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2024

FACULTY OF MEDICINE
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CENTRAL NERVOUS SYSTEM AND SPECIAL SENSES

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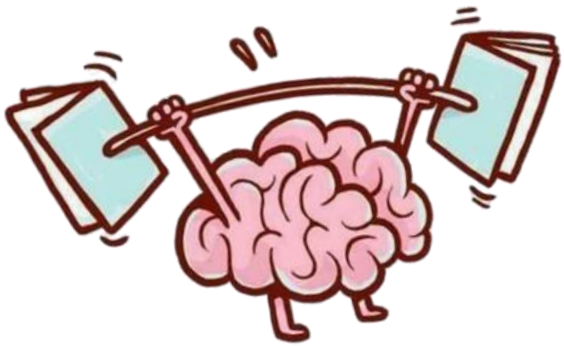

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PHYSIOLOGY

Nervous system

I. Anatomical organization of the nervous system:

(1) Central nervous system (CNS):

a) Brain b) spinal cord.

(2) Peripheral nervous system (PNS):

12 pairs of cranial nerves and 31 pairs of spinal nerves.

II. Functional organization of the nervous system:

1. **Sensory system:** Detects changes in internal and external environments and informs the CNS about them.
2. **Motor system:** Initiates and controls the motor activities of skeletal muscles, plain muscles, cardiac muscles and even glands.
3. **Intellectual nervous system:** Provides basis for consciousness, memory, learning, intelligence, thoughts and behavior.

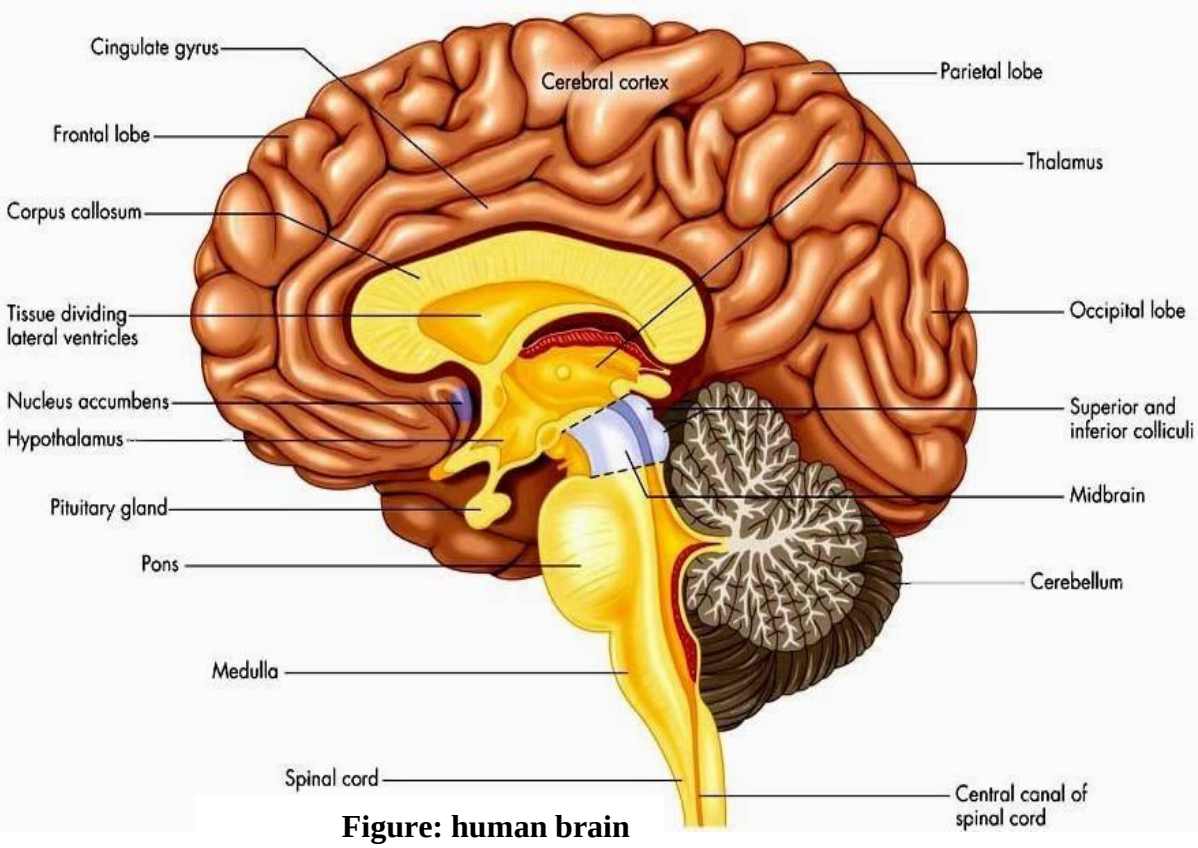


Figure: human brain

Sensory system

☒ **Def:** It is the division of the nervous system concerned with the **detection of the stimuli** (as regard nature, locality and intensity) and **informs the specialized centers in CNS** to adopt adequate **responses**.

