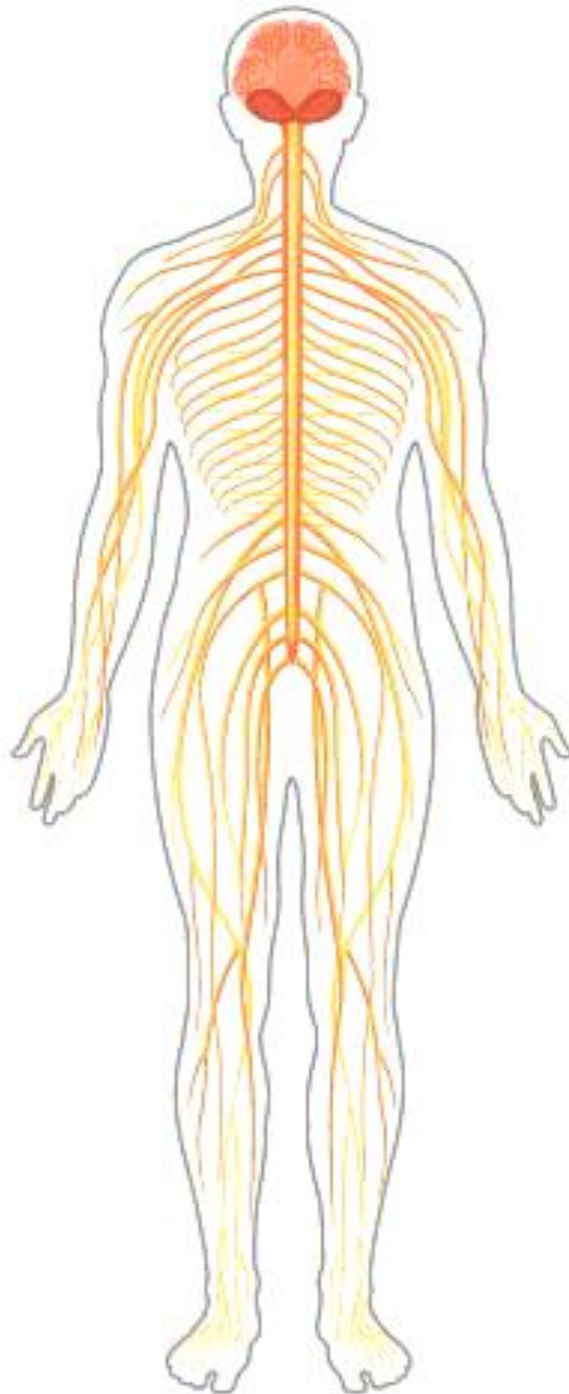


# NERVOUS SYSTEM

NER 202



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## Nervous tissue

- ❖ **Structurally**, nervous tissue consists of two cell types: nerve cells (neurons) and glial cells.

### Neurons

- ❖ **Definition:** The structural and functional unit of the nervous system, constitute more than 100 million cells.

- ❖ **Histological Structure:** Most of neurons consist of 2 parts;

A- **Cell body (Perikaryon):** is a part of the neuron receptive to stimuli and is containing nucleus and surrounding cytoplasm.

- **Size:** varies from **4µm** as in granular cells in cerebellar cortex to **100µm** as in motor neurons in spinal cord.
- **Shape:** depends on the number of cells processes;
  - Unipolar has **globular** shape,
  - Bipolar have **fusiform** shape
  - Multipolar are **stellate, pyramidal or pyriform**.

a) **The nucleus:**

- It is usually large spherical, euchromatic with a prominent nucleolus reflecting the intense synthetic activity of these cells.

b) **The cytoplasm:**

- 1- It contains highly developed rough endoplasmic reticulum and numerous polyribosomes suggesting that these cells synthesize both structural proteins and proteins for transport. When stained, rER, free ribosomes and polysomes appear under the light microscope as basophilic granular areas called Nissl bodies. Their number varies according to neuronal type & functional state.

2- **The Golgi complex** is present around the nucleus.

3- **Mitochondria**

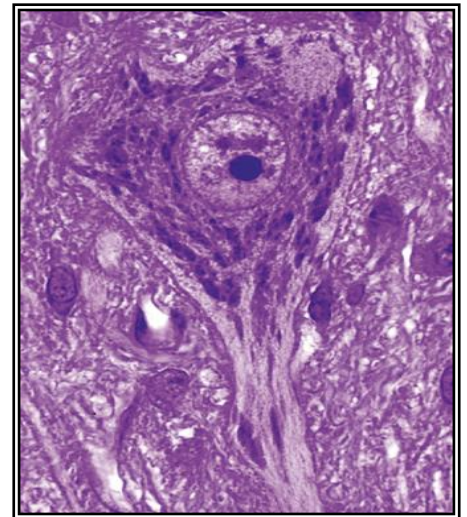
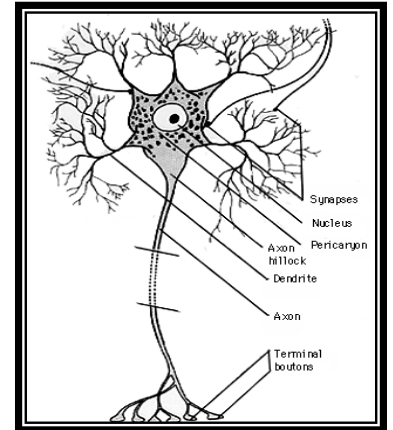
- 4- **Neurofilaments:** intermediate filaments with diameter of 10nm) are abundant in Perikaryon and processes. They bundle together as a result of the action of fixatives to form neurofibrils (2 µm in diameter) that are visible by the light microscope (stained brown by Ag). They provide structural support.

5- **Microtubules** (20-28 nm in diameter) are arranged in parallel bundles in perikaryon and processes. They are involved in axonal transport of neurotransmitter substances, enzymes and other cellular constituents.

6- **Centrioles** are not seen as neurons cannot divide.

7- **Inclusions in form of:**

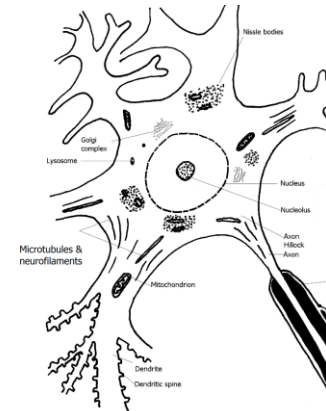
- **Lipofuscin** pigment which is golden brown. It is a residue of undigested material by lysosomes. Its amount increases with aging.



- **Melanin** pigment which is dark brown or black. It is found in neurons of the substantia nigra of the mid brain.
- **Lipid droplets** in cytoplasm as energy reserve or products of abnormal metabolism.

#### B- The processes:

- **Dendrites are multiple** processes that receive stimuli from the environment or other neurons and carry it **to** the cell body.
- **Axon is a single** process that conveys information **away** from the cell body to other neurons or effector cells as the muscle cell.
- Both the dendrites and axon have mitochondria, neurofibrils and microtubules

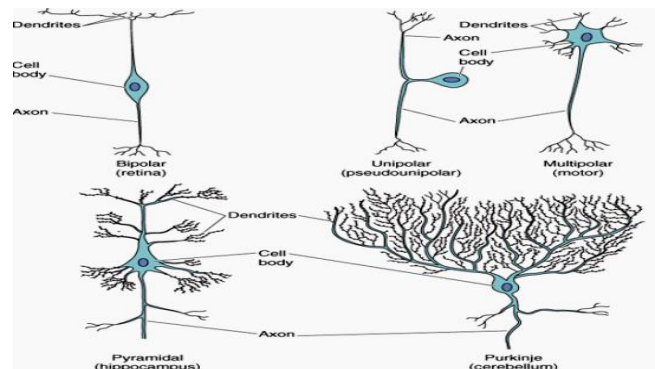


Dendrites	Axon
1-Usually numerous	1-Single originates from axon Hillock
2-Short.	2-Long.
3-Thick.	3-Thin.
4-Branching like a tree. Branches arise at <b>acute angle</b> .	4-Not branching except at the end. It may give collateral branches near the cell body that arise at <b>right angle</b>
5-Become thinner & they are subdivided into branches.	5-Has a constant diameter
6-Contain Nissl bodies	6-Does not contain Nissl granules.

#### ❖ Classification of neurons:

##### A. -They are classified according to number of processes into:

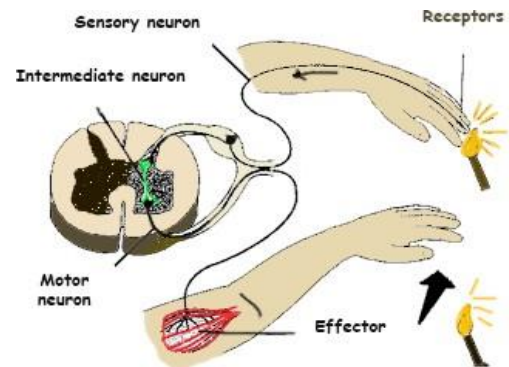
- 1- **Unipolar:** have a single process that is close to the Perikaryon and divides into 2 branches to form a T shape, with one branch extending to peripheral ending to act functionally as a dendrite but its structure is similar to that of axon and the other towards the central nervous system to represent the axon. The stimuli that are picked by the dendrites travel directly to the axon without passing through the Perikaryon. It is found in the spinal ganglia and mesencephalic nucleus of trigeminal nerve.
- 2- **Bipolar:** have one dendrite and one axon. This type is present in cochlear and vestibular ganglia in ear, retina in eye and the olfactory mucosa.



- 3- **Multipolar:** have one axon and many dendrites. They take different forms:
  - a- Stellate as the anterior horn cells in spinal cord.
  - b- Pyramidal as pyramidal cells in cerebral cortex.
  - c- Pyriform as Purkinje cells in cerebellar cortex.

#### B. According to function:

- 1- **Sensory** (Efferent) neurons receive sensory stimuli as cells of dorsal root ganglion .
- 2- **Motor** (afferent) neurons control effector organs such as muscles and glands as anterior horn cells in spinal cord.
- 3- **Interneurons** connect neurons in retina and spinal cord.



#### C. According to length of axon:

- 1- **Golgi type 1:** neurons have long axon that leaves the grey matter and enters white matter as motor neurons in spinal cord, pyramidal cells in cerebral cortex and Purkinje cells in cerebellar cortex.
- 2- **Golgi type 2:** neurons have short axon that does not leave the grey matter as in interneurons in cerebral and cerebellar cortex.

### Nerve fiber and their covering

❖ **Nerve fibers:** consists of an **axon** covered by axolemma and contains axoplasm (cytoplasm). It arises from a conical extension of cell body called axon hillock.

#### ❖ **Types of nerve fibers:**

- 1- **Unmyelinated nerve fibers:** have no myelin sheath and is divided into:
  - a- Unmyelinated fibers without sheath of Schwann cells (neurolemma) as in gray matter (Naked).
  - b- Unmyelinated nerve fibers with sheath of Schwann cells as in sympathetic post ganglionic fibers.
- 2- **Myelinated nerve fibers:** have myelin sheath and is divided into:
  - a- Myelinated nerve fibers without sheath of Schwann cells as in white matter.
  - b- Myelinated nerve fibers with sheath of Schwann cells as in peripheral nerve fibers.

#### ❖ **The sheath of Schwann (Neurolemmal sheath)**

- It consists of flattened cells with flattened nuclei called Schwann cells that form thin chain around the myelin of a nerve fiber.

#### • **Functions:**

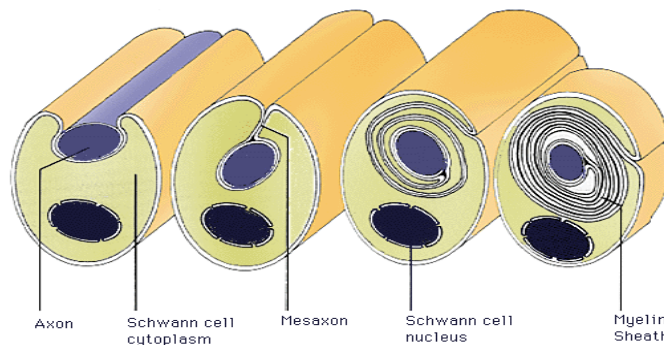
- 1) Formation of myelin sheath in the peripheral nerves.
- 2) Electric insulation.
- 3) Regeneration where axon grows from the proximal stump formed by Schwann cells.

#### ❖ **Myelin Sheath:**

- **Formation:** It is formed by rotation of Schwann cells (in peripheral nervous system) or Oligodendroglia processes (in central nervous system) around the axon several

turns. Each Schwann cell wraps around one segment of a single axon. while each oligodendroglia cell wraps around one or more segments of many axons (10-60).

- **Structure:** It is made of many layers of modified cell membranes with a higher proportion of lipids than other cell membranes.
- **LM:** After routine fixation Lipoprotein dissolves. It can be stained black with **osmic acid**.
- **E/M:** It appears as fused spiral laminae of plasmalemma.
- *It shows gaps called nodes of Ranvier that represent the spaces between adjacent sheath cells.*
- *The sheath of myelin is thus divided into segments by the nodes which are called internodal segments.*
- **Functions:** enhances the speed of nerve impulse.
- **Stages of myelination (Formation of myelin sheath):**
  1. Axon **invaginates** into near sheath cell (Schwann cell in peripheral nervous system or oligodendroglia in central nervous system).
  2. Further invagination so axon is surrounded by a **single turn of cell membrane**.
  3. The single turn progresses into **many turns** (up to 50 turns) in a spiral form mostly due to rotation of the sheath cell.
  4. The intervening cytoplasm is pushed to the cell body leading to **compaction** of the turns.
  5. **Fusion** of cell membranes of the spirally arranged turns to form myelin sheath.



**Diagram showing steps of myelin sheath formation by Schwann cells**

## Peripheral Nervous System

- It consists of Nerves, ganglia and nerve endings.

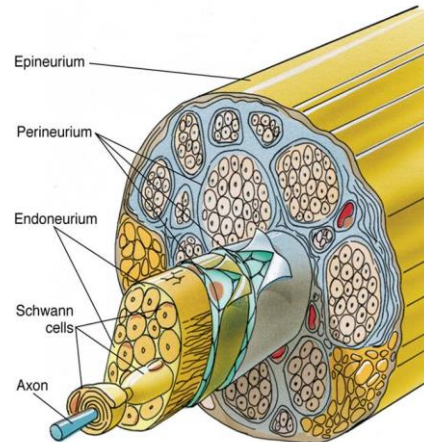
### Peripheral Nerve

❖ **Definition:** Bundles of nerve fibers held together by connective tissue.

- The nerve is covered by **dense** connective tissue called **epineurium**.
- Nerve bundles are surrounded by **perineurium**. It is formed of flattened epithelium-like cells joined by **tight** junctions. This forms a barrier to protect the nerve fibers.



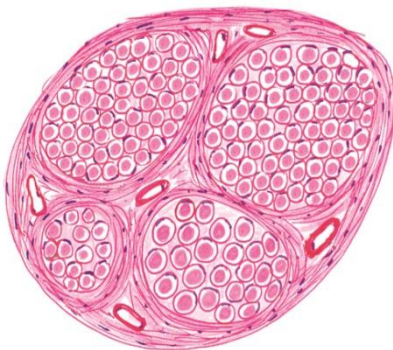
- Inside the bundle the nerve fibers are connected by **endoneurium** (sheath of Henle). It consists of **reticular fibers** formed by Schwann cells.



**Diagram showing structure of peripheral nerve**

❖ **In histological preparations**, the appearance of nerve fibers depends on the stain:

1. Preparations stained by H & E., the lipid component of myelin have been dissolved during dehydration, leaving behind central faintly stained axon.
2. Preparations stained by osmic acid, the lipid component is preserved and appears as black ring around the site of the axon.



**Diagram showing nerve trunk stained with H&E**



**Diagram showing nerve trunk stained with osmic acid**

## Degeneration and regeneration of nerve tissue

- In a wounded nerve fiber, there are **two distinct types of changes**:

**A- Retrograde degeneration (Traumatic degeneration):** In nerve cell and proximal part of nerve fiber

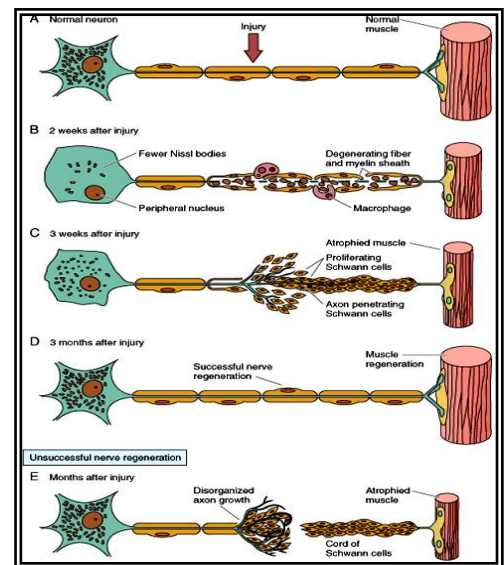
- **Chromatolysis**: disappearance of Nissl bodies with decrease in basophilia.
- Increase in volume of Perikaryon with loss of dendrites so becomes globular.
- Migration of nucleus to peripheral position.
- Disappearance of Golgi body and mitochondria.
- Fragmentation of neurofibrils.
- Lysosomes **increase**

**B- Wallerian degeneration:** in distal part of nerve fiber.

- Axon: neurofibrils appear **beaded**, then **segmented**, then **granular** and finally **disappear**.
- Myelin sheath shows widening of nodes of Ranvier. The internodal segments are termed **fermentation chambers** as fat split into fatty acids.
- Schwann cells **proliferate** giving rise to cellular columns that act as guide for the growing axons during regeneration.

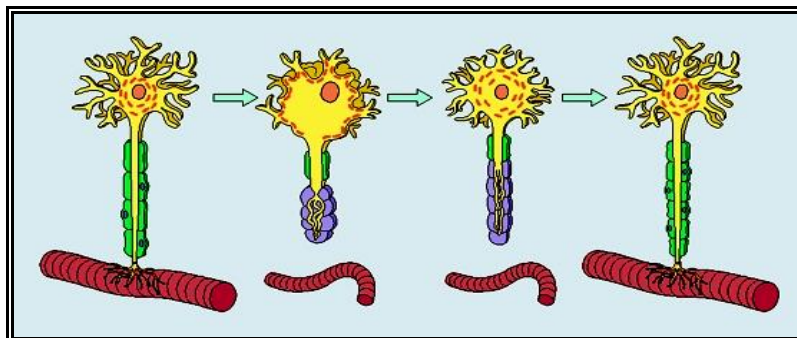
### ❖ Stains of degeneration:

1. **Silver**: to demonstrate changes in Golgi body and Neurofibrils.
2. **Osmic acid**: to demonstrate changes in myelin sheath.
3. **Basic stains**: to demonstrate changes in Nissl bodies.



### ❖ **Regeneration** takes place where;

1. **Macrophages** remove debris and secrete **interleukin 1** (substances secreted by cells of the immune system) which stimulates **Schwann cells** to secrete substances that promote nerve growth.
2. Growth of axons in proximal part in direction of the columns of Schwann cells. Regeneration is efficient when the fibers and the columns of Schwann cells are directed to the correct place.



**Diagram showing steps of nerve fibers regeneration**



## Ganglia

- **Definition:** collection of nerve cells and glial cells outside CNS supported by connective tissue.
- **Types:** Craniospinal and autonomic (sympathetic or parasympathetic).

Spinal ganglion	Sympathetic
1. Covered by thick connective tissue capsule.	1. Covered by thin connective tissue capsule.
2. Blood vessels are less.	2. Blood vessels are more.
3. Cells are arranged in groups or rows.	3. Cells are scattered
4. Cells are variable in size.	4. Cells are uniform in size.
5. Cells are larger.	5. Cells are smaller.
6. Cells are unipolar	6. Cells are stellate multipolar.
7. Cells have glomeruli formed by coiling of the axon around the cell body before splitting in a T form.	7. No glomeruli.
8. Cells are surrounded by large number of <b>satellite cells</b> in a continuous layer	8. Few <b>satellite cells</b> in discontinuous layer (interrupted by the dendrites)

## NEUROGLIA

- Glial cells are 10 times more abundant in the mammalian brain than neurons. They surround the cell bodies and processes.
  - **Central neuroglia:** include Astrocytes, Oligodendrocytes, Microglia and Ependymal cells.
  - **Peripheral neuroglia:** include Schwann cells and Satellite cells.

	Astrocytes ( <b>Macroglia</b> )	Oligodendrocytes	Microglia ( <b>Mesoglia</b> )
<b>Origin</b>	Ectodermal	Ectodermal	Mesodermal
<b>Site</b>	Grey matter and white matter		
<b>Shape</b>	Large star shaped cells with multiple processes	Medium sized cells which have few processes.	- Smallest cells with many branches. - The cell body and the branches are decorated by spines.
<b>Nucleus</b>	Large pale	Medium dark	Small dark
<b>Cytoplasm</b>	Intermediate filaments (GFAP)	highly dense	Many lysosomes
<b>Centrioles</b>	Present so can divide and form tumors		Absent

<b>Subtypes</b>	<b>1- Cytoplasmic astrocytes:</b> <ul style="list-style-type: none"> <li>In grey matter</li> <li>Granular cytoplasm</li> <li>Many short processes</li> </ul> <b>2- Fibrous astrocytes</b> <ul style="list-style-type: none"> <li>In white matter</li> <li>Fibrous cytoplasm</li> <li>Many long processes</li> </ul>	<b>1- Satellite cells:</b> <ul style="list-style-type: none"> <li>In grey matter.</li> <li>closely associated with the cell body of neurons.</li> </ul> <b>2- Interfascicular</b> <ul style="list-style-type: none"> <li>In white matter</li> <li>Between bundles of axons.</li> </ul>	
<b>Function</b>	1. They have processes with expanded end feet linked to endothelium of blood capillaries so can control metabolic exchanges between nerve cell and blood. 2. Blood brain barrier. 3. Structural support. 4. Repair process by formation of scar tissue.	1- Support nerve cells. 2- Formation of Myelin sheath. 3- Electric insulation.	Phagocytic cells so can be stained by <b>trypan blue.</b>

### Peripheral neuroglia

#### a- Ependymal cells

- Line central canal of spinal cord and ventricles of brain.
- They form simple cuboidal or columnar epithelium that may be ciliated in places. Cilia may be involved in propulsion of CSF.
- Ectodermal in origin.

#### b- Schwann cells

- In peripheral nervous system.
- Responsible for myelin production, electric insulation and regeneration.
- Ectodermal in origin.

#### c- Satellite cells

- Low cuboidal cells
- In peripheral nervous system.
- Around nerve cells in ganglia

### Synapse

- Site of **functional** contact between neurons or neurons and other effector cells (as muscle & gland cell). Its main function is to transmit impulse from the **presynaptic** cell to **postsynaptic** cell.

#### ❖ Classification:

##### a) According to method of transmission of nerve impulse:

- Chemical:** most common, in which conduction of impulses takes place by release of **neurotransmitters**.

2. **Electrical:** contain **gap junctions** that allow movement of ions between cells and so permit the spread of electric current. They have been demonstrated in cerebellum.
- b) **According to the site of contact of the axon:**
  - 1- **Axosomatic:** axon forms synapse with cell body.
    - Most excitable because: a- large number of  $\text{Na}^+$  channels
    - b-Lower threshold (11 mv depolarization)
    - Least numerous
  - 2- **Axodendritic:** axon forms synapse with a dendrite.
  - 3- **Axoaxonic:** axon forms synapse with an axon
    - Least excitable (15 mv depolarization).
    - Most numerous

❖ **By electron microscope:**

➤ **Synaptic knobs:**

- Has protein on its membrane called t-snare
- It contains Vesicles: Contain protein called v-snare

- **Types :**

1. Clear vesicles: Containing rapidly acting transmitter e.g. Acetyl choline
2. Granular vesicles: Containing slowly acting chemical transmitter
  - It contains also Mitochondria

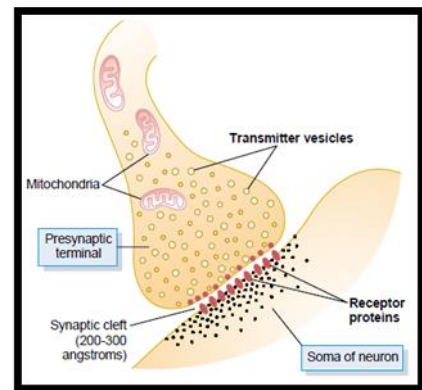
➤ **Synaptic cleft:** - 30- 50nm width

- It contains extracellular fluid

(ECF):  $\text{Na}^+$ ,  $\text{Cl}^-$

➤ **Post-synaptic membrane:** Contain receptors formed of:

- Binding protein (to unite with the transmitter).
- Ligand channels: (1  $\text{Na}^+$  channels: Allow  $\text{Na}^+$  entry (influx)
- (2  $\text{Cl}^-$  channels: Allow  $\text{Cl}^-$  entry (influx)
- (3  $\text{K}^+$  channels: Allows  $\text{K}^+$  exit (efflux)



**Synaptic transmission**

- It is Chemical transmission
- Is transmission of impulse (action potential) from one neuron to another
- It is chemical by release of chemical Transmitter.

❖ **Mechanism Synaptic Transmission:**

1- **Release of Chemical Transmitter:**

- The action potential in the presynaptic nerve reaches the terminal knob
- Opens the voltage gated  $\text{Ca}^{++}$  channels present on membrane thickening called active zone.
- $\text{Ca}^{++}$  enters the knob according to concentration & electric gradient
- The vesicles move to the active zone
- v-snare fuses with t- snare leading to rupture of vesicles
- Release of chemical transmitter in synaptic cleft
- The amount of transmitter released is directly proportionate to amount of  $\text{Ca}^{++}$  entered

2- **Union of chemical transmitter with its receptors**

3- **Synaptic potential:** Changes in ion fluxes through membrane lead to change in resting membrane potential (RMP) of postsynaptic membrane to become:

- a. **Less negative:**Causing Excitatory Postsynaptic Potential (EPSP)
- b. **More negative:** Causing Inhibitory Postsynaptic Potential (IPSP)

- 4- **Removal of neurotransmitters and termination of response** :By one of the following
- Inactivation of transmitter→By specific enzymes at post synaptic membrane
  - Passive diffusion away from synaptic cleft
  - Active re-uptake of transmitter by axon terminal to be stored or destroyed(
  - Removal by glial cell

### Synaptic Potentials

#### 1) **Presynaptic Potentials (PSP) :**

##### - **Types:**

##### **A-Pre-synaptic inhibition**

- By 3rd inhibitory neuron:
- Its axon terminal anastomoses with the axon terminal of an excitatory presynaptic neuron (before it reaches the synapse)
- **Releases an inhibitory chemical transmitter which either:**
  - Closes voltage gated  $Ca^{++}$  or
  - Closes  $Na^{+}$  channel or
  - Opens  $K^{+}$  or  $Cl^{-}$  channels
- The end result is reduced  $Ca^{++}$  entry to synaptic knob which in turn decrease release of chemical transmitter .

##### **B-Pre-synaptic facilitation:**

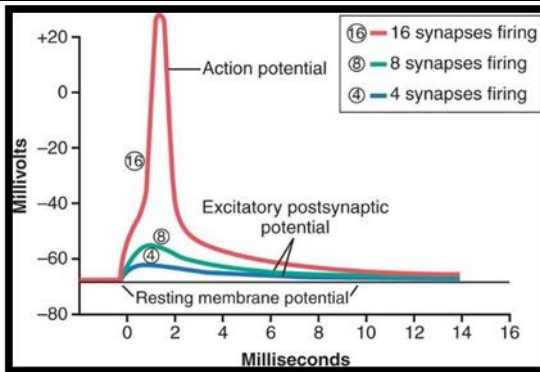
- **Sensitization By 3rd excitatory neuron:**
  - Secretes excitatory chemical transmitter (serotonin)
  - Serotonin increase cAMP in pre-synaptic terminals → activate kinase which phosphorylate  $K^{+}$  channels → closure of  $K^{+}$  channels → prevent repolarization & prolong the action potential.
  - The action potential → opens  $Ca^{++}$  channels → increase  $Ca$  entrance → increase release of chemical transmitter (may continue for 3 weeks) .
  - It is the base of sensitization involved in learning & memory.

#### **C-Postsynaptic Potentials (PSP) :**

##### ➤ **Types:**

- Excitatory Post-Synaptic Potential [EPSP]
- Inhibitory Post-Synaptic Potential [IPSP]
- Grand Post-Synaptic Potential [GPSP]

1-Excitatory Post-Synaptic Potential [EPSP]	2-Inhibitory Post-Synaptic Potential [IPSP]
<b>1 .Post-synaptic membrane is in a state of:</b>	
Local partial depolarization (excitatory state)	Local partial hyperpolarization (inhibitory state)
<b>2 .Produced by:</b>	
Combination of excitatory chemical transmitter (e.g. acetyl choline) with its specific receptor	Combination of inhibitory chemical transmitter (e.g. GABA) with its specific receptor.
<b>3 .Occurs after:</b>	
0.msec from pre-synaptic nerve stimulation	5msec from pre-synaptic nerve stimulation
<b>4 .Reaches max after:</b>	
1.5 msec	1.5msec
<b>5 .Lasts for:</b>	
5 msec	3msec

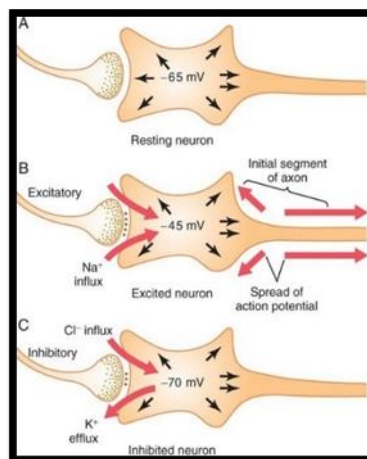
6 .During this period:													
The membrane is facilitate (ie needs weaker stimulus to be excited) "high excitability"	The membrane is inhibited (ie needs higher stimulus to be excited) "low excitability" because the potential is away from firing level												
7 .It is caused by:													
<ol style="list-style-type: none"> <li>1. Opening of ligand gated Na<sup>+</sup> channels which allow: Na<sup>+</sup> entry (according to concentration&amp; electric gradients)</li> <li>2. Opening of ligand gated Ca<sup>++</sup> channels.</li> </ol>	<ol style="list-style-type: none"> <li>1. Opening of ligand gated Cl<sup>-</sup></li> <li>2. Opening of ligand gated K<sup>+</sup> channels</li> <li>3. Closure of ligand gated Na<sup>+</sup></li> <li>4. Closure of ligand gated Ca<sup>++</sup> channels</li> </ol>												
8 .It can be summated													
To reach the threshold value, it must be summated													
Summation could be:													
<table border="1"> <thead> <tr> <th>Temporal (time)</th><th>Spatial (space)</th></tr> </thead> <tbody> <tr> <td>One pre- synaptic knob is stimulated repetitively</td><td>Several pre-synaptic knobs are stimulated simultaneously(40)</td></tr> <tr> <td colspan="2">When excitation reaches firing level, action potential starts.</td></tr> <tr> <td colspan="2">Up to 50 EPSPs have to summate to reach the threshold value</td></tr> </tbody> </table>	Temporal (time)	Spatial (space)	One pre- synaptic knob is stimulated repetitively	Several pre-synaptic knobs are stimulated simultaneously(40)	When excitation reaches firing level, action potential starts.		Up to 50 EPSPs have to summate to reach the threshold value		<table border="1"> <thead> <tr> <th>Temporal (time)</th><th>Spatial (space)</th></tr> </thead> <tbody> <tr> <td></td><td></td></tr> </tbody> </table>	Temporal (time)	Spatial (space)		
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 <p><i>Excitatory postsynaptic potentials, showing that simultaneous firing of only a few synapses will not cause sufficient summated potential to elicit an action potential, but that simultaneous firing of many synapses will raise the summated potential to threshold for excitation and cause a superimposed action potential</i></p>													

### 3-Grand Post-Synaptic Potential [GPSP]

- It is the sum of all EPSPs and IPSPs occurring at the same time in one post synaptic neuron.
- If EPSP equal to IPSP input: GPSP is zero
- If EPSP is slightly greater than IPSP input: GPSP will be depolarization but do not reach firing level
- If EPSP is much greater than IPSP input: GPSP is depolarization reach firing level
- If IPSP is greater than EPSP: GPSP is hyperpolarization



Post-synaptic Potential	Action Potential
1. Not obey all or law	1. Obey all or non law
2. Graded	2. Can not be graded
3. No absolute refractory period	3. there Is absolute refractory period
4. Summated	4. Can not be summated
5. Not propagated	5. Propagated
6. 20msec	6. 1msec
7. Make the membrane more or less negative	7. Always make the membrane less negative



### Three states of a neuron.

- A. Resting neuron, with a normal intraneuronal potential of (-65 millivolts).  
 B. Neuron in an excited state, with a less negative intraneuronal potential (-45 millivolts) caused by sodium influx.  
 C. Neuron in an inhibited state, with a more negative intraneuronal membrane potential (-70 millivolts) caused by potassium ion efflux, chloride ion influx, or both.

### Characters of synaptic transmission

- Forward direction** → Impulses are conducted from pre-synaptic to post-synaptic neuron (as neurotransmitter is released from pre- synaptic neuron)
- Synaptic delay:**
  - Is the time taken by an impulse to be conducted through synapse
  - It equals 0.5 msec "Millisecond"
  - It is taken by: 1-Release of chemical transmitter      2 - Union with receptors  
3-Opening ionic gates      4-Building post-synaptic potential
- Central delay** → Time of conduction of impulse along the synapses  
→ Equals: Number of synapses in reflex arc multiplied by 0.5 msec
- Fatigue** → It is decreasing rate of discharge of impulse from post-synaptic neuron after long period of high frequency stimulation of pre-synaptic neuron
  - **Cause:** a) Exhausted pre-synaptic vesicles      b) Inactivated post-synaptic receptors

- **Benefit:** Stops CNS over excitation, as in epileptic fits where fatigue stops convulsions
- 5- **Synaptic Plasticity** → Change in functions according to demand placed on synapse. So, synaptic transmission can be strengthened or weakened for short or long duration

### Factors affecting synaptic transmission

#### 1. **Changes in composition of internal environment:**

##### a- ***PH of blood:***

- 1) **Alkalosis** → Increases excitability → increases synaptic transmission → convulsions eg Hyperventilation

- **Mechanism:** In alkalosis, protein carry more negative charge → combine with ionized Ca → decrease ionized Ca → open Na<sup>+</sup> channels → depolarization

- 2) **Acidosis** → Decreases excitability → decreases synaptic transmission → coma eg diabetes → acids (as β-hydroxy butyric acid)

##### b- ***Hypoxia:*** -Decrease synaptic transmission

- Because decrease O<sub>2</sub> supply → Pyruvate & lactic acids accumulate
- Interrupted cerebral circulation for 3-5 sec → unconsciousness

##### c- ***Hypoglycemia:*** - Decrease synaptic transmission

- Because glucose is the only fuel for brain for energy production
- Energy is needed for formation of transmitter & active re-uptak

- d- ***Hypocalcemia:*** Low Ca<sup>++</sup> facilitate synaptic transmission As it increases the excitability of postsynaptic membrane

##### e- ***Hormones:*** -May inhibit or facilitate synaptic transmission

- e.g. thyroid hormones facilitate synaptic transmission

#### 2. **Drugs:**

- a. ***Theophylline & caffeine*** → Facilitate synaptic transmission (as they lower the threshold of excitability & depolarize post-synaptic membrane)

- b. ***Hypnotics, Analgesics & Anaesthetics*** → Decrease synaptic transmission by:

- i. Stabilizing cell membrane → hyperpolarization Or
- ii. Interfere with transmitter synthesis

- c. ***Strychnine*** → Competes with glycine (Inhibitory chemical transmitter) leaving excitatory pathway unaffected → convulsions & spasm.

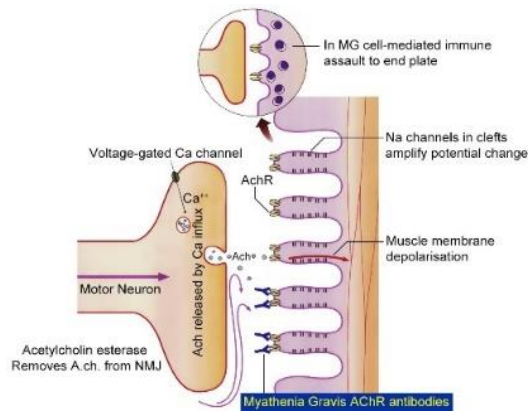
#### 3. **Diseases:**

- I. ***Parkinsonism*** → A disease of basal ganglia

- Causing decrease release of Dopamine (inhibitory chemical transmitter) leaving acetyl choline (excitatory chemical transmitter) → Hypertonia (rigidity)

- II. ***Tetanus*** → Decrease release of GABA (inhibitory chemical transmitter) leaving excitatory chemical transmitter → spastic paralysis muscle spasm → locked jaw & asphyxia

- III. ***Myasthenia Gravis "MG"*** → Autoimmune disease: Antibody against acetyl choline receptors in neuromuscular junction → severe muscle weakness.



