorylation of light chain myosin molecule to activate myosin cross-bridge reactions.

Sarcoplasmic reticulum - Tubular system

- Muscle cells also contain a special structure called sarcotubular system which has two sets of tubules. Longitudinal tubules (L-Tubules) and transverse tubules (T-Tubules).
- `L' Tubule system
  - Present parallel to myofibrils. At both the ends of the tubule, bulbous structures known as *terminal cisternae* function *as a* storage place for the Ca^{++} ions and play a key role in muscle contraction.
- `T' Tubule System
  - The T system consist of set of tubules formed by the invaginations of the plasmalemma. This tubule run perpendicular to the long axis of the muscle cell and lie between the cisternae of two successive "L" tubules.
  - The "T"' tubules are located at the junction of "A" and "I" bands which pass through the fibres, open into the inter-fibre space, permits the flow of extracellular fluid.
  - For every sarcomere 1 or 2 T-tubules are observed (preferably at Z disc region). Lumen of T-tubule is actually the extra cellular space. T - Tubule brings action potential from sarcolemma to the interior of the muscle cells. As sarcoplasmic reticular membranes approach the T-tubule, they coalesce to from 2 large sacs called the lateral cisternae, one on each side.

Triad

- It is a paired cisternae and a "T" tubule in between the cisternae. One T- tubule and 2 lateral cisternae associated with it forms a 'Triad'. They have remarkable ability to accumulate Ca^{2+} against a concentration gradient. Calcium pump an energy dependant -

operating in the L-tubules which can transport 2 Ca^{2+} with an expense of one ATP from the sarcoplasm to the lumen of sarcoplamic reticulum.

- The ATPase enzyme found associated with ca – pump, keeps free of Ca^{2+} concentration in the sarcoplasm of a resting muscle at a very low level (10^{-8}M) and the most of Ca^{2+}found in the lateral cisternae bound to a protein called *calsequestrin*. In the cytoplasm, the Ca^{2+} is bound with *calmodulin***,** which permits the transports cytoplasmic Ca^{2+} to its site of action.
- When an action potential pass along with T-tubule, Ca^{2+} from the lateral cisternae become disgorged go to the sarcoplasm thereby rising the free Ca^{2+} concentration from (10^{-8}M) to (10^{-5} to 10^{-6}M) and this intracellular Ca^{2+} triggers muscle contraction.

Proximate composition of mammalian skeletal muscle

- Water: 55 – 78% by wt: Water content varies inversely with lipid content.
- Protein: 15-23%
- Lipid: 1 to 20%
- Carbohydrate: 1-2%: mostly glycogen or lactic acid
- Ash: 1% mostly K^+, less Na^+, Cl^- and Mg 2^+
- Nucleic acid: < 1% - 25 – 30 mg DNA/100g and 100mg RNA/100g.
- Other soluble organic composition: 1% - 8-5 mM ATP, 20mM phosohcreatine, 350 mg carnosine /100g.

EXCITATION CONTRACTION COUPLING

- The arrival of an Action Potential at Sarcoplasmic Reticulum causes release of Ca^{2+} down the concentration gradient to sarcoplasmic reticulum.Released Ca^{2+} causes conformational changes to effect contraction. As action potential passes,$Ca^{2}$are pumped again to sarcoplasmic reticulum and relaxation happens. This cycle is known as Excitation Contraction Coupling.

EXCITABILITY

- It is the ability of any living cell or tissue to exhibit an electrochemical change (action potential) to a stimulus. However, nerve and muscle cells are highly excitable cells than other cells.

Events of action potential

Action potential of nerve and muscle fibres

- The action potential is caused by a sequence of changes or events occurring in the membrane permeability to Na^+ and K^+ ions. When an excitable cell is stimulated, action potential aids the transmission of impulses through nerve and muscle fibres. Action potential is the rapid changes in the membrane potential from its normal negativity to positive potential inside the cell membrane which last for few milliseconds, and then returns back to its original resting negative potential level.
    - *Polarised membrane* is the resting cell membrane with a normal negative resting membrane potential
    - *Depolarization stage*: It is the *first event* of action potential is characterised by rapid increase in the permeability to Na^+ ions (5000 folds) to interior of the cell generating more positive electrical potential inside of the cell.
- This is followed by a gradual inactivation of Na^+ channels (closure) that occur within another few milliseconds and the membrane becomes impermeable to Na^+ ions. It is associated with gradual opening of *voltage gated K^+ channels* to allow K^+ ions outflow to the exterior of the cell membrane. The potential inside cell is re-established to its normal resting level (- 75mV). This stage is called as the *repolarisation stage*.

- Higher concentration of K^+ ions in the exterior of the cell towards the end of the action potential continues for a short period creates more negativity inside referred to as *hyper-polarised state*. At this state, re-excitation of the cell will not occur.
- The *final event* is characterised by *electrogenic pump mechanism*, which aids in the transport of three Na^+ ions to the exterior for every two K^+ ions to interior of the cell and create the normal resting potential (- 75 mV) on the inside of the cell membrane.
- The whole action potential lasts about 1 - 2 milliseconds in most nerves, but longer in many muscle cells.
- Channel systems of cell membrane
    - $Na^+ – K^+$ leakage channels
    - Voltage gated Na channels and K channels
    - *$Na^+ – K^+$ leakage channels*
    - These channels are 100 times more permeable to K^+ ions than Na^+ ions and are exceedingly important in determining the level of normal resting membrane potential.
- Voltage - gated channels of the cell membrane
    - The *voltage-gated Na^+ channel* causes both depolarisation and repolarisation of the nerve/muscle membrane during the action potential. The *voltage-gated K^+ channel*also plays an important role in establishing the repolarisation of the membrane. These two voltage-gated channels are present in the cell membrane.
- Voltage - gated Na^+ channel
    - The voltage gated Na^+ channels have two gates, the *external gate or activation gate* which opens to outside of the cell. The other gate is at the interior end and opens to inside of the cell referred as *internal gate or inactivation gate***.**
    - The activation gate is closed during resting stage (- 75 mV), while the inactivation gate is opened. This prevents free passage of Na^+ ions from outside to interior of the cell.During depolarisation stage the resting membrane potential drops from – 75 mV or to - 70 to - 50 mV causes opening of the activation gate due to conformational changes results in increased Na^+ ion permeability as much as 500 to 5000 folds into the cell through the channel system.
    - A gradual increase to positivity following the opening of the activation gate also closes the inactivation gate comparatively at a slow speed. The time lapse between the activation and inactivation of the channels causes the passage of Na^+ ions to the interior of the cell for few milliseconds.
    - During repolarisation stage, the inactivation gate is completely closed and prevents Na^+ ion entry from outside to the interior of the cell membrane. The inactivation gate will not reopen until the disturbed membrane potential returns nearly to the original resting membrane potential level of -70 to- 80 mV.
- Voltage - gated potassium channel
    - This channel has only one gate at the interior of the membrane. It may either close or open to the interior of the cell. During resting stage this gate is inactivated and prevents the passage of K^+ ion to the exterior of the cell through this channel system. When the electrical potential drops towards zero, Na^+ channels get inactivated causes the activation of K^+ channels to allow increased K^+ ions diffusion to outside of the cells.
    - Electro-chemical changes during action potential Spike potential (over shoot)
    - It is the steep change in the negativity of the cell from - 75 mV to more positivity of + 40 mV in the membrane potential due to rapid increase in the permeability of the Na^+ions to the interior of the cell.

- In large fibres, the electrical potential during depolarisation stage overshoots slightly positive beyond the zero level whereas in the small fibres and many CNS neurons the potential does not over shoot beyond zero.

- Positive after potential
  - During repolarisation, the membrane potential drops little more negative than the normal resting value of – 75mV due to excess of K^+ ion diffusion to out side the cell. This is caused by the prolonged opening of K^+ channels for several milliseconds even after repolarisation.

MEMBRANE POTENTIAL

- The interstitial fluid and the intracellular fluid contain 147 mEq/litre of positive ions (cations) outside the cell, and about 155 mEq /L, of negative ions (anions) inside the cell. Higher concentration of Na^+ ions (142 mEq/L) and lower concentration of K^+ ions (5 mEq/L) characterise the interstitial fluid.
- The intracellular fluid has more of K ions (140 mEq/L) and less of Na^+ ions (14mEq/L).
- This concentration difference of ions across a selectively permeable cell membrane creates an electrical potential difference.
- This electrical potential difference across the cell membrane is called as *"membrane potential"*.

Basic mechanisms of membrane potential

Three major factors cause the membrane potential.

- Differential permeability of the membrane to diffusion of ions.
  - During resting state the cell membrane K^+ ions is 50 to100 times more odiffusable to out side than to Na^+ ions through *non-gated leak channels due to* their concentration gradient.
  - This contributes accumulation of positive charges immediately outside the membrane.
  - The resting membrane is almost completely impermeable /very slightly permeable to Na^+ ions.
- The Na^+, K^+ electrogenic pump
  - It generates positive membrane potential out side the cell by actively pumping 3 Na^+ ions out of the cell for every 2 K^+ ions pumped into the cell against their concentration gradient.
- Trapping of negatively charged anions inside the cell
  - Many intracellular anions are large molecules proteins, organic SO_4 and PO_4 are trapped within the cell and are attracted to the inner surface of the cell membrane generate negative electrical potential inside the cell.
  - These three factors are the primary cause of membrane potential. The magnitude of this potential produced by diffusion of ions can be predicted by the *Nernst equation*.
    - $E_x = (-60mV/z) \times \log[X_{inside}/X_{outside}]$ E_x = equilibration potential for ion X
    - z = valence of the ion – 1 for Na & K
    - [X] = Concentration of ion X

- The diffusion potential caused by K and Na ion diffusion would give a membrane potential of about. An additional giving a net resting membrane potential of – 90 mV.

The resting membrane/ diffusion potentials of skeletal muscle fibres

- During resting stage, the muscle fibres have an electrical potential of - 90 mV inside the fiber (range from - 75 to - 90 mV) of which – 86 mV is determined by K diffusion and the remaining – 4mV is contributed by the electrogenic Na^+-K^+ pump.

SERIES ELASTIC COMPONENT OF A MUSCLE

- The components such as sarcolemmal sheath at the end of the muscle fibres, the tendon and the hinged arms of the cross bridges of the myosin filaments are known as *series elastic components* of the muscle. stretch slightly as tension increases. Consequently, the contractile unit must shorten an extra 3-5% to make up for the stretch of these elements. During isometric contraction, these series elastic components develop greater tension that opposes the contraction of the myofibrils. Hence the contraction becomes zero, but the tension is very high.
- In isotonic contractions, the contractile elements shorten and stretch the series elastic components. This causes the tensionto rise just to exceed the force of contraction due to the effect of the weight. Thereafter the tension in the muscle remains constant.

Types of muscles

	Slow Muscle fibres		Fast Muscle fibres
1	Smaller fibres	1	Much larger fibres
2	Innervated by small nerve fibres	2	Innervated by comparatively large nerve fibres
3	Have extensive blood supply, hence referred as *"Red muscle"*, shows prolonged performance of work (Long contraction time).	3	Have less blood supply, hence called as "*White muscle"*, shows quick and repetitive contractions (Short contraction time).
4	Increased number of sarcosomes	4	Fewer sarcosomes
5	Muscle metabolism by aerobic or oxidation of glucose, fatty acids and amino acids, causes the	5	Glycolysis or anaerobic type of metabolism liberating 2 molecules of lactic acid and 2

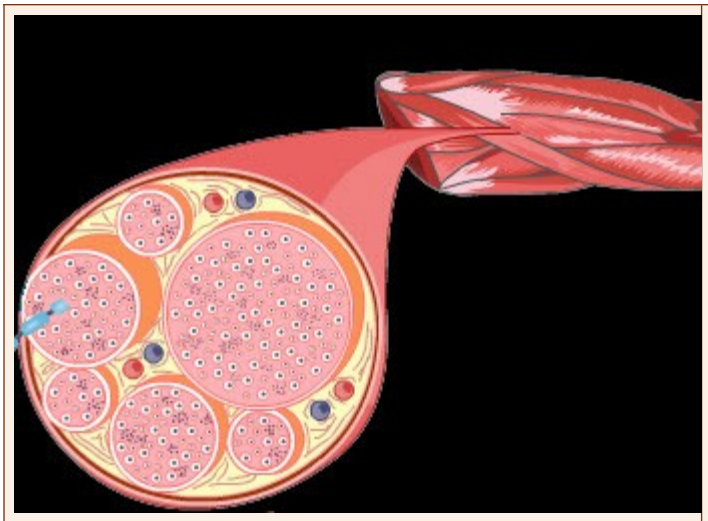
	release of 38		molecules of ATP.
6	Large amount of myoglobin in sarcoplasm.	6	Lack of myoglobin.
7	Less sarcoplamic reticulum	7	Extensive sarcoplasmic reticulum
8	Less Ca^{++} ion release	8	Rapid Ca^{++} ion release
9	Has large motor units (More muscle fibres/ neuron), no fine degree ofcontrol.	9	Has few motor units (less muscle fibres/ neuron), higher degree of fine control.
10	Adapted for prolonged, continued muscle activity – like support of the body against gravity	10	Adapted for rapid and powerful muscle contractions – like jumping, running

- Based on the duration of contraction, the *muscle fibres are classified* as slow (tonic) and fast (twitch) fibres. Every muscle in the body is composed of slow and fast muscle fibres.
- Based on energy source and rate of contraction, skeletal muscle fibres can be classified into slow-twitch (type-I) /oxidative and fast-twitch (type-II) /glycolytic fibres. Type-I fibres are always oxidative and slow muscle fibres. Type-II is either oxidative or glycolytic and rate of contraction varies from slow to fast and superfast.

The motor units of the muscle

- Each motor neuron leaves the ventral horn of the spinal cord and innervates many muscle fibres. All the muscle fibres in a muscle that are innervated by a single motor neuron (all the muscle fibres supplied by a single motor neuron) are called as *motor unit*.
- The ratio of motor nerve to the number of muscle fibres innervated in a given skeletal muscle is called *innervation ratio***.** The number of muscle fibres per motor unit differs as per the function for which the muscle is used in the body.
- *Small muscles which act rapidly and which require finer control of movement have an innervation ratio of 1:2 to 1:4. Large muscles that do not require finer control have an innervation ratio of 1:800 or more.*

MODULE-16: MUSCLE CONTRACTION



LEARNING OBJECTIVES

- This module helps to,
  - learn about properties of muscle contraction,
  - appreciate thermal changes occurs in muscle during work and
  - understand rigor mortis.

TYPES OF WHOLE MUSCLE CONTRACTION

- Muscle contraction is principally of two types
  - Isometric contraction
    - Muscle contraction without shortening in length that occurs during the manifestation of the process of muscle contraction.
    - In isometric contraction, the muscle contracts between two fixed points. Hence during the process of contraction it does not shorten in its length and develops the force of contraction.
    - Therefore in isometric (same length) contraction, there is no work performance, less force of contraction and low Fenn effect due to liberation less energy.
  - Isotonic contraction
    - On stimulation, the muscle contracts between one fixed and one moveable points (eg. Lifting the weight) shows shortening in length, but the tension on the muscle remains constant.
- Contractions of muscle in the body
  - In the body, most of the muscular contractions are a mixture of both isometric and isotonic contractions. During standing posture the quadriceps shows isometric contraction, to tighten the knee joint to keep the legs stiff. Contraction of the biceps is isotonic when the hand lifts the weight.
  - Alternate isometric and isotonic contractions of the quadriceps and gastrocnemius (calf muscle) help to effect running or walking. The quadriceps

contracts isometrically when the foot hit the ground, while the calf muscle contracts isotonically when the foot is lifted off the ground.

MOTOR END PLATE

- The axon terminals of the motor neurons innervate each muscle cell. The innervation ratio is the number of muscle fibers or cells innervated by a single motor neuron (motor unit).
- In muscles where delicate control is required the innervation ratio is small (3 to 6) as in extrinsic eye muscles. In the muscles of limb where the fine control is not necessary innervations ratio may be as high as 1000.
- The muscle cell plasmalemma at the motor end plate has got large numbers of infoldings - 0.5 to 1 µm deep 50 – 100 nm width.
- The axon terminal (contains 1,00,000 synaptic vesicles) sends finger like processes into these infoldings but they remain separated by a space of 40 – 60 nm.
- The nerve impulse propagated along the motorneuron and its axon collaterals reaches the neuromuscular junction.

Motor end plate or neuromuscular junction

NEUROMUSCULAR JUNCTION

- The motor neuron branches at its end and each branch comes into a close opposition with the skeletal muscle at a specialised area called the *neuromuscular junction* or *motor end plate*. This synapse has a *presynaptic membrane,* a narrow space between the nerve and muscle, called *synaptic cleft* and a *post synaptic membrane sarcolemma*.
- The presynaptic knob is the terminal portion of the axon of the motor neuron; the extends from the CNS to the muscle cell. The axoplasm contains a large number of vesicles called *synaptic vesicles*; contain the excitatory neurotransmitter substance *acetylcholine*. These vesicles are in clustered located very close to the presynaptic membrane. Acetylcholine is synthesised in the cytoplasm of the nerve terminal and stored in the synaptic vesicles.
- The presynaptic terminal also contains many mitochondria, required for the synthesis of neurotransmitter substance.
- Synaptic cleft is a narrow space of 20 to 30nm wide separates the presynaptic membrane and postsynaptic sarcolemma membranes. The synaptic cleft is filled with extracellular fluid and spongy reticular filaments called basal lamina. The synaptic cleft contains an enzyme, *acetylcholinesterase*, to hydrolyse acetylcholine.
- The postsynaptic cell membrane has a series of invaginations called *junctional folds* that increase the surface area of the postsynaptic membrane. Acetylcholine receptors are located on the postsynaptic membrane at the entrance of these junctional folds.

Transmission of impulse across the neuromuscular junction When the action potential reaches the presynaptic terminal of the motor neuron, the depolarisation opens *voltage-gated* Ca^{++} *channels* ; and extracellular Ca^{++} diffuses into the presynaptic nerve cytoplasm. The increased intracellular Ca^{++} level causes the synaptic vesicles to fuse with the presynaptic membrane; the fused synaptic vesicle opens and releases the acetylcholine into the synaptic cleft by exocytosis.

ACETYLCHOLINE RECEPTORS

- The released acetylcholine diffuses across the synaptic cleft, reaches the postsynaptic membrane (sarcolemma), and binds with acetylcholine-specific receptors. This causes opening of *ligand-gated ion channels* in the sarcolemma**. And diffusion of sodium**

ions into the muscle cell generating local potential change called *end plate potential*.

- Depolarization in the end plate potential opens voltage-gated Na^+ channels at the postsynaptic membrane and leads to the generation of an action potential on the muscle cell membrane. Presence of the neurotransmitter in the presynaptic nerve terminal permits the transmission of action potential unidirectionally from the motor nerve to the skeletal muscle fibre.
- The binding activity of acetylcholine with its receptor remains for a very brief period. The acetylcholine is rapidly removed from the receptors by
    - Enzymatic hydrolysis of *cholinesterase*, located on the postsynaptic membrane hydrolyses acetylcholine into acetyl and choline molecules.
    - Diffusion of acetylcholine out of the synaptic cleft and is no longer available to act on the muscle.
- *Myasthenia gravis* is a neuromuscular disorder in which autoantibodies are produced against acetylcholine receptors. Hence, neuromuscular transmission is impaired and leads to paralysis.

MUSCLE CONTRACTION

- It is accomplished by a sliding together or telescoping of the interdigtating thick and thin filaments and as a result narrowing and eventual disappearance of the H zone and shortening of I band happen.

Summary of events

- Before contraction ie in the absence of Ca^{2+} in the sarcoplasm, troponin T strongly binds with tropomysion, troponin I and troponin C. At the same time troponin I firmly attached to actin. Here actually the tropomyosin blocks or hides out the binding site of myosin with actin. This is achieved mainly by the association of troponin - I with the actin.
- An action potential travels along a motor nerve to muscle fibre
- At the neuro muscular junction the nerve secretes a neurotransmitter – acetylcholine (Ach).
- Acetylcholine acts on the muscle sarcolemma and opens Ach-gated ion channels
- Flow of Na^+ ions to the interior of the muscle fibre membrane at the point of the nerve terminal initiates an action potential in the muscle fibre
- The action potential travels along the muscle fibre membrane
- The action potential also travels deeply into the muscle cell through the sarcoplasmic reticulum releases Ca^{++} from the cistern into the myofibrils
- When action potential reaches triad then Ca^{2+} released, Ca^{2+} binds with troponin – C leading to some confirmational change (Structural change in the tt – complex and exposure of "G" actin to myosin head) on the C molenucle leading to troponin – I to loose its affinity towards actin.
- When troponin I looses linkage with actin, troponin – T can no longer hold the tropomyosin strand out of the groove. Only when tropomyosin is placed outside the groove formed by the double stranded actin helix, then only myosin biding site on actin is marked.
- When actin groove occupied by tropomysin, binding site exposed to myosin.

- Myosin heads or cross bridges attach to actin's binding site and swivel it simultaneously and then dissociate in a sarcomere at a time only 5-20% of the total cross bridge attached to the thin filament at a given instant.
- Now the thin and thick filament slide part each other at a uniform rate without any jerk. Time required for one cycle of cross bridge is 0.1 milliseconds.
- Swiveling or rotating of the cross bridge in an inclined way cause actin filament to move towards the center of the sarcomere.
- Now the thin and thick filament slide past each other at a uniform rate with out any jerk. Time required for one cycle of cross bridge is 0.1 ms.
- Swiveling or rotating of the cross bridge cause actin filament to move towards the center of the sacromere.
- Once swiveling is over ATP is hydrolyzed and energy liberated and this energy used dissociation of cross bridge from the actin. So ATP acts as a dissociator and soon reorientation of the utilization of energy. In other words for swiveling action, no energy is needed but for only dissociation and reorientation of myosin head energy is utilized.
- This series of event continue till Ca^{2+} is rebound to sarcoplasmic reticulum.
- New ATP get bound to the spent cross bridge and hydrolysis of ATP happens only after swiveling.
- After death all myosin cross bridge stop attach with actin at an angled position and results in rigor mortis.

SLIDING MECHANISM OF MUSCLE CONTRACTION

"Walk- along theory" of contraction (Sliding mechanism of contraction)

- In the relaxed state, actin filaments lie adjacent and parallel to the myosin filaments. In contracted state, the actin filaments extending from the z-discs are also pulled inward by head portion of the free ends of myosin filaments.
- Thus, muscle contraction occurs by sliding action actin over myosin filament.
- In the relaxed muscle, the troponin -tropomyosin complex covers active binding sites "G" actin filaments and prevents its attachment with myosin heads to cause contraction.
- In the presence of large amounts of Ca^{++}, troponin-C readily binds with Ca^{++}, the troponin complex undergoes a conformational change and moves the tropomyosin molecules deeper into the groove between two stands of actin strands.
- This effect "uncovers" the active site "G" actin and the myosin head binds with the active sites and initiates muscle contraction.

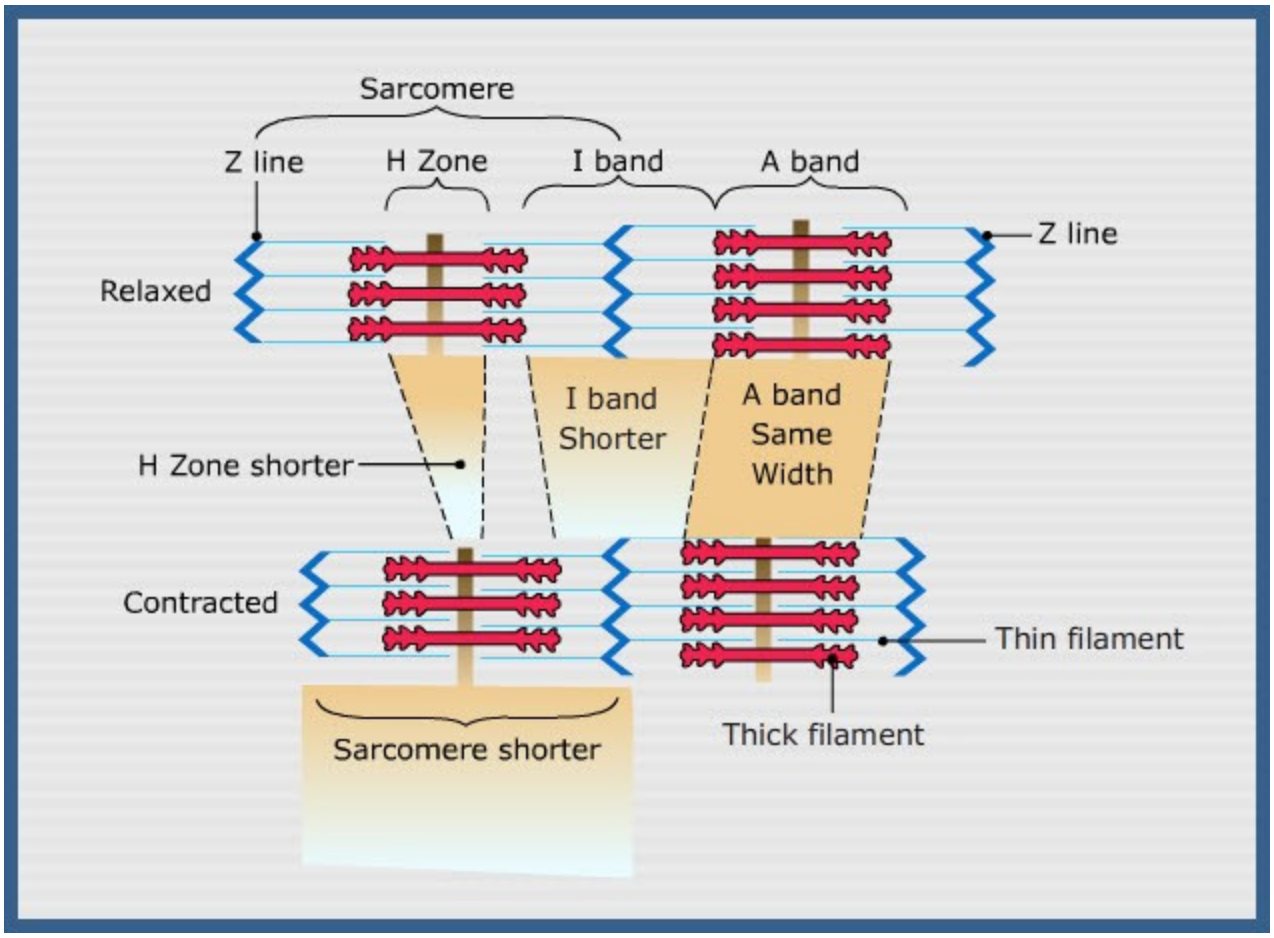
Interaction between actin and myosin filaments

- As soon as the actin filament becomes activated by the Ca^{++}, the heads of the cross bridge of the myosin filaments are immediately attracted to the active sites, "G"actin. This causes sliding movement of actin filament over the myosin filament, which is known as "*Walk along*" theory (*"ratchet" theory*) of contraction.
- ATP molecule binds with heads of the cross-bridges of myosin molecule. ATPase activity in the myosin head causes a partial hydrolysis of ATP to ADP and the inorganic phosphate (Pi). The head extends perpendicular to the actin filament and shows high affinity to actin filament
- The troponin - tropomyosin complex binds with Ca^{++}. Active sites the "G"actin are uncovered.

- The bond between the head of the cross-bridges and “G” actin cause a conformational change in the head causes complete hydrolysis of ATP and release of ADP and Pi. The head shows tiling towards the arm of the cross-bridge. This known as the *“power-stroke”* which pulls the actin filaments in wards. The actin filaments slide over the myosin filament.
- Once the head of the cross-bridge is tilted, ADP and Pi are released. Now a new molecule of ATP binds with the head of cross-bridge detaches the myosin head from the “G” actin.
- The new ATP is cleaved to begin the next cycle leading to power-stroke, i.e. the energy ‘*cocks*’ the head back to its perpendicular position ready to begin another power-stroke cycle again.
- Similar repeated back and fourth movements of the cross bridge makes the heads walk along the actin filament step by step thus pull the actin filament towards the centre of the sarcomere, until the z-membrane reaches the ends of the myosin filaments.

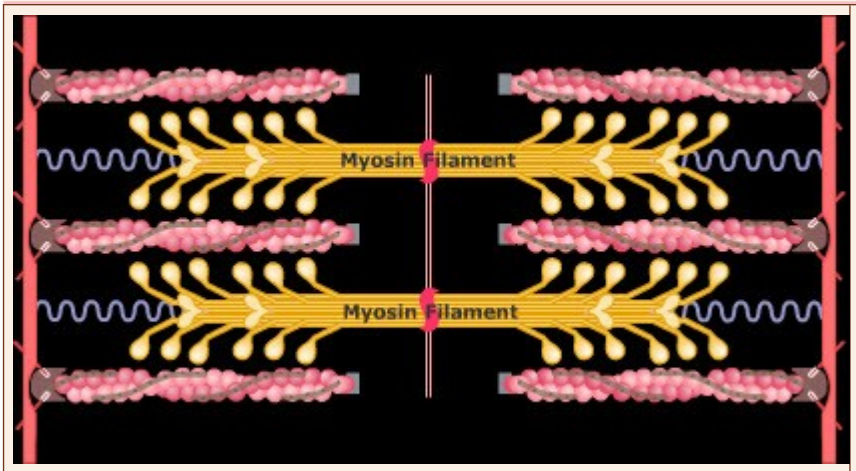
The role of Ca^{++} in muscle relaxation

- The Ca^{++} does not remain in the myofibrils for more than few milli seconds. As the action potential is over, the `L' tubules almost immediately reabsorb the Ca^{++} from the sarcoplasm, and stored it in the cisternae.
- When the Ca^{++} concentration drops in the sarcoplasm, the strong affinity of Ca^{++} for troponin `C' is lost. This causes the movement of tropomyosin molecule to its original position to cover the active binding site, the “G”actin results in relaxation of the muscle.



- **Contracted state Vs relaxed state**

MODULE-17: PROPERTIES OF MUSCLE CONTRACTION



LEARNING OBJECTIVES

- To learn about properties of muscle conraction.
- To appreciate thermal changes occurs in muscle during work.
- To understand rigor mortis.

CHARACTERISTICS OF MUSCLE CONTRACTION

Stimulus

- It is an external agent, when applied to an excitable tissue provoke a visible *response* .
- Types of Stimuli (Based on strength)
    - *Sub threshold :* sub minimal/ low intensity, unable to produce a response
    - *Threshold :* minimum intensity, strong enough to initiate an action potential
    - *Sub maximal :* higher strength than threshold
    - *Maximal :* highest threshold strength
    - *Supra maximal :* destructive to tissues
- Classification of stimulus
    - *Mechanical :* Pain, Pressure, and Touch
    - *Chemical :* Acid, Alkali; *Thermal*: Warmth, Cold

- *Osmotic :* Hypertonic solution, Hypotonic solution

PROPERTIES OF MUSCLE CONTRACTIONS

- When a muscle fibre is stimulated by minimal or maximal effective stimuli, the whole fibre contracts to the maximum or it will not contract at all. This law is applicable to single motor unit (motor nerve and all the muscle fibres it supplies).
- *Whole cardiac muscle obeys this law because of syncytium*.

Recruitment

- Because different motor neurons in a nerve has different threshold levels, an increase in intensity of the stimulus applied to the nerve evoke action potential in additional motor neurons and contraction in additional muscles fibers in the muscle served by that nerves..This increase in tension development of a muscle caused by gradual increase in intensity of the electrical stimulation is due to recruitment of additional motor units to the contractile state.
- Recruitment occurs because a nerve contains many different motor neurons having different threshold levels for initiating an action potential. Generally motor neurons having small diameters have low threshold values and are the first motor units recruited by a given stimulus. These small motor neurons are associated with somatic fibres. Largest motor neurons innervate FG fibers have highest threshold levels.

Simple muscle contraction *(Single muscle twitch)*

- Application of single threshold level of stimulus (electrical stimulation) causes a single muscle contraction followed by relaxation. The single muscle twitch has three phases.
  - Latent period
    - It is the period between the application of stimulus and beginning of contraction (about 10m.second).
  - Period of contraction
    - This period indicates the actual shortening (about 40m.second).
  - Period of relaxation
    - It is the period between the point of maximum contraction and the period of complete relaxation (about 50m.second).

Refractory period

- It is a brief period during which a muscle undergoing contraction for a first stimulus is unable to respond to a second stimulus. The earliest chemical change during muscular contraction is the breakdown of ATP. So long as the breakdown ATP is not resynthesised in adequate amounts, the muscle cannot be excited.
- Refractory period is that period during which this resynthesis of broken ATP takes place. Following stimulation of a motor neuron or a muscle cell a brief period exists during which the motor neurons or sarcolemma is unresponsive to the II stimulus is called resting potential.
- It is of two types
  - Absolute refractory period
    - It is the time interval between the twin impulses (less than 3millisecond) during which the muscle can not be stimulated even by stronger stimuli. This is due to the rising phase of the action potential when Na^+ conductance to the interior of the cell is high.
  - Relative refractory period
    - It is the period of reduced excitability, which requires increased intensity of second stimulation to generate another action potential. It is characterised by after depolarization stage of action potential during

which the K^+ permeability is very high and the Na^+ channels are recovering their excitability.

Treppe *(Staircase phenomenon)*

- When a stimulus of constant strength and duration is repeated once or twice per second (below tetanising frequency)causes increased contractions during the first few stimulations, which finally reach a constant response. This is due to development of physical and chemical changes i.e. reduced viscosity of the sarcoplasm, increased heat production, increased Ca^{++} availability for binding with troponin during first few contractions, referred as *beneficial effects***.**

SUMMATION OF MUSCLE CONTRACTION

- Summation is the added effect of individual muscle twitches to get strong and powerful muscle contraction.
- Summation occurs in two different ways
    - By increasing the number of motor units to contract simultaneously.
    - By increasing the rapidity of contraction of individual motor unit of a contracting muscle.
- Multimotor unit summation (Spatial summation)
    - The strength or the force of contraction of a muscle increases progressively with respect **to increasing number of contracting motor units by increasing the strength of stimulation**.
    - The strength of resulting contractions in a skeletal muscle is proportional to the size or the number of motor units contracted at the time, which in turn is directly proportional to the strength of the stimulus; i.e**. increasing the strength of stimulus increases stimulation of motor units.**
- Wave summation (Temporal summation)
    - The frequency of stimulation is increased to a motor unit or units in such a way that the **successive stimuli stimulate additional motor units during its contraction phase**.
    - When a motor unit is excited by a rapid succession of weak stimuli, it may evoke stronger contractions. Applying stimuli in rapid succession to a muscle increases the excitatory potential of the postsynaptic nerve ending. This increased excitatory potential is often referred to as *excitatory postsynaptic potential (EPSP).*
    - The second stimulus arrives before the completion of the first contraction, which initiates the second contraction. This gives greater strength or force, as well as duration to the already progressing contraction.

FACTORS INFLUENCING THE STRENGTH OF CONTRACTION

- Size and the number of motor unit stimulated.
- Rapidity with which individual motor unit of a muscle is stimulated.

Starling's law

- The first factor is governed by the strength of stimulus. The second is mostly by the rate of effective stimuli. The last is by the initial length of the muscle fibre.
- In cardiac muscle, mechanical *summation is impossible* because of prolonged action potential (250msec.) almost completely overlaps with long twitch (300 m sec.).

- In smooth muscle, the action potential is relatively short (5 -10 m. sec.), hence no overlapping of twitches, thus *summation is possible*.
- Starling's law of muscle contraction
    - The energy of contraction of the muscle is directly proportional to the initial length of the fibre. This law can be proved by the load and after load experiment on the gastrocnemius muscle of the frog.

Tetanisation

- It is the fusion of successive twitches when the frequency of stimuli is given at a rapid rate.
- Experimental tetanus
    - The experimental tetanus of a muscle may be defined as fusion of individual contractions caused by repeated experimental stimulation of a viable muscle, by which two kinds of tetanus can be produced by using gastrocnemius muscle of the frog.
- Complete tetanus
    - If the frequency of the successive stimulation to a muscle is so adjusted that the subsequent effective stimuli fall during the preceding contraction phase, a complete tetanus or complete fusion of contractions can be obtained ***(tonic contraction)***.
- Incomplete tetanus
    - When the subsequent effective stimuli are applied to fall during the relaxation phase of the preceding contraction, then incomplete tetanus or incomplete fusion of contractions can be obtained **(*clonic* contraction)**.
    - Cardiac muscle fibres do not functionally tetanise, since, mechanical summation is not possible due to prolonged action potential (250msec.), which almost completely overlaps with long twitch (300msec.) duration.
- Critical frequency
    - **It is the lowest frequency required to produce a complete tetanus.**

Factors responsible for tetaniszation

- Viscose property
    - Viscose inertia of the sarcoplasm, sarcolemma, epimysium, perimysium and facia provide a resistance to change in the length immediately after contraction.
- Fusion of activation process
    - Successive pulsatile stimuli at rapid rate causes fusion of activation or the manifestation of muscle contractions by providing free Ca^{++} continuously to the sarcoplasm.

MUSCLE FATIGUE

- Fatigue is the decrease in the working capacity of a muscle or tiredness of the muscle when it is continuously stimulated.
- It is **characterised by diminished force of contraction, increased latent period and contraction period and prolonged relaxation period**. The relaxation is incomplete i.e., the muscle is in a state of contracture, (the muscle contracts even without the presence of action potential). At this stage the muscle cannot be excited or do any more work.

- In the locomotor system of the skeletal muscle, there are three sites, which are easily fatigued.
    - Synapses of CNS.
    - Neuromuscular junction.
    - The muscle.

Causes of fatigue

- Continuous stimulation of the nerve fibre or continuous stimulation of the muscle that too under ischemia (impaired blood supply) causes,
- *Lack of energy sources:* Depletion of O_2 from myoglobin; depletion of muscle glycogen; depletion of ATP
- *Depletion of neurotransmitters:* Prolonged muscle activity diminishes neurotransmitter acetylcholine concentration in the neuromuscular junction, thereby reduces the transmission of the impulses to muscle which causes diminished muscle contraction.
- *Accumulation of metabolic end products such as lactic acid:* In oxygen lack, the muscle glycogen broken down by anaerobic glycolysis to give pyruvic acid which is then reduced to lactic acid by the action of lactic dehydrogenase. But in an intact muscle the blood supply minimises the above effect by continuously supplying the O_2 and nutrients to a functioning muscle.

RIGOR MORTIS

Muscle exhibits

- In-excitable
- Shortens in length
- Increases in thickness
- Become viscous and losses translucency
- Acidic pH 5.8
- Stiff
- Glycogen disappears
- Gives off H_2CO_3

- Rigor mortis starts in the 2nd hour and is completed in 3 hrs after death. Rigor mortis disappears 24 – 36 hrs after death due to autolysis.
- Deficiency of ATP causing establishment of permanent link between actin and myosin. When ATP falls to 85% and creatine PO_4 to 30% of its initial value, symptoms of rigor mortis begin to appear.
    - Ca^{++} pumps run out of ATP
    - Ca^{++} cannot be removed
    - Continuous contraction
    - Eventually tissues break down
- This is major physiological different between cardiac and skeletal muscles. Skeletal muscles ordinarily contracts only when stimulated by nerve impulse.
- In contrast cardiac muscles tissue can contract with out our nerve stimulation. Its source of stimulation is conducting tissue of specialized muscle with in the heart.
- Nerve stimulation causes the conducting tissue to increase or decrease its rate or discharge. Cardiac muscle tissue has got an extra long refractory period.

THERMAL CHANGES DURING MUSCLE CONTRACTION

- Out of total energy liberated by the hydrolysis of ATP in a contracting muscle, only 40-45% can be converted into work energy and the rest is evolved as heat; i.e. the efficiency

of muscle contraction is about 45%. It is **recorded by using *thermopile***. Thermopile has plates of antimony and bismuth connected to galvanometer. In a single twitch 0.001° to 0.005° C temperature produced.

- Total heat Produced = Wt. of muscle (gm) × Sp. Heat × Extent of temperature.

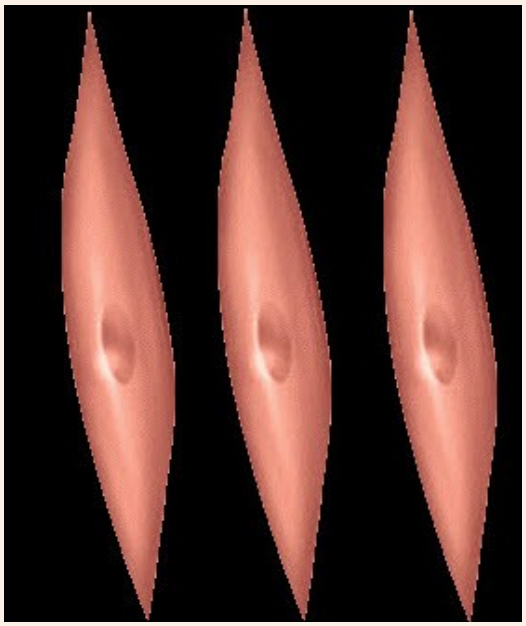
Fenn effect

- When a work is performed by the muscle and energy is required. **Heat generation by a muscle is directly proportional to its work performance due to increase hydrolysis of ATP**. This Of the total energy liberated from ATP, the muscle utilises 40 to 50% energy in performing work and the rest is liberated as heat to maintain body temperature.
- The liberated heat is classified as
    - *Resting heat:* Used for biochemical reactions during resting state
    - *Initial heat***:** It is produced both at initiation and during the course of muscle contraction. It is dependant on aerobic change in the muscle due to breakdown of ATP and creatine PO_4 and formation of lactic acid. It consists of
        - *Activation heat:* produced due to Ca transport associated with initiation of contraction
        - *Shortening heat:* Liberated by sliding reaction, muscle lifts load and does external work.
        - *Maintenance heat:* Heat liberated in a muscle that is stimulated but does not lead to physical work (isometric contraction); it is proportional to duration of contraction and tension developed during contraction.
        - *Recovery heat:* Heat liberated after contraction of muscle fibre. It is due to pumping of Ca^{++} back into the tubules and resynthesis of ATP for next cycle.

Effect of temperature in the muscle

- **An increase of temperature shortens the latent and contraction periods whereas relaxation is not much affected.**
- A decrease of temperature has the opposite effect causing increased latent and contraction period and prolonged relaxation period.
- When temperature exceeds a few degrees above 40 ° C, irreversible changes take place in the sarcoplasm.
- There is a minimum temperature (near 0°c) is required for muscle contraction, below which the muscle fibres fail to respond to stimulation; but the loss of excitation is reversible.

MODULE-18: MUSCLE METABOLISM AND SMOOTH MUSCLE PHYSIOLOGY



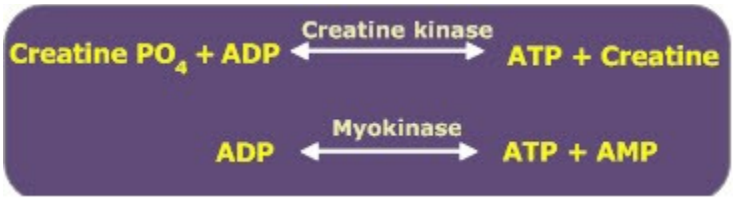
LEARNING OBJECTIVES

At the end of this module, the learner will learn the following,

- energy for muscle metabolism and work done by them,
- smooth muscle and
- muscle pathologies.

MUSCLE METABOLISM

- Sarcoplasm contains creatine kinase and also myosin kinase. ADP degraded to AMP and ATP. **AMP produced is degraded to IMP – inositol monophosphate by adenylic deaminase**, which again converted to uric acid and excreted.

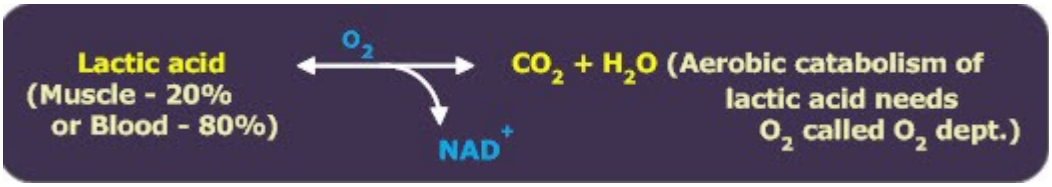


- Hydrolysis of ATP produces 7.3 kcal/mol

METABOLISM OF GLUCOSE IN MUSCLE

- ATP formed during metabolism used for phosphorylating creatine, so creatine PO_4 formed. This creatine PO_4 used during contraction for phosphoylating ADP to form ATP and later ATP is hydrolyzed.
- ATP is also produced from FFA. Eg Palmitic acid generates 140 ATP
- FFA ----------> CO_2 + H2O + ATP
- Hence creatine kinase is used for restoring creatine PO_4 as well as to restore ATP. Approximately 0.3 µmol ATP is hydrolysed per gram of muscle during single twitch. Liver and skeletal muscle store glycogen of the animal body in equal proportion (9 to 16g of glycogen from 1 kg of skeletal muscle).
- FG muscles rely mostly on anaerobic glycolysis as the product of ATP is rapid and happens with out O_2. SOG and FOG cells relay on anaerobic metabolism for their energy production.

- Longer time required to obtain ATP through aerobic metabolism of glucose. Such muscle can sustain activity for longer periods of time (heart: only brief rest periods).
- During initial stages of contraction pH of sarcoplasm increases due to libration of creatine from creatine PO_4. But later pH decreases due to accumulation of lactic acid especially in anaerobic conditions.
- In anaerobic breakdown of glucose, lactic acid production is more which can alter the pH by altering the buffering capacity. So this type of metabolism is self limiting one. Lactic acid brings about fatigue.
- Liver can prepare glycogen from lactic acid more quickly than it is done by the muscles. Muscle can form glycogen more readily from glucose that it is done by the liver. Pyruvic acid partly converted to lactic acid in anaerobic condition.



TYPE OF MUSCLE FIBRES

- FG cells have a
  - Shorter contraction time (5 – 50ms).
  - Less amt of myoglobin as FG cells go for anaerobic meth myoglobin with in the stage for O_2 is less needed.
  - Have more phosphorylase needed for degraded glycogen).
  - Larger cell diameters (fast twitching).
  - Fewer mitochondria (more numbers needed for aerobic metabolism).
  - More glycogen needed for anaerobic glycolysis.
  - Much less lipids (lipids are oxidized aerobically by β-oxidation).
  - Less blood flow.
  - Slower rate of protein turnover do not depend AA metabolism for energy.
  - Narrower Z disc 66 nm compared to 144 nm by SO cells – rapid contraction.
  - Fairly less red in colour (less myoglobin).
  - A more extensive and highly organized sarcotubular system (more Ca^{2+} storage for stronger contraction).
  - Less resistance to fatigue, and are innervated by large motor neurons,
  - Higher contractile speed (myosin dependant ATPase activity of FG fibers has 2 – 3 times more than SO fibers. FOG cells have intermediary characteristics between FG and SO cells. 2 disc width is 88 nm. Speed of contraction higher than SO but lower than FG, have shorter contraction periods.