☒ **Components of the sensory nervous system**:

a) Sensory **receptors**. Then,

b) **Afferent nerve** fibers that carry impulses to,

c) **Specific areas** in the brain & spinal cord (sensory centers).

Figure: sensory system

Sensory receptors

☒ **Def of receptors:**

Receptors are specialized microscopic structures located at the peripheral terminations of the afferent nerves.

☒ **Functions of receptors:**

They detect the stimuli and transduce (convert) these stimuli into nerve impulses which are then conducted along the afferent nerves to the sensory centers in central nervous system i.e. the receptors act as "detectors and transducers".

Physiological classification of receptors

I. According to the location of the receptors: They are classified into:

A. External receptors: on the body surface mainly in skin.

B. Internal receptors: in deeper structures & viscera.

II. According to nature of the stimulus: They are classified into:

1. Mechanoreceptors:

They are stimulated by the **mechanical forms of energy**, they **include:**

a. Touch receptors in the skin.

b. Proprioceptors in the muscles e.g. muscle spindle & Golgi tendon organs.

c. Pressure receptors e.g. pacinian corpuscles.

d. Baroreceptors in the aortic arch & carotid sinus that detect the changes in arterial blood pressure.

e. Sound receptors.

f. Vestibular receptors that detect the changes in the equilibrium.

g. Stretch receptors as in alveoli, urinary bladder & right atrium.

2. Chemoreceptors:

They respond to the **chemical stimuli e.g.**

a. **Peripheral chemoreceptors** in the aortic and carotid bodies.

b. **Central chemoreceptors** in the brain stem.

c. Taste & smell receptors.

d. Hypothalamic glucoreceptors & osmoreceptors.

3. Thermal receptors:

- They respond to **changes in temperature**.
- They include **cold receptors** which respond to the drop of temperature & **warm receptors** which respond to the increase in temperature.

4. Pain receptors (Nociceptors):

They respond to the **injurious or painful stimuli**.

5. Photoreceptors or electromagnetic receptors:

They respond to the **electromagnetic waves of light** in the retina.