- IV. **Botulism toxin** → Block the release of acetylcholine (excitatory chemical transmitter) at neuromuscular junction leading to flaccid paralysis.

#### Clinical Application

- Improperly prepared salted fish may contain Botulinum toxin causing botulism, which may end in respiratory failure
- We inject Botulinum toxin (Botox) into muscle for therapeutic purposes as:
- a-Anti-wrinkle treatment (Cosmetology)      b-Achalasia of the cardia      c-Anal fissure

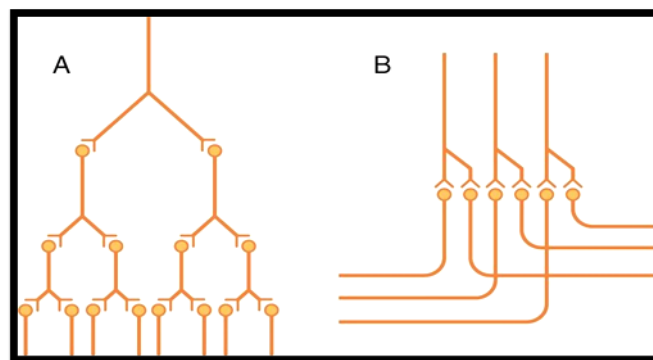
#### Organization of Neurons in Neuronal Pool

❖ **Definition:** Neuronal pool is a collection of neurons having the same function in CNS

❖ Similarities of organization:

##### 1- Divergence:

- **Def.:** One neuron stimulates many neurons
- **Function:** 1-**Amplification:** e.g. one pyramidal cell in motor cortex stimulates 100- 1000 AHCs in spinal cord
- 2- **Distribution of signals:** e.g. painful stimulus stimulate AHCs of muscles on same & opposite side (flexor withdrawal reflex)

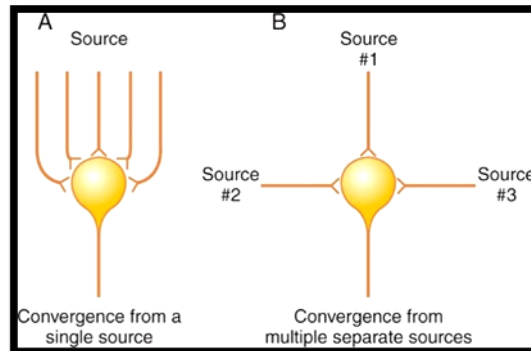


"Divergence" in neuronal pathways.

- A. Divergence within a pathway to cause "amplification" of the signal.  
 B. Divergence into multiple tracts to transmit the signal to separate areas.

## 2- **Convergence:**

- **Def.:** Many neurons stimulate one neuron
- **Function:** 1-Intensification of stimulus due to spatial summation
- Interpretation of information carried from different sites & received by one neuron



"Convergence" of multiple input fibers onto a single neuron .

A. Multiple input fibers from a single source .

B. Input fibers from multiple separate sources

## 3- **Excitation Field:**

- **Def.:** It is number of neurons with which one afferent neuron synapse

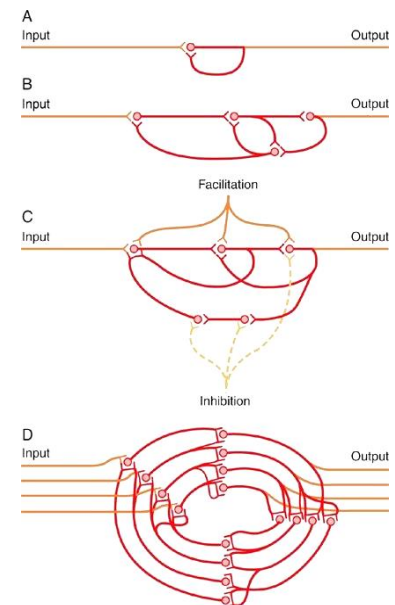
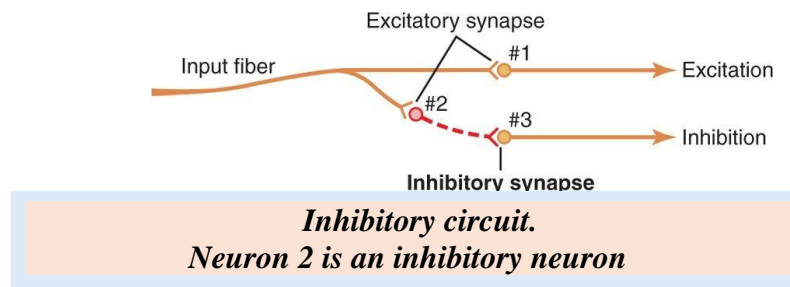
Central neurons in excitation field	Peripheral neurons in excitation field
<ul style="list-style-type: none"> <li>- Discharge zone</li> <li>- When afferent neuron is stimulated, these cells are stimulated &amp; reach threshold value and discharge</li> <li>- If overlap occurs in the center</li> </ul>	<ul style="list-style-type: none"> <li>- Facilitation zone (subliminal fringe)</li> <li>- Which cannot reach threshold value and so, they are only facilitated</li> <li>- The stronger the stimulus → the wider the discharge zone</li> <li>- The weak the stimulus → the small excitation field formed mainly of subliminal fringe</li> </ul>

- **Overlap between excitation field may lead to:**

4- <b>Occlusion</b>	5- <b>Facilitation</b>
<b>Due to:</b> Decrease the number of discharge zone	<b>Due to:</b> Increase the number of discharge zone are
<p><b>Discharge" and "facilitated" zones of a neuronal pool.</b></p>	

## 6- Inhibitory Circuits:

- Lateral inhibition:** A central neuron is stimulated while the neurons at the periphery are inhibited by one excitatory input through inhibitory interneuron  
Importance: Sharpen the sensation
- Negative feedback inhibition:** Input fiber stimulate output fiber which in turn inhibit the input by inhibitory inter neuron
- Reciprocal innervation:** It is stimulation of one muscle and inhibition of its antagonist by excitation of one nerve. This is carried through inhibitory interneuron



## 7- Activating Circuits: “After discharge”

- **Def.:** The output continues to discharge after stoppage of stimulation of the input
- **Mechanism:**
  - Parallel circuits:** -The input is connected to the output by many parallel circuits, each contains different number of synapses
    - This leads to arrival of successive impulses to output neuron to prolong the discharge
  - Reverberating circuits “Oscillatory circuits” (closed circuits):**
    - The output neuron sends collateral to restimulate itself.
    - It can be stopped by fatigue of the synapses or inhibitory impulses from outside.

## Skin

### ❖ Structure:

- Epidermis:**
  - Outer epithelial layer (**keratinized stratified squamous epithelium**).
  - Derived from **ectoderm**.
- Dermis:**
  - Thicker deep CT layer.
  - Derived from **mesoderm**.

### N.B.

**Hypodermis:** is not a part of the skin (Greek; hypo = under, dermis = skin).

### ❖ Types of skin According to thickness of epidermis, skin is classified into **thick** and **thin**

## Thick (Non-Hairy) Skin

- It has a thick epidermis (400-1400  $\mu\text{m}$ ) and a thick horny layer
- Present in palms and soles.
- It is formed of epidermis and dermis.

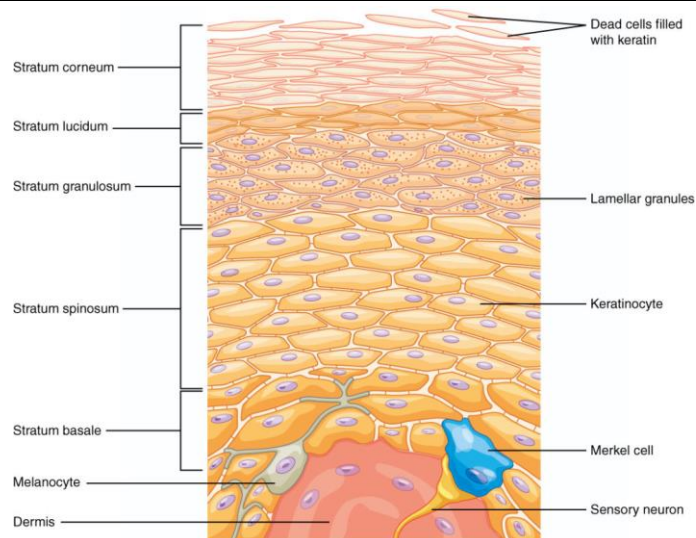


## The Epidermis

- It is a keratinized stratified squamous epithelium.
- Thicker over soles than palms.
- Avascular layer receiving its nutrition by diffusion.
- Rich in free nerve endings.
- The epidermis is formed of **keratinocytes and non-keratinocytes**.

### a- Keratinocytes

- 85% of the cells in epidermis.
- Deeper layers are continuously dividing, differentiating, and accumulating keratin filaments (keratin formation) while progressing upwards.
- Superficial layers are continuously shed off.
- According to **keratinocytes maturation, epidermis consists of 5 layers:**



**Diagram showing layers of skin**

#### - **Stratum Basale or (Basal Cell Layer):**

##### ➤ **LM:**

- Single layer of low columnar or cuboidal cells, resting on a clear wavy basement membrane.
- Basophilic cytoplasm with large basal oval nucleus.
- Intense mitotic figures (**responsible for renewal**).
- Melanocytes and Merkel's cells are found in this layer

##### ➤ **EM:**

- Attached to each other and to the following layer by desmosomes and to basement membrane by hemi-desmosomes.
- Rich in free ribosomes and polysomes with few other organelles (G.A, mitochondria and rER).
- Keratin intermediate filaments ending in desmosomes.

- **Stratum Spinosum (Prickle Cell Layer):**

➤ **LM:**

- 4-8 layers of polyhedral cells are present above the basal cell layer.
- Less basophilic cytoplasm than cells of stratum Basale.
- Cells have central rounded nuclei.
- Borders of cells appear to be separated from one another by small spaces that are traversed by fine spine-like processes (desmosomes), giving prickly appearance.
- Langerhans cells are present in this layer.

❖ **Malpighian layer:** Consists of both stratum Basale and stratum spinosum.

- **EM:** bundles of **intermediate filaments (Tono-filaments)** that end into the dense plaques of numerous desmosomes along highly inter- digitating cell boundaries.

- **Stratum Granulosum (Granular Cell Layer):**

➤ **LM:**

- layers of spindle-shaped cells above the spinous cell layer.
- Deep basophilic and granular cytoplasm with flat pale nuclei.

- **EM:** The cytoplasm shows 2 types of granules.

A. **Keratohyalin granules:**

- **Non membranous.** - Aggregate to form keratin filaments (tonofilaments)

B. **Membrane-coated lamellar granules:**

- Membranous granules. - Release a **lipid-rich secretion that fills spaces between cells.**

**4- Stratum Lucidum (Clear Layer):**

➤ **LM:**

- Thin, lightly stained, clear, homogeneous layer.
- Formed of much flattened cells.
- Nuclei are on their way to disappear by karyolysis.

➤ **EM:**

- Thickened cell membranes.
- Few remnants of desmosomes.
- Organelles disappear (by lysosomal activity).
- Nuclei appear as ghosts or completely absent
- Densely packed keratin filaments (Tono- fibrils) embedded in an electron-dense matrix formed by keratohyalin granules.

**5- Stratum Corneum (Horny Layer):**

- **LM:** Thick eosinophilic layers formed of heavily keratinized dead cells, called scales.

➤ **EM:**

- Thickened cell membranes attached together by remnants of desmosomes.
- Filled with mature keratin filaments (**Tono-fibrils**) embedded in amorphous matrix.
- No nuclei nor organelles.

## Non-Keratinocytes

### 1- Langerhans Cells:

- **Origin:** Bone marrow precursors migrate via blood to the dermis then epidermis.
- **LM:**
  - Represent 3-8% of epidermal cells.
  - They are stellate-shaped cells found mainly between cells of the stratum spinosum of epidermis.
  - In H.&E. skin sections; cell appears with a dark-staining nucleus and a pale clear cytoplasm.
  - They can be identified using vital stains.
- **EM:**
  - A prominent Golgi complex and numerous lysosomes
  - Special tennis-racquet-shaped granules (Birbeck's granules). Some may contain hydrolytic enzymes.
  - The nucleus is dark and highly irregular.
  - Absence of keratin filaments and desmosomes.
  - Absence of melanin granules.
  - Absence of cell junctions between them and keratinocytes.
- **Function:** Acts as antigen presenting cell; capable of binding antigen that contacts skin and then presenting it to T-lymphocytes. So, they have a significant role in skin immunological reactions (**allergic dermatitis**).

### 2- Merkel's Cells:

- **Origin:** Ectodermal in origin. They are modified epithelial cells.
- **LM:**
  - They resemble epidermal cells.
  - Present in-between cells of the basal layer. Abundant in highly sensitive skin like that of fingertips and at the bases of some hair follicles.
  - Free nerve fiber (sensory) traverses basal lamina to terminate as disc-shaped expansions beneath Merkel's cell forming Merkel cell-neurite **complex**.
- **EM:**
  - Cells are attached to neighboring keratinocytes by desmosomes.
  - Cytoplasm contains electron-dense granules resembling those of neuroendocrine cells elsewhere (APUD).
  - Deeply invaginated nucleus.
- **Function:** - Mechanoreceptors for light touch sensation.  
- Neurosecretory function (granules).

### 3- Melanocytes:

- **Origin:** Precursors arise from neural crest (ectoderm) and migrate to the skin early in development and differentiate to melanocytes.
- **LM:**
  - Cell bodies of melanocytes are present in-between and just below the cells of stratum Basale.
  - They have rounded cell bodies from which long irregular cytoplasmic processes extend between keratinocytes. Tips of these extensions terminate in invaginations of the cells present in stratum Basale and stratum spinosum.

- Cells have rounded pale-stained nuclei.
- **The H.&E-stained** skin sections **do not** demonstrate melanocytes
- **EM:**
  - Cell shows all characters of active protein synthesizing cells: abundant rough endoplasmic reticulum, prominent Golgi apparatus and mitochondria.
  - Granules are known as melanosomes.
  - Nucleus shows euchromatin and a prominent nucleolus.
  - No desmosomes between melanocytes and keratinocytes.
  - Hemidesmosomes are present to bind melanocytes to basal lamina.
- **Function of melanocytes:**
  - Melanin pigment is formed by the epidermal melanocytes (**as they can synthesize tyrosinase enzyme which is essential for melanin synthesis**).
  - Ultraviolet light speeds melanin synthesis.

### The Dermis

- Connective tissue under epidermis. - Thicker than epidermis.
- Irregular surface having projections (dermal papillae) which fit into concavities in the epidermis (epidermal ridges).
- Formed of **2 layers**: Papillary layer and Reticular layer

1. Papillary layer	2. Reticular layer
<ul style="list-style-type: none"> <li>• <b>Thinner</b> superficial layer</li> <li>• Forms dermal papillae.</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Thicker</b> deep layer</li> </ul>
<ul style="list-style-type: none"> <li>• Formed of <b>loose C.T.</b></li> </ul>	<ul style="list-style-type: none"> <li>• Formed of <b>dense C.T.</b></li> </ul>
<ul style="list-style-type: none"> <li>• <b>More cellular</b> (fibrocyte, lymphocyte, macrophage, mast cell, adipocyte).</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Less cellular</b> (fibrocyte, macrophage, lymphocyte, mast cell, adipocyte).</li> </ul>
<ul style="list-style-type: none"> <li>• Fine C.T. fibers (type III collagen &amp; elastic fibers).</li> </ul>	<ul style="list-style-type: none"> <li>• C.T. fibers type I (bundles) &amp; elastic fibers.</li> </ul>
<ul style="list-style-type: none"> <li>• More vascular (to nourish epidermis)</li> </ul>	<ul style="list-style-type: none"> <li>• Less vascular</li> </ul>
<ul style="list-style-type: none"> <li>• <b>Receptors:</b> Meissner's corpuscles.</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Receptors:</b> Pacinian corpuscles, Ruffini's end organ &amp; Krause's end bulb</li> </ul>

- **Dermal-epidermal junction:**
- Zigzag-like interdigitations between dermal papillae and epidermal ridges forming the fingerprints which are of medico legal importance.

**- Its importance:**

- Provide attachment of epidermis to dermis.
- Surface area for nutrition of epidermis.

❖ **Factors fixing epidermis to dermis:**

- 1- The basement membrane of epidermis.
- 2- Hemidesmosomes: between basal epidermal cells & basement membrane.
- 3- Dermal papillae interdigitating with epidermal ridges

### Thin (Hairy) Skin

- It covers all the body except palms, soles, tips and sides of fingers and toes.
- Eyelid has got the thinnest skin in the body.
- Thin skin has the basic skin structure as thick skin but with some differences.

### Differences between thick and thin skin.

	Thick skin	Thin skin
<b>Sites</b>	<ul style="list-style-type: none"> <li>• Palms &amp; soles</li> <li>• Tips, sides fingers &amp; toes</li> </ul>	Rest of the body
<b>Epidermis:</b>	Thicker	Thinner
1- Malpighian layer	Thicker	Thinner
2- Granular layer	Thicker (3-5)	Thinner(single)
3- Clear layer	Present	Less apparent
4- Horny layer	Very thick	Very thin
<b>Dermal papillae</b>	More, large, regular	Fewer, small, irregular
<b>Appendages:</b>		
Hair follicles	Absent	Present
Sebaceous glands	Absent	Present
Arrector pili muscles		
Sweat glands	More numerous	Less numerous

### Sweat gland

- **Type:** Simple tubular coiled glands.
- **Site:** Deep in the dermis, all over the body except: glans penis & nail beds.

	Eccrine sweat glands	Apocrine sweat glands
<b>Site</b>	<ul style="list-style-type: none"> <li>• All over the body except glans penis &amp; nail beds</li> <li>• More numerous</li> <li>• More in thick skin</li> </ul>	<ul style="list-style-type: none"> <li>• Thin skin of axillary, pubic &amp; perineal regions</li> <li>• Less numerous</li> <li>• Not present in thick skin</li> </ul>
<b>Mode of secretion</b>	<b>Merocrine (by exocytosis)</b>	
<b>Secretory part</b>	<ul style="list-style-type: none"> <li>• Small &amp; Narrow lumen</li> <li>• Formed of <b>three types of cells:</b> <ol style="list-style-type: none"> <li><b>1. Large (Clear) cells:</b> <ul style="list-style-type: none"> <li>▪ More numerous</li> <li>▪ Broad base, narrow apex.</li> <li>▪ Pale cytoplasm (glycogen).</li> <li>▪ <b>Intercellular canaliculi</b> between clear cells.</li> </ul> </li> <li><b>2. Small (dark) cells:</b></li> </ol> </li> </ul>	<ul style="list-style-type: none"> <li>• Large in size &amp; Wide lumen</li> <li>• Formed of <b>two types of cells:</b> <ol style="list-style-type: none"> <li><b>1. Simple cubical cells:</b> <ul style="list-style-type: none"> <li>▪ Eosinophilic cytoplasm</li> <li>▪ The apical cytoplasm contains numerous small granules that discharge their content by</li> </ul> </li> </ol> </li> </ul>



	<ul style="list-style-type: none"> <li>▪ Less numerous</li> <li>▪ Narrow base, wide apex</li> <li>▪ Dark cytoplasm (dark granules containing glycoprotein).</li> </ul> <p><b>N.B.:</b> Watery secretion of clear cells passes through canaliculi to lumen where it mixes with protein product of dark cells.</p> <p><b>3. Myoepithelial cells</b></p>	<p>exocytosis.</p> <p><b>2. Myoepithelial cells</b></p>
<b>Excretory duct</b>	<ul style="list-style-type: none"> <li>• Spiral course in dermis &amp; epidermis</li> <li>• Opens into epidermis</li> <li>• Lined by 2 layers of cubical cells</li> <li>• Appears darker than secretory part</li> </ul>	<ul style="list-style-type: none"> <li>• Spiral course in dermis</li> <li>• <b>Opens into a hair follicle</b></li> <li>• Lined by 2 layers of cubical cells</li> </ul>
<b>Function</b>	<ul style="list-style-type: none"> <li>• Sweat is a clear watery fluid (water, NaCl, urea &amp; ammonia) with low protein content.</li> <li>• Its main function is body temperature regulation.</li> </ul>	<ul style="list-style-type: none"> <li>• Start function at puberty.</li> <li>• They secrete viscous odorless secretion that becomes offensive by bacterial action.</li> </ul>

### Sebaceous Glands

- **Development:** develop as outgrowths of the external sheath of the hair follicle.
  - **Type:** Simple alveolar (acinar) or branched alveolar exocrine gland.
  - **Sites:** In the dermis of thin skin:
    - Usually associated with hairs.      - Rarely without hairs: eyelids.
  - **Structure:**
    - a) **Secretory part: each alveolus is lined by:**
      - **Basal flattened germinal cells:** large polyhedral cells are produced by mitosis of these basal cells.
      - **Large polyhedral vacuolated cells:** The cells gradually become filled with lipids.
    - b) **Excretory duct:**
      - Short & wide and opens in upper 1/3 of hair follicle.
      - Lined by stratified squamous epithelium continuous with hair follicle.
  - ❖ **Mode of secretion:** by holocrine secretion
    - The cell undergoes programmed cell death (apoptosis) and both the secretory product and cell debris are discharged from the gland through their short ducts.
- N.B. :** Hypodermis: is not a part of the skin (Greek; hypo = under, dermis = skin).

### Nerve Endings

- A. Receptors:** Receive external or internal stimuli and convert them to nerve impulses:
  - Exteroceptors: receive external stimuli.
  - Proprioceptors: receive stimuli from the muscle.
  - Interoceptors: receive internal stimuli.
- B. Effectors** that bring efferent nerve impulses to effectors (muscle or gland).

## Nerve Endings in Epithelium

### A- Receptors are exteroceptors

#### a) Free nerve endings:

- In epidermis of skin and cornea of eye.
- They are mechanoreceptors for pain, temperature and touch
- Nonencapsulated. Myelinated nerve loses its myelin below the basement membrane and passes in between the epithelial cells.

#### b) Merkel endings:

- Epidermis of hairless skin.
- Mechanoreceptors for touch.
- Nonencapsulated.
- The nerve loses its myelin sheath and forms a disc like expansion under Merkel cell near the base of the epidermis.

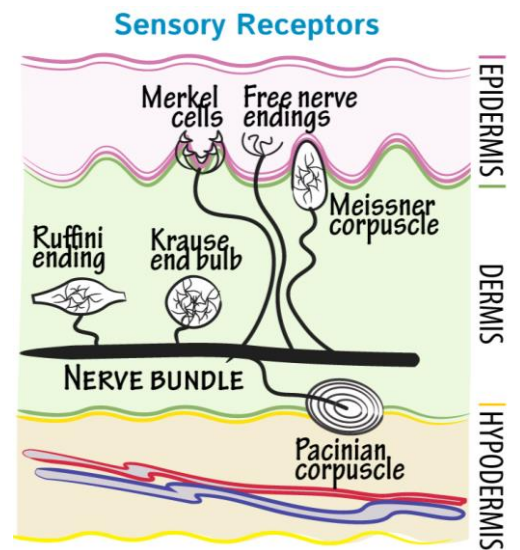
#### c) Peritracheal nerve endings:

- Present in hairy skin around hair follicle
- Mechanoreceptors for touch and movement of hair.
- Nonencapsulated.

#### d) Neuroepithelium endings:

- Taste buds in tongue for taste.
- Organ of Corti in ear for hearing.
- Macula utriculi, macula sacculi and cristae ampullaris for equilibrium.

**B) Effectors:** These are autonomic nerve endings supplying glandular epithelium as lacrimal and salivary glands. The unmyelinated nerve fibers form networks just outside the basal lamina of the epithelium. From there, branches penetrate the lamina and end between the bases of the glandular cells.



## Nerve Endings in Connective Tissue

- All are receptors;

#### 1- Free nerve endings:

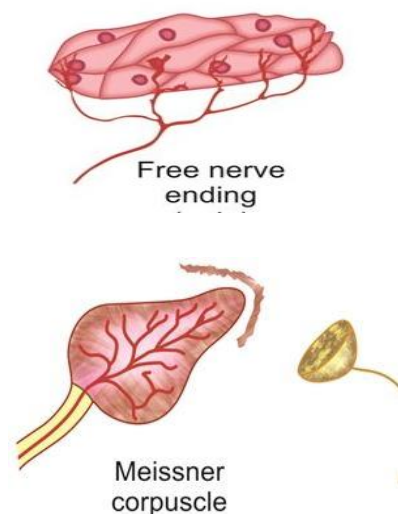
- Similar to those in epithelium.
- Present in dermis of skin and stroma of cornea.

#### 2- Meissner's corpuscle:

- Dermal papillae of skin especially in palm of hands and sole of feet.
- It is a mechanoreceptor for **touch**.
- Encapsulated, oval in shape.
- Axon loses its myelin to enter the corpuscle and spirals up between modified flattened Schwann cells, arranged transversely until it ends at upper pole of corpuscle.

#### 2- Krause's end bulb:

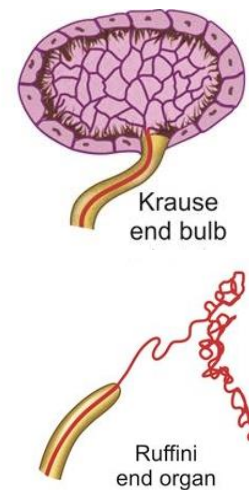
- Deep in dermis
- It is a mechanoreceptor for touch.



- Encapsulated, ovoid bodies.
- Axon enters the corpuscle after losing its myelin and branches repeatedly inside.

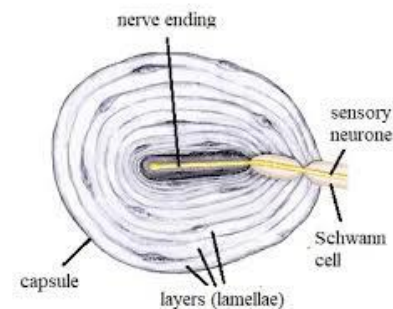
### 3- Ruffini corpuscles:

- Deep in dermis of skin especially in sole.
- It is a mechanoreceptor for stretching and twisting of skin.
- Encapsulated, fusiform bodies.
- The axon enters the capsule after losing myelin sheath and branches between parallel collagen fibers inside.



### 4- Pacinian corpuscle:

- Dermis & hypodermis of **skin**, periosteum of **bone**, **joint** capsule and C.T. of some organs as **pancreas**, **wall of the rectum & urinary bladder**.
- It is a mechanoreceptor for vibration and pressure that responds to displacement of the capsule lamellae. The Pacinian corpuscle in joint capsule is one of the **proprioceptors**.
- Encapsulated large ovoid up to 1mm in length
- It has a thin C.T. capsule enclosing 20-60 concentric lamellae consisting of very thin flat cells (probably modified Schwann cells) separated by narrow spaces filled with gel like material.
- Towards the center, the lamellae become closely packed.
- Myelinated nerve fiber enters the corpuscle at one pole. Its Schwann cell sheath becomes continuous with the capsule while myelin sheath ends inside the corpuscle. Naked nerve fiber runs parallel to the longitudinal axis and ends in a small expansion.



## Nerve Endings in Muscular Tissue

### A- Receptors: Muscle spindles:

- **Site:** in skeletal muscles. More numerous in muscle involved in fine movements as intrinsic muscle of hand and in antigravity muscles.
  - It is a mechanoreceptor for **stretch-muscle length**. **It is one of the Proprioceptors** within is responsible for regulation of the muscle tone through stretch reflex. It also keeps the CNS informed about the length of the muscle thereby indirectly influencing the control of voluntary muscle.
  - **Shape:** fusiform. They lie **parallel** to muscle fibers.
  - **Size:** up to 6 mm long but less than 1 mm in diameter.
  - **Structure:** Capsule surrounding lymph filled space that contains intrafusal muscle fibers and nerve fibers.
- **Intrafusal fibers:** much smaller than skeletal muscle fibers and they have central non striated area containing the nuclei. They are of 2 types:

- Nuclear bag type: the central nuclear area is dilated.
- Nuclear chain type: no dilatation and the nuclei are in the form of chain.
- **Afferent nerves**: unmyelinated sensory nerve fibers that envelope the intrafusal muscle fibers.

### Effectors: Motor end plate (Neuromuscular junction)

#### Sensory Receptors

- **Definition:** They are modified nerve endings of afferent fibers which receive (detect) different stimuli & convert (transform) them into action potentials
- **Functions:**
  - Detectors: Detect changes in the surrounding environment
  - Transducers: Transform any form of energy in the stimulus into action potentials
- **Classification:** According to
  1. **Its site:** - Superficial “Cutaneous”    -Deep    -Visceral    -Special sense
  2. **Physiological:**
    - i. **Mechanoreceptors:** Detect mechanical deformity in the receptors as:
      - Touch    - Pressure    - Sound (cochlear receptors)
      - Acceleration (vestibular receptors)
      - Blood pressure (baroreceptors)
      - They are found in: -Skin    -Mucous membrane    -Muscle    -Tendons  
-Joints (Proprioceptors)    - Blood vessels    -Lungs    -Inner ear
    - ii. **Thermoreceptors:**
      - In hypothalamus for body temperature regulation
      - In skin, mucous membrane: Detect cold & warm energy
    - B. **Chemoreceptors:** - Taste    - Smell    - Osmoreceptors    - Glucoreceptors  
- CO<sub>2</sub>    - O<sub>2</sub>    - H<sup>+</sup>
    - C. **Nociceptors:** Detect pain    D. **Electromagnetic:** Detect light
- **Properties:**
  1. **Specificity: (Muller's law):**
    - Each receptor is sensitive to one type of sensation called adequate stimulus eg light for photo receptors
    - Other forms of energy can stimulate the receptor, but it needs stronger stimulus than the adequate one
  2. **Excitability: Generator potential “Receptor potential” [RP]:**
    - **Def.:** It is a state of partial depolarization in the receptor membrane which occurs when the receptor is stimulated
    - Receptor potential spreads passively with decreasing its magnitude to :
      - Adjacent part of sensory nerve (unmyelinated) or
      - 1<sup>st</sup> node of Ranvier (myelinated nerves)
    - **If depolarization** reaches the firing level → it leads to action potential which is propagated by salutatory conduction
    - **As long as** there is receptor potential with enough magnitude to generate action potential → there is train of nerve impulses

- **Ionic basis of RP:** The energy of the stimulus causes nonspecific opening of Na<sup>+</sup> channels → Na<sup>+</sup> entry leading to partial depolarization
- **Number of opened channels:** Is directly proportional to intensity of stimulus.
- In some receptors (as photoreceptors) → the electromagnetic waves cause closure of Na<sup>+</sup> channels → hyperpolarization

**NB: Receptor potential is studied in Pacinian corpuscle (mechanoreceptor): It is stimulated by mechanical pressure which leads to deformity & generates receptor potential**

Receptor Potential	Action Potential
<ol style="list-style-type: none"> <li>1. A local state of partial depolarization which spreads passively</li> <li>2. Due to non-specific increase in permeability to Na<sup>+</sup></li> <li>3. Not obey all or non-law. <ul style="list-style-type: none"> <li>- It has a variable magnitude.</li> </ul> </li> <li>4. Can be graded &amp; its amplitude is increased by increasing intensity of stimulus.</li> <li>5. No absolute refractory period</li> <li>6. Can be summated</li> <li>7. Its duration is 5- 10 msec (longer than AP) → allow repetition of AP</li> <li>8. Not blocked by local anesthesia</li> </ol>	<ol style="list-style-type: none"> <li>1. It is complete depolarization followed by overshoot, reversal of polarity</li> <li>2. It Is due to increase in Na<sup>+</sup> &amp; K<sup>+</sup> permeability.</li> <li>3. Obey all or non-law . <ul style="list-style-type: none"> <li>- It has a fixed magnitude.</li> </ul> </li> <li>4. Can not graded</li> <li>5. Followed by absolute refractory period</li> <li>6. Can not be summated</li> <li>7. Its duration of spike: 2 msec</li> <li>8. Blocked by local anesthesia</li> </ol>

### 3. Adaptation of receptors:

- **Definition:** Adaptation is decline in the receptor potential and frequency of impulses inspite of constant maintained application of the stimulus

- **Classification:** According to rate of adaptation, receptors are classified into:

- **Rapidly adapting receptors (phasic)** eg touch receptors
  - They adapt rapidly to continuously applied stimuli but respond rapidly if change take place
- **Moderately adapting receptors** As: Temperature, Smell & Taste
- **Slowly adapting receptors (tonic)** eg:- Pain receptors - Muscle spindle
  - Alveolar stretch receptors
- Pain receptors are slowly adapting or they do not adapt at all
- Their function is: To keep the brain continuously informed about dangerous changes in environment.
- **Mechanism:** Each receptor has its own property of adaptation
  - **eg: 1- Rods & cones:** Adapt by changing the concentration of their pigment
  - 2- **Mechanoreceptors:** Adapt by:
    1. Remodeling (readjustment) of the receptor structure: Where maintained pressure → steady displacement in outer lamellae but inner lamellae of nerve fiber slip back to original. Position ending distortion → decline in generator potential
    2. Inactivation of Na<sup>+</sup> channels in terminal nerve fiber
    3. Inactivation of Na<sup>+</sup> channels in 1st node of Ranvier.



## Sensory Code

- **Definition:** It is the ability of CNS to recognize type “Modality”, site “Locality” & strength “Intensity” of sensation
- i. **Code For Type of Sensation:**
  - Each receptor is most sensitive & specialized to one type of stimuli
  - The sensation perceived to brain will be the same whatever the method of stimulation
  - This known as **MULLER LAW**.
- ii. **Code For Site of Sensation:**
  - Each part of body send sensory signal to particular area of the brain & the brain project the sensation to the same part of the body
  - This known as **LAW OF PROJECTION**
- iii. **Code For Strength of Sensation:**
  - Brain depends on frequency of action potential to determine the strength of sensation
  - Increase frequency mean increase in strength

## Somatic Sensations

- **Definition:** Feeling produced by application of stimulus
- **Classification:** Classified into:
  - General Sensations:
    - Somatic sensations      - Organic Sensation (Thirst, hunger, sexual desire)
  - Special sensation: - Hearing      - Vision      - Taste      - Smell      - Emotional: As fear
  - Somatic sensations

## Mechanoreceptive Sensation

### a- Tactile sensation:

#### 1- Touch: Types: **1- Crude touch:**

- **Receptors:** Free nerve ending & Hair end organs
- **Afferent:** A $\delta$  fibers
- **Pathway:** Ventral spino-thalamic tract
- Poorly localized      e.g. feeling of clothes & hair comb
- **Tested by:** A piece of cotton passed on skin while eyes are closed

#### **2- Fine touch:**

- **Receptors:** Merkel's & Meisner's
- **Afferent:** A $\beta$  fibers
- **Pathway:** Dorsal column      - Well localized

**a- Tactile localization:** It is the ability to localize the point touched while eyes are closed

**b- Tactile discrimination:** It is the ability to feel two points touched simultaneously as two separate points while eyes are closed

- The distance between the two touched points should be above the threshold distance.
- Threshold distance is shorter if:
  - A. Number of receptors is: More      B. Number of afferent fibers is: More
  - C. Area of cortical representation is: Greater      D. Central convergence of afferent is: Less

**c- Texture of materials:** It is the ability to know the texture of materials eg silk or wool by touching them while eyes are closed

#### 2- Tickling & itching: - Receptors: Free nerve endings

- **Afferent:** C fibers (different from pain fibers)
- **Pathway:** Ventral spino-thalamic tract
- Tickling is ability to feel light moving things on the skin as insects which cause local repeated mechanical stimulation
- **Itching** is the sensation caused by chemical substance secreted near the receptors as histamine, Kinins & proteolytic enzymes

3- **Stereognosis:** - Receptors: Mixture of receptors of different sensations

- **Afferent:** A $\beta$  fibers - Pathway: Dorsal column
- It is the ability to recognize the nature of familiar objects put in hand with both eyes closed It depends on:- All cutaneous & deep sensation  
- Previous knowledge about the object

4- **Pressure:** - **Receptors:** Pacinian corpuscle

- **Afferent:** - Crude: A $\delta$  fibers Fine: A $\beta$  fibers
- **Pathway:** Dorsal column
- It enables the person to know the weights of objects & discriminates between different weights

5- **Vibration:** - **Receptors:** -Meissner's corpuscle: Responds to vibration up to 80 cycles/sec

- Pacinian corpuscle: Responds to vibration up to 500 cycles/sec
- These receptors contribute to sense of roughness when hand is passed over rough
- **Afferent:** A $\beta$  fibers
- **Pathway:** Dorsal column
- Vibration is rhythmic repetitive pressure sensation
- It is felt when tuning fork put on bony prominences (as leg malleoli) to allow magnification of stimulus and avoid its damping by soft tissues
- Impaired vibration sense: is an early diagnostic sign in degeneration of posterior column of spinal cord
- e.g. : 1- Uncontrolled Diabetes mellitus "DM " 2- Pernicious anemia "PA"

**b- Kinesthetic sensation: Proprioceptive sensation:**

- **Receptors: Types:** -Rapidly adapting: Pacinian corpuscle (for rate of movement)  
- Slowly adapting: Muscle spindle & Golgi organ
- **Sites:** A) In: - Small joints as fingers - Large joints as knee  
B) In ligaments & tendons
- **Pathway:** Dorsal column
- **They inform the CNS about:**
- 1- Static: Sense of position of different parts of body
- 2- Kinetic (dynamic): Sense of movements & Rate of movements of different parts of body

**NB:** - Joints→ For each degree of angulations, there is specific receptors in joints which discharge to specific area in cortex .