WORK DONE BY THE MUSCLE

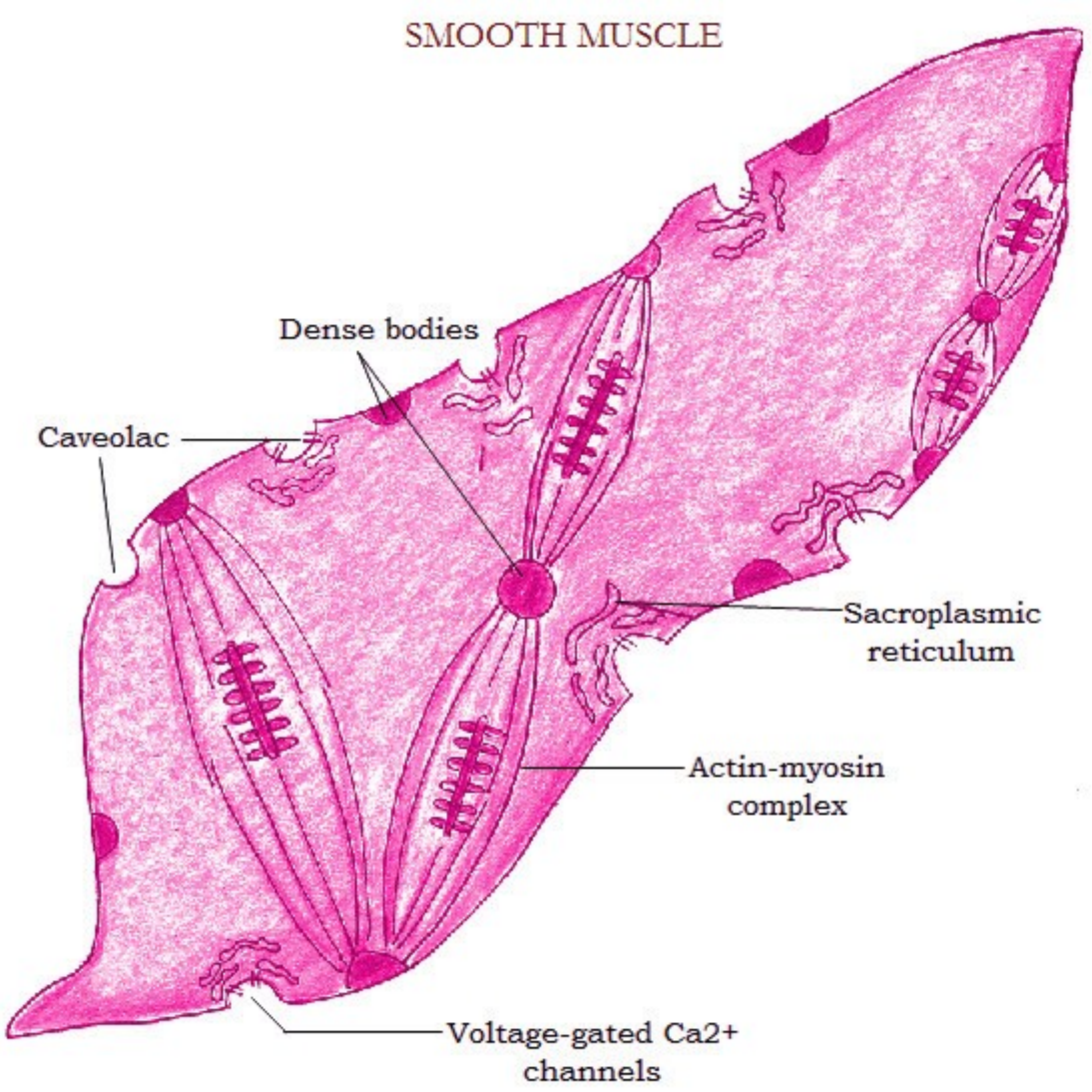
Work done (W) = (Hxl)/L

  - L – Length bet fulcrum and the tip of the lever
  - L – Length bet fulcrum and the weight load
  - H – Observed HT on contraction
- The chemical energy liberated during contraction is party converted into mechanical energy with manifibers ency indicated paction of total energy liberated is converted into work.
- Untrained animals = 20%
- Trained – 25 – 30%

- Isolated muscle – 40%

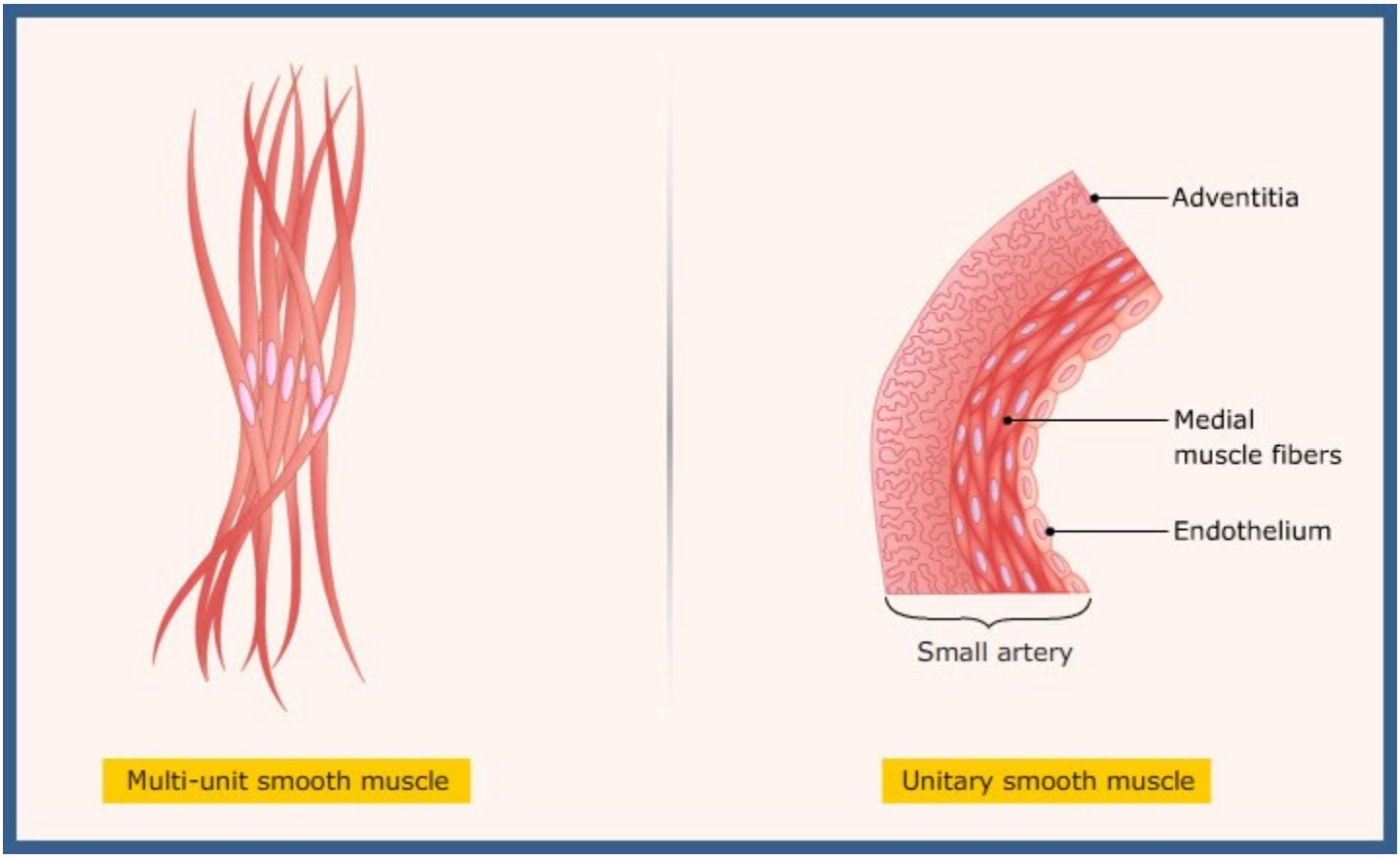
SMOOTH MUSCLE TISSUE

- Contains action and myosin filaments with are not orderly arranged. So no striations.
- **Two kinds**
    - *Visceral smooth muscles:* About 99% of the smooth muscles are of the unitary type. The fibers are tightly bound together top form continuous network called '*syncytium*' and wrap around sheets that form part of the walls of hollow visceral such as uterus and stomach, intestines, urinary bladder etc. When a neuron stimulation a fiber impulse travels over the *other fibers via 'gap junctions' so that contraction occurs in wave over many adjacent fiber direct electrical conduction*
    - *Multi unit smooth muscle tissue (Direct electrical conduction):* consist of individual fibers each with its own motor nerve endings, similar to that of skeletal muscles. About 1% of the smooth muscle is present as multiunit smooth muscle. Seen in the walls of blood vessels (sympathetic stimulation), **erector pili muscles that attach to hair follicles, intrinsic muscles of eye such as iris, nictitating membrane.**



- Both kinds of smooth muscles can contract and relax more slowly than skeletal muscles tissue (peculiar arrangement of thin and thick filaments). Smooth muscles can maintain forceful contraction for longer time (labour pain of uterus) than skeletal muscles. Smooth muscles can be stretched with out developing tension eg., Urinary Bladder, stomach wall etc.
- **The actin filaments are attached to protein – dense bodies** which in turn are attached to cell membrane. There are only 1 myosin filaments to every 12 – 15 actin but each myosin filament for more numbers of cross bridges – 3 kg/cm^2 pressure. *Latent period 150 – 200 ms and total time 1 to 3 sec for contraction and relaxation with in about 30 times as long as the single twitch of skeletal muscle*. Swiveling action of cross bridge is much slower ie., less ATPase activity. This economy of energy utilization by smooth muscle is important to overall function of the body, because organs such as intestines, UB, GB, must maintain moderate tone throughout life.
    - **Contration duration is longer in smooth muscles.**
    - Muscle proteins loosely organized so no myofibrils but force of contraction is almost equal to skeletal muscles.
    - Extra cellular materials like collagen, elastin are produced by smooth muscle.

- Smooth muscles are seen as sheets (GIT tract) or bundles (Erector pili) and **have no tendons except gizzard (Central tendon)**
- **Actin molecules are held by dense bodies (similar to Z-lines)**
- Contain α- actin similar to Z line
- **No tropomyosin, instead Calmodulin**
- In smooth muscle, myosin and actin happens only when light chain is phosphorylated.
- More of voltage gated Ca^{2+} channels - slow channels. These channels allow entry even in the absence of action potential.
- ECF (Ca^{2+}) has got strong influence on force contraction.
- Similar to cardiac muscle.
- **Prolonged contraction and relaxation period (200-300 msec.).**
- **No T-tubules**
- Stretching – contraction because of single unit smooth muscle depolarised and spread over large area (Gut).
- **Multi-unit smooth muscle found in ciliary body, iris, ductus deference and walls of large arteries. Here each muscle fiber in innervated separately & contracts only when it receives synaptic stimulation**.



Action Potential in smooth muscle

- They are two types
  - Spike potentials and
  - AP with plateaus ie., prolonged repolarization causing sustained contraction as in uterus.

ACTION POTENTIAL IN SMOOTH MUSCLE

Slow wave rhythm

- Some smooth muscles are self excitatory ie; elicite AP with out an extrinsic stimuli; due to waxing and waning of pumping of Na^+ outward – if rapid sudden decrease in electronegativity, if slow gradual decrease in electronegativity and once reaches – 35 mv causing action potential. ie., most of the peaks of slow waves, one or more AP occurs leading to rhythmical contraction of smooth muscle (Pacemaker waves). This type of activity is prominent in gut, ureter etc.
- Excitation of visceral smooth muscle by stretch also possible, here slow wave potential and decrease of membrane potential caused by stretch are the causes. Eg., gut loaded by ingesta --------> stretch --------> peristalsis; Uterus at full term -------> delivery.
- **In case of multi unit smooth muscle, depolarization is cased by neurotransmitters contraction with out generation of its own action potential.** Because the fibers are two small to generate an action potential where as in visceral smooth muscle 30 to 40 smooth muscle fibers getting depolarized simultaneously ie., self propagating AP ensures. Yet even without an AP in the multiunit smooth muscle fibers the local depolarization (caused by NT) spreads itself electronically over the entire fiber and it is all that is needed to cause the muscle contraction.
- Mechanism of Ca^{2+} in smooth muscle contraction: An effective troponin system is lacking Ca^{2+} itself excites contraction in smooth muscle fibers by activating ATPase activity of myosin head.
- *Local tissue factors and hormones causing smooth muscle contraction with out AP generation*: In fact probably half or most of all smooth muscle contraction is initiated not AP but by stimulatory factors like *non – nervous and non-AP stimulatory factors like local factors & hormones.* Eg., Contraction of met-areterioles, pre-capillary sphincters where virtually nervous connection is not there (smaller the size, little or no nervous supply), local changes like lack of O_2,excising of CO_2, excess H^+ cause vasodilatation. Hormones such as nor-epinephrine, epinephrine, Ach, angiotensin, vasopressin, oxtocycin, serotonin, histamine can cause vaso-constriction/dilatation depending upon the receptors in the smooth muscle (Excitatory receptor or Inhibitory receptor).
- Some of the hormones viz., nor-epinephrine, vasopressin and angiotensin have powerful excitatory effect causing spasm, of blood vessels for hours together.

Action potential in smooth muscles

- The smooth muscles have relatively lower resting membrane potential and short action potential (5 - 10 m sec.) than the skeletal and cardiac muscles. **The resting potential of the smooth muscle cells range from – 50 mV to – 60 mV. The action potential is regulated by Ca^{++} pump.**
- Action potential in visceral smooth muscle occurs in two forms:
  (1) spike potential (2) action potential with plateau.
- **Spike potential***:* Typical spike potential as in skeletal muscle occurs in smooth muscles which is elicited by electrical stimulation, hormones, transmitter substance from nerves, by stretch or spontaneously.

- **Action potential with *plateau*** occurs in visceral smooth muscle cells similar to cardiac cells to prolong the period of contraction in smooth muscles of ureters, uterus and vascular smooth muscles. In smooth muscle cells, the voltage-gated Ca^{++} channels are comparatively more in number than the Na^{+} channels. *Ca^{++} generate the action potential in the smooth muscles. Since the Ca^{++} channels are slow to open and close, the on set of smooth muscle contractions are slower.*

CARDIAC MUSCLE

- Involuntary, single centrally located nucleus, numerous mitochondria. **The T-tubular of mammalian cardiac muscles are larger (esp. in Ventricles) than those of skeletal muscles and are located at the Z lines rather than at the A – I band junction as in skeletal muscles fibers.** While the groups of skeletal muscle fibers an arranged in a parallel fashion, those of cardiac muscles branch freely with other fibers to form 2 separate net works.
    - Muscular walls and septum of atria
    - Muscular walls of septum of ventricles
- When a single fiber of either network is stimulated all the fibers in the network become stimulated as well. Thus each network contracts as a functional unit. Each fiber in a network is separated from the next fiber by an irregular transverses thickening of sarocolima called intercalated disc. Thus cardiac muscle can act as a *Syncytium* (which provides more rapid spread of impulses between fibers).
- Under normal conditions cardiac muscles tissue contracts & relaxes rapidly continuously and rhythmically with out stopping.
    - AP spreads cell to cell through "*Gap Junction*s", and in this way to entire heart (in skeletal muscles each fiber must be separately stimulated by a motor neuron).
    - **T – tubules poorly developed in atrial musculature. In verticals, they are much larger in diameter as compared to skeletal muscle.**
    - Location: They lie over Z-lines sarcoplam reti is not well developed;
    - No lateral cisternae – **So no Triads (ie., have *diads*).**
    - AP = 100 – 250 ms duration (Skeletal muscles = 2-3 ms duration.
    - Catechols – increase the Ca^{2+} release which causes force and frequency increase
    - Purkinje fibres specialized cardiac fibers for impulse conduction, part of the pace maker
    - **Have extensive Ca^{++} - Na^{+} exchange system.**

Rhythmicity

- Repetitive discharge of impulses normally occurs in the pace maker cells of SA node, smooth muscle and many neurones of CNS in which the resting membrane potential is only **- 55 to - 60 mV** which is not enough to close the Na^{+} and Na^{+}- Ca^{++} channels. This cause inward flow of Na^{+} and Ca^{++} creates still less negativity inside these cells and generates spontaneous and cyclic action potential. More over their cell membranes are naturally leaky to Na^{+} to generate the action potential at a faster rate.

MEMBRANE POTENTIAL IN CARDIAC MUSCLE

Resting membrane potential in cardiac muscle

- **The resting membrane potential in cardiac muscle is – 90 mV, but has long action potential (250msec).**
    - **Cardiac muscle = - 85 to - 95 mV**
    - Conduction system = - 90 to -100 mV
    - Ventricle muscle = -100 to -105 mV

- **S.A. node = - 50 to - 55 mV**

Action potential in cardiac muscle

- Cardiac muscle has an inherent property of generating its own action potentials rhythmically, independent of nerve stimulation. This occurs in the peacemaker cells of the S.A. node, which depolarises faster than any other parts of the heart.
- The onset of action potential in cardiac muscle is slower but prolonged than skeletal muscle which lasts for 150msec. in atria and 300 m.sec. in ventricle.In cardiac muscle, repolarisation does not occur immediately after depolarisation The positivity generated as the spike potential by the depolarisation remains as a plateau near the peak. This plateau lasts for a few-hundred m.sec prolongs the contraction of the cardiac muscle.
- *The reason for the prolonged action potential* in cardiac muscle cells is due to the presence of two separate channel systems
  - *Voltage activated Na channel (fast channel).*
  - *Voltage activated Na - Ca channel (slow channel).*
- Activation of the fast Na channels causes the spike potential of the action potential, **whereas the slow channel prolongs the passage of Ca^{++} and Na^{+} into the interior of the cell, thus establishes the plateau in the action potential.**
- *The inflow of Ca^{++} in to the cardiac muscle cells decreases K^{+} permeability by about 5 fold. This delays the K^{+} permeability to outside which in turn delays the re-polarisation process of the action potential in cardiac muscle*. This prolonged action potential (250 – 300 m.sec) provides longer contraction period in the cardiac muscle cells than the skeletal muscles. Hence cardiac muscle is not functionally tetanized.

MUSCLE PATHOLOGIES

- Skeletal muscle pathologies are classified into 3 categories
  - Muscle atrophies that have a neural involvement that derive form disease of ventral root cells, motor nerve roots or peripheral nerves
  - Disorders of neuro muscular transmission including myasthenia gravis, poisoning and various acetyl cholinesterase compounds botulism and tick paralysis
  - Disorder of muscle cell itself which are genetically determined myopatheis, muscle damage by external agents including physical damage, toxins and drugs such as steroids with chloroquine, inflammatory reactions due to viral or bacterial or parasite infestations and autoimmune disease (polymyositis), muscle disorders associated with endocrine or metabolic disease, myopathies associated with malignant disease such as rhabadomyeloma, tumors, amyloidosis and paroxysmal myoglobinuria.

CHARACTERISTICS OF SKELETAL, SMOOTH AND CARDIC MUSCLES

Property	Skeletal	Smooth	Cardiac
Cell shape, size and interactions and cell organelles	Cylindrical 10 - 100 µm diameters 2-3 cm long, no electrical	Elongated fusiform 1 – 12 µm dai., 15 – 500 µm	Multi branched 2 – 20 µm dia., 20-200 µm long,

	coupling (cell to cell conduction), no branching, prominent T-tubules, multiple nuclei, varying degree mitochondria present, triad is prominent.	long, functional syncytium, no branching. Moderately developed sarcoplasmic reticulum system, less prominent, T-tubules, few mitochondria	intercalated disc provide electrical coupling. Abundant mitochndria. No lateral cisternae, fairly developed sarcoplasmic reticular system.
Rhythmicity	Nil	Present	Present & characteristic
Conductivity	Very fast	Slower	Slower
All or none law	True for single fiber	True for single fiber	True for the whole heart.
Contractility	Simple muscle curve	Slow- all periods of the curve longer	Contraction longer than relaxation
Refractory period	**Short (with in latent period)**	*Longer*	**Longest** (whole contraction period is absolute refractory)
Tetanus	Possible	Not so	Impossible (long

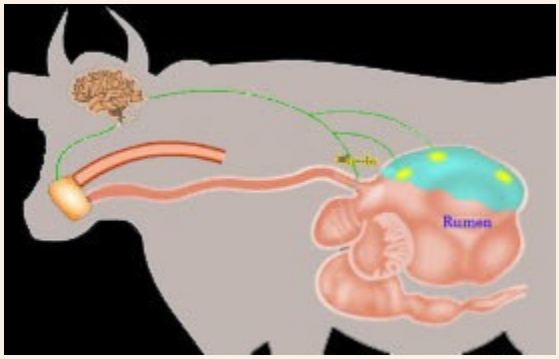
			refractory period ensures recovery)
Fatigue	Possible	Possible	Impossible (long refractory period ensures recovery)
Tonicity	Depend on nerve	Independent of nerve	Independent of nerve
Action Potential	**RMP = -70 mV,** AP is 1 msec long, AP depends on Na^+ and K^+ gradient. No spontaneous activity.	**RMP = – 55mV** (-50 to -60), larger resting N a^+permeability. AP depends on Ca^{2+} gradient. AP 10 ms long, AP is Ca^{2+} permeability dependent (SLOW CHANNEL). Stretch and pacemaker activation.	**RMP = -90 mV.** AP dependent gradients of Ca^{2+} K^+ and Na^+. Spontaneous pacemaker activity, no stretch induced activity, AP 250 msec long.
Actomyosin	Well	Lowest	Moderate

ATPase	developed	actomysion ATPase.	amount of actomysin ATPase.
Ca^{2+}	Ca^{2+} removes inhibition due to troponin. $Ca^{2+}$from sacrcoplasmic reticulum only, Ca^{2+}increases the activity of ATPase during contraction.	No troponin system. sparse sarcoplasmic reticular Ca^{2+}. Ca^{2+} form ECF (by diffusion). Ca^{2+} so latent period is more prolonged. Ca^{2+}pump works slowly causing relaxation, so more contraction time.	Ca^{2+} from ECF and sarcoplasmic reticulum. Troponin system present. Extensive Ca^{+}, Na^{+}exchange system. Ca^{+} ↑es strength of contraction and duration of systole.
Na^{+}	Excitation	Probably same	Initiates and maintains heart beat.
K^{+}	Reduce excitability and hastens fatigue	Probably same	Inhibits contraction and produces relaxation
Protein	maximum	Less	Less
Glycogen	less	More	More
Carnosine	maximum	Less	Less
Fats	Mostly neutral	Mostly neutral	More

	fats	fats	phospholipids and cholesterol than in other
Inorganic	Na^+/K^+ = 1/5 Ca^{2+}	About same	Na^+/K^+ = ½ Ca^{2+} ie., more Na^+
Energy metabolism	Glycolysis and oxidative metabolism.	Primarily glycosysis	Oxidative metabolism with high O_2 need. Also glycolysis & fatty acid metabolism.
Lactic acid	Oxidized less easily than glucose and often incomplete	Same as skeletal	**Completely and more readily than glucose**
Glycogen	Decreased metabolism of glycogen during starvation	Same as skeletal	Increased glycogen metabolism during starvation.
Blood supply and O_2 consumption	moderate	Less	High
Control	Voluntary	Not so,	Not so,

		involuntary	involuntary
Innervations	**Single innervation** with Peripheral NS A-ch as neurotransmitter.	Dually innervated by Autonomic NS. Excitation and inhibition modulates ongoing activity	Dually innervated by ANS. Parasympathetic slows down activity and sympathetic increases.
Electrical events	Short AP (1 ms) does not over lap with twitch event (30 ms). Summation possible.	Relatively short Ap (5-10 ms), does not over lap with prolonged twitches. Summation possible	Very long AP (250 ms), almost completely overlaps with long twitches (300 ms). No tetanus and no summation possible.

MODULE-19: DIGESTIVE SYSTEM OF MONOGASTRIC ANIMALS AND RUMINANTS



LEARNING OBJECTIVES

At the end of this module, the learner will be able to know,

- the difference between ruminant and monogastric gastro intestinal tract,

	• factors of digestion and • functions of saliva and it's importance in the ruminant animal will be known.

PHYSIOLOGY OF DIGESTION AND ABSORPTION

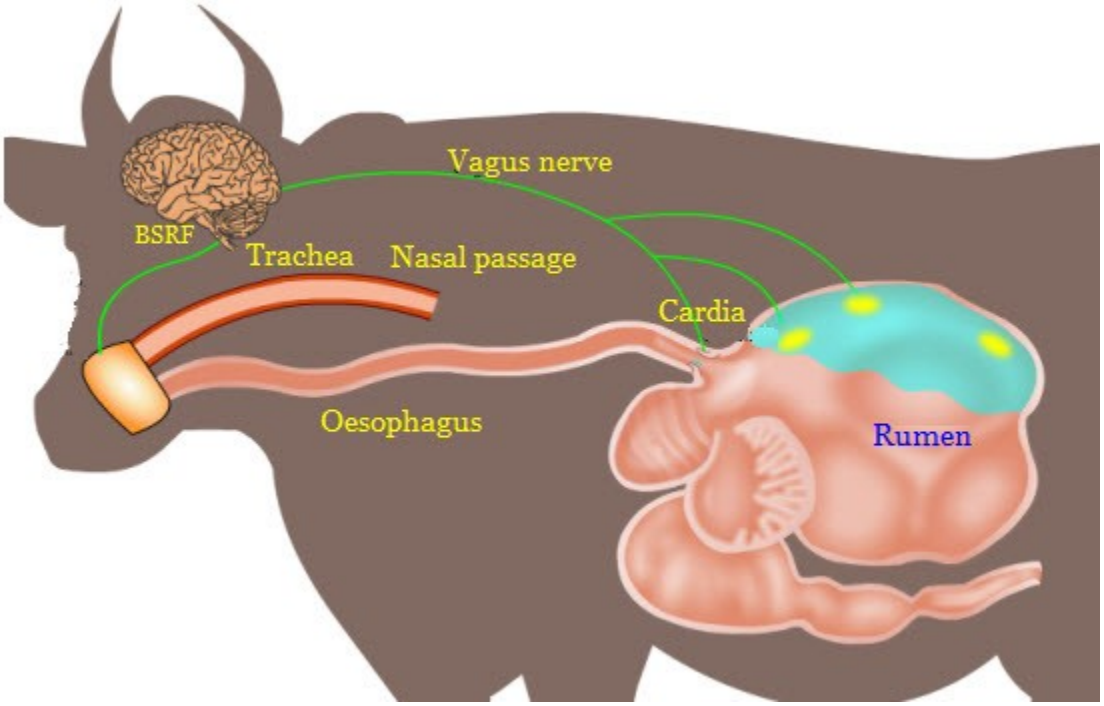
- Digestion is the process of breakdown of complex food into simpler form by the activities of the alimentary tract and glandular secretions for absorption of nutrients and the rejection of their residues.

Food

- Food is a complex mixture of substances like carbohydrates proteins, fats, vitamins, inorganic salts and water to meet the nutritive requirements of an animal.
- *Herbivorous animals* (*Cattle, sheep, horse, goat* etc.,) derive their nutritive requirements from plant sources.
- *Carnivorous animals* (dog, cat etc.,) obtain their food from animal sources.
- *Omnivorous animals* (*man, pig, etc*) get their foods from both animals and plants sources.

Alimentary tract

- It extends from the lips, mouth, pharynx, oesophagus, stomach, small intestine (Duodenum, jejunum and ileum), large intestine (Caecum, colon and rectum) and anus .
- In carnivores, alimentary tract is small and simple.
- The simple stomach herbivores(horse, rabbit), are also referred as *hind-gut digesters* because they have relatively simple stomach portion,but the large intestine is much more complex and voluminous than the carnivores.
- In ruminants (cattle, sheep and goat), the stomach is extensively large and complex, whereas the large intestine is relatively small , hence they are known as *fore-gut digesters*.



Functions of GI tract

- To assist in the acquisition of nutrients.
- To prepare nutrients for digestion.
- To digest the nutrients.
- To felicitate absorption of products of digestion.
- Absorbtion of water.
- As excretory organs to help in elimination of waste products.
- As an endocrine gland to influence digestion and other metabolic functions.
- Motility of the GI tract.

Prehension of food

- Prehension is the seizing and conveying of food into the mouth. In bipeds (Primates) the hands are the prehensile organs. Dogs and Cats hold their pray with the forelimbs which is passed into the mouth by the head and jaw movements. In horse, upper lip, tongue and the incisor teeth are the main prehensile organs to collect the food. The clefted upper lip in sheep favours close grazing, on contrast the unclefted upper lip in goat. In cattle, large strong, rough protrudeable tongue and incisor teeth of the lower jaw are the prehensile organs. The pointed lower lip functions as a prehensile organ in swine.

FACTORS OF DIGESTION

Mechanical factors

- Mastication (Grinding the food)
- Deglutition (Swallowing)
- Regurgitation (Return of the cud from stomach to mouth)
- Rumination (Chewing of cud)
- Remastication (Regrinding)
- Redeglutition (Reswallowing)

- Intestinal motility
- Eructation (Elimination of gases)
- Defecation (Elimination of fecal matters)

Chemical factors

- Digestive enzymes and hormones
- Non-enzymatic chemicals: HCl, HCO_3

Microbiological factors

- Bacteria
- Protozoa
- Fungi

MASTICATION

Definition

- Extensive chewing of the feed causes mechanical reduction in the size of the food. The finely divided food particles provide greater surface area for enzymatic action and proper mixing with salilva for easy swallowing.
- This act is achieved by diduction and occlusion of both the upper and lower molar teeth.
- Temporo mandibular joint is involved. Hence, lateral forward and backward movement is possible.
- Most of the animals masticate on one side at a time due to the anatomical arrangement of the dental table (wider upper jaw and narrower lower jaw).
- Molar teeth are chisel shaped with the arrangement of inner most lower teeth and outer most teeth. Both are sharp edged.

Importance of mastication

- In herbivores mastication is of greater significance due to the coarse bulky nature of food.
- In ruminants, only during remastication the food is thoroughly ground.
- In herbivores, mastication of food material is by lateral movement of the lower jaw and to-and-fro movement.
- In herbivores, the upper jaw is wider than the lower jaw and mastication of food occur on only one side at a time.
- The molar teeth are chisels shaped with sharp edged lower teeth pointed towards inner side and that of upper teeth towards outer side. Incisor teeth are used to cut and lacerate the food
- In ruminants, the upper incisors are absent, but modified as *dental pad* and in the lower jaw they are loosely and obliquely placed in the sockets.
- Grazing
    - *Traditional grazers* (sheep, cattle)
        - Grass and roughage eaters.
        - Mostly graze on monocotyledons
        - Use their small mouth and long tongue to grasp grass and hay.
        - Tongue is curved around the grass
    - Browser ruminants (deer, giraffe and moose)
        - Graze on dicotyledons
        - Have large mouth opening and use their incisors to gnaw on fruits and flowers, trees.
    - *Intermediary* – opportunistic feeders (goat)
        - Adapt to both the pattern of feeding.
        - They prefer low fiber dicotyledons .
        - Preferred food can be sought by climbing

- Bovine
  - Keratinized papillae of the bovine helps in the passage of food in the oral cavity.
  - As the tongue pushes the cell grass between the lower incisors and upper dental pad, simultaneous mandibular severing reduces the size of the particles.
  - As rumination is the predominant activity, they spend less time in initial mastication.
- Sheep and goat
  - Mandibular grinding
- Horse
  - Incisors thrust the feed into the oral cavity with the propulsive movement of mandible,maceration of grass at its base is achieved.
  - Masticate thoroughly prior to swallowing.
- Omnivores occupy a position between herbivores and carnivoresin the aspect of timing.
- Pig
  - Use incisors, tongue and propulsive movements of head for mastication.
  - Rhodents have the unique property of mastication due to their ability to shift their teeth in a proplineal pattern.
- In carnivores, mastication is imperfectly performed by vertical movement of the lower jaw.
- Dog and cat
  - Mastication is done by teeth with food in oral cavity by propulsive head and mandibular movements.
  - In cats, papillae of the tongue (dorsal lingual spicules) help in pushing the feed into the oral cavity.
- In carnivores and omnivores, the upper and lower jaws are equal width and the teeth are relatively simple.

Drinking

- *Dogs and cats*
  - Fluid is drawn into the oral cavity by the rapid extension and retraction of the tongue by making the free end of the tongue as laddle like structure to convey the liquid into the mouth.
- *Horse, Bovine, Sheep and Goat*
  - Drinking of fluid is by suction by creating negative pressure by keeping closed mouth beneath the fluid and tongue.

Suckling

- It is effected by creating negative pressure in the mouth largely by the back ward movement of base of the tongue.
- Milk is forced from the teat into the mouth due to pressure gradient.

FUNCTION AND MECHANISM OF MASTICATION

Fuction

- Physical breakdown increases the surface area of food, which improves the microbial digestion.
- Assist in appreciating the flavor of the food.
- Improves salivary and gastric activities.
- Initial digestion of carbohydrates is facilitated.
- Contributes to dilution and buffering of ruminoreticular fluid.

Mechanism

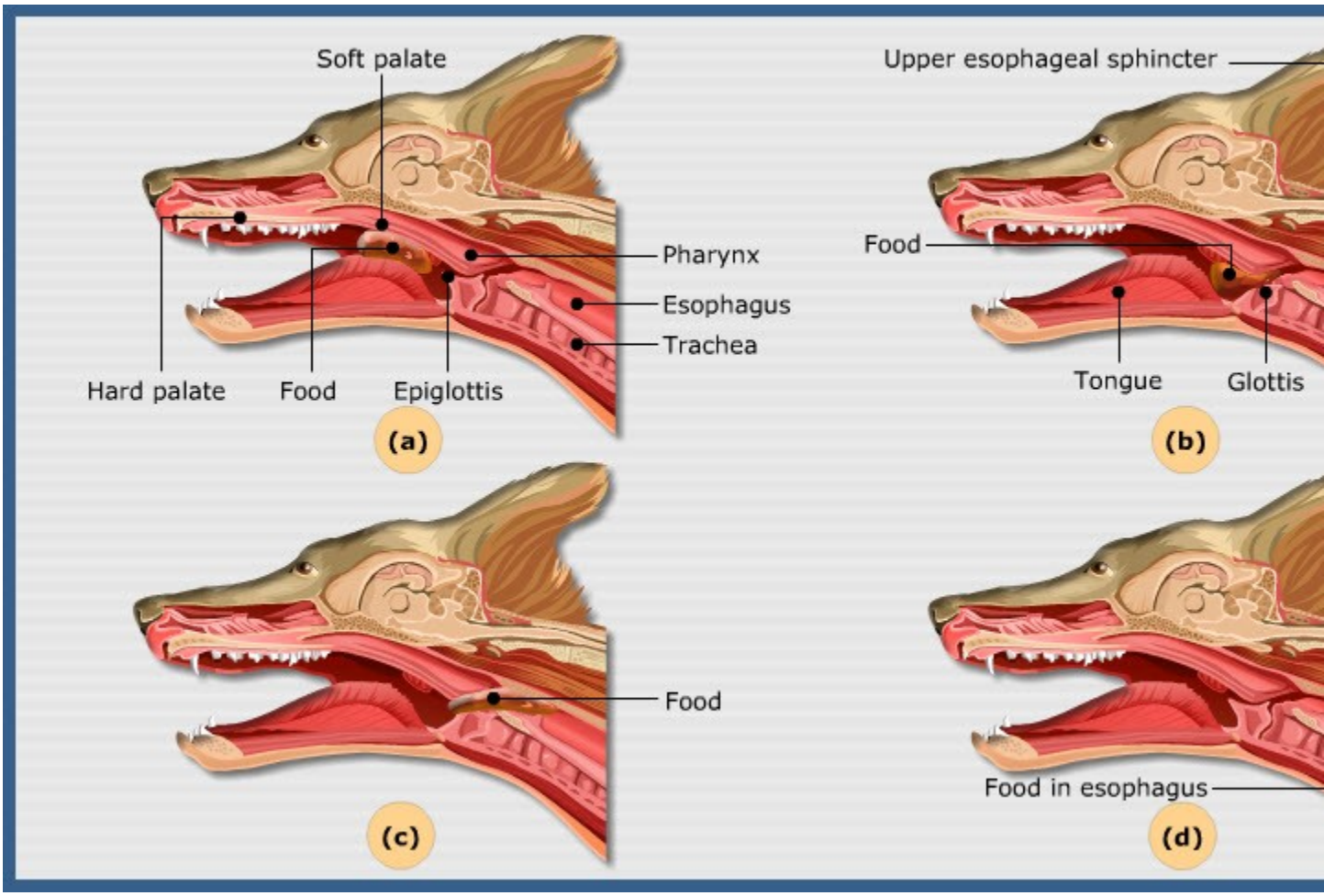
- Reflex activity under the control of CNS.
- Mastication is basically a voluntary act but usually takes place involuntarily.
- Mastication reflex or chewing reflex is the rhythmic movements of mandible.
- Lowering pf mandible due to extension of tongue(mainly in bovine) is known as **LINGUO MANDIBULAR REFLEX.**
- Stimuli for masticatory reflex is the presence of food in the oral cavity.
- These are receptors in tongue and oral mucosa which initiates mastication by the sense of food.
- **Sensory impulses are carried via trigeminal, facial, and glossopharyngeal nerves to brain stem.**
- Efferent via trigeminal supplied to mastigatory muscles.
- This in turn causes rhythmic movement of the mandible in relation to the maxilla.
- This results in shearing and crushing of food.
- The main mastigatory muscles include temporalis with the assistance from massetor muscle for shearing and massetor with the assistance from pterygoid muscles for grinding.

DEGLUTITION (Swallowing)

- Deglutition is the act of passage of food from the mouth to the stomach through pharynx and oesophagus. It starts, as a voluntary act then becomes an involuntary reflex during its execution. The afferent nerves originate from receptors located in the posterior part of the mouth and pharynx. **Deglutition center is situated in the medulla.**
    - It is the motor activity involving the integrated movement of muscles of tongue, pharynx and oesophagus. (including the peristaltic movement)
    - It is under direct neural control of brain.
    - Complex action of tongue, to place the bolus centrally between the tongue and the hard palate. Pressure of the bolus in the pharynx stimulates pharyngeal pressure receptors to intiate swallowing reflex.

Act of swallowing

- It takes place in three phases
    - From mouth to pharynx (voluntary act)
    - From pharynx into the oesophagus (reflex mechanism)
    - From the oesophagus into the stomach (reflex mechanism)
- Contraction of mylohyoid and hypoglossal muscles.
- Pressing of the tongue against the hard palate and pulling the root of the tongue backwards.
- The tongue acts like a plunger driving bolus towards pharynx.
- Elevated soft palate is to cut off communication with nasal passage.
- Forward pulling of hyoid bone and the larynx,cause opening of the entrance of oesophagus.
- Closure of the larynx by epiglottis make the bolus to enter directly into the oesophagus.



STAGES OF SWALLOWING

- Pharyngeal stage - Phryngeo oesophageal sphincter
- Oesophageal stage - Significance of lower esophageal sphincter.

Pharyngeal stage

- Relaxation of pharyngeo oesophageal sphincter.
- Peristaltic contractions of the pharynx to propel the food bolus from the base of the tongue into laryngopharynx.
- Propulsion of the bolus via relaxed pharyngeo oesophageal sphincter to the esophagus.
- **Pharyngeo oesophageal sphincter**
    - It is also known as upper oesophageal sphincter formed by the cricopharyngeal muscle and oesophageal circular muscle.
    - As the bolus proceeds to upper oesophagus, simultaneous contractions of this sphincter to a closed state to initiate next stage of swallowing reflex.
    - The bolus travels from cranial esophagus to caudal oesophagus via gastro esophageal junction.
    - Gastro esophageal junction is guarded by a lower oesophageal sphincter.
    - Reflex, contraction of the oesophageal muscles to propel the bolus down.
    - This reflex is completed by vagus.

- Accumulation of several boluses in the oesophagus causes local myogenic stimulus initiates more powerful peristalsis to push the food to gastro oesophageal junction.

Oesophageal stage

- Lower oesophageal sphincter
  - It differentiates esophagus and stomach.
  - Physiologically is in a high pressure zone.
  - The incoming bolus exert force to open this sphincter.
  - This is an active reflex mediated by vagus to increase oesophageal pressure.
  - Synchronized act of relaxation of lower oesophageal sphincter with oesophageal wave propel the bolus into the stomach.

SWALLOWING REFLEX

- **Swallowing centre is located in the brain stem (medulla oblongata).**
- Stimulation of the receptors in the soft palate, pharynx (posterior wall) and epiglottis (dorsal surface) by food material.
- Sensory fibers emerge through vagus, glossopharyngeal and hypoglossal to mylohyoid and hypoglossal muscles.
- Contraction of mylohyoid and hypoglossal muscles press the tongue against hard palate. Backward pulling of the tongue elevates soft palate.
- The tongue forces the bolus in the opened oesophagus.
- Pulling action of hyoid bone and larynx opens the oesophagus.
- Larynx is closed by epiglottis.
- This reflex involves internucial neurons from reticular formation.
- Swallowing centre also activates the neighboring respiratory regulatory neurons.
- This interrupts respiration during swallowing to avoid aspiration of food particles into respiratory passages.

Mechanism of regurgitation

- Common in ruminants.
- Initiated with closed glottis and raised palate.
- Drop in intrathoracic and intraesophageal pressure due to inspiratory effort of the tongue.
- Opening of cardia, clearing of cardia.
- Extra reticular contraction (regurgitation contraction) pushed ruminoreticular cud to the mouth via esophagus.

OESOPHAGUS AND STOMACH

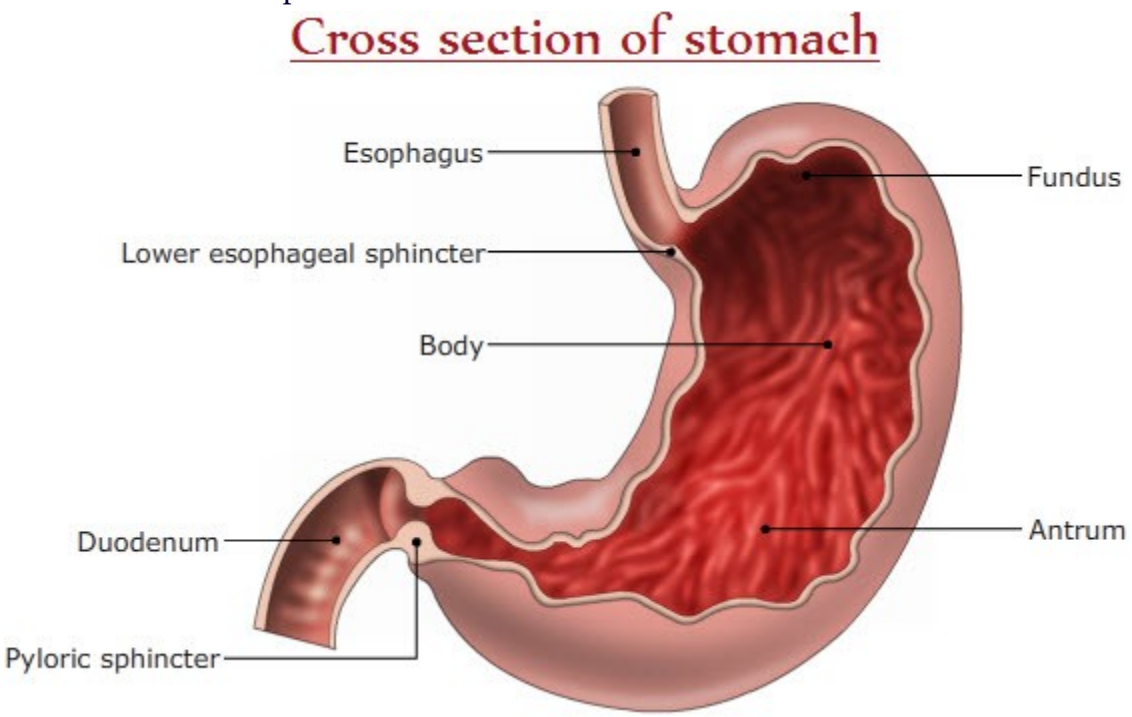
- Oesophagus is a muscular tube like structure extends from the pharynx to the stomach. In dog, cattle and sheep, the muscular layer is striated throughout the length of the oesophagus, whereas in pigs and horse, it begins as striated but becomes smooth muscles at caudal oesophagus.
- The *pharyngeo – oesophageal* junction is normally closed by *oesophageal sphincter*.
- Vagus is the main motor nerve regulates the motility of the oesophagus.
- During swallowing, the peristaltic wave travels from pharyngeo - oesophageal sphincter towards *cardiac sphincter* which is located at *gastro-oesophageal junction*.
- Reverse peristalsis/antiperistalsis is involved in bringing the gastric contents into the oesophagus during belching and regurgitation.
- Peristaltic waves, bucco - phryngeal pressure and gravity are responsible for the movement of food bolus through oesophagus, of which bucco - pharyngeal pressure is important for the passage of liquids.

Cardia

- The point of opening of oesophagus into the stomach is called cardia.
- It is provided with a sphincter muscle known as cardiac sphincter.
- It prevents back flow of food from stomach to oesophagus.
- Cardia is ordinarily closed except during swallowing and regurgitation.
- The cardiac sphincter is well developed and powerful in horse.
- The activity of cardiac sphincter is under the control of CNS.

Stomach

- It functions as a reservoir of food.
- Actively involved in grinding the food to reduce their size
- Initiates enzymatic digestion of food materials
- Controls the rate of passage of food to the small intestine for final digestion and absorption.
- Produces the intrinsic factor for the absorption of vitamin B12 from the intestine, which involves in hematopoiesis.



- Based on structure and function of stomach, domestic animals fall into two general classes.
    - Non-ruminants/ simple stomach animals – Horse, cat, dog, and pig.
    - Ruminants – Cattle, sheep , goat, camel and buffalo
- The stomach of nonruminants is simple consisting of only one compartment, whereas the stomach of ruminants is complex, consisting of four compartments (rumen, reticulum, omasum and abomasum) of which only abomasum secretes the gastric juice
- The stomach is a hollow, sac like organ made up of four layers - serous, muscular, submucosa and mucosa from outside to inside.
- The stomach mucosa of simple stomach animals, is divisible into *oesophageal (glandless)* region and *glandular* region. The glandular area includes *cardiac, fundic (parietal)*and *pyloric* regions.

- In horse, oesophageal region is extensive up to 1/3 to 1/5 of the surface area of stomach. In the glandular region, the cardiac gland zone is very narrow, while the fundic gland zone is very wide.
- In pig, the oesophageal region of the stomach is limited to a small area around the cardia. The cardiac gland zone is very extensive, whereas the fundic and pyloric gland zones are similar to those of horse.
- In dogs, the oesophageal region is absent, the cardiac glands are found as a narrow zone scattered along the lesser curvature of the stomach around the cardia. The fundic glandular zone is extensive occupying about 2/3 of gastric mucous membrane.

RUMINANT STOMACH

- Ruminants are animals capable of regurgitating their food from their stomach and remasticate them.
- Capacity of the stomach varies with age and size of the animal.
- All herbivorous animals have spacious compartments in their G.I tract. It favours retention of bulky fibrous plant for soaking, mixing and microbial fermentation.
- In ruminants and kangaroo, stomach(Rumen) provides an additional space for microbial fermentation.
- Bacteria, protozoa and fungi in the rumen are responsible for extensive fermentative digestion in the rumen. It is supported by the mechanical activity of the three compartments(rumen,reticulum and omasum).
- Only the abomasum, the true stomach secretes gastric enzymes and HCl. Ruminants are animals which can regurgitate and remasticate.
- Abomasum is the largest compartment in new born ruminants.
- As age advances, the rumen and reticulum grow at a faster rate than abomasum.
- In adults, rumen and reticulum occupies 69%, omasum 8% and abomasum 23% of the stomach portion. View image...
- Omasum is not well developed in sheep and goat, it **is absent in Camel and Llama(Tylapoda)**
- Oesophagus opens into the rumen through cardia.
- Rumen has two sacs, dorsal and ventral sacs that are freely communicating with each other.
- Rumen is connected to reticulum by rumino – reticular folds.
- Reticulum is communicated with omasum through reticulo –omasal orifice.
- Oesophageal/reticular groove extends from the cardia to reticulo – omasal orifice.
- It is a gutter like invagination. This groove is more functional in young ruminants. View image...
- During suckling the receptors in the pharynx and mouth get stimulated causes reflex closure of reticular groove to conduct liquid and milk directly from the oesophagus into reticulo – omasal orifice, bypassing rumen and reticulum.
- In calves, reticular groove/oesophageal groove acts as a bypass route for the passage of milk directly from the oesophagus into the omasum and abomasum.
- Closure of this groove is mediated by behavioural, psychological resposed and also by chemicals.
- Administration of chemicals like NaCl, $NaHCO_3$, $CuSO_4$ and sugar solutions reflexly close this groove, but $CuSO_4$ is less effective in calf and older ruminants, but more effective in sheep.
- Sodium salts like $NaHCO_3$ (60ml of 10% solution) stimulates closure in calves.

OTHER STRUCTURES

Liver

- Liver and gall bladder represent accessory structures of the digestive system.
- Metabolic organ, participate in digestion, metabolism and also in circulatory/immune system.
- Special and unique organ as it receives double blood supply, seat of metabolism and is of diagnostic purpose.