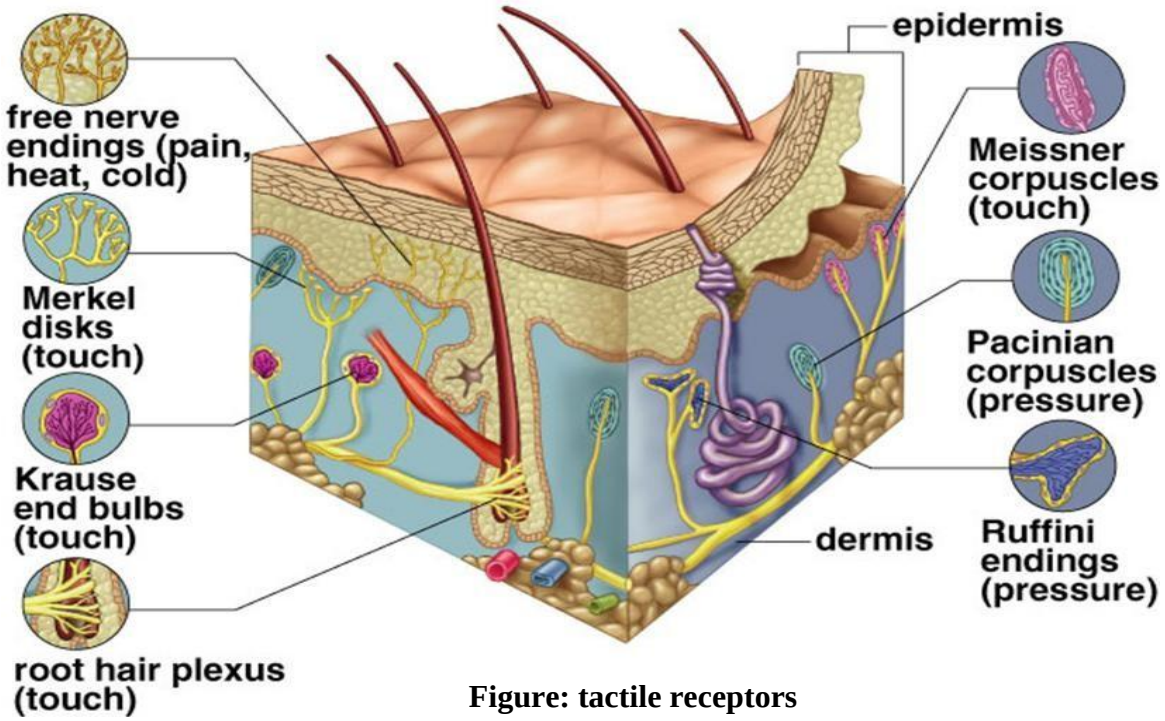


Figure: tactile receptors

Properties of receptors

1. Specificity (the adequate stimulus).
2. Excitability (receptor potential).
3. Rate of discharge from receptors.
4. Adaptation of receptors.

1. Specificity (Muller's law):

☒ **Def:** "Each type of receptors is highly sensitive to a particular type **(only one type)** of stimuli called the **adequate stimulus** and when stimulated it gives rise to only **one type of sensation** whatever the way of stimulation".

☒ **Example:**

- Retinal receptors are highly sensitive to the light waves.
- Auditory receptors are highly sensitive to the sound waves…etc.

☒ However, the receptors may respond to stimuli other than their specific or adequate ones, provided that these stimuli are very strong; but still the response is the same modality to which the receptor is specialized.

☒ **e.g retinal receptors** are normally stimulated by the light waves and give rise to sense of vision. But if heavy mechanical stimuli applied to the eye as in heavy blow, the retinal receptors can be stimulated and eye sees flashes of light.

2. Excitability (Receptor potential):

☒ **Def of excitability:** It is the ability of the receptors to respond to their adequate stimuli.

☒ **Mechanism of stimulation of receptors:**

- **Most** of the body receptors on adequate stimulation show **depolarization** through the increased permeability of their membranes to Na^+.
- **Only the visual** receptors (Rods & Cones) when stimulated adequately, they show **hyperpolarization.**

☒ **Receptor potential (RP)**

It is **best studied in pacinian corpuscles:**

- **Nature:** mechanoreceptors
- **Site:** present in the skin, and deep tissues
- **Involved in:** the sensations of touch, pressure and vibrations).
- **Structure:**
  - Is a vesico-elastic structure
  - Consists of several concentric layers of connective tissues like an onion surrounding a central nerve terminal.
  - The ending of the sensory nerve is not myelinated, but the first node of Ranvier is also located inside the capsule.
- **Pacinian corpuscles preferred because they are:**
  - Easily stimulated by microglass rods under microscope.
  - Large in size and easily dissected.

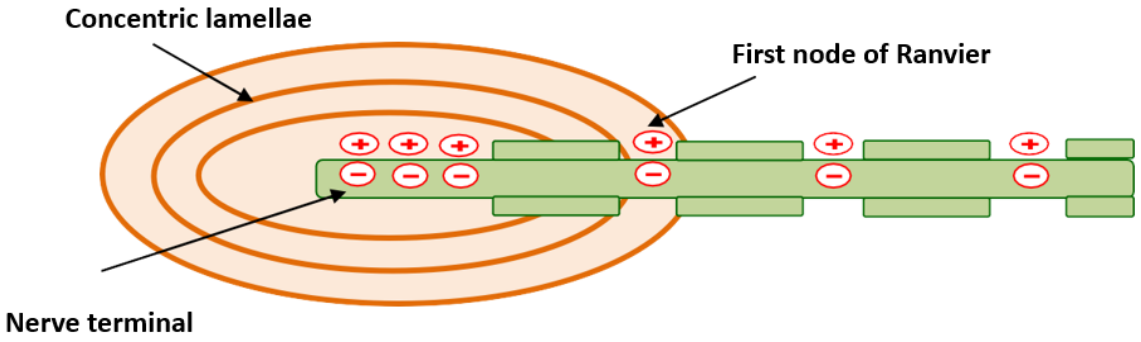
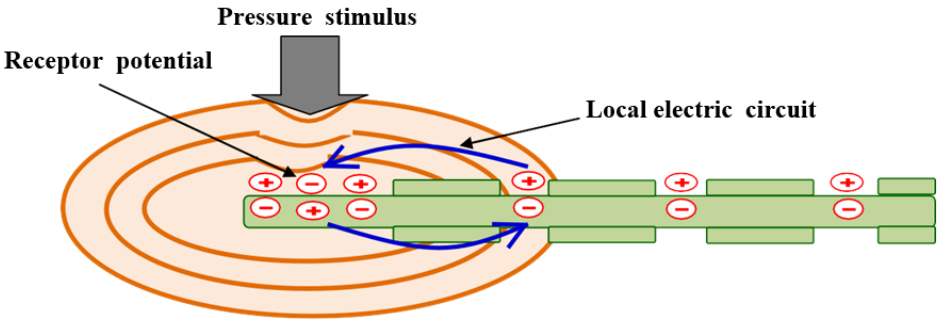