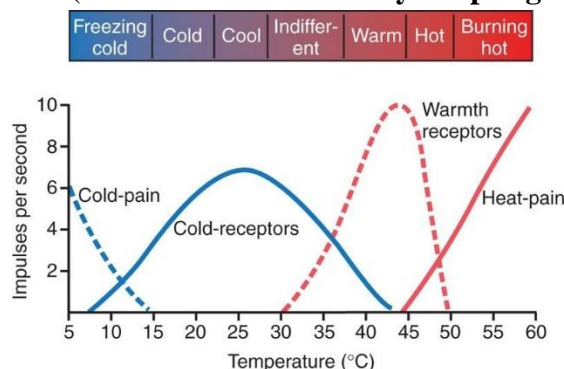
In thalamus, there is specific neuron for slow rate of movement and other for high rate of movement

- **Proprioceptive impulses go to:**
  - Cerebellum: Via spino-cerebellar tract to keep equilibrium
  - Cerebral cortex: Via dorsal & ventro-lateral tract.

### Thermal Sensation

- **Definition:** Sense of: - Warm                      -Cold
- **Thermoreceptors :**
  - **Types:**
    - **Cold receptors:** Free nerve ending attached to: C & A $\delta$  fibers
    - **Warm receptors:** Free nerve endings attached to: C fibers
    - **Two subtypes of pain receptors** (high threshold receptors):
- **Cold pain receptors:** For freezing cold
- **Heat pain receptors:** For burning hot sensation
- **Characters: -** Are located immediately under the skin
  - **Number:** Cold receptors: Are more numerous than warm receptors
  - **Distribution:** Greatest in: Lips    Moderate in: Fingers tips    Least in: Trunk
  - **Mechanism of stimulation:** Stimulated chemically by:
    - ✓ Accumulated metabolites due to change in metabolic rate
    - ✓ Each 10° Change increase the concentration of metabolites two folds
  - **Adaptation:** Warm receptors → Adapt more rapidly than cold receptors

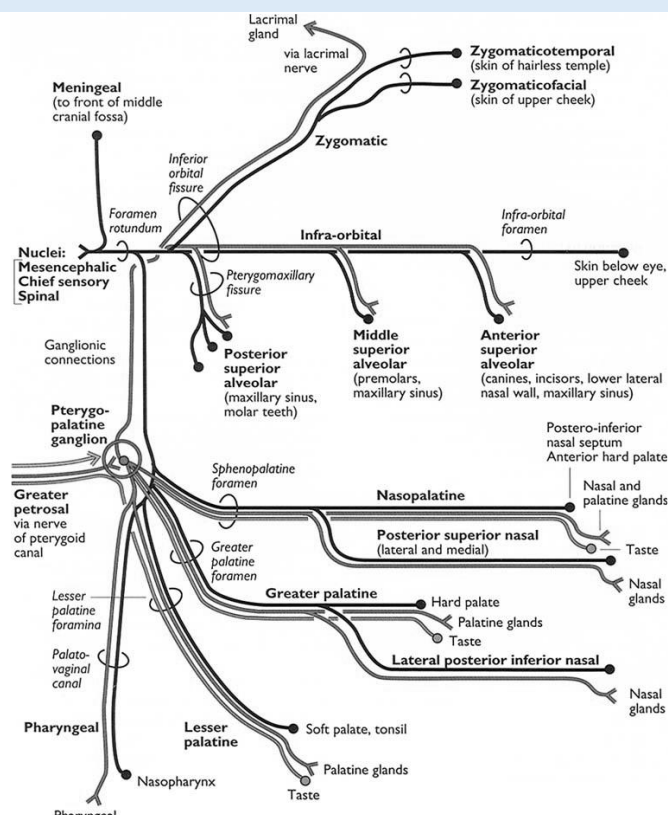
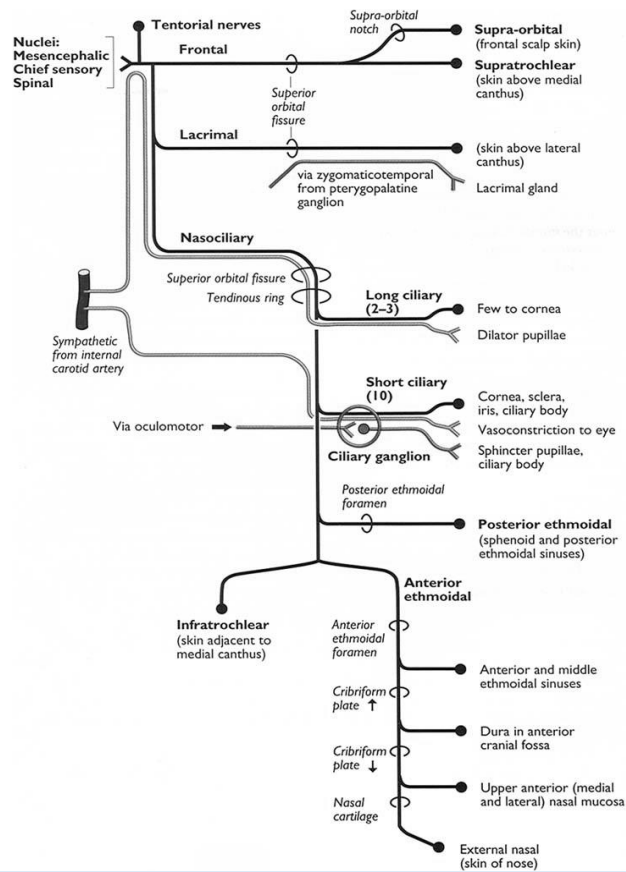
(but both are moderately adapting receptors)



***Discharge frequencies at different skin temperatures of a cold-pain fiber, a cold fiber, a warmth fiber, and a heat-pain fiber***

- **Detection of thermal sensation:**
    - **According to range of temperature they detect:**
      - **Cold receptors:** - Stimulated from 10-43° - Maximum rate of discharge at 25°C
      - **Warm receptors:** - Stimulated from 30-50°C -Maximum rate of discharge at 45°C
      - **Cold pain receptors:** - Stimulated from 5-10°C - Maximum rate of discharge at 5°C
      - **Warm pain receptors:** Stimulated above 45°C
- NB: - At 0°C :** Degree Centigrade “Celsius” there is no action potentials ie anesthesia
- **At 35°C:** - Comfort zone exist where awareness of temperature disappears
    - Due to equal discharge of warm & cold receptors
- **Temperature sensation perceived depends on:**
    - The original skin temperature
    - The rate of temperature change
    - The surface of the skin exposed to temperature change

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## TRIGEMINAL NERVE

## Cranial nerves

- ❖ It is attached to pons.
- ❖ It contains sensory & motor fibers.
- ❖ It divides into 3 branches (ophthalmic, maxillary & mandibular).

### OPHTHALMIC NERVE

- ❖ It contains sensory fibers.
- ❖ Divides into 3 branches (lacrimal, frontal & nasociliary). They all pass through sup orbital fissure.

#### **Branches and Distribution:**

<i>Branch</i>	<i>Course, branches &amp; distribution</i>
<b>Lacrimal</b>	<ul style="list-style-type: none"> <li>• To lacrimal gland.</li> <li>• Palpebral branch → upper lid</li> </ul>
<b>Frontal</b>	<ul style="list-style-type: none"> <li>• Supratrochlear N → skin of forehead</li> <li>• Supraorbital N → supraorbital foramen → skin of forehead</li> </ul>
<b>Nasociliary</b>	Supply skin over bony & cartilaginous nose, cornea & ethmoidal & sphenoid air sinuses

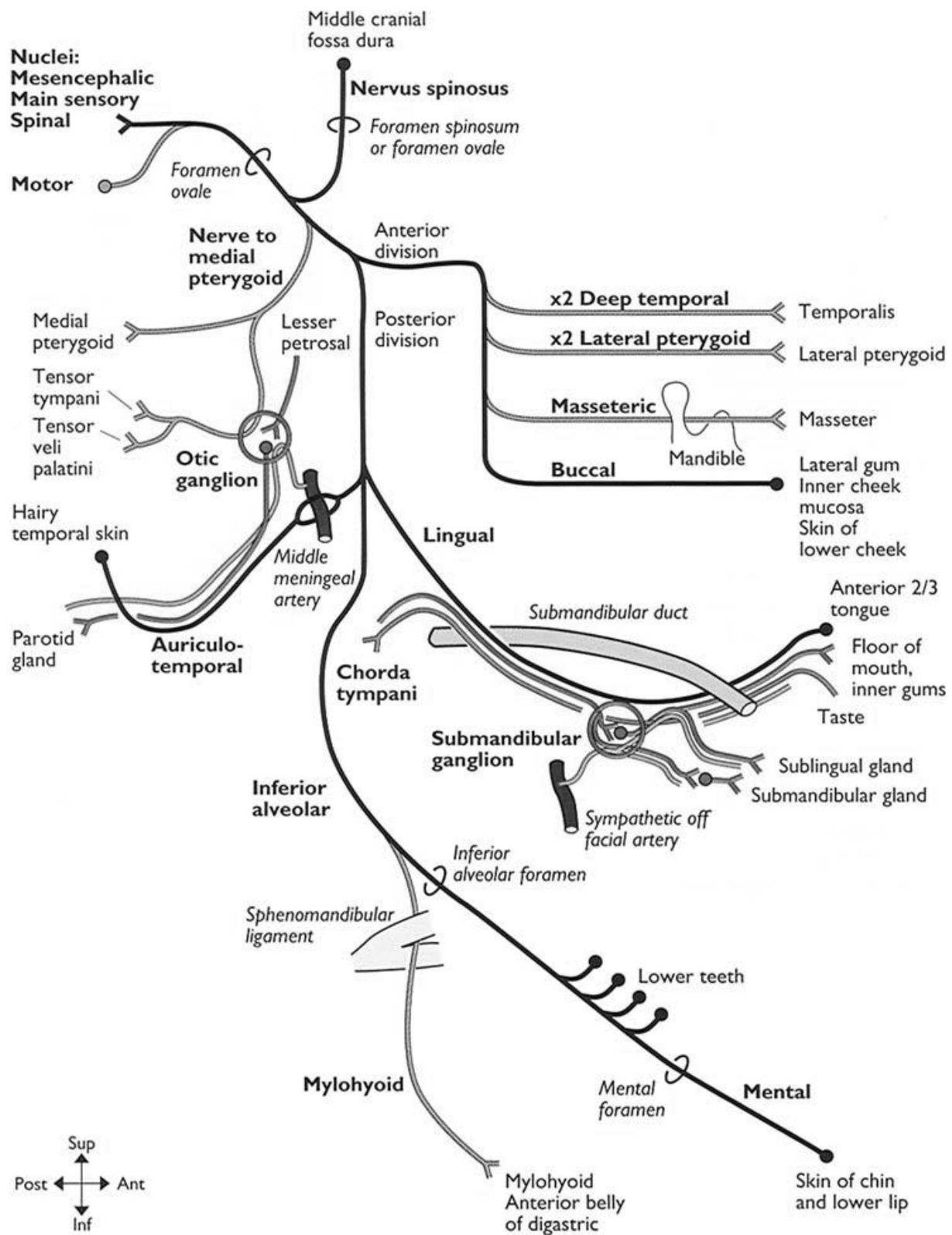
### MAXILLARY NERVE

- ❖ It contains sensory fibers.
- ❖ Passes through foramen rotundum to inf orbital fissure.

#### **Branches and distribution:**

<i>Branch</i>	<i>Course, branches &amp; distribution</i>
<b>Meningeal</b>	Supply meninges
<b>Zygomatic</b>	Passes through inf orbital fissure <ul style="list-style-type: none"> <li>• Zygomaticofacial → skin of the cheek (upper part)</li> <li>• Zygomaticotemporal → non hairy temporal region</li> </ul>
<b>Sphenopalatine</b>	Supply the nose
<b>Pharyngeal</b>	Supply the pharynx
<b>Greater &amp; lesser palatine</b>	Supply the palate
<b>Sup alveolar (post, middle &amp; ant)</b>	Supply upper jaw & maxillary sinus
<b>Infraorbital</b>	<b>Palpebral</b> Lower lid
	<b>Nasal</b> Ala of nose
	<b>Labial</b> Upper lip





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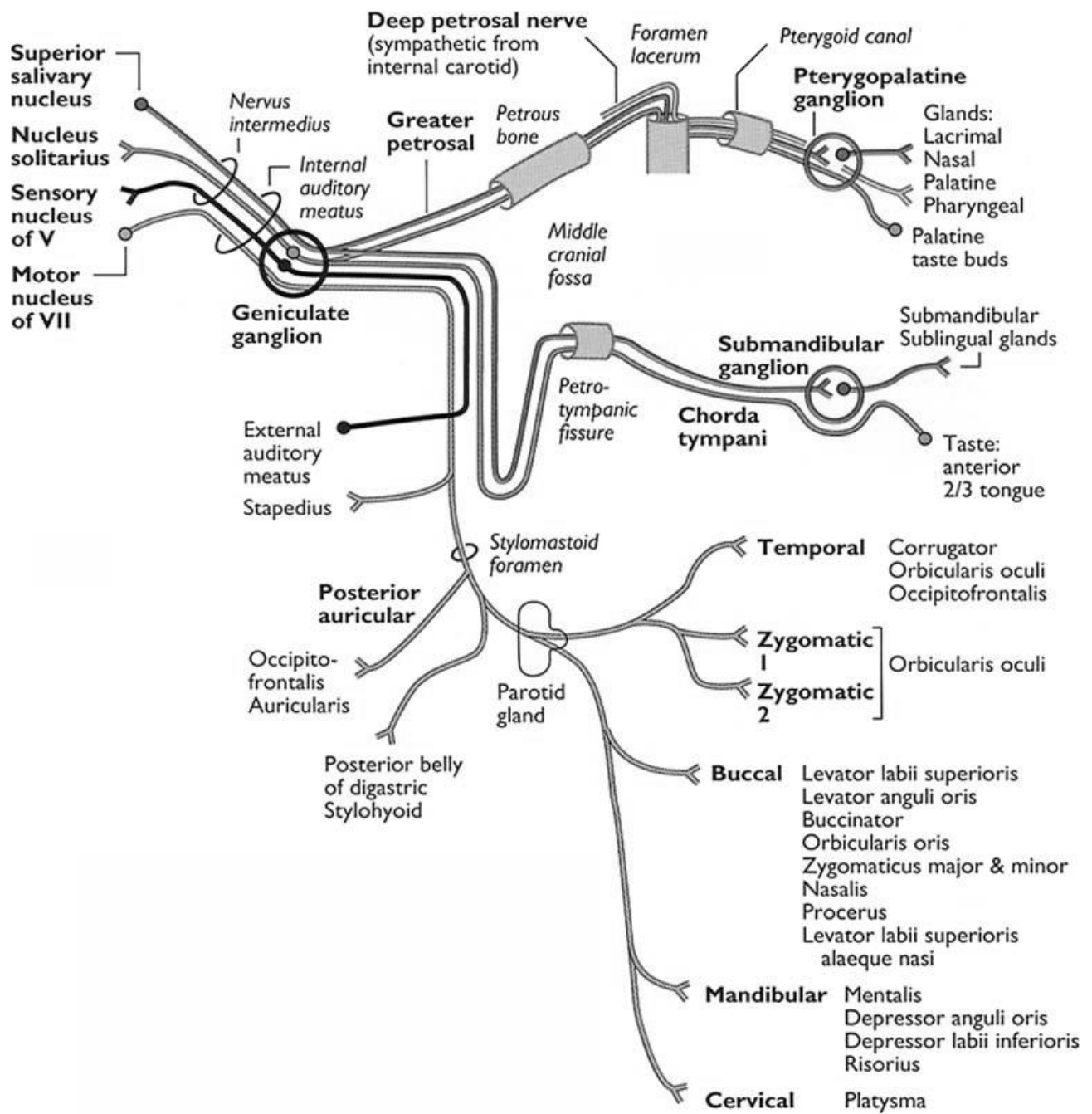
## Mandibular nerve

## MANDIBULAR NERVE

- ❖ It contains sensory & motor fibers.
- ❖ Passes through foramen ovale.
- ❖ Divides into ant and post divisions.

### Branches and Distribution:

<i>Branch</i>		<i>Course, branches &amp; distribution</i>
<b>Trunk</b>	<b>Meningeal (nervus spinosus)</b>	Reenter skull through foramen spinosum & supply meninges
	<b>N to med pterygoid</b>	Supply med pterygoid, tensor palati & tensor tympani
<b>Ant division</b>	<b>Ns to lat pterygoid</b>	Lat pterygoid
	<b>N to masseter</b>	Masseter
	<b>Deep temporal Ns</b>	Temporalis
	<b>Buccal</b>	Skin over buccinators
<b>Post division</b>	<b>Auriculotemporal</b>	<ul style="list-style-type: none"> <li>• Passes deep to neck of mandible</li> <li>• Supply outer surface of auricle &amp; hairy temporal region</li> </ul>
	<b>Lingual</b>	<ul style="list-style-type: none"> <li>• Passes near the lower 3<sup>rd</sup> molar</li> <li>• Supply ant 2/3 of the tongue with general sensations</li> <li>• <i>Joined by chorda tympani N (of facial) which supply the same area with taste</i></li> </ul>
	<b>Inf alveolar</b>	<ul style="list-style-type: none"> <li>• Gives <u>mylohyoid N</u>: runs in mylohyoid groove → supply mylohyoid and ant belly of digastric muscle</li> <li>• Passes through mandibular foramen &amp; supply lower teeth</li> <li>• Emerges from mental foramen as mental N &amp; supply chin &amp; lower lip</li> </ul>



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## Facial nerve

## FACIAL NERVE

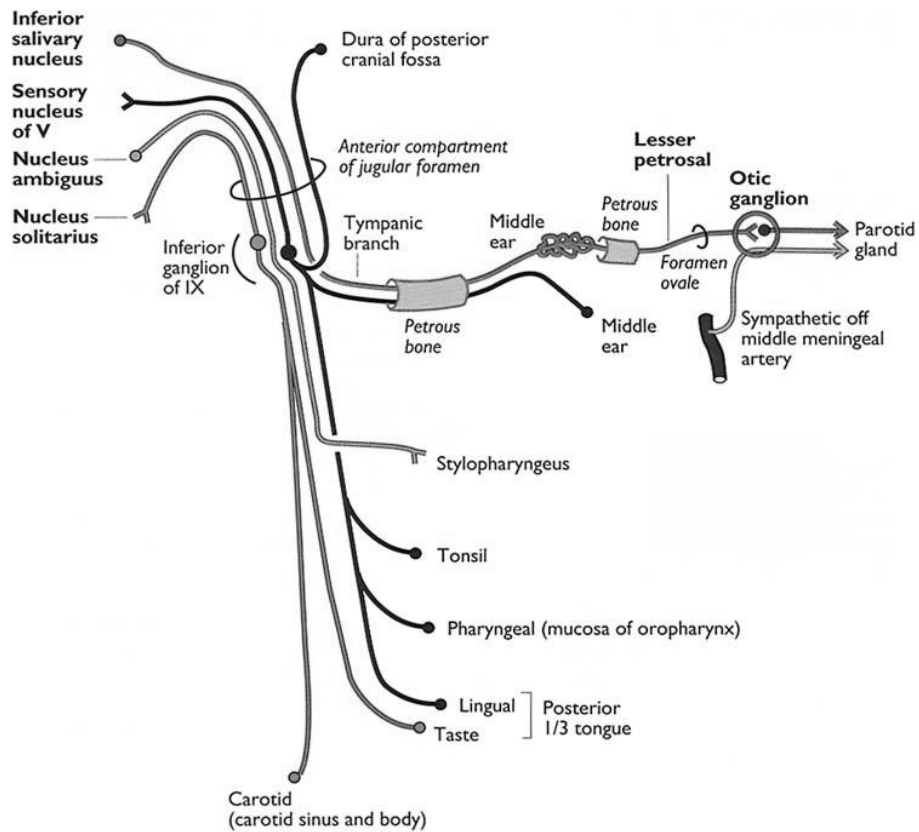
- ❖ It is attached to pons.
- ❖ It contains motor, sensory, taste & parasympathetic fibers.
- ❖ It passes through internal auditory meatus → facial canal (in the petrous bone) → stylomastoid foramen → parotid gland.

### **Branches and Distribution:**

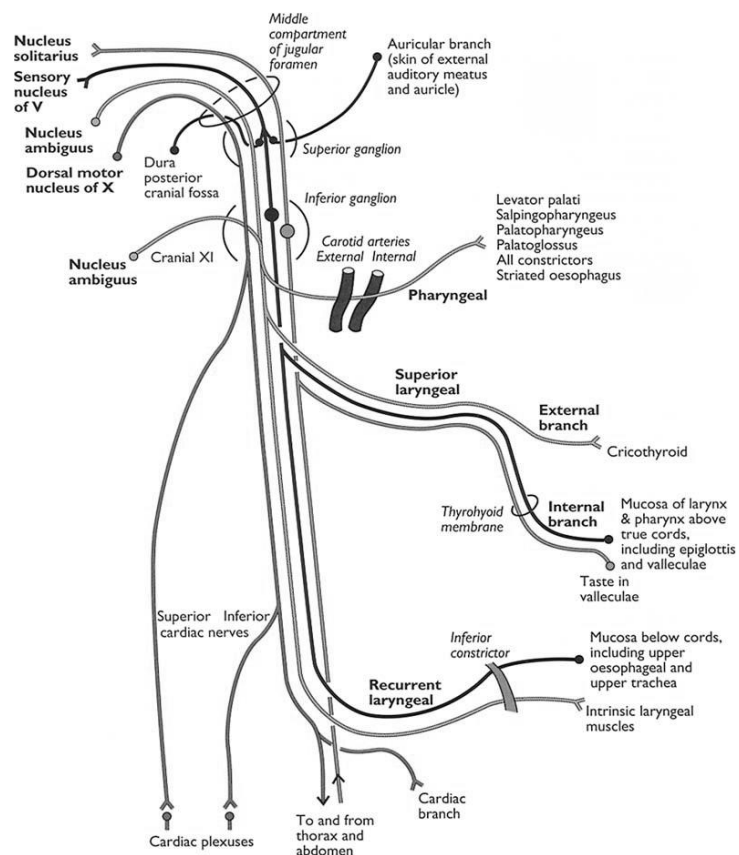
<i>Branch</i>	<i>Course, branches &amp; distribution</i>
<b>Greater petrosal N</b>	<ul style="list-style-type: none"> <li>• Arises in middle ear → passes through its foramen</li> <li>• Supply lacrimal gland, nose, pharynx &amp; palate with parasympathetic fibers</li> <li>• Supply palate with taste</li> </ul>
<b>Chorda Tympani</b>	<ul style="list-style-type: none"> <li>• Arises in middle ear → passes to infratemporal fossa → join the lingual N (of mandibular)</li> <li>• It supplies submandibular &amp; sublingual salivary glands with parasympathetic fibers</li> <li>• It supplies ant 2/3 of tongue with taste</li> </ul>
<b>N to stapedius</b>	Arises in middle ear & supply stapedius
<b>Sensory branch</b>	Sensory to external ear
<b>Post auricular</b>	Occipital belly of occipitofrontalis
<b>Digastric</b>	Post belly of digastric
<b>Stylohyoid</b>	Stylohyoid muscle
<b>Temporal</b>	Frontal belly of occipitofrontalis & orbicularis oculi
<b>Zygomatic</b>	Muscles near zygomatic arch & orbicularis oculi
<b>Buccal</b>	Buccinators
<b>Mandibular</b>	Muscles of lower lip
<b>Cervical</b>	Platysma

### **Control of facial motor nucleus:**

- The cerebrum (through corticonuclear fibers) controls the whole facial motor nucleus of the opposite side. But it only controls the upper part of the nucleus of the same side. So, the upper part of the facial motor nucleus (supplying muscles of upper part of face) receives bilateral corticonuclear fibers, while the lower part (supplying muscles of lower part of face) receives only contralateral fibers.
- Accordingly:
  - Lesion above the facial motor nucleus will lead to paralysis of the muscles of lower part of opposite side only.
  - Lesion of the nucleus or the facial nerve will lead to paralysis of all the muscles of the same side.



### Glossopharyngeal nerve



### Vagus nerve

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## GLOSSOPHARYNGEAL NERVE

- ❖ It is attached to medulla.
- ❖ It contains motor, sensory, taste & parasympathetic fibers.
- ❖ It passes through jugular foramen.

### **Branches and Distribution:**

<i>Branch</i>	<i>Course, branches &amp; distribution</i>
<b>Meningeal</b>	Reenter skull through jugular foramen & supply meninges
<b>Tympanic N</b>	<ul style="list-style-type: none"> <li>• Enters the middle ear → sensory innervation</li> <li>• Continue as lesser petrosal N → foramen ovale → Parasympathetic to parotid gland</li> </ul>
<b>N to stylopharyngeus</b>	Stylopharyngeus
<b>Pharyngeal branches</b>	Sensory to pharynx & tonsils
<b>Lingual branches</b>	Sensory & taste to post 1/3 of tongue

## VAGUS NERVE

- ❖ It is attached to medulla.
- ❖ It contains motor, sensory, taste & parasympathetic fibers.
- ❖ It passes through jugular foramen.

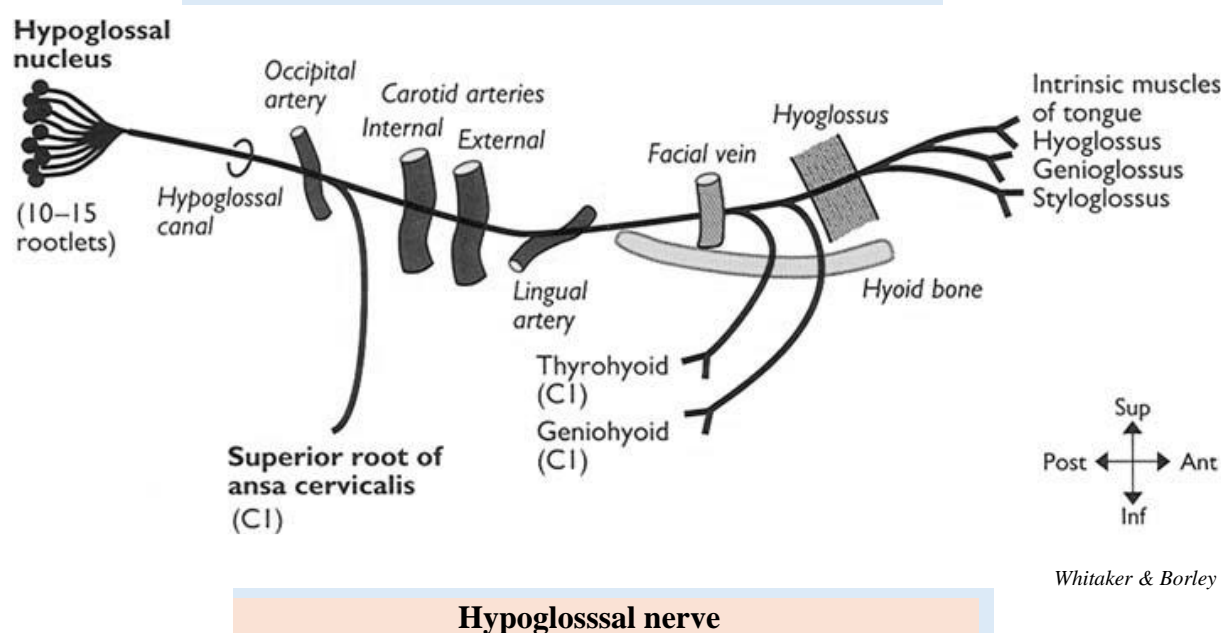
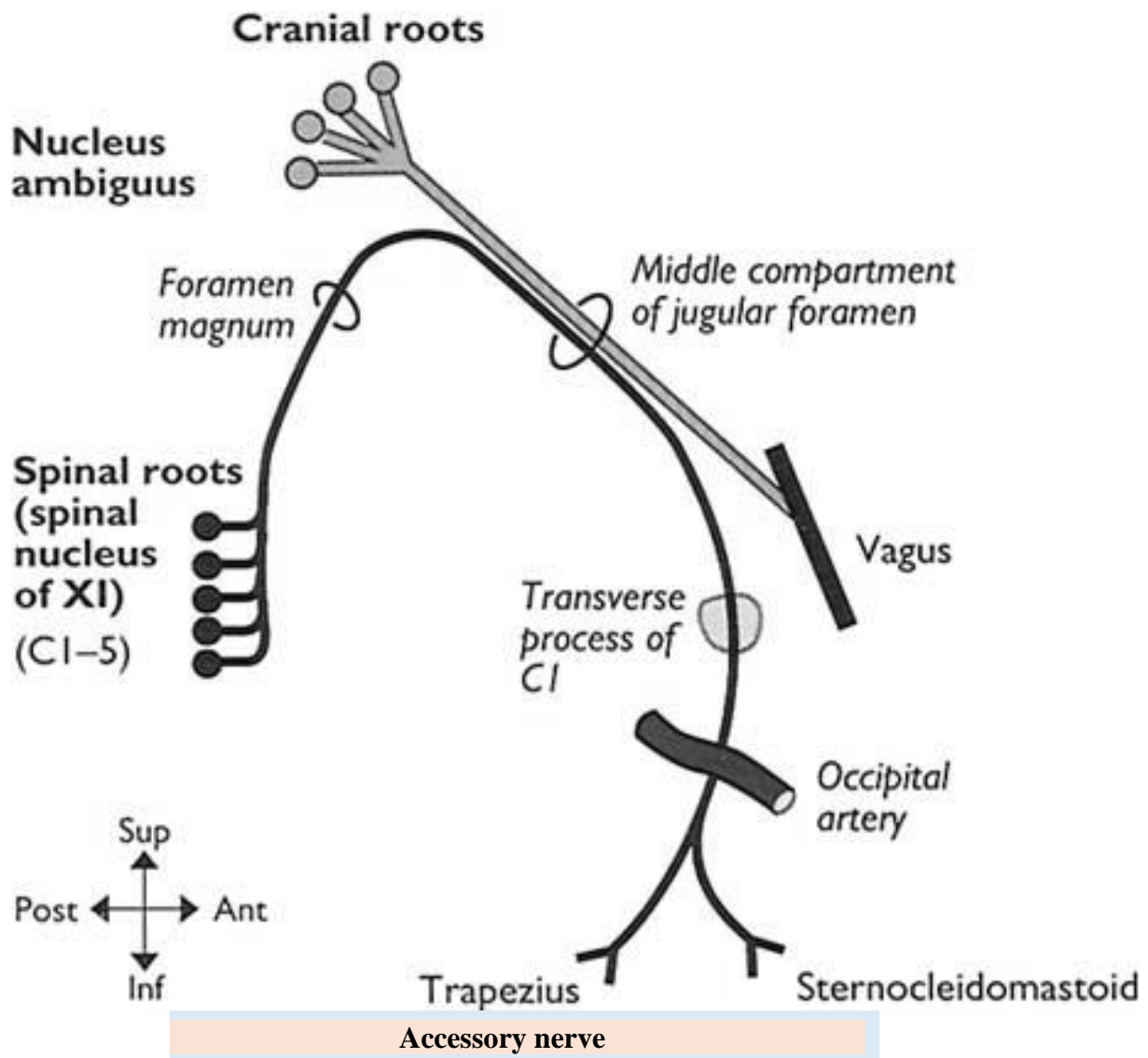
### **Branches and Distribution (In the head & neck):**

<i>Branches</i>	<i>Course, branches &amp; distribution</i>
<b>Meningeal</b>	Reenter skull through jugular foramen & supply meninges
<b>Pharyngeal</b>	<ul style="list-style-type: none"> <li>• <i>Its fibers are mainly from cranial accessory (through vagus)</i></li> <li>• <i>Supply all Ms of Pharynx except stylopharyngeus &amp; all Ms of Palate except tensor palati</i></li> </ul>
<b>Sup laryngeal N</b>	a) <u>Internal laryngeal N</u> : supply root of tongue & epiglottis (general & taste sensations) & larynx (general sensation) b) <u>External laryngeal N</u> : supply cricothyroid
<b>Recurrent laryngeal N (Rt)</b>	<ul style="list-style-type: none"> <li>• The sensory fibers from vagus (supply the larynx)</li> <li>• <i>The motor fibers from cranial accessory (through vagus) → supply all muscles of larynx except cricothyroid</i></li> </ul>

### **N.B.:**

- The italic branches are branches of cranial accessory N (through vagus).
- External & recurrent laryngeal nerves are closely related to the arteries of thyroid gland & could be injured during thyroid operations. Injury of recurrent laryngeal N leads to hoarseness of voice, while injury of external laryngeal N leads to loss of high pitched voice.
- The vagus N gives other branches in thorax & abdomen (parasympathetic to viscera).





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## ACCESSORY NERVE

### CRANIAL ACCESSORY NERVE

- ❖ It is attached to medulla.
- ❖ It contains motor fibers only.
- ❖ It is joined by spinal accessory intracranial.
- ❖ It passes through jugular foramen, where spinal accessory separates from it.
- ❖ It joins the vagus N & distributes its fibers through branches of vagus.
- ❖ It supplies all muscles of pharynx except stylopharyngeus and all muscles of palate except tensor palati (through the pharyngeal branch of vagus). And supplies all muscles of Larynx except cricothyroid (through the recurrent laryngeal branch of vagus).

### SPINAL ACCESSORY NERVE

- ❖ It is not a cranial nerve, it is formed of fibers from C1-5 (ant rami).
- ❖ It enters the skull through foramen magnum → join the cranial accessory N → passes through jugular foramen → leaves the cranial accessory N.
- ❖ It supplies sternomastoid & trapezius.

## HYPOGLOSSAL NERVE

- ❖ It is attached to medulla.
- ❖ It contains motor fibers only.
- ❖ It passes through hypoglossal (ant condylar) foramen.

#### **Branches & distribution:**

- It supplies all muscles of the tongue except (palatoglossus).

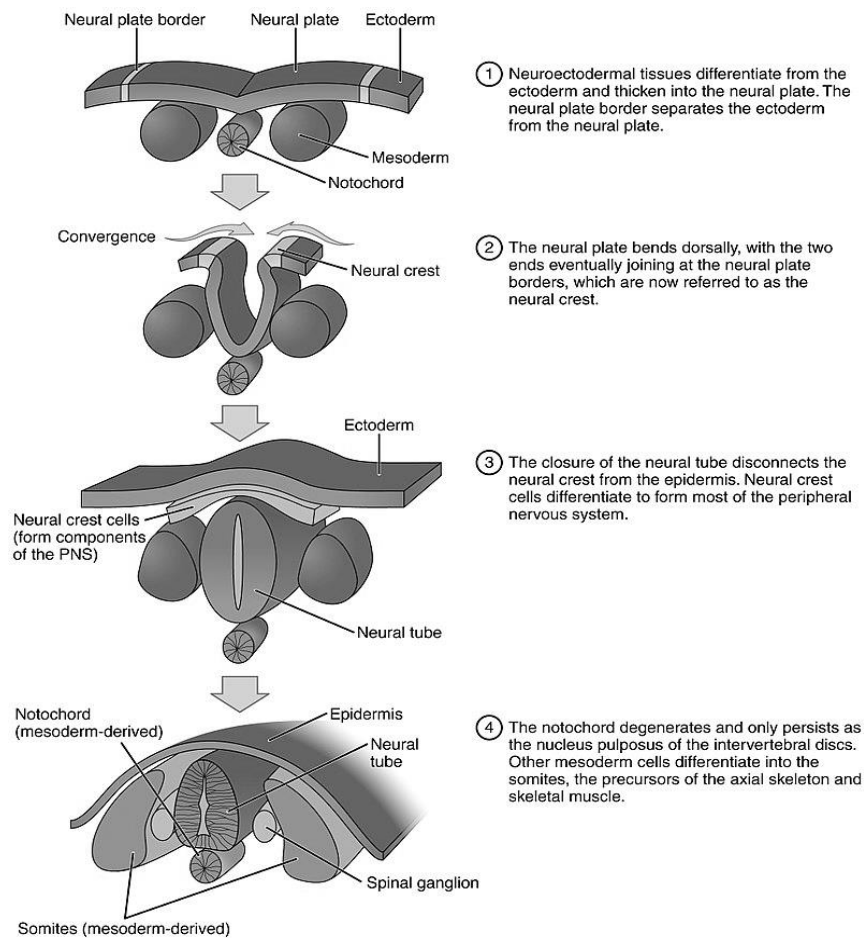
**N.B.:** hypoglossal N is joined by fibers from C1. These fibers give the following branches:

- 1) **Meningeal branch:** supply meninges.
- 2) **N to geniohyoid.**
- 3) **N to thyrohyoid.**
- 4) **Descendens hypoglossi:** it joins descendens cervicalis (C2-3) to form ansa cervicalis, which supply all infrahyoid muscles except thyrohyoid.