Pancreas

- Representing one of the accessory structures of the digestive system secretes clear, colorless liquid representing water, enzymes and salts like sodium bicorbonate.

Small Iniestine

- Has 3 portions Duodenum, Jejunum and Ileum. Concerned with digestion and absorption.

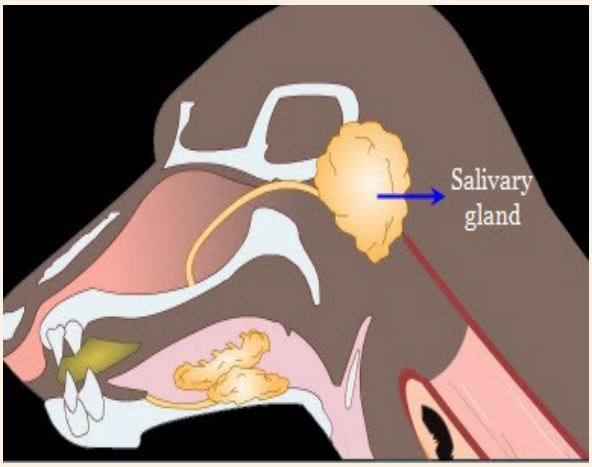
Large intestine

- Has 3 major portions viz. cecum, colon and rectum. Main function includes formation of certain vitamins, completion of absorption, formation of dung and its expulsion.

Gastro-intestinal motility

- The walls of GI tract are muscular and capable of generating slow waves of electrical depolarization which are originated by the presence of food/ingestion as a stimuli from various areas of gut lumen.
- These motility aims to propel ingesta from one area to the other, to promote digestion and to aid absorption.
- Movement popularly known as motility are of propulsive, reventire or mixing.

MODULE-20: SALIVARY SECRETION, FUNCTION AND REGULATION



LEARNING OBJECTIVES

At the end of this module, the learner will understand ,

- the basic unit of salivary secretion,
- mechanism of salivary secretion and
- it's control and importance in animals.

SALIVARY GLAND AND ITS SECRETION

- **Salivon is the functional salivary unit.**
- It begins most proximally as several Acini which converge into a intercalated duct.
- Numerous intercalated ducts unite to form a striated duct. A group of these ducts directly drain their content into glandular tubule which pour their content into fewer excretory ducts.
- Finally, the excretory ducts converge to form a single excretory duct, which leads to oral cavity.

Salivary gland and secretion

- Saliva is the mixed secretion of three pair of main salivary glands, namely parotid, sub maxillary or sub mandibular and sublingual and also many small glands found in the mucous membrane of the mouth.
- Glands in general are divided into serous, mucous and mixed types.
- Serous glands give rise to thin, watery secretion containing protein without mucin, mucous glands produce a secretion containing the glycoprotein in mucin ; mixed glands produce both serous and mucous secretions.
- Cells that gives rise to a serous secretion also secrete enzymes. **Zymogens granules are the precursors of enzyme stored in the serous cells.**
- Mucous gland is collected in a system of ducts which discharge their content through larger ducts into the mouth.
- The absorptive and secretary activities of the cells lining the ducts affect the composition of the saliva.
- In most of the mammals, parotid glands are serous. In some animals the secretion of this glands is devoid of enzymes .
- The sub maxillary glands is mixed in ungulates, dogs and cats but it is serous in rodents.
- The sublingual gland of the horse, ox, pig, dog and cat is a mixed gland and that of rodents is mucous.

Salivary glands of ruminants

- Parotid, submaxillary and sublingual are the major salivary glands of ruminants.
    - In addition, sheep and cattle have two inferior molar glands, small and numerous buccal and labial glands in cheek and lips, palatine glands in hard and soft palate and pharyngeal glands in the pharynx and roof of the tongue.
    - *Inferior molar is a* serous gland
    - *Buccal, Pharyngeal* and *Palatine* are mucous glands
    - *Labial is a m*ixed gland
- Based on the composition of saliva salivary glands are classified as
    - *Alkaligenic glands* (Parotid, Inferior molar, Buccal and Palatine) secrete more of HCO_3 and low content of mucin.
    - *Mucogenic glands* (Submaxillary, Sublingual and Pharyngeal) secrete more of mucin with low concentration of HCO_3

Pattern of secretion

- The parotid glands secrete spontaneously and continuously. Its secretion is rapid during feeding and rumination on the side of bolus chewing. Its flow is about 2ml/min. at rest and 30 to 50ml/min. during rumination. Mechanical

stimulation of mouth, cardia, reticulo-omasal orifice, lips of oesophageal groove and walls of reticulum reflexly stimulate parotid secretion.

- Secretion of inferior molar occur only during feeding, whereas buccal and palatine glands shows slow resting rate of secretion. Flow of saliva in cow is 60 to 160litres/day; in sheep 6.0 to 16litres/day.
- In dogs, submaxillary and sublingual glands show free flow of saliva during chewing of normal meat (no secretion by parotid), whereas dry meat powder excites abundant secretion from the parotid.
- In horse, parotid secretion occurs only during feed intake, whereas in ruminants, parotid secretion is continuous.
- Sheep show slight increase in parotid secretion as a result of feeding.
- Numerous small glands like inferior molar, buccal, labial, palntine and pharyngeal do contribute to the quantity of ruminat saliva. Volume of saliva produced by adult cattle is 90-190 litre per day.
- Salivary secretion is continuous.
- Flow of saliva varies with activity and increase with feeding and rumination to aid deglutition.
- Type of ration influences rate of salivation.
- Saliva is predominantly of two types i.e. serous and mucus.
- Serous saliva is rich in carbonate ions and is secreted continuously.
- Mucus saliva helps to reduce foaming by increasing surface tension and is secreted when animal is feeding and is rich in mucopolysaccharides.

Methods of studying salivary secretion

- Mixed saliva may be obtained directly from the mouth.
- By means of cannulation of the appropriate salivary ducts.

SALIVA - COMPOSITION AND SECRETION

Spontaneous secretion of saliva

- Some salivary glands possess the innate ability to secrete in the absence of any from of stimulation and this type of secretion is known as spontaneous secretion. This mechanism exists for maintaining the moist mucous membrane of the mouth and pharynx. In ruminant, the parotid salivary glands secrete spontaneously.
- Stimulation of salivary buccal receptors by the entry of the food in the mouth reflexly stimulate copious salivary secretion. Normal foodstuffs cause salivary secretion rich in mucin and enzymes to facilitate easy swallowing, while dry or noxious materials cause watery secretion with little mucin.

Composition and formation of saliva

- Saliva like all digestive secretions, is formed from the blood.
- Mixed saliva obtained from the mouth is a colorless, slightly opalescent liquid containing small amounts of electrolytes, protein and in some animals, a carbohydrate splitting enzymes- salivary alpha amylase, desquamated cells from buccal mucosa and lymphocytes derived from the lymphoid tissues in the mouth and pharynx are also present.
- Dog parotid saliva is highly fluid and thin like water,whereas dog sub maxillary glands saliva is highly viscous. The protein of saliva are complex and the term mucin is the galactosamine containing muco proteins. In some animals the resting serous cells of salivary glands contains numerous zymogen granules which are the precursors of the salivary enzymes, alpha amylase, and which disappear after prolonged secretion.

- During para sympathetic stimulation, the rate of secretion of both the sub maxillary and parotid glands is almost linear to the rate of stimulation, some of the inorganic constituents of the saliva change their concentration as the rate of secretion increases, the sodium and chloride concentration in the saliva are greater at high rates of secretion than at lower rates whereas the concentration of bicarbonates and potassium are higher at higher secretory rates.

Composition of Ruminant saliva

Inorganic salts	Nacl, KCl, $CaCO_3$, $NaHCO_3$, PO4
Organic components	Mucin, Ptyalin, Urea,Uric acid, Creatinine and Amino acids.
Suspended organic matters	Leukocytes and epithelial cells
Gases	CO_2, O_2, H_2, N_2 and water vapours

Reaction of saliva

- Slightly acidic in man, slightly alkaline in most of the domestic animals (except ruminants) and distinctly alkaline in ruminants.

Amount of saliva

- Amount of salivary secretion is inversely related to moisture content in the food. Quantity of salivary secretion:
  - Horse- 50 ml / minute during mastication
  - cow- 100 to 200 L/ day
  - single parotid gland of sheep- 930 to 1840 ml/24hrs.

NERVE SUPPLY AND FUNCTION

Innervation

- In addition to neural or hormonal stimuli the secretory cells of the salivary glands secrete saliva spontaneously. Neural stimulation produce more secretion in most species. The salivary glands receive both efferent innervations of sympathetic and para sympathetic nervous system which mainly act synergistically on the salivary glands.

Sympathetic supply

- The sympathetic fibers leaves the spinal cord as pre ganglionic fibers in the ventral roots of the first two or three thoracic nerves and pass through the cervical sympathetic chain to the superior cervical ganglion. The post ganglionic

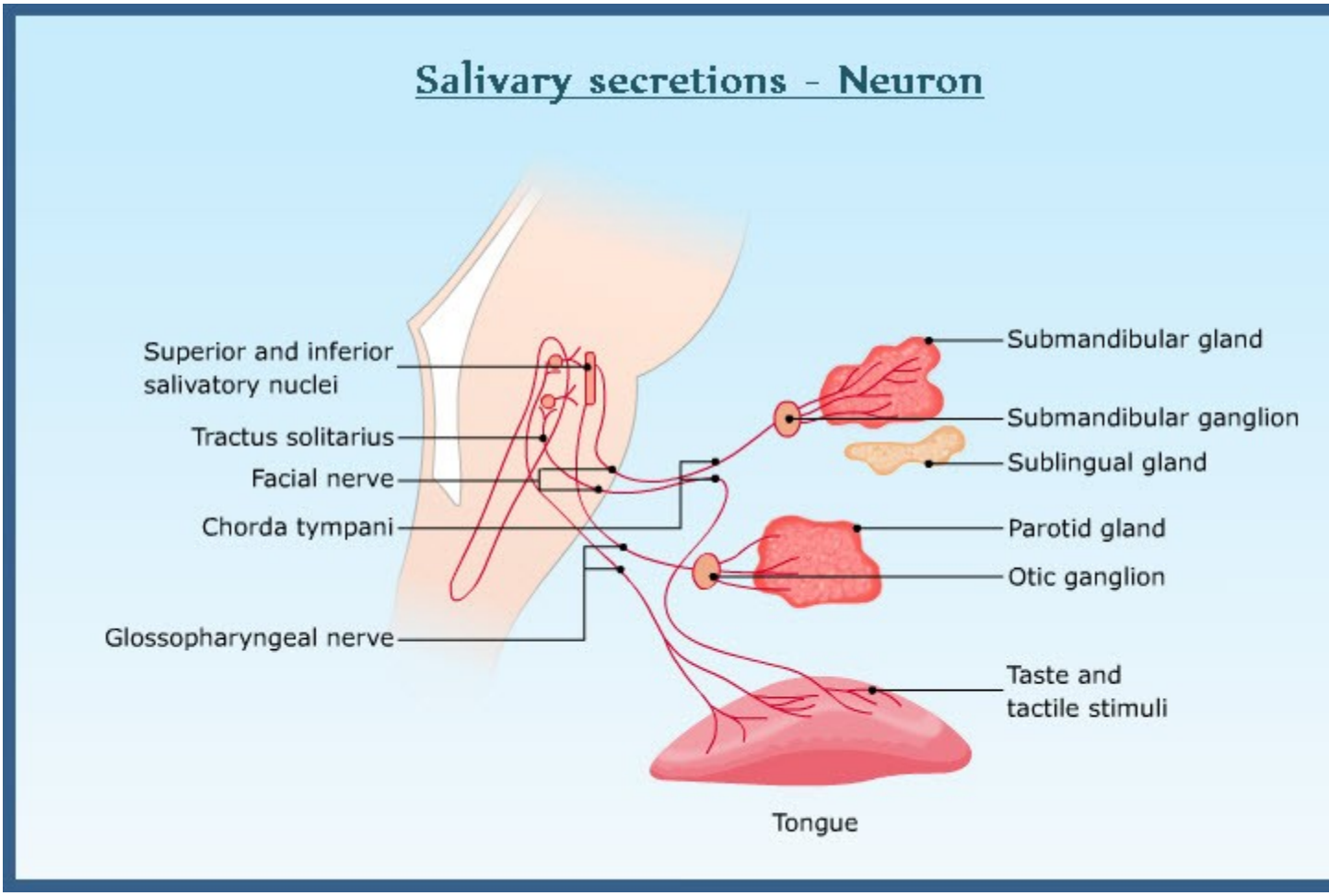
fibers (adrenegic nerves) from the superior cervical ganglion are distributed to blood vessels of the salivary glands and the secretory cells.

Para-sympathetic supply

- The preganglionic fibers of the para sympathetic fibers leave the brains stem through glosso-pharyngeal and trigeminal nerves, synapse with the otic ganglion which privides post ganglionic fibers to the parotid gland. The preganglionic parasympathetic fibers to the sub maxillary and sub lingual glands leave the brain stem in the facial nerve and travel along the chorda tympani to join the lingual nerve before their synaptic junctions with sub maxillary ganglion. This ganglion provides cholinergic post ganglionic prasysmpathetic fibers to sub maxillary and sub lingual glands.
- Two salivary secretory centers are located in the central nervous system-Brain stem (Medulla), one is concerned with the sub maxillary gland, and the other with the parotid. However stimulation of any one of these two areas causes secretion by both glands.
- The medullary salivary nuclei acts as center of the gustatory reflex, It is also regulated by inhibitory or excitatory signals from higher centers of the brain , particularly from certain regions of the diencephalon and cerebral cortex. Afferent impulses from the mouth, pharynx, and olfactory areas are carried by the trigeminal and glossopharyngeal nerves to the salivary centers.

Regulation of salivary secretion

- Nerve supply
  - *Trigeminal* and *glossopharyngeal* are the sensory/afferent to the salivary centers, located in *medulla oblongata*. The motor/efferent fibers are formed by both sympathetic and parasympathetic nerves of the autonomic nervous system.
  - Stimulation of sympathetic nerves causes vasoconstriction in the salivary glands results in thick salivary secretion rich in mucin and protein.
  - ***Facial* and *glossopharyngeal* nerves are the parasympathetic efferent fibres to salivary glands**. They stimulate cholinergic receptors in the salivary acini, causes vasodilation and copious salivary secretion rich in water and HCO_3, but low content of protein.
  - ***Bradykinin* a vasodilator polypeptide, formed by parasympathetic stimulation of the salivary glands.**
  - Anticipation of food intake produces increased parasympathetic response results in increased salivary secretion.



Effects of nerve stimulation

- Stimulation of the parasympathetic efferent fibres results in a copious secretion of saliva, with high mucoprotein content from the sub maxillary glands, and serous or watery secretion from the parotid glands. The amount and composition of the secretion vary with intensity of stimulation. Stimulation of the parasympathetic efferent fibres shows marked vasodilatation which greatly increases the blood flow to the glands.
- **Vasodilatation is also brought about by specific vasodilator substance like bradykinin.**
- The response of stimulation of sympathetic efferent fibers is variable and differences are found in different glands among different species.In the cat, there is a considerable flow the sub maxillary gland and none from the parotid. Sympathetic stimulation immediately followed by para sympathetic stimulation produce saliva containing much higher proportion of mucus than para sympathetic stimulation alone.

Effect of denervation

- Sectioning of the nerve supply of the salivary glands leads to complete cessation of the salivary secretion except the glands which exhibit the property of spontaneous secretion. Atrophy of the glands develops after denervation accompanied by histological changes by hypersensitivity to chemical or hormonal

agents like epinephrine, nor epinephrine, acetylcholine and pilocarpine. Claude Bernard in 1864 observed increased secretion (paralytic secretion) from the sub maxillary gland after sectioning the chorda tympani by removing the inhibitory action of these gland cells.

REGULATION OF SALIVARY SECRETION

- When food enters the mouth, a copious secretion of saliva takes place by reflex stimulation of the salivary glands through the buccal receptors and secretory centers.
- Normal foodstuffs causes salivary secretion rich in mucin and enzymes to facilitate easy swallowing, while dry or noxious materials causes watery secretion with little mucin.
- The types and volumes of secretion varies with diverse range of stimuli. The chewing of meat cause a flow of saliva from its sub maxillary and sublingual glands but not from parotid gland. While dry bread promoted abundant parotid watery saliva which contains little mucin.
- The saliva produced from one gland differs from that of the other. These may be mixed together in differing proportions. A single gland may be composed of different type of cells and their relative contributions to the saliva produced by that gland may vary. The secretion from a gland composed of only one type of secretory cell also varies in composition at differing rates of secretion .There is a general mechanism by which change in the composition of saliva can occur.
- The secretion of saliva in response to food in the mouth is an unconditioned reflex,and the stimulus producing it is termed as unconditioned stimulus .It is not necessary for food to enter the mouth to provoke a flow of saliva because the sight,smell or even the thought of food may stimulate salivation .The extent to which this psychic secretion occurs varies in different species and it is particularly marked in dog. The nature of the secretion produced varies,the sight of meat evokes a thick,stringy, mucus secretion from the sub maxillary and sublingual glands, while the sight of dry bread results in an abundant secretion of watery parotid saliva.
- Psychic reflexes were termed as conditioned reflexes by Pavlov [1910] because they were dependent on certain conditions for their development known as acquired reflexes.The conditioned reflex is that when a stimulus which in itself does not provoke secretion.
- The optic and olfactory nerves function as afferent/sensory pathways for this reflex activity. Psychic salivary secretion is exhibited by goats and pigs, but it is feeble or absent in horse and sheep. Food is a *natural stimulus* for salivary secretion and salivation during feeding is an *inherited reflex*. When a dog is conditioned by a *neutral stimuli* (bell sound at the time of feeding) for certain period of time, only the bell sound without food is sufficient for increased salivary secretion by way of *acquired reflex*.

FUNCTIONS OF THE SALIVA

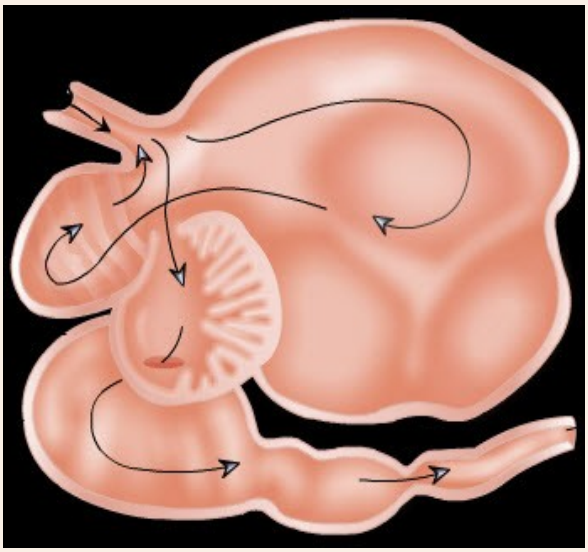
- Saliva has lubricating function that facilitates the mastication and swallowing of ingested food.
- The mucin content provides an adhesive to food to form bolus for swallowing.
- Water soluble components of food get dissolved in saliva which gain access to the taste buds to distinguish different tastes which in turn produces large quantity of saliva.
- Spontaneous secretion of saliva even during sleep has an important protective function by keeping oral mucosa moist and lubricated even in the absence of food.

- Increased secretion during eating also enhanced protection to the mucosa and serous layer by diluting harmful substances.
- Pronounced salivary secretion prior to vomiting protects the mucous membrane during subsequent passage of acid vomitus
- Saliva of pig, rabbit, dog and man contain an amylolytic enzymes *ptyalin or salivary amylase* that hydrolyses alpha 1_4, glucosidic linkages of the statch and leads to the formation of series of dextrin which are finally broken down to maltose (87%) and glucose (13%).
- S***alivary amylase is absent in horse, cattle, sheep and goat.***
- The optimum hydrogen ion concentration for salivary amylase is around pH 6.2; it is active over a wide range of pH and continues its digestive action in the stomach. Most of the carbohydrates are partly brokendown by salivary amylase in the stomach. In man, amylolytic activity continue up to 30mintues after the entry food into the stomach.
- Many other enzymes like lipase, maltase, peroxidase, mucolytic enzymes are also found in saliva, but they are derived from the bacteria normally residing in the mouth or from the break down of desquamated cells from the buccal mucosa .
- Young animals have another enzyme, *lingual lipase*, for hydrolysing the fat
- Saliva possesses bacteriostatic properties due to the presence of lysozyme to dissolve bacteria
- Saliva is aslo involved in thermoregulation as evoprative heat loss, and is significant in dogs and cats.

Functions of ruminant saliva

- Excellent buffer due to rich contents of bicarbonate and phosphate ions with pH of 8.10
- *In ruminants* , saliva provides a proper media for the bacterial growth and activity in the rumen.
- HCO_3 and PO_4 content of saliva neutralize the Volatile fatty acids produced during microbial fermentation.
- *Urea* is a non protein source supplies nitrogen for the bacterial growth and microbial protein synthesis
- *Phosphates* are utilized for nucleoprotein and phospholipid synthesis.
- Mucin content of saliva has anti-foaming characteristic and reduces foaming tendency of the diet.

MODULE-21: RUMINANT DIGESTION



LEARNING OBJECTIVES

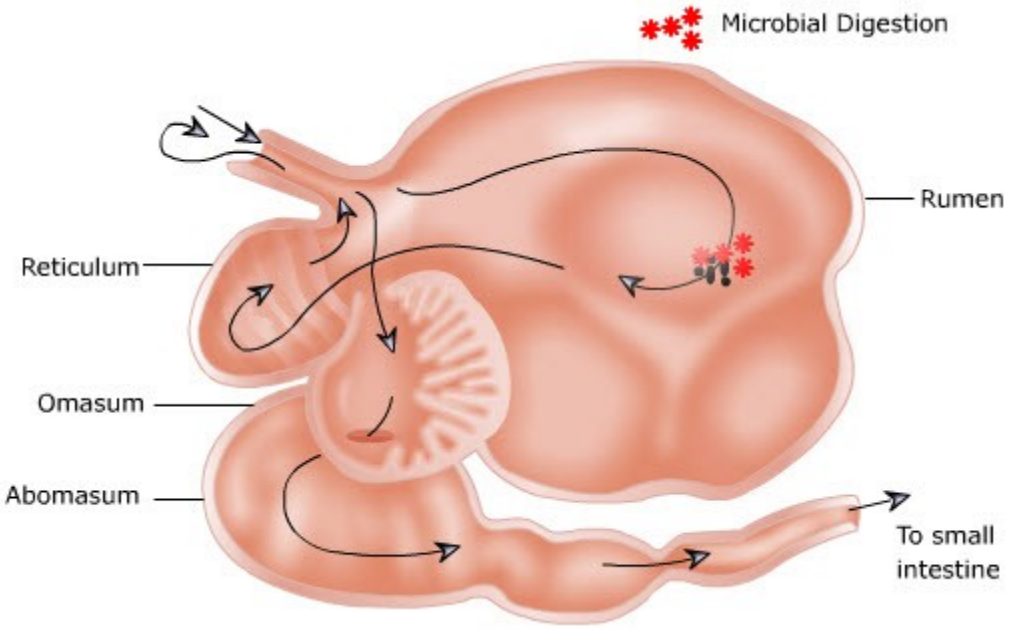
At the end of this module learner are confident to explain the following,

- features of digestion in ruminants,
- mechanical factor of digestion in ruminants,
- nervous control of rumination and
- eructation-its mechanism and significance.

DIGESTION IN RUMINANT STOMACH

Features of digestion in ruminants

- Gastro intestinal tract has colonies of microbes. As the animal grows the type of microbes gets modified according to the type of diet. Host animal and its populations of gut microbes interact. There is a complex interaction between the host animal and microbial population. Host animal does not produce enzymes degrading cellulose and other plant polymers, hence depends on metabolic activities of gut microbes to utilize the fibrous food. Microbial cellulose digestion is a slow process hence they are retained for longer period in the gut.



- Value of microbial products are more to the host (VFA/ Vitamin B Complex)
- They are well absorbed in rumen and lower stomach
- Ammonia and non protein nitrogen ,metabolized by microbes to synthesize good quality microbial protein which is later digested by the host.
- Large fibrous particles are selectively retained in the reticulo-omasal orifice for mechanical breakdown.
- Large quantity of gases produced by metabolism is readily expelled by eructation.
- Large output of saliva provides high buffering action against VFAs and also media for microbial growth.
- Toxic substances are detoxified during fermentation before getting into the small intestine.

Mechanical factor of digestion in ruminants

Mastication	Grinding of the food particles
Deglutition	Swallowing of patially graind food materials (Cud) from the mouth into oesophagus
Rumination	Chewing of the cud. This occurs in four phases
	Regurgitation: Reentry of cud, the liquid portion from the reticulum in to the mouth
	Remastication: Regrinding of the cud

	Reinsalivation: Additional salivary secretion to the bolus
	Redeglutition: Reswallowing of the bolus from the mouth into oesophagus
Eructation	Elimination of CO_2 and CH_4 from GI tract

RUMINATION

- This consists of four processes
  - Regurgitation
  - Re-mastication
  - Reinsalivation
  - Redeglutition
- Rumination is a reflex initiated by mechanical stimulation of mucosal receptors of reticulum, ruminireticular fold, rumen and cardia.
- Particles of the feed influences the time on rumination.
- Feeding of hay diet requires eight hours of rumination. Feeding well chapped smaller pieces of grass reduces time of rumination.
- Rumination starts with third contraction of reticulum viz regurgitation contraction which aids in clearing the cardia for opening.
- Regurgitated bolus is primarily of liquid ingesta.
- From reticulum it is pushed reflexly to opened cardio oesophageal sphincter.
- Lower intra oesophageal pressure at this point causes the pressure gradient to flood the ingesta from the stomach to cardia.
- Forceful inspiration with closed glottis causes decrease in intrapleural and intra oesophageal pressure.
- The presuure gradient is purely achieved by forceful inspiratory effort mediated by the contraction of costal muscles and not by ruminal/ reticular contraction.
- Reverse peristalsis moves the regurgitated bolus from esophagus to mouth. In the mouth, the liquid ingesta from the bolus is squeezed and swallowed. This is followed by reinsalivation and remastication.
- Vagus provides the afferent fibres and the rumination center is located in the brain stem.
- Efferent fibres supply to salivary gland, esophagus, reticulum, muscles for inspiration, mastication and deglutition.

MECHANISM AND NERVOUS CONTROL OF RUMINATION

- Rumination
  - It is the process of bringing back the *cud* from the rumen and reticulum to the mouth for further *chewing*.
- Regurgitation
  - The cud that returns to the mouth is mainly the liquid from the rumino reticulam.
  - The regurgitated cud consists of small particulate matter highly mixed with liquid and in advanced stage of fermentation.

    - Freshly eaten forages whose particle size is too great to be suspended in the rumen fluid for extensive maceration and are not regurgitated.
    - The glottis is closed by the elevated soft palate and inspiratory effort with tongue causes a drop in intra-thoracic and intra-oesophageal pressure.
    - The cardia and caudal oesophageal sphincter get open, simultaneously extra-reticular contractions force the cud from the retuculum into the oesophagus due to negative intra-thoracic pressure.
    - An antiperistaltic wave of oesophagus carries the cud to mouth.
- Remastication
    - In the mouth, the liquid portion of the cud is squeezed and swallowed. The remaining solid mass is chewed with slow, regular chewing movements for about 40-seconds.
- Reinsalivation
    - During the process of remastication saliva is added from parotid gland followed by reswallowing
- Redeglutition
    - It is the act of reswallowing of the cud
    - Time spent in rumination varies in different animals and with different rations.
    - Average daily duration for rumination in cattle is 10 hours on hay diet.
    - The proportion of grain and roughage in ration influences rumination time.
    - With low roughage diets or finely ground roughage,total rumination time may be reduced to 3 hours/ day.
    - Peak rumination occurs during afternoon and in the middle of the night.
- Nervous control of rumination
    - Rumination is a reflex act, but it can also be influenced by voluntary control.
    - The receptors for rumination are in the reticular wall, cranial pillars of rumen and rumino-reticular fold.
    - Vagus provides afferent nerve fibres to the rumination centre in the medulla.
    - The efferent nerves are the motor nerves controlling muscles of larynx, oesophagus, and reticulum.

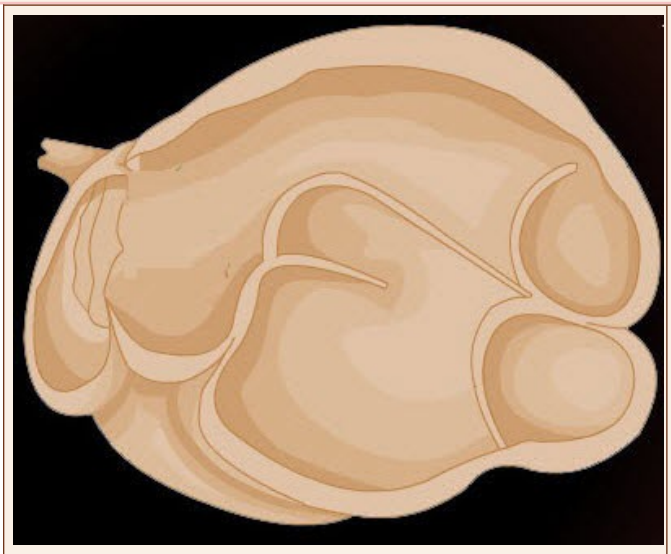
ERUCTATION

- It is the expulsion of fermentation gases like CO_2 and methane that has accumulated in the rumen.
- Receptors for eructation reflex are the *tension receptors* located in the reticulum, cardia, and cranial rumen sac, which are stimulated by accumulation of gas.
- Vagus provides both afferent and efferent fibres. Eructation centre is present in medulla.
- Volume of gas produced in rumen of a dairy cow is ½ to 1 litre/minute. The gas layer is moved cranially by the secondary contraction of the dorsal sac.

- The cardia and lower oesophageal sphincter open, and the gas enter into the relaxed oesophagus. By an antiperistaltic wave in the oesophagus and elevation of soft palate the gas is expelled through the mouth.
- Free gas found at the top of the ingesta in the dorsal rumen sac move cranially and ventrally to the cardia. Cardia remains closed by contact with watery ruminal content. Cardia gets free of ingesta during the contractions of dorsal sac, cranial pillar and caudal pillar.
- Accumulation of gas in the dorsal sac is the primary stimulus of eructation. Increase in the pressure in the dorsal sac of the rumen increases the eructation frequency and amount of gas expelled.
- Eructation occurs once in two ruminoreticular contractions. Inhibition of eructation isobserved during blokage of ruminoreticular contraction. Block of eructation leads to bloating of the rumen, called as TYMPANY which can also happen when gas production is higher than the elimination.
- Rumen distension decreases the lung volume and alters breathing pattern. Mechanical activity of the diaphragm is inhibited. Oils and non absorbable surfactants are used to treat bloat.
- Biphasic increase in pressure in the esophagus is observed during eructation. In the first phase, gas enters the esophagus. In the second phase,sharp increase in pressure accompanied by esophageal contraction.
- High grain feeding and feeding of lush alfalfa results

in trapping of gases in the rumen called " feedlot bloat" or "legume bloat". This is due to formation of foam in the ruminoreticulum which traps many small gas bubbles. This can be prevented by reducing feeding of grains or lush pastures.

MODULE-22: RUMEN CONTRACTIONS AND ACT OF VOMITING



LEARNING OBJECTIVES

- At the end of this module the knowledge on
  - the basic mechanism of ruminoreticular motility,
  - control of rumination will be gained and
  - vomiting, its mechanism and the significance in non-ruminant.

MOTILITY IN RUMEN AND RETICULUM

- There are two patterns of motility are seen in reticulo-rumen
  - Primary or *mixing contractions* called primary cycle
  - Secondary or *eructation contractions* known as secondary cycle
- Primary contractions
  - The primary cycle consists of
    - a biphasic contraction of reticulum
    - a caudal moving single contraction of dorsal sac

        - a contraction of ventral sac of rumen.
    - In the primary cycle, rumino-reticular contractions begin from the reticulum as biphasic contractions of which the *first contraction known as mixing contraction.*
    - It then relaxes.
    - The second contraction with strong force is called as evacuation contraction.
    - During feeding, the contractions occur at 75 seconds intervals.
    - Functions of reticular contractions
        - Direct liquid flow caudally to the cranial ruminal sac
        - Direct low density ingesta into the dorsal sac
        - Assist in regurgitation
        - Regulate the flow of ingesta from reticulo-rumen to omasum
- Secondary contraction
    - During second contraction of the reticulum, the rumen starts contracting from the dorsal sac of the rumen as caudally moving contraction towards caudal sac.This is followed by caudally moving ventral sac contractions.
    - Then the dorsal and ventral sacs show cranial moving contraction called the primary cycle. It is involved in mixing of ingesta and separation of large and small particles.
    - Secondary contractions is cranially moving begin from the caudo-dorsal blind sac moving over the dorsal sac.
    - The function of the secondary contraction is to expel the gases out of the rumen.
    - The reticulo-rumen contractions occur at a frequency of 1 to 3/ min. It is increased during eating.
    - During rumination, triphasic contractions occur in the reticulum in which the stronger extra contraction precedes the normal biphasic contraction.
    - The extra contraction in the reticulum as primary wave is referred as regurgitation contraction.
    - During rumination, the primary wave of the ventral sac is absent, but shows strong and prolonged ventral sac movements as secondary wave.
- Nervous control of stomach motility in ruminants
    - Tension receptors and epithelial/mucosal receptors are sensory receptors of fore-stomach stimulated by both mechanical (coarseness of rumen material) and chemical (decrease in pH, increase in VFA) stimuli.
    - Sensory afferents through vagus regulates the major contractions of rumen and reticulum.
    - Total vagotomy abolishes rumen and reticular contractions, rumination, eructation and reticular groove reflex.
    - Vagus is also the motor nerve to abomasum.
    - Sympathetic nerves are inhibitory to ruminant stomach, but their actions are not very important.
    - The intrinsic nerves of reticulo-rumen also cause weak and non cyclic contractions.

RUMINAL CONTRACTIONS

Contractions of rumen

- Cyclic, spontaneous contractions occur in the first three compartments. Frequency of cycle varies with the type of activity. Three types of activity prevails normally during

    - resting
    - eating
    - ruminating
- Resting activity is the contractile activity of the stomach when the animal is neither eating nor ruminating. During rest, cyclic motility is less rhythmic with low frequencies.
- Eating: During feeding, strength of contractions and frequencies of contractions are greatly increased.

Cycle of contraction during feeding follows a pattern

- Cycle of contraction begin at reticulum.
- Two contractions occur during feeding or at rest.
- First contraction is mixing contraction and is weak.
- Second contraction is evacuation contraction which is strong.
- Between these two contractions, a complete relaxation of reticulum occurs.
- Third contraction follows the second strong contraction during rumination. This third contraction is the strongest of the three and is referred to as *extra or regurgitation contrction of the reticulum*.
- Regurgitation of the bolus occurs at the peak of this contraction
- Primary functions of biphasic/triphasic contraction of the reticulum are,
    - To direct the flow of liquid into the cranial sac of rumen.
    - To direct low density digesta into the dorsal sac.
    - To regulate liquid ingesta flow from the ruminoreticulam to the omasum.
    - To assist in regurgitation by flooding the cardia by the ingesta.

Ruminal contractions

- During second contraction of the reticulum, cranial sac of rumen also contracts.
- Cranial pillars start contracting and form a barrier between the cranial and caudal rumen.
- At the end of the contraction of cranial sac the ingesta in the cranial sac are pushed into relaxed reticulum. At this point, vigorous contraction of entire rumen pillars, sac and other parts of rumen occur to mix the ingesta well with rumen fluid.
- This rumen contraction is said to be primary and secondary contractions occuring in the frequency of 6-8 contractions / 5 minute. Cardia is always submerged in the liquid ingesta, gets cleared prior to eructation by contraction of pillars of the rumen and walls of the dorsal sac.
- Bubble of gas transferred from dorsal sac to the cardia cranially. This process occurs during reticular relaxation corresponding to the time of contraction of pillars of the rumen.

NERVOUS CONTROL OF RUMINANL CONTRACTIONS

- Cyclical contractions of the first three compartments which begins early in life continue through out life without any interruption.
- Cyclical contractions are disturbed during pathological conditions affecting firstly rumen (impaction, intestinal intussusceptions) resulting cessation of rhythmic spontaneous contractions.

- Smooth muscle fibres of rumen receives sympathetic and parasympathetic (vagus) innervations which provide rhythmic propulsive motility.
- Rumination is an indicator of good health because of all the nervous pathways and neuromuscular functions of the stomach must be functioning well forexecution of the complex rumination reflex.
- The ruminal stomach is supplied with an extensive network of afferent nerve fibres that carry information from in the stomach to the CNS. Tension receptors are more in reticulum and cranial sac.
- Epithelial receptors are more in reticulum and cranial sac and pillars of rumen.
- Mucosal receptors are rich in abomasum and duodenum and are sensitive to both mechanical and chemical stimuli.

MECHANICAL FACTORS INFLUENCING MOTILITY

- When animal feeds, heavier boli they pass from oesophagus to cranial sac of rumen and are immediately passed into reticulum and omasum through reticulo-omasal opening. Heavier feed are retained less time for microbial fermentation.
- Coarse particles of hay are retained for more hours than finely chopped hay. Fermentative activity and contractions of the pillars of rumen and reticulum result in physical breakdown of particles. Lighter particles (hay/straw) leave the cardia of the oesophagus to the dorsal sac of the rumen. They remain there for several days get soaked in the ruminal fluid for microbial action (rumen bacteria, protozoa and fungi).
- Mixing and powerful crushing activity of contractions of the pillars help in through microbial digestion. This results in further breakdown because of microbial action and physical breakdown of particles during contraction of pillars and walls of the rumen and reticulum. This results in reduction of hay particles. Due to this the density increases and they settle down in the ventral sac. During contraction, the ingesta is pushed from ventral sac to cranial sac through cranial pillar of the rumen. From cranial sac via reticulo-omasal opening they are pushed into omasum and subsequently into abomasum.

Omasal transfer of substances

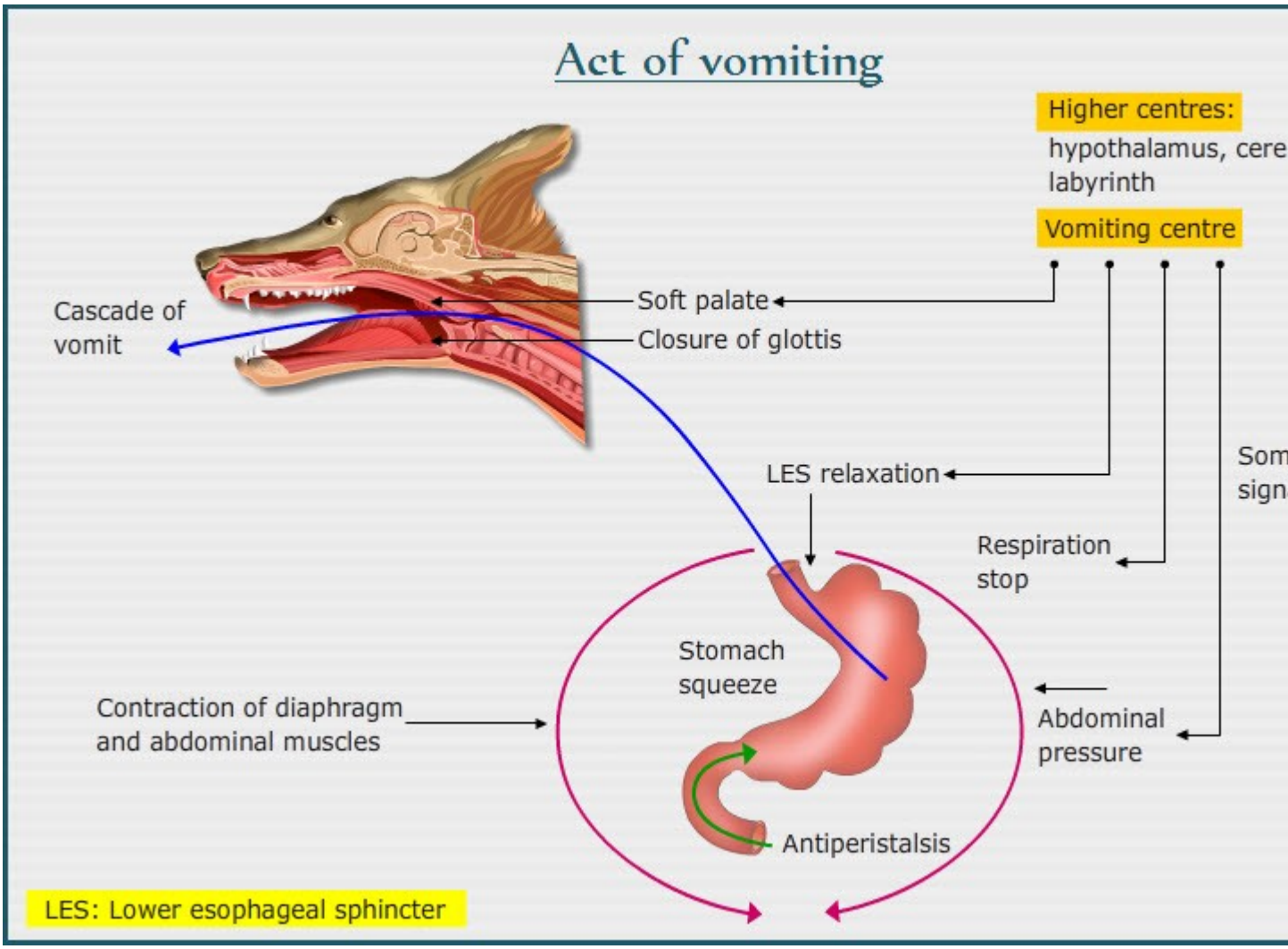
- Ingesta from reticulum to abomasum is transferred via omasum. Omasum removes water and electrolyte from ingesta and reduces the size of the ingesta. Omasal canal act as pump and forces the ingesta into abomasum due to omasal contraction.
- Contractile activity of the reticulo- omasal and omaso abomasal opening, walls of reticulum, omasal body and abomasum create the pressure gradient which aids in the flow of ingesta. Increase in reticular pressure dilates reticulo-omasal opening to push the ingesta into abomasum. Abomasum does not show rhythmic contraction similar to other three.

FOREIGN OBJECTS IN RUMEN

- Indigestible objects which are occasionally swallowed without proper mastication pass to the rumen. If the surface of the piece is sharp, it causes inflammatory reaction in the mucosa of reticulum and rumen.
- This leads to infectious spread on pericardium, peritoneum or pleuaral membrane (Traumatic Reticulo Pericarditis).
- High density material pass via cranial sac, sink to the floor of the cranial sac.
- Heavy indigestible objects always remain in the floor of reticulum as reticulo- omasal orifice lie dorsal to the floor of reticulum.

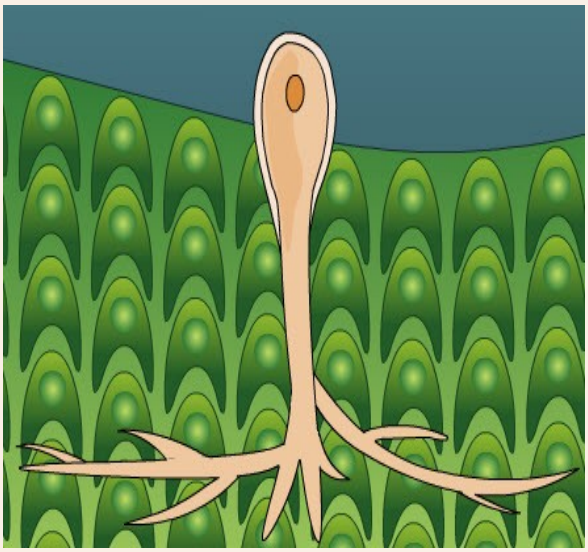
VOMITING (EMESIS)

- Vomiting is the spasmodic and forceful ejection of the stomach contents to mouth through dilated oesophagus.
- Vomiting is very rare in horse due to the presence of well developed and powerful cardiac sphincter and distant position of the stomach from the abdominal walls.
- In carnivores and omnivore vomiting is common.
- Herbivores and rodent never vomit.
- The vomiting centre is located in the lateral reticular formation of the medulla which is stimulated by afferent impulses from pharynx, stomach, duodenum, heart and uterus.
- In other non-vomiters, the vomiting center may be absent or rudimentary.
- The cranial nerves 5, 7, 9, 10 and 12 to the upper gastro-intestinal tract and spinal nerves to the diaphragm and abdominal muscles are the efferent nerves involved in the reflex act of vomiting.
- Act of vomiting
    - It is composed of four phases
        - Oesophageal dilatation
        - Gastric emptying
        - Gastric reflux
        - Oesophageal collapse



- After a deep involuntary inspiration, the glottis and the nasopharynx are closed by elevation of soft palate.
- Relaxation of oesophagus, gastro-oesophageal junction and the body of the stomach followed by strong pyloric contraction.
- The intra-thoracic pressure is increased by the contraction of diaphragm and abdominal muscles.
- Additional pressure exerted by the contraction of abdominal muscles and the diaphragm, force the stomach contents into mouth through the relaxed oesophagus.
- Massive antiperistalsis originates from the small intestine which reflux into the stomach.

MODULE-23: RUMEN MICROBES



LEARNING OBJECTIVES

- This module explores,
  - the microbial habitat in rumen,
  - their types,
  - their nature and number and
  - their characteristics and benefits.

RUMEN FERMENTATION

- The unique feature of digestive physiology in the ruminants is the fermentative digestion known as microbial digestion which occurs in the rumen and reticulum. Microbial digestion of food also occurs in the three chambered ruminats, camel, lama and in the stomach of marsupials and in hippopotamus.
- Anaerobic *ciliate protozoa* and non-spore forming *anaerobic bacteria* and *anaerobic fungi* are the major microbes in rumen.Some facultative bacteria are also present. The microbes have a volume of 3.6 % of strained rumen liquor of which 50% is contributed by cilitate protozoa and the remaining 50% by the bacteria.The number of rumen fungi is negligible but their activity is of great importance.
- The bacteria and protozoa grow on the substrates of the food in the fore stomach of the ruminants.

Establishment of bacteria in young ruminants

- Development of bacterial flora in young ruminants occurs at a very early age.
- The nature and rate of development is affected by type of diet fed and degree of isolation of young from adult animals. Under normal conditions, bacteria of adult type establish at about 6^{th} week of age in young animals.
- The ciliates may not become established in young animals unless they are maintained in close contact with animals harbouring them or are inoculated.
- Rumen microbes digest all major carbohydrates of ruminant diet such as cellulose, hemicellulose, pectin and xylose etc. These group of carbohydrates are not digested by mammalian digestive enzymes. The fermentation of cellulose is a slower process and is incomplete in rumen, but the digestion of cellulose and hemi-cellulose is almost completed in the rumen.

- Microbes derive their energy for their growth by fermenting cellulose, hemicellulose, pectin, soluble sugars, starch, the carbohydrates of major plant constituents .
- Rumen microbes are responsible for the digestibility of about 70 to 85% dry matter of the diet in ruminants, results in the production of *volatile fatty acids* (Acetic, Butyric and propionic acids) gases like CO_2, methane (CH_4) , ammonia (NH_3)with small amounts of N_2, H_2, and O_2 and microbial cells.
- From carbohydrates, certain organic isoacids, NH_3 and minerals, the microorganisms can synthesise good quality microbial proteins and B complex vitamins required for their growth and metabolic activities.
- They also hydrolyses lipids, unsaturated fatty acids. Proteins and NPN substances of dietary and salivary sources get degraded by the microbes and the released amino acids, $NH_3$are utilized for microbial growth and microbial protein synthesis. Thus the ruminant animal can be maintained on diets free of essential amino acids.
- In animals maintained in green pasture, the number of bacteria is higher than those fed dry rations. When ciliate protozoa are absent, viable bacterial count increases. Rate and*method of feeding also affects bacterial count*.
- The pH of the rumen liquid ranges from 5.8 to 7.0, which get decreased after feeding.

Rumen as microbial habitat

  - Maintenance of constant temperature of 40°C
  - Maintenance of constant pH of 6 – 7 by the HCO_3 & HPO_4 buffers of saliva
  - Aqueous environment by continuous salivary secretion
  - Continuous supply of substrates for microbial activity
  - Mixing of the ruminal contents by rumino-reticular contractions
  - Continuous removal of the fermentative end products.