Figure: Pacinian corpuscle

☒ Mechanism of RP:

- When the pressure is applied to the corpuscle ➔ it compresses the concentric lamellae ➔ deformation of the nerve terminal ➔ opening of Na+ channels ➔ increasing Na+ influx ➔ **partial state of depolarization** in the nerve terminal known as **"RP".**
- The maximal amplitude of RP around 100 mv that occurs when maximal opening of Na+ channels in the receptor membrane.
- When the **RP** reaches certain threshold, it generates **local electrotonic current** which flows to the first node of Ranvier ➔ gradual depolarization till the firing level is reached & action potential (AP) is generated ➔ AP is propagated along the afferent nerves to the CNS.



- The amplitude of **electrotonic current** is determined by the **amplitude of the RP** which by its turn depends upon the **intensity of the stimulus**.
- As long as the amplitude of the **electrotonic current** is strong, ➔ the **1st node of Ranvier** can be depolarized in short time ➔ this increases the rate of discharge.

☒ **Properties of the RP:**

1. **Graded amplitude**: i.e. its amplitude is directly related to the intensity of the stimulus i.e. does not obey the all or none rule.
2. Can be **summated:** multiple RPs can be summated with each other.
3. **Passive localized spread**.
4. It has a **short duration (5 msec)**.
5. It can initiate repeated action potentials at the 1st node of Ranvier.
6. It is **not blocked by local anesthetics**.

3. Rate of discharge from receptors:

☒ **Weber- Fechner 's Law:**

- The frequency of impulses discharged from the receptors through afferent nerves is directly proportionate with the logarithm intensity of the stimulus.
- R = log S x K (Where R = rate of discharge, S = strength of stimulus, K = constant).
- To increase the rate of discharge twice, you must increase the intensity of the stimulus 100 times.

☒ **Increasing the intensity of the stimulus increases the rate of discharge by:**

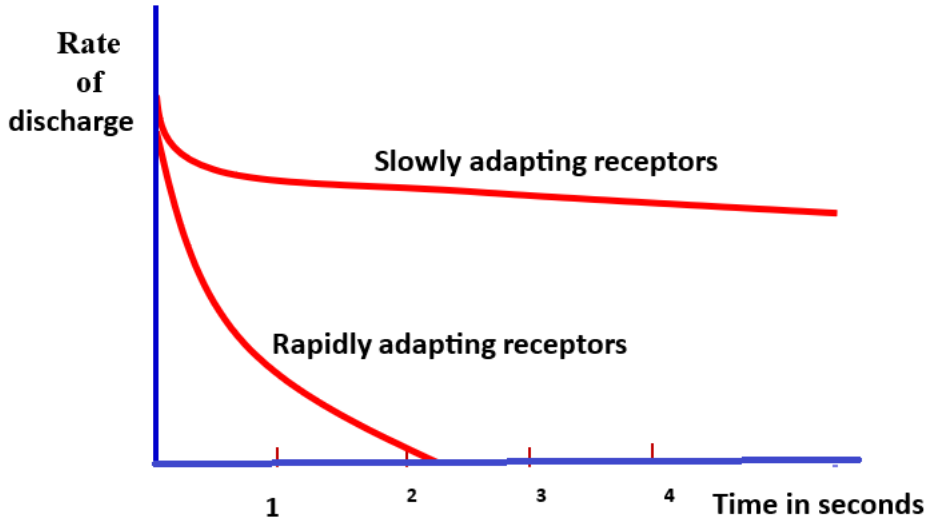
- Increasing the **rate of discharge from each receptor**.
- Increasing the **number of excited receptors (recruitment).**

4. Adaptation of receptors:

☒ **Def:** decline "decrease" in the rate of discharge from the receptors in spite of continuous constant stimulation.