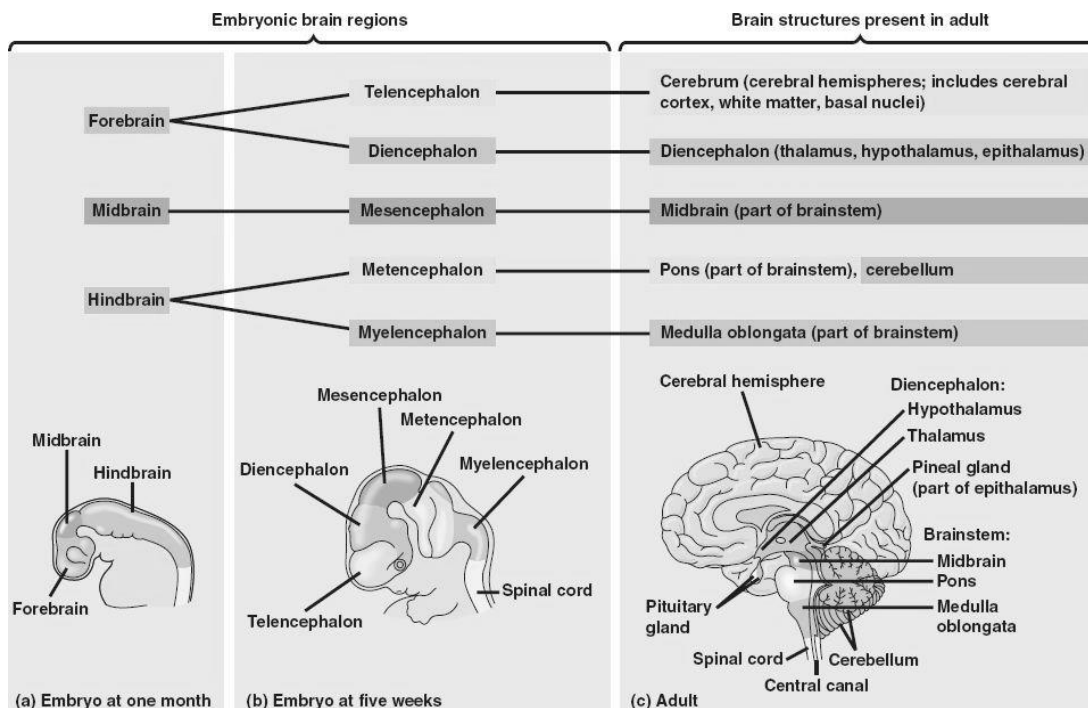
#### **Control of hypoglossal nucleus:**

- The cerebrum (through corticonuclear fibers) controls the hypoglossal nucleus of the opposite side, But not of the same side.
- Accordingly:
  - Lesion above the hypoglossal nucleus will lead to paralysis of the opposite hypoglossal nerve.
  - Lesion of the nucleus or the hypoglossal nerve will lead to paralysis of the nerve at the same side.

**Applied Anatomy:** injury to hypoglossal N will lead to paralysis of genioglossus (responsible for deviation of tongue to opposite side), leading to a deviation of tongue to the same side.



## Neural tube



## Development of brain

Pinterest

## Embryological Preview

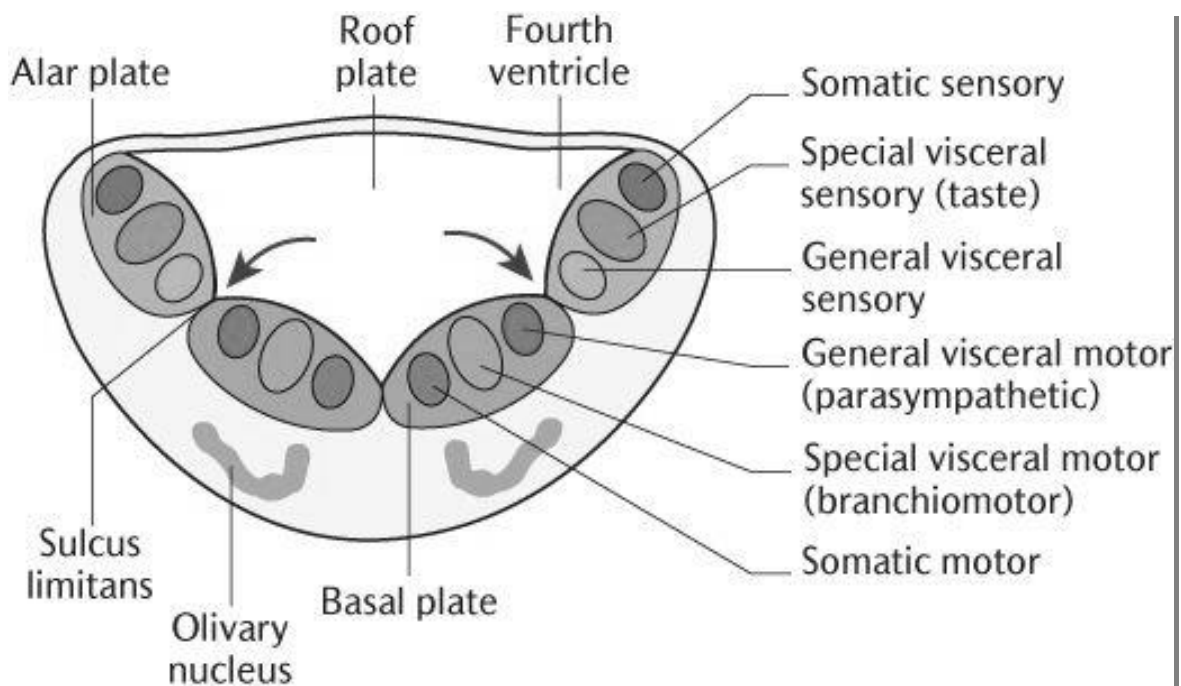
### Neural tube

#### ❖ Formation of the neural tube:

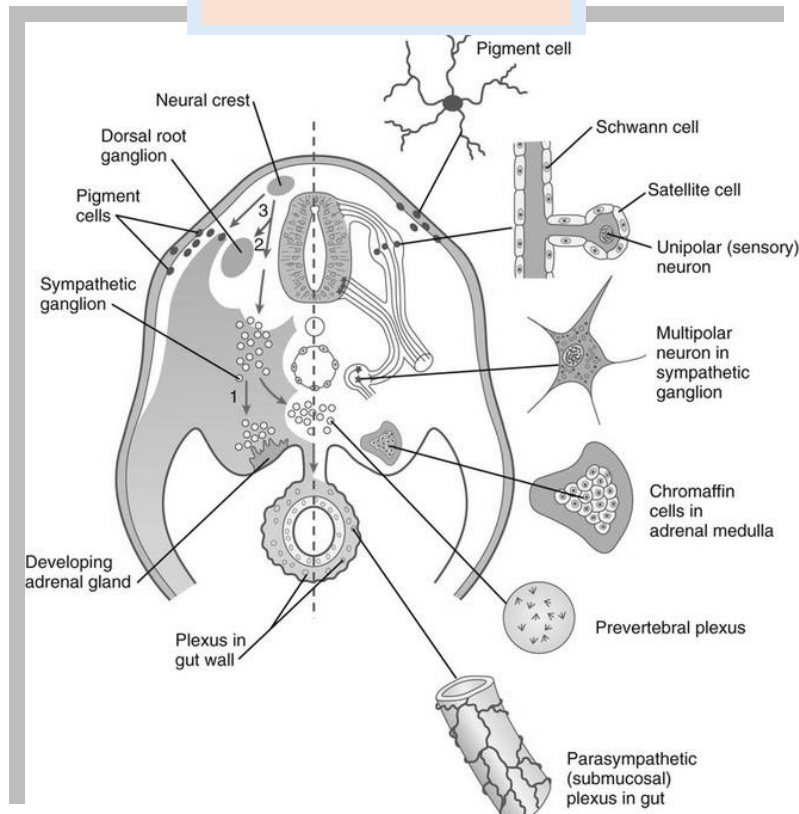
- The central part of the ectoderm between primitive node and prechordal plate thickens to form **neural plate**.
- The neural plate invaginates to form **neural groove**, which has two **neural folds** on its sides. The junction between the ectoderm and the neural groove on each side shows a longitudinal strip called **neural crest**.
- The neural folds fuse with each other to form the **neural tube**.
- The neural tube separates from the surface ectoderm and sinks down below it but above the notochord. The neural crest becomes dorsolateral to the neural tube.
- The neural tube has two openings at its ends called the cranial and caudal **neuropores**, which close by the end of the 4<sup>th</sup> week.

#### ❖ Differentiation of the neural tube

- The **lateral wall** of the neural tube is thickened forming 2 lateral walls, each is further divided into:
  - Basal lamina:** ventral, develops into motor cells
  - Alar lamina:** dorsal, develops into sensory cells
- The **cranial** part of the neural tube enlarges and develops into the **brain**. While the **caudal** part develops into the **spinal cord**
- The enlarged cranial part shows 3 dilatations (**brain vesicles**):
  - 1] **Prosencephalon** (forebrain): further develops into:
    - a) **Telencephalon:** develops into cerebral hemispheres and its lumen becomes lateral ventricles
    - b) **Diencephalon:** develops into (thalamus, hypothalamus and epithalamus). and its lumen becomes third ventricle
  - 2] **Mesencephalon:** develops into the midbrain and its lumen becomes cerebral aqueduct.
  - 3] **Rhombencephalon:** further divided into
    - a) **Metencephalon:** develops into the pons
    - b) **Myelencephalon:** develops into the medulla
    - c) **Cerebellum**
- The alar laminae in the Rhombencephalon shifts laterally so that the lumen becomes posterior and widens forming the fourth ventricle. Accordingly, the alar laminae become lateral and the basal laminae become medial.



### Brain stem columns



### Derivatives of neural crest

*Pocketdentistry/ Basicmedicalkey*



- In the brain stem, the alar lamina divides into 4 longitudinal sensory columns while the basal lamina divides into 3 longitudinal motor columns. These **columns** will further divide into cranial nerves nuclei and They are (from lat to med):
  - 1] **Special somatic afferent (GVA):** develops into nuclei receiving auditory and equilibrium sensations.
  - 2] **General somatic afferent (GVA):** develops into nuclei receiving somatic sensations.
  - 3] **Special visceral afferent (SVA):** develops into a nucleus receiving taste sensation.
  - 4] **General visceral afferent (GVA):** develops into nucleus receiving visceral sensations.
  - 5] **General visceral efferent (GVE):** develops into nuclei supplying viscera with parasympathetic fibers.
  - 6] **Special visceral efferent (SVE):** develops into nuclei supplying somatic muscles derived from pharyngeal arches.
  - 7] **Special efferent (SE):** develops into nuclei supplying somatic muscles derived from somites.
- In the spinal cord, the lateral wall also divides into:
  - Basal lamina:** ventral, develops into the motor cells (ventral horns).
  - Alar lamina:** dorsal, develops into the sensory cells (dorsal horn).
- The caudal part of the spinal cord is stretched and transmitted into **filum terminale**.

#### ❖ **Congenital anomalies:**

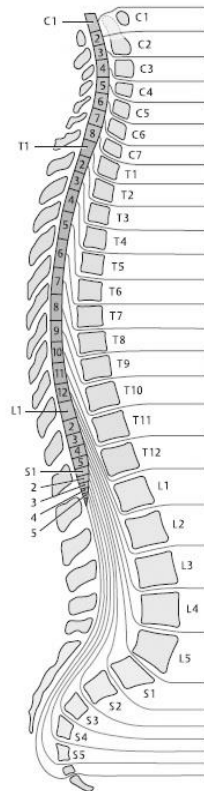
- **Hydrocephalus:** enlarged ventricles (and skull) due to obstruction in the lumen of the neural tube (usually cerebral aqueduct).
- **Anencephaly:** failure of closure of the cranial neuropore. The cerebral hemisphere (as well as the covering skull vault) is not developed.
- **Spina bifida:** failure of fusion of the laminae of the vertebrae. It may be occult or accompanied by protrusion of meninges, spinal cord, or both.
- **Meningocele:** a meningeal sac protrudes through a vertebral defect, The neural tube develops normally.
- **Meningomyelocele:** part of spinal cord and meninges protrude through a vertebral defect. The neural tube is usually fused normally.
- **Myelocele:** the spinal cord is exposed through a vertebral defect. This is due to failure of fusion of the neural folds into neural tube.

**N.B.:** the development of the neural tube is the inducer of the development of the surrounding skull and vertebral column. This is why combined congenital anomalies are common.

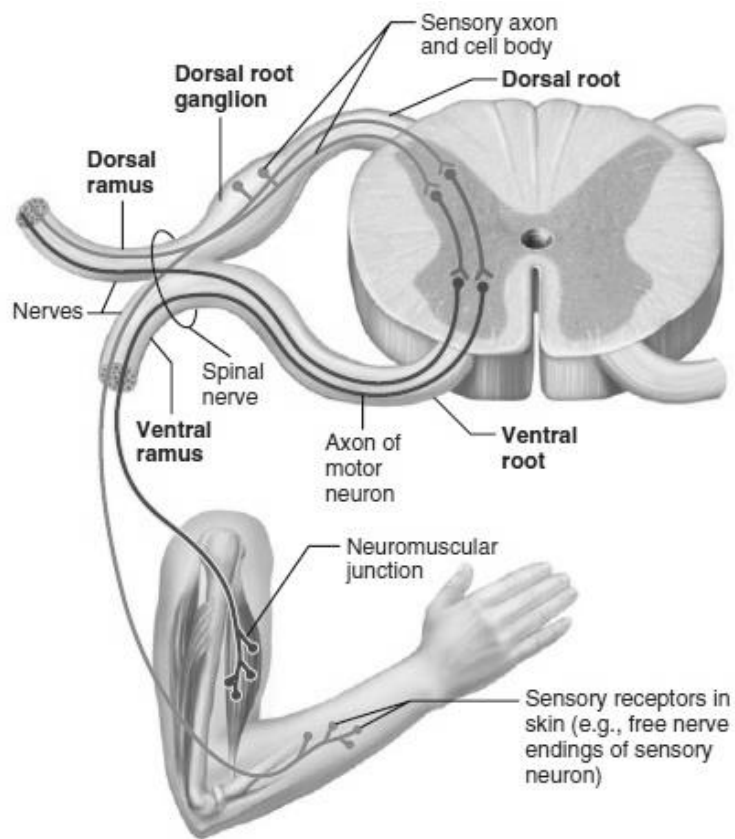
#### ❖ **Derivatives of the neural crest**

- Spinal dorsal root ganglia
- Sensory ganglia of cranial nerves
- Autonomic ganglia
- Suprarenal medulla (considered as a modified autonomic ganglion)
- Schwann cells (responsible for myelination of peripheral nerves)
- Arachnoid and pia (the dura is derived from the sclerotomes)
- Melanoblasts of the skin





**levels of spinal segments**



**Spinal cord and spinal nerve**

# CENTRAL NERVOUS SYSTEM

## SPINAL CORD

**Length:** 45 cm.

**Extent:**

**Sup:** at the lower border of foramen magnum.

**Inf:** the lower end is called conus medullaris & at the following levels:

**3rd month of intrauterine life:** same length of vertebral column.

**At birth:** L3 vertebra.

**After 3rd month:** lower border of L1 vertebra (45 cm in adults).

**Segments & its levels**

- 31 segments (8 C, 12 T, 5 L, 5 S & 1 Cc).
- From each segment arises a pair of spinal nerves.

**Levels:**

- Cervical segments = number of vertebra +1 (e.g.: C5 segment is at the level of C4 vertebra).
- T1-T6 segments = number of vertebra +2.
- T7-T12 segments = number of vertebra +3.
- Lumbar segments: level of T10 & T11 vertebrae.
- Sacral & coccygeal segments: level of T12 & L1 vertebrae.

**Spinal nerves**

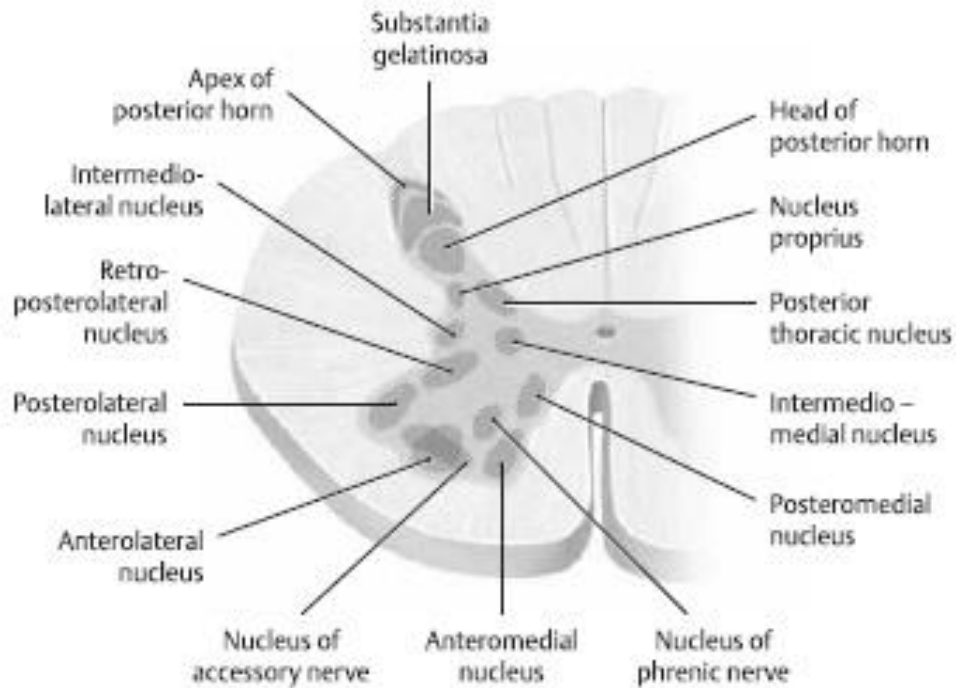
- 31 pairs (8 C, 12 T, 5 L, 5 S & 1 Cc).
- It has 2 roots: Post (dorsal) root (sensory) & ant (ventral) root (motor).
- The 2 roots unite to form the spinal nerve (mixed).
- The spinal nerve divides into 2 rami:

**Ant (ventral) ramus:**

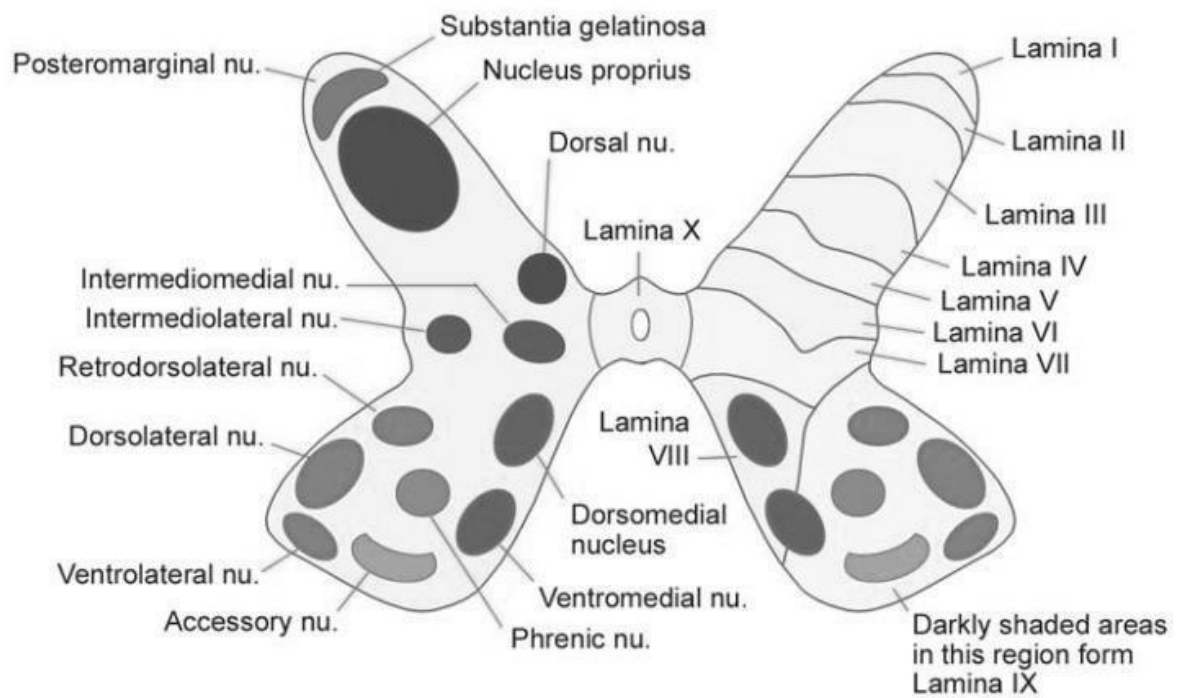
- Mixed.
- Form plexuses (except in thoracic region).
- Supplies muscles & skin of anterolateral sides of trunk & limbs.

**Post (dorsal) ramus:**

- Mixed.
- Does not form plexuses.
- Supplies muscles & skin of the back (post to vertebral column).
- Important segmental innervation levels:
  - Skin just below xiphoid process is supplied by T7.
  - Skin around the umbilicus is supplied by T10.
  - Skin of inguinal region is supplied by L1



**Nuclei of spinal cord**



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**Lamination of spinal cord**

### **Cross section of the spinal cord**

- ❖ **White matter:** formed of myelinated axons (ascending & descending tracts & crossing fibers).

Ant columns (2): ant to grey matter.

Lat columns (2): lat to grey matter.

Post columns (2): post to grey matter.

- ❖ **Grey matter:** H shaped & consists mainly of nuclei (nerve cells within CNS).

Post horns (2): sensory.

Lateral horns (2): autonomic (some segments).

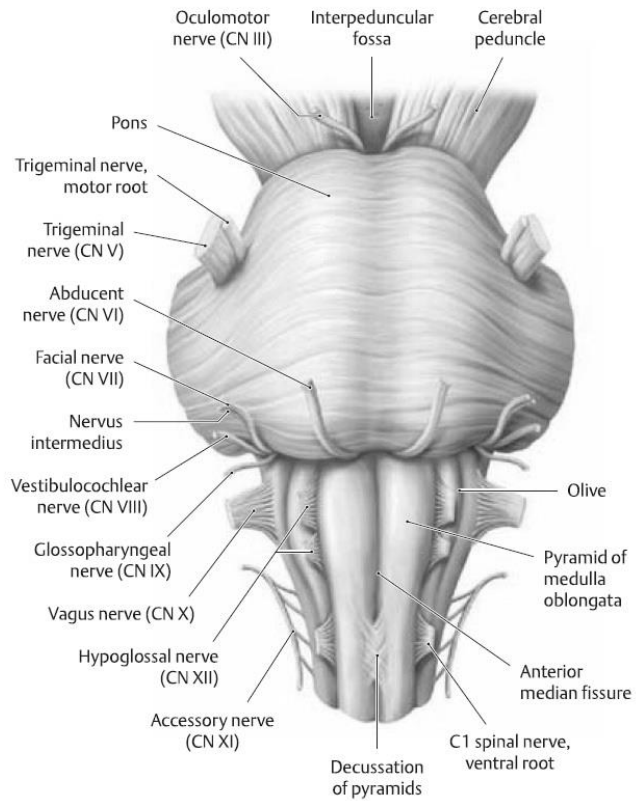
Ant horns (2): motor.

- ❖ **Central canal:** contains CSF, Superiorly it is continuous with central canal of medulla.

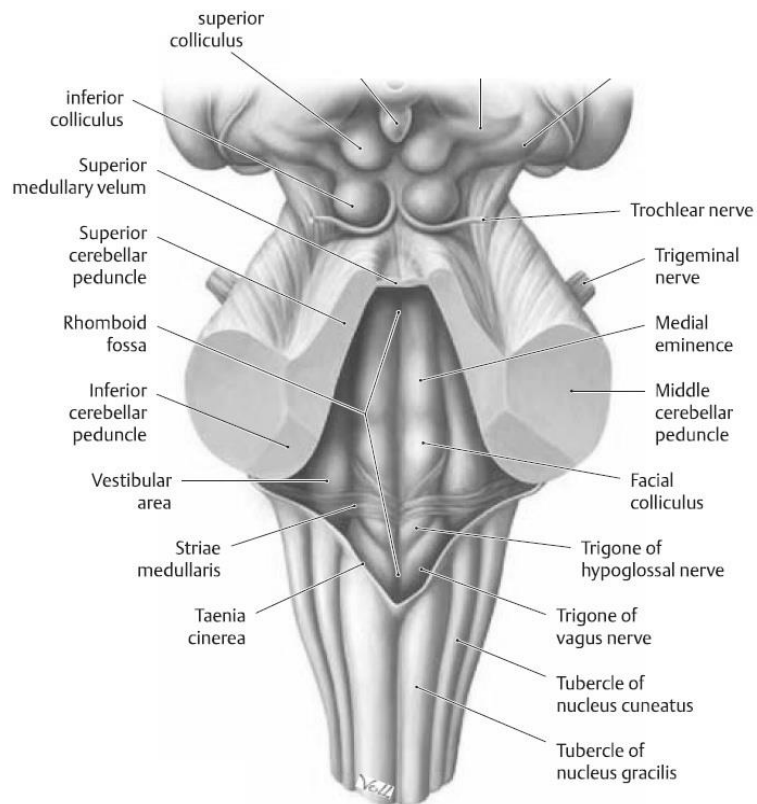
### **Lamination & nuclei of grey matter:**

<i>Lamina</i>	<i>Site &amp; extent</i>	<i>Corresponding nuclei</i>	<i>Function</i>
<b>I</b>	Post horn (tip) of all segments	Posteromarginal nucleus	Pain & temperature
<b>II</b>	All segments	Substantia gelatinosa (of Rolandi)	Pain modulation
<b>III</b>	All segments	Main sensory nucleus (nucleus proprius)	<ul style="list-style-type: none"> <li>• Touch &amp; pressure</li> <li>• Pain</li> </ul>
<b>IV</b>			
<b>V</b>	Post horn (neck)		Proprioception
<b>VI</b>	Post horn (base)		
<b>VII</b>	Between ant & post horns of T1-L3 segments	Dorsal (Clarke's) nucleus	Unconscious proprioception
	Between ant & post horns of L1-S3 segments	Spinal border nucleus	Unconscious proprioception
	T1-L3 & S2-4 segments	Intermediolateral nuclei	Autonomic (gives preganglionic efferent fibers)
	T1-L3 & S2-4 segments	Intermediomedial nuclei	Autonomic (receives visceral sensations)
<b>VIII</b>	Ant horn (med) of all segments	Commissural nucleus	Interneurons which relay in lamina IX
	All segments	Dorsomedial nucleus	Supplies trunk flexors & proximal limb muscles
	All segments	Ventromedial nucleus	Supplies trunk extensors
	C5-T1 & L1-S3	Dorsolateral nucleus	Supplies limb flexors
	C5-T1 & L1-S3	Ventrolateral nucleus	Supplies limb extensors
<b>IX</b>	Ant horn (lat)		AHCs
<b>X</b>	Around central canal	Grisea centralis	Glial cells

**Gate pain modulation:** substantia gelatinosa receives impulses from Gracile, Cuneate, lat spinothalamic & corticospinal tracts & many CNS nuclei. Substantia gelatinosa cells secrete enkephalins which inhibit impulses from pain fibers of dorsal root ganglia (DRG) to posteromarginal & main sensory nuclei (lat spinothalamic tract).



### External features of brain stem (Ant)



### External features of brain stem (post)

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## BRAIN STEM

### EXTERNAL FEATURES OF BRAIN STEM

#### ❖ **Medulla:**

**Ant** (from med to lat):

**Ant median fissure.**

**Pyramid:** marking pyramidal tract.

**Anterolateral fissure:** attachment of 12<sup>th</sup> cranial N.

**Olive:** marking inf olivary nucleus.

**Posterolateral fissure:** attachment of 9<sup>th</sup> 10<sup>th</sup> & 11<sup>th</sup> cranial Ns.

**Inf cerebellar peduncle:** connecting medulla to cerebellum.

**Post & sup:**

**Medullary stria:** between pons & medulla.

**Inf fovea:** inverted V shaped depression marking nuclei of 12<sup>th</sup> cranial nerve (med), 10<sup>th</sup> (deep) & 8<sup>th</sup> (lat).

**Post & inf** (from med to lat):

**Post median fissure.**

**Gracile tract & nucleus.**

**Cuneate tract & nucleus.**

#### ❖ **Pons:**

**Ant** (from med to lat):

**Median groove:** for basilar A.

**Transverse ridges:** marking transverse pontine fibers, it shows attachment of 5<sup>th</sup> cranial N, the 6<sup>th</sup> cranial N is at its inf border.

**Middle cerebellar peduncle:** connecting pons to cerebellum.

**Pontocerebellar angle:** between pons, medulla & cerebellum, it is site of attachment of 7<sup>th</sup> & 8<sup>th</sup> cranial Ns.

**Post (from med to lat):**

**Median fissure.**

**Medial eminence & facial colliculus:** facial colliculus is caused by fibers of facial N encircling 6<sup>th</sup> cranial N nucleus.

#### ❖ **Midbrain:**

**Ant** (from med to lat):

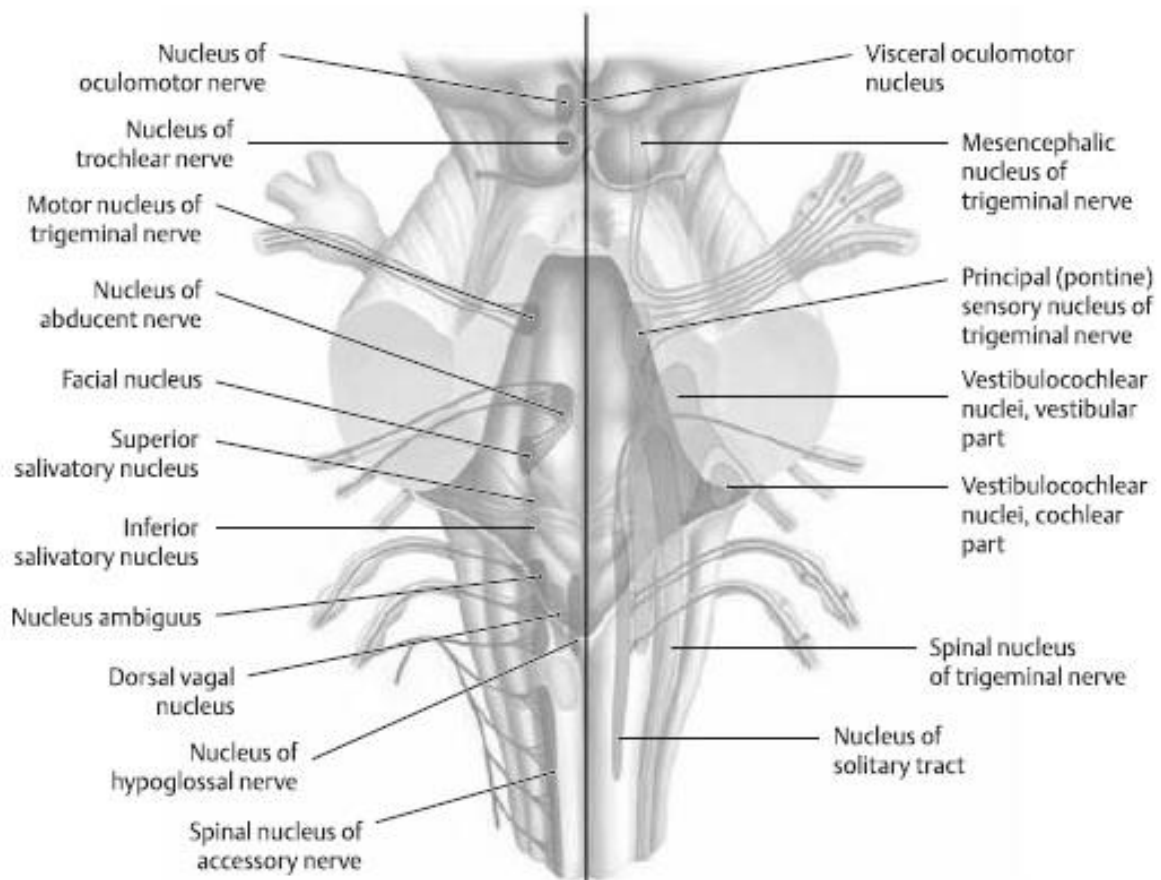
**Interpeduncular fossa:** site of attachment of 3rd cranial N.

**Cerebral peduncles:** marking pyramidal tract.

**Post & sup: 2 sup colliculi:** concerned with visual reflexes.

**Post & inf: 2 inf colliculi:** concerned with auditory reflexes. Below inf colliculi is the site of attachment of 4<sup>th</sup> cranial N.