- Abomasal secretions are dependent on volume of material flowing into it and pyloric distension. A rise in abomasal pH, short chain fatty acid level stimulate HCl and gastrin secretion. Parasympathetic nerves and gastrin also involved in abomasal secretion.
- Microbes derive their energy for their growth by fermenting cellulose, hemicellulose, pectin, soluble sugars, starch, the carbohydrates of major plant constituents .They result in the production of acetic, butyric propionic and lactic acids and gases like CO_2, methane and H_2.
- Abomasum receives a continuous flow of these materials and functions as a true stomach by secreting gastric juice. More of gastric secretion is from the fundic glands but the pyloric secretion is low. Gastric juice in the fundus region contain pepsin and HCl, has a pH close to 1.0. Pyloric secretions are slightly alkaline with little peptic activity.

RUMEN BACTERIA

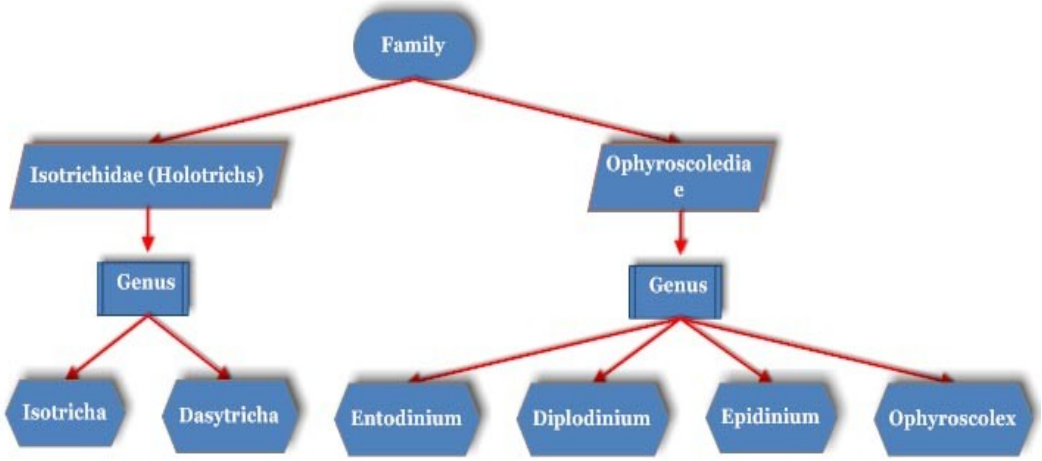
1. Cellulolytic Species	• Fibrobacter succinogenes • Ruminococcus albus & R. flavifaciens • Butyrivibrio fibrisolvens
2 Hemicellulolytic Species	• Butyrivibrio fibrisolvens • Ruminococcus sp. & • Bacteroides ruminicola
3. Pectinolytic Species	• Butyrivibrio fibrisolvens

	• Bacteroides ruminicola • Succinivibrio dextrinosolvens
4. Amylolytic Species	• Bacteroides amylophilus • Streptococcus bovis • Succinomonas amylolytica
5. Ureolytic Species	• Succinivibrio dextrisolvens • Selenomonas sp. • Butyrivibrio sp • Bacteroides ruminicola
6. Methane producingSpecies	• Methanobrevibacter ruminantium • Methanobacterium formicicum • Methanomicrobium mobile
7. Sugar-Utilising Species	• Treponema bryanti • Lactobacillus sp.
8. Acid-Utilising Species	• Megasphera elsdenii • Selenomonas ruminantium
9. Proteolytic Species	• Bacteroides amylophilus • B. ruminicola • Butyrivibrio fibrisolvens • Streptococcus bovis
10. Ammonia Producing Species	• Bacteroides ruminicola • Megasphera elsdenii
11. Lipid-Utilising Species	• Anaerovibrio lipolytica • Butyrivibrio fibrisolvens • Micrococcus sp.
Bacterial number is about 10^{10} to 10^{11} per ml rumen fluid	

RUMEN PROTOZOA

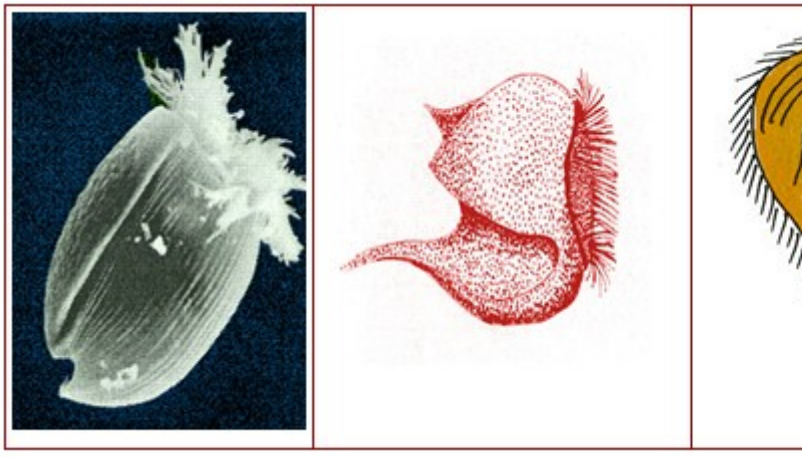
- Many species of protozoa are active in rumen.
- All protozoa are strictly anaerobes and found only in ruminants.
- Ciliates form the bulk of protozoa and flagellates are present to a very limited extent.

- The ciliates belong to two families.

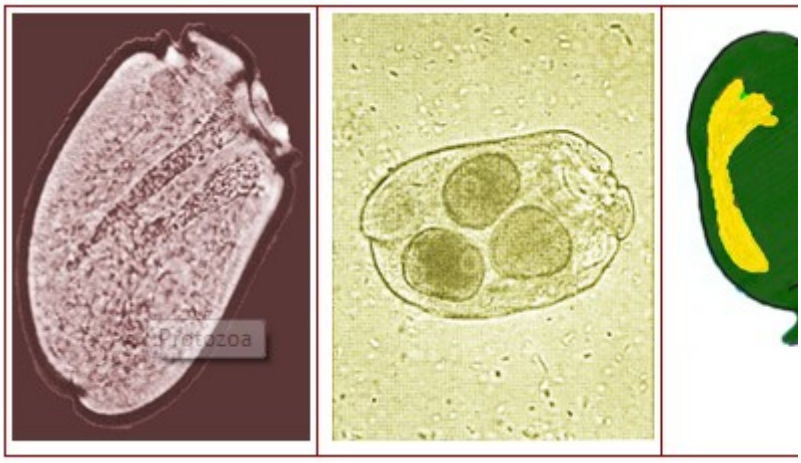


- Many species of micro-organisms are present in the rumen and variations occur in number of certain species with time after feeding, dietary regime and individual differences.
- Protozoal number is affected by pH (<5.5), type and composition of diet, season and frequency of feeding. Highly digestible diets increase their number.
- Protozoa store large quantities of reserve starch, which is used when exogenous energy supply is exhausted. Some facultative bacteria are also present.
- The microbes have a volume of 3.6% of strained rumen fluid and this volume contains 50% ciliate protozoa and 50% bacteria.
- Metabolic activity of bacteria is far greater than protozoa though total volume of small bacteria might be same as ciliate protozoa, which is due to greater surface area provided by the bacteria.
- Protozoal number range between 10^5 and 10^6 per ml fluid. Most of the rumen bacteria and protozoa are strict anaerobes.

Isotrichidae family



Ophyroscoledia family



Role of protozoa

- Increase in digestibility and weight gain is observed in faunated animal than in defaunated animals. But the absence of protozoa does not affect the animal performance.
- The protozoa help to stabilise the rumen fermentation, by ingesting feed particles and storing reserve polysaccharides and they may control the availability of substrates by sustaining uniform fermentation between feedings.
- Mixed protozoal-bacterial protein is better in quality than bacterial protein alone in contributing essential nutrients to ruminant animal.

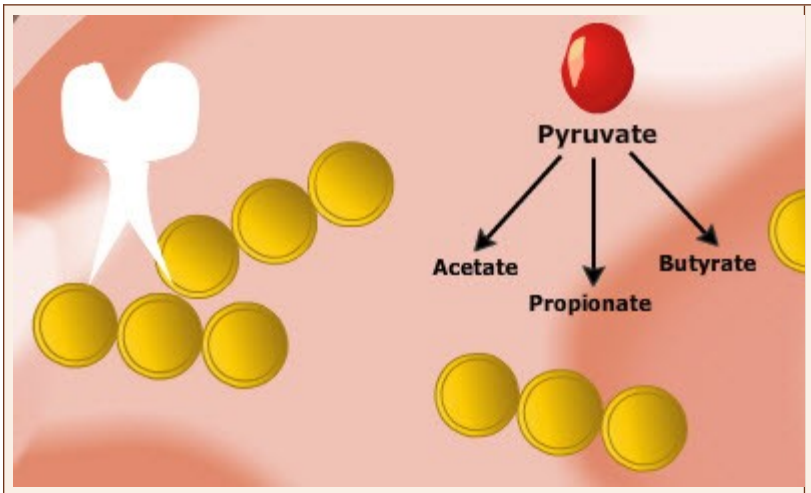
RUMEN FUNGI

- Anaerobic fungal zoospores are found in rumen. Several are flagellate organisms. *Neocallimastix frontalis, Sphaeromonas communis* and *Piromonas communis* are identified in rumen. Presence of plant cellwall carbohydrates facilitate increase inthe fungal population (Spores) and thus further help in lignocellulosic digestion.
- The fungi are important in the digestion of plant cell wall, their number ranges from 10^5 to 10^7 per gram of rumen contents.
- Feeding of high roughage diet increases their number as shown in animation below.
- Fungi play a significant role in adhesion with plant cell wall.
- It is difficult to culture fungi *in-vitro* as they are strict anaerobes.

FUNCTIONS OF RUMEN MICRO-ORGANISMS

- Ferment the dietary carbohydrates including the cell wall constituents of plants, which can not be enzymatically digested by the mammals.
- Produces short chain fatty acids like acetic, butyric, propionic and lactic acids and gases such as CO_2, Methane, and H_2.
- The short chain fatty acids are absorbed from the rumen and are the major energy source of the ruminants.
- By microbial enzymes the dietary proteins are broken down in to ammonia and branched-chain VFAs.
- The short chain fatty acids and NH_3 are utilised for growth of microbes and microbial protein synthesis.
- The microbial proteins are utilised by the host animal as a source of quality protein.
- Triglycerides are hydrolysed to glycerol and fatty acids. The glycerol is converted to propionic acid. The unsaturated fatty acids are hydrogenated .
- Microbes synthesize vitamin K and B complex vitamins.

MODULE-24: DIGESTION OF CARBOHYDRATES IN RUMINANTS



LEARNING OBJECTIVES

This module explains,

- fermentation of carbohydrates in the rumen,
- the pathways leading to the formation of major VFAs,
- role of VFAs with energy production cycles and
- methods to improve ruminal fiber digestibility.

FERMENTATION OF CARBOHYDRATES

- Speed of carbohydrate fermentation varies with their availability and solubility.
- Soluble sugars are rapidly fermented but starch is less rapidly fermented.
- Cellulose and hemi-cellulose are slowly fermented.
- Starch is a glucose polymer with alpha 1, 4 glucose linkage.
- The fructosans are polymer of fructose units with beta linkage.
- In roughages, most of the carbohydrates are structural and found in plant cell wall (cellulose, hemicellulose and pectin).

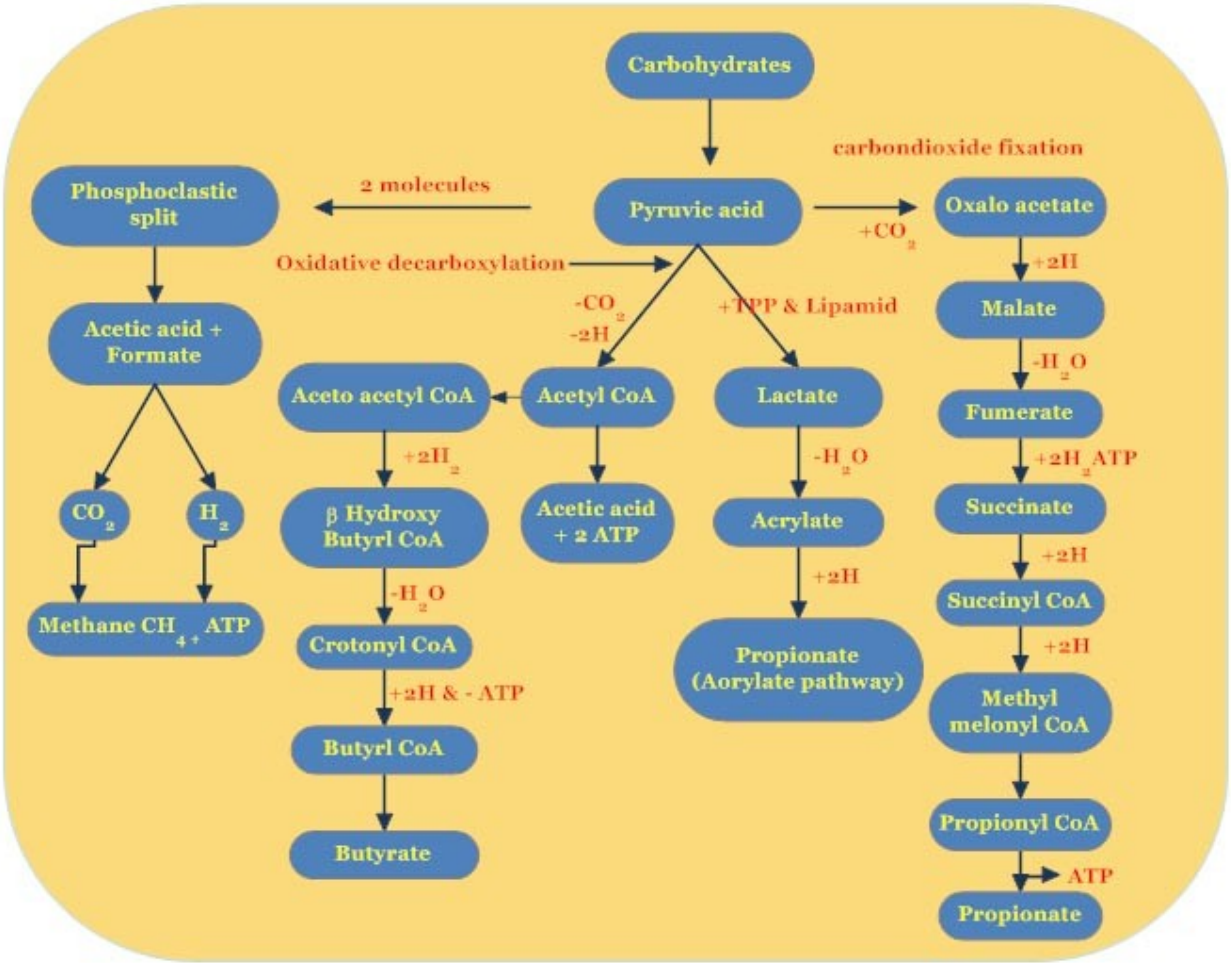
- Cellulose is beta 1,4 glucose linkage polysaccharide and hemicellulose is polysaccharide composed of beta linked xylose units and few hexoses.
- Pectin, found in cell wall and intracellular is beta linked galacturonan (polysaccharide based on galactose with uronic acid).
- The alpha linkage can be readily hydrolysed by amylases, whereas the beta linkage can be digested only by microbial enzymes, but not by mammalian enzymes.
- Lignin, a phenolic compound, a constituent of plant cellwall is resistant even to microbial enzymatic digestion. Only a small portion of dietary lignin is digestible due to the action of rumen fungi.
- The lignin reduces the digestibility of cell wall carbohydrates.
- Lignin and cellulose content increase with the age of the plant and temperature.
- Fructosans are more in young grasses.
- Xylose is the most abundant sugar in grasses.

DEGRADATION OF DIFFERENT CARBOHYDRATES

Four steps are involved in the degradation of carbohydrates.

- Adherence
  - This is the most important factor in fibre digestion.
  - Coccoids show preferance to get attached to plant cell wall.
  - Adherance helps the bacteria to be retained for a longer time and fecilitates sustained action.
  - This attachment helps the cell bound enzymes of adhered bacteria to come into intimate contact with substrate and ensure that resulting degradation products are preferrentially available.
- Factors affecting the adherence
  - pH: At a pH below 5.0 adherence decreases and is fecilitated at the pH of 5.5 to 7.8
  - Temperature: Adherence is maximum at 40 ^{o}C.
  - Lignin and lignified portions of the plant cell wall are inhibitory. Soluble cellulose derivatives like carboxy methyl cellulose and methyl cellulose are inhibitory.
  - Certain compounds like phenyl propionic acid increases attachment with plant cell wall.
- Disaggregation
  - The fibrous feeds are soaked in the rumen fluid and are broken to small pieces.
  - Starch granules are easily attacked when ground. Lignin inhibits degradation of structural carbohydrates.
- Extra-cellular degradation
  - The rumen liquor is the best source of bacterial and protozoal enzymes, which are secreted by the microorganisms and released into the rumen liquor.
  - The food substances that are soaked in the rumen fluid are acted by these microbial enzymes and degraded into short chain oligosaccharides and sugars.
- Intra-cellular degradation
  - The oligosaccharide and disaccharides are degraded to simple sugars prior to engulfement by bacteria.
  - The simple sugars enter into the bacterial cell for further metabolism by the microbes.The sugars are metabolised in the microbes by phosphoroclastic cleavage by intracellular enzymes and leads to the formation of pyruvate, phosphoenol pyruvate, short chain fatty acids,CO_2 and methane (CH_4). During this process, 2 NAD are reduced to NADH.

- Starch is degraded by bacterial enzymes to maltose and some glucose. Maltose is further fermented to glucose. Glycolysis is the major pathway of fermentation of glucose and other monosaccharides. Conversion of hexose to two molecules of pyruvate yields two ATPs, the main energy source for growth and maintenance of bacteria.
- **Cellulose is converted to glucose by cellulases and then to pyruvate by a complex process. Cellulose exists in amorphous and crystalline forms; crystalline form is the most difficult to degrade in the rumen. Hemicellulose is also degraded by cellulases similar to cellulose. Pentose sugars are produced from hemicellulose.Pectins are degraded to galacturonic acid, methyl esters of galacturonic acid and finally converted to short chain fatty acids.**
- **Pyruvate is the intermediate product of carbohydrate metabolism in ruminants which is converted to short chain fatty acids, CO_2 and CH_4. During this process, ATPs are formed which are utilised for microbial growth and multiplication.**
- The microbes do not require CO_2 and CH_4 for their growth, whereas the short chain fatty acids are the major energy source for the host animal (ruminants). Concentration of short chain fatty acids in the rumen is within a range of 60 to 120mmol/L of rumen liquor.



FORMATION OF VOLATILE FATTY ACIDS

Acetic acid formation

- Oxydative decarboxylation of pyruvic acid
  - Pyruvic acid is converted into Acetyl-CoA by the removal of CO_2 and H_2, in the presence of thiamine pyrophosphate (TPP) and lipomide. The Acetyl-CoA yields acetic acid.
- Phophoroclastic split
  - Two molecules of pyruvic acid yield one molecule of acetic acid and formic acid. The formic acid is converted to CO_2 and H_2. The methanogenic bacteria utilises a portion of this H_2 for CH_4 production, whereas the other portion of H_2 will be utilised for the production of succinate, propionate, butyrate, lactate as well as hydrogenation of unsaturated fatty acids.

$$2CH_3\text{-}CO\text{-}COOH \; CH_3\text{-}COOH + HCOOH \quad CO_2 + H_2 + ATP + CH_4$$

Propionic acid formation

- By CO_2 fixation
  - CO_2 combines with pyruvic acid to form oxalo acetic acid ($CH_2COOH\ CO\ COOH$) which is then reduced by hydrogenation (+2H) to malic acid;
  - On removal of one water molecule malic acid is converted to fumaric acid (CHCOOH CHCOOH).
  - Addition of H_2 and one molecuel of ATP to fumaric acid results in the formation of succinic acid
  - Decarboxylation (- CO_2) of succinic acid yields propionic acid (CH_3CH_2COOH).
- By acrylate pathway
  - Pyruvic acid on hydrogenation (+2H) forms lactic acid ($CH_3CHOH\ COOH$)
  - On removal of water lactic acid is converted to acrylic acid ($CH_2CH\ COOH$) on hydrogenation (+2H) it yields propionate.
- Butyric acid
  - Two molecules of acetyl-CoA condense to form acetoacetyl-CoA and $2H_2$. On reduction (+2H) acetyl-CoA is converted to beta hydroxy butyrl CoA, which by the removal of one molecule of H_2O is converted to crotonyl CoA. Reduction of crotonyl CoA leads to formation of Butyrl CoA along with one molecule of ATP . The butyrl CoA yields butyrate ($CH_3CH_2CH_2COOH$).
  - During the formation of acetate and butyrate NAD is generated.The production of acetate leads to generation of ATP and formation of excess NADH. During the formation of propionate NAD is regenerated with a release of free hydrogen and this H is subsequently used to reduce CO_2 to CH_4 and H_2O.
  - Thus there is a direct relationship between acetate and CH_4 production.when more acetate is produced from pyruvate, more CH_4 is also produced.
  - Likewise, there is a reciprocal relation between propionate production and CH_4 formation; as more pyruvate is converted to propionate production, CH_4 formation is reduced.

END PRODUCTS OF CARBOHYDRATE FERMENTATION

Short Chain Fatty Acids (acetic, propionic and butyric acids).

- Isoacids like valeric, isovaleric, isobutyric and 2-methylbutyric acids.
- Gases produced are CO_2, CH_4 and H_2 .
- The CH_4 accounts for nearly 30 to 40% of the total rumen gas production and CO_2 accounts for 50 to 60%.

- The short chain fatty acids are available asrespective sodium salts. In cattle fed a mixed diet, the proportions of VFAs are acetate 60-65%, propionate 15-20% and butyrate 10-15%. The ratio of A: P: B ranges from 70:20:10 for high forage diets to 60:30:10 for high grain diets. Fluctuation in the VFA concentration occurs on daily ration.
- The normal total VFA content of the rumen ranges from 60 to 120mEq/L. The type of diet, quantity and quality of feed, health of the animal alter the concentrations of individual acids. Total VFA production is higher in animals fed high starch diet than high fibre diet. Propionic acid decrease in animals fed on hay.
- The rumen ecosystem adapts to the type of diet. Lactic acid production is increased in the animals fed with large quantities of easily digestible carbohydrates like starch, sugar or rapidly changing the diet from high roughage to high starch diet.
- Un-dissociated acids do get absorbed from rumen and the rate of metabolism follows similar pattern of butyrate to propionate to acetate.
- Rate of absorption of volatile fatty acids increases when the pH of the rumen ingesta decreases.
- This helps in regulating rumen pH by removal of acidic materials and constant pH is being maintained.
- Loss of VFA results in accumulation of carbon di oxide(as bicarbonate and as CO_2) and concentration of HCO_3 ion increases as that of plasma.
- Lactate production is relatively low. High starch diet if fed too high cause accumulation of high concentration of lactate.
- This follows lactacidemia (high lactate in blood) due to absorption from the rumen.
- Metabolism of propionate in the ruminal epithelium increases as the concentration of lactate.
- Increased lactic acid formation in the rumen reduces rumen pH, leading to lactic acidosis.There is an increase in the number of Streptococcus bovis.This causes suppression of the growth of other types bacteria as they are sensitive to pH,causes rumen dysfunction.Dehydration results due to osmotic imbalance.

Significance of short chain fatty acids in ruminants

- The propionate is glucogenic acids and provides glucose through gluconeogenesis by entering into the Kreb's cycle at the level of succinate.
- Acetate and butyrate contribute the energy needs of the ruminant animal by entering Kreb's cycle as acetyl-CoA. They are ketogenic acids cause the formation of the ketone bodies, acetone, acetoacetic acid and beta hydroxy butyric acid. The ketone bodies serve as energy source in tissues like CNS and heart.
- **The acetate is the precursor for milk fat synthesis**.

Methods to improve ruminal fiber digestibility:

- Physical and mechanical treatments
  - Soaking with water
  - Grinding and pelleting
  - Increase the fiber intake
  - Increase surface area for microbial degradation
  - Irradiation by Heat/steam treatments

These treatment break the chemical bonds

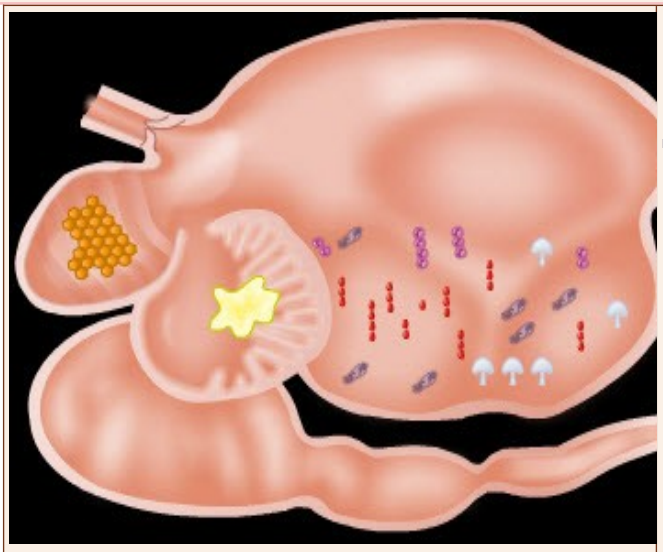
- Chemical treatments
  - Alkali treatment
  - Treating with Ammonia and urea
  - Chlorine compounds – Improves cell wall digestibility
  - Ozone - Decreases lignin content and increases cell wall contents
  - Sulphur dioxide – Solubilizes hemicellulose

- Alkaline hydrogen peroxide – Solubilizes approximately 50% of lignin
- Treatment with fungi

SIGNIFICANCE OF METHANE PRODUCTION

- The carbohydrate fermenting bacteria produce formate, hydrogen and CO_2.
- The methanogens trasform the H_2 and CO_2 into CH_4.
- The formate is converted into H_2 and CO_2.
- Methanogens preferrentially use formate as substrate for methanogenesis.
- The methanogens act as an electron sink and favoures acetate production.
- This is known as interspecies H_2 transfer that helps to maintain low partial pressure of H_2.
- This favours acetate production from pyruvate and discourages the formation of ethyl alcohol.
- Upon the accumulation of H2,the formation of H_2 from NADH is inhibited and NADH formed during glycolysis is reoxidisde to form alcohol.

MODULE-25: PROTEIN DIGESTION IN RUMINANTS



LEARNING OBJECTIVES

This module eloborates,

- the fate of protein in rumen,
- advantages of non-protein nutrition,
- participation of rumen bacteria in protein degradation and
- end products of nitrogen metabolism

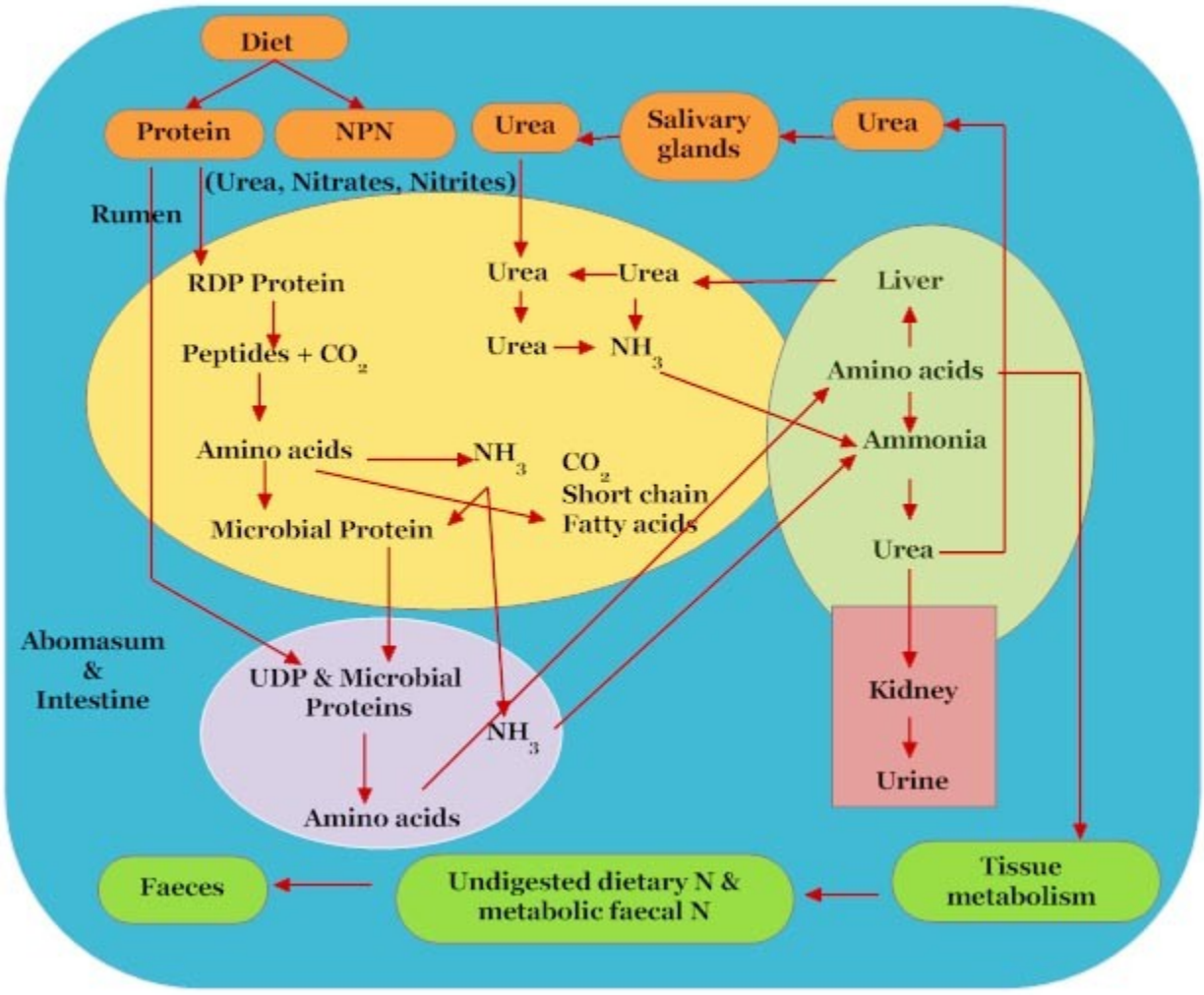
	and their values.

PROTEIN DIGESTION IN RUMINANTS

- Rumen microbial population have proteolytic activity. The diet of ruminants contains proteins and non-protein nitrogenous (NPN) substances (ammonia, nitrates, urea). Of the total proteins entering the rumen, 20 to 100% will be degraded to ammonia which are referred as rumen degradable protein (RDP).
- The fraction whch is not degraded by the microbes in the rumen escape and by-pass the microbial digestion, called as rumen undegradable protein (UDP); this fraction reaches the small intestine for enzymatic digestion by the animal.
- When the dietary proteins enter the rumen, the RDP fraction is hydrolysed by extracellular microbial proteases and produce short-chain peptides as end products.
- The peptides are absorbed into the microbial cell bodies. Within the microbial cells, the peptides can either be used for the formation of microbial protein or enter in to VFA pathways for energy production**.**
- The amino acids on deamination yield ammonia and a carbon skeleton; the carbon structures of many amino acids enter directly into various steps of the VFA pathways, leading to the formation of three major VFAs (Acetic, Butyric and Propionic acids).
- Three branched-chain amino acids valine, lucine and isoleucine are involved in the biosynthesis of branched-chain VFAs, the iso acids (isobutyrate, isovalarate and 2–methyl butyrate) which are growth promoters of cellulolytic rumen microbes.

NITROGEN METABOLISM IN RUMEN

- Some proteins are converted to amino acids extra cellularly. The amino acids are absorbed by the microbial cells and are utilised by the bacteria for incorporating into the microbial protein or microbial cell wall or in the nucleic acids.
- The amino acid requirement of the ruminant is met by microbial proteins synthesized by bacteria utilizing dietary protein,NPN substances,urea from saliva,urea through rumen epithelium and un degraded proteins that escapes degradation by rumen microbes (UDP).
- Protein breakdown in the rumen is proportional to solubility, the degree of secondary and tertiary structures, cleavage of disulphide bonds, cross linking between amino acids and also the concentration of ammonia in rumen fluid.
- The merit of conversion of dietary protein to microbial protein,depends upon the composition of food protein.
- Proteolytic activity is well pronounced in Bacteroides sp, Selenomonas sp, Butyrivibrio sp, megasphaera elsdeni and Succinivibrio dextrisolvens.
- Proteolysis results in oligopeptides which undergo degradation to smaller peptides and amino acids. Peptides are more effectively incorporated into bacterial protein whereas amino acids undergo rapid deamination providing NH_3 for bacterial growth. The amino acids on deamination give rise to NH_3, CO_2 and VFA.



AMMONIA NITROGEN IN THE RUMEN FLUID

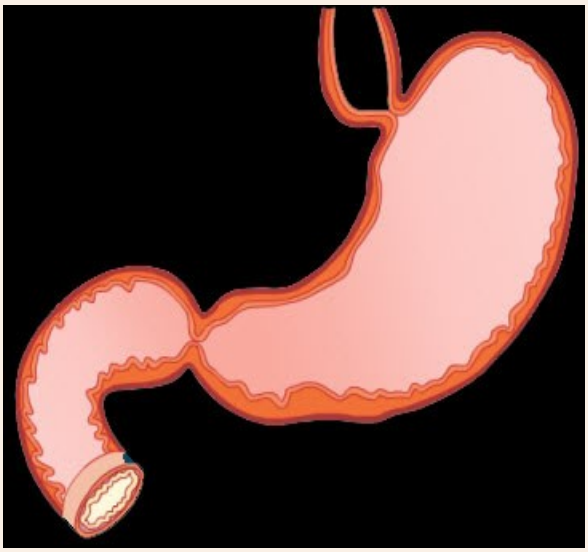
- Ammonia is an important source of N for the growth of rumen microorganisms. About 92% of rumen bacteria utilize ammonia as a nitrogen source.
- Ammonia nitrogen in the rumen fluid varies with diet(2mg to 100 mg/ dl) (**normal range is 5-25mg/dl**)
- High concentration of starch diet tends to reduce rumen ammonia.
- Urea, frequently used to replace true protein in ruminant ration as a non-protein source is rapidly cleaved in rumen by ureolytic bacteria to ammonia.

- Ammonia toxicity is most frequent sequelae of urea feeding where rumen pH may rise to 7.3. But urea toxicity is tolerable if pH is maintained within 7.0.
- The route by which NH3 utilized depends upon the concentration of NH3 in the rumen fluid. When the NH3 concentration is low, the energy dependent GS/GOGAT systems is utilized whereas when the concentration is high, GDH system is utilized. This is the pathway by which NH3 is converted to microbial protein. When NH3 present in the form of ammonium ion and it requires active transport.
- **Glutamine occupies a central role in the nitrogen metabolism of rumen bacteria. As there is no functional TCA cycle (Ketoglutarate is not formed) it is synthesised by reverse TCA cycle.**

AMINO ACID BIOSYNTHESIS

- The NH_3 is taken up by the bacteria and fixed to glutamate. Based on the source of carbon atom amino acids are divided into groups like glutamate family (glutamine, proline, arginine).
- Serine family (Serine, glycine, cysteine).
- Aspartate family (Aspartate, lysine, methionine, threonine, isoleucine).
- Pyruvate family (Alanine, isoleucine, leucine, valine).
- Aromatic family (Phenylalanine, tyrosine, tryptophan and histidine).

MODULE-27: GASTRO INTESTINAL MOTILITY



LEARNING OBJECTIVES

- At the end of the module the learner will know the following,
  - the importance of gastric motilityand how it assists in gastric mixing and emptying and
  - the types of intestinal motility and their physiological significance.

GASTRIC MOTILITY

Mechanism of gastric motility

- Function of the stomach is to regulate the flow of food to the small intestine at a controlled rate .
- The proximal region (fundus) near the oesophageal end serves storage function and the distal region serves grinding and sieving function.
- Muscular activity of the fundus shows weak continuous contraction, but capable of relaxation without changing intraluminal pressure as the food enters the stomach . Thus, the fundus serves as a food storage area and not involved much in the mixing of food.
- The body of the stomach serves as a mixing site of the gastric juice with the food.
- The distal stomach, the antrum shows intense slow wave of muscular contractions.
- It acts as a gastric pump and regulates the propulsion of food through the pyloric sphincter into the duodenum.

- The antral contractions also show reverse peristalsis of the pyloric contents, thus delay the passage of solid particles from the stomach.
- The peristaltic waves movement of the stomach begins near the middle of the body of the stomach and runs towards pylorus.
- The sphincter gets closed only when a peristaltic wave reaches it.
- Bile and duodenal contents flow into the stomach through the opened sphincter.
- As gastric digestion proceeds, the peristaltic wave becomes stronger and small quantities of gastric contents are carried into the pylorus.
- As the peristaltic wave comes near the pylorus, the pylorus constricts and blocks the exit of gastric contents excepts those particles smaller than 2mm in size.
- Larger particles are retropelled back into the corpus for further mixing and regrinding.
- Thus, the distal stomach serves to propel the food for mixing and grinding and acts as gastric pump, regulating the rate of gastric emptying (View animation).
- Termination of pyloric peristaltic wave follows as duodenal contraction to carry the ingesta along the duodenum.
- Reverse peristaltic waves are also noticed in the stomach.
- The rate of passage of solids is regulated by the rate at which the solids are broken down to small particles, which in turn is controlled by the motility of distal stomach.
- Greater the motility of antrum, faster the material is broken down.
- Liquids leave the stomach more quickly than solids and it is less dependent on antral motility.
- Emptying of solid material depends on fat content. Low fat meals leaves the stomach in 3 to 4 hours.

Regulation of gastric motility

- The stomach muscle possess a high degree of automaticity.
- Gastric motility is regulated by the vagi and sympathetic nerves.
- Stimulation of vagus increases peristaltic activity of the distal stomach, but suppresses muscular activity of the proximal stomach.
- Anticipation of eating increases vagal activity.
- Entry of food into the stomach provokes peristaltic contractions, through reflex arcs involving, receptors in stomach mucosa, vagus nerves and vagal nucleus in medulla.
- Sympathetic nerves inhibit peristalsis.
- Gastrin increases gastric motility, whereas secretin and CCK suppress gastric motility.

Enterogastric reflex

- The enterogastric reflex involves both extrinsic and intrinsic nervous system and endocrine system.
- This reflex regulates gastric emptying by gastric motility. These reflexes have their afferent receptors in duodenum which are activate by low pH, high osmolality, and presence of fat.
- Vagus is the extrinsic nerves stimulation of which brings about increased gastric motility, whereas inhibition of vagus nerve causes a decrease in gastric motility.
- Intrinsic nerves with their receptors and motor nerves also alter gastric motility through interconnections between stomach and duodenum.
- Osmotic pressure and acidity of duodenal contents are detected by duodenal chemoreceptors which alter the vagal activity. Increase in osmotic pressure and decrease in acidity depresses gastric motility.

Endocrine control of gastric motility

- The endocrine system controlling the gastric motility include secretin, produced by low duodenal pH; CCK released in response to fat in duodenal contents and GIP release in

response to carbohydrates. These hormones enter into the blood, carried to stomach and inhibit gastric motility.

Hunger

- Hunger or urge to eat is a discomfort or pain localised in the epigastric region caused by a need for food.
- The feeling of hunger is marked by rhythmic contraction related to motor activity of the stomach which is determined by low blood sugar level.
- Hunger contractions appear even before the stomach has completely emptied itself.
- Hunger sensations mainly act through the hypothalamic hunger center, which determines food intake and the satiety center, which regulates satisfaction of eating.

ABOMASAL MOTILITY

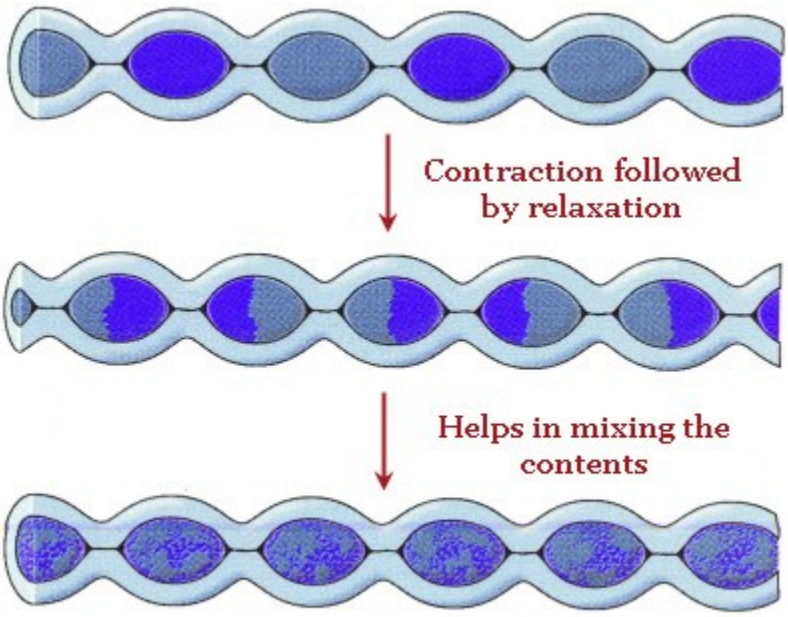
- Does not show cyclical rhythmic activity as that of the three compartments. Emptying of duodenum increases abomasal contractions.
- Enteric hormones (secretin, CCK, pancreozymin) produced by duodenal mucosa decreases abomasal activity and secretion.
- Distension of abomasum has negative effect on other three compartments i.e. distension of abomasum decreases the contractions of other compartments and delays the passage of food from omasum to abomasum.
- Duodenal receptors which are sensitive to composition of abomasal contents play a major role in abomasal emptying. Eg. osmolality of gastric chyme is the primary factor influencing abomasal emptying.
- Abomasum is always filled up each time as omasum contracts. Contraction of abomasum spreads through its walls forces the ingesta to move towards duodenum.
- Abomasum has two compartments pyloric antrum, body of the abomasum. Pyloric antrum of abomasum is more active prior to feeding. Other than vagi, neuromuscular activity in the walls of the abomasum is of importance in maintaining abomasal motility.
- Abomasal motility is ceased when ruminant fed on high concentrate and low roughage diet, due to high VFA production.
- High concentration of butyrate, propionate limits abomasal motility other than the total volume of VFA produced.
- Contraction of abomasum expels abomasal gas back to reticulum.
- Grain feeding increases abomasal methane production. Methane poorly absorbed across the epithelium and is trapped in the abomasum and causes abomasal dysfunction like displacement.

INTESTINAL MOTILITY

- The functions of the intestinal movements are
    - To mix the ingesta with digestive secretions
    - To bring the digested products in contact with intestinal mucous membrane for absorption
    - To move the food masses from place to place in the intestine
    - To expel the residue from the rectum through anus
    - To assist in flow of blood and lymph through vessels of intestinal wall

Motility in small intestine

- Motility of the small intestine occurs in two phases:
    - one during digestive period following food intake and
    - the second phase during interdigestive period, when less food is present in gut.
- During digestive phase, two patterns of motility occurs: propulsive/peristalsis and nonpropulsive/segmentation.



Segmentation - Small intestine

Types of motility during digestive phase

Rhythmic segmentation

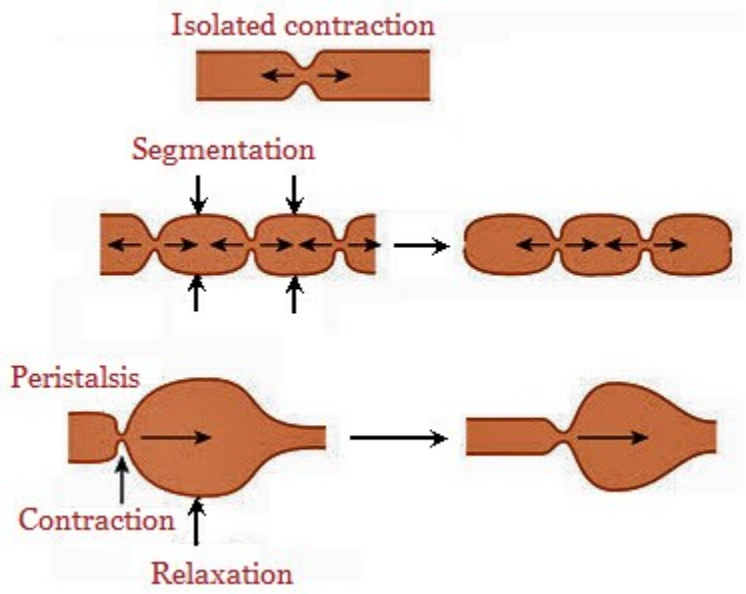
- It is produced by contraction of circular muscles.
- During segmentation, a mass of food lying in a length of intestine (3-4cm long) is divided into smaller ovoid pieces by constrictions caused by circular muscles.
- Within few seconds, the constricted portions relax and new areas get constricted.
- Segmentation may be taking place in many different areas of small intestine at the same time.
- The amplitude of segmentation varies and is strong after feeding.
- The effect of segmentation is to mix the food material with digestive secretions and to expose the mixture to the absorptive mucosa.
- Slight onwards movement of ingesta also occurs during segmentation. This segmentation is myogenic in origin and is increased by vagal stimulation and inhibited by epinephrine.
- Segmentation occurs in dogs 17-18 times a minute in the upper jejunum and 12-14 times a minute in the ileum.

Peristalsis

- This is the main mechanism for the onward movements of semisolid intestinal contents.
- It is achieved by creation of a rings of contraction, which pushes the bowel contents to succeeding relaxed areas.
- A stimulus at any point in the intestine can cause contraction above and distension below.
- The wave of contraction and relaxation moves along the intestine as a peristaltic wave, which carries the ingesta towards the lower end of the tract. This movement is neurogenic and is carried out by intrinsic nerves.
- Digestive phase peristalsis in contrast to interdigestive phase peristalsis, pass over only short segments.
- A combination of segmentation and slow wave movement by brief peristalsis ensures complete absorptive process.
- Movements during interdigestive phase: small intestine shows powerful peristaltic contractions at times travels the entire length. These waves are called as migrating

myoelectric complexes (MMC) which begins in the duodenum as slow waves leading to spike and muscle contraction.

- It serves to push undigested materials out of the small intestine.



Spiral motility

- Spiral motoility exposes the inner contents of the food to the intestinal mucosa for absorbtion.

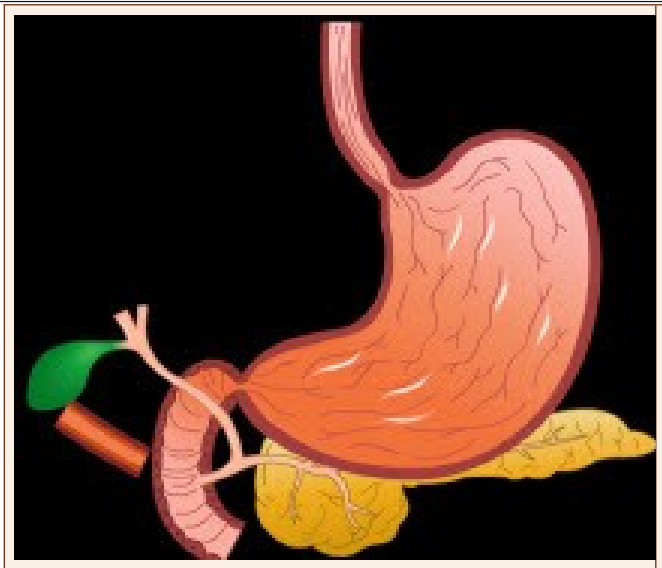
Antiperistalsis

- Peristalsis towards oral direction is designated as antiperistalsis or reverse peristalsis.
- It occurs throughout the digestive tract, but it is not powerful as peristalsis. It helps to
    - Delay the movement of food down the intestinal tract.
    - To ensure adequate mixing.
    - To regurgitate duodenal contents into stomach.
- Ileocaecal sphincter
    - The ileocaecal sphincter is at the junction of small and large intestine to prevent back flow of colon contents into the ileum.
    - It is a circular muscle that remains constricted most of the time.
    - There is a flap of mucosa that acts as one-way valve, which further blocks the back flow of colon contents to ileum.
    - The sphincter relaxes when a wave of peristalsis reaches it, and allows movement of material from ileum to colon.