☒ **Types:** According to the speed of decline "Rate of adaptation" in the rate of discharge from receptors, we can classify the receptors into:

- Rapidly adapting receptors (Phasic receptors).
- Slowly adapting receptors (Tonic receptors).



	Rapidly adapting receptors = Phasic receptors	**Slowly adapting R. = Tonic receptors**
Def.	They first discharge at high rate, then the rate decreases rapidly to zero after 1 or 2 seconds in spite of continuous stimulation	They continue to discharge at a lower rate as long as the stimulus is applied.
Examples	• Pacinian corpuscle. • Meissner 's corpuscle. • Hair follicle receptors. • Some joint receptors.	• Muscle spindle and Golgi tendon organ (GTO). • Pain receptors. • Cold receptors.
Pattern of discharge	They discharge **only at**: • **onset** of stimulation • **termination** of stimulation • **change in strength** of stimulation *so they are called **phasic** receptors*	They discharge **continuously** to CNS as long as the stimulus is applied. *So they are called **tonic** receptors*
Importance	• CNS only needs **to** receive impulse at the **start, termination & change in strength** of stimulation. • **Continuous** from these receptors **isn't necessary, otherwise** they **would be distracting. (e.g.** no need to continuously inform CNS about contact of clothes).	• Impulses from muscle spindle, GTO & vestibular receptors helps to maintain **posture & equilibrium**. • Impulses from baroreceptors & chemoreceptors maintain **ABP & HR.** • Pain & cold receptors inform CNS about **harmful** stimuli & initiate **protective reflexes.**

Coding of sensory information

☒ **Def:** It is the ability of higher centers of the brain to identify:

a) Type of the stimulus (modality discrimination)

b) Intensity of the stimulus (intensity discrimination)

c) Locality of stimulus (locality discrimination)

although action potential is the same in all nerves

1. Modality discrimination

It's the ability of the CNS to **discriminate the type** of a sensation (e.g touch, pain ,sound, …) **it depends on:**

A. Peripheral mechanism:

- Occurs at the level of receptors and depends on **Muller's law**.
- According to **muller's law**: each type of receptor gives one type of sensation when stimulated by its adequate stimulus.
- **e.g.** stimulation of retinal receptors gives rise to light sensation.
- So that **specificity** of receptors represents **the first step** in the coding of different modalities (types) of stimuli.

B. Central mechanism:

Depends on *"labelled line principle"* which is an extension to Muller 's law.

Labelled line principle states that:

*"There's **a specific anatomical connections (**pathways) for each sensation which begins at a **specific receptor** then through a **specific tract** to terminate at a **specific center (area)** in the cerebral cortex".*

- Stimulation of this pathway at any point gives rise to a specific sensation **e.g** stimulation of the visual pathway at any point gives rise to visual sensation.
- This means that there are **specific pathways** for transmission of different modalities and that **each pathway carries only one sensory modality**.

2. Intensity discrimination

It's the ability of the CNS to **discriminate the intensity** of a sensation, **it depends on**:

A. Peripheral mechanism: which depends on:

a. **Rate of impulse discharge from each receptor**: the **higher the** rate of discharge, the **stronger is** the stimulus.

b. **The number of stimulated receptors (recruitement of receptors)**: the **more the number** of stimulated receptors, the **stronger is** the stimulus.

B. Central mechanism:

- **Depends on the number of afferents reaching CNS**: the more **the number** of **afferents** reaching CNS the **stronger is** the stimulus.

3. Locality discrimination

☒ It's the ability of CNS to **discriminate the site** of a sensation, **it depends on:**

☒ **Somatotopic map:**

- Each area in the body e.g hand or leg is **represented** in a specific area in the cerebral cortex with **accurate anatomical pathways** from the receptor to the center in the cerebral cortex.
- So when the impulse reaches specific area in the cerebral cortex, the sensation isn't felt in the cortical neuron but it is **referred (projected)** to its **original site** in the body this principle is called **law of projection**.

Pain sensation

☒ **Def of pain:** Unpleasant sensory and emotional experience caused by actual tissue damage.

☒ **Significance of pain**: It is a **protective** sense, where it directs the person to get rid of the injurious agents.