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### Cranial nerves nuclei

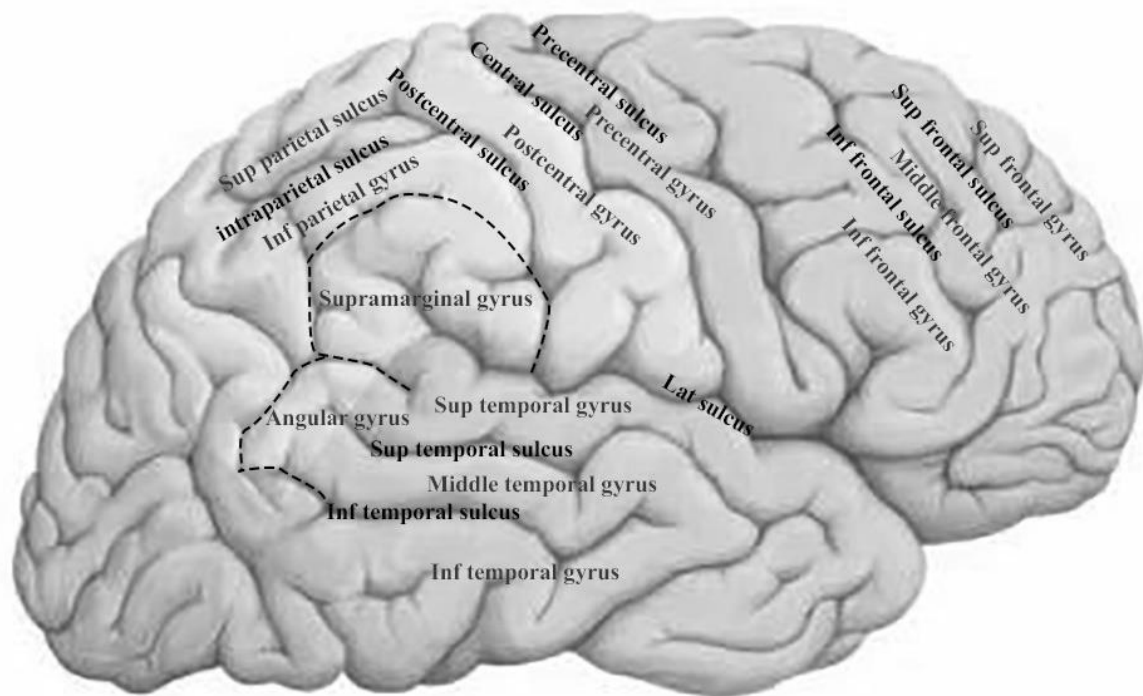
### **CRANIAL NERVES TYPES OF FIBERS & NUCLEI**

- ❖ **Types of fibers:** Cranial nerves has 7 types of fibers. Their nuclei in brain stem are arranged in 7 longitudinal columns, they are (from lat to med):

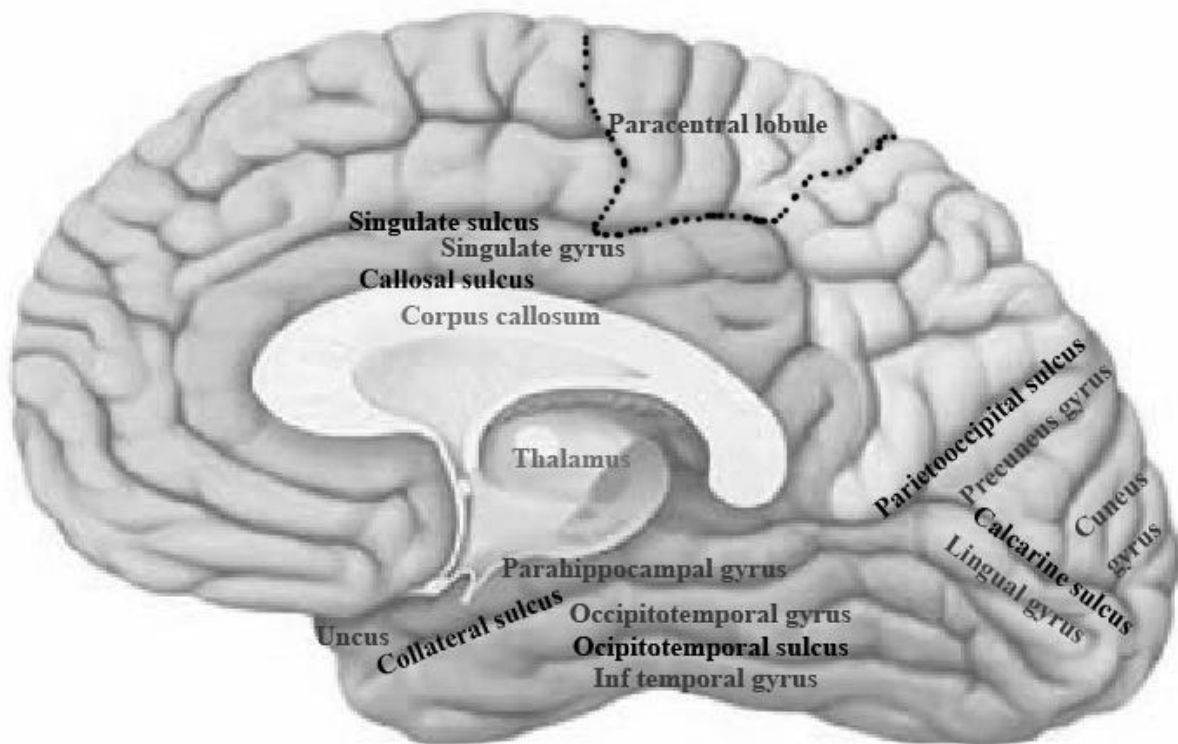
<i>Fibers</i>	<i>Function</i>	<i>Cranial nerves</i>
<b>SSA</b>	Vision, hearing & equilibrium	2 & 8
<b>GSA</b>	General sensations	5,7,9 & 10
<b>SVA</b>	Taste & smell	1 & solitary nucleus (7,9 & 10)
<b>GVA</b>	Visceral sensations	Solitary nucleus (9 & 10)
<b>GVE</b>	Parasympathetic efferent	3,7,9 & 10
<b>SVE</b>	Supply somatic muscles	5,7 & Ambiguous nucleus (9,10,11)
<b>SE</b>	Supply somatic muscles	3,4,6 & 12

- ❖ **Cranial nerves nuclei:**

Cranial nerve		Attachment	Fibers	Nuclei	Function
1	Olfactory	Cerebrum	SVA	---	smell
2	Optic	Cerebrum	SSA	---	vision
3	Oculomotor	Mid brain	GVE	Edinger Westphal	Parasympathetic to eye
			SE	Oculomotor	Motor to eye
4	Trochlear	Mid brain	SE	Trochlear	Motor to eye
5	Trigeminal	Pons	GSA	• Spinal trigeminal • Main sensory • Mesencephalic	Sensory to face
			SVE	Trigeminal motor	Motor to muscles of mastication, tensor tympani, tensor palati, mylohyoid & ant belly of digastric
6	Abducent	Pons	SE	Abducent	Motor to eye
7	Facial	Pons	GSA	Spinal trigeminal	Sensory to external ear
			SVA	Solitary	Taste from ant 2/3 of tongue
			GVE	• Special lacrimal • Sup salivary	Parasympathetic to lacrimal glands, orbit, nose, palate & pharynx & Submandibular & sublingual glands
			SVE	Facial	Motor to muscles of face & scalp, platysma, post. belly of digastric & stylohyoid
8	Vestibulocochlear	Pons	SSA	Vestibular	equilibrium
				Cochlear	Hearing
9	Glossopharyngeal	Medulla	GSA	Spinal trigeminal	Sensory to post 1/3 of tongue & pharynx
			SVA	Solitary	Taste to post 1/3 of tongue
			GVA	Solitary	Visceral sensations
			GVE	Inf salivary	Parasympathetic to parotid
			SVE	Ambiguous	Motor to stylopharyngeus
10	Vagus	Medulla	GSA	Spinal trigeminal	Sensory to root of tongue & larynx
			SVA	Solitary	Taste to root of tongue
			GVA	Solitary	Visceral sensations
			GVE	Dorsal motor	Parasympathetic to viscera
			SVE	Ambiguous	Motor to cricothyroid
11	Cranial accessory	Medulla	SVE	Ambiguous	Motor to most of muscles of palate, pharynx & larynx
12	Hypoglossal	Medulla	SE	Hypoglossal	Motor to muscles of tongue (except palatoglossus)



**Cerebrum (external features of superolateral surface )**



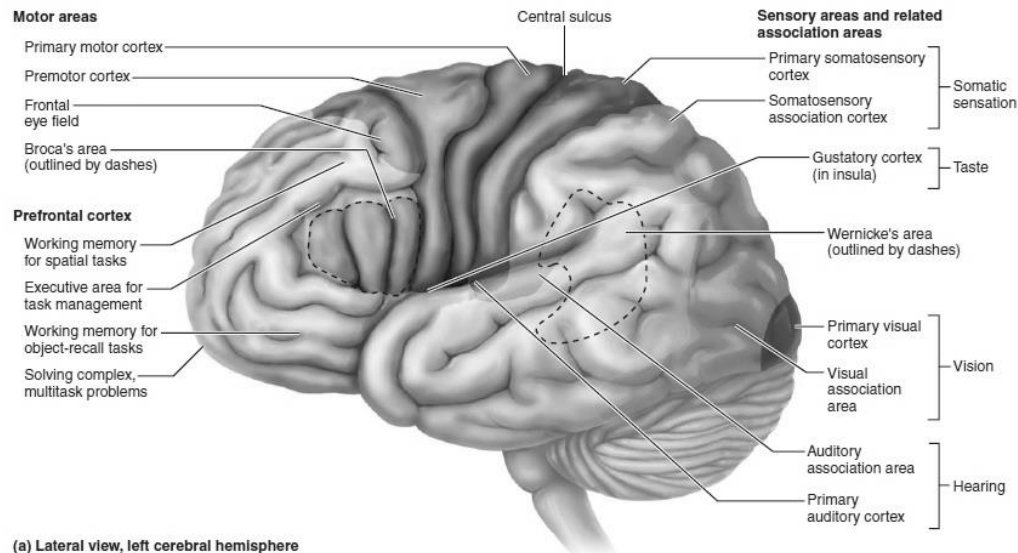
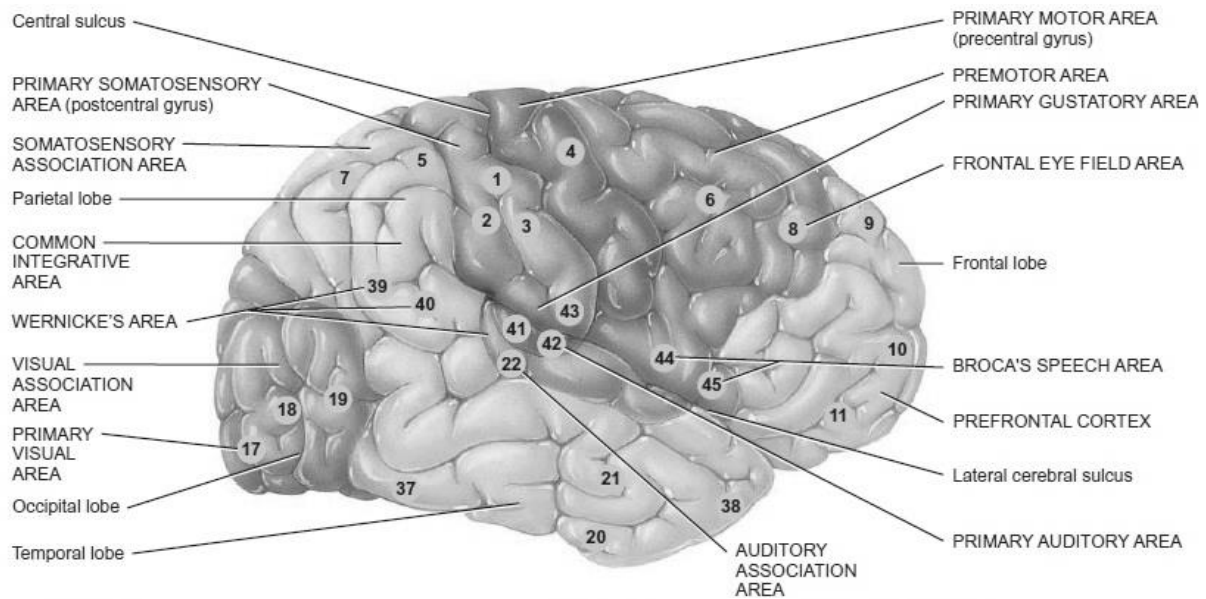
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**Cerebrum (external features of med & inf surfaces )**

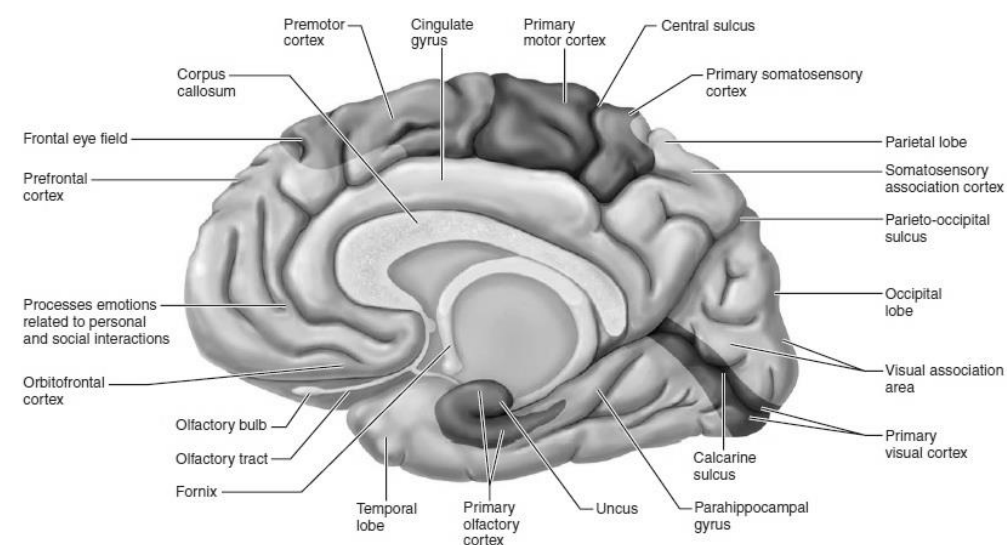
## CEREBRUM

### FEATURES OF CEREBRAL HEMISPHERE

- ❖ The cerebral hemisphere has 3 surfaces (lat, med & inf), it shows fissures (sulci) & lobes in between (gyri). It is divided into 4 main lobes (frontal, parietal, temporal & occipital) mainly by central, lat & parietooccipital sulci.
- ❖ **Lobes, sulci and gyri:**
  - Lat sulcus:** transverse fissure, extends on lat & inf surfaces. The **supramarginal gyrus** surrounds its post end
  - Central sulcus:** vertical fissure on lat surface & extends to the med surface with **paracentral lobule** surrounding it.
  - Parietooccipital sulcus:** oblique fissure, extends on med surface between ant  $\frac{3}{4}$  & post  $\frac{1}{4}$ .
  - Frontal lobe** shows **precentral sulcus** which is ant to central sulcus with **precentral gyrus** between them. Ant to it, frontal lobe shows **sup & inf frontal sulci** dividing it into **sup, middle & inf frontal gyri**. Medially the frontal lobe shows **cingulate & callosal sulci** with a **cingulate gyrus** in between.
  - Parietal lobe** shows **postcentral sulcus** which is post to central sulcus with **postcentral gyrus** between them. Post to it, the parietal lobe shows **intraparietal sulcus** dividing it into **sup & inf parietal gyri**.
  - Temporal lobe** is divided by **sup & inf temporal, occipitotemporal & collateral sulci** into **sup, middle & inf temporal, occipitotemporal & parahippocampal gyri**. The **angular gyrus** surrounds the post end of sup temporal sulcus, while the ant end of parahippocampal gyrus is called **uncus**.
  - Occipital lobe** shows **calcarine sulcus** which extends mainly on med surface from post pole anteriorly, below it is the **lingual gyrus**, above it is **cuneus gyrus** with the **precuneus gyrus** ant to it.
- N.B.:** the med surface of cerebral hemisphere shows the thalamus, a cut section of corpus callosum (fibers connecting both sides) & lat ventricle (large cavity containing CSF) in between.



(a) Lateral view, left cerebral hemisphere



(b) Parasagittal view, right hemisphere

Tortora & Nielsen / Marieb

## Cerebrum (Functional areas)

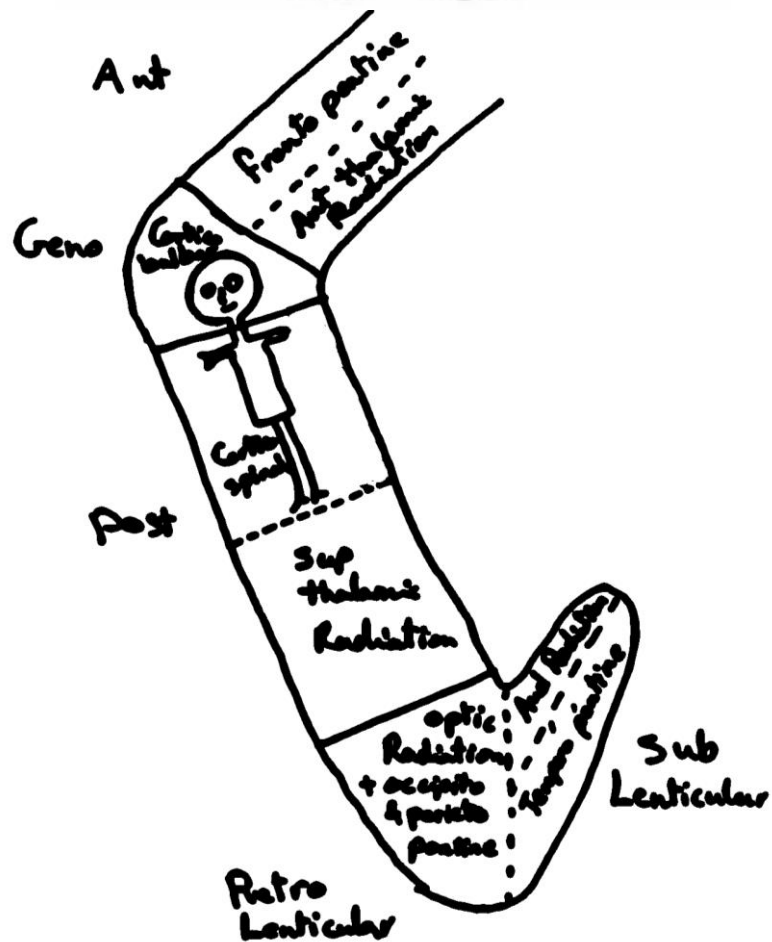
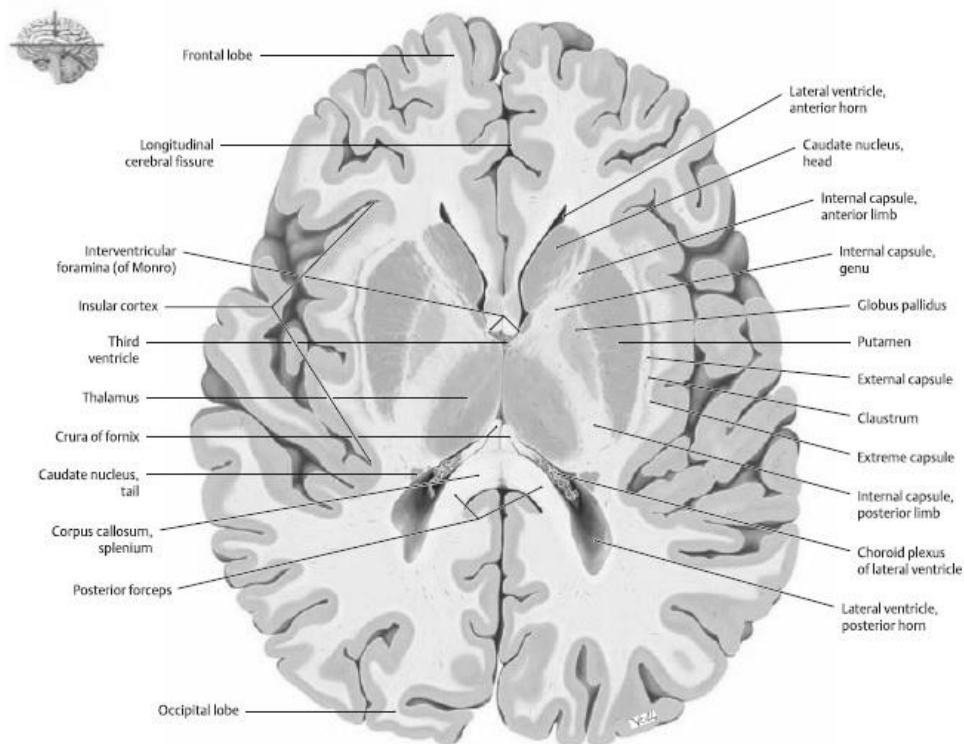


## CORTICAL FUNCTIONAL AREAS

<i>Functional area</i>	<i>site</i>	<i>function</i>	<i>lesion</i>
<b>1ry motor area (4)</b>	<ul style="list-style-type: none"> <li>• Precentral gyrus.</li> <li>• Paracentral lobule</li> </ul>	Voluntary movements of opposite side	Contralateral hemiplegia
<b>Premotor area (6)</b>	Anterior to 1ry motor area	Learned movements	Apraxia (loss of learned movements)
<b>Frontal eye field area (8)</b>	middle frontal gyrus (post)	Movement of both eyes to opposite side	Deviation of both eyes to same side
<b>Motor speech (Broca's) area (44&amp;45)</b>	inferior frontal gyrus (post) of dominant hemisphere	Coordinate speech muscles	Motor aphasia (loss of speech)
<b>Prefrontal area (9,10,11&amp;12)</b>	Ant ½ of frontal lobe	Personality, behavior & will	Personality changes
<b>1ry sensory area (3,1&amp;2)</b>	<ul style="list-style-type: none"> <li>• Postcentral gyrus</li> <li>• Paracentral lobule</li> </ul>	Receives sensations from opposite side	Contralateral hemianesthesia
<b>1ry gustatory area (43)</b>	Postcentral gyrus (inf)	Taste	Taste hallucinations
<b>Sensory association area (5&amp;7&amp;40)</b>	Sup parietal gyrus	Understanding sensations	Astereognosis (inability to identify objects by touch)
	Supramarginal gyrus (40)	Understand body image	
<b>1ry auditory area (41&amp;42)</b>	Sup temporal gyrus (middle)	Receives hearing impulses from the 2 sides (mainly opposite)	Bilateral hearing defect (mainly opposite side)
<b>Auditory association (Wernick's) area (22)</b>	Sup temporal gyrus (post)	Understand sounds	<ul style="list-style-type: none"> <li>• Auditory agnosia (inability to identify sounds)</li> <li>• Sensory aphasia</li> </ul>
<b>1ry olfactory area</b>	Uncus	Olfaction	Olfactory hallucinations
<b>1ry visual area (17)</b>	Around calcarine sulcus	Receives visual impulses	Visual field defect
<b>Visual association area (18,19&amp;39)</b>	Around area 17	Understand vision	Visual agnosia (inability to identify objects by vision)
	Angular gyrus (39)	Understand writing	<ul style="list-style-type: none"> <li>• Alexia (inability to read)</li> <li>• Agraphia (inability to write)</li> </ul>
<b>Sensory speech area</b>	Supramarginal gyrus (40) Wernick's area (22) Angular gyrus (39)	Understand body image, sounds & writing → Broca's area (speech)	

**N.B.:** in 1ry motor & 1ry sensory areas, the body is represented upside down.





Schuenke / Bondok

Internal capsule

## WHITE FIBERS

### Types:

**Projection fibers:** ascending or descending fibers connecting cerebral hemisphere to a lower level, e.g.: internal capsule.

**Association fibers:** fibers connecting 2 different areas at the same hemisphere.

**Commissural fibers:** fibers connecting 2 similar areas of both hemispheres, e.g.: corpus callosum.

## INTERNAL CAPSULE

**Definition:** a collection of projection white fibers lying between lentiform nucleus (lat), caudate nucleus (med & ant) & thalamus (med & post).

### Parts and fibers passing:

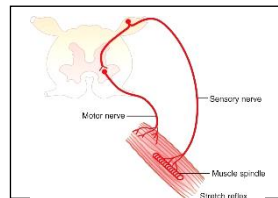
<i>Part</i>	<i>Fibers</i>		<i>From</i>	<i>To</i>	<i>Function</i>	<i>Lesion</i>
<b>Ant limb</b> (between lentiform & caudate)	Frontopontine		Frontal cortex	Pontine nuclei → cerebellum	Transmit information to cerebellum	
	Ant	thalamic radiation	Thalamus	Prefrontal area	Limbic	Personality changes
<b>Genu</b> (between the 3 nuclei)	Corticospinal		Cerebral cortex	Cranial Ns nuclei	Motor to cranial Ns	Contralateral hemiplegia of some cranial Ns
<b>Post limb</b> (between lentiform & thalamus)	Ant ½	corticospinal	Cerebral cortex	AHCs	Motor to spinal Ns	Contralateral hemiplegia
	Post ½	Sup (main sensory) thalamic radiation	PLVNT PMVNT	Sensory area	Sensory pathway	Contralateral hemianesthesia
<b>Retrolenticular</b> (behind lentiform)	Post thalamic (optic) radiation		Thalamus	Visual area	Visual pathway	Visual field defect
	Occipito & Parietopontine		Occipital & parietal lobes	Pontine nuclei → cerebellum	Transmit information to cerebellum	
<b>Sublenticular</b> (below lentiform)	Inf thalamic (auditory) radiation		Thalamus	Auditory area	Auditory pathway	Hearing defect
	Temporopontine		Temporal lobe	Pontine nuclei → cerebellum	Transmit information to cerebellum	

## The Reflexes

- The skeletal muscles are controlled by many levels of the central Nervous system (CNS) including motor cortex, basal ganglia (BG), cerebellum, brain stem and spinal cord
- The reflex arc: Is the functional unit of the nervous system .
- A sensory stimulus initiates a motor response directly in a simple neural circuit
- The reflex arc consists of :
  1. Receptor: The sense organ
  2. An afferent neuron
  3. An efferent neuron
  4. One or more synapses
  5. An effector organ

### Spinal Reflexes

A- **Monosynaptic reflex:** Stretch reflex

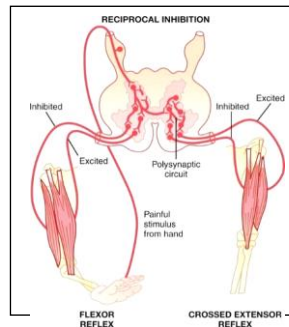


#### Neuronal circuit of the stretch reflex

B- **Bisynaptic reflex:** Inverse stretch reflex (Golgi tendon reflex)  
 - Marked stretch → Reflex Relaxation Golgi tendon organ

C- **Polysynaptic reflexes:**

a) **Flexor withdrawal reflex**



#### Flexor reflex crossed extensor reflex, and reciprocal

- b) **Crossed extensor reflex**
- c) **Reflexes of posture & locomotion**
  1. Positive supporting reaction
  2. Stepping and walking movement
- d) **Superficial skin reflexes**
  1. Abdominal reflexes (upper & lower)
  2. Cremasteric reflex
- f) **Autonomic reflexes in the spinal cord**
  1. Micturition reflex

2. Defecation reflex
3. Changes in vascular tone
4. Sweating: Resulting from local skin heat.

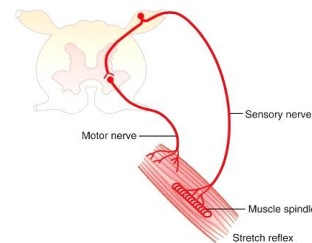
## Spinal Reflexes

### 1- Monosynaptic reflexes

- There is only one synapse.      - No interneuron

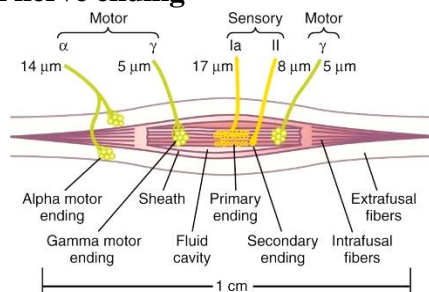
### Stretch reflex:

- Is the only monosynaptic reflex
- It is a spinal reflex
- **Def:** It is reflex contraction of muscle in response to stretch
- **Pathway:**
  - **Stimulus:** Stretch of muscle (extrafusal fibers) → stretch of midportion of muscle spindle (intrafusal)
  - **Receptors:** Muscle spindle (central portion) ↓
  - **Afferents:** Thick myelinated fibers (primary & secondary)
  - **Center:**
    - Alpha motor neuron in spinal cord (AHCs)
    - It is monosynaptic spinal reflex.
  - **Efferent:** Thick myelinated A  $\alpha$  fibers
  - **Response:** Muscle contraction



### Innervation of muscle spindles

#### ❖ Structure: as discussed in nerve ending



*Muscle spindle, showing its relation to the large extrafusal skeletal muscle fibers. (Note also both motor and sensory innervation of the muscle spindle)*

#### ❖ Innervation :

Sensory innervations	Motor Innervations
<b>1<sup>st</sup> ending:</b> Encircle central part of bag & chain <b>2<sup>nd</sup> ending:</b> Encircle nuclear chain only	Peripheral contractile part of receptor receives motor supply from gamma motor <b>dynamic:</b> For peripheral part of bag <b>static:</b> For peripheral part of chain
<u>Stimulation of receptor</u>	
Stretch the whole muscle	Contraction of peripheral part of receptor

- **Types:** There are two components of stretch reflex:
  - **Static stretch reflex:**
    - The stimulus is: Slow sustained stretch
    - The receptor is :Nuclear chain which is type of muscle spindle

- **The afferent** is :Primary & secondary nerve endings
- **The response** is :Continuous contraction of the muscle
- **It is the basis of:** Muscle tone
- **Dynamic response**
- **The stimulus** is: Sudden quick stretch
- **The receptor** is: Nuclear bag which is type of muscle spindle
- **The afferent** is: Primary nerve endings
- **The response** is: Sudden strong contraction followed by sudden relaxation within a second
- **It is the basis of:** Tendon Jerk
- **Properties of stretch reflex:**
- 1- It is monosynaptic
- 2- It is the fastest reflex in body
- 3- It is local (restricted to the stretched muscle)
- 4- It is more in the antigravity muscle
- 5- It shows reciprocal innervation inhibition of antagonistic muscle
- 6- It does not show fatigue
- **Supraspinal regulation of stretch reflex:**
- **Stretch reflex is a spinal reflex which is controlled by Supraspinal centers:**

Supra spinal facilitatory area	Supra spinal (inhibitory area)
Impulses from these area Increase activity of gamma motor neuron - <b>Facilitatory RF “reticular formation”</b> which: Send impulse to gamma through ventral reticulo spinal tract. It has intrinsic activity - <b>Vestibular nucleus:</b> Send impulse to gamma through vestibulospinal tract - <b>Neo cerebellum:</b> Send impulse to gamma indirectly through facilitatory RF - <b>Primary motor area 4</b>	Impulses from this area decrease activity of gamma motor neuron - <b>Inhibitory RF “reticular formation” which:</b> Send impulse to gamma through lateral reticulo spinal tract. It has no intrinsic activity - <b>Red nucleus:</b> Send impulse to gamma through rubrospinal tract - <b>Paleocerebellum:</b> Send impulse to gamma indirectly through inhibitory RF - <b>Basal ganglia:</b> Send impulse indirectly - <b>Cortical suppressor area</b>

- **Functions:**
- 1. Static stretch reflex is the basis of muscle tone.
- 2. Stretch reflex has a role of in controlling voluntary motor activity
- a) **Damping function of stretch reflex:**
- Brain discharges irregularly to motor neurons: Leading to jerky (oscillation) movements
- Stretch reflex :
- Prevents oscillations of movement & makes them smooth because:

- There is simultaneous discharge to  $\gamma$  (gamma) motor neuron (coactivation of  $\alpha$  (alpha) &  $\gamma$  (gamma) motor neurons  $\rightarrow$  causing extra & intrafusal to contract at same time)

**b) Servo-assist function during muscle contraction :**

- During a normal movement (e.g. lifting a weight) :
- The motor cortex sends signals to both  $\alpha$  (alpha) &  $\gamma$  (gamma) motor neurons i.e. there is coactivation  $\alpha$  (alpha) &  $\gamma$  (gamma) motor neurons) & this maintains constant position of contracted muscle in spite of application of different loads.

**NB:**

**A. The impulses sent to  $\alpha$  (alpha) motor neurons stimulate the extrafusal fibers**

**B. The impulses sent to  $\gamma$  (gamma) motor neurons stimulate intrafusal fibers**

**❖ Clinical importance**

**1. Muscle tone: Static stretch reflex**

- It is observed as a degree of resistance when the neurologist flexes and extends the muscles alternatively

**- Definition:**

- It is reflex sub tetanic alternating contraction of skeletal muscle fibers especially the antigravity muscle (extensors of lower limb & back and flexors of upper limbs)

**- *During rest, the muscle spindle is continuously stretched because :***

- The muscle length is shorter than the distance between origin & insertion
- There is continuous  $\gamma$  (gamma) efferent discharge (from higher centers) during normal condition (which keeps the muscle spindle stretched)

**- *Skeletal muscle tone is maintained without fatigue because :***

- The reflex contraction is sub tetanic
- The alternating activity of different motor units

**- Functions of muscle tone:**

1. Keeps body position against gravity
2. Keeps viscera in position
3. Helps to maintain body temperature
4. Helps venous return & lymph drain.

**2. Tendon jerk (Deep reflexes): Dynamic stretch reflex**

- Sudden striking of tendon produces sudden stretch of muscle resulting in reflex rapid contraction followed by rapid relaxation.

**- *It is facilitated by:***

- a) Putting the muscles in a stretched position
- b) Increasing  $\gamma$  (gamma) efferent discharge by :
  - i. Clenching the teeth
  - ii. Pull the hand apart while fingers are flexed & hooked together

**- *Examples of tendon jerks :***

**a) Biceps jerk:**

- A sudden tap on biceps tendon of semi flexed elbow  $\rightarrow$  reflex contraction of biceps & flexion of elbow
- **Center:** C5 & C6



**b) Triceps jerk:**

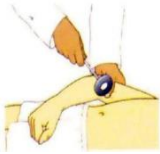



- A sudden tap on triceps tendon → reflex contraction of triceps & extension of elbow
- **Center:** C6 & C7

**c) Knee jerk:**

- A sudden tap on patellar tendon → reflex contraction of quadriceps & extension of knee
- **Center:** L2, L3, L4

**d) Ankle jerk:**

- A tap on Achilles tendon → reflex contraction of gastrocnemius & plantar flexion of ankle
- **Center:** S1, S2

Deep tendon reflexes of upper limb	
<b>Biceps jerk C5 (C6)</b> 	<b>Knee jerk (center: L2, L3, L4)</b>  (legs must not be in contact with each other)
<b>Triceps jerk C6, C7</b> 	<b>Ankle jerk of recumbent patient (S1)</b> 

❖ **Clinical significance of skeletal muscle tone & tendon jerk**

- Muscle tone and tendon jerks are affected together in the same manner (ie they are absent, inhibited or facilitated together)
- Exaggerated tendon jerk & hypertonia: Occurs in UMNL (upper motor neuron lesion)
- Weak tendon jerk & hypotonia: Occurs in LMNL (lower motor neuron lesion)

**Inverse stretch reflex (Golgi tendon reflex)**

❖ **Pathway:**

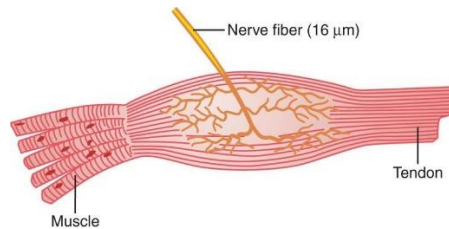
- **Stimulus:** Increased tension in muscle & its tendon e.g. marked stretch or strong active contraction
- **Receptor:** Golgi tendon organ:
  - Is a high threshold receptor which is stimulated by: High tension in the muscle
  - Found in the tendon in series with muscle fibers
- **Afferent:** Large, myelinated nerve fibers (Ib)
- **Center:** Spinal cord, it is **bisynaptic spinal reflex**
- **Efferent:** Alpha motor neuron, which inhibits the muscle fibers.
- **Result:** Reflex relaxation of the muscle → decrease muscle tone

❖ **Aim:** It prevents the development of too much tension on the muscle

❖ **Clinical application:** Lengthening reaction (in clasp knife rigidity)

- **NB:** Clasp knife means initial resistance then sudden release.

- **Mechanism :**
- **If upper limb is passively flexed:**
  - Extensors are stretched & lengthened
  - Stimulation of their muscle spindle → increasing the tone and resistance
  - The high tone & tension in the muscle → stimulates Golgi tendon receptor → inhibit  $\alpha$  (alpha) motor neuron → leading to muscle relaxation



*Marked stretch → Reflex Relaxation*

*Golgi tendon organ*

### Polysynaptic reflexes

#### 1. **Flexor withdrawal reflex:** Nociceptive reflex

- **Pathway:**
  - Stimulus: Injurious (painful) stimulus applied to a limb
  - Receptors: Free nerve endings
  - Afferent: A delta & C
  - Center: In spinal cord. It is polysynaptic containing 4 to 5 interneurons at least
  - Efferent: Alpha motor neuron
  - Response: Flexion & withdrawal of the limb
- **Properties:**
  - A. The pattern of the reflex **depends on the locality of the stimulus** ie stimulation of inner side of the limb produces: Flexion & abduction
  - B. **Divergence:** Is present to allow the spread of excitation to several flexor muscles
  - C. **Reciprocal innervation:** contraction of flexors is accompanied by relaxation of extensors. This is done through lateral inhibition of the extensors
  - D. **Recruitment:** The tension in contracting muscle rises gradually (due to gradual increase in number of activated motor units)
  - E. **Tetanus:** Is of reflex nature
- **Means:**
  - Continuous contraction of muscle due to repeated stimulation of afferent nerve
- **Characterized by:**
  - Long latent period (due to impulse conduction in afferent nerve & interneuron)
  - The tension rises gradually (i.e. recruitment) then declines due to synaptic fatigue and persists for a short time after the stimulus is removed (after discharge).

#### **NB: Motor tetanus:**

- Is due to: Repeated stimulation of motor nerve of muscle (efferent)
- **Is characterized by:**
  - A. Short latent period

**B.** The tension rises rapidly, maintained & then drops rapidly after the stimulus is removed

**2. Crossed extensor reflex:** Application of injurious stimulus to a limb produces:

- Reflex flexion of the ipsilateral limb
- Reflex extension of the contralateral limb to support the body weight
- **Properties:**
  - a) The latent period is longer than the flexor reflex
  - b) The after discharge is longer than the flexor reflex.
  - c) Reciprocal innervation is present, as excitation of the extensor is associated with inhibition of the flexor muscles.