Motility in large intestine

- These movements are more sluggish than that of small intestine, favours prolonged bacterial attack on cellulose and other substances and also function as a reservoir of faecal matter.
- Sometimes the contractions become powerful leading to effective propulsion.

MODULE-28: GASTRIC SECRETIONS AND REGULATION



LEARNING OBJECTIVES

- At the end of the module the following will be explained,
  - the components of gastric juices and it's celluar origins,
  - the mechanism of HCl secretion,
  - the control of gatric secretion and it's three phases and
  - the

		functions of the components of the gastric juices.

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GASTRIC GLANDS

- The glandular mucosa of the stomach has many pores known as *gastric pits*.
- The surface area of the stomach lining the pits is covered with mucous cells which secrete mucus to protect the surface epithelium.
- Secretions of gastric glands
  - Cardiac glands secrete only mucus
  - Parietal/fundic glands secrete HCl and pepsinogen
  - Pyloric glands secrete mucus and gastrin.
- Cell types of fundic glands
  - Fundic gland contain three main types of cells.
    - *Body chief cells or peptic cells* are locate at the base of the gland secrete *proteolytic enzymes (Pepsin and Rennin)*
    - *Parietal or oxyntic cells* are present at the upper third of the gland is the site of *HCl* secretion.
    - *Neck chief cells,* placed near the surface epithelium near the upper part of the gland secret *mucus* and a mucoprotein *"Intrinsic factor"* required for *Vit.*B_{12} absorption from the intestine is necessary for erythropoiesis.

Cells of pyloric glands

- The pyloric glands are structurally similar to the parietal glands
- Has body chief cells and neck chief cells only.
- Parietal cells are absent.
- "G" cells secrets Gastrin (Gut hormone).

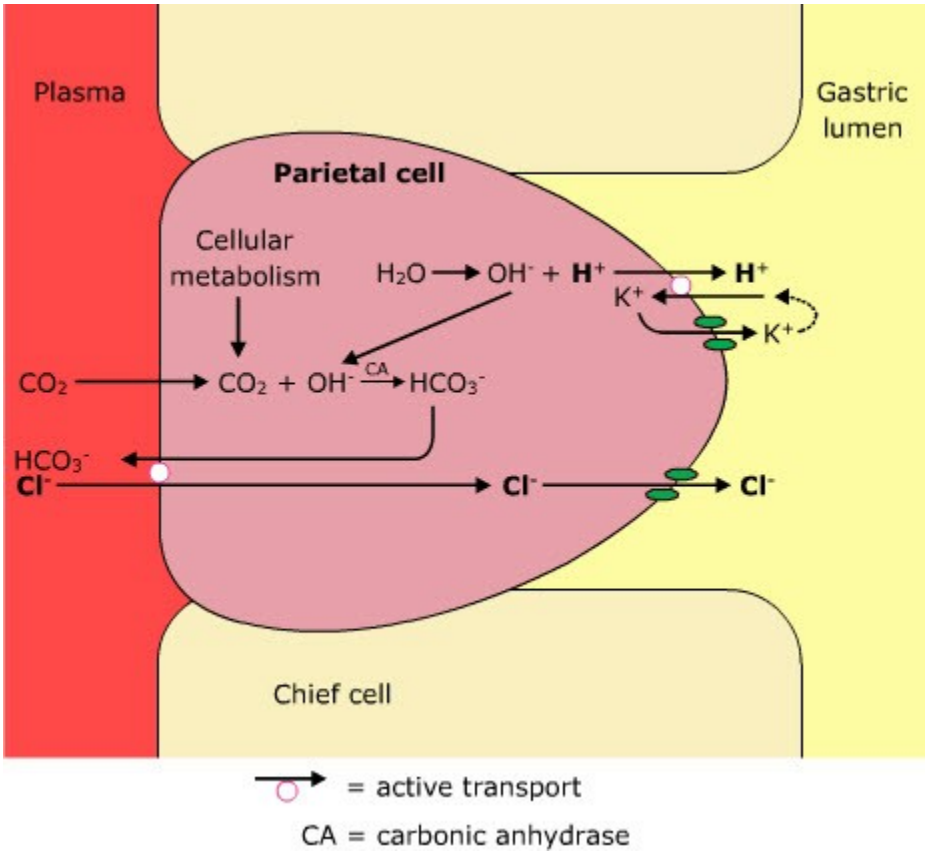
GASTRIC JUICE - COMPOSITION

- It is a colourless fluid, containing HCl, enzymes and mucus. Concentration of HCI in the stomach content varies with the nature of food, stage of digestion, amount of saliva to be neutralized etc

Hydrochloric acid

- It is actively secreted by the parietal/oxyntic cells of the fundic glands involves expenditure of energy, which is derived from the oxidative metabolism.
- Diffusion of CO_2 from the plasma into parietal cells
- Higher concentration of carbonic anhydrase in the parietal cells
- Chemical reaction of CO_2 with cellular water in the presence of "carbonic anhydrase"
- Formation of carbonic acid (H_2CO_3) in the parietal cells

- Dissociation of H_2CO_3 in to HCO_3^- + H^+
- Diffusion of HCO_3^- ions into plasma with a exchange of Cl^- ion from the plasma
- During active digestion, the concentration of HCO_3 increases very high and increases the pH of blood, called as **alkaline tide**.
- Active exchange of H^+ and K^+ ions between parietal cell and luminal surface of the stomach by of H^+ - K^+ ATPase, enzyme present in the luminal surface of the stomach
- H^+ ion is actively secreted into the luminal surface of the parietal cell with a exchange of K^+ ions into the parietal cell
- Reaction of K^+ ions with Cl^- ion and formation of KCl in the parietal cell
- Release of KCl into the luminal surface
- Reaction of KCl with H^+ ion and the formation of K^+ ion and HCl



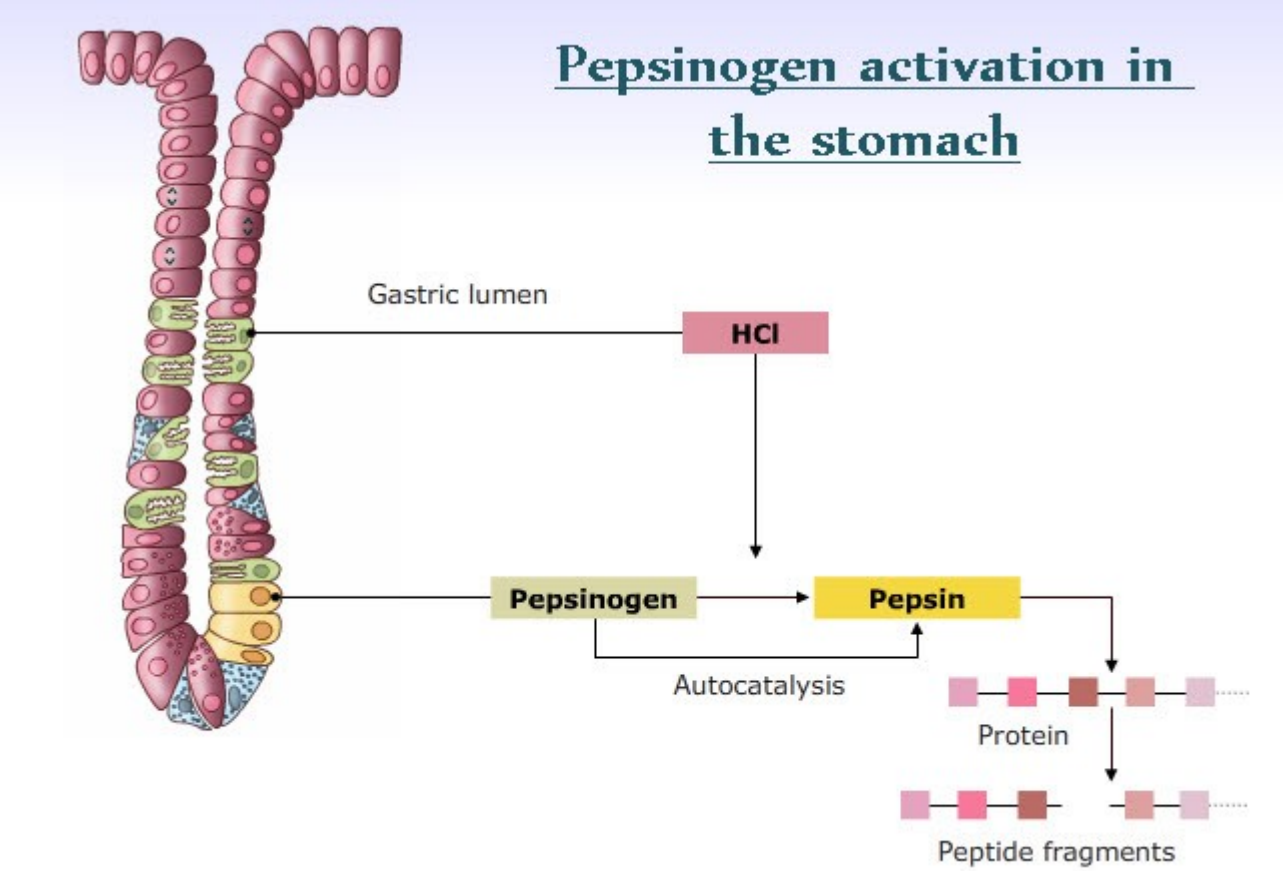
Functions of HCl

- Activates pepsinogen, the inactive form of enzyme into active pepsin, hydrolysing enzyme of protein
- Slight hydrolysis of sucrose
- Also function as antiseptic in the stomach.

GASTRIC ENZYMES

Pepsin

- Proteolytic enzyme, involved in hydrolysis of proteins into polypeptides
- Synthesized as “Pepsinogen” (inactive form of pepsin)
- Pepsinogen is activated by HCl
- Optimum pH of 1.5 – 3 is required for pepsin activity



Rennin(Chymosin, Rennet)

- It is a milk coagulating enzyme, present in young animals(Calf, Lamb, piglet etc.,)
- Secreted as prorennin (inactive form of rennin)
- Prorennin is activated by HCl
- Rennin reacts with casein (Milk protein) in the presence of calcium ion forms calcium paracaseinate to delay the passage of milk through stomach for prolonged action of pepsin on casein

Gastric lipase

- Acts on emulsified fat
- Hydrolysis fat in to fatty acids and glycerol
- Require the optimum pH of 5.5 – 7.5
- Its concentration in carnivores is low
- **Absent in birds and ruminants.**

CONTROL OF GASTRIC SECRETION

- In man and horse, the secretion of gastric juice is continuous but it is intermittent in dogs and cats.
- The rate of secretion increases during feed intake.
- The secretions of gastric glands are regulated by nervous and chemical mechanisms.
- The gastric secretion takes place in three phases
- Cephalic phase
- Gastric phase
- Intestinal phase

Cephalic phase

- Stimulation of sensory endings in mouth and pharynx or psychic/conditioned reflex due to the impulses originating from the smell, sight of food sensation provoke the cephalic phase of secretion. It contributes about 45% of gastric secretion. The extent of psychic secretion is well developed in dogs and also present in pigs.

Gastric phase

- Entry of food into the stomach causes copious secretion of gastric juice. This contributes about 45% of the gastric secretory response.
- Basically two principle stimuli are responsible for gastric phase
    - Mechanical stimuli
    - Humoral /hormonal stimuli
- Mechanical stimulation
    - Stimulation of intrinsic nerve system
    - Vago-vagal reflex from fundic area
        - Contact of food bolus with the receptors of stomach mucous membrane and the distension of the stomach causes the releases of acetylcholine. Both "G" cells and parietal cells of the gastric glands are stimulated by acetylcholine results in increased secretion of gastrin and HCl respectively.

Hormonal stimulation

- Major portion of gastrin, a gut hormone is produced by the "G" cells of the pyloric glands. Small amount of gastrin is also released from the fundus, duodenum and small intestine. Vagal stimulation during anticipation of eating and distension of stomach stimulates gastrin release and HCl secretion.
- Histamine present in the gastric mucosa is also a powerful stimulator of gastric acid secretion**.**Histamine is secreted by enterochromaffin-like cells (ECL) in parietal mucosa. Acetylcholine produced by parasympathetic nerve endings also stimulate HCl secretion by the parietal cells. Vagus conditioned the parietal cells and potentiates the action of gastrin on HCl secretion. Gastrin stimulates the gastric juice with high HCl content and low pepsin activity. The pepsin release is not hormonally stimulated, but its secretion is enhanced by vagal stimulation.

Intestinal phase

- Accumulation of food in the intestine excite gastric secretion by humoral mechanism due to entry intestinal gastrin and cholecystokinin (CCK) from duodenum into gastric gland through blood stream. This phase contributes about 10% of the gastric secretion.
- Secretion and functions of mucus
    - The gastric mucus is derived from cardiac and pyloric glands, neck chief cells of fundic glands and surface epithelium of stomach. Mucus secretion is independent of secretion of water, HCl and enzymes. Vagus controls the mucus secretion. Mucous functions as a lubricant and protects the to gastric mucous membrane of stomach wall against the highly HCl content.
- Inhibition of gastric secretion
    - Gastric secretion may be inhibited by higher nerve centers via smell or sight of unappetizing food. The autonomic nervous system is involved in marked inhibition of gastric secretion during pain, anger and other emotional states.
    - Accumulation of acid (< pH 2.5) in the stomach inhibits further HCl production by inhibiting gastrin release from pylorus.
    - Entry of fat, sugar, or high acid contents into the duodenum, causes the release of gastric inhibitory polypeptide (GIP), from the duodenum. It is transported to stomach via blood stream and inhibits gastric secretion. Secretin and CCK

secretions from the duodenum are also involved in the inhibition of gastric secretion, when acid contents of stomach enter the duodenum.

GASTRIC SECRETION IN RUMINANTS

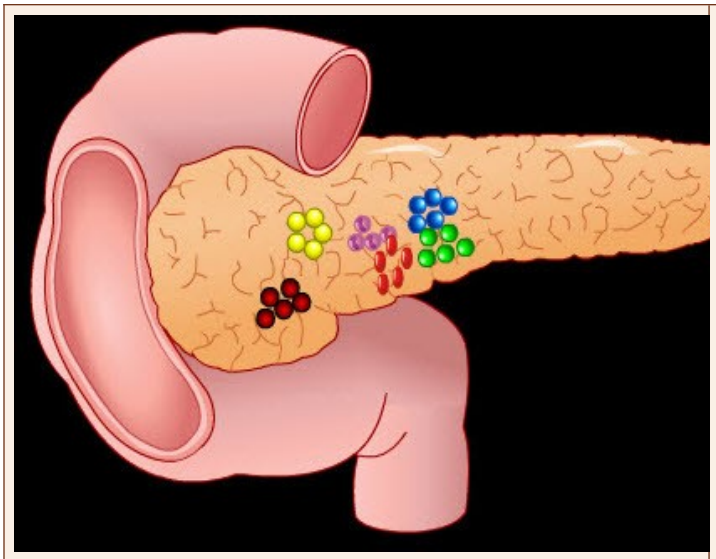
Gastric secretion

- Abomasum is the only part of the ruminal stomach secreting digestive juices.
- Fundic abomasums is rich in HCl, pepsin and in young ruminant rennin- a milk coagulating enzyme is found.
- pH of abomasal juice is approx 1.0 to 1.3.
- Buffered ingesta with volatile fatty acids entering abomasum increases abomasal secretion.
- Regulation of abomasal secretion is compelx. It involves humoral and neural factors.
- Gastrin, G.I tract hormone is secreted by abomasal mucosa in response to cholinergic stimuli.

Absorption

- Ruminal wall is composed of stratified, squamous, highly vascular which facilitates transport of nutrient and other components from rumen to blood and vice versa.
- Water, electrolytes, volatile fatty acids, alkaloids, iodide, sodium cyanide, potassium ion and are readily absorbed from the rumen.
- 60 to 70% of the digestible organic matter is readily absorbed from the rumen and other two compartments.

MODULE-29: SMALL INTESTINE AND PANCREATIC SECRETIONS



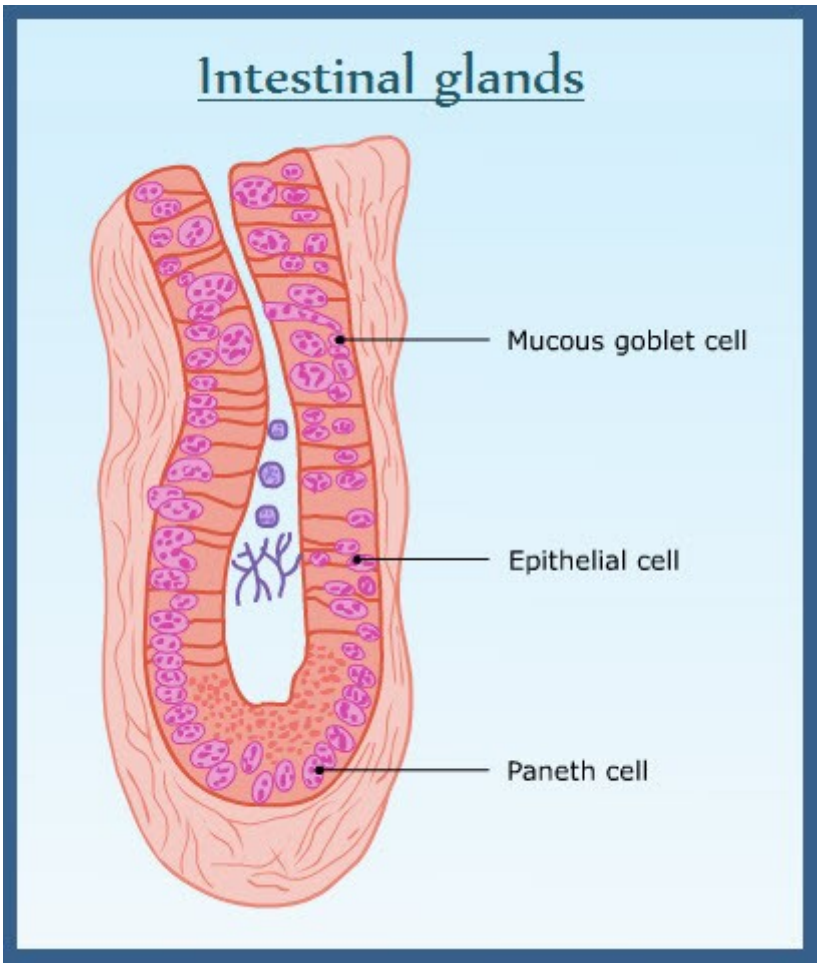
LEARNING OBJECTIVES

- This module explains,
  - the composition of the pancreatic juice and it's nervous and hormonal regulation and
  - composition and functions

	of intestinal juice.

SMALL INTESTINE

- Small intestine is the predominant site of digestion and absorption. This begins at the end of pyloric sphincter and goes upto large intestine. This is highly coiled structure, has few glands to assist digestion.

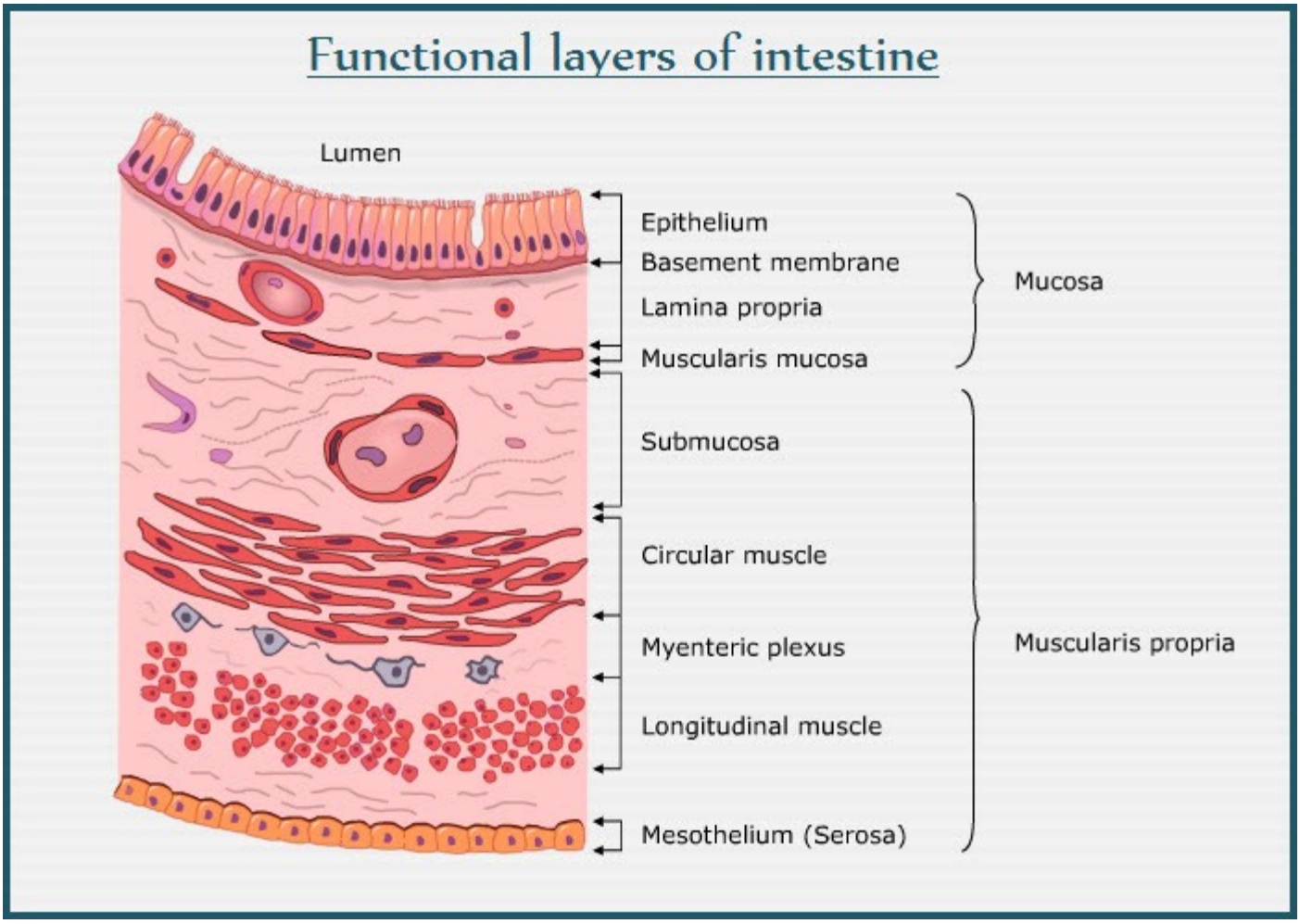


- It is composed of 4 layers-serosal (outer), muscular, submucosa and innermost mucosal layer. Mucosa is the functional layer involved in digeston and absorption.
- Has three major portions namely duodenum, jejunum and ileum, with specific functions.

DIGESTIVE ENZYMES IN THE INTESTINAL JUICE

- *Enterokinase:* activates trypsinogen to trypsin.
- *Dipeptidase* : converts proteases to peptones and amino acids.
- *Aminopeptidases* : converts peptones to amino acids.
- *Maltases :* converts maltose to glucose
- *Lactases :* converts lactase to glucose and galactose
- *Sucrase* : coverts sucrose to glucose and fructose

- *Nuclease :* converts nucleic acids to mononucleotides.
- *Nucleotidase and nucleosidases:* convert nucleic acids to purines, pyrimidine bases, phosphoric acid and petose sugars.
- *Lipases :* act on fat liberating fatty acids and glycerol.
- *Amylases :* act on starch resulting in dextrins and maltose.

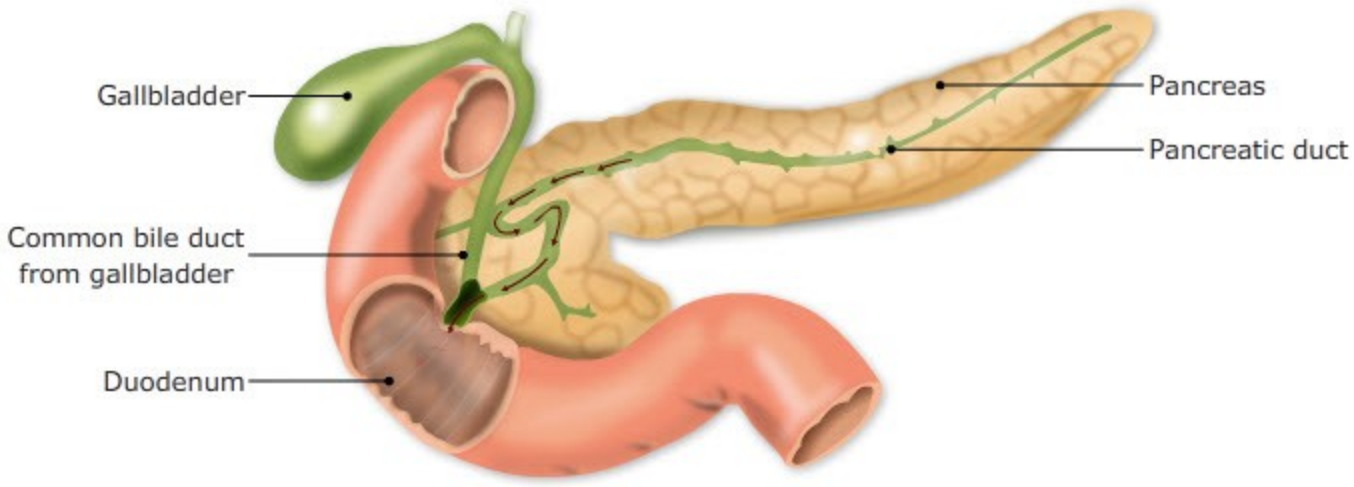


Optimum pH in various compartments of the G.I tract

- Stomach contents: 4.60
- Duodenum : 7.30
- Jejunum : 7.47
- Ileum: 7.55
- Caecum: 7.09
- Colon: 7.09
- Rectum: 6.24

PANCREAS

- Pancreas has both endocrine and exocrine portions. The endocrine portion of the pancreas is made up of *islets of langerhans*, secrets hormones like gulcagon (alpha cells), insulin (beta cells) and somatostatin (delta cells) into the blood. The major portion of pancreas is exocrine in function.



- Secretions
  - The enzymes of the pancreatic juice are synthesized and secreted by the acinar cells.
  - The small duct system contain high level of carbonic anhydrase is responsible for the secretion of water and electrolytes.
  - In most species, the pancreatic duct empties directly into duodenum.
  - Horse, dog and fowl usually have two pancreatic ducts.
  - In sheep, pancreatic duct joins with common bile duct before entering into duodenum.
- Composition of pancreatic juice
  - Pancreatic juice is a clear alkaline fluid made up of the secretions of two separate phases , aqueous and organic phases
  - The aqueous phase causes a higher concentration of HCO_3 and lesser amounts of Cl. The HCO_3 is important for partial neutralisation of the acid chyme from the stomach and maintenance of H^+ ion concentration suitable for digestive activities of pancreatic enzymes.
- The organic phase produces more of pancreatic enzymes. The amount of juice secreted in Horse – 10 to 12, Cattle – 3 to 5, Sheep – 0.5 to 1 L /100kg body weight/day

Pancreatic enzymes

- There are three major groups of enzymes namely *proteases, lipases and amylase* capable of digesting proteins, fats and carbohydrates respecively.
- The following proteolytic enzymes of pancreas are secreted as zymogen granaules or proenzymes.
  - Trypsinogen
  - Chymotrysingon
  - Procarboxy peptidase A and B
  - Proelastase.
- Trypsingoen is converted to active trypsin either by the action of an enzyme enterokinase present in duodenal and jejunal juice or by autocatalysis.
- Chymotrysingoen, procarboxy peptidases and proelstases are activated by trypsin.
- Trypisn, elastase and chymotrypsin are endopeptidases; carbodxy pepetidase is a exopeptidase.

- ***Pancreatic amylase* (*amylopsin*) is secreted as an active state**. It acts on starch and produces *oligosacharides* and *maltose*. It requires an **optimum pH of 6 to 9 and chloride ions for this action.**
- ***Pancreatic lipase* (*steapsin*)** is secreted as an active form.It splits fats into free fatty acids and glycerol. Calcium ions, polypeptides, peptidees and bile salts enhance lipase activity.
- *Cholesterol esterase and phospholipase* act on choleterol esters and phospholipids producing non-esterified fatty acids, cholesterol and lysophospholipid.
- *Ribonuclease* and *deoxy ribonuclease* present in pancreatic juice reduce ribose nucleic acid and deoxy ribonucleic acids to mononucleotides.

REGULATION OF PANCREATIC SECRETION

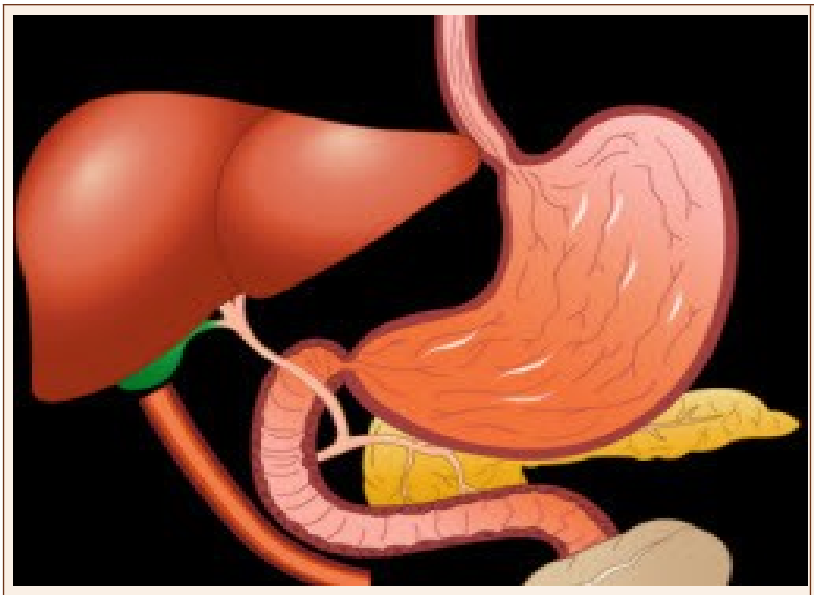
Nervous regulation

- In three phases
  - Cephalic phase.
  - Gastric phase.
  - Intestinal phase.
- *Cephalic phase:* The cephalic phase of gastric secretions , simultaneously transmit the impulses along the vagi to pancreas; results in pancreatic secretion rich in enzymes, but little water and electrolytes.
- *Gastric phase:* Distension of stomach due to entry of food into the stomach casuse reflex stimulation of pancreatic secretion through vagovagal reflex.
- *Intestinal phase:* Distension of intestine following the entery of food into the small intestine, stimulates the production of pancreatic enzymes and their secretion. This phase is controlled by both intrinsic nerves of the intensine and vagus. Acetylcholine released by the vagal action and local nerve reflexes sensitise the pancreas for the action of secretin and CCK.

HORMONAL REGULATION

- Secretin and CCK are the important hormones regulate pancreatic secretion.
- Secretin is the gastro intestinal hormone secreted by the duodenal mucosa of small intestine. Presence of acid ingesta, peptides, soaps and amino acids, HCl in the stimulate the release of secretin. When the duodenal pH falls below 4.0 secretin causes increased secretion of thin watery pancreatic juice with high concentration of HCO_3 with less or no enzyme referred as hydrolytic secretion. This type of HCO_3 release is to neutralise the acidity of duodenal contents. It inhibits gastric secretion.
- Cholecystokinin (CCK) stimulates the pancreatic secretion rich in enzymes referred as ecbolic secretion identical to the action of vagal stimulation. CCK also causes contraction of gall bladder and also delays gastric emptying.
- Vasoactive intestinal polypeptide (VIP) another intestinal hormone, stimulates pancreatic HCO_3 secretion, whereas the pancreatic polypeptide, inhibits pancreatic HCO_3 and enzyme secretions.

MODULE-30: SECRETION OF LIVER AND THEIR REGULATION



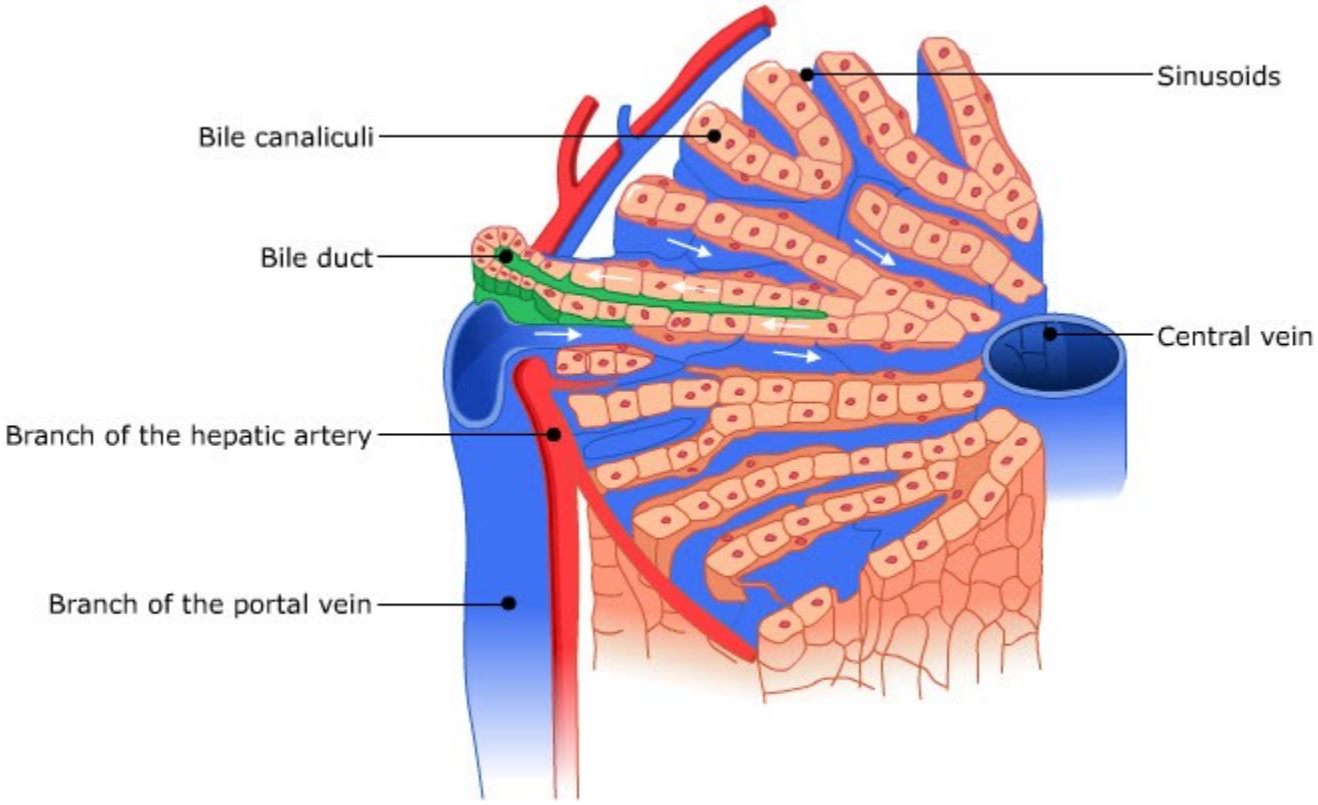
LEARNING OBJECTIVES

This module explains the following,

- the functions of the liver,
- the composition of bile with a brief introduction on jaundice and regulation of bile secretion and it's functions and
- entero-hepatic cycling of bile.

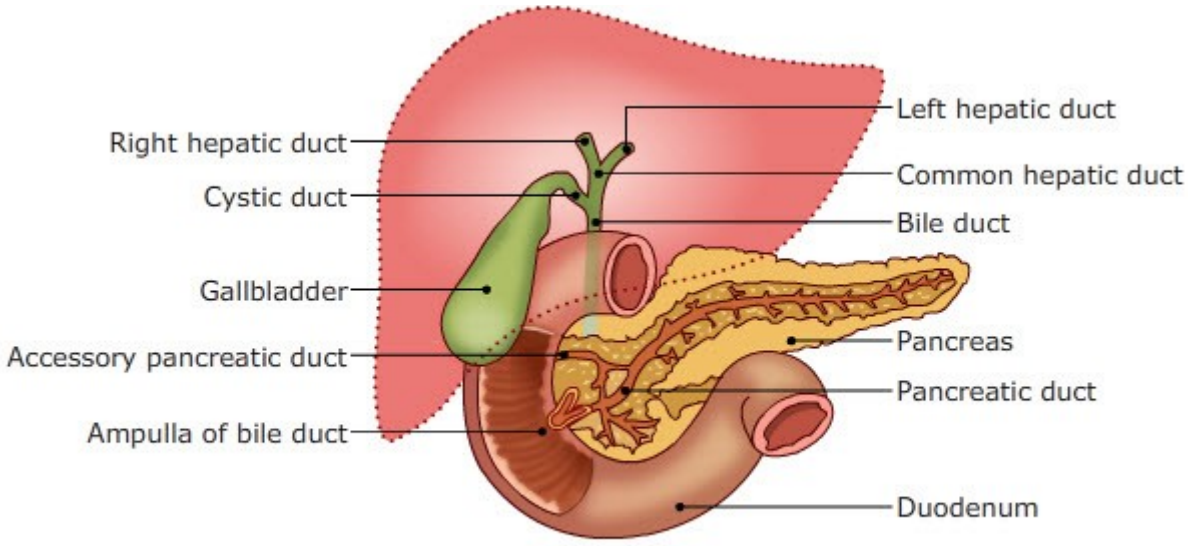
LIVER AND BILE

- Liver is the largest gland in the body and has number of important functions.
  - Secretion of bile
  - Formation and storage of glycogen
  - Regulation of glucose level in the systemic circulation.
  - Deamination of NH_3 and formation of urea.
  - Destruction of uric acid
  - Synthesis of fatty acids from carbohydrates and proteins.



- Phosphorylation of fats, introversion of fatty acids, partial oxidation of fatty acids and formation of ketone bodies.
- Detoxification of poisonous substances brought to it by blood.
- Destruction of old erythrocytes
- Storage and distribution of anti – pernicious anemia factors
- Formation of fibrinogen and other plasma factors.
- Formation of prothrombin
- Destruction of estrogen.
- Metabolism of hormones.

- Secretion of bile
  - Secretion of bile as a source of bile acids which is necessary for fat digestion and absorption in the jejunum
  - Bile pigments provides the excretory route for certain endogenous metabolites and drugs.
  - Additional buffer to neutralize H^+ ions in the proximal duodenum.
- Gall Bladder
  - It is a storage organ of the bile for continuous secretion of bile. The walls of the gall bladder secrete mucin and absorb H_2O from the bile inorder to concentrate the bile.
  - The horses, rat, deer, elk, moose, giraffe, camel, elephant and pigeon do not possess a gall bladder.
  - Removal of the gall bladder, does not result in any great physiological disturbance.
- Bile
  - Bile is both a secretive and an excretive substances. It plays an important role in the solubilization and absorption of fat.



PHYSICAL PROPERTIES OF BILE

- Bile from hepatic duct is a viscid, greenish or greenish yellow with golden tinge liquid with a bitter taste.
- The compositions varies upon whether the bile is obtained from gall bladder or from the ducts of the liver.
- The constituents of the bile are
    - Bile pigments
    - Bile acids or salts of bile acids
    - Cholesterol
    - Lecithine
    - Mucin and alike substances
    - Fat, soap, urea
    - Inorganic substances like Na, K, Ca, Cl and HCO_3

Composition of bile

	Hepatic bile	Gall bladder bile
Water	97.5 gm%	92 gm %
Bile salts	1.1 gm%	6 gm %
Bilirubin	0.04 gm%	0.3 gm %
Cholesterol	0.1 gm%	0.3 - 0.9 gm %
Fatty acids	0.12 gm%	0.3 – 1.2 gm %

Lecithin	0.04 gm%	0.3 gm %
Na+	145 mEq /1	130 mEq/1
K+	5 mEq/1	12 mEq/1
Ca+	5 mEq /1	23 mEq/1
CI	100 mEq/1	25 mEq/1
HCO_3	28 mEq/1	10 mEq/1
pH	7.1-7.3	6.9 – 7.7

Amount of bile secreted in different species

Horse	250-300 ml/ hour
Ox	98-111 ml/hour
Sheep	7-154 ml/hour
Pig	70-140 ml/hour
Dog	7-14 ml /hour
Man (Adult)	300-1200 ml/ hour

- The volume of bile secretion depends on many factors
  - Blood flow to the liver,
  - Digestive state of the animal
  - Composition of food.

Methods of bile collection

- Bile can be obtained by gall bladder fistula from gall bladder.
- Direct connection of the common bile duct also helps in getting the bile from animals.

FUNCTIONAL ANATOMY OF BILIARY SECRETION

- The basic functional unit of the liver is the liver lobule, which is constructed around a central vein.The lobule is composed of many hepatic cellular plates that radiate away from the central vein. Between the cells in the hepatic plates is the bile canaliculi that collect the bile secreted by the liver cells and empty them into terminal bile ducts. These bile ducts join with the cystic duct to form the common bile duct in the species which have gall bladder.
- The common bile duct terminate as a slight swelling in the duodenal mucosa as bile duct papilla which is controlled by a sphincter muscle known as *Sphincter of oddi*.This sphincter is well defined in carnivores but not so prominent in herbivores.
- In human, dogs, cats and horses the bile and pancreatic ducts open closely together into the duodenum. In sheep and goats the pancreatic duct empties directly into the common

bile duct so that the mixture of bile and pancreatic juice enters the duodenum. In pigs and cows bile and pancreatic ducts lie some distance apart.

- Bile is secreted continuously in all species.Bile is stored in the gall bladder in animals which feed once or twice daily. Gall bladder is the storage organ of bile and has a ability to concentrate the bile up to 20-30 times during inter digestive periods by the absorption of NaCl or $NaHCO_3$ and H_2O . So gall bladder bile differs in composition as that of hepatic bile. The degree of concentrating ability varies with species of animals. In ruminants and pigs only slight absorption of water takes place. More over these animals are **continuous feeders hence need continuous flow of dilute bile in to the intestine. In horse, gall bladder is absent, hence large and continuous flow of hepatic bile to the duodenum.**

Emptying of the gall bladder

- Basic conditions are necessary for the gall bladder to empty.
    - Relaxation of sphincter of oddi allows the bile to flow from the common bile duct into the duodenum
    - Contraction of the gall bladder provides the force required to move the bile along the common duct. Meal rich in fat, shows both of these effects.
- Fat as well as partially digested proteins in the food entering into the small intestine causes the release of cholecystokinin from the intestinal mucosa of upper small intestine. It is absorbed through circulation passes to gall bladder, causes contraction of the gall bladder muscle. This provides the pressure that forces bile towards the duodenum.
- Vagal stimulation associated with the cephalic phase of gastric secretion causes an additional weak contraction of the gall bladder.
- Neurogenic or a myogenic reflex from the gall bladder to the sphincter of oddi inhibits sphincter of oddi. Chloecytokinin may also have a direct inhibitory action on the sphincter.
- Presence of food in the duodenum causes increased peristalsis in the duodenal wall. When peristaltic wave travels towards the sphincter of oddi momentary relaxation referred as “Receptive Relaxation” of sphincter of oddi occurs before the peristaltic contraction of sphincter of oddi adjacent to intestinal wall.

Formation of bile

- Bile secretion involves two components.
- First is the *bile salt dependant* secretary flow.
- Bile is a major route of cholesterol excretion. Bile salts are synthesized in the liver from cholesterol, have cyclo pentano per hydro phenanthrene ring structure.
- The primary bile acids in most species are cholic acid and chenodeoxy cholic acid conjugated with either taurine or glycine which lower the pH of bile salt .
- The secondary bile acids (deoxy cholic acid and litho colic acid) are derived from bacterial de hydroxylation in the colon.
- the pH of intestinal content is close to pH 6, leads to failure of conjugation and accumulation of large amounts of un-ionized, hydrogenated bile acids.
    - Limited H_2O solubility of these acids leads to absorbtion by a passive diffusion. Thus conjugation of bile salt provides concentration of ionized bile salts which is required for normal fat absorption.
    - The bile salts are actively transported from the hepatocyte into the bile canaliculi. Bile is iso osmotic because of passive flow of cations and H_2O. Bile salts are re circulated from the intestine(Entero hepatic circulation) which inturn stimulates hepatic bile flow.

- Second component of the bile secretion is the *bile salt independent* flow and involve the ductular epithelium. Active transport of Na^+ accompanied by Cl, HCO_3, and H_2O provides buffer to the duodenum. This phase is under the control of secretin, cholecystokinin, and gastrin to increase HCO_3 concentration and bile flow.

BILE ACIDS AND SALTS OF BILE ACIDS

- Bile salts are Na or K salts of glycocholic and tauro cholic acids formed in the liver and found in the bile. In carnivores, man, sheep, goat and birds, tauro cholic acid predominate. In pig and rabbit , it is the glyco cholic acid predominates. Glycocholic acid is a compound of glycine (simplest amino acid), cholic acid (derived from cholesterol). Taurocholic acid is a compound of taurine (sulphur containing nitrogenous substance derived from an essential amino acid cystine) and cholic acid. **Chief bile acid is cholic acid. Others are deoxycholic, lithocholic and chenodeoxy cholic acid .**

Functions of bile salts

- They have powerful surface tension reducing ability (Detergent effect) and thereby act as a strong emulsifying agent and assist in fat emulsification. This allows the agitation in the intestinal tract to break the fat globules into minute sizes.
- Activates pancreatic lipase.
- Activates cholesterol esterases
- They help in the absorption of fatty acids, monoglycerides, cholesterol and other lipids from the intestinal tract, by forming minute complexes of lipids which are called MICELLES . These are highly soluble because of the electrical charges of the bile salts. The lipids are “ferried” in this form to mucosa where they are absorbed. Without the bile salts about 40% of the lipids are lost into the stools.
- Helps in absorption of fat soluble vitamins

Enterohepatic circulation

- Approximately 94% of the bile salts are reabsorbed by an active transport process through the intestinal mucosa in the dorsal ileum.
- On reaching the liver by portal circulation almost entire bile salts are absorbed by hepatocyte from venous sinusoids and recirculated into the bile so that these salts can circulate about 18 times before being voided in the feces.
- Loss of bile salts are replaced by the liver. This recirculation of the bile salts is called entero hepatic circulation.
- The amount of bile salt in the enterohepatic circulation alters the bile secretion.

BILE PIGMENTS

- The bile pigments are the waste products of the haemoglobin (Hb) breakdown give yellow/green colour to bile. *Bilirubin,*the brownish yellow pigment is readily oxidized into*biliverdin* which gives green colour to the bile of the herbivores.
- Bilirubin is produced from Hb with destruction of RBC in the reticuloendothelial system (RES) of the body (eg. spleen, liver and bone marrow).
- It is normally present in the blood in low concentration. Bilirubin is highly soluble in all the cell membranes. But high concertration of bilirubin is very toxic, needs excretion through bile,one of the very important functions of the liver.
- When the RBC have lived out their life span of 120 days they have become too fragile to exist longer in the circulatory system, their cell membrane rupture and release Hb.

- Released Hb undergo phagocytosis by tissue macrophages (RES). Haemoglobin is split into haem and globin of which globin is readily transported to protein pool of the body for reutilization.
- Haem ring gives (a) free iron that is transported in the blood by transferrin and (b) 4 pyrol nuclei , the substrate for bile pigments. The first pigment formed is biliverdin and is rapidly reduced to free bilirubin , which is gradually released into the plasma.
- Free billirubin immediately and strongly combine with the plasm albumin and transported through the blood and the interstitial fluid. Bilirubin bound with plasma protein called as "Free bilirubin" is insoluble that can't pass through kidney.
- Within hours, this free billirubin pass through the hepatic cell membrane, where it is released from the plasma albumin, but instantaneously combines with one of the 2 protein (Y and Z proteins) inside the liver cell which traps the bilirubin.
- Soon after bilirubin is released from these proteins it conjugated with glucuronic acid, phosphate and sulphate to form bilirubin glucuronide and 10% as bilirubin phosphate and rest as billirubin sulphate respectiely.
- These conjucated forms are excreted by active transport into the bile canaliculi.