☒ **Pain receptors (Nociceptors):**

- **Nature:** They are **free nerve endings**.
- **Subtypes of pain receptors: They are functionally classified according to their sensitivity response into 4 subtypes:**
  1. **Mechanical pain receptors:** Respond only to the **mechanical trauma** e.g. heavy pressure.
  2. **Chemical pain receptors:** Respond to tissue damage produced by **chemical agents** e.g. concentrated H2SO4 or high concentration of HCl in esophagus and environmental irritants
  3. **Thermal pain receptors:** Respond to tissue damage produced by **thermal stimuli (temperatures > 45 C^O & < 10 C^O)**.
  4. **Polymodal pain receptors:** Respond to the tissue damage produced by a wide variety of painful stimuli **(combination of the above stimuli).**

☒ **Adaptation of pain receptors:** They are **slowly adapting** receptors even non adapting receptors, and this is very important because it directs the subject to get rid of the injurious agent

☒ **Distribution of pain receptors:**

- **More in**: Skin, periosteum, arteries, dura.
- **Less in:** Deep tissues and viscera.
- **Absent in:** Parenchymatous organs e.g liver, brain & lung alveoli.

Thus, diseases affecting the parenchyma may not cause pain early. However, later on they cause severe pain when they invade the serous covering e.g peritoneum and pleura which is richly supplied by pain receptors.

☒ **Threshold of pain receptors:** They are of **high threshold**: the pain receptors need sufficient degree of tissue damage to be stimulated. The lowest intensity of injurious agent needed to stimulate the pain receptors and produces pain sensation is known as **Pain Threshold**

☒ **Mechanism of stimulation of pain receptors:**

Tissue damage ➔ Release of chemical agents called **pain producing compounds (PPCs)** which are of **2 types:**

- **Direct stimulators:** includes K+, serotonin, histamine, bradykinin, acids and proteolytic enzymes.
- **Sensitizers:** Sensitizing the receptor membrane by lowering its threshold e.g. substance P and PGE2

Cutaneous pain

☒ **Def:** Pain sensation results from the stimulation of pain receptors in the skin

☒ **Types:** 1- Pricking (fast) pain. 2- Burning (slow) pain.

☒ **This dual pain sensation** is due to **dual pain pathway**.

	1. Pricking (fast)	2. Burning (slow)
Locality	well localized	Diffuse
Quality	Pricking	Burning
Onset	**Rapid** [felt immediately after injury (0.1 second)].	**Slow** [felt shortly after injury (1 second or more).
Duration	**Short** (less than 1 second)	**Long** (several minutes)
Conduction	**Fast**, where it is transmitted by rapidly conducting A-δ nerve fibers **(6-30m\sec)** "**neospinothalamic tract**".	**Slow**, where it is transmitted by slowly conducting, C nerve fibers **(0.5-2m\sec)** "**paleospinothalamic tract**".
Center	**cerebral cortex**.	**thalamus**, so still can be felt after the damage of the cerebral cortex.
Initiate	Somatic protective reflexes	Autonomic & somatic reflexes
Lost by	Pressure & hypoxia	Local anaesthetic drugs

☒ Reactions to cutaneous pain

1. Somatic reactions: In the form of **skeletal muscle contraction** e.g. flexion withdrawal reflex

2. Autonomic reactions:

i) Mild to moderate cutaneous pain is associated with **pressor (sympathetic)** effects as ↑ heart rate, ↑ arterial blood pressure.

ii) Severe cutaneous pain is associated with **depressor (parasympathetic)** effects as ↓ heart rate, ↓ arterial blood pressure, nausea and vomiting.

3. Emotional and psychic reactions: e.g anxiety & depression.

4. Hyperalgesia

	a) Primary hyperalgesia (Allodynia):	**b) Secondary hyperalgesia:**
Def:	↑ pain sensitivity in the red inflamed area (flare) surrounding the site of injury.	↑ pain sensitivity in the healthy skin area surrounding the red (flare) area.
In this area	Non painful stimuli (as touch) produce pain.	Mild painful stimuli produce severe pain.
Onset & duration	It develops **30 to 60 minutes** following skin injury and lasts for **several hours or days**.	Its duration is **shorter than the 1ry hyperalgesia**.
Pain threshold	Lowered	Not lowered