**3. Reflexes of posture & locomotion:**

**A. Positive supporting reaction:**

- Deep pressure on the sole of the foot produces reflex Contraction of both flexors & extensors to convert the limb into a rigid column to support the body weight (the reflex shows no reciprocal innervation)

**B. Stepping and walking movement:**

- Rhythmic stepping of the limb & reciprocal stepping of the other limb indicating that pattern of walking is in spinal cord.

**4. Superficial skin reflexes:**

- **Abdominal reflexes (upper & lower):** Stroking (scratching) the skin of the abdomen leads to reflex contraction of:
  - Upper abdominal muscle (Center: T7 to T10)
  - Lower abdominal muscle (Center: T10 to T12)
- **Cremasteric reflex:**
  - Scratching the skin of the inner aspect of the thigh → contraction of Cremasteric muscle & elevation of testis
  - Center: L1

**5. Autonomic reflexes in the spinal cord:**

- a) Micturition reflex: Distension of bladder results in:
  - Reflex contraction of bladder
  - Reflex relaxation of urethral sphincters
  - Center: S<sub>2</sub>, S<sub>3</sub>, S<sub>4</sub>
- b) **Defecation reflex:** Distension of rectum results in:
  - Reflex contraction of rectum
  - Reflex relaxation of anal sphincters - Center: S<sub>2</sub>, S<sub>3</sub>, S<sub>4</sub>
- c) **Changes in vascular tone:** Resulting from local skin heat or cold
- d) **Sweating:** Resulting from local skin heat.

- **NB:**

➤ **Decerebrate rigidity:**

- Caused by transverse section at brain stem between superior & inferior colliculi.
- **This section:**
  - a. Removes the inhibitory effect of Supraspinal centers & red nucleus
  - b. Leaving the strong facilitatory effect of facilitatory reticular formation and vestibular nuclei

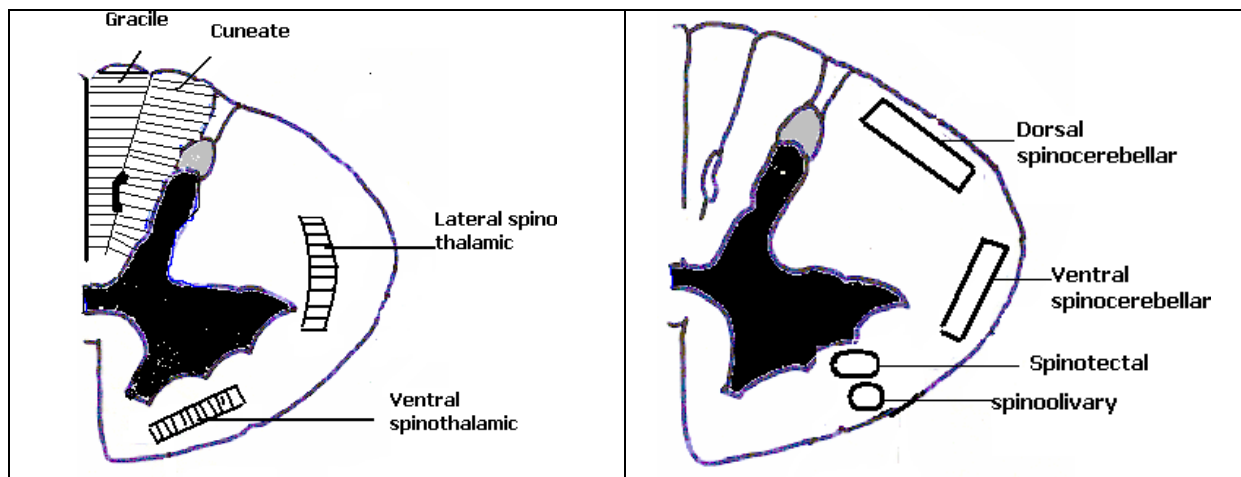
- **Effect:** The tone increases markedly in the antigravity muscle, so the animal shows extended neck, back, limbs & elevated tail.
- A similar condition occurs in man when there is lesion of internal capsule

### Tracts of the spinal cord

❖ Tracts are

- 1- **Long:** ascending or descending.
- 2- **Short:** both ascending and descending.

4 tracts carrying sensations that reach the cerebral cortex	4 tracts that carry impulses to sub cortical level
1- Gracile tract.	1- Dorsal spinocerebellar tract.
2- Cuneate tract.	2- Ventral spinocerebellar tract
3- Lateral spinothalamic tract.	3- Spino-olivary tract
4- Ventral spinothalamic tract.	4- Spino-tectal tract



### Pathway of proprioception and fine touch from the body

- ❖ **Proprioception:** sense of position, movement and vibration.
- ❖ **Fine touch:** sense of tactile localization, tactile dis-crimination and stereognosis.
- ❖ **Receptors for Proprioception:** Muscle spindle , tendone spindle & Pacinian corpuscles
- ❖ **Receptors for fine touch:**
  1. Meissner's corpuscle.
  - 2- Ruffini's corpuscle.
  - 3- Merkel's disc.
- ❖ **First order neurons:**
  - They are the **large cells** in spinal ganglia. They receive impulses from receptors by peripheral **Thick** myelinated nerve fibers and send them to spinal cord by central branches that enter the spinal cord through the **medial** division of posterior roots.
  - Branches from sacral, lumbar and lower thoracic segments ascend as **gracile** tract on the same side.
  - Branches from upper thoracic and cervical segments ascend as **cuneate tract on the same side.**

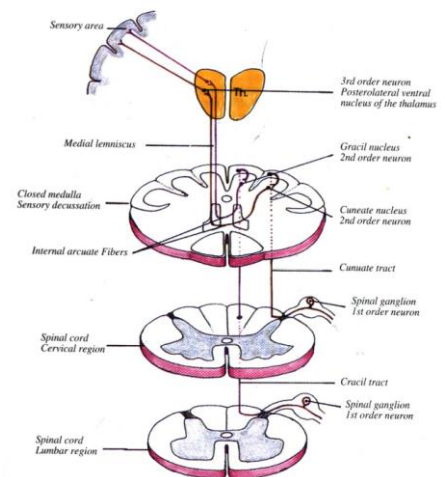
Gracile and Cuneate tracts end in the gracile and cuneate nuclei in medulla on the same side.

❖ **Second order neurons:**

- They are Gracile and Cuneate nuclei in the medulla. They give rise to internal arcuate fibers that cross to the opposite side at the upper half of closed medulla (sensory decussation) to form medial lemniscus.

❖ **Third order neurons:**

They are the cells of ventral posterolateral nucleus (V.P.L.N) of thalamus. Their axons ascend in sensory radiation to reach sensory area in post central gyrus of cerebral cortex (area 3,1,2).

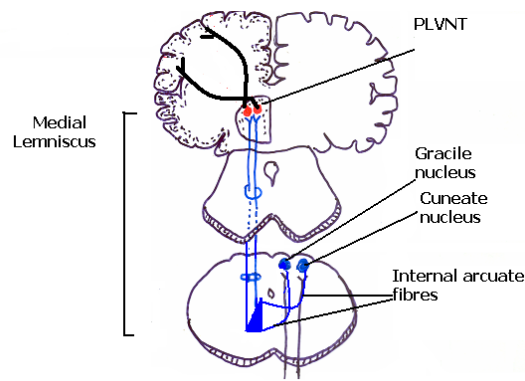


Tract	Gracile tract	Cuneate
<b>Definition</b>	Long ascending sensory tract	
<b>Origin</b>	Large cells in spinal ganglia that receive impulses by peripheral thick myelinated fibers & send central branches that enter the <b>medial</b> division of the post. Roots.	
<b>Course</b>	-Posterior column of white matter. -in all levels of spinal cord.	-Posterior column of white matter. -Cervical & upper Thoracic levels.
<b>Termination</b>	-Ipsilateral Gracile Nucleus in closed medulla.	-Ipsilateral Cuneate Nucleus in closed medulla.
<b>Function</b>	Proprioception & fine touch from lower ipsilateral half of body.	Proprioception & fine touch from upper ipsilateral half of body.

- **Lemniscus:** bundles of secondary sensory fibers within the brain stem which terminate in specific relay nuclei of the diencephalon.

**Medial lemniscus**

- Definition:** ascending sensory bundle in the brain stem.
- Origin:** gracile and cuneate nuclei in closed medulla of opposite side that give rise to internal arcuate fibers. The fibers cross to opposite side in upper half of closed medulla (sensory decussation).
- Course:** ascend in brain stem in a medial position.
- Termination:** V.P.L.N in thalamus.
- Function:** carries Proprioception and fine touch from opposite side of the body.



**Diagram for Medial lemniscus**

### **Clinically important point**

#### **❖ Tabes dorsalis**

- It is a bilateral progressive degeneration of gracile and cuneate tracts.
- Occurs in syphilis.
- Results in loss of proprioception and fine touch.
- The patient suffers from sensory ataxia which is a marked disturbance of gait and unless the patient can see the movements of his limbs and correct them he may fall.

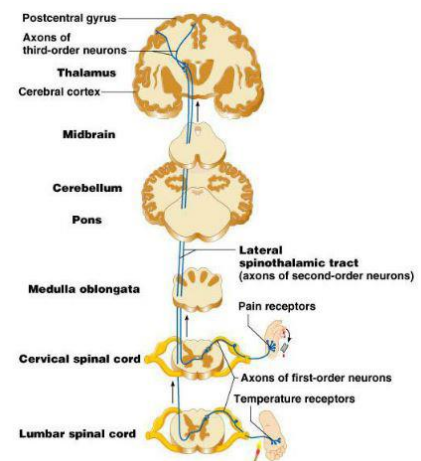
#### **Pathway of pain and temperature from the body**

- **Receptors:** Free nerve endings.

#### • **First order neurons:**

They are the **small cells** in spinal ganglia. They receive impulses from receptors by peripheral **thin** myelinated nerve fibers and send them to spinal cord by central branches that enter the spinal cord through the **lateral** division of posterior roots. Fibers travel up or down 1 or 2 segments in Lissauer's tract then end in **substantia gelatinosa of Rolandi** nucleus.

- **Second order neurons:** they are cells of Substantia Gelatinosa of Rolandi. Their axons cross to the opposite side anterior to the central canal in the anterior white matter. It ascends through the brain stem. In the pons it joins the ventral spinothalamic tract to form spinal lemniscus that ends in the **V.P.L.N** of the thalamus.
- **Third order neurons:** They are the cells of ventral posterolateral nucleus (**V.P.L.N**) of thalamus. Their axons ascend in sensory radiation to reach sensory area in post central gyrus area of cerebral cortex (area 3, 1, 2).



#### **Pathway of crude touch from the body**

#### **Receptors:**

1. Free nerve endings.
2. Merkel's disc.
- 3- Peritrichial nerve endings.
- 4- Meissner's corpuscle.



- **First order neurons:**

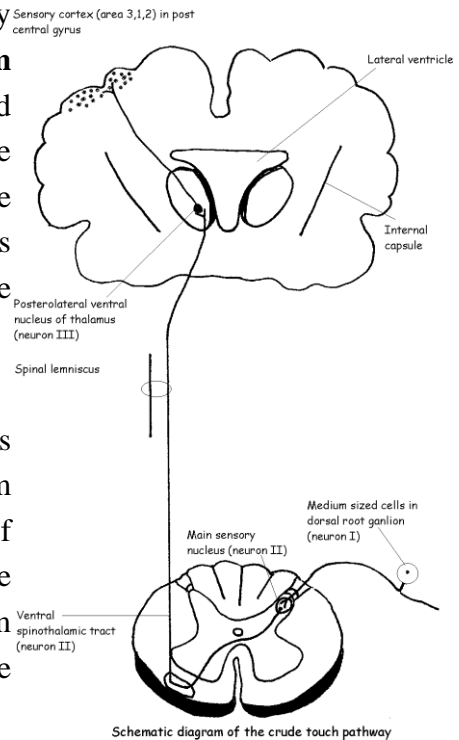
- They are the **medium sized cells** in spinal ganglia. They receive impulses from receptors by peripheral **medium sized** myelinated nerve fibers and send them to spinal cord by central branches that enter the spinal cord through the **medial** division of posterior roots. The fibers ascend in the spinal cord for few segments to synapse with the nucleus proprius. While ascending they send collaterals to a large number of nucleus proprius.

- **Second order neurons:**

- They are cells in nucleus proprius. Their axons cross to other side in anterior white commissure to form the ventral spinothalamic tract the ventral column of white matter. It ascends through the brain stem. In the pons it joins the lateral spinothalamic tract to form spinal lemniscus that ends in the P.L.V.N of the thalamus.

- **Third order neurons:**

They are the cells of ventral posterolateral nucleus (V.P.L.N) of thalamus. Their axons ascend in sensory radiation to reach sensory area in post central gyrus of cerebral cortex (area 3,1,2).



Tract	Lateral Spinothalamic	Ventral Spinothalamic
<b>Definition</b>	Long ascending sensory tract in spinal cord.	
<b>Origin</b>	Cells of SGR of opposite side.	cells of MSN of opposite side.
<b>Course</b>	<ul style="list-style-type: none"> <li>• Crossed.</li> <li>• Lateral column of spinal cord (all levels).</li> <li>• Joins ventral spinothalamic tract at the pons to form spinal lemniscus.</li> </ul>	<ul style="list-style-type: none"> <li>• Crossed</li> <li>• Ventral column of spinal cord(all levels).</li> <li>• Joins lateral spinothalamic tract at the pons to form spinal lemniscus.</li> </ul>
<b>Termination</b>	ventral posterolateral nucleus (V.P.L.N) of thalamus.	
<b>Function</b>	Pain, temperature from opposite side of body.	crude touch from opposite side of the body.

### Spinal lemniscus

- **Definition:** Ascending sensory bundle in the brain stem formed by lateral and ventral spinothalamic tracts.
- **Course:** in pons → mid brain.
- **Termination:** PLVNT.

➤ **Function:** pain, temperature and crude touch from opposite side of body.

	<b>Proprioception &amp; Fine touch</b>	<b>Crude touch</b>	<b>Pain &amp; Temperature</b>
<b>Receptors</b>	<ul style="list-style-type: none"> <li>• <b>Proprioception:</b> Muscle spindle, tendon spindle, Pacinian corpuscle</li> <li>• <b>Fine Touch</b> <ul style="list-style-type: none"> <li>• Meissner's corpuscle,</li> <li>• Rufini's Corpuscle</li> <li>• Merkel's disc.</li> </ul> </li> </ul>	1- Free Nerve ending 2- Peritrichial N. endings. 3- Merkel's disc 4- Meissner's Corpuscle	<ul style="list-style-type: none"> <li>• Free nerve endings.</li> </ul>
<b>1<sup>st</sup> order Neuron</b>	<ul style="list-style-type: none"> <li>• <b>Large cells</b> in spinal ganglia: <b>thick</b> myelinated fibers enter the <b>medial</b> division of the post. Roots.</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Medium sizes cells</b> in spinal ganglia: <b>Medium sized</b> myelinated fibers &amp; enter the <b>medial</b> division of the post. Roots.</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Small cells</b> in spinal ganglia: <b>thin</b> myelinated nerve fibers &amp; enter the <b>lateral</b> division of posterior root.</li> </ul>
<b>2<sup>nd</sup> order Neuron</b>	<ul style="list-style-type: none"> <li>• <b>Gracile &amp; Cuneate</b> nuclei in medulla.</li> <li>• They give rise to internal arcuate fibers that cross to opposite side at the upper half of medulla (sensory decussation) to form medial lemniscus.</li> </ul>	<b>Main Sensory Nucleus (MSN)</b> <ul style="list-style-type: none"> <li>• Axons cross to opposite side to form ventral spinothalamic T. in the ventral C. of white m.</li> <li>• In pons it joins the lateral spinothalamic T. to form spinal lemniscus.</li> </ul>	<b>SGR</b> <ul style="list-style-type: none"> <li>• Axons cross to opposite side to form lateral spinothalamic T. in the lateral C. of white m.</li> <li>• In pons it joins ventral spinothalamic T. to form Spinal lemniscus.</li> </ul>
<b>3<sup>rd</sup> order Neuron</b>	V.P.L.N of thalamus. Their axons ascend in the posterior limb of internal capsule & corona radiate to reach sensory area in the post central gyrus of cerebral cortex (area 3,1,2).		

### The short tracts of the spinal cord

❖ These are tracts that start and end in the spinal cord

<b>Tract</b>	<b>Fasciculi Proprii</b>	<b>Lissauer's</b>	<b>Septomarginal</b>	<b>Comma-shaped</b>
<b>Site</b>	- Around grey matter of all segments of the spinal cord	- All segments of spinal cord	- Posterior column of white matter in sacral, lumbar, and lower thoracic segments	- Posterior column of white matter in Cervical & upper thoracic segments
<b>Origin</b>	Axons of associative nuclei	Small cells of dorsal root ganglia	Gracile tract	Cuneate tract

<b>Course</b>	Ascend and descend for few segments surrounding grey matter like a ring	Enter spinal cord through lateral division of post root to ascend and descend for 1 or 2 segments	Short descending fibers
<b>Termination</b>	Associative nuclei of other spinal cord segment	SGR	AHCs
<b>Function</b>	Coordinate function of different segments of spinal cord	pain and temperature sensations	Carry proprioceptive sensation to complete stretch reflex arc and maintain muscle tone

### Pathway of sensory impulses to subcortical levels

1 <sup>st</sup> O.N.		Large cells of dorsal root ganglia					Cells of dorsal root ganglia
2 <sup>nd</sup> O.N.	<b>origin</b>	Gracile and cuneate nuclei	Accessory cuneate nucleus	Clark's nucleus in lamina VII	Cells in laminae V-VII in post. horn	Cells in laminae IV&V in post. horn	Cells in laminae I&V in post. horn
	<b>Tract</b>	External arcuate fibers (ant. & post.)	Cuneo-cerebellar tract	Dorsal spinocerebellar tract	Ventral spinocerebellar tract	Spino-olivary tract	Spinotectal tract
	<b>Course</b>	Not in the spinal cord		Lat. Column of spinal cord (upper lumbar, thoracic, & cervical) + closed medulla	Lat. Column of spinal cord (all levels) + brain stem	All levels of spinal cord	All levels of spinal cord + brain stem
	<b>Termination</b>	Cerebellum through inf. Cerebellar peduncle	Cerebellum through inf. Cerebellar peduncle	Cerebellum through inf. Cerebellar peduncle	Cerebellum through sup. Cerebellar peduncle	Inf. Olivary n. then via olivocerebellar tract to Cerebellum through inf. Cerebellar peduncle	Tectum of superior colliculus of midbrain
<b>function</b>		Carry proprioceptive sensations to the cerebellum					Spino-visual reflex
<b>Sensation coming from:</b>		All spinal cord segments	above C8	C8-L2	lumbar, sacral, and coccygeal segments	All spinal cord segments	All spinal cord segments

### Pathway from the Face & Head

#### 1- Proprioception Pathway

- **Receptors:** muscle spindles & tendon spindles in muscles of mastication. Pacinian corpuscles in deep dermis.
- **First order neurons: are inside the CNS.** They are the only exception to the rule. They are located in the **mesencephalic nucleus**.
- **Second order neurons:** The axons of the mesencephalic nucleus descend to synapse with the cells in **main sensory nucleus**. Their axons cross and enter the trigeminal lemniscus.

- **Third order neurons:**

They are the cells of **PMVN of the thalamus**. Their axons end in the sensory area in cerebral cortex.

## 2- **Pain and temperature pathway**

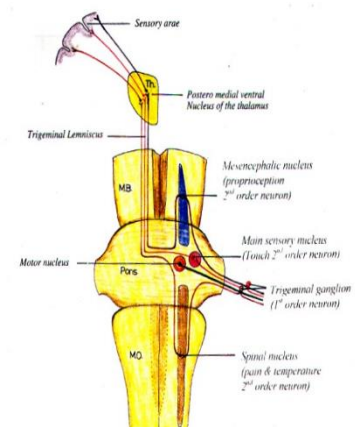
- **Receptors:** as in body.
- **First order neurons:** cells in the **trigeminal ganglion**.
- **Second order neurons:** cells in the **spinal nucleus**. Their axons cross and enter the trigeminal lemniscus.
- **Third order neurons:**  
They are the cells of **PMVN of the thalamus**. Their axons end in the sensory area in cerebral cortex.

## 3- **Simple touch pathway**

- **Receptors:** as in body.
- **First order neurons :** cells in trigeminal ganglion
- **Second order neurons:** cells in the main sensory nucleus . Their axons cross and enter trigeminal lemniscus
- **Third order neurons:** they are the cells of PMVN of the thalamus. Their axons end in sensory area in cerebral cortex  
definition: ascending sensory fibers carrying sensations from the face

### **Trigeminal lemnisci**

- **origin:** 2nd order neuron in sensory pathways from face
  - **Spinal nucleus of trigeminal nerve**
  - **Main sensory nucleus.**
- Their axons cross to opposite side to form trigeminal lemniscus
- **Course:** in upper & middle level of pons & mid brain
- **Termination:** PMVNT.
- **Function:** carries pain, temperature, simple touch and proprioception from face and scalp of opposite side



## **Lesions of Sensory System**

### **[A] Hyperalgesia:    Hypersensitivity to pain**

<i>Primary hyperalgesia</i>	<i>Secondary hyperalgesia</i>
- It occurs in inflamed skin (red area) as in sun burn or abscess - Bradykinin & K <sup>+</sup> are released → lower threshold of pain → so, non-painful stimuli become painful	- It occurs in normal skin (no red area) - Lesion in thalamus or spinal cord → increase the threshold of pain (so, Pain receptors need stronger stimulus but once pain is elicited → it is very severe)

### **[B] Patterns of sensory loss:**

#### **I.    Peripheral nerves**

##### **❖    Peripheral neuropathy:**

- Lesion of peripheral nerves    (peripheral neuritis)

- Sensory neuropathy: Leading to loss of all sensation in the area of supply
- Polyneuropathy :
  - Is diffuse lesion of all peripheral nerves
  - Loss of sensations (especially pain) starts distally leading to socks& gloves sensory loss

## II. Root Affection

### ❖ Herpes zoster:

- It is a virus which infects dorsal root ganglion (DRG)→ excitation of pain neuronal cells → severe pain in the dermatomal segment supplied by infected ganglion.
- The virus migrates to the cutaneous terminals → rash & vesicles.

## III. Spinal cord lesions

### ❖ Tabes dorsalis: Syphilitic “Spirochetes” disease

- Affects: Posterior column:
  - Severe pain: As it irritates pain fibers at first, then followed by loss of pain sensation
  - Degeneration of posterior column:
    - Leading to Loss of fine touch, pressure, vibration & proprioceptive sensation
    - Resulting in :
      - Sensory ataxia: Incoordination of voluntary movement in absence of paralysis
      - +Ve Romberg's sign: The patient maintains his erect position by visual impulses ie if he closes his eye, he falls

### ❖ Syringomyelia:

- Widening of the central canal of the spinal cord (usually cervical)
- Damage: Pain & temperature fibers & later on fibers of crude touch & pressure (as they cross immediately in front of central canal)
- This leads to loss of: Pain, temperature, crude touch & pressure on both sides at the level of the lesion → Jacket sensory loss
- The sensations carried in the dorsal column e.g. fine touch, pressure, vibration, Kinesthesia are not affected i.e. dissociation of cutaneous sensations occurs.

### ❖ Brown Squared syndrome: Hemi section of spinal cord

#### • Results in:

#### 1- *At the level of the lesion: At the same side*

- Sensory: Loss of all sensations at the corresponding dermatome
- Motor: Lower motor neuron lesion ie flaccid paralysis loss of reflexes

#### 2- *Below the level of the lesion:*

##### ➤ *On the same side:*

- Sensory: Loss of fine touch, pressure, vibration & kinesthesia (posterior column)
- Motor: Upper motor neuron lesion (UMNL) i.e. spastic paralysis, hyper-reflexia & +ve Babinski sign

##### ➤ *On opposite side:*

- Sensory: Loss of pain, temperature, crude touch
- Motor: No loss

**NB: So, touch is not lost but decreased in both sides**

## ❖ Thalamic syndrome

### • Cause:

- Thrombosis of thalamo-geniculate artery (branch of posterior cerebral artery)
- This artery supplies Posteroventral nucleus of thalamus & lateral ventral nucleus of thalamus

### • Effects:

#### 1. **Contralateral loss of all sensations**

#### 2. **After few months :**

- Return of some crude sensations
- Return of pain (thalamic pain = very severe unpleasant pain) characterized by: Increase threshold i.e. needs stronger stimulus to produce it, Once produced, it is very severe
- 3. **Mixed ataxia:** i.e. combination of:
  - Sensory ataxia: Due to loss of proprioceptive sensations
  - Cerebellar ataxia: Due to loss of connection between cerebellum & cortex

**NB: This connection passes through the lateral ventral nucleus**

#### 4. **Emotional disturbances**

#### 5. **Brain stem lesions:** Contralateral loss of all sensations

#### 6. **Cortical lesions:**

- Lesion of sensory cortex: Leading to contralateral loss of cortical sensations
- Lesion of somatic association area: Leading to inability to recognize complex objects

## **Pain Sensation**

### ➤ **Definition:**

- Pain is unpleasant sensation for body protection
- It occurs when there is tissue damage

### ➤ **NB:**

- Cerebral cortex is not essential for perception Pain
- Pain perception can occur at level of thalamus and reticular formation
- The cortex role in perception of pain is to localize site of pain and discrimination of intensity and modality of pain

### ➤ **Pain receptors:** Are free nerve ending of Aδ fibers & C fibers

#### ▪ Types:

- Mechanical pain receptors:** Stimulated by mechanical injurious stimuli
- Thermal pain receptors:** - Cold pain - Warm pain
- Chemical pain receptors:** Stimulated by chemical injurious stimuli eg:
  - ❖ HCl in case of peptic ulcer disease “PUD ”
  - ❖ Other injurious stimuli (chemical mediators of pain) include :
    - Histamine - Serotonin - Bradykinin (most painful)
    - Prostaglandin - Proteolytic enzyme - K<sup>+</sup>
  - ❖ These chemicals stimulate chemical pain receptors & lower threshold of other pain receptors

#### ▪ Distribution of pain receptors:

### ➤ **More in:**

- Skin - Joint surfaces - Arteries
- Periosteum - Falx cerebri - Tentorium cerebelli & cranial sinuses



- **Less in:** Deep tissues
- **Absent in:** - Liver parenchyma - Lung alveoli - Brain (pain insensitive)
  - Nerve fibers: A delta and C fibers
  - Adaptation: Slowly or non-adaptive receptors
  - Threshold of pain:

- Is the same for all people but reactions differ from one person to another
- Pain felt when skin temperature is 45°C

- Reaction to pain:

**a) Motor Reaction:**

- Fast: Withdrawal reflex (Cutaneous pain)
- Slow: Increase muscle tone (Visceral pain)

**b) Emotional Reaction:**

- Fast: Screaming & anxiety (Acute pain)
- Slow: Depression (Chronic pain)

**c) Autonomic Reaction:**

- Fast: Tachycardia & increase ABP (Cutaneous pain)
- Slow: Bradycardia & decrease ABP (Visceral pain)

**d) Arousal Reaction:** Pain pathways give collateral to reticular formation & none specific thalamic to **enhancing wakefulness & alertness**

- Types of Pain sensations

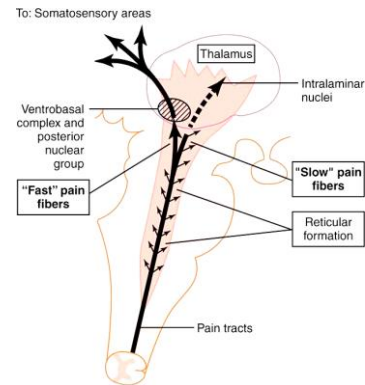
❖ Pain sensations could be classified into:

- 1-Fast pricking pain      2- Slow burning pain

OR

❖ Pain sensations could be classified into:

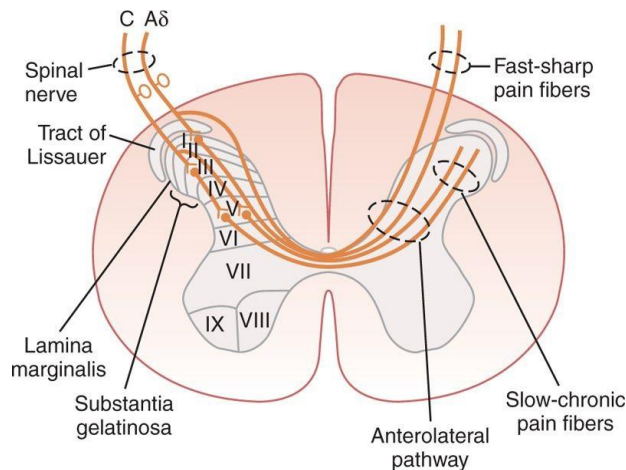
- 1- Cutaneous pain      2- Deep pain      3- Visceral pain



*Transmission of pain signals into the brain stem, thalamus, and cerebral cortex by way of the fast pricking pain pathway and the slow burning pain pathway*

Types	Fast pricking pain	Slow burning pain
	Acute Pain	Chronic Pain
<b>Quality</b>	Immediate, sharp	Aching, throbbing
<b>Onset</b>	Felt within 0.1 second	After 1 second
<b>Duration</b>	Short duration	Long & annoying
<b>Receptors</b>	Mechanical & thermal	Elicited by <b>all</b> types of receptors
<b>Carried by</b>	A delta Fibers	C fibers
<b>Localization</b>	Well localized	Poorly localized (diffuse)
<b>Center</b>	<b>Ends in:</b> Cerebral cortex	<b>Ends in</b> <ul style="list-style-type: none"> <li>• Reticular formation</li> <li>• Brain stem</li> <li>• Non- specific: Thalamic nuclei then to whole cortex</li> </ul>
<b>Felt in</b>	1-Skin 2-Parietal surfaces	1- Skin 2- Deep structures (Viscera)
<b>Blocked by</b>	1.Hypoxia 2.Compression	-Local anesthetic as Cocaine (applied to certain areas of the body As smooth, through “acts by blocking conduction of nerve impulses”)

<b>Pathway</b>	Neospinothalamic	Paleospinothalamic
<b>Chemical transmitter</b>	Glutamate	Substance P
<b>Motor response</b>	Withdrawal reflex	Increase muscle tone
<b>Autonomic response</b>	<b>Increase:</b> 1- ABP 2- HR 3-Sweating	<b>Decrease:</b> 1-AB 2- HR 3- Sweating



*Transmission of both "fast-sharp" and "slow-chronic" pain signals into and through the spinal cord on their way to the brain*

### **Pain sensations could be classified into:**

#### **1- Cutaneous pain:**

- Is produced by stimulation of pain receptors in the skin
- Starts as fast pricking followed by prolonged slow burning pain
- Is accurately localized due to:
  - a. The high density of pain receptors in the skin
  - b. The fast pain fibers reach the sensory cortex there localization is accurate.

#### **2- Deep pain:**

- **Conducted along:** C fibers
- **Characters:** Poorly localized (Diffuse), dull aching with depressor effects
- **Produced from:** - Muscle - Tendons - Ligaments  
- Joints - Periosteum
- **Causes:**

##### **1. Ischemia:**

- Ischemic pain: It is type of deep pain
- **Mechanism:**
  - Decreased blood supply to a tissue due to vessel narrowing by:
  - Thrombosis

##### **2. Inflamed vessel (Vasculitis)**

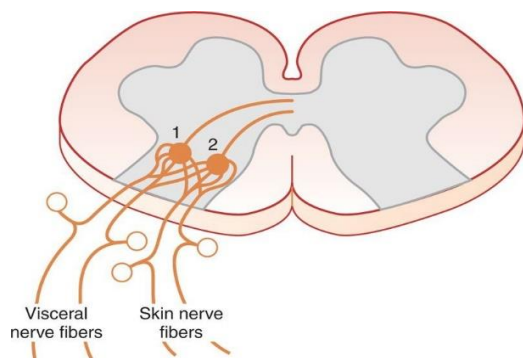
- **Leading to:**
  - Accumulation of metabolites as lactic acid
  - Release of proteolytic enzymes from ischemic tissue

- Resulting in stimulation of pain receptors
  - **Example:**
    - **Angina pectoris:** Ischemia of cardiac muscle
    - **Intermittent claudication:** Ischemia of skeletal muscle Due to decrease blood supply (eg narrowing of arteries) supplying muscles of lower limb
    - **Visceral pain:** This pain arises from viscera of thorax and abdomen
- **Conducted along :**
  - Pain from viscera is carried along C fibers
  - Pain from peritoneum, pleura or pericardium is carried along: A delta fibers
- **Most of viscera contain only pain receptors**
- **It differs from cutaneous pain :**
  - Sharp cut in the viscera does not cause pain
  - Diffuse stimulation of pain nerve endings causes severe pain
- **Causes:**
  1. Irritation: Chemical irritation by HCl in peptic ulcer disease “PUD”
  2. Overdistension of hollow viscous (as urinary bladder) → mechanical stimulation
  3. Spasm of a hollow viscous (as gut, gall bladder or ureter) →
    - Mechanical stimulation of pain receptors
    - Ischemic pain: Due to obliteration of BV
  4. Ischemia: Causing accumulation of acidic metabolites, bradykinin, proteolytic enzymes.
  5. Peritonitis (Inflamed peritoneal covering of viscera)
- **Characters:**
  1. Dull aching or cramps
  2. Diffuse & poorly localized
  3. Depressor (parasympathetic): Autonomic changes :
    - HR: Bradycardia
    - ABP: Hypotension
  4. Nausea & vomiting
  5. Rigidity of muscles overlying the affected area
  6. Referred to the surface area i.e. referred pain

### Referred pain

- **Definition:**
  - Pain is felt on a surface area originating from the same dermatome of the diseased viscous or supplied by the same dermatome
- **Simply Mechanism:**

Convergence Projection Theory	Facilitation Theory
<ul style="list-style-type: none"> <li>- Afferent pain fiber from diseased viscus &amp; afferent from skin rise from same dermatome <b>converge</b> on same neuron in <b>SGR</b> &amp; reach the same area in cerebral cortex</li> <li>- The brain project sensation to skin &amp; not to diseased viscus</li> </ul>	<ul style="list-style-type: none"> <li>- Afferent visceral pain fiber give collateral that end on posterior horn cell receiving pain from the skin produce EPSPS on them lead to its stimulation.</li> </ul>



### Mechanism of referred pain

#### • Examples

- 1- Cardiac pain
  - Retrosternal      - Root of the neck
  - Outer part of the chest      - Inner part of left arm
  - Epigastrium
2. Gastric pain: Is felt between the umbilicus & xiphoid process
3. Gall bladder pain: Is felt in :
  - Epigastrium      - Tip of right scapula
4. Appendix pain: Is felt around umbilicus
5. Renal pain: Is felt in :
  - The back      - Inguinal region      - Testicles

### Pain control

#### 1- Gate Inhibition

##### -SGR:

- Acts as gate (through which pain impulses reach lateral spino-thalamic tract)
- It can be closed by impulses from:
  - A beta fiber → So Rubbing of skin → inhibits pain
  - A delta fiber → So Aquapuncture → inhibit pain
  - Corticofugal fibers → So thinking → inhibit pain
- All these fibers cause pre-synaptic inhibition of pain fibers by activation an interneuron which secrete GABA

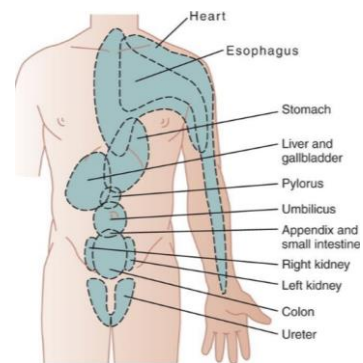
#### 2-Supraspinal Analgesia System

##### a-Periaqueductal gray area :

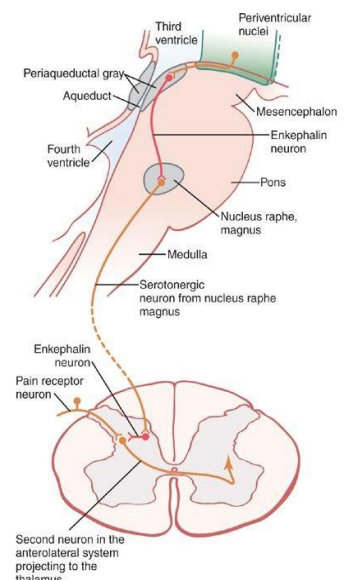
- In midbrain & upper pons:
- Neurons in this area are stimulated by:  $\beta$ -endorphin reaching from pituitary .
- They secrete Enkephalin & send their signals to Raphe magnus

##### b- Raphe magnus nucleus:

- In lower pons & medulla
- Neurons of Raphe magnus secrete serotonin & send their signals down the dorsolateral column to pain inhibitory area in spinal cord.