Formation and fate of urobilinogen

- In the intestine, ½ the conjugated bilirubin is converted into highly soluble urobilinogen and stercobilinogen by bacterial action.
- Some of the uro bilinogen gets absorbed from intestinal mucosa into the blood.
- Most of them re-excreted into the gut by the liver
- After exposure to air the urobilinogen is oxidized to urobilin and excreted through urine, giving yellow colur to urine.
- Stercobilinogen is converted into stercobilin. and excreted through the feces.

JAUNDICE

- lt is much a symptom than a disease.
- It gives a yellowish tint to the body tissues, including the skin and deep tissues.
- Usual cause of jaundice is the presence of large quantities of bilirubin in the ECF, either free or conjugated form.
- Normal plasma concentration of bilirubin (both free and conjugated) is about 0.5 mg/100 ml of plasma.
- In abnormal conditions, it can rise up to 40mg/100 ml. Skin may appear yellow when the concentration of bilirubin rises to about 1.5 mg/100 ml.
- Physiological classification of jaundice:
    - Haemolytic jaundice
    - Obstructive jaundice

Hemolytic jaundice

- It is due to excessive destruction of RBC with rapid release of bilirubin in to the blood. In this condition excretory function of the liver is not impaired
- Plasma concentration of both free and conjugated form of bilirubin are elevated much above the normal level .
- The rate of formation of urobilinogen in the intestine is also increased.

Obstructive jaundice

- Obstruction in the bile ducts or damage to the liver cells leads to improper excretion of the usual amounts of bilirubin in to the G.I tract.
- In this condition the rate of bilirubin formation is normal.

- The free bilirubin gets into the liver cell for conjugation. Rupture of thebile canaliculi directly empties conjugated bilirubin into the lymph, hence most of the plasma bilirubin are of conjugated type rather than free bilirubin.

DIAGNOSTICS DIFFERENCES

Differntial diagnosis of haemolytic and obstructive jaundice

- Vanden Berg test is the specific test to differentiate free and conjugated bilirubin in the plasma. In the case of *direct Vandenberg reaction* Vandenberg reagent shows immediate reaction with conjugated bilirubin.
- Free bilirubin in the presence of alcohol precipitates the protein and releases the bilirubin, which reacts with Vandenberg reagent. Hence it is called as *indirect Vandenberg test*.
- Indirect Vandenberg reaction is the confirmatory test of haemolytic jaundice due to high content of free bilirubin in the plasma, whereas obstructive jaundice can be confirmed by direct Vandeberg reaction due to increased content of conjugated bilirubin.
- In the case of total obstruction of bile flow , lack of bilirubin in the intestine prevents the conversion of bilirubin in to urobilinogen by bacterial action. Urobilinogen is not available for reabsorbtion through portal blood and the excretion of urobilin through urine, henc test for urobilinogen in urine is completely negative .
- The stools become clay coloured due to lack of stercobilin and other bile pigments.
- Kidney can excrete only highly soluble conjugated bilirubin but not the albumin bound "free bilirubin".
- In severe case of obstructive jaundice large quantities of conjugated bilirubin froms foam and becomes intense yellow colour while shaking the urine.

CHOLESTEROL

They belong to the group of steroid present in animal fat. About 10% of the bile is the cholesterol, secreted by hepatic cells. There are two principle sources of cholesterol in the bile.

- Synthesised by the hepatic cells
- By absorption from the intestine through portal circulation to the liver

Gall stones and their formation

- Two kinds of gall stones are formed
  - Cholesterol and bile pigments
  - Cholesterol,bile pigments and $CaCO_3$ with other fatty substances.
- The cholesterol is insoluble in the water. Bile salts, fatty acids and lecithine present in the bile provide hydrophobic property to cholesterol and keep it as solution in bile . When the bile becomes concentrated, these hydrophobic substances also get concentrated.
- Under abnormal conditions, cholesterol may be precipitated which results in the formation of gall stones in the bladder.
- The following are the conditions that cause cholesterol precipitation:
  - Excessive absorption of water from the bile
  - Excessive absorption of hydrophobic substances
  - Excess secretion of cholesterol in bile
  - Inflammation of the gall bladder epithelium.
- Inflammation of gall bladder epithelium alters the absorption of water, bile salts or other hydrophobic substances through gall bladder mucosa.

- Excessive absorption of water, bile salts or other hydrophobic substances, leads to precipitation of cholesterol .
- Many small cholesterol crystals act as a nidi or nucleus which favours further deposition of cholesterol crystals leads to occurrence of multiple gall stones.

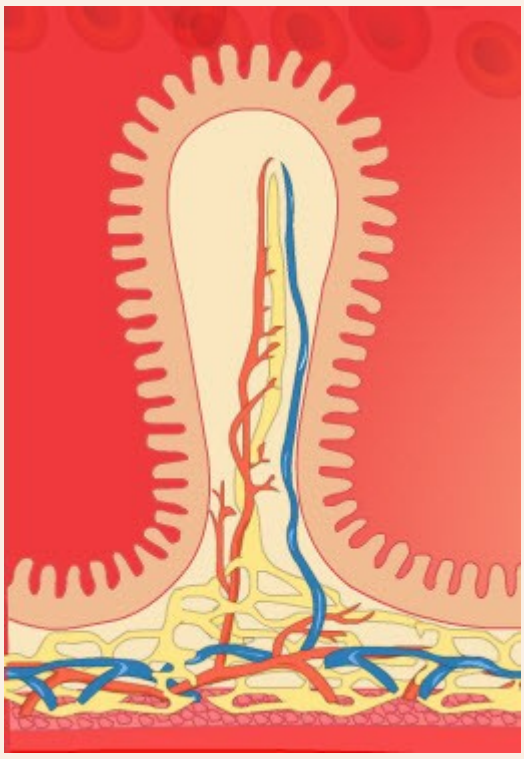
FUNCTIONS OF GALL BLADDER

- Storage of bile and concentrating the bile.
- Delays the absorption of bile salts from the intestine by the addition of mucin to the bile.
- Prevents excess absorption of bile.
- Assisting stabilization of fat emulsion in the intestine.

Function of bile as whole

- Bile acids brings about the absorption of fat and fat soluble vitamins like vit.A,D, E and K.
- High content of HCO_3 in the bile maintains alkalinity for optimal enzymatic reaction in the intestine .
- Mucin and pseudomucin in the bile act as a stabilizers of fat emulsion in the intestine.
- Bile has a marked antiseptic property and regulates the bacterial growth in the bowel.
- Bile has a mild laxative effect.
- In the absence of bile in the intestine, fat absorption is reduced and other food particles like proteins are coated with fat or fatty acids, escape enzymatic digestion leads to putrification of protein which gives offensive odour to feces.

MODULE-31: PROCESS OF DIGESTION

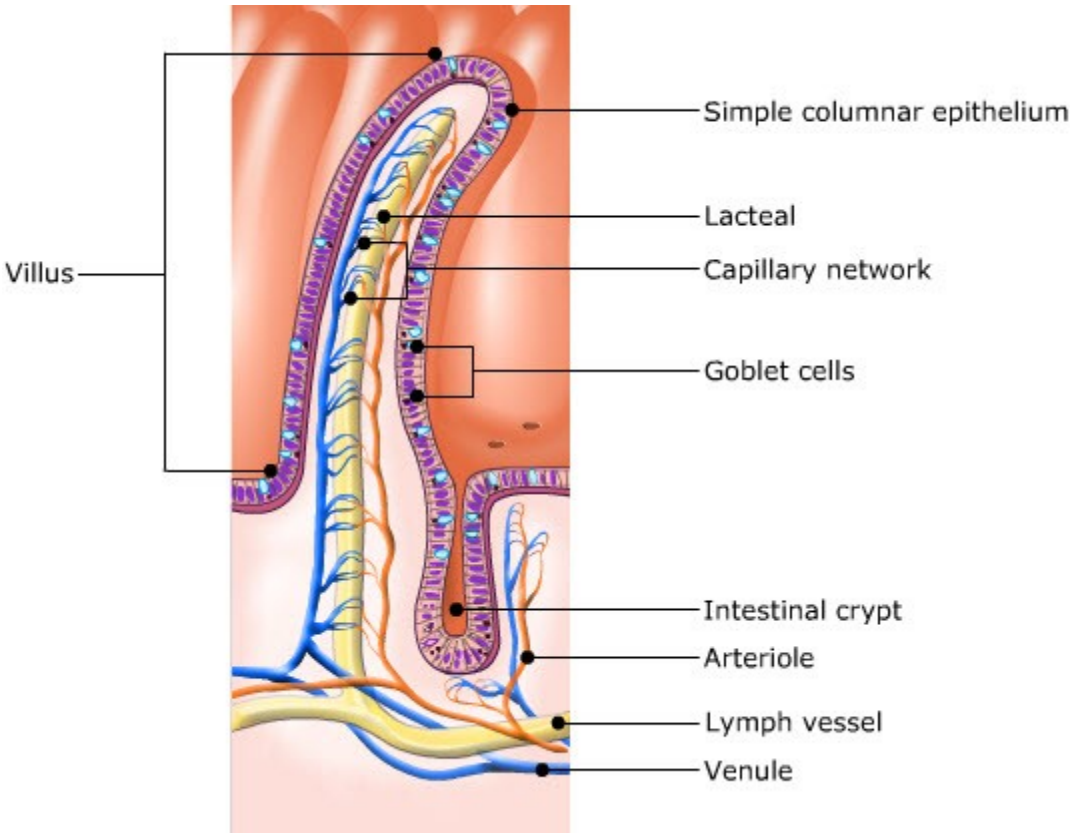


LEARNING OBJECTIVES

- This module deals with,
  - duodenal and intestinal secretions and their composition and functions,
  - the regulation of intestinal secretions,
  - the digestion of carbohyhdrate proteins and lipids at molecular/celluar level and
  - the luminal and membranous phases of digestion and the

	functions of enzymes.

STRUCTURE OF VILLI



- Surface area of the small intestine is enormously increased by large folds of mucosa known as ***plica circularis*** to facilitate contact between mucosa and lumen contents.
- The mucosal surface area is covered with finger-like epithelial projections called as *villi* to increase the surface area by about 10 to 14 fold.
- The villi are covered with brush like surface membrane known as *brush border*, composed of *microvilli* causes further increase the surface area. **The gland like structure at the base of the villi is known as *crypts of Lieberkuhn*.**
- The villi and crypts are covered with a layer of epithelium.
- The epithelial cells covering the villi and the crypts are called as enterocytes.
- The enterocytes facing towards the lumen is called apex which are covered with apical membrane. This apical membrane is provided with the microvilli (brush border).
- A jelly-like layer of glycoproteins known as *glycocalyx* covers the microvilli . Digestive enzymes and other proteins are attached to microvilli and project into glycocalyx.
- That part of enterocyte facing opposite to lumen is called as the basolateral membrane.
- Nutrients absorbed into enterocytes exit the cell through basolateral membrane before entering into blood.

CHEMICAL DIGESTION OF NUTRIENTS

- Enzymatic digestion of nutrients takes place in two phases
    - Luminal phase
    - Membranous phase
- Chemical digestion of each major nutrient is by hydrolysis *glycosidic* bonds in carbohydrates, *peptide* bonds in proteins, *ester* bonds in fats and *phophodiester* bonds in nucleic acids by the insertion of water molecule.
- Hydrolysis of nutrients in the digestive tract is catalysed by the action of enzymes secreted by salivary, gastric and pancreas glands. These glands pour their enzymes in the lumen of the GI tact for mixing with ingesta hence referred to as *luminal phase* of digestion. This phase of digestion results in incomplete hydrolysis of nutrients leads to the production of short-chain polymers of original macromolecule.
- In the *membranous phase* of digestion, the enzymes are synthesised within the enterocytes and transported to the apical membrane. Direct contact of these enzymes in the epithelium with the substrates derived from luminal phase of digestion exhibit final break down of the products of the short-chain polymers of luminal phase of digestion into monomers inside the epithelium of small intestine, hence referred to as *membranous phase* of digestion.
- It is followed by the absorption of end products of nutrients across the intestinal epithelium. .

Carbohydrate digestion

- Dietary carbohydrates are mainly monosaccharides (Glucose, galactose and fructose) disaccharides (lactose and sucrose) and fibrous carbohydrates (cellulose, hemicellulose).
- Oligosaccarides (maltose, isomaltose and maltotriose are rarely present in the diet, but they are formed in the gut during the course of carbohydrate digestion.
- Starches is present as amylose and amylopectin.
- Amylose contains glucose monomers linked by a -1, 4 glycosidic linkage, whereas amylopectin also contain glucose linked by *a* -1, 4 glycosidic linkage, but the chains are branched, having a -1, 6 glycosidic linkage at branched points.

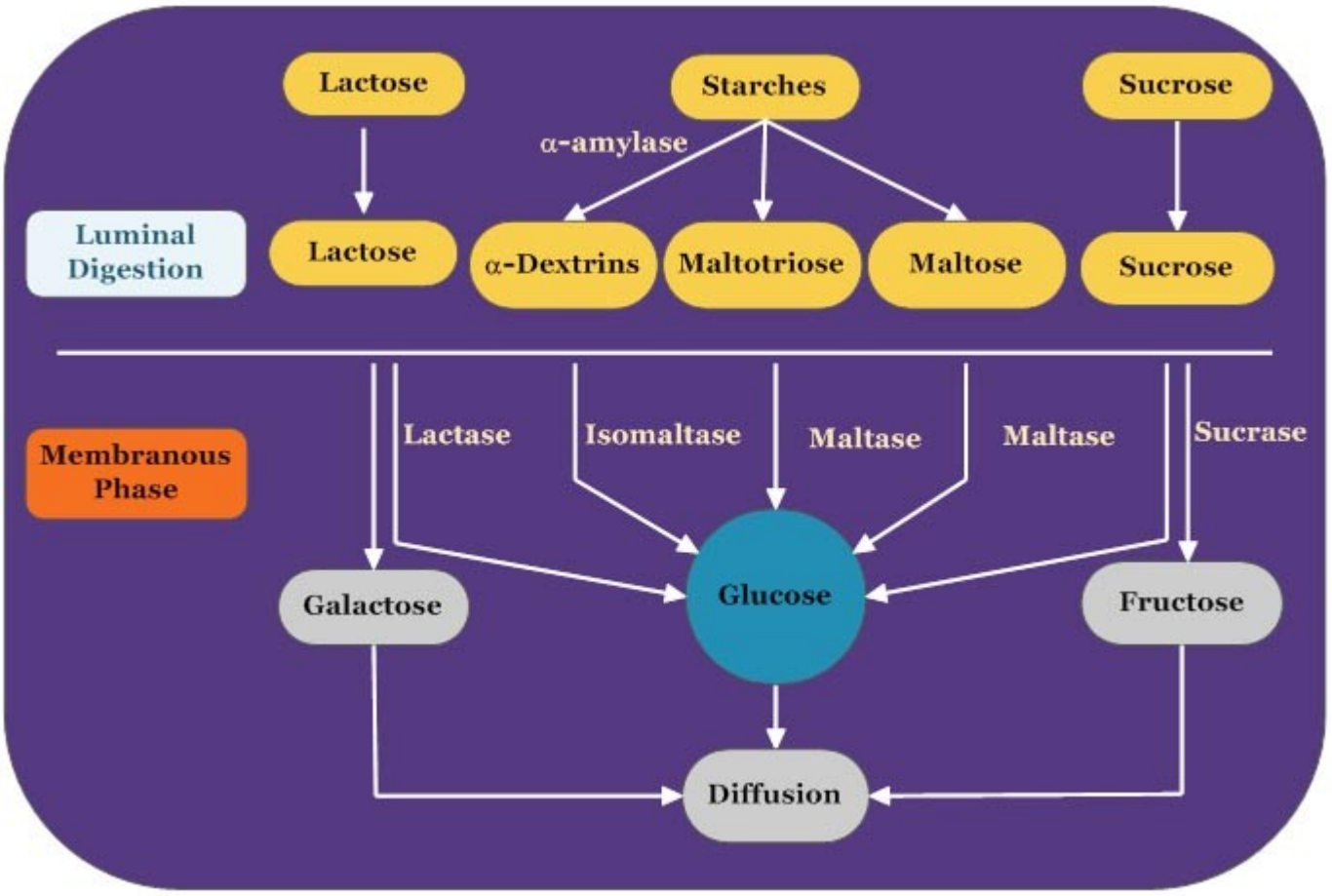
LUMINAL AND MEMBRANOUS PHASE OF DIGESTION

Luminal phase

- In luminal phase of digestion, *alpha amylase* is secreted by the salivary glands (eg. pig, dog and rabbit), and pancreatic amylase hydrolyses starches to yield *oligosaccharides (a -dextrins, maltotriose, maltose* without free glucose),whereas fibrous carbohydrates (eg. Cellulose and hemicellulose) can not be hydrolysed by *alpha amylase of mammals*.
- Hydrolysis of *amylopectin* produces branched-chain oligosacchrides, *limit dextrins* and alpha 1, 6-linked disaccharide, *isomaltose*.

Membranous phase

- The oligosaccharides, di- and tri-saccharides are hydrolysed by saccharidases enzymes like *maltase, isomaltase, sucrase and lactase* in the membranous phase.
- In the glycocalyx of enterocytes, these enzymes hydrolyse the oligosaccharides (eg. maltose, sucrose and lactose) to monosaccharides *(glucose, galactose, and fructose)*.
- Most of the monosaccharides are absorbed into the portal blood and carried to liver. some are also absorbed through lymph stream.



PROTEIN DIGESTION

- Dietary, endogenous, microbial and shed mucosal cells proteins are capable of being hydrolysed by *endopeptidases*, the proteolytic enzymes present in gastric , pancreatic and intestinal juices break the proteins at internal peptide points.
- In the luminal phase of digestion, gastric proteases (eg. pepsin and rennin) and pancreatic proteases (eg. trypsin, chymotrypsin, carboxy peptidase a & b) yield *oligopeptides* and some amino acids.
- These oligopeptides are further hydrolysed by *oligopeptidases* in the glycocalyx to produce *amino acids, di- and tri- peptides*.

Luminal phase of digestion

- The proteolytic enzymes are secreted from gastric glands and pancreas as inactive *zymogens*. In the stomach, *pepsinogen and prorennin (chymosinogen)* are activated by HCl.
- Pepsin also autocatalytically activates pepsinogen.
- Trypsinogen from pancreas is activated as trypsin by the action of *enterokinase,* an enzyme produced from duodenal mucosa.
- **Trypsin autocatalytically activates trypsinogen.**
- The active trypsin inturn activates other proteolytic pancreatic enzymes (Chymotrypsinogen and procarboxypeptidase a & B) .
- The HCl of stomach also has hydrolytic properties on protein

Membranous phase of digestion

- In the membranous phase of digestion, the e*xopeptidases* present on the enterocyte apical membrane act at the ends of peptide chain to release free amino acids at the surface of mucous membrane.
- Some long-chain peptides are incompletely hydrolysed leading to the production of di- and tri-peptides.
- These di- and tri-peptides are easily absorbed by the epithelial cells; where they are subsequently hydrolysed by the intracellular peptidases, forming free amino acids.
- Thus, the free amino acids are produced at two sites: on the surface of the enterocytes and the second within the cell.

Enzyme	Source	Precursor	Activator	Action
Pepsin	Gastric glands	Pepsinogen	HCl & Pepsin	Endopeptidase
Chymosin (Rennin)	Gastric glands	Pro-rennin	HCl	Endopeptidase
Trypsin	Pancreas	Trypsinogen	Enteokinase & Trypsin	Endopeptidase
Chymotrypsin	Pancreas	Trypsinogen	Trypsin	Endopeptidase
Elastase	Pancreas	Pro-elastase	Trypsin	Endopeptidase
Carboxypeptidase A	Pancreas	Procarboxypeptidase A	Trypsin	Endopeptidase
Carboxypeptidase B	Pancreas	Procarboxypeptidase B	Trypsin	Endopeptidase

LIPID DIGESTION

- Lipids make up a large portion of diet in carnivores, where as they form only a minor portion of diets in herbivores.
- Primary dietary lipid is *triglyceride*; other lipids include *cholesterol and cholesterol esters* from animal sources, waxes from plant sources and *phospholipids* from both plant and animal sources.

- Lipid digestion occurs in four phases; *emulsification, hydrolysis, micelle formation and absorption***.**

- Emulsification is a process of reducing lipid droplets to a smaller size for their suspension in water.
- In the gut, lipid globules are broken down to droplets by the mixing and agitating actions of distal stomach.
- Emulsification is completed in the small intestine by the detergent action of bile acids and phospholipids.
- Bile salts reduce the surface tension of the lipid droplets and further, reduce in size of the fat droplets.
- The bile coated or emulsified droplets are subjected to hydrolytic enzyme action.
- *Triglycerides* are the major dietary lipid, undergo hydrolysis by the action of gastric, pancreatic *lipase and co-lipase*, which are secreted as active form.
- The co-lipase "make a pathway" through the bile product coating the emulsified lipid droplet, giving access to the lipase to reach the underlying triglyceride.
- Lipase cleaves the fatty acids from the end of triglyceride molecule resulting in the formation of two free nonesterified fatty acids and a monoglyceride.
- *Cholesterol esterase and phospholipase* are the other lipid digesting enzymes of pancreas.
- The products of these enzymes are *nonesterified fatty acids, cholesterol and lysophopholipid***.** The fatty acids, monoglycerides etc., combine with bile acids and phospholipids to form very small lipid droplets, *micelles* . The micelles are water soluble allow the lipids to diffuse through glycocalyx and into close contact with absorptive surface of the enterocytes.

LARGE INTESTINE

Large intestine of herbivores

- Large intestine is of great importance in herbivores. In simple stomached animals, the enormous caecum and colon are involved in the microbial fermentation hence they are called as ***hind gut digesters***. The absorption of the fermented end products of cellulose and digestible products synthesised by bacteria occur in large intestine of simple stomached herbivores.

Structure

- Caecum and colon of simple-stomached herbivores are very capacious and sacculated, whereas in ruminants, they are simple and non-sacculated. Glands and villi are present in large intestine of herbivores. The glands secretes mainly mucous but has no enzymatic digestive function. In carnivores c olon is short and non-sacculated, caecum is poorly developed, intestinal glands are present throughout large intestine but villi are absent. The glands of large intestine secretes only mucous not the enzymes.

Bacterial action

- No bacterial fermentation occurs in small intestine of carnivores. However, in large intestine, putrifactive (proteolytic) and cellulolytic type of bacteria act on the ingesta which have escaped digestion in small intestine. The products of bacterial action in large intestine are indole, skatole, paracresol, VFA, NH_3 and gases CO_2, CH_4, H_2S and B complex vitamins. These products may be absorbed into the portal blood and carried to liver.

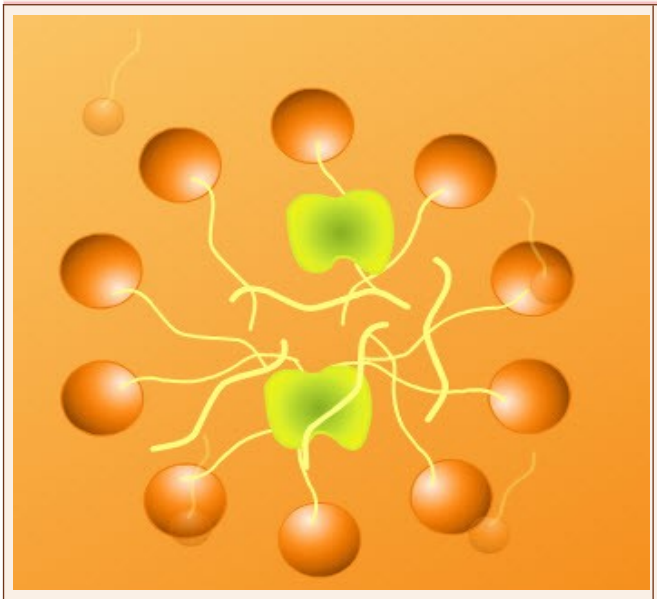
Digestive process

- In monogastric animals, hind-gut maintains conditions favourable for microbial fermentation, which includes substrate availability, control of pH and osmolality, anaerobiosis, retention of substrate and removal of end products of fermentation. There is extensive urea recycling in caecum and colon supplies N_2 for microbial growth.
- Bacterial action in large intestine is mainly on structural and non-structural carbohydrates and proteins. The digestion of cellulose in large intestine yields VFA, CO_2 and CH_4. Ammonia is produced from proteins and urea is absorbed from large intestine of horse.
- In ruminants, enzyme digestion occurs after microbial fermentation and the host animal also utilises the microbial cell bodies. In simple stomached herbivores, microbial fermentation follows after enzymatic digestion and only fermentation products and not the microbial cell bodies are available for absorption by the host. The VFAs absorbed from the large intestine contributes to the energy needs of the host animal.
- Volatile fatty acids acetic, propionic and butyric acids are found in the large intestine of ruminants and horse. Appreciable quantities are also produced in pigs, rabbit and fowl. Very small amounts are found in large intestine of cat and dog. Bacterial synthesis of B complex vitamins occurs in caecum and colon.
- The gases found in large intestine are CO_2, CH_4 and very small amounts of H_2S, O_2 and considerable quantities of N_2 which are expelled in part through anus and in part absorbed into the blood and eliminated through lungs.

Functions of large intestine

- The digestive processes are practically complete in the small intestine. Materials escape absorption in small intestine are gradually propelled into the large intestine through the***ileocaecal valve***. Large intestine is involved in the functions of reabsorption of water that has been poured out by digestive glands. It also acts as reservoir for waste material that constitutes the *faeces*, which are expelled at intervals by the act of defecation.

MODULE-32: ABSORPTION



LEARNING OBJECTIVES

This module explain the following,

- absorption - basic histology of the villi of intestine and venous and lymph,
- various transport machanism,
- the mechanism of digestion of

	carbohydrates, proteins and lipids and • the importance of bile in lipid absorption.

ABSORPTION

- It is the process whereby the products of digestion and the digested foodstuff form the lumen of the gut is transferred to the blood or the lymph across the epithelial cell membrane.

Site of absorption

- No absorption of food or end products of digestion in the mouth and oesophagus
- In the monogastric animal, absorption in the stomach is very limited.
- However certain drugs can be absorbed from the pharynx and to a limited extent from the oesophagus.
- The small intestine is the chief site of absorption in the carnivores and omnivores.
- Villi is the the chief site of absorption in small intestine
- The large intestine is the chief organ of absorption in all herbivores (eg. horse) and to a limited extent in the carnivores and man where it is restricted to the initial colon.
- In ruminants, the digestion and absorption of contents is of special importance in the anterior part of the digestive tract.
- The large intestine has specific absorptive sites with respect to water and electrolytes.
- In herbivores, especially in equines, the large intestine absorbs volatile fatty acids and ammonia.

ROUTES OF ABSORPTION

Small intestine has extremely well developed lymphatic and blood system which function as a route of absorption of digestive products.

- Lymph
  - In the core of the villus lymph capillary originates as *lacteal* near the tip of the villus and enters into a plexus of lymph vessels lying just on the inner side of the muscular coat. Branches of these plexus then enter into the submucosa and form a loose plexus of large lymphatics, finally pass into mesentry.
  - The lymph capillaries drain their content into large lymph vessels, which intern empty into the mesentric vessels. These mesentric vessels are then connected with mesentric lymph nodes. The contents of the mesentric vessels empty into the *cisterna chyli* which is continued forward as thoracic duct, finally empties into the venous system anterior to heart.

- Glycerides, long chain fatty acids, cholesterol and the immuno globulins during the first 24 hours of life are absorbed by the lymphatic system. The rate of lymph flow increases after a meal.

- Blood
  - Each villus contains several small arteries, which enter the base of the villus and form a dense capillary network immediately under its epithelium. Near the tip of the villus, one or two veins arise from a capillary network and run downward.
  - The venules and veins, drain into the portal vein. The portal vein enters into the liver where its blood is mixed with that of hepatic artery. The hepatic vein conveys the blood from the liver to the posterior vena cava.
  - Amino acids, monosaccharides, free glycerol, water, inorganic salts and short chain fatty acids are absorbed through blood route. After a meal, rapid flow of blood causes increased absorption rate, but this increase is less than that of lymph.

MECHANISM OF ABSORPTION

- The possible mechanisms of absorption are broadly classified into three groups:
  - Non-carrier mediated transport (passive diffusion)
    - It depends on the electro-chemical gradient, occurs through channel pathways of ions.
    - Non-carrier mediated process aids in the absorption of short chain fatty acids, inorganic salts and lipid soluble compounds.
  - Carrier mediated transport – includes
    - Facilitated transport from higher to lower concentration
    - Exchange diffusion Na+/H+ exchanger: transports H+ out and Na+ into the cell
    - Active transport against concentration gradient with expenditure of energy
      - The carrier-mediated process may help water-soluble materials to pass the lipid layer of the cell membrane, whereas glucose and amino acids are absorbed by active transport.
  - Pinocytosis transport of intact luminal materials in the form of vacuoles into the mucosal cells. This is important for absorption of intact proteins and intact triglycerides.

CARBOHYDRATE ABSORPTION

Carbohydrate absorption

- Monosaccharides (eg. glucose, fructose) are absorbed by active transport mediated by carrier and sodium pump.

Absorption of glucose

- Glucose gets attached to specific transport proteins that lie on the luminal side of the enterocytes. These transport proteins have two binding sites one for glucose and one for sodium.

- Once glucose and Na^+ occupy the binding sites, the transport protein moves across the cell membrane and unload the glucose and Na^+ into the cell. Hence, this process is referred to as sodium co-transport.
- The transport of glucose will not occur unless Na+ is present.
- Within the cell, glucose moves down by concentration gradient through the basoleteral membrane by facilitated diffusion, to extra-cellular space and then into the blood and finally to liver where the monosaccharides are stored as glycogen.
- **Galactose is absorbed more rapidly than glucose but fructose absorption is slower than glucose absorption.**
- **Fructose absorption is by facilitated diffusion and not energy dependent. Hence, fructose can not be absorbed against concentration gradient.**
- Mannose, xylose and arabinose are poorly absorbed by diffusion.
- Maltose, sucrose and lactose as such are absorbed very slightly.
- Disaccharides do not generally enter into the blood stream because of the presence of disaccharidases in the brush border of mucosa, which converts them to monosaccharides.

PROTEIN ABSORPTION

- The free amino acids are readily absorbed chiefly by active transport requiring Na -co transport system.
- Three types of carriers are involved in the transport of acidic, basic and neutral amino acids.
- L-isomer forms of plant and animal protein are more readily absorbed than D-isomers, acidic basic and meutral amino acids
- Some di and tri peptides are also absorbed. Intracellular peptidase hydrolyses these peptides to amino acids.
- Intracellular amino acids diffuse across the basolateral membrane to reach liver via portal blood, whereas intact proteins are absorbed via lymph pathway.
- Immediately after birth immunoglobulins from colostrum are absorbed by a process of pinocytosis particularly in lambs, piglets, kids, calves and pups.
- The immunoglobulin absorption decreases with time after birth and ceases after 24-36 hours.

LIPID ABSORPTION

- Lipid absorption begins in the dental duoderium and ends in proximal part of the jejunum.
- As the micelles come in close contact with surface of enterocytes, the lipid components diffuse through the glycocalyx to the apical membrane by a special fatty acid binding proteins which aids the transport the fatty acids across the cell membrane.
- Other components in the micelle such as monoglycerides, cholesterol and vitamin A diffuse into the apical membrane.
- Bile salts get detached from the micelles during fat absorption and remain in a free state. In the ileum, Na-co transport system function as specific bile acid transport which nearly complete the absorption of bile salts.
- After absorption, the bile salts are transported to liver by the portal blood.

- The liver extracts bile acids and maintains the normal concentration of bile acids in systemic blood. This process of recirculation of between liver and intestinal lumen is referred as *enterohepatic circulation of bile***.**
- Glycerol is absorbed by passive diffusion into the mesentric venous blood.
- Short chain fatty acids up to C^{10} are water-soluble get into mesentric portal blood.
- Monoglycerides and long chain fatty acids enter the microvilli and pass on to the lacteal by simple diffusion.
- Only free form of cholestrol can be absorbed, whereas cholestrol esters must be hydrolyzed by pancreatic brush border hydrolases..
- Cholesterol is absorbed less efficiently than triglycerides. Presence of hydro cholesterol or plant sterols inhibits cholesterol absorption.
- In the epithelial cells, cholesterol is re-esterified before their transfer to lacteals.
- Before absorption phospholipids are hydrolysed to free fatty acids and lysophospholipids by phospholilpase of pancreas and intestinal epithelium.
- Within the epithelial cells, long chain fatty acids are converted into fatty *acyl-CoA* involving co-enzyme A and *ATP*.
- The fatty acyl co-enzyme reacts with monoglycerides to form di and tri glycerides.
- The newly formed triglycerides differ from that of dietary fat. GlycerolPO_4 derived from glucose metabolism provides glycerol residue for the triglyceride synthesis.
- In addition, phospholipids and cholesterol esters are produced in the epithelial cells. Small amounts of proteins are added to the lipid droplet before their transfer from epithelial cells to lymph.
- *Chylomicrons* are the products containing high amount of triglycerides, low level of phospholipids, cholesterol esters and proteins. They leave the cell by *reverse pinocytosis*and enter into the lacteals.
- Lipid absorption begins in the distal duodenum and completed in the proximal jejunum.
- The absorbed fat is in the form of an emulsion and imparts a milky appearance to the lymph,called as *"chyle"***.** This leave the cell by reverse pinocytosis and enter in the lacteal. Though lymphatic channel and thoracic duct it is added into the blood for its distribution to tissues.
- **Short chain fatty acids are absorbed by blood from colon and caecum in sheep and horse and ceecum in pigs**.

MECHANISM AND ABSORPTION OF MINERAL AND WATER

- Sodium is transported as sodium co-transport along with glucose and amino acids.
- Sodium transport is also coupled transport with chloride ion
- Sodium ion also shows diffusion across the electrochemical gradient.
- Potassium is transported by passive diffusion across the concentration gradient
- Bicarbonate ions are transported actively or rarely with sodium ion.
- Magnesium ion is transported actively, but poorly absorbed.
- Calcium ion is also transported actively by the calcium-binding protein produced under the influence of vitamin D_3
- Phosphorous is actively absored related to calcium absorption.
- Copper ion is absorbed in small quantities.
- Cobalt and manganese ions are readily absorbed.
- Iron absorption is related to its level in mucosal cells and is mediated by apoprotein carriers.

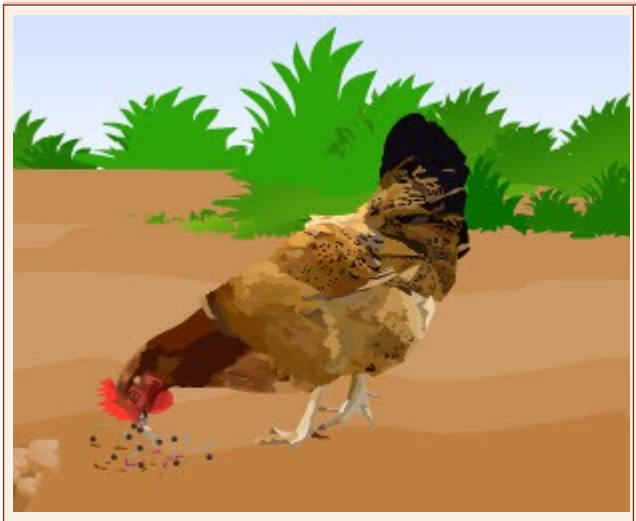
- Water is transported passively

ABSORPTION OF VITAMINS

Absorption of vitamins

- Fat soluble vitamins (A, D, E, K) pass through the intestinal mucosa by passive diffusion.
- Water soluble vitamins (except B12) are also absorbed by passive diffusion but may also be transported actively.
- Vitamin B12 requires an intrinsic factor, secreted by the gastric glands of the stomach, for its absorption by and active transport process.

MODULE-33: AVIAN DIGESTION



LEARNING OBJECTIVES

This module explores,

- the difference between the alimentary tract of chicken and mammals and
- the digestion and absorption of food form the avian G.I tract.

AVIAN DIGESTION -ALIMENTARY CANAL

- In birds, the alimentary canal is a long tube like organ starting from the beak at the head and ending with the vent or cloaca in the abdominal region.

Special features of the avian digestive system includes

- Presence of beak
- Absence of teeth
- Proventriculus
- Gizzard
- Paired caeca
- Vent

MOUTH STRUCTURE

- In the fowl ,the lips and cheeks are replaced by the beak - an area of dense and horny skin lying over the mandible.

- Absence of teeth, but so called egg tooth found on the end of the beak of newly hatched chickens to aid their escape from the egg at the time of hatching which disappears after a day or two.
- The hard palate, forming the roof of the mouth. It has five transverse rows of backwardly pointing, hard, conical papillae.
- Numerous ducts of the salivary glands pierce the hard palate to release their secretions into the mouth cavity.

SALIVARY GLANDS

- A thick layer of stratified squamous epithelium covers the free surface.
- The salivary glands run the whole length of the hard palate, the groups of glands merging to form one mass of glandular tissue under the epithelium.
- Lymphoid tissue is found in most glands.
- The salivary glands are:
    - Maxillary - in the roof of the mouth
    - Palatine - on either side of the nasal opening in the roof of the mouth
    - Apheno-pteryoid glands - in the roof of the pharynx on each side of the common opening for the eustachian tubes
    - Anterior sub-mandible glands
    - Posterior sub-mandibular glands
    - Lingual glands - in the tongue
    - Crico-arytenoid glands - around the glottis
    - Small gland in the angle of the mouth.

PHARYNX AND TONGUE

- The pharynx is continuous with or follows the mouth.
- The combined cavity of the mouth and the pharynx is often referred to as the oropharynx.
- The common opening for the two eustachian tubes is located in the middle of its dorsal wall (roof).
- The tongue is long and pointed and conforms to the shape of the beak in which it operates.
- The epithelium of the tongue is thick and horny, especially towards the tip.
- A transverse row of simple, large and horny papillae with their tips directed towards the rear of the mouth cavity are located on the posterior end.
- The hyoid bone provides the framework to support the tongue. The entoglossal bone extends longitudinally in the median plane.
- Small patches of lymphatic tissue are located throughout the corium. Mucous glands are located in the tongue with short ducts directed towards the rear.
- Some but not others believe that there are taste buds located on the tongue.
- In any case the sense of taste appears to be very weak if at all present.
- The mouth has two major functions:
    - To pick up the food particles and direct the food into the oesophagus.

OESOPHAGUS AND CROP

- Oesophagus is wide which connects the mouth region to the crop.
- The wall of the oesophagus is composed of four layers of tissue, the innermost being mucous membrane.
- The mucous membrane is an important barrier to the entry of microbes.

- It secretes mucous to lubricate and to aid the passage of the food along the alimentary canal.
- The crop is a large dilation of the oesophagus located just prior to the oesophagus entering the thoracic cavity. In some birds there are two crops and **carnivorous birds donot have crop.**
- The crop provides the capacity to hold food for some time before the commencement of digestion. This capacity enables the bird to take its food as "meals" at time intervals and permits continuous digestion.
    - The crop structure is similar to that of the oesophagus except there are no glands present in fowls.
    - **Ducks and geese have glands in the crop mucous membranes.**
    - **In pigeons, the surface cells of the crop slough off during brooding to form pigeon's milk - used to feed the baby pigeons in the nest.**
- Inside the thoracic cavity, the oesophagus becomes the proventriculus very glandular part of the digestive tract often called as glandular stomach.

PROVENTRICULUS AND GIZZARD

Proventriculus

- The glandular stomach or proventriculus is relatively small and tubular.
- The wall is very thick composed of five layers:
    - Outer serous membrane.
    - Muscle layer composed of three separate layers:
        - Two thin longitudinal layers.
        - One thick circular layer.
    - Layer of areolar tissue containing blood and lymph vessels.
    - Thick layer composed mainly of glandular tissue.
    - Inner mucous membrane.

Gizzard

- The muscular stomach or gizzard is located immediately succeeding the proventriculus.
- It is placed partly between the lobes and partly behind the left lobe of the liver.
- Under the outer layer very powerful masses of red muscle are located.
- The inner surface is lined with a creamy colored, thick, horny tissue raised in ridges.
- The gizzard almost always contains quantities of hard objects such as gravel or other grit that aids in the disintegration of food - the primary function of the gizzard.
- The gizzard consists of number of layers of tissues in some of which straight tubular glands are located.
- The innermost layer is a strong, flexible skin able to withstand the potentially damaging effects of the muscular action of grinding the food often in the presence of stones or other insoluble material.
- The glands of the gizzard produce a liquid, keratinized material that passes to the surface of the horny lining where it hardens to replace tissue worn away by the grinding action of the organ.

DIGESTION IN BIRDS

Enzymatic digestion

- After ingestion, the food is mixed with saliva and mucous to moisten the food. Amylase, is produced by the salivary and oesophageal glands.
- The secretions of the proventriculus or glandular stomach are hydrochloric acid, pepsin that acts on protein and the hormone gastrin that stimulates the production and release of gastric juice in the proventriculus and pancreatic juice from the pancreas.
- *Gizzard* is a very powerful muscular organ actively involved in breaking the food particles into smaller sizes. The enzymes released into the food with the saliva and by the proventriculus are also thoroughly mixed with the food. This breaking and mixing function of the gizzard is enhanced by the presence of insoluble grit such as stones.
- Pancreatic juice and bile from the liver enters via ducts located at the distal end of the duodenum at about the junction of the duodenum and the jejunum. The digestive process starts prior to the entry point to the small intestine due to back flow of pancreatic juice and bile towards the gizzard.
- In addition to enzymes, the pancreas produces insulin and sodium bicarbonate. Insulin is involved in the maintenance of blood sugar levels while the sodium bicarbonate, being strongly alkaline, will increase the pH of the intestinal contents.
- The small intestine also produces enzymes that play their part in the digestive process of reducing the complex food compounds into simple building blocks that can be absorbed across the intestinal wall for the transport to the organ for further processing or storage.
- Food materials that escape enzyme action are subjected to bacterial breakdown in the caeca.

SMALL INTESTINE

- Small intestine begins at the exit from the gizzard and ends at the junction of the small intestine, caeca and colon.
- It is relatively long and has a constant diameter. Of the three parts of the small intestine duodenum, jejunum and ileum, only the duodenum can be easily distinguished in the fowl.
- There is no clear demarcation between the jejunum and ileum.
- Much of the digestion of the food and all of the absorption of the nutrients takes place in the small intestine
- Structures of small intestine
    - Outer serous membrane.
    - A layer of longitudinal muscle
    - A layer of thick circular muscle
    - Structures located between the two muscle layers are:
        - Blood vessels.
        - Lymph vessels.
        - A network of nerve fibers.
    - An ill-defined sub-mucosa
    - Mucous membrane consisting of:
        - Thick muscularis mucosae of longitudinal and circular muscle.
        - Corium - many glands, lymphoid tissue, muscle fibers and a variety of free cells.
        - Inner epithelial surface.

Duodenum

- The duodenum starts at the gizzard and forms an elongated loop about 20 centimeters long. The pancreas lies between the arms of the loop and being attached to each arm of the duodenum actually holds the two arms together.
- Lymphoid tissue in the duodenum is very plentiful and is usually located in the corium.
- Bile ducts from the gall bladder attached to the liver and two to three pancreatic ducts enter the small intestine by a common papilla at the caudal end (closest to the rear) of the duodenum.
- Pancreas is located closely associated with the duodenum being attached to each side of the duodenal loop and lying between the two arms.

Villi

- It is a long flattened, fingerlike projections extending into the lumen of the intestine like flexible fingers.
- A single layer of columnar epithelium together with goblet cells covers the lining. The goblet cells secrete mucous.
- A lacteal (lymph vessels), capillaries, bundles of plain muscle fibres, nerves and other tissues and cells occupy the core of the villus. The villi have the function of providing a vastly increased surface area for the more efficient absorption of the nutrients.
- The villi are very actively involved in the absorption process.
- The efficiency of the absorption is influenced by the surface area available for the nutrients to move through.

Jejunum and the ileum

- The jejunum and the ileum, together about 120 cm long, commence at the caudal end of the duodenum where the bile and the pancreatic duct papilla are located and terminates at the ileo-caecal-colic junction. It is a junction of small intestine, the two caeca and the colon. This portion of the small intestine is similar in structure to the duodenum except that:
    - The villi are shorter
    - There is less lymphoid tissue
- Meckel's diverticulum is a constant feature about half way along the small intestine appearing as a small projection on the outer surface of the small intestine. This projection represent this point of attachement of yolk sac during the development of the embryo.

Functions of small intestine

- Produces number of enzymes involved in the digestive process
- Site of final digestion of the food
- Site of absorption of the end products of digestion

LARGE INTESTINE

- The large intestine is very short and ends at the cloaca.
- This section includes paired caeca, colon and rectum and the rectum being the terminal part.
- The bursa of fabricius is located immediately above the cloaca of young birds, but disappears when the birds have reached approximately one year old.

Caeca

- Paired caeca or blind pouches are about 16-18 centimeters long in the adult.

Structure of the caeca

- Outer serous membrane

- Outer longitudinal muscle
- Circular muscle
- Inner longitudinal muscle forming the muscularis mucosae of the mucous membrane

Cecal function

- Microbial digestion of cellulose.
- Reflux of urine into the ceca exposes the cecal microflora to urea and uric acid, which are then degraded; the nitrogen is not recycled for use by the host.
- Microbial synthesis of B compex vitamins

Cloaca

- It is a tubular cavity opening to the exterior of the body provides a common passage to the digestive and urogenital tracts.
- It divides into three chambers as follows:
    - *The copradaeum* - a continuation of the colon-rectum
    - *The urodaeum* - middle part into which the ureters and genital ducts open
    - *The proctodaeum* - opens to the exterior of the vent. Birds less than one year old have a dorsal opening leading into the blind, rounded sac - the bursa of fabricius.

ABSORPTION AND EXCRETION

Absorption

- Absorption of glucose occurs via both passive and carrier mediated transport system.
- Passive transport appears to predominate in the duodenum and jejunum. Chicken has a sodium dependent carrier system for the active transport of sugars.
- Carrier medicated transport of D -glucose is facilitated by a Na^+-glucose co-transpoter protein.
- Amino acids are also transported by Na^+ dependent and energy dependent carrier mediated process in birds.
- Four system of amino acids tansport have been identified in chicks:
    - Neutral amino acids system
    - Basic amino acids system
    - Acid amino acids system
    - A system for proline, beta alanine and related amino acids.
- Neutral amino acids are transported more rapidly than basic or acidic amino acids.

Faeces

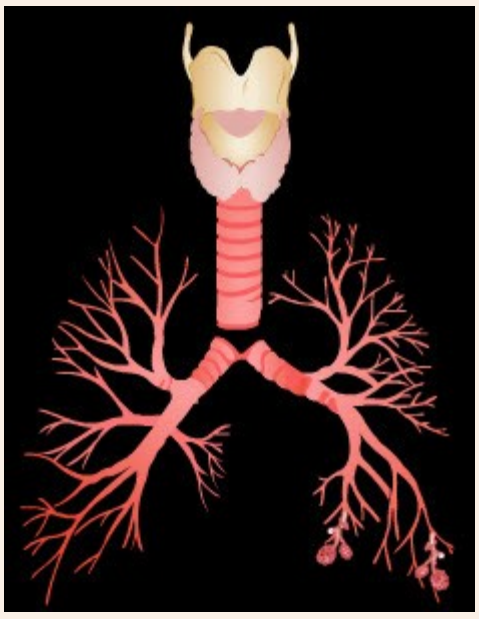
- This material consisting of waste and undigested food mixed with the urine in the cloaca and eliminated from the body as faeces.
- Typically it is a rounded, brown to grey mass topped with a cap of white uric acid from the kidneys.

ABSORPTION OF SALT AND WATER

- Sodium, K^+ and Cl^- ions are almost completely absorbed. Na^+ ions are involved in the transport of water, monosaccharides, amino acids, pyramidine and bile salts.