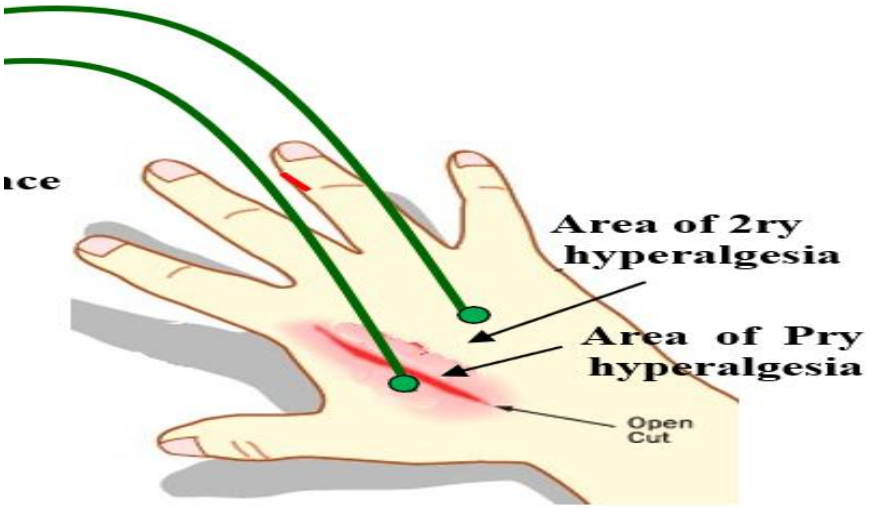


Figure: types of hyperalgesia

Deep pain

☒ **Def:** A type of pain produced by stimulation of pain receptors in the deep tissues **e.g** muscles, tendons, joints & ligaments.

☒ **Causes:**

(i) Injury of deep tissues.

(ii) Inflammation e.g arthritis and myositis.

(iii) Ischemia (ischemic pain).

☒ **Characters:**

1. **Quality:** Dull aching or throbbing.
2. **Locality:** Diffuse and poorly localized.
3. **Transmitted** via the C-non myelinated nerve fibers.
4. **Associated with:**
   - **<u>Reflex spasm of the nearby muscles</u>** ➔ reduce movements of injured part ➔ minimizes the tissue damage.
   - **<u>Depressor (parasympathetic) effects</u>**: as ↓HR and ↓ABP

Visceral pain

☒ **Def:** Pain sensation results from the stimulation of pain receptors in the viscera.

☒ **Causes:**

1. **Ischemia:➔** accumulation of metabolites as lactic acid➔stimulation of pain receptors. Ischemia results from:
   a) **Thrombosis** as in superior mesenteric artery or coronary artery.
   b) **Spasm** of the smooth muscles in the wall of the viscus (**Colic)➔** compression of the blood vessels.
   c) **Overdistension** of hollow organs **e.g.:** Stomach, uterus & urinary bladder➔ collapse of the blood vessels that pass in its wall.
2. **Trauma.**
3. **Inflammation** e.g cholecystitis, appendicitis.
4. **Chemical irritation** e.g. irritation by HCl (heart burn)

☒ **Characters:**

1. **Quality:** Colicky, burning, or dull aching.
2. **Locality:** Diffuse, poorly localized.

N.B: when the disease reaches the **parietal layer** of the serous membranes, pain become **sharply localized** & felt in its origin.

3. **Transmission:**

The visceral pain pathway reaches the C.N.S by **2 separate routes (Parietal pathway & Visceral pathway**)

Parietal pathway	Visceral pathway
* **Arise from** the parietal layers of the serous membranes & some retroperitoneal organs as kidney.	* **Arise from** the viscera itself & the visceral layers of the serous membranes.
* **Transmitted by:** A-δ & C- nerve fibers	* **Transmitted by:** C-nerve fibers
*** Join** the somatic nerves.	*** Join** the autonomic nerves

4. **Associated with:**
   - **Somatic reactions** in the form of contraction of the overlying muscles (**Guarding reponse**) to protect the underlying inflamed viscus.
   - **Parasympathetic manifestations** as ↓ in H.R, ↓ in A.B.P
5. **It is usually referred.**

Referred pain

☒ **Def:** Viscera pain is **poorly localized** and **is not felt in the affected viscera**, but in the **skin area or somatic tissue** (dermatome) supplied by the same spinal dorsal roots which innervate the diseased viscus **i.e.** ***pain arises frm a viscus & is felt in a related somatic structure***.

NB: Both the viscus and somatic structure originated from the **same embryonic segment or dermatome**.