### Surface areas of referred pain from different visceral organs



### Pain inhibitory complex area:

- In dorsal horn of spinal cord:
- It consists of many interneurons which release Enkephalin. They cause pre-synaptic inhibition of SGR (Substantia Gelatinosa of Rolandi) → preventing release of chemical transmitters (substance P).

## 2- Brain Opiate System

### a- Morphine is a powerful pain killer (analgesic):

- It is exogenous opioid
- Extracted from : Plant (called opium)
- It combines to receptors in CNS

### b-Endogenous opioid peptides

- They cannot cross BBB “Blood Brain Barrier” (So IV injection is ineffective)

#### • Types:

#### ➤ **β Endorphins:** Is 30 amino acids

- **Present in:** - Hypothalamus - Pituitary
- They are secreted in stress conditions (eg battle) → reaching opioid receptors in body causing analgesia (stress analgesia)

#### ○ **N.B.**

■ **Endorphins in hypothalamus act as: Neurotransmitters**

■ **Endorphins in pituitary act as: Neurohormone**

#### ➤ **Enkephalins:**

- Meta & leu enkephalins are : Pentapeptides (5 amino acids)
- They are derived from proenkephalin
- They are present in different parts of CNS eg:
  1. Periaqueductal grey matter
  2. SGR “Substantia Gelatinosa of Rolandi”
  3. Limbic system

#### ➤ **Dynorphin:**

- They are: 17amino acids
- Very potent analgesic
- Responsible for addiction & tolerance for opiates

#### ➤ **Opiate receptors:**

#### • Types:

○ **μ Receptor (Mu):** Have high affinity to Endorphins

○ **δ Receptor (Delta):** Have high affinity to Enkephalins

○ **K Receptor (Kappa):** Have high affinity to **Dynorphin**

■ **Sites:** -Periaqueductal gray area - Raphe magnus nucleus: In **medulla**

■ **Blocked by: Naloxone** (Which used for their identification)

### Headache

-Headache is referred pain as brain itself is insensitive to pain

-Pain sensitive intra-cranial structures include:

- 1- Arteries: Dural arteries especially the middle meningeal A.
- 2- Veins: Venous sinuses
- 3- Nerves: V, IX & X
- 4- Dura
- 5- Tentorium:

- Stimulation of pain receptors **above tentorium** is referred along ophthalmic nerve causing **frontal headache**
- Stimulation of pain receptors **below** tentorium is referred along 2<sup>nd</sup> cervical nerve causing **occipital headache**

#### -Causes

#### 1- **Headache of Intra-cranial origin :**

##### -Causes :

**A-Migraine headache :** Caused by abnormal vascular phenomenon due to unknown cause

- Aura prodromal: Tension or emotion: Causes vasospasm of cerebral vessels → ischemia → nausea, visual & sensory manifestations
- Headache: As a result of prolonged ischemia → accumulation of metabolites → vasodilatation → strong pulsation (throbbing pain)

**B- Meningeal irritation :**

- Meningitis: Headache is referred over entire head
- Brain tumor: Headache is referred to localized area of
- Operative trauma: Headache for several days

**C-Hypertension:** Headache due to marked expansion of cerebral vess

**D- Intra-cranial pressure:** whether increased or decreased

#### ❖ **Clinical Application**

- Decrease ICP after lumbar puncture (removal of 20 ml CSF) → brain descent → traction of Dura → headache

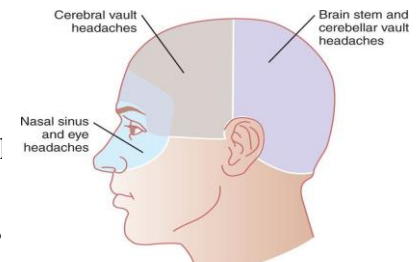
**E- Alcoholic:** Produces direct meningeal irritation

**F- Constipation :** Meningeal irritation (due to absorption of toxic substances)

#### 2. **Headache of Extra-cranial origin**

##### -Causes :

- Muscular spasm of scalp & neck - Irritation of nasal sinuses
- Eye disorders:
  - Glaucoma
  - Errors of refraction: Due to spasmodic contraction of ciliary muscle & extra-ocular muscles
- Otitis media - Toothache
- Systemic disorders as: anemia, infection.



Areas of headache resulting from different causes

#### **Ascending Reticular Activating System (ARAS) or (RAS)**

- RAS is the ascending branches of neurons of the facilitatory reticular area
- The fibers of RAS extend upwards to all areas of cerebral cortex either :
  - Directly
  - Through nonspecific thalamic nuclei (reticula-thalamo-cortical pathway)

#### • **Functions of RAS:**

- Responsible for the:
  - Alert - Conscious - Wakefulness state of person
- Plays an important role in control of sleep
- Its depression leads to sleep while its damage leads to coma

#### • **Factors affecting activity of RAS:**

➤ **Factors that increase RAS activity**



1. All sensory signals from sensory pathway tracts:
  - Auditory are more effective than visual
  - Pain and proprioceptive signals are more effective
2. Signals from cerebral cortex through Corticofugal fibers to RAS: e.g.:
  - Motor signals from motor cortex → so performance of voluntary movements help person to resist desire for sleep
  - Signals from temporal & frontal lobe in emotions
3. Drugs: Sympathomimetics eg:
  - Adrenaline                      - Noradrenaline                      - Dopamine
  - Amphetamine                      - Aminophylline                      - Caffeine

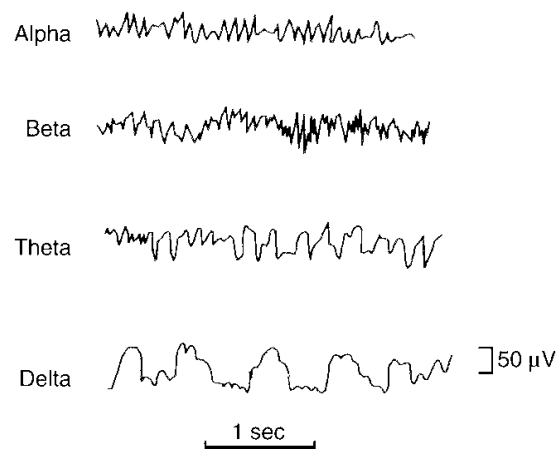
➤ **Factors that decrease RAS activity:**

1. Reduction of signals from sensory pathways
2. Reduction of signals from cerebral cortex
3. Stimulation of sleep centers
4. General anesthesia & drugs e.g. alcohol, morphine, narcotics
5. Extensive damage of RAS e.g. tumors

**Electro-encephalogram (EEG)**

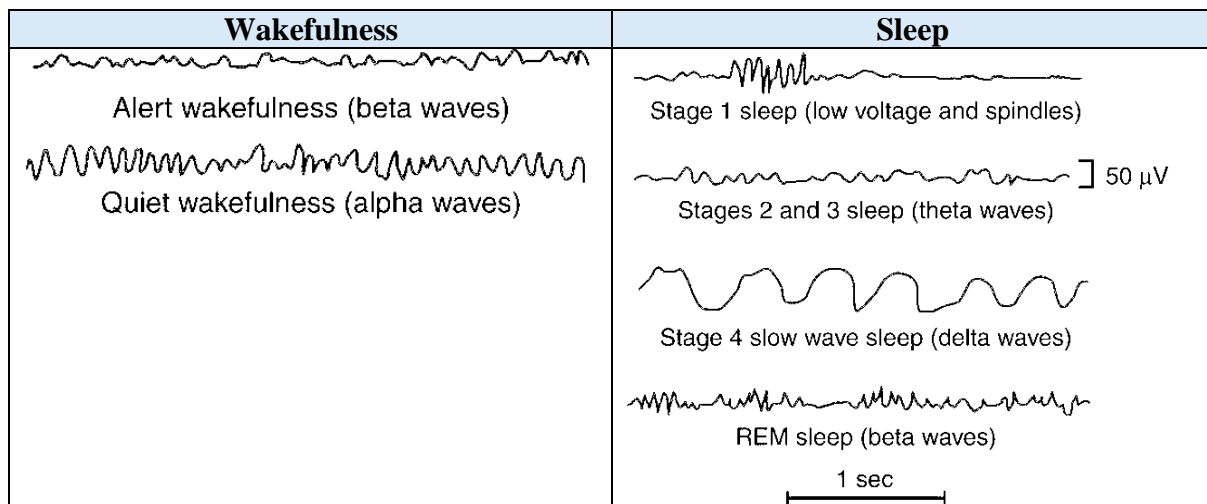
It is recording of the electrical activity of the brain in conscious subjects through intact skull  
The normal waves recorded by EEG are:

- Alpha                      - Beta                      - Theta                      - Delta                      - Lambda



**Different types of brain waves in the normal electroencephalogram**

- Their frequency is inversely proportional to amplitude
- ❖ **Alpha waves (α) Have:**
  - Low frequency                      - High amplitude
  - Recorded in adults who are relaxed with eye closed
- ❖ **Beta waves (β) Have:**
  - High frequency                      - Low amplitude
  - Recorded in adults with open eyes, at anxiety, alert & sensory stimuli



*Progressive change in the characteristics of brain waves during different stages of wakefulness and sleep*

❖ **Sleep:** It is a state of unconsciousness from which a person can be aroused by proper sensory stimuli

- Sleep is two types that alternate with each other:

**Slow wave sleep (non-rapid eye movement) (non REM)**

- Which is the first to occur when the person falls sleep
- It is orthodoxically sleep
- It is the first to occur at start of sleep
- It is about 80% of sleep
- It persists for 90 minutes
- It is associated with non-rapid eye movement
- Decrease:
  - Heart rate                      - Arterial blood pressure (ABP)
  - Respiratory rate            - Basal metabolic rate
- The muscle tone is reduced
- No dreams or teeth grinding
- No swallowing, erection or ejaculation
- **EEG show four stages:**

➤ **Stage I:** Waves are characterized by:

- Low amplitude      - High frequency

➤ **Stage II:**

- The waves are spindle shaped (light sleep)

➤ **Stage III:** Waves are characterized by:

- High amplitude            - Low frequency moderate sleep

➤ **Stage IV:** Very large waves (deep sleep)

- Rapid eye movement (REM) or paradoxical sleep
- It is paradoxical sleep
- It occurs after 4th stage of non-REM
- It is about 20% of sleep
- It persists for 20 minutes
- It is associated with rapid eye movement

**Rapid eye movement (REM) or paradoxical sleep**

- It is paradoxical sleep
- It occurs after 4<sup>th</sup> stage of Non REM

- It is about 20% of sleep
- It persists for 20 minutes
- It is associated with rapid eye movement
- **Increase:**
  - Heart rate      - Arterial blood pressure (ABP)
  - Respiratory rate
- The muscle tone is reduced due to activation of inhibitory reticular area
- The dreams occur in this stage
- **It is associated with:**
  - Teeth grinding                      - Swallowing
  - Erection                                - Ejaculation
- EEG shows small rapid irregular  $\beta$  waves i.e. like an alert person. So, it is termed paradoxical as the waves are like that of alert person while he is difficult to be aroused

### Mechanism of Sleep:

- Sleep is secondary to inhibition of RAS by the following mechanisms:
  - 1) Passive mechanism (theory) → Passive inhibition of RAS by:
    - a. Fatigue of its neurons after a period of wakefulness
    - b. Elimination of its exciting stimuli e.g.: Visual & Auditory
  - 2) Active mechanism (theory)
    - Active inhibition of RAS by signals discharged from subcortical centers
    - The chemical transmitters of sleep are:
      - Serotonin                      - Prostaglandin                      - Acetyl choline                      - Noradrenaline

### Descending Tracts

- They are divided into upper motor neuron and lower motor neuron
  - **Upper motor neuron:**
    - The nerve cells present in cerebral cortex or subcortical level and terminate at motor nuclei of cranial nerves or anterior horn cells of spinal cord.
  - **Lower motor neuron:**
    - The motor nuclei of cranial nerves and the anterior horn cells give axons that terminate at the muscles.
  - The upper motor neurons are classified into pyramidal and extrapyramidal tracts.

#### a-Pyramidal Tracts

- 1- Corticobulbar tract.
- 2- Corticospinal tract.

#### 1. Corticobulbar tracts:

- The fibers arise from cerebral cortex and terminate in motor nuclei of cranial nerves in brain stem. It is further subdivided into lateral Corticobulbar and medial Corticobulbar.

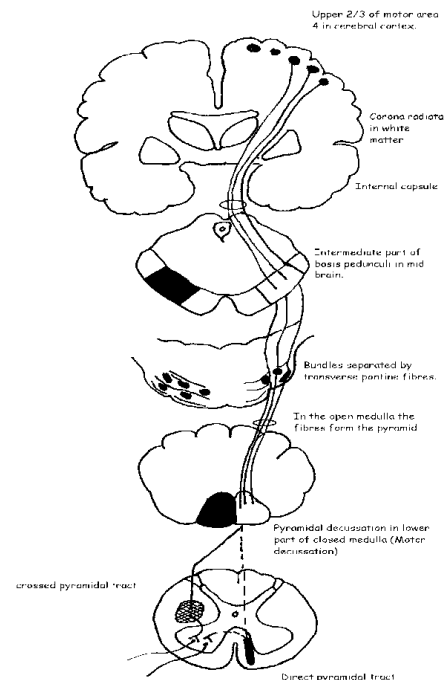
**a- Medial Corticobulbar tract:**

- **Origin:** Motor area 8 in cerebral cortex.
- **Course:** the fibers descend in corona radiata and then lie in the genu of internal capsule. In the mid brain they are present in the basis pedunculi very close to the middle line.
- **Termination:** they end on the motor nuclei of cranial nerves 3, 4, & 6 on both sides.

**b- Lateral Corticobulbar tract:**

- **Origin:** lower 1/3 of motor area 4 in cerebral cortex.
- **Course:** the fibers descend in the corona radiata and then in the genu of the internal capsule. In the mid brain they pass in the basis pedunculi lateral to the corticospinal fibers
- **Termination:** they end on the motor nuclei of the cranial nerves; 5, 7, 9, 10, 11, 12 on both sides **except**

- The portion of hypoglossal nerve that provides innervation for tongue protrusion
- The part of facial nerve that innervates the muscles of the lower face.
- They only receive contralateral innervation from the pyramidal tract.



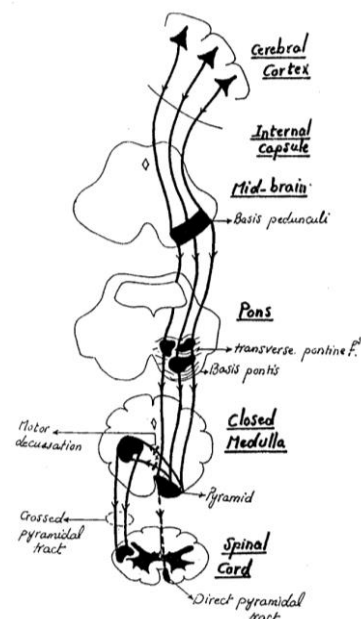
**2. Corticospinal tracts:**

- The fibers arise from cerebral cortex and terminate in anterior horn cells of the spinal cord.

- **Origin:** Betz cells & others in upper 2/3 of motor area 4 in cerebral cortex.

- Corona radiata in white matter.
- Genu & anterior 2/3 of posterior limb of internal capsule.
- Intermediate part of basis pedunculi in mid brain.
- Basis pontis as bundles separated by transverse pontine fibers.
- Pyramid in upper Medulla.
- Pyramidal decussation in lower part of closed medulla (Motor decussation) where 80-90% of the fibers cross to opposite side.
- In the spinal cord the crossed pyramidal tract is present in lateral column of white matter in all levels while the direct pyramidal tract is present in the anterior column of white matter in cervical and upper thoracic levels.

- **Termination:** In anterior horn cells of the opposite side. Some end on the same side.



**N.B.: Direct pyramidal tract crosses in the spinal cord to end on the anterior horn cells of the opposite side. Few fibers end on the same side.**

- **Function:** control voluntary movement and increases tone and reflexes in muscles

#### **b- Extrapyramidal tracts**

- They are descending motor fibers that do not pass through the pyramids of the medulla.
- *They can be divided into main 2 groups:*
  - a) Extrapyramidal tracts that arise from cerebral cortex and terminate in the brain stem.
  - b) Extrapyramidal tracts that arise from brain stem and terminate in the anterior horn cells of the spinal cord.

Single tracts	Paired tracts
<ul style="list-style-type: none"> <li>• <b>Rubrospinal.</b></li> <li>• <b>Olivospinal.</b></li> <li>• <b>Sulco- marginal.</b></li> </ul>	<ul style="list-style-type: none"> <li>- <b>Ventral and lateral reticulospinal.</b></li> <li>- <b>Ventral and lateral tectospinal.</b></li> <li><b>Ventral and lateral vestibulospinal</b></li> </ul>

### **The motor cortex**

**is divided into:**

<b>[A] Primary motor area</b>		<b>[B] Premotor area</b>
Paralysis of muscles of opposite side	<b>Lesions</b>	Paresis (muscle weakness) of opposite side
Hypotonia (flaccidity)	<b>Motor</b>	Hypertonia (rigidity)
<b>Reflexes</b>		
Hyporeflexia of deep reflexes	<b>Deep</b>	Hyper-reflexia of deep reflexes
Loss of superficial reflexes	<b>Superficial</b>	Reappearance of grasp reflex Aphasia
<b>Babinski sign:</b> - Scratching of outer aspect of sole of foot leads to: - Dorsiflexion of big toe - Fanning of lateral 4 toes	<b>Plantar reflex</b>	<b>Plantar reflex shows:</b> - Fanning of lateral 4 toes but - No dorsiflexion of big toe - Reappearance of grasp reflex - Aphasia      - Apraxia

### **Cortical Control of Motor Functions**

**For performance of voluntary movements: 2 neurons are essential:**

#### **1- Upper Motor Neuron [UMN]:**

##### **a. Pyramidal tracts:**

- **Origin:** Originates from primary motor area, premotor areas and somatic sensory area posterior to central sulcus
- **Types**

1. Cortico-bulbar tract→Supplying motor nuclei of cranial nerves

2. Cortico-spinal tracts:

- **Functions of pyramidal system:**

- Responsible for complex fine skilled voluntary movements of fingers, toes and face
- Facilitatory to muscle tone and deep reflexes

- **Lesion results in:**

- Paralysis of muscles (if the lesion above medulla: Paralysis will be contralateral ie of opposite side) .
- Pure pyramidal Lesion (which is uncommon) also results in:
  - Hypotonia (flaccid paralysis).                      - Hyporeflexia of deep reflexes

b. **Extrapyrmidal:**

- **Def.**→All parts of the brain and brain stem that are concerned with motor control other than the pyramidal system.

- **Origin**→ Premotor area, basal ganglia, reticular formation, red nuclei and vestibular nuclei.

- **Extrapyrmidal tracts:**

1. Rubrospinal tract                      2. Reticulospinal tract                      3. Tectospinal tract
1. Vestibulospinal tract                      5. Olivo spinal tract

- **Functions:**

- I. Control gross movement that involves a group of muscles which are required for fixation
- II. Facilitatory or inhibitory to muscle tone

**2- Lower Motor Neuron [LMN]:**

- ❖ Cranial motor nuclei (in brain stem) & their axons (motor cranial nerves)
- ❖ Anterior motor neurons (in spinal cord) & their axons (motor nerves)

Effects	Upper motor neuron lesion	Lower motor neuron lesion
(1) <b>Paralysis:</b> -Distribution -Side -Type -Recovery	<b>Contralateral hemiplegia</b> -Wide spread. -Opposite side -Spastic (++ muscle tone) - There is permanent loss of voluntary movements of hands & fingers.	-Localized -Same side -Flaccid (-- muscle tone) -May occur because nerves have <b>neurolemma</b>
(2) <b>Reflexes:</b> <b>stretch reflex &amp; muscle tone</b>	- <b>Spasticity</b> = ++ muscle tone, more in the antigravity muscles -The upper limb is adducted & flexed at elbow & wrist -The lower limb is adducted & extended at hip & knee. -The spasticity is of <b>clasp knife</b> . It is caused by damage of inhibitory pathways to stretch reflex	- <b>Flaccidity</b> = muscle tone (absent muscle tone)
-Deep reflexes -Superficial reflexes -Planter reflex	- Exaggerated - Absent  - + <b>Ve Babinski sign</b>	-Absent -Absent



<b>-Muscle wasting</b> <b>-Response to electrical stimuli</b>  <b>-Gait</b>	<ul style="list-style-type: none"> <li>Minimal wasting of paralyzed muscle</li> <li>Normal response of paralyzed muscle to electrical stimuli i.e. No reaction of degeneration</li> </ul> <p>Circumduction gait (drag the paralyzed limb slowly towards the intact limb in intact manner)</p>	<b>-Marked atrophy</b> <b>-Abnormal response i.e. reaction of degeneration:</b> Chronaxie is prolonged -Faradic current: no response -Galvanic current: Anodal closing current is powerful than cathodal closing current & both are irregular
<b>Causes</b>	Mostly due to lesion in <b><u>post limb of internal capsule</u></b> caused by hemorrhage or thrombosis which result in the following: 1- Contralateral hemiplegia: UMNL (spastic) 2-Contralateral hemianesthesia but there is some recovery of pain, temperature, crude touch. 3- Crossed homonymous hemianopia 4- Hearing is slightly affected (decrease auditory acuity)	-Damage of LMN as in poliomyelitis (AHCs) -Damage of motor nerves as: diabetes mellitus, B12 deficiency. -Neuromuscular block as in myasthenia gravis

### Spinal Cord Lesions

#### Complete transection of the spinal cord:

- **Results from:** Penetrating wounds or accidents
- **Effects:**
  - Permanent loss of All sensations below the level of the lesion*
  - Permanent loss of Voluntary motor movements below the level of lesion (UMNL)*
    - Upper cervical lesions: results in respiratory failure & death
    - Lower cervical lesions: results in quadriplegia & respiration is diaphragmatic
    - Mid thoracic lesions: results in paraplegia & respiration is normal
- **Why Permanent?**
  - Because Tracts (either ascending [sensory] or descending [motor “pyramidal”]) are myelinated with No neurolemmal sheaths → so, once damaged, they never regenerate (as neurolemmal sheaths is important for regeneration)
- c. *Reflexes: Pass into two stages*
  - Spinal shock
  - Recovery of reflexes

#### **A) Spinal shock:**

- *Complete loss of all reflexes below the level of the lesion: eg:*
  - Stretch reflex (muscle tone & tendon jerk): Complete atonia & areflexia
  - Flexor withdrawal reflex is lost

- Arterial blood pressure (ABP): The higher the level of the lesion, the lower the ABP due to: separation of the vasoconstrictor center in medulla from the sympathetic lateral horn cells in thoracolumbar region leading to vasodilatation.
- Autonomic reflexes:
  - Micturition, defecation, erection reflexes are lost.
  - Micturition: Retention with overflow
  - Vasoconstriction, vasodilatation & sweating are lost. So, venous return & blood flow of immobile limbs are reduced
- Skin (of paralyzed part): Is cold, blue, dry & liable to form ulcers and bed sores
- Muscle wasting develops: (as there is catabolism of body protein & negative nitrogen balance).

➤ ***Duration of spinal shock:***

- Depends on degree of brain development (encephalization) i.e. phylogenetic level of animal e.g.:
  - In frogs: It lasts minutes
  - In dogs: It lasts 1-2 hours
  - In monkeys: It lasts days
  - In man: It lasts 2-6 weeks

➤ ***Cause of spinal shock:***

- Sudden withdrawal of Supraspinal facilitatory impulses (in reticulospinal, vestibulospinal & corticospinal tracts)
- Leads to hyperpolarization of the spinal motor neuron

❖ **Recovery of reflexes:**

1- **Stretch reflex (muscle tone & tendon jerk):**

- First reflex to recover - Muscle tone is weak
- Tone of flexors appears first (results in paraplegia in flexion)

2- **Flexor withdrawal reflex :**

- Plantar noxious stimulus → dorsiflexion of big toe & abduction of other toes (Babinski sign)
- Then reflex become stronger in form of flexion of foot, knee, hip

3- **Deep reflexes:** Ankle jerk appear after knee jerk & is weak

**4-Mass reflex: Stimulus:** Scratching skin of lower limb or abdominal wall Response:

- a) Flexion of both lower limb
- b) Contraction of abdominal wall
- c) Evacuation of urinary bladder & rectum
- d) Sweating & pallor of skin below lesion
- e) Arterial blood pressure (ABP) rises

5- **Autonomic reflexes:**

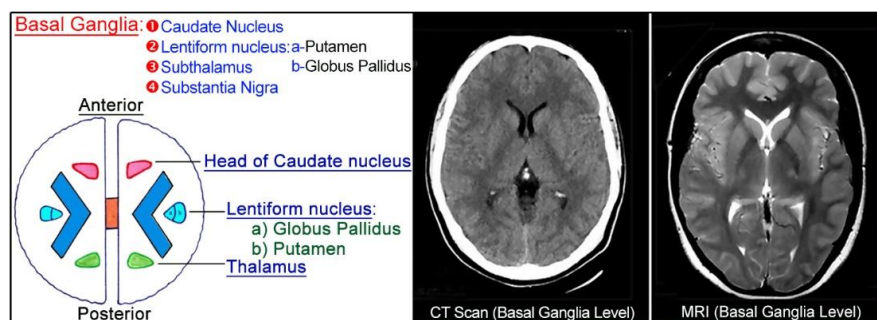
- Reflex micturition & defecation occur )i.e. automatic bladder & rectum similar to that in children
- The blood pressure rises to normal at rest
- Sexual reflexes (coitus reflex): Genital manipulation in male produces: Erection & ejaculation [but normal complex sexual activity cannot be executed]

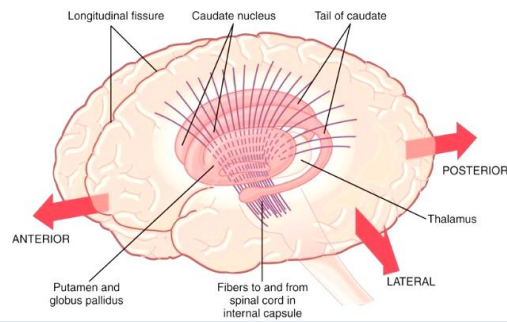
- 1- **Skin:** Warm, good color & heal
- 2- **Six months after cord transection :**
  - Marked reflex activity appears in extensor muscles
    - a. Tone of extensors: Becomes greater than that in flexors (results in paraplegia in extension)
    - b. Flexor withdrawal reflex: Is accompanied by crossed extensor reflex.
    - c. Mass reflex: Disappears:
    - d. New reflexes appear as: - +ve supporting reaction - Stepping reflex
  - **The recovery of reflex is due to:**
    1. Denervation hypersensitivity
    2. Increased collaterals from remaining input
  - **Stage of failure of reflexes:**
  - If urinary tract infected & bed sores are severe → reflexes disappear & patient die from septicemia & uremia
  - **Care of patients with transected spinal cord:**
  - Proper care allows transition from stage of spinal shock to stage of recovery without complications:
    1. Catheterization: To prevent urine stasis & infection
    2. Rectal enema
    3. Frequent mobilization of patient in bed to prevent bed sores
    4. Antibiotics: To prevent any infection

### Basal ganglia

- **Definition:** Inter connected nuclei found Deep to the cerebral cortex and Lateral to thalamus
- **They include:** 5 structures on each side of the brain:

3 Large nuclei:	2 Functionally related nuclei
a. Caudate: Corpus striatum b. Putamen c. Globus pallidus (divided into an external and internal segment) <div style="background-color: #ffe0b0; padding: 10px; margin-top: 10px;"> <p><b>NB:</b></p> <ul style="list-style-type: none"> <li>Caudate + putamen are called corpus striatum</li> <li>Putamen + globus pallidus are called "lenticular nucleus"</li> </ul> </div>	a. Sub thalamus b. Substantia nigra





### Anatomical relations: of the basal ganglia to the cerebral cortex & thalamus (shown in three-dimensional view)

#### ➤ Nervous connection of basal ganglia:

##### 1- Cortical connections:

- a- Caudate Circuit: Concerned with planning the sequence of pattern of movement
- b- Putamen Circuit: Execution patterns of movement

##### 2- Efferent pathway from the basal ganglia:

- **There are interconnection** between different nuclei of basal ganglia
- **Outflow tracts** from G to brain stem

##### - **Globus pallidus:**

- Is the **chief efferent pathway** of basal ganglia.
- It sends impulses to the sub thalamic nuclei and substantia nigra → reticular formation in brain stem → motor neurons of spinal cord

#### ➤ Neurotransmitters in basal ganglia:

- 1- Excitatory Neurotransmitters: - Acetyl choline - Noradrenaline
- 1- Inhibitory Neurotransmitters: - Dopamine - GABA

#### ➤ Functions of BG: depends on balance between excitatory & inhibitory neurotransmitters:

- 2- Inhibit muscle tone: Diffuse stimulation of BG reduces muscle tone
- 3- Control voluntary movements: BG & motor cortex control complex pattern of movements
- **Caudate Circuit: Important for Planning sequences of patterns of movements**
  - Converts thought into plans and pattern
  - Modifying the timing of these patterns of movement occurs slowly or rapidly
  - Modifying their spatial dimensions e.g. one can write very small or very large letter.

### **NB: Damage of caudate: Inability to write or draw figures with a fixed scale**

#### - **Putamen circuit:**

- Helps the cortex to execute subconscious learned pattern of movement: they store programs of familiar automatic pattern of voluntary activity e.g writing the letters of alphabet, cutting with scissors or hammering nails.

- **N.B. Damage of putamen: leads to motor apraxia i.e. inability to do familiar movements in absence of muscle paralysis e.g. one's writing becomes crude.**

#### c- **Globus pallidus:** May be responsible for:

- Posture taken by the body to perform a particular voluntary movement

- Thus facilitate the fine movements of the hand

**d-BG:** Initiation and regulation of the gross intentional movements of the body eg swinging of the arms while walking and facial expressions

**NB: In birds & fish: BG perform all motor functions & Voluntary movements**

➤ **Metabolic characteristics of BG:**

A. BG has high oxygen consumption.

B. BG (especially the substantia nigra) has high copper content.

➤ **Lesions of BG:** All are characterized by the presence of involuntary movements:

	<b>Athetosis</b>	<b>Parkinsonism</b>	<b>Chorea</b>
- <b>Site of lesion</b>	Globus pallidus		Caudate & putamen
- <b>Involuntary movements</b>	- Continuous slow snake like movements - Hypertonia		- Rapid involuntary dancing jerky movements - Hypotonia
			<b>NB:</b> <ul style="list-style-type: none"> <li>- <b>Hemiballismus:</b></li> <li>- <b>Sub thalamus</b></li> <li>- <b>Involuntary, intense violent movements of one limb</b></li> </ul>

**Parkinsonism (Paralysis agitans)**

- It is caused by lesion in substantia nigra which leads to loss of dopaminergic neurons leading to loss of dopaminergic inhibition of putamen

➤ **Causes:**

1. Idiopathic: It occurs in elderly
2. Cerebral atherosclerosis (old age): Loss of dopamine receptors
3. Phenothiazine (group of tranquilizers): Block D2 dopamine receptors
4. Repeated head trauma

➤ **Manifestations:**

**A- Akinesia:**

- Difficulty in initiating voluntary movements
- Decrease in associative movements

• **Characters:**

- Mask face (expressionless)
- Slow monotonous speech
- Gait :
  - Shuffling gait (i.e. patient walks in short steps)
  - Decrease in associative movements i.e. walking without swinging his arms

• **NB: The patient is usually bent forward as rigidity is more in flexors muscle**

**B- Rigidity: (i.e. resistance all through limb bending)**

- Lead pipe or cog wheel rigidity

- It occurs in both antigravity & progravity muscles **but more in flexors**, so, the patient develops the generalized flexion attitude
- **Mechanism:** Due to excess impulses transmitted along the corticospinal tract to both alpha AHCs and gamma ACHs

C- **Hyperkinesia: Involuntary Static tremor:**

- Involuntary - Static (present at rest)
- Disappears: During voluntary movement & sleep
- Rhythmic - Rapid (At a rate of 4-8 cycles/sec)
- Affecting **distal** joints - Alternating contractions of the antagonistic muscles

➤ **resulting in:**

- Pill rolling movements of hands
- Up & down movement of **mandible**

➤ **Treatment:**

1. Anticholinergic drugs: To reduce Acetylcholine activity
2. L-dopa (Levodopa):
  - Is a Dopamine precursor that cross the **BBB** (Blood Brain Barrier)
  - We **can not** give Dopamine itself as it does not cross the **BBB**
3. Implantation of dopamine-secreting tissue in near the BG

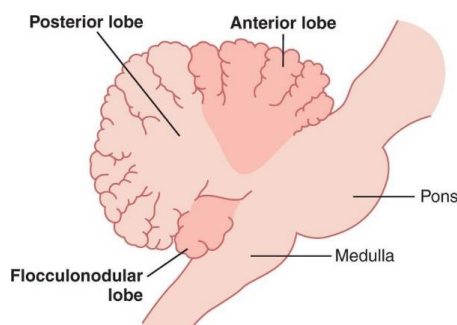
**Cerebellum**

❖ **External features of cerebellum**

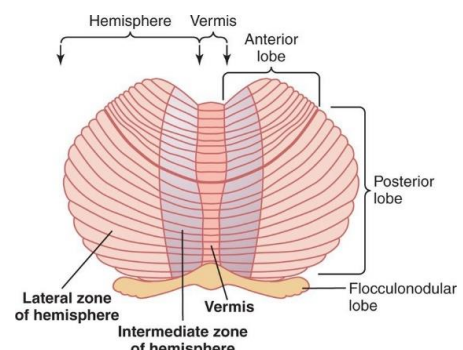
- It consists of **2 hemispheres** & a **vermis** connecting them.
- Superiorly the cerebellar hemisphere shows **primary fissure**. The part ant to primary fissure is the **ant lobe**.
- Inferiorly, the cerebellar hemisphere shows **posterolateral fissure**. The part ant to posterolateral fissure is called floccule & is connected to a part of the vermis called nodule to form **flocculonodular lobe**.
- The rest of the cerebellum is the **post (middle) lobe**, including a **horizontal fissure** between sup & inf surfaces.
- Inferiorly, part of the hemisphere projects through foramen magnum called **tonsils**.
- The cerebellum shows outer grey matter lobules called **folia**. It has an inner tree shaped white matter called **arbor vitae**.

➤ **Cerebellum is vital to the control of rapid muscular activities as:**

- Writing - Running - Typing - Talking -Playing piano



**Anatomical lobes of the cerebellum**  
(as seen from the lateral side)



**Functional parts of the cerebellum** (as seen from the postero inferior view) with the inferior most portion of the cerebellum rolled outward to flatten the surface



## Histology of cerebellum

- It is formed of two hemispheres joined by vermis
- Section has tree like appearance due to presence of many folds called folia
- Each folium is formed of central white ( medulla) covered by gray matter ( cortex)

### ❖ Cerebellar cortex : 3 layers

#### a) **Molecular layer: the outermost layer formed of:**

- Two types of inhibitory interneurons: the stellate cells ( molecular) and basket cells . both cells form synapse onto Purkinje cell and dendrites
- It also contains dendrites of Purkinje neurons
- End of climbing cells that synapse with dendrites of Purkinje cells. Climbing fibers come from inferior olivary Nucleus. Each Purkinje cells receive input from a single climbing fiber in the form of powerful excitatory signals.
- Parallel axons from the granule cells (extending from granular layer) that synapse with dendrites of Purkinje cell. Each Purkinje cells receive excitatory input from 100,000 to 200,000 parallel fibers.

#### b) **Purkinje layer: the middle layer contains only one type of cells that is Purkinje cells**

- Purkinje cells are the Primary integrative neurons of the cerebellar cortex
- Purkinje cells are large Pyriform multipolar cells arranged in one row.
- Purkinje cells dendrites are with hundreds of spiny branches reaching up into the molecular layer.