- Na^+ is transported as
  - Na-co transport
  - Cl^- coupled transport and
  - Diffusion by electro -chemical gradient.
- Chloride ions are transferred through Cl^- coupled Na^+ transport
- Association with Na^+ co-transport of glucose
- Diffusion by electro-chemical gradient.
- K^+ is absorbed by passive diffusion due to concentration gradient.
- HCO_3 absorption is by active transport.
- Water is transported passively.
- Intestinal absorption of Ca^{++} is by active transport. Vitamin D induces mucosal Ca^{+} $^{+}$ binding protein and increases Ca^{++} absorption.
- Mg^{++} is absorbed by active transport but its absorption is poor. Absorption of phosphorus is active process and related to active transport of Ca^{++}.
- Absorption of Fe^{++} is related to its level in mucosal cell. Absorption is limited by binding capacity of apoprotein (carrier protein).
- Cu is absorbed in small amounts.
- Co and Mn are readily absorbed.
- Fat-soluble vitamins A, D, E and K pass through mucosa passively as also water-soluble vitamins. Vitamin B_{12} requires an intrinsic factor secreted by stomach for its absorption by active transport.

MODULE-34: RESPIRATORY APPARATUS AND PHYSICAL PRINCIPLES OF GAS EXCHANGE



LEARNING OBJECTIVES

This module deals with,

- what is respiration?
- the structures associated,
- basics of gaseous transport and
- terms related to capacity of lung during various phases.

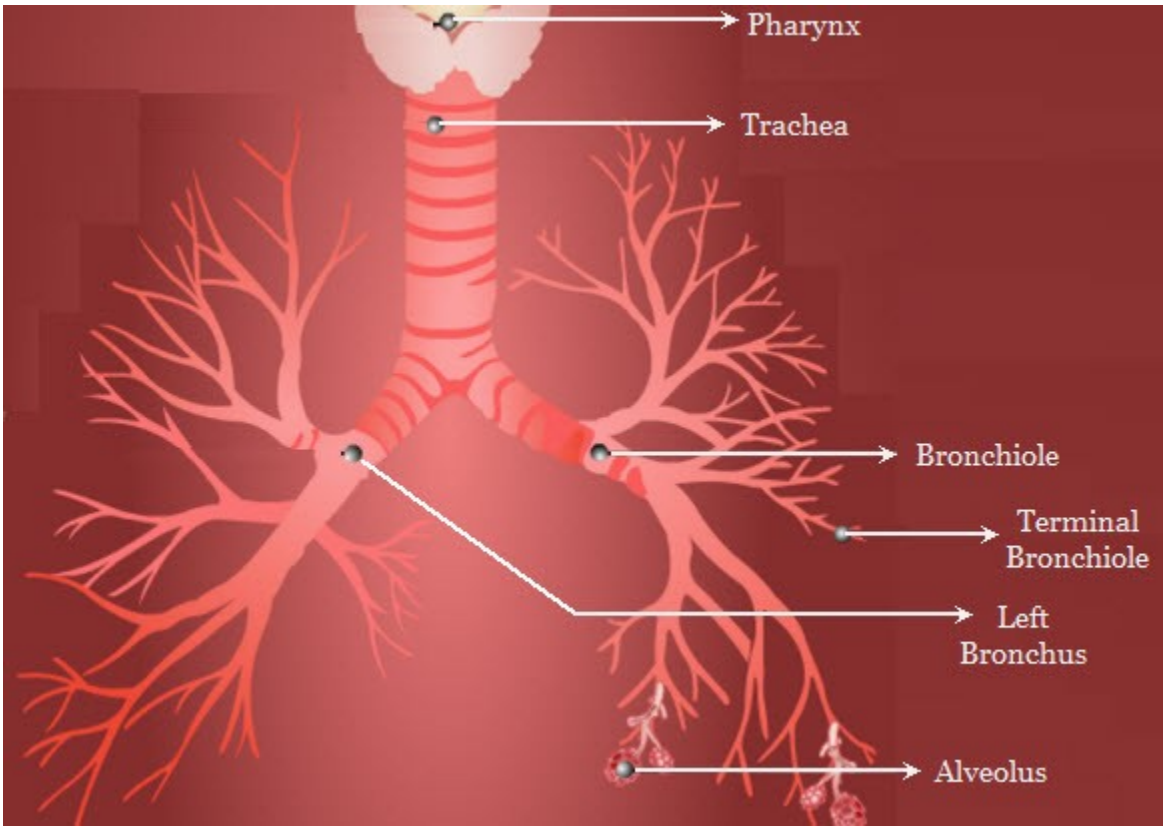
RESPIRATORY TRACT

- It is the conducting portion or airway consists of nose, pharynx, larynx, trachea, bronchi, bronchioles, and terminal bronchioles.
- Pharynx is a common passageway for air and food. The opening from the pharynx leading to the continuation of the airway is the larynx, the organ of phonation (sound production) in mammals.

- It is produced by the controlled passage which causes vibration of vocal cords of larynx.
- The organ of phonation in birds called the syrinx which is located at the junction where trachea divides into bronchi.
- The glottis is the slit-like opening between the vocal cords. Extending craniad from the larynx is the epiglottis.
- It is a leaf shaped plate of cartilage covered with mucous membrane.
- It is located at the root of the tongue, which is passively bent over the larynx during the act of swallowing, thereby preventing the entrance of food into the trachea.

TRACHEA

- The lungs are paired organs located within the thorax.
- In general, the left and right lungs have two and four lobes, respectively. Trachea is the primary passageway of air to the lungs. It is located between larynx and bronchi.
- The tracheal wall contains cartilaginous rings to prevent collapse of the tracheal airway.
- Each tracheal ring is incomplete (not joined dorsally), which permits variations in diameter by the tracheal smooth muscle.
- The right and left bronchi and their subdivisions (bronchioles) continue all the way to the alveoli. The walls of the airways into the alveoli, particularly the bronchioles, create resistance to airflow.



- The larger the diameter of the airway,less the resistance to airflow. The diameter of the airways can be altered by the degree of contraction of the smooth muscle in these airways.

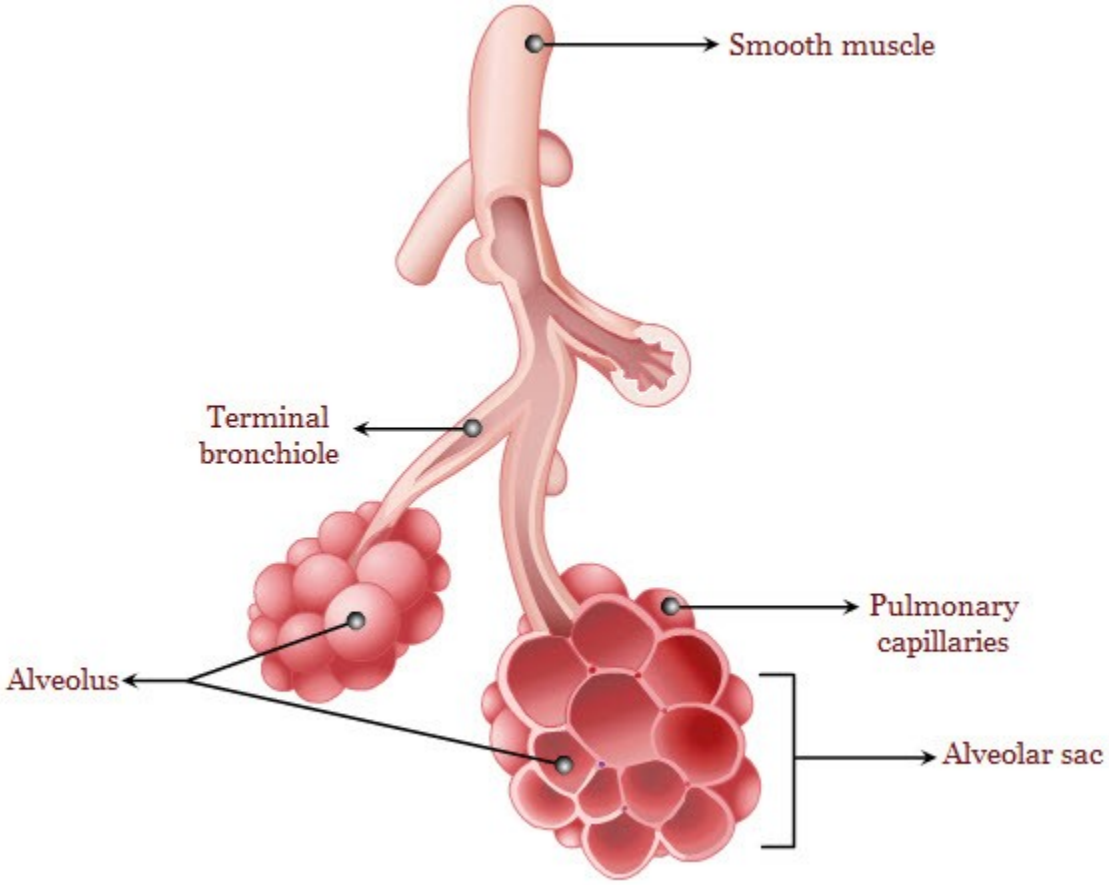
- Stimulation of the sympathetic nervous system causes relaxation of these walls, which allows air to more readily enter the lungs.
- The respiratory portion is the site of gas exchange between the air and blood and consists of the respiratory bronchioles, alveolar ducts, alveolar sacs, and alveoli. This extensive branching of the respiratory channels is called the bronchial tree.
- The alveoli are thin-walled sacs where gaseous exchange occurs.

PLEURAL MEMBRANES

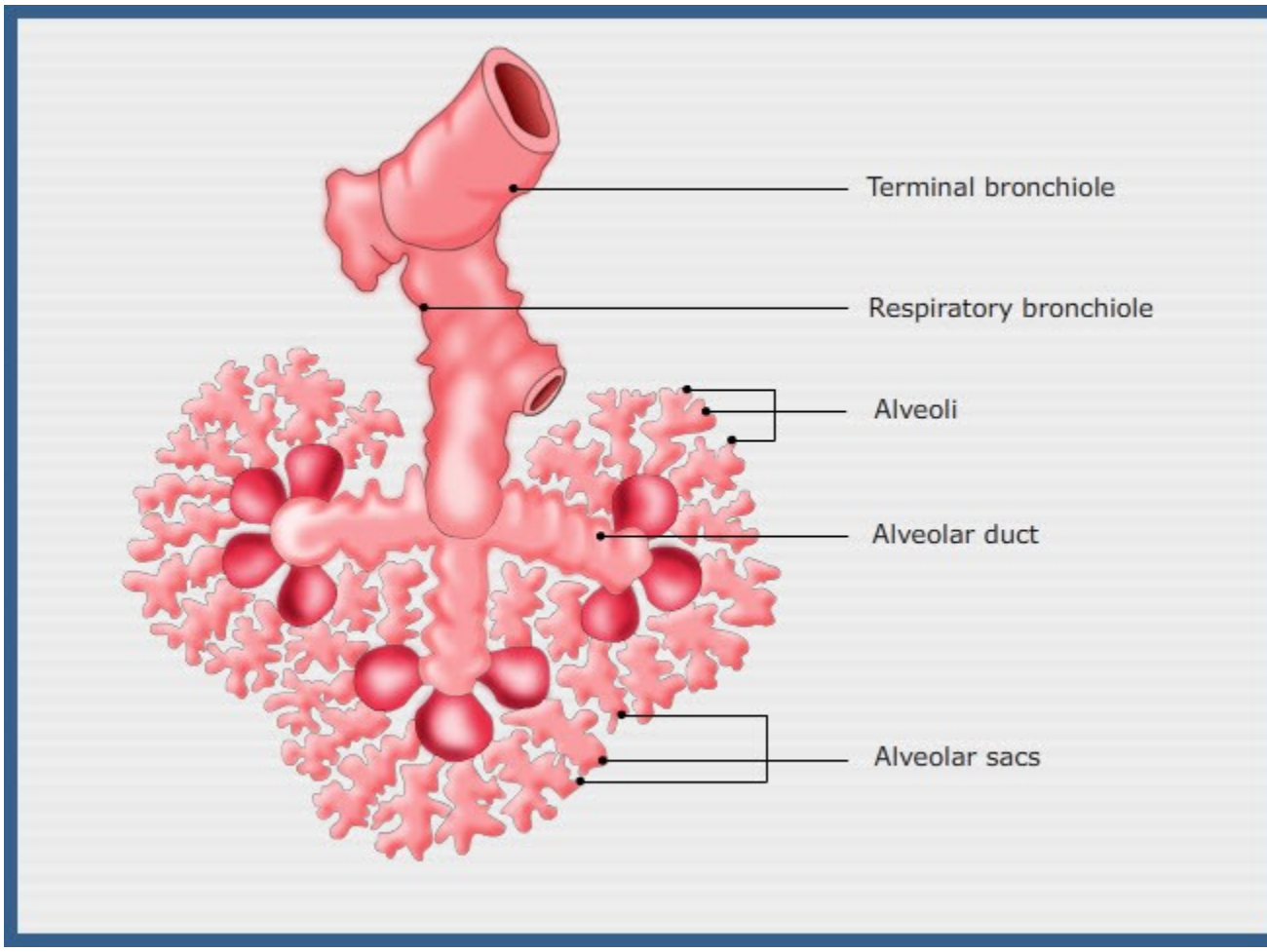
- The lungs are surrounded by a serous membrane called as pleural membrane. The superficial layer lining the thoracic cavity is the parietal pleura and the layer closely adhering to the lungs is the visceral pleura.
- The narrow parietal space between these two layers contains a small amount of pleural fluid that allows the two layers to slide over one another during breathing.
- The lungs have an almost friction-free movement within the thorax because of the pleura. Inflammation of the pleural membrane is called pleurisy.
- After the first breath, the lungs become less dense. If the lung floats in water, it indicates that the animal took at least one breath, and therefore was born alive. This fact allows one to determine whether a newborn animal is stillborn or not.
- The pressure inside the intrapleural space is negative due to continuous removal of fluid that is secreted . This negative pressure is vital for the expansion of the lungs.
- If an injury to the chest wall punctures the pleural membrane, it can allow air to enter the intrapleural space, resulting in a condition called as "pneumothorax".

ALVEOLUS

- The pulmonary alveoli are the principal sites of gas diffusion between the air and blood.
- The separation of air and blood, and thus the diffusion distance, is minimal at the alveolar level.



- The alveolar epithelium and the capillary endothelium are intimately associated. Different cells are seen, such as,
    - **Type I alveolar cells, predominant,which are simple squamous epithelium and the main site of gas exchange.**
    - **Type II alveolar (or septal) cells, cuboidal epithelial cells containing microvilli that secrete alveolar fluid containing surfactant.**
    - Alveolar macrophages remove debris from the lungs.
        - Fibroblasts produce elastic fibres.



RESPIRATORY MEMBRANE

- The respiratory membrane is where O_2 and CO_2 diffuse across the alveolar and capillary walls. It is a very thin membrane about 0.5 µm thick and consists of four layers. Exchange between alveoli and capillaries.

- Gas moving from alveolus to blood must pass through:
  - Thin layer of pulmonary surfactant
  - Alveolar epithelium : A layer of type I and type II alveolar cells, and alveolar macrophages.
  - The epithelial basement membrane.
  - The capillary basement membrane.
  - Capillary endothelium
  - Plasma
  - Red blood cell membrane
  - Red blood cell to reach hemoglobin
- The pulmonary artery carries deoxygenated blood, while oxygenated blood returns to the left atrium via the pulmonary veins. The darker purple color of venous blood becomes

bright red arterial blood during the saturation of hemoglobin with oxygen that has freshly diffused from the alveoli.

- During exercise, cardiac output can increase by as much as eightfold. During this time, blood flow to the lungs must increase. Pulmonary blood vessels dilate. In the horse, pulmonary arterial pressure can be so high as to cause erythrocytes to leak from pulmonary capillaries, a condition called as exercise-induced pulmonary hemorrhage, in athletic horses.
- Pulmonary ventilation
    - Respiration, the process of gaseous exchange, occurs in three steps:
        - Pulmonary ventilation, or breathing, is the mechanical movement of air into (inspiration) and out (expiration) of the lungs.
        - External respiration is the exchange of gases between the lungs and the pulmonary capillaries, which occurs across the respiratory membrane. The blood gains O_2 and loses CO_2.
        - Internal respiration is the exchange of gases between systemic capillaries and tissue. The blood gains CO_2 and loses O_2.

PULMONARY VOLUMES AND CAPACITIES

- Pulmonary volumes and capacities are recorded by Spirometer.The recordings are known as Spirogram. It shows the following:
    - *Tidal Volume (VT)* - the volume of air entering or leaving the nose or mouth per breath. It accounts 70% of the total lung capacity. If an animal inhales more forcefully, it can increase the volume of air entering the lungs above normal tidal volume.
    - *Inspiratory Reserve Volume (IRV)* - the volume of gas inhaled into the lungs during a maximal forced inspiration starting at the end of a normal tidal inspiration.
    - *Residual Volume (RV)* - the volume of gas left in the lungs after a maximal forced expiration. Determined by the force generated by the muscles of expiration and the inward elastic recoil of the lungs as they oppose the outward elastic recoil of the chest wall. Dynamic compression of the airways during the forced expiratory effort is also an important determinant of the residual volume - as airway collapse occurs gas is trapped in the alveoli.
    - *Total Lung Capacity (TLC)* - the volume of air in the lungs after a maximal inspiratory effort. Determined by the strength of contraction of the inspiratory muscles in opposition to the inward elastic recoil of the lungs and chest wall.
    - *Inspiratory Capacity (IC)* - the volume of air inhaled into the lungs during a maximal inspiratory effort that begins at the end of a normal tidal expiration.
    - *Functional Residual Capacity (FRC)* - the volume of gas remaining in the lungs at the end of a normal tidal expiration. Balance point between the inward elastic recoil of the lungs and the outward elastic recoil of the chest wall.
    - *Vital Capacity (VC)* - the volume of air expelled from the lungs during a maximal forced expiration starting after a maximal forced inspiration. About 4.5 liters.
    - *Expiratory Reserve Volume (ERV)* - the volume of gas expelled from the lungs during a maximal forced expiration that starts at the end of normal tidal expiration.

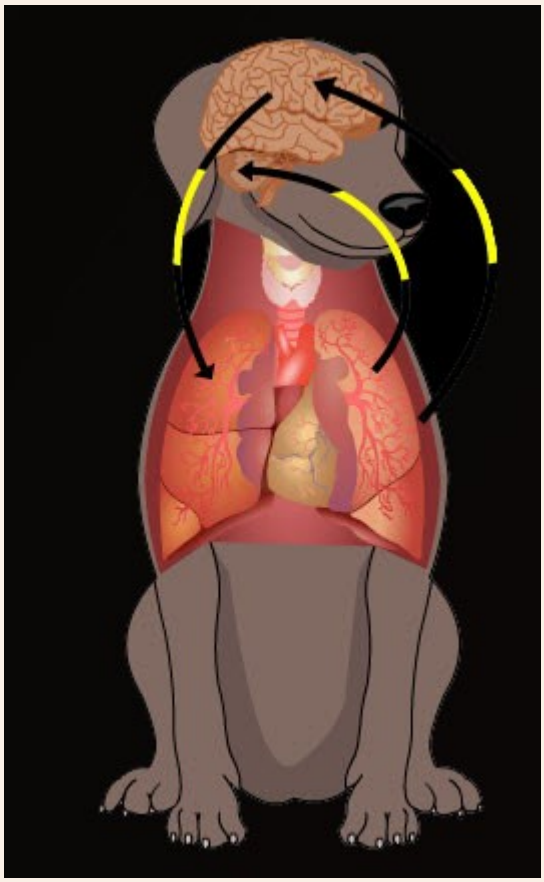
GAS LAWS

- Avogadro's hypothesis

    - Equal volumes of different gases at equal temperature contain the same number of molecules.
    - Equal numbers of molecules in the same volumes at the same temperature will exert the same pressure. (One mole of any gas will contain $6.02x10^{23}$ molecules and will occupy a volume of 22.4 L at a temperature of 0°C and a pressure of 760 mmHg.)
- Dalton's law
    - In a gas mixture, the pressure exerted by each individual gas in a space is independent of the pressures of other gases in the mixture.
    - e.g. $PAl_v = PH_2O + PO_2 + PCO_2 + PN_2$
      Partial Pressure of O_2= $\%O_2$ content X Total partial pressure
- Boyle's Law: $P_1V_1 = P_2V_2$ (at constant temperature)ie at constant temperature pressure of the gas varies inversly with its volume.
- Charles' law or Gay-Lussac's Law
    - $V_1/V_2=T_1/T_2$
    - $P_1/P_2=T_1/T_2$
    - ie at constant pressure the volume of given mass of the gas increases by 1/273 of its volume at zero degree rise in temperature.
- Henry's Law
    - The weight of a gas absorbed by a liquid with which it does not combine chemically is directly proportional to the pressure of the gas to which the liquid is exposed (and its solubility in the liquid).
- Graham's Law
    - The rate of diffusion of a gas (through the gas phase) is inversely proportional to the square root of its molecular weight.
- Diffusion
    - All gas moves across the blood-gas interface by passive diffusion; that is, net movement is from an area of high partial pressure to low.
- Diffusion of O_2 and CO_2 obey Fick's Law
    - Rate of diffusion or flow of a gas is directly propotional to
      $A \times D \times (P_1-P_2)/T$
    - where: A = area , T = thickness, D = diffusivity, P_1-P_2 = partial pressure gradient
    - The volume of gas per unit of time moving across a tissue sheet is directly proportional to the surface area of the sheet, the diffusibility, and the difference in gas concentration between the two sides, but is inversely proportional to the tissue thickness.
    - The surface area is in several square meters depends upon size of the lung. The thickness is generally ½ micron. This large surface area and small thickness are excellent for diffusion.
- Diffusivity or Diffusion constant
    - D = Solubility / Squreroot of Mol.Wt.
    - CO_2 diffuses about 20% slower because of its molecular weight but 24 times faster due to its greater solubility. Therefore the diffusivity of CO_2 is about 20 times that of O_2.
- Dalton's law
    - Dalton's law states that each gas within a mixture exerts its own pressure independent of the other gases present.,
    - Atmospheric air is a combination of nitrogen (N_2),oxygen (O_2), carbon dioxide (CO_2), and water vapor. At sea level, atmospheric pressure is 760 mmHg.

    - Atmospheric air is 78.6% nitrogen, 20.9% oxygen, 0.04% carbon dioxide, 0.06% other gases, and varying water vapor, depending on the humidity. PH_2O presence would cause a dilution of the other gases, and thus their partial pressures would be lowered to maintain the total pressure at 760 mm Hg. The ventilation process does not evacuate the alveoli completely with each breath, but rather it is a gradual replenishment and evacuation
- The approximate composition of alveolar air can be
    - PO_2 = 104 mm Hg
    - PCO_2 = 40 mm Hg
    - PN_2 = 569 mm Hg
    - PH_2O = 47 mm Hg
    - **Total = 760 mmHg**
- All **the components are diluted by water vapor, which is equal to 47 mm Hg in the alveolar air. PH_2O = 47 mm Hg represents 100% humidification of alveolar air at body temperature**.
- The PO_2 is lower and the PCO_2 is higher than their respective atmospheric pressures because oxygen is continually diffusing from alveolar air to the tissues (where it is used) and CO_2 is continually diffusing from the tissues (where it is produced) to the alveolar air (where it is expelled).
- The PN_2 of alveolar air is lower than its value in atmospheric air primarily because of its dilution by water vapor.
- Altitude - air pressure at 10,000 ft = 563 mm Hg
- Scuba diving - air pressure at 100 ft = 3000 mm Hg
- Henry's law
    - Henry's law states that the quantity of a gas that will dissolve in a liquid is proportional to its partial pressure and its solubility coefficient.
    - Gases will dissolve in body fluids more readily if they have a greater partial pressure and solubility coefficient.
    - The solubility coefficient of CO_2 is 24 times higher than that of O_2. Therefore, CO_2 dissolves in blood more readily than O_2.
    - In contrast, the solubility of nitrogen is very low, so even though atmospheric air has 79% N2, it has no effect on body functions.

MODULE-35: MECHANISM OF RESPIRATION AND EXCHANGE OF GASES



LEARNING OBJECTIVES

- This module explains,
  - inspiration and expiration mechanics ,
  - basic physics prevailing possibility of lung expansion,
  - respiratory passage and its resistance,
  - pulmonary blood flow,
  - vasculr resistance,
  - pulmonary frequencies,
  - physology of ventilation,
  - importance of dead space and
  - physiology of gas exchange.

MECHANISM OF RESPIRATION

- Boyle's law states that at constant temperature and pressure, there is an inverse relationship between volume and pressure of a gas:
  - $P_1V_1 = P_2V_2$
  - where P is the pressure of the gas (mm of Hg), and V is the volume of gas (ml).
- Therefore, the pressure inside a closed container will decrease as the volume of the container increases, and vice versa.
- When this law is applied to the lungs, the pressure inside the lungs decreases as the volume of the lungs increases.
- Air moves into the lungs as a result of a decrease in air pressure within the lungs.
- In most animals, inspiration is an active process.

- **The main muscles responsible for quiet inhalation are the diaphragm and external intercoastal muscles.** The diaphragm is a dome-shaped muscle innervated by the phrenic nerves.
- As the diaphragm contracts, it increases the horizontal dimensions of the thoracic cavity, thus increasing the volume of the thorax.
- Diaphragmatic contraction enlarges the thorax in a caudal direction, and intercoastals muscle contraction enlarges the thorax in a craniad and outward direction. This causes the volume of the lungs to expand and thereby decreases the pressure inside the lungs. This results in inspiration.
- Contraction of the external intercoastals muscles causes the ribs to move cranially and ventrally, thus increasing the diameter of the thorax. This accounts for about 25% of the entry of air into the lungs.
- In a horse at rest, the intrapleural pressure is negative, about 754 mmHg. As inspiration begins, this pressure drops to approximately 744 mmHg.
- Atmospheric pressure is 760 mmHg at sea level. As the volume of the thoracic cavity increases during inspiration, the parietal pleura is pulled outward, and the visceral pleura is pulled with it. As a result, the pressure inside the lungs, (the alveolar pressure) decreases. Air then flows from an area of high pressure (the atmosphere) to an area of lower pressure (the alveoli).
- As an animal increases the force of inspiration, additional muscles are engaged. These include the sternocleidomastoid muscles that move the sternum rostrally, the scalene muscles that pull the first two ribs forward, and the pectoralis minor muscles that pull several other ribs forward.

EXPIRATION

- Normal expiration is a passive process involving no active muscle contraction. Like inspiration, it is due to pressure gradients, but in an opposite direction. Because of the elastic recoil of the lungs and chest wall, there are two inwardly directed forces resulting 1) the elastic fibers that were stretched during inhalation, and 2) the inwardly directed force due to the surface tension arising from the alveolar fluid.
- As the neural signals to the diaphragm cease, it relaxes and this dome-shaped muscle moves rostrally, thus decreasing the volume of the thoracic cavity.
- The external intercostals also relax, and allow the ribs to move dorsally and caudally, thus further decreasing the volume of the thoracic cavity. This decreases lung volume and causes alveolar pressure to increase approximately 2 mmHg above atmospheric pressure. As a result, air flows out of the lungs to an area of lower pressure.
- **During forceful exhalation, the abdominal and internal intercostals muscles** contract. This causes the ribs to move caudally and dorsally compressing the abdominal viscera and decreasing the thoracic volume. This increases pressure inside the thoracic cavity and forces air outward.

TYPES OF BREATHING

- There are two types of breathing: *abdominal* and *coastal.*
    - *Abdominal breathing* is characterized by visible movements of the abdomen, Normally in animals the abdominal type of breathing predominates.
    - The *coastal breathing* is characterized by pronounced rib movements. During painful conditions of the abdomen, such as peritonitis, in which movement of the viscera would aggravate the pain, coastal breathing can predominate. Similarly, during painful conditions of the thorax, such as pleuritis, abdominal breathing will be more apparent.
- Eupnea is the normal quiet breathing, with no deviation in frequency or depth.

- Dyspnea is difficult breathing, in which visible effort is required to breathe. The animal is conscious of this state.
- Hyperpnea refers to breathing characterized by increased depth, frequency, or both after severe exercise. The animal is not actually conscious of this state.
- Polypnea is rapid, shallow breathing, similar to panting. Polypnea is similar to hyperpnea in frequency, but not in depth.
- Apnea refers to a cessation of breathing.

SURFACE TENSION OF ALVEOLAR FLUID AIDS IN EXPIRATION

- Alveolar fluid coats the inside surface of the alveoli. The surface tension produces an inwardly directed force causing the alveoli to assume the smallest possible diameter.
- In order to expand the lungs, this surface tension must be exceeded. This surface tension accounts for approximately two thirds of the lung's elastic recoil.
- Surfactant, produced by type II alveolar cells, is a complex of lipids and proteins that reduces the surface tension in much the same way the soap allows lipids to dissolve in aqueous solutions.
- Surfactant decreases surface tension which increases pulmonary compliance (reducing the effort needed to expand the lungs) reduces tendency for alveoli to collapse.
- Since surfactant is one of the last compounds produced during embryonic development, premature animals often have respiratory distress as a result of the underdeveloped respiratory system.
- In the case of sheep, surfactant is released into the alveolar spaces near the beginning of the fourth month of gestation. Its release correlates with a rise in plasma cortisol levels.

COMPLIANCE OF LUNGS

- The distensibility of the lungs is referred to as lung compliance. High lung compliance means that the lungs will expand easily.
- Compliance is seen decreased
    - pulmonary edema resulting from accumulation of fluid in the lungs
    - insufficient of surfactant.

RESPIRATORY FREQUENCY

- Respiratory frequency refers to the number of respiratory cycles each minute.
- It is an excellent indicator of health status, respiratory frequency can be affected by other factors, such as:
    - body size,
    - age,
    - exercise,
    - excitement,
    - environmental temperature,
    - pregnancy, and
    - breed.
- Pregnancy and digestive tract filling increase frequency because they limit the movement of the diaphragm during inspiration.

- When expansion of the lungs is restricted, adequate ventilation is maintained by increased frequency. Thus when cattle lie down, the large rumen pushes against the diaphragm and restricts its movement, and the respiratory frequency is seen to increase.
- It indicates the number of breaths per minute during normal quiet respiratory activity.
- Rate of respiration varies with age, sex, body size, exercise, external environmental temperature pregnancy, fullness of digestive tract, rumination, etc. Pregnancy and fullness of the GI tract increases the frequency because they limit the movement of diaphragm during inspiration.
- Frequency also increases as the environmental temperature rises, to help in the thermoregulation.

Respiratory rate of different animals

Horse	10 – 14 / min (12)
Pig	32 – 58 (40)
Cattle	26 – 35 / min. (29)
Dog	20 – 34 (24)
Fowls	15 – 30 / min
Man	12 – 20
Cat	20 – 40 / min
Rat	97 / min
Sheep & Goat	20 – 34 / min (25)

ARTIFICIAL RESPIRATION

- Artificial respiration is resorted to in cases of
  - cessation of respiration while under general anaesthesia
  - drowning where the animal has been rescued from water – mainly applicable for small animals;
  - poisoning by narcotics or paralytic substances
  - asphyxia from fumes, smoke, gases etc.

Method of administration

In large animals

- The animal is released from all restraints, head and neck are extended to allow a straight passage of air into the lungs and the tongue is pulled out. The elastic ribs are compressed by alternately leaning the whole weight of the body of a person on the hands kept pressed on the ribs and then releasing the pressure about once every 4 or 5 seconds, for the purpose of stimulating normal movements of breathing. As an alternative, a heavy person may sit himself with some vigour astride the ribs for about 4 or 5 seconds, rise for a similar period and then reseat himself.

- Inhalation of strong of ammonia upon a piece of cotton and held about a foot from the upper nostrils assists in inducing a gasp, which is sign of returning of respiration. The animal is turned on its sides every 2 or 3 minutes to prevent stasis of blood. As long as the heard continues to beat, attempts at resuscitation should be pursued. Resuscitators or mechanical ventilators are useful to give artificial respiration. For pigs and sheep, the same procedures can be applied.

Dogs and cat

- Mouth-to-mouth or mouth-to-nose ventilation, which uses exhaled air to provide 16% O 2 can be used for artificial ventilation. The preferred technique is use of endotracheal intubation and providing ventilation with an anesthetic machine or mechanical ventilator.
- In another technique, the animal is laid on its side with the head at a lower level than the rest of the body. The palm of a hand is placed flat over the upper side of the abdomen and the other hand is placed on the rib cage, weight is placed on the hands for a second or two and then the pressure is released. The motions of artificial respiration should be faster than normal respiration, but a slight pause should always be observed before each rhythmic movement.

Resuscitators

- A frequently used resuscitator consists of mechanism for applying intermittent positive pressure and a facemask or a connector to connect the equipment with endotracheal tube. These apparatus forces air through the mask into the lungs during positive pressure cycle an allow air to flow passively out of lungs during the remaining periods.
- For controlled positive pressure ventilation, either orotracheal intubation or tracheotomy is indicated. The technique is used in comatose, anaesthetized or sedated animals

RESPIRATORY PASSAGEWAY RESISTANCE

- *Upper respiratory passageways* - relatively large, very little resistance to airflow (unless obstruction such as from food lodging or cancer)
- *Lower respiratory passageways* - from medium-sized bronchioles on down, can alter diameter based on autonomic stimulation
- *Parasympathetic* - causes bronchioconstriction
- Sympathetic - inhibits bronchioconstriction
- *Epinephrine* - used to treat life-threatening bronchioconstriction such as during asthma and anaphylactic shock.

PULMONARY BLOOD FLOW

- Dual circulation of the lung
    - Bronchial circulation - arterial supply of tracheobronchial tree (as far as the terminal bronchioles), and other thoracic structures. About 2% of cardiac output.
    - Pulmonary circulation - site of gas exchange between alveolar air and capillary blood. Mixed venous blood in pulmonary artery.
- Main pulmonary artery is much thinner-walled than the aorta. Much less smooth muscle in the walls of the vessels of the pulmonary arterial tree. No highly muscular arteriole.
- As a result low resistance to pulmonary blood flow. Pulmonary vascular resistance (PVR) is about 1/10 of systemic vascular resistance.
- Pulmonary vessels are more distensible than systemic vessels. Blood at a time seen about 30% arteries, 40% capillaries; 30% veins. This can change with lung inflation or during hypoxia.

- Pulmonary capillaries in the adult:280 billion capillaries supply 300 million alveoli with 50-100 m^2 surface area. Diffusion distance normally less than 0.5 micron.

PULMONARY VASCULAR RESISTANCE

- Although pulmonary vascular resistance is very low at rest, it can decrease further, as in exercise, during which blood flow increases. Neural : Sympathetic nerves to larger vessels - NE released.
- Effects somewhat controversial - most likely increases pulmonary vascular resistance and decreases distensibility of larger vessels. Parasympathetic - Ach decreases PVR if tone elevated.
- Humoral : Increase PVR: Norepinephrine, alpha adrenergic agonists, serotonin, prostaglandins F_2 and E_2, angiotensin, endothelin, alveolar hypoxia (hypoxic pulmonary vasoconstriction), alveolar hypercapnia, low pH of mixed venous blood.
- Histamine constricts pulmonary veins. Decrease PVR: Acetylcholine, beta adrenergic agonists, bradykinin, prostaglandin E_1 and I_2 (prostacyclin), nitric oxide.

ALVEOLAR GAS EXCHANGE

- Usually, gas pressure is considered in terms of total pressure, regardless of whether it is a single gas or a mixture of gases. However each gas in the mixture separately contributes to the total pressure.
- It is defined as the pressure exerted by a particular gas in a mixture of gases. The sum of the partial pressures of the gases within a mixture equals the total pressure.
- Because oxygen is consumed and carbondioxide is produced by cells, the venous blood will have a high PCO_2 and a lower PO_2 and vice-versa for arterial blood.
- A more active location would consume more O_2 and produce more CO_2 than less active locations. Because of these differences, the jugular vein blood may not be representative of whole body venous blood (i.e., blood from the right atrium).
- Gases diffuse from an area of their higher concentration to an area of their lower concentration.
- Two gas laws are applicable to gas exchange .
- Dalton's law explains how gases move by diffusion based on pressure differences while Henry's law describes the diffusion of gas based on its solubility.

EXTERNAL AND INTERNAL RESPIRATION

- External respiration, also called pulmonary gas exchange, is the diffusion of O_2 and CO_2 from the alveoli to pulmonary blood. Blood circulating through the body picks up $CO_2$and delivers O_2. As this blood travels through the pulmonary capillaries, CO_2 diffuses into the alveoli while O_2 diffuses from the alveoli to pulmonary blood. The exchange of these gases occurs independently and passively.
- Pulmonary gas exchange is facilitated by a very thin respiratory membrane.
- Ventilation is generally regarded as the process by which gas in closed places is renewed or exchanged. As it applies to the lungs, it is a process of exchanging the gas in the airways and alveoli with gas from the environment. The main function of breathing is to provide gas for ventilation.
- In addition, there is a close association between the amount of gas reaching the alveoli (ventilation), and the blood flow through the pulmonary capillaries (perfusion).

- Internal respiration, or systemic gas exchange, occurs at the tissue level, where there is an exchange of O_2 and CO_2 between systemic capillaries and tissue. O_2 diffuses from the capillaries into the cells; CO_2 diffuses from the cells into the systemic capillaries.

VENTILATION-PERFUSION RELATIONSHIPS (V/Q)

- For optimal gas transfer to occur in the lung, ventilation and perfusion must be matched. In man for the whole lung, alveolar ventilation and pulmonary blood flow are both about 5 L/min. Therefore, for the whole lung V/Q is about 0.8 - 1.2. Local airway responses and hypoxic pulmonary vasoconstriction help match ventilation and perfusion.
- Low Oxygen in alveolus→ vasoconstriction
- High Oxygen in alveolus→ vasodilation
- High CO_2 in alveolus→ dilate bronchioles
- Low CO_2 in alveolus → constrict bronchioles

DEAD SPACE VENTILATION

- The tidal volume is used to ventilate not only the alveoli, but also the airways leading to the alveoli. Because there is little or no diffusion of oxygen and carbon dioxide through the membranes of most of the airways, they compose part of dead space.
- The other part of dead space ventilation is made up of alveoli with diminished capillary perfusion.
- Ventilating these alveoli is ineffective in producing changes in the blood gases. Ventilation of nonperfused alveoli and the airways, because neither accomplishes exchange of the respiratory gases. is referred to as physiologic dead space.
- Physiologic dead space is defined as the volume of gas that is inspired but takes no part in gas exchange in the airways and alveoli. **Therefore, the tidal volume has a dead space component and an alveolar component.**
- More ventilation of lower (with respect to gravity) regions of the lung than upper regions of the lung. Intrapleural (intrathoracic) pressure is less negative at the bottom of the lung than at the top because of the weight of the lung and the configuration of the chest wall.
- Therefore the transpulmonary pressure gradient is greater at the top of the lung than at the bottom.
- Therefore the alveoli at the top of the lung are at a higher, less compliant point on the pressure-volume curve than those at the bottom.
- Therefore the alveoli at the bottom of the lung increase their volume more with each inspiration and decrease their volume more with each expiration during eupnea (from FRC).
- Dead space ventilation is a necessary part of the process of ventilating the alveoli and is not totally wasted. It assists in humidifying inhaled air and in cooling the body under certain conditions, such as when panting is necessary.
- During panting, the respiratory frequency increases and the tidal volume decrease so that alveolar ventilation remains approximately constant.

PHYSIOLOGY OF GAS EXCHANGE

- Ventilation brings O_2 to the alveoli and removes CO_2. Because O_2 is being consumed in the tissues, a pressure difference exists for its diffusion from alveoli to venous blood (which then becomes arterial) and from arterial blood to the tissues. Because CO_2 is being produced in the tissues, a pressure difference exists for its diffusion from tissue to

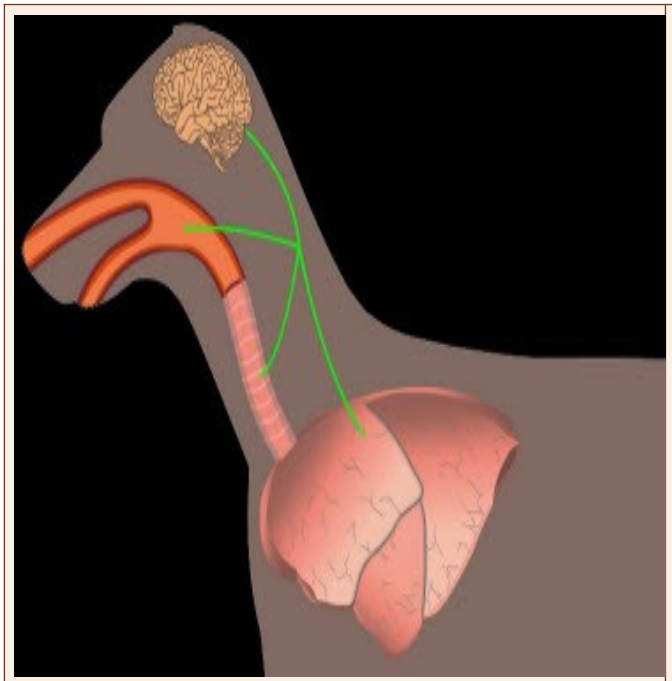
arterial blood (which then becomes venous) and from venous blood to the alveoli. **(Animation831-After title correction)**

Gases	Venous Blood	Alveolar Air	Arterial Blood	Tissues
O_2	40	104	100	30 or less
CO_2	45	40	40	50 or more
N_2	569	569	569	569
Water vapor	47	47	47	47
Total	701	760	756	696

Values are in mm of Hg

- The total pressure in venous blood is somewhat less than atmospheric pressure because the volume of CO_2 produced is lower than the volume of O_2 consumed.
- As because not all of the blood going to the lungs is arterialized (nonperfused alveoli) the difference in PO_2 exists.

MODULE-36: CONTROL OF RESPIRATION



LEARNING OBJECTIVES

- This module helps to gain knowledge on
  - regulation of respiration,
  - means of regulation,
  - structures associated,
  - mechanical factors assisting the regulation and
  - hormonal

	participation.

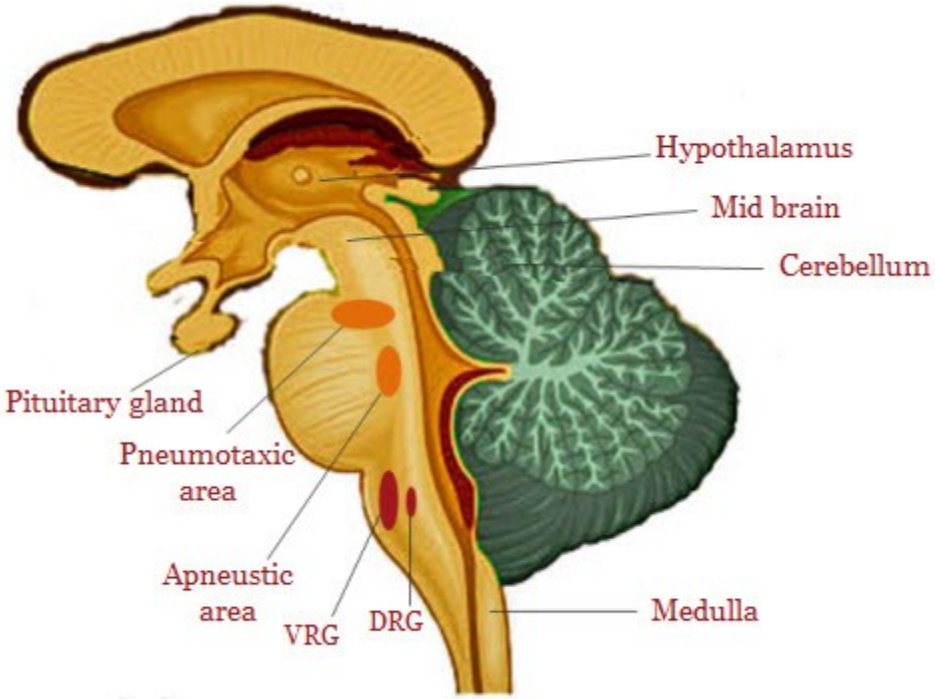
NEURAL CONTROL

- Pulmonary ventilation is regulated closely to maintain the concentrations of H^+, CO_2, and O_2 at relatively constant levels while meeting the needs of the body under varying conditions.
- If either the H^+ or the CO_2 concentration increases or if the O_2 concentration decreases, their levels will be returned to normal by increasing ventilation.
- Conversely, if either the H^+ or CO_2 concentration decreases or if the O_2 concentration increases, pulmonary ventilation will be decreased. This regulatory mechanism is controlled by changes in tidal volume, frequency of respiratory cycles, or both.

Last modified: Saturday, 4 June 2011

RESPIRATORY CENTRES

- The central mediator of these changes is the respiratory center in the brain stem which has four specific regions .
- The medullary rhythmicity area is located in the medulla oblongata, and it controls the basic respiration rhythm.
- It consists of two areas, the inspiratory and expiratory areas, also called the dorsal respiratory group and ventral respiratory group, respectively.
    - *Dorsal respiratory group:* group of neurons predominately associated with inspiratory activity (lung inflation and termination of inspiration).
    - *Ventral respiratory group:* group of neurons containing inspiratory and expiratory neurons (assist in inspiration begun by those in the dorsal respiratory group and also assists expiration).
- The respiratory center is gray matter in the pons and the upper medulla, is very sensitive to the PCO2 in the arteries and to the pH level of the blood.



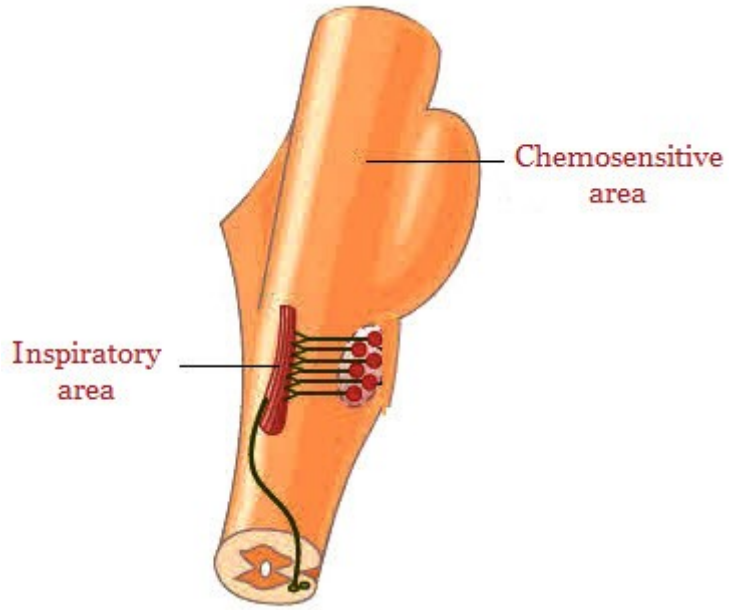
- The CO_2 can be brought back to the lungs in three different ways; dissolved in plasma, as carboxyhaemoglobin, or as carbonic acid. That particular form of acid is almost broken down immediately by carbonic anhydrase into bicarbonate and hydrogen ions. This process is then reversed in the lungs so that water and carbon dioxide are exhaled.
- The medulla oblongata reacts to both CO_2 and pH levels which triggers the breathing process so that more oxygen can enter the body to replace the oxygen that has been utilized.
- The medulla oblongata sends neural impulses down through the spinal chord and into the diaphragm.
- There are two other ways the Medulla Oblongata can be stimulated.
    - The first type is when there is an oxygen debt (lack of oxygen reaching the muscles), and this produces lactic acid which lowers the pH level. The medulla oblongata is then stimulated.
    - The second type occurs when the major arteries in the body called the aortic and carotid bodies, sense a lack of oxygen within the blood and they send messages to the medulla oblongata.
- The inspiratory area sends signals to the diaphragm via the phrenic nerve and to the external intercostal muscles via the intercostal nerves. These signals cause muscle contraction resulting in inspirations. When these signals cease, inspiration is concluded, which allows the diaphragm and external intercostal muscles to passively relax, during which time the elastic recoil of the lungs and thoracic walls causes the volume of the thoracic cavity to decrease.
- Transection between the spinal cord and medulla oblongata stops breathing.
- Although not active during quiet breathing, forceful expiration requires signals from the expiratory area that cause contraction of the internal intercostals and abdominal muscles.
- Contraction of these muscles further decreases the volume of the thoracic cavity, thus increasing exhalation.