#### c) **Granular layer: the innermost layer composed of:**

##### A- Granule cells

- Small dark closely packed nerve cells
- Each granule cell has a few short dendrites within the granule cell layer
- Their dendrites make synapse with excitatory mossy fibers coming from pontine nuclei
- The granule cells send their T- shaped axon known as parallel fibers up into the superficial molecular layer, where they form hundreds of thousands of synapses with Purkinje cell dendrites

##### B- Golgi cells

- Large cells
- Their dendrites branch in different directions
- Their axons synapse with granular cells to provide inhibitory feedback on them
- Axons of Purkinje, climbing fibers and mossy fibers

## Functional anatomy

### • Cerebellum comprises the following:

- Vermis (midline structure)    - Two cerebellar hemispheres    -Flocculonodular lobe

### ❖ From the **functional** point of view, cerebellum is divided into 3 parts:

	Connected To	Concerned with
1. <b>Archicerebellum</b> = Vestibulo-cerebellum (Flocculonodular lobe)	Vestibular nuclei	Equilibrium
2. <b>Paleocerebellum</b> = Spino-cerebellum	AHCs + Cerebral	1. Responsible for coordination of

	cortex	movements 2. It is inhibitory to the muscle tone (Intermediate zone of hemisphere)
3. <b>Neocerebellum</b> = Cerebro-cerebellum	Cerebral cortex	1. Planning & programming of movements 2. It is facilitatory of the muscle tone (lateral zones of hemisphere)

- **Connections of cerebellum:**

- **The cerebellum has:**

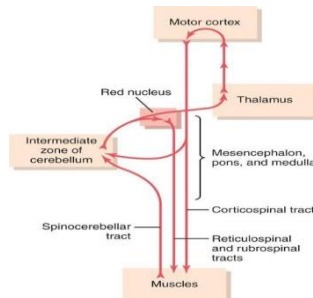
- External layer of **gray matter** (cerebellar cortex)
- Inner **white matter**: Embedded in it 3 deep nuclei:

Fastigial (medially)	Interpositus	Dentate (laterally)
Globose & emboliform Input pathways to cerebellum ( <b>afferent</b> )		Output pathways ( <b>efferent</b> )

- **Afferents:** It receives from:

- 2- Cerebral cortex
- 2- Vestibular apparatus
- 3- Spinal cord

**Efferents:** It sends to: 1- Cerebral cortex 2. Basal ganglia (BG)



### Cerebral and cerebellar control of voluntary movements, involving especially the intermediate zone of the cerebellum

- **Functions of cerebellum:**

1. **Control of posture & equilibrium:**

- **During rapid movement:**

- The vestibular apparatus send signals to the **archicerebellum** (flocculonodular lobe) → output signals → brain stem → reticulospinal & vestibulospinal tracts → maintain equilibrium through changes in tone of muscles

2. **Effect on muscle tone (stretch reflex):**

A. **Neocerebellum:** Is facilitatory to stretch reflex (through Facilitatory reticular formation) → increase muscle tone

B. **Paleocerebellum:** Is inhibitory to stretch reflex → decrease muscle tone

3. **Function of cerebellum in control of voluntary movements:**

A- **Servocomprator:**

- **The Paleocerebellum (spinocerebellum):**

- **Is informed about:**

- The intended **plan** of motor cortex
- The **performance** of movement (via spinocerebellar tracts)

- **Compares performance of muscles with motor cortex intention**

- If not appropriate it sends corrective signal

- **NB: The spinocerebellum:**

- **At the onset of movements:** It turns on the agonist muscles & turns off the antagonist muscles
- **At the end of movements:** It turns off the agonist muscles & turn on the antagonist muscle
- **The point at which reversal of excitation between agonist & antagonist depends on the on the rate of movement**

**A- The braking effect of the cerebellum (Prevent overshoot) (*Damping movement*)**

- All movements of our body are pendular & they have a momentum & tend to overshoot
- The cerebellum assesses the rate of movement calculates the length of time needed to reach the intended point and then transmits inhibitory impulses to the motor cortex to inhibit the agonist and excite the antagonist muscles thus brakes are applied to stop the movements at the precise intended point.

- **NB: If the cerebellum is damaged → There is overshooting (oscillatory movement around the intended point) Resulting in kinetic tremors**

**B- Planning and timing function of the cerebellum**

- The lateral zones of cerebellar hemisphere plan for rapid movements
- The ability to progress smoothly from one movement to the next depends on cerebellum that plans for the next movement at the same time the present movement is occurring
- The cerebellum also provides appropriate timing for each movement
- The neocerebellum is important for the smooth progression of movement to the next movement especially rapid movements e.g. running

**Clinical abnormalities of Cerebellar lesion:**

- Lesion in deep cerebellar nuclei → **neocerebellar syndrome**

▪ **Manifestations:**

**b- Ipsilateral (i.e. they appear on the same side of the lesion):**

- 1- **Hypotonia:** Due to loss of facilitatory effect of neo cerebellum on muscle tone
- 2- **Asthenia:** The patient feels muscle weakness (as there is difficulty in maintaining muscle contraction)
- 3- **Cerebellar ataxia:**

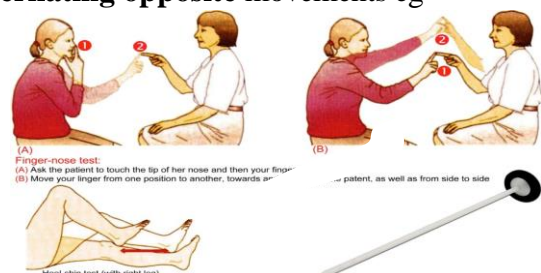
- **Definition:** Incoordination of voluntary movements **in absence of** motor lesion (i.e. UMNL or LMNL)

- **Manifestations:**

1. Dysmetria: Movements overshoot their intended point.
2. Decomposition of movements
3. Intention kinetic tremors: Due to: Absence of damping function of cerebellum

**NB: 1, 2, 3 are shown by finger to nose test**

4. Dysdiadochokinesia: Inability to do **rapid alternating opposite** movements eg repeated pronation & supination
  5. Dysarthria: Staccato speech
- Difficulty in producing clear correct speech
  - Due to Failure of smooth progression of



movements in muscles of larynx, mouth & respiratory muscles

6. Cerebellar nystagmus i.e. Eye ball tremors

**7. Rebound phenomenon:**

- Inability to stop the motor act in the proper time
- Due to: Absence of cerebellar brake

8. **Staggering gait:** The patient walks on a wide base swinging from side to side & may fall on the diseased side (drunken gait)

**Ataxia**

➤ **Definition:** Incoordination of voluntary movements **in absence of** motor lesion (UMNL or MNL)

➤ **Types:**

1. Sensory ataxia: Due to lesion in proprioceptive pathway eg Tabes dorsalis, pernicious anemia
2. Motor ataxia: **Cerebellar ataxia:** Due to lesion in neocerebellum
3. Mixed ataxia: Thalamic syndrome (sensory & motor)

➤ **Organization of motor cortex, cerebellum & basal ganglia:**

**1. Planning:**

- a) The **idea** of voluntary movement: Originate in **cortical association area**
- b) **Basal ganglia:** Puts the **plan** for the **slow** gross movements
- c) **Lateral portions of cerebellar hemisphere** puts the **plan** for the **rapid** movements
- d) Plans are sent to **motor & premotor**

**2. Execution:**

- a) The **motor cortex** sends the final motor commands through **pyramidal** tracts
- b) The intermediate cerebellum (**spinocerebellar**) **monitors the performance** of movements & **corrects any deviation** from the plan

**Role of brain stem in controlling motor functions**

❖ **The brain stem consists of :** - Midbrain - Pons - Medulla

- Parts of the diencephalon (the diencephalons consist of :

- a. Thalamus
- b. Sub thalamus
- c. Hypothalamus

❖ **The brain stem contains reticular formation (a dense network of neurons) :**

• **They include centers for:**

1. CVS
2. Respiratory
3. Swallowing
4. Vomiting
5. Sleep
6. Eye movement centers

• **Reticular nuclei :** - Pontine - Medullary

• **Vestibular nuclei:** - Locus coeruleus - Raphe nuclei

❖ **The reticular nuclei are divided into 2 functional divisions**

➤ **The pontine reticular nuclei (Facilitatory reticular area)**

- Lie in the middle and lateral pons & midbrain (mesencephalon)
- They discharge spontaneously
- They send excitatory output fibers in 2 directions:

Upwards	Downwards
<ul style="list-style-type: none"> <li>• i.e. Ascending reticular activating system (RAS)</li> </ul>	<ul style="list-style-type: none"> <li>• i.e. Ventral reticulospinal tract</li> <li>• They facilitate stretch reflex</li> </ul>

<ul style="list-style-type: none"> <li>• It stimulates the cerebral cortex resulting in the alert state</li> </ul>	<ul style="list-style-type: none"> <li>• They maintain tone in antigravity muscles</li> </ul>
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- **Pontine reticular nuclei are:**

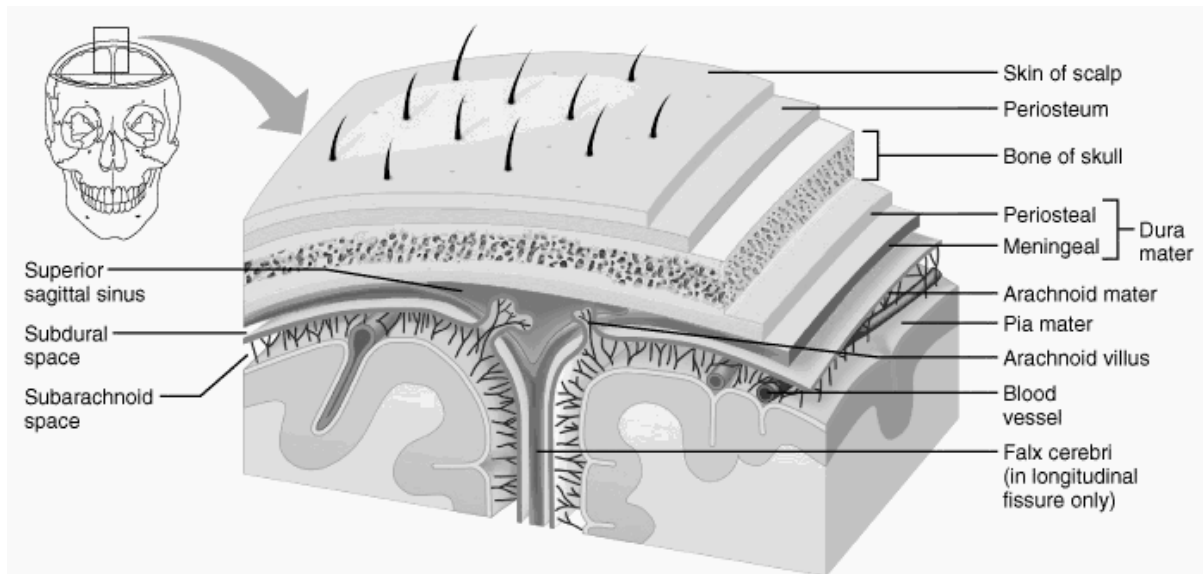
- Excited by: Signals from vestibular nuclei & neocerebellum
- Inhibited by: Signals from medullary reticular nuclei

➤ **The medullary reticular nuclei :**

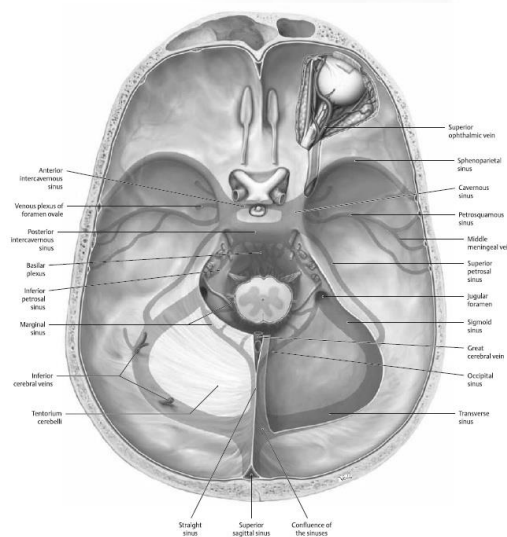
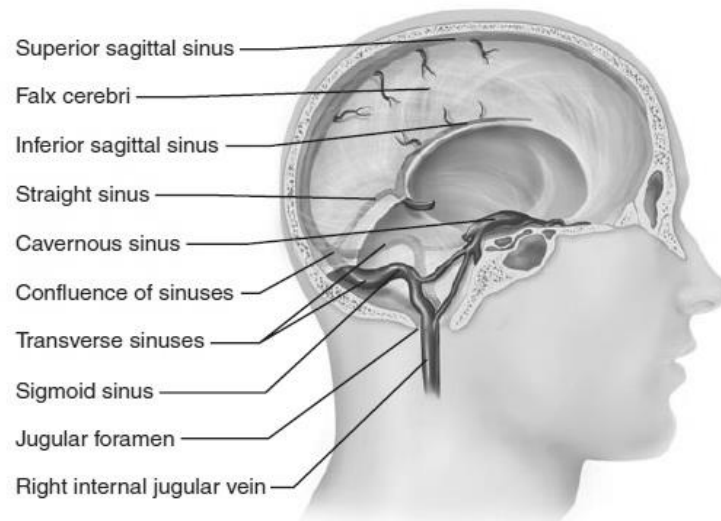
- Lie in the medial ventral part of **medulla**
- They have **no** intrinsic activity, but they are **activated by** signals from:  
A. Red nucleus      B. Paleocerebellum      C. Basal ganglia (BG)
- They send signals along **lateral reticulospinal tract** to inhibit:
  - 1- Stretch reflex
  - 2- Gamma motor neuron

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## Meninges



## Venous folds & sinuses

Cummings / Marieb / Schuenke

## **MENINGES**

**Definition:** three membranes surrounding the CNS (dura, arachnoid & pia).

**Meninges and its related spaces:** (from outside inwards):

**Extradural space:** cranially it contains middle meningeal artery (no veins).

**Dura** (the outer tough layer): formed of a single layer around the spinal cord, but cranially it is subdivided into two layers:

**Outer endosteal** lining the skull.

**Inner meningeal** covering the brain.

- Fused to the outer layer except in certain sites where they separate to form ***dural sinuses***.
- Stretched in some sites forming ***dural folds***.

**Subdural space:** potential space, contains thin film of fluid. Cranially it is traversed by cerebral veins (no arteries).

**Arachnoid** (the middle trabecular layer).

**Subarachnoid space:** contains fine trabeculae (threads), CSF and cerebral vessels.

**Pia** (the inner tender layer): closely attached to the external surface of CNS. The pia covering the spinal cord forms:

**Denticulate ligaments:** 21 pairs of projections piercing the arachnoid and attached to the dura at the sides of vertebral canal, aiding vertical support to the spinal cord.

**Filum terminale:** the lower end of pia below the spinal cord extends passing in vertebral canal and attached to coccyx, aiding to horizontal support of the cord.

## **DURAL FOLDS**

### **Falx cerebri**

- Sickle shaped.
- Lies in the sagittal plane between 2 cerebral hemispheres

**Parts and related sinuses:**

**Apex:** attached to frontal crest and crista galli.

**Base:** attached to tentorium cerebelli (upper surface) with ***straight sinus*** in between.

**Upper border:** convex and attached to the skull cap (inner surface) with ***superior sagittal sinus*** enclosed.

**Lower border:** concave and free (above corpus callosum) with ***inferior sagittal sinus*** enclosed.

### **Tentorium cerebelli**

- Tent shaped, it is elevated at its superior surface where the falx cerebri is attached.
- Forms the roof of posterior cranial fossa separating the cerebellum from the cerebrum.

**Parts and related sinuses:**

**Attached border:** attached to the superior petrosal groove (with the ***superior petrosal sinus*** enclosed) and transverse groove (with the ***transverse sinus*** enclosed)

**Free border:** U-shaped surrounding the midbrain.

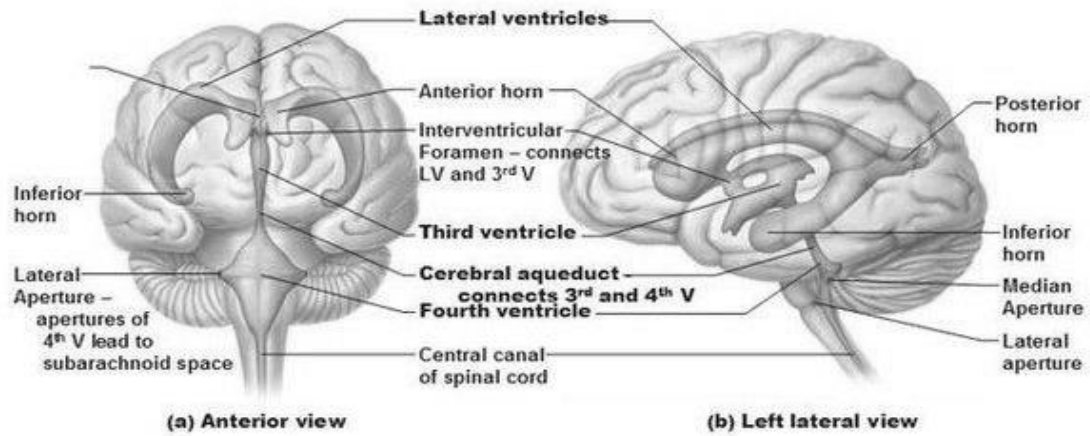
**Superior surface:** the falx cerebri is attached to it (with the ***straight sinus*** in between)

**Inferior surface.**

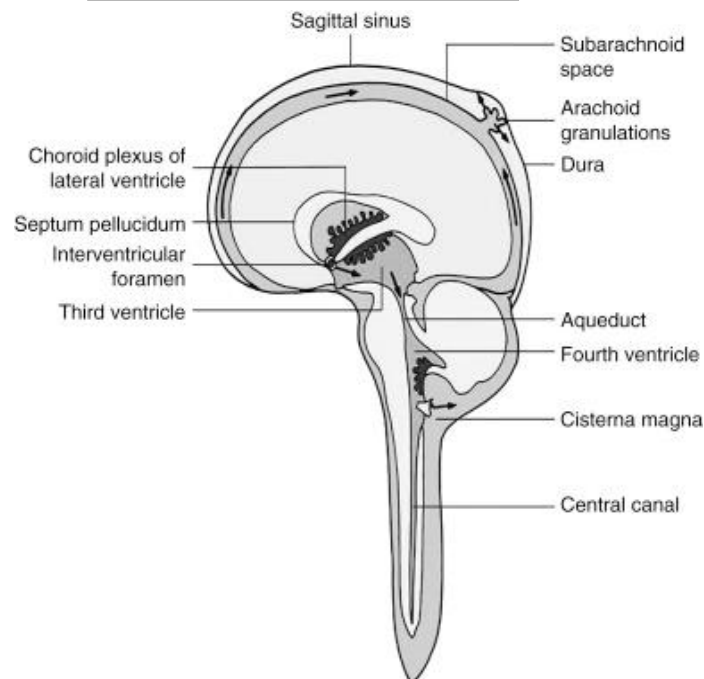
**Cavum Trigeminal:** part of tentorium cerebelli which covers the trigeminal ganglion.

**Falx cerebelli** attached to the internal occipital crest separating the two cerebellar hemispheres and contains the ***occipital sinus***.

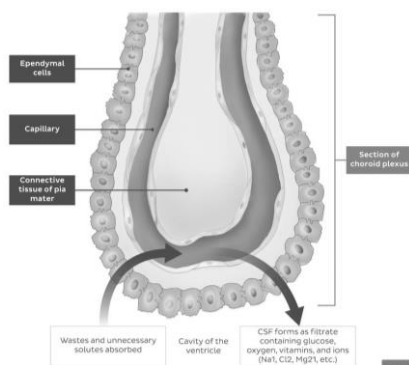
**Diaphragma sellae** it roofs the pituitary gland and pierced at its centre by the infundibulum connecting the hypothalamus to the pituitary. It Contains ***intercavernous sinuses***.



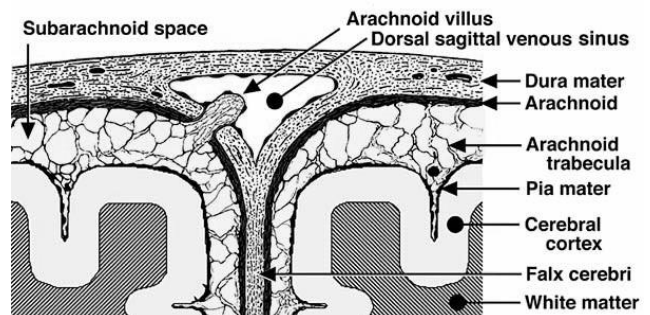
### Ventricles and central canal



### CSF circulation



### Choroid Plexus



### Arachnoid villi

## **VENTRICULAR SYSTEM AND CENTRAL CANAL**

**Definition:** they are the cavities inside the CNS.

**Parts:**

**Lateral ventricles:** the two cavities of the cerebral hemispheres.

**Interventricular foramina** (of Monro): between the two lateral and third ventricles.

**Third ventricle:** in the midline between the two thalami.

**Cerebral aqueduct** (of sylvius): the cavity of the midbrain.

**Fourth ventricle:** between pons and upper medulla (ant) and cerebellum (post).

**Central canal:** the cavity of the lower medulla and spinal cord.

## **CERBROSPINAL FLUID (CSF)**

**Definition:** clear fluid filling the ventricular system and subarachnoid space.

**Amount:** 130 ml, 400-500 ml are produced daily (renewed 3-4 times).

**Formation:**

- Mainly by the secretion of the choroid plexuses of the ventricular system (90% in the lateral ventricle).
- The choroid plexus is formed of capillaries in the subarachnoid space pushing the pia and a thin layer of ependymal cells into the cavity of the ventricles.
- The CSF is filtered through the endothelium of the capillary and the ependymal layer into the ventricular cavity.

**Circulation:** lateral ventricles → interventricular foramina → 3<sup>rd</sup> ventricle → cerebral aqueduct → 4<sup>th</sup> ventricle →

- 1) Median foramen (of Magendie) and lateral foramina (of Luschka) → subarachnoid space (around whole CNS) → absorption.
- 2) Central canal of the lower medulla and spinal cord.

**Absorption:**

- Mainly by arachnoid villi and granulations into the blood of the dural venous sinuses (specially superior sagittal sinus).
- Arachnoid granulations (macroscopic) and villi (microscopic) are arachnoid protrusions piercing the dura and reaching inside the venous sinuses.
- The excess CSF is filtered through the arachnoid and endothelial cells to the sinus blood.

**Functions of CSF:**

- 1) Protection of CNS (water jacket).
- 2) Lightens the brain weight.
- 3) Maintenance of intracranial pressure: The volume of the brain + CSF + blood is constant, any alteration is managed by modification of CSF or blood (through emissary veins).
- 4) Nourishment of CNS.
- 5) Removal of metabolites (as the brain has no lymphatics).

**Applied anatomy:**

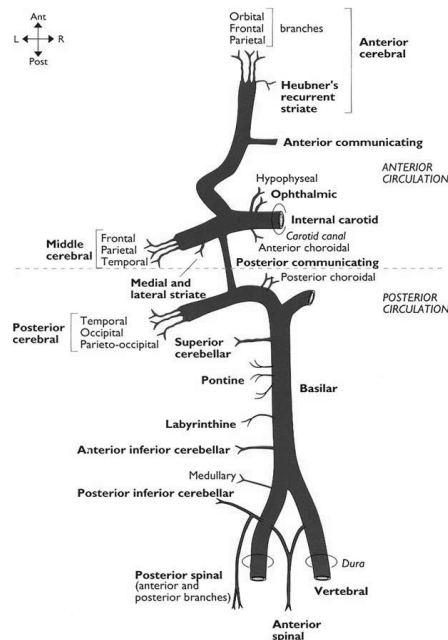
**Hydrocephalus:** increased production or obstructive drainage will lead to excessive CSF, dilatation of ventricles and enlargement of skull.

**Papilledema:** increased CSF pressure will lead to congestion and bulging around the optic nerve. It may cause nerve atrophy and blindness.

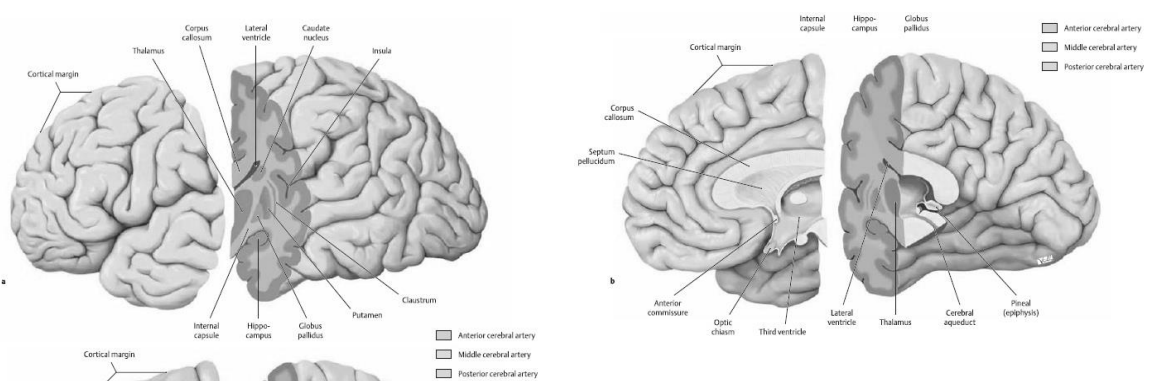
**Drug administration** (spinal anesthesia).

**Lumbar Puncture:** (a sample of CNS obtained between L3-4 or L4-5).

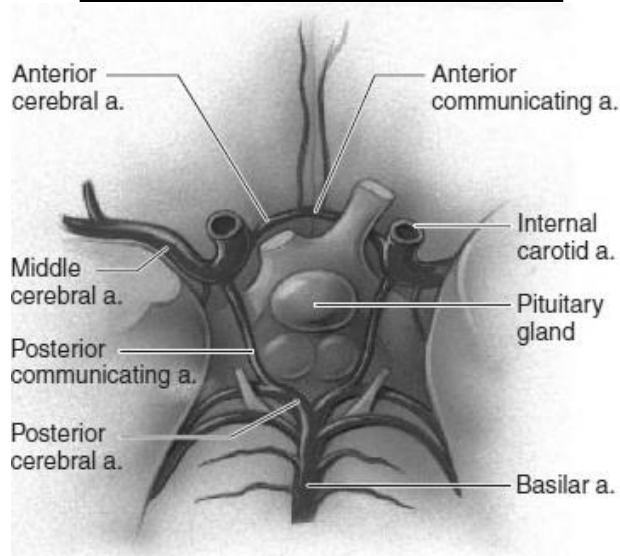
- It is used for diagnosis in CNS diseases.
- Sudden decrease in spinal CSF pressure may lead to suction of the lower medulla into foramen magnum which is fatal.



### Vertebrobasilar system & ICA



### Blood supply of cerebral hemisphere



### Circle of Willis

Whitaker & Borley / Schuenke / Shier



## ARTERIAL BLOOD SUPPLY OF THE CNS

- ❖ The blood supply of CNS depends mainly on 2 arterial systems: the vertebrobasilar system & the internal carotid system.

### **Vertebral A:**

- It begins as a branch of subclavian artery.
- It passes through the foramen transversarium of C6-1 vertebrae, then through foramen magnum & ascends anterior to medulla to meet the other vertebral artery at its upper end.
- Each vertebral artery gives ant and post spinal arteries. The 2 ant spinal arteries unite forming a single one descending ant to spinal cord, while the post spinal arteries descend posterolateral to it. The spinal cord is also supplied also by radicular branches from nearby arteries (vertebral, intercostal, lumbar and lat sacral).
- Beside the spinal cord, the vertebral artery supplies the medulla and cerebellum.
- It ends by uniting with the other vertebral artery forming the basilar artery.

### **Basilar A:**

- It begins by the union of 2 vertebral arteries
- It ascends in the median groove of pons & ends at its upper end by dividing into 2 post cerebral As.
- It supplies pons and cerebellum.
- It ends by dividing into two post cerebral As.

### **Post cerebral A:**

- It begins as terminal branches of basilar artery
- supplies midbrain, occipital lobe & lower part of temporal lobe.

### **Internal carotid A:**

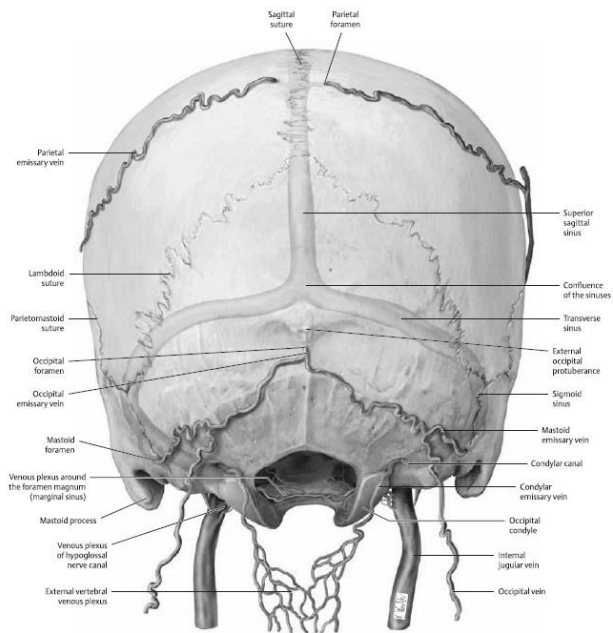
- It begins as one of two terminal branches of common carotid artery between C3-4 vertebrae.
- It passes inside the carotid sheath → carotid canal → foramen lacerum → traverses cavernous sinus and end by dividing into ant and middle cerebral As.
- It supplies the eye & pituitary gland
- It ends by dividing into ant & middle cerebral As.

**Ant cerebral A:** supplies med surface of frontal & parietal lobes & part of their lat surface.

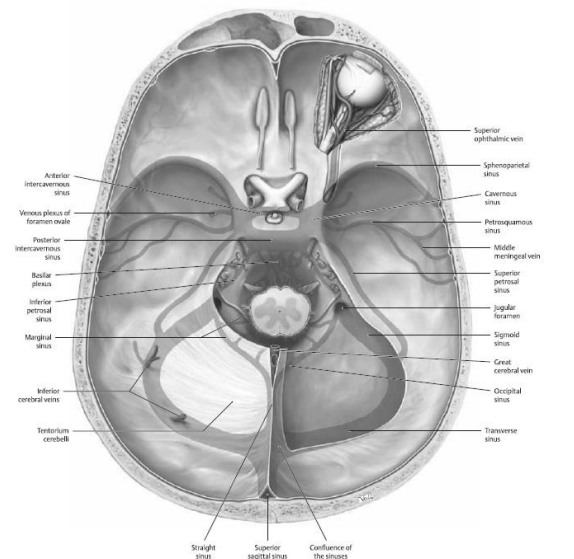
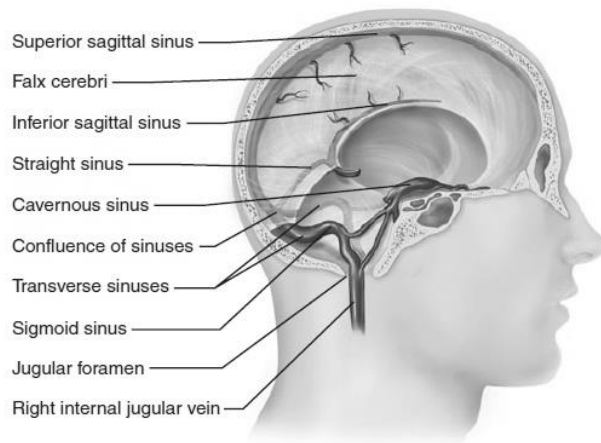
**Middle cerebral A:** supplies lat surface of frontal & parietal lobes & upper part of temporal lobe.

### **Arterial circle (of Willis):**

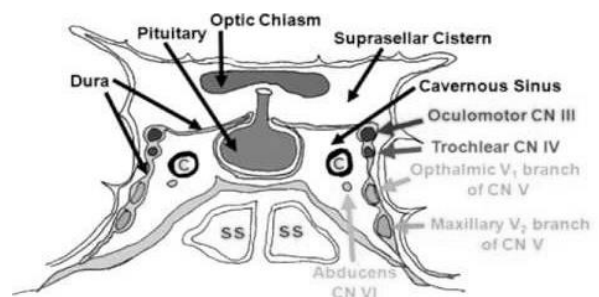
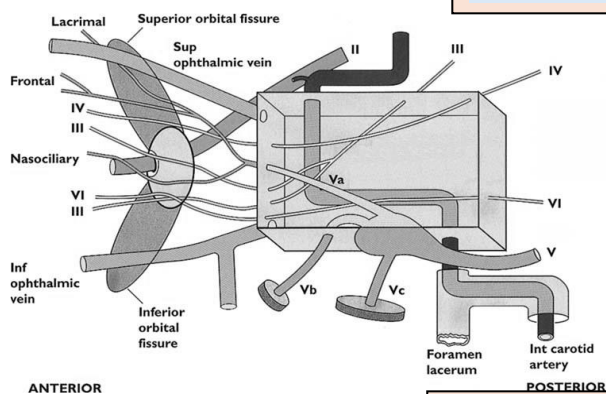
- It is formed by 2 post cerebral As, 2 internal carotid As, 2 post communicating As connecting post cerebral to internal carotid, 2 ant cerebral As & 1 ant communicating A connecting them.
- It is a connection between the 2 main arterial systems of both sides. It maintains equal pressure in cerebral As and compensates arterial occlusion.



### Emissary vein



### Dural venous sinuses



### Cavernous sinus

Schuenke / Marieb / Healthdocbox / Pinterest



## VENOUS DRAINAGE OF THE CNS

- ❖ The spinal cord veins correspond to their arteries and drain into the internal vertebral venous plexus in the epidural space.
- ❖ The veins of the brain are divided into superficial and deep groups. The superficial group lies in the subarachnoid space and drains the cortex, while the deep group drains the deeper structures. Both groups drain into the dural venous sinuses.

### DURAL VENOUS SINUSES

- ❖ Valveless venous spaces between two layers of dura. They are lined by endothelium but lack the rest of the histological features of the Vs. They drain the brain, skull and CSF. They may be:

**Single sinuses:** e.g.: sup sagittal (grooves the skull cap), inf sagittal, straight and occipital sinus (along internal occipital crest).

**Paired sinuses:** sphenoorbital (along the lesser wing of sphenoid), cavernous (beside the pituitary fossa), sup and inf petrosal (along sup and inf borders of petrous bone respectively), transverse and sigmoid (related to transverse and sigmoid grooves respectively).

- ❖ The sigmoid sinus passes through the jugular foramen to continue as IJV, which drain all the venous sinuses.
- ❖ Usually, drainage occurs from before backwards. Being valveless, obstruction in the blood flow may reverse the direction of drainage.
- **Cavernous sinus:** it lies at the side of pituitary and sphenoid air sinus, it extends from the orbit anteriorly to the petrous bone posteriorly.

**Structures inside:** oculomotor, trochlear, ophthalmic and maxillary branches of trigeminal N (at the lat wall), abducent N and ICA.

#### **Connections:**

**Ant:** venous drainage of the eye and sphenoorbital sinus.

**Post:** drains to sup and inf petrosal sinuses.

**Med:** venous drainage of pituitary and the other cavernous sinus.

**Inf:** connected by emissary Vs (passing through foramen ovale, lacerum and carotid canal) to pterygoid and pharyngeal venous plexuses.

**Applied anatomy:** infection may spread to cavernous sinus through its connections leading to cavernous sinus thrombosis. The patient may complain of eye oedema (obstructed venous drainage), squint (paralysis of oculomotor, trochlear and/or abducent Ns responsible for eye movements), sensory loss of some areas of the face (paralysis of ophthalmic and/or maxillary Ns), and in late cases, meningitis or encephalitis.

### EMISSARY VEINS

- ❖ Valveless veins connecting veins outside the skull with intracranial venous sinuses.

**Function:** maintain intracranial pressure.

**Applied anatomy:** they may transmit infections to venous sinuses leading to sinus thrombosis, meningitis (inflammation of meninges) or encephalitis (inflammation of brain), both may be fatal.

## **Brain Barriers**

### **A) Blood brain barrier:**

- **Definition:** It is the barrier between the blood and the nerve cells.
- **Structure:** It is formed of:
  - Tight junction between non fenestrated endothelium lining capillaries.
  - Thick continuous basement membrane (Basal lamina).
  - End feet of astrocytes firmly applied on capillaries.
- **Function:**
  - Prevents harmful materials from reaching the nerve cells.
  - Allows nutrients and precursors of neurotransmitters to pass by facilitated diffusion and active transport.

### **B) Blood -CSF harrier**

- **Definition:** it is the barrier that separates blood from CSF.
- **Structure:** it is formed of;
  - Endothelium of choroidal capillary.
  - Basement membrane of the choroidal capillary.
  - Basement membrane of ependymal cells forming the choroid plexus.
  - Tight junctions between ependymal cells forming the choroid plexus.
- **Function:**
  - Control of substances pass from blood to CSF.
  - Maintenance and constancy of CSF.

### **C) Arachnoid barrier:**

- **Definition:** It is the barrier between extracerebral capillaries and subarachnoid space
- **Structure:** it is the arachnoid barrier layer formed of cells joined by tight junctions and desmosomes.
- **Function:** block substances leaving extracerebral capillaries from reaching subarachnoid space, brain tissue and ventricles.

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