PNEUMOTAXIC AND APNEUSTIC AREA

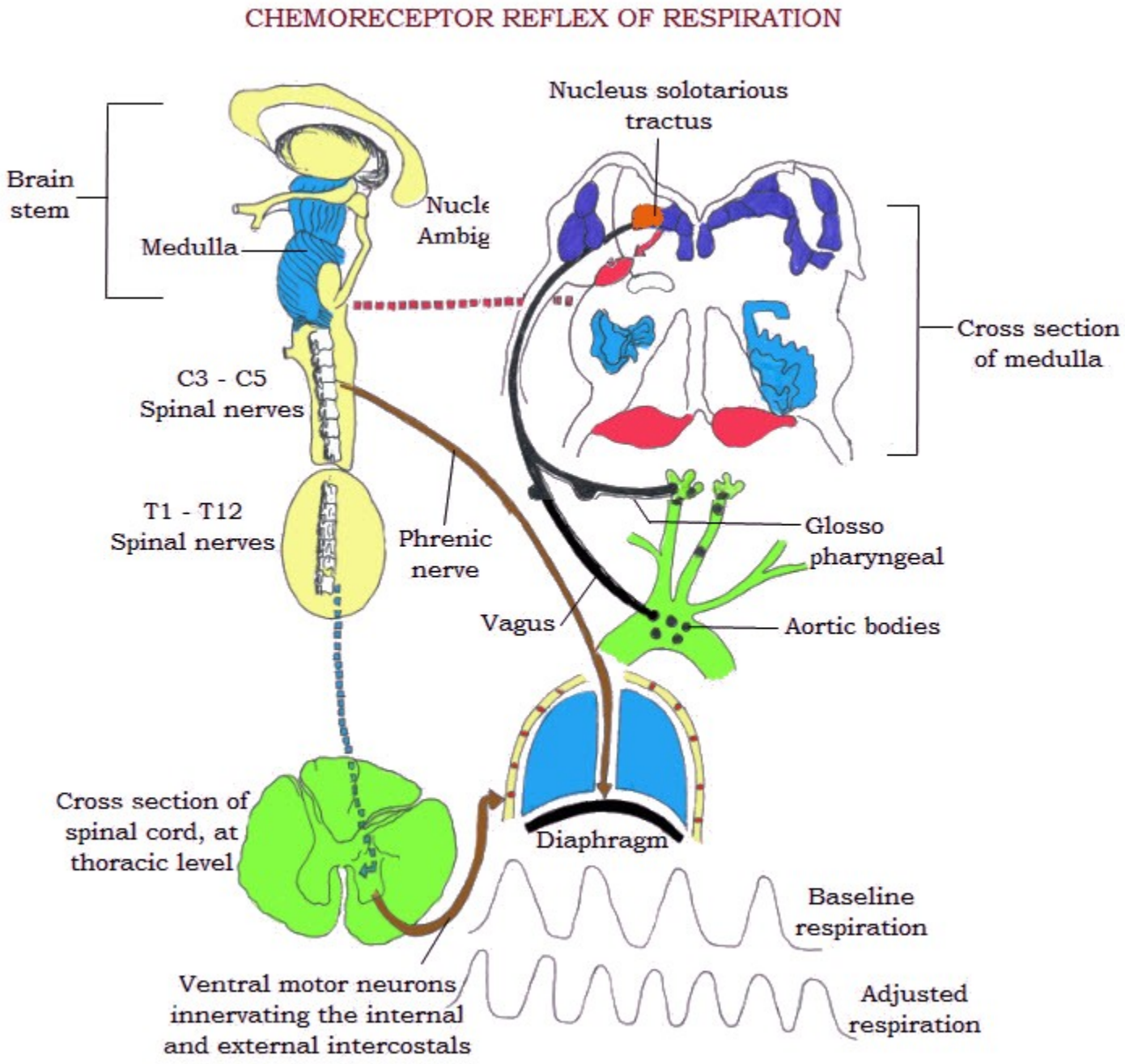
- Pneumotaxic centre believed to modulate respiratory center sensitivity to inputs that activate termination of inspiration and facilitate expiration .
- **Apneustic centre believed to be associated with deep inspirations.**
- The **pneumotaxic area, also called the pontine respiratory group**, sends inhibitory signals to the inspiratory area. These signals primarily function to prevent overfilling of the lungs.
- Conversely, the apneustic area **located in the lower pons** sends stimulatory signals to the inspiratory area that prolongs inspiration.
- The pneumotaxic area can override the apneustic area. Impulses going to the respiratory center (afferent impulses) from several receptor sources have been identified. Importantly the Hering-Breuer reflexes.

HERING - BREUER REFLEX

- The receptors for these reflexes are located in the lungs, particularly in the bronchi and bronchioles.
- The nerve impulses generated by these receptors are transmitted by fibers in the vagus nerves to the respiratory center.
- The effect of inflation-receptor stimulation is to inhibit further inspiration (stimulation of neurons in the dorsal respiratory group) and to stimulate expiratory neurons in the ventral respiratory group. However the tidal volume can be increased by a person with the modulation of pneumotaxic centre.
- There are other peripherally located receptors that modify the basic rhythm. Stimulation of receptors in the skin are excitatory to the respiratory center, and deeper than usual inspiration can be noted.
- Their excitation to the inspiratory area is through the apneustic area because inspiratory gasps are noted. Advantage is taken of these receptors when breathing stimulation is desired in newborn animals.



- Rubbing the skin with a rough cloth often initiates the breathing cycles. Several respiratory reflexes originate from receptors in the upper air passages.
- Stimulation of the mucous membranes in these regions causes reflex inhibition of breathing. Eg: inhibition of breathing that occurs during swallowing; also, in diving birds and mammals, there is a reflex inhibition of breathing when they submerge.



- Stimulation of the laryngeal mucous membrane in the unanaesthetized animal causes not only inhibition of breathing, but also usually powerful expiratory efforts (coughing and sneezing).
- Ordinary respirations proceed involuntarily. They can be altered voluntarily hastened, slowed, or stopped altogether, for a while. Phonation and abdominal pressure in the expulsive acts of defecation, urination, and parturition are examples of complete voluntary control of the respiratory movements.

- Afferent impulses from pressure receptors in the carotid and aortic sinuses have as their principal function a role in the regulation of circulation, but impulses from these receptors also go to the respiratory center.
- **The impulses are inhibitory in nature-the higher the blood pressure, the greater the inhibition to respiration. Because of the influence of inspiration on return of blood to the heart, it can be seen that the reduction in inspirations would slow down the return flow of blood to the heart and thus help to lower blood pressure**.

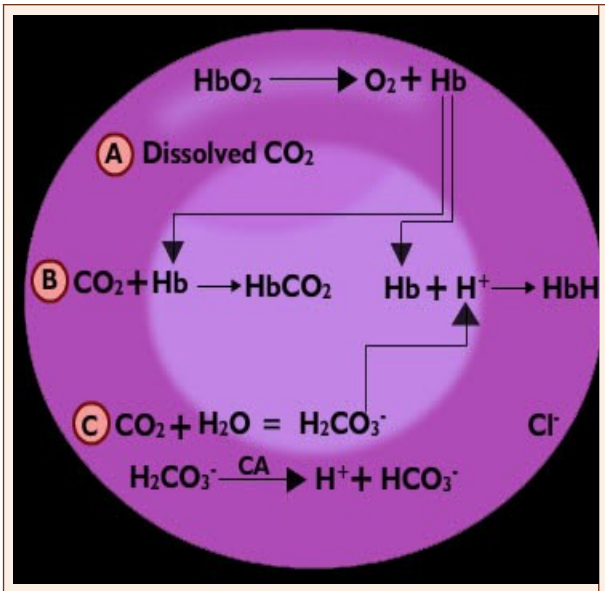
HUMORAL CONTROL

- Humoral control refers to those factors in the body fluids that influence ventilation like CO_2, O_2 and H^+ .
- Their concentrations in the blood affect alveolar ventilation in several ways:
    - Carbon dioxide increase causes alveolar ventilation to increase; its decrease causes alveolar ventilation to decrease.
    - H^+ increase causes alveolar ventilation to increase; its decrease causes alveolar ventilation to decrease.
    - Oxygen decrease causes alveolar ventila tion to increase; its increase causes alveolar ventilation to decrease.
- The respiratory system functions to bring in O_2 and eliminate CO_2 from the body. This function is assisted by specialized receptors called chemoreceptors that monitor the levels of CO_2, O_2 and H^+, and then send such information to the respiratory center.
- These chemoreceptors are located in several locations. There are central chemoreceptors found in the medulla oblongata that respond to changes in cerebrospinal fluid H^+ and PCO_2. Because of the much greater diffusibility of carbon dioxide, as compared with H^+, it is distributed more quickly from the blood to the interstitial fluid of the medulla and to the cerebrospinal fluid than hydrogen ions.
- The H^+ concentration of the interstitial fluid of the brain stem is the deciding stimulus for respiratory drive. The influence of CO_2 is exerted by its conversion to H^+ through the hydration reaction.
- Peripheral chemoreceptors include the aortic bodies and carotid bodies whose removal eliminates a respiratory response to hypoxia.
- The aortic bodies are a cluster of chemoreceptors in the aortic arch; the carotid bodies are oval nodules in the wall of the left and right common carotid arteries, where they bifurcate into the internal and external carotid arteries.
- Axons from the chemoreceptors in the aortic bodies are part of the vagus nerve (cranial nerve X), whereas those of the carotid bodies project in the glossopharyngeal nerves (cranial nerve IX).
- The levels of CO_2 and H^+ are highly correlated.
- Throughout the body, CO_2 is quickly converted to carbonic acid catalyzed by the enzyme carbonic anhydrase. Carbonic acid dissociates into HCo_3^- and H^+. Therefore, increase in PCO_2 lead to increases in H+ while decreases in CO_2 lead to decreases in H^+. As a result, has a large affect on respiration, whereas P O_2 affects respiration only if its levels change substantially.
- Increases in arterial blood CO_2, called hypercapnia, cause an increase in H^+. This has a particularly large effect on central chemoreceptors since there is little protein within the cerebrospinal fluid to buffer the H^+. Activation of the central chemoreceptors causes increased respiration rate, possibly causing hyperventilation. Conversely, low arterial blood CO_2, called hypocapnia, inhibits respiration. Large drops in arterial PO_2 increase ventilation by stimulating peripheral chemoreceptors.

INFLUENCES OF PO_2 IN VENTILATION RATE

- The influence of oxygen is transmitted from the carotid and aortic bodies to the respiratory center. The carotid and aortic body receptors also respond to carbon dioxide and hydrogen ion concentration, but the effectiveness of the carotid and aortic body response to carbon dioxide and hydrogen ions is far less than the response from the brain stem.
- Thus, the carotid and aortic bodies are considered to be the most influential for the regulation of oxygen. These bodies are distinct structures with an abundant blood supply located just outside the aortic arch, at the division of the carotid arteries. They respond to changes in the PO_2 (arterial) of blood.
- Blood with reduced amounts of hemoglobin, and consequently less oxygen, has the same PO_2 as blood with normal hemoglobin and oxygen, and thus no ventilation response would be elicited because there is no change in PO_2.
- In anemia ventilation might be increased, not because of less oxygen, but because of greater H+ concentration caused by reduced buffering associated with the hemoglobin decrease. In the case of carbon monoxide poisoning and lack of oxygen carried by hemoglobin, ventilation is not increased, not only because the PO2 is normal, but also because there is adequate hemoglobin present for buffering hydrogen ions.
- Arterial blood PO2 must be in the range of 30 to 60 mm Hg for the respiratory center to receive stimulation to ventilation from the carotid and aortic bodies. At this stage hemoglobin is still about 90% saturated with oxygen at a PO2 of 60 mm Hg.
- Also, the slowing effect of an increased arterial PO2 would not normally be observed in animals breathing atmospheric air because the arterial PO2 seldom increases above 100 mm Hg.
- The slowing is noted in anesthetized animals breathing an oxygen-enriched atmosphere, in which the arterial PO2 could increase to 350 to 400 mm Hg.
- The regulation of ventilation by oxygen is not ordinarily thought to be important. There is usually no problem in maintaining arterial blood PO2 in the range of 80 to 100 mm Hg, and it is not advantageous to have it higher than 100 mm Hg because hemoglobin is almost saturated at that partial pressure.
- Ventilation could even be reduced to about 50% of normal and hemoglobin still would be considerably saturated. The most important chemical factor in the regulation of ventilation is the concentration of carbon dioxide; relatively small changes can have an effect.
- The regulation of ventilation by oxygen becomes more important in such conditions as pneumonia and pulmonary edema, in which gases are not diffused as readily through the respiratory membrane.
- Decreased diffusion is more noticeable for oxygen than for carbon dioxide because of the smaller diffusion coefficient for oxygen. Hyperventilation caused by oxygen lack can therefore reduce the carbon dioxide concentration (because CO2 readily diffuses) and thus reduced formation of hydrogen ions , so that they become ineffective in stimulating increased ventilation.
- The oxygen deficiency mechanism (originating from the carotid and aortic bodies) continues to function and provides the drive to increase ventilation.

MODULE-37: TRANSPORT OF GASES



LEARNING OBJECTIVES

- This module explains to understand
  - various means of oxygen and corbondioxide transport,
  - their significance and
  - factors modifying their transport.

OXYGEN TRANSPORT

Oxygen is transported in blood in two forms :

- as physically dissolved O_2
- O_2 in combination with haemoglobin

PHYSICALLY DISSOLVED O_2

- The O_2 diffuses across the alveolar membrane and the lung capillary endothelium into the blood plasma where it is physically dissolved according to its solubility co-efficient and partial pressure.
- 0.003ml of O_2 is dissolved in 100ml plasma at a PO_2 of 1mmHg.
- At a PO_2 of 100mmHg, 0.31ml O_2 gets dissolved in each 100ml blood.

TRANSPORT OF O_2WITH HAEMOGLOBIN

- After entry into the blood plasma, most of the O_2 enters across the red cell membrane into the cell. The major portion of O_2 is carried by blood is not in physical solution but is associated with haemoglobin molecule inside the red cells.
- If plasma is exposed to an atmosphere of 100mm.Hg partial pressure of O_2 only 0.3ml of O_2 is taken up, But when blood is similarly allowed to equilibrate at an O_2 tension of 100mmHg, it can carry 19 – 20 ml of O_2/ 100ml of blood.
- Hb present within erythocytes does the extra uptake.
- Each Hb molecule contains 4 heme groups. Each heme molecule contains one Fe^{++} atom in a reduced state.
- Each molecule of Hb can combine with 4 molecules of O_2 depending on the relative concentration of Hb and O_2 in blood. When reduced Hb combines with O_2 it has been oxygenated then it is called Oxy – Hb.
- Oxygen binding with Hb is a four step process; the O_2 affinity of a particular heme is influenced by the oxygenation of other hemes in that haemoglobin molecule. These

heme-heme interactions are responsible for the sigmoid shape of the oxyhemoglobin curve.

- Greater the concentration of Hb in blood greater the amount of O_2 carrying capacity.
- At 150 mm Hg PO_2, the blood is nearly saturated.

OXY HEMOGLOBIN DISSOCIATION CURVE

- The Loading and unloading of O_2 ability of the Hb in the form of a graph referred as oxy – hemoglobin dissociation curve.
- This graph is obtained when the Hb is allowed to equilibrate with various PO_2 and the values of percentages of Hb saturation (X axis) against the PO_2 (Y axis), are plotted. For *oxy Hb* the curve is *"S" or sigmoid shaped* and for *myoglobin* the dissociation curve is *rectangular hyperbola* in shape.
- Under normal conditions, at a PO_2 of 100mm. Hg, blood leaving the lungs is 95 – 98% saturated with O_2. Further increase in PO_2 do not increase O_2 carrying capacity of blood but increase the amount of O_2 in physical solution according to Henry's law.
- One gram of Hb can transport 1.34 ml of O_2. The average hemoglobin concentration is 15 g/ 100 ml of blood. In atrial blood at a PO_2 of 100 mm.Hg, Hb is 97.5% saturated with O_2 and transport 15 x 1.34 x 97.5/100 = 19.6 ml / 100 ml or 19.6 volumes percent.
- 100 ml of blood carries 19.9 ml of O_2 of which 19.6 ml in combination with hemoglobin and remaining 0.3 ml in physical solution As the arterial blood reaches the tissue, O_2 is unloaded from the blood to tissues, the O_2 saturation falls to about 72% in venous blood.
- At 72% saturation of O_2, the blood will have 14.5 ml O_2. Hence each 100 ml blood unloads approximately 5 volume percent of O_2 to tissues. PO_2 of venous blood is 40 mm Hg.
- Shift of dissociation curve to right results is greater release of O_2 from oxy Hb due to decreased affinity of Hb to O_2. A shift to left increases the affinity of Hb to O_2 and decreases O_2 released from Hb. Variation occur in O_2 dissociation of foetus and adults.
- The extent of oxygen dissociation from the oxy hemoglobin dissociation curve is influences by.
    - PO_2
    - PCO_2
    - H^+ ion concentration
    - Temperature
    - Concentration of DPG (2 – 3 diphosphoglycerate) in erythrocytes.
- Increase in H^+ ion concentration and CO_2 level shifts the curve to down the right as also increase in temperature and 2 – 3 DPG. The 2-3 DPG level increases in hypoxia. Shifting the curve to down and right causes increase in release of O_2 from the Hb.
- The shift of oxy-Hb dissociation curve to down and right by increased CO_2 tension is termed as *Bohr's effect*. In tissues as O_2 is unloaded, CO_2 is simultaneously taken up by blood and this enhances unloading of O_2.

CARBON DIOXIDE TRANSPORT

- The CO_2 produced during metabolism is a waste product and has been eliminated. The flow of CO_2 is effected under a continuous pressure gradient.

Tissues	Venous blood	Alveolar air	Expired air	Atmospheric air
50 mm Hg	46 mm Hg	40 mm Hg	32 mm Hg	0.3 mm Hg

- The transport of CO_2 is effected in the following ways.
    - As physically dissolved CO_2

- Transport in chemical combination

PHYSICALLY DISSOLVED CO_2

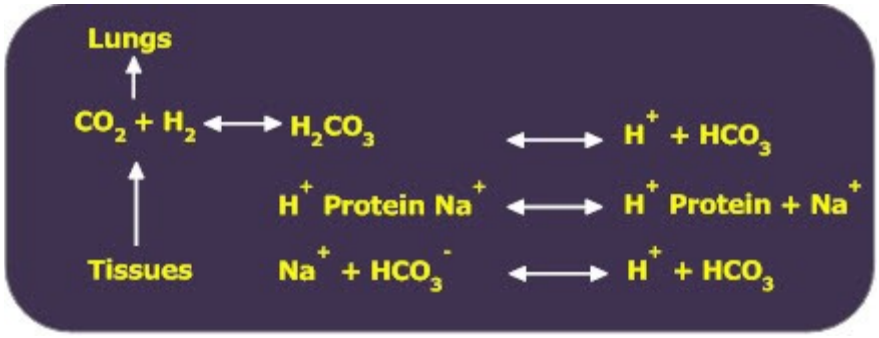
- Compared with O_2, CO_2 is 24 times more soluble in blood plasma. Only about 5 – 7 % of total CO_2 carried by blood is in a simple physical solution.
- The factors that determine the transport are the partial pressure of CO_2 (Henry's law) and temperature.
- Both plasma and cells can transport CO_2 in a physically dissolved state. (The solubility factor per litre for CO_2 at 38°C is 0.03 for plasma and 0.025 for cells).

TRANSPORT IN CHEMICAL COMBINATION

- By far the greater proportion of CO_2 is transported in blood in chemical combination as HCO_3.
- Majority of the CO_2 diffusing into the blood combines with water *forms carbonic acid*, which ten rapidly dissociates into HCO_3ions and H^+. This reversible reaction is kept moving to the right because the H^+ is buffered by plasma proteins / Hb.
  - Formation of HCO_3 in plasma
  - Formation of HCO_3 by RBCs *(Isohydric Transport of CO_2)*

FORMATION OF HCO_3 IN PLASMA

- The Chief buffers of plasma that provides for buffering action by combining with H^+ is protein system (Proteinate / Protein)
- The reaction is plasma is as follows :

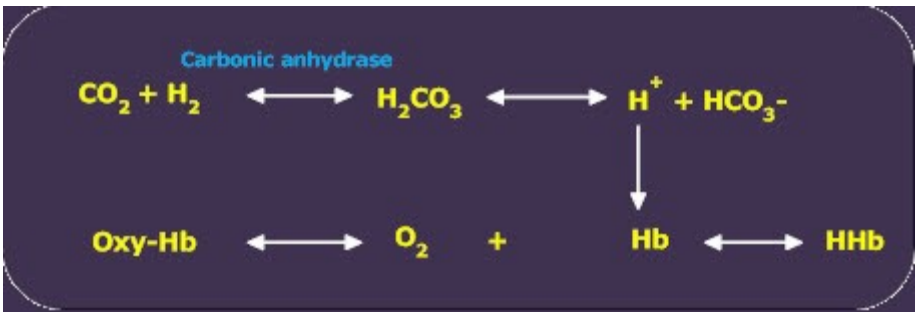


- The PCO_2 in tissues is higher than in arterial blood causes diffusion of CO_2 into blood and forces the preceding reversible reaction to the right causing an increase in HCO_3. This increase in HCO_3 represents transport due to plasma proteins.
- When venous blood reaches the lungs, CO_2 diffuses into alveolar air and is exhaled out. This causes the preceding reaction to shift to left.
- The pH of arterial plasma decreases about 0.025 units in becoming venous plasma.
- The transport of CO_2 as HCO_3^- by plasma proteins represents about 4% of total CO_2 transport.

FORMATION OF HCO_3 BY RBCs

- The CO_2 from tissues enter plasma then into the RBCs. H_2CO_3 formation by the reaction of CO_2 with water is too slow to less of importance in plasma but inside the RBCs, the enzyme carbonic anhydrase catalyses the reaction between CO_2 and H_2O accelerating the rate of about 5,000 fold.

- H_2CO_3 rapidly and spontaneously dissociates into H^+ and HCO_3. Since an increase in H^+ concentration is severely detrimental to an organism, a base buffer must be available to remove the H^+ ions. The Hb provides the buffering, driving the reaction to the right.
- In the tissue Oxy-Hb delivers O_2 and becomes deoxygenated Hb. The deoxygenated Hb is a weaker acid than Oxy-Hb and function as a better buffer readily combines with $H^+$and facilitates the formation of HCO_3 form CO_2.



- Hb is a major buffer in blood that removes free H^+ from blood and an equal quantity of HCO_3 is left dissolved in fluid. The HCO_3 diffuse out of RBC into the plasma due to concentration gradient by exchanging choloride ions from the plasma across the RBC membrane referred as *chloride shift or Hamburger shift*.
- The conversion of CO_2 via H_2CO_3 to HCO_3 ion in erythrocytes accounts for 70% for CO_2transport.
- In the lungs, high PO_2 favours diffusion of O_2 into the red cells and oxygenates Hb. On oxygenation HHb becomes Oxy Hb and releases H^+ ions. This H^+ ion combine with HCO_3 and drives the reaction to the left.

TRANSPORT AS CARBAMINO HEMOGLOBIN

- Haemoglobin contains terminal amino group (NH) reversibly react with CO_2 to from an unstable *carbamino compound*.
- About 20% CO_2 is transported as carbamino haemoglobin (Though plasma proteins can also form carbamino compounds, this reaction in plasma is negligible because free NH group is relatively less in plasma proteins).

CO_2 EQUILIBRATION CURVE

- The total quantity of CO_2 combined with blood in all forms of transport of CO_2 depends on PCO_2, which can be expressed through the CO_2 equilibration curve.
- The PCO_2 ranges between 40mm. Hg in the atrial blood and 45mm. Hg in venous blood. At the capillary bed the concentration of CO_2 rises to 52 volumes percent and the level falls to 48 volumes percent as the blood passes though lungs, hence 4 volumes percent of this is actually exchanged in the process of transporting CO_2 from tissues to lungs.
- The combining of CO_2 with Hb is influenced by degree of oxygen saturation of Hb. Greater the O_2 saturation, lesser is the CO_2, carrying power, more the displacement of CO_2referred as *Haldane effect* .
- On oxygenation Hb becomes a stronger acid. (Reduced Hb being a weaker acid and displaces CO_2 from carbamino Hb. Moreover, increased acidity of oxy-Hb causes increased release of H^+ ion which combines with HCO_3^- to form H_2CO_3. In the lungs H_2CO_3 on dissociation releases CO_2 and H_2O.

HYPOXIA

- It is a state of inadequate O_2 supply to tissue. Absence of O2 is referred as anoxia. The Cerebral effects seen will be mostly as excitement, hallucination, restlessness

and unconsciousness. When blood O_2 below 13%, breathing is stimulated. The anoxia can be classified into the following types.

Anoxic hypoxia (Ambient hypoxia)

- This is due to reduced alveolar ventilation and reduced O_2 tension in blood caused due to obstruction of air passage, paralysis of respiratory muscle, pulmonary disease or congenital diseases of heart. Ambient anoxia is caused by low pO_2 in environmental air in high altitudes or closed space. Symptoms seen are dyspnoea, alkalemia, high cardiac output, increased pulse pressure, dilatation of peripheral vessels.

Anemic anoxia

- Decrease in O_2 carrying capacity of Hb due to low concentration of Hb seen in haemorrhages, anaemia, CO poisoning. In this case the partial pressure of O_2 is normal but insufficient O_2 delivery to tissue results in increased cardiac output and rapid circulation time.

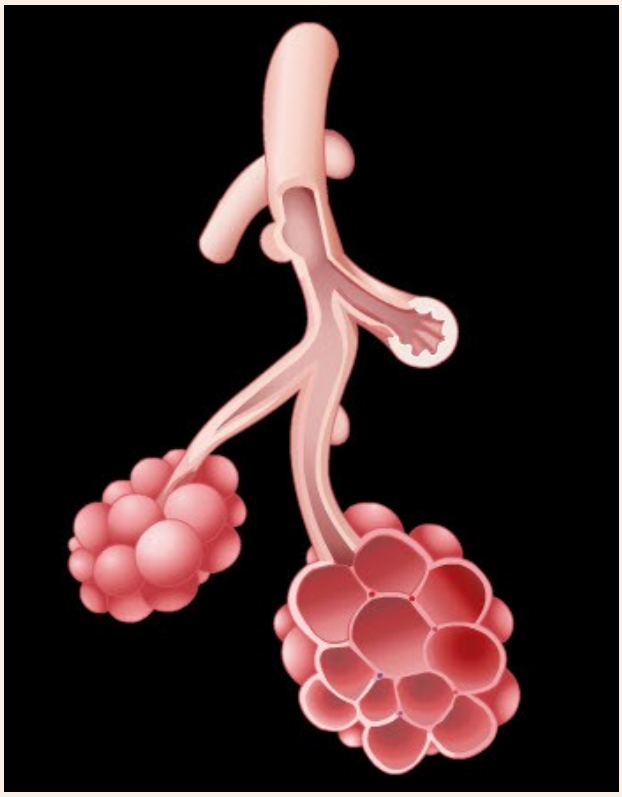
Stagnant hypoxia

- The O_2 content of arterial blood is normal, but the tissues receive low O_2 supply because general or local circulation failure.

Histotoxic hypoxia

- The tissue oxidation is interfered due cyanide poisoning. Paralysis of cytochrome oxidase system is responsible for this condition. The amount of O_2 and pO_2 are normal in arterial blood and above normal in venous blood.

MODULE-38: ROLE OF RESPIRATORY SYSTEM IN ACID – BASE BALANCE



LEARNING OBJECTIVES

- This module deals with,
  - acid-base balance of body,
  - their importance,
  - respiratory support to restore the imbalance and
  - other non respiratory functions of lungs.

ROLE OF RESPIRATORY SYSTEM

- Blood PCO_2 can be varied extensively because the partial pressure of CO_2 in alveoli determines the amount of CO_2 dissolved in blood.
- The respiratory mechanism depends upon the sensitivity of respiratory control systems to change in blood PCO_2 and pH.
- A small increase in PCO_2 or decrease in pH stimulates pulmonary ventilation, so that CO_2 expiration increases.
- If an acid is added to body fluids, chemical buffering results in formation of additional H_2CO_3 and leading to a depletion of HCO_3

$H^+ + HCO_3^- \text{-----} > H_2CO_3 \text{-----} > CO_2 + H_2O$

- When the production of CO_2 is increased or pulmonary hypoventilation occurs, it leads to the accumulation of CO_2 in blood Therefore, the pH falls slightly.
- However, the increase in CO_2 and decrease in pH stimulate respiration, causing a rapid expiration of extra CO_2. Then blood PCO_2 decreases and pH returns to normal.
- When an alkali is added to blood or pulmonary hyperventilation occurs, this causes a decrease in H_2CO_3 {CO_2} level in blood. The respiratory system is inhibited and additional CO_2 is retained in ECF. These increase PCO_2 to balance the increased HCO_3 resulted from added alkali.

METABOLIC ACIDOSIS

- In *metabolic acidosis*, (ketosis, diabetes mellitus, renal acidosis and diarrhoea) blood HCO_3 falls either as a result of a reaction with acid or due to direct loss from ECF and pH falls. This results in fall of the blood buffer bases.

- Usually no change in plasma PCO_2 because of buffer action can be detected. However, a fall in pH results in increased alveolar ventilation and a fall in PCO_2.
- Decreased PCO_2 will bring the ratio of conjugate base to weak acid back to normal . However, the total bases will be less than normal and this requires renal correction – the excretion of H^+ and restoration of plasma HCO_3^-.
- The academia stimulates secretion of H^+ ion by the renal tubule. This ensures reabsorption of all HCO_3 from tubular fluid and the excess H^+ will begin to acidify the urine. For each H^+ ion secreted one HCO_3 will be reabsorbed in to plasma.

METABOLIC ALKALOSIS

- Metabolic alkalosis, (vomiting, K^+ deficiency) involves the gain of base (OH^- or HCO_3^-) or loss of strong acid by ECF. In these conditions, there is an increase in HCO_3 in ECF, resulting in increased base content.
- The response of the body is opposite to the one observed in metabolic acidosis.
- Alkalemia results in rise in pH which will depress pulmonary ventilation and PCO_2 will rise. This respiratory compensation thus will bring pH back to normal.
- Renal correction consists of decreased secretion of pH ions and so increased excretion of HCO_2.

RESPIRATORY ACIDOSIS

- If excretion of CO_2 by the lungs falls below the rate of CO_2 production in the body, respiratory acidosis develops.
- There will be increase in blood PCO_2 *(hypercapnia)* and the primary defect will be in the inability of lungs to expire CO_2 at a normal rate. This may be due to
    - Depression of respiratory centres in CNS.
    - Abnormality of chest wall or respiratory muscles, which prevents enlargement of thorax.
    - Obstruction to gas movement in lungs
- A rise in PCO_2 cause increase in H_2CO_3 and buffer reaction prevents the fall of pH caused by rise in H_2CO_3.
- Renal compensation then follows. Low pH stimulates secretion of H^+ into urine with a rise in plasma HCO_3^-.

RESPIRATORY ALKALOSIS

- When alveolar hyperventilation occur the expiration of CO_2 may exceed the rate of its production within the body and respiratory alkalosis develops. There will be low plasma PCO_2 *(Hypocapnia)* and alkalemia.
- Hyperventilation is caused by abnormal stimulus to respiratory centres either directly as in NH_3 toxicity or through hypoxemia acting through peripheral chemoreceptors. Buffer reaction follows :

$HHb + HCO_3 \text{----}> Hb^- + H_2CO_3 \text{----}> CO_2 + H_2O$

- The HCO_3 falls. Renal compensation begins ; alkalemia depresses H^+ ion secretion by renal tubules and excretion of filtered HCO_3 rises. This result in further fall of plasma HCO_3 and the ratio of HCO_3 to H_2CO_3 moves back to normal.

NON - RESPIRATORY FUNCTIONS OF LUNG

- Animals are exposed to pollutants like dusts, ammonia, pungent gases carbon monoxide, products of plant and animal origin, parasites, bacteria, viruses, spores, endotoxins, diesel fumes, ozonized oxides of nitrogen.

- During transport the animals and animals reared under intensive housing are exposed to stressor promoting agents like pneumonia/pleuritis.
- Non-infectious stress for prolonged time leads to chronic airway diseases.
- These treats are handled by variety of defense mechanism of the lung.

Non-specific immunity/Innate immunity

- Protects against harmful inhaled substances. This includes mucociliary system; cough reflex, phagocytic activity of the alveoli.

Toll-like receptors

- Proteins on the surface of the cell membrane that can recognize the molecules which are common to many bacteria/fungi. On stimulation of these receptors initiates the activities of proinflamatory cytokinins.

Specific defense against specific agents (Bacteria/virus)

- It takes several days for the activation of the process of immune memory to protect future attack of the same organism.

MUCOCILIARY SYSTEM

Functions

- Aerosol is the collection of particles/lipid droplets which are small enough to remain suspended in the air for a period of time.
- Aerosols suspended in air are inhaled
- Aerosols are classified as inhalable/PM 10 (10μ or less) and respirable/PM 2.5 (2.5μ or less)
- These inhaled particles are trapped by the moist surface of the tracheobronchial tree depends on the size of the particles.
- Large particles (> 5μ) are trapped by inertial impaction
    - Inertial impaction occurs as bends in the large air ways
    - Large particles (> 5μ) travel at high velocity are unable to cross these bends.
    - Inertial impactions are provided by the lymphoid tissues in the tonsils, bronchi associated with lymphoid tissues.
- Particles < 4μ settle down by means of sedimentation on the wall of the airways and remain in the lung for ever.
- Particles that diffused into the alveoli epithelium are exhaled out.
- Type of breathing alters the settlement of the particles in the respiratory tract
- Slow, deep breathing transport the particles deep into the lung
- Rapid, shallow breathing enhances inertial deposition in the air ways
- Bronchoconstriction enhances the deposition in the central airways
- Bronchodilatation favors peripheral deposition

Deposition of particles

- Toxic gases get deposited based on their solubility and concentration
- Highly soluble sulphur dioxide at lower concentration is removed by the nose, but at higher concentration it will go deep into the lung
- Less soluble gases also go deep into alveoli
- Inhalation of toxic gases initiates protective reflexes like cough, sneeze, high mucous secretion and bronchospasm.

Anatomical specialties of mucociliary blanket of the respiratory tract

- It consists of sol and gel mucous layers overlying the epithelial cells

- Particles deposited in the lung are transported by the mucociliary escalator to the pharynx for its swallowing
- Sol layer is a low viscous layer over which the cilia beats and baths surface of the epithelial cells
- Gel layer is more viscous that traps the inhaled particles
- Forward beating of the cilia propels the particles to tracheobronchial system or nasal cavity
- Rate of ciliary beating depends on the surface area and also gravity
- Slow ciliary beating in the bronchiole than bronchi and trachea

Respiratory mucous secretion

- Clara cells are the non ciliated portion of bronchioles in the smaller airways
- Goblet cells are located in the large air ways secrete mucous
- Bronchial glands also secrete serous and mucous via sub mucosal glands
- Mucous secretions are under the influence of autonomic nervous system
- On the surface of the epithelial cells, the microvilli assist the ions fluid exchange
- The composition of the mucous varies with the nature of stimuli
- During bacterial overload increased viscosity of mucous secretion, lesser the clearance rate
- Transepithelial movements of water and ions changes the composition of the mucous layer

Cough reflex

- It is a protective reflex initiated by irritation of the sub epithelial layer or stimulation of stretch receptors in the large bronchi by the foreign bodies
- Inflammation of the air passage and injury to respiratory epithelium also causes hyper responsive cough reflex
- It clears the mucous secretions from the trachea and large bronchi

EFFECT OF ALVEOLAR MACROPHAGES

- It is the first line of defense
- In the lungs, macrophages are in the alveolar lining fluid
- Surfactant proteins, complement proteins, opsonins and lysozymes in the respiratory secretions assist in the phagocytosis of particles like bacteria.
- Some of the destroyed particles are removed by microciliary system. Others cross the alveolar wall and enter into the lymphoid tissues of the airways.
- Lung's immune response of the functioning macrophages viz antigen presenting cells
- Hypoxia depressed the macrophage activity
- Endogenous glucocorticoids/synthetic corticoids suppresses macrophages activity
- Excessive administration of synthetic corticoids causes increased susceptibility to bacterial infection in the lung
- Animals transported to a longer distance show stress induced macrophage dysfunction
- Viral infection decreased macrophage functions and contributes the secondary bacterial infection.

Effect of other WBCs

- Neutrophils are also involved in the phagocytosis of inhaled particles
- The invaded bacteria is destroyed by the release of toxic oxygen radicals and proteolytic enzymes
- The free radicals also damage the lung tissues also; Antioxidants and protease inhibitors protect the lung tissue from this effect.

Role of cytokinines and chemokinines

- Cytokinines and chemokinines are proteins released by the macrophages, lymphocytes, epithelial cells during inflammatory process in response to lung injury by infectious agents, allergy or inhalation of toxic gases.
- These proteins attract the inflammatory cells (Neutrophils) to the site of injury and provide communication between neutrophils during inflammatory process.
- These proteins are also involved in tissue remodeling and healing process
- They act as a potent chemo attractant of the inflammatory cells (Neutophils) and produce agents for prolonged inflammatory response

FLUID EXCHANGE

- Continuous exchange of water and solutes between the alveolar epithelium and interstitial cells through interstitial septum
- Hydrostatic and oncotic pressures also favors fluid exchange
- Diffusible particles get exchanged
- Alveolar epithelium is impermeable to certain substances, hence prevents the leak of fluid into the alveoli
- The fluid between pleura has less protein, lubricates the pleura
- Fluid from the interstitium as well as pleural fluids are cleared by lymphatic system and by pumping of the lung during respiration

METABOLIC FUNCTIONS OF THE LUNG

- Endothelial surface is good enough to clear the blood of substances produced in other part of body.
- More over pulmonary capillary blood receives total cardiac output which favours cleansing.
- Endothelial surface is studded with clveolae which houses many enzymes involved in metabolism of vasoactive substances.
- Monoamino oxidases neutralizes serotonin and norepinephrine.
- Angiotensin converting enzymes metabolizes bradykinin and convert angiotensin I to II.Neutralizing enzymes of PGE2, F2 and leukotrienes are present.
- Toxic exogenous substances are also neutralized in lungs.

OTHER NON-RESPIRATORY FUNCTIONS OF THE LUNG

- Sneezing
- Phonation
- Cooling of blood going to the brain
- Olfaction
- Panting in dogs
- Purring in cats

MODULE-39: RESPIRATION IN BIRDS

	LEARNING OBJECTIVES • This session explores, ◦ anatomy of avian

- respiratory tract,
  - its merits and adaptations,
  - mechanism and regulation of respiration in birds.

MODULE-39: RESPIRATION IN BIRDS

LEARNING OBJECTIVES

- This session explores,
  - anatomy of avian respiratory tract,
  - its merits and adaptations,
  - mechanism and regulation of respiration in birds.

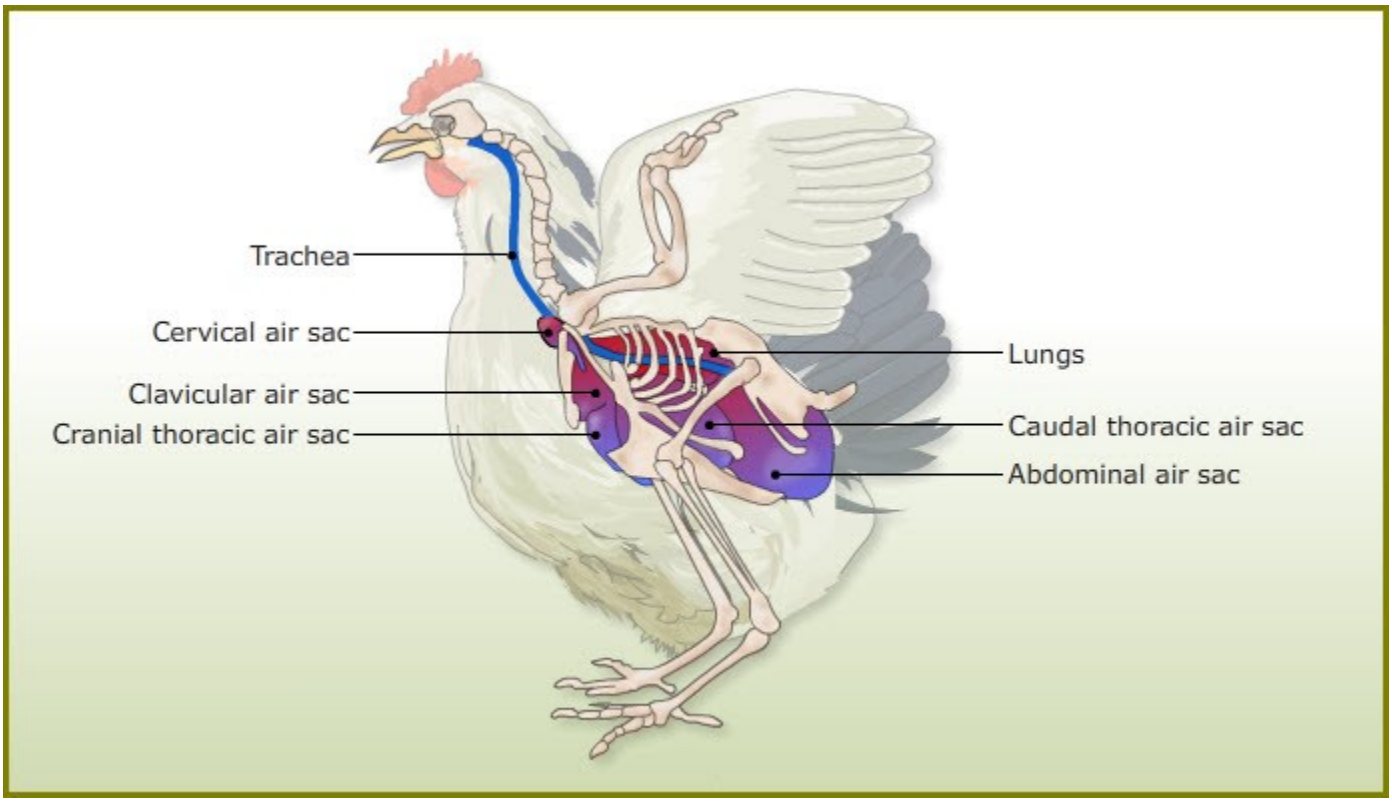
RESPIRATION IN BIRDS

- The lungs are small and attached to ribs and are rigid; they do not expand or contract during the respiratory cycle. Large discrete air sacs are present. Both inspiration and expiration are active.
- Respiratory system beginning from external nares leads to nasal cavities, which open into pharynx. The air also passes through the mouth in to the respiratory system.
- Trachea begins with glottis and divides into two bronchi. At the division is the syrinx, which is the vocal organ in birds. The length and volume of the trachea is greater in birds than in mammals.
- Each lung contains one main intrapulmonary *primary bronchus*, which divides into these sets of *secondary bronchi*.

    - The Secondary bronchi divide into *tertiary bronchi or parabronchi***.**
    - The three sets of secondary bronchi are
        - **Mediodorsal**
        - **Medioventral**
        - **Lateroventral.**
- The parabronchi connect the mediodorsal and medioventral secondary bronchi and also connect some secondary bronchi to the airsacs.
- Those parabronchi (structures that contain gas exchange tissues in their walls) that passes between mediodorsal and medioventral secondary bronchi are nearly parallel and are called as *paleopulmonic parabronchi*.
- Those that pass from mediodorsal and lateroventral secondary bronchi and intrapulmonic primary bronchus to the caudal airsacs are called *neopulmonic parabronchi*. Exchange of gases between lungs and blood occur in parabronchi.

AIRSACS

- These large thin-walled airsacs arise from some secondary bronchi. They lie outside the lungs in the body cavity. They function as airways. Since they are avascular, no gasesous exchange occurs.
- There are 9 airsacs ; (5 anterior and 4 posterior) unpaired *inter clavicular* sac, paired *cervical* and anterior *thoracic airsacs*) are anterior air sacs. Paired *posterior thoracic* and large *abdominal sacs* are the posterior air sacs.
- Diverticula from some of the airsacs are connected to many of the bones. Hence, many of the bones in birds are pneumatic and the humerus is an important *pneumatic bone*.
- The humerus a bone is connected to interclavicular air sac. Lungs can be ventilated via humerus and birds can suck air through broken and opened humerus.
- Gas volume of the airsacs is approximately 10 times more than lungs.



MECHANICS OF RESPIRATION

- There is no diaphragm in birds. So, there is no division of abdominal and thoracic cavities.
- Pressure occurring during respiratory cycle is referred to as thoraco-abdominal pressure. Respiration is caused by changes in body volume.
- During inspiration, the transverse and dorso-ventral diameter of thorax increase because of the ventral cranial movement of sternum and lateral movement of ribs.
- During inspiration, some gas moves into the medio dorsal secondary bronchi, pass through the paleopulmonic parabronchi and enter into the cranial airsacs.
- The pressure increase in expiration in all air sacs and air is forced out of the air sacs, which moves through lungs to outside. Thus, gas flows through the avian lungs during both inspiration and expiration.
- During expiration, gas from the caudal airsacs passes again through the neopulmonic parabronchi and lateroventral secondary bronchi in the opposite direction and then moves into the mediodorsal secondary bronchi and passes through the paleopulmonic parabronchi in the same direction as during inspiration.
- Gases from the cranial airsacs move into the medioventral secondary bronchi and out of the lungs without passing through the gas exchange area.
- The unidirectional movement of gas through paleopulmonic parabronchi, which is the gas exchange portion of avian lungs, increases efficiency of ventilation.
- Gas exchange can occur in the paleopulmonic parabronchi during both inspiration and expiration.
- The remainder the gas moves through the neopulmonic parabronchi, lateroventeral secondary bronchi into the caudal airsacs.
- During expiration these diameters decrease. In air sacs pressure drops and volume increase during inspiration and air move through the lungs into the airsacs.

RESPIRATORY RATES

- Respiratory rates of resting birds vary from 5/min in ostrich to 100 in small birds.
- Respiratory rates during flight are 3 – 18 times greater than at rest.
- Chicken, male 17 and female 27, Pigeon 28, House sparrow 59, and Goose 14/min.

TRANSPORT OF BLOOD GASES

- The difference in gas transport and diffusion between mammals and birds are not great. O_2 dissociation curve is same as in mammals except that it is to the right of mammalian curve. i.e. avian blood is less saturated with O_2 than mammalian blood at same temperature and partial pressure and release of O_2 to tissues is greater than mammalian blood.
- PO_2 for the arterial blood ranges 90 - 96 mm Hg. O_2 saturation is 88 – 90% in arterial blood and 40% in venous blood which are lower than mammalian blood. PCO_2 fowl blood is 28 – 34 mmHg. Arterial pH is generally higher in birds (7.44 to 7.58).

REGULATION OF RESPIRATION

- Respiratory centres as are as in mammals, Chemoreceptors are also important for regulation of respiration in birds Most of these receptors are present in lungs and they detect CO_2 levels in lungs and not of blood.
- They are stimulated by low CO_2 level and once stimulated they reduce respiration. The central chemoreceptors of brain respond to PCO_2 or H^+ ion concentration.
- Carotid and aortic chemoreceptors are also present in birds. Stretch receptors are present in lungs and their activity is modified by CO_2 level.

- Mechanoceptors are chemoceptors in muscle or joints activated by movements or build up of metabolites increases ventilation. Thermoceptors of skin, muscle and hypothalamus on stimulation lead to rapid shallow, panting type of respiration.
- During heat stress in birds, respiratory frequency markedly increases, while tidal volume decreases and panting occur (dead space ventilation increase for evaporative water loss).
- There is no marked change in arterial blood gases and pH. However, in chicken, there is severe hypocaprina and alkalosis during panting.
- Birds hyperventilate during running or flying, and arterial PCO_2 decreases.
- In high altitude due to low PO_2 of air, hyperventilation occurs.
- The birds become highly alkalotic but they tolerate this condition much better than mammals.