☒ **Examples of Referred pain:**

Type of visceral pain	Referred to
1-Cardiac pain:	- Retrosternal region, - Base of the neck, - Left shoulder, - Inner side of the left arm, fore-arm, or little finger. - Epigastric region.
2-Renal & ureteric pain:	- Inguinal region. - Testicle & scrotum
3- Gall bladder pain:	- Epigastric region to the right. - The right shoulder **if diaphragm is irritated**.
4- Appendicitis pain:	skin area surrounding the umbilicus. **N.B.** later on localized to the **right iliac fossa** when the **peritoneal covering** is irritated.
5-Gastric pain:	Epigastric region
6-Esophageal pain:	- Pharynx - Lower neck - Midline chest region
7-Uterine pain:	-Suprepubic -Perineum -Lower back

☒ Mechanism of referred pain: [Convergence projection theory]:

- The pain carrying fibers from the diseased viscus & from the related somatic structures **converge on** the same SGR cells (Dorsal horn cells) and **ascend to** the same cortical neurons.
- The cortical sensory areas **accustomed to** receive pain impulses from the somatic structure.
- So when the viscus is **injured or inflamed** the impulses from it are perceived by the cortex **as if** coming from the **somatic structure** so, the pain sensation is projected to the **somatic structure.**

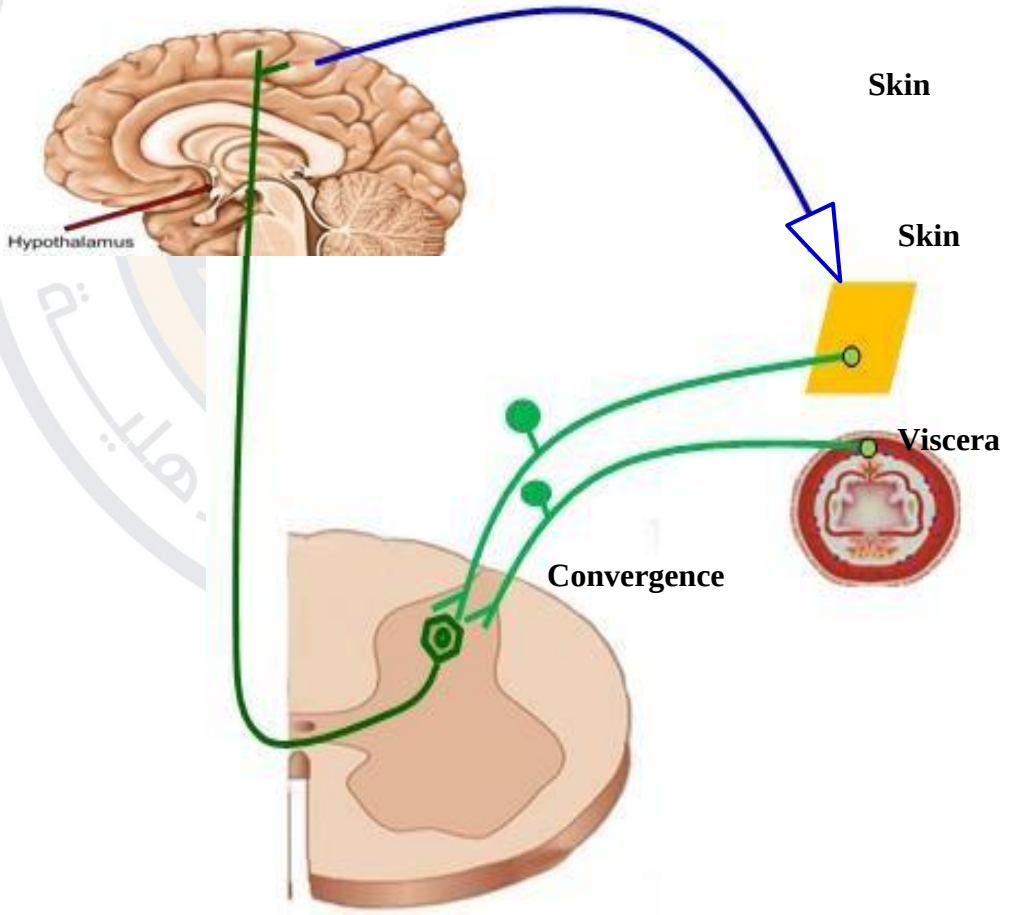


Figure: Convergence projection theory

Neuropathic pain

☒ **Def:** A chronic type of pain caused by damage to or pathological changes in the nerve fibers either in the peripheral or central nervous system

☒ **Examples:**

- Trigeminal neuralgia.
- Herpes zoster.
- Diabetic peripheral neuropathy.

☒ **Characters:**

1. Described as excruciating, burning or shooting pain.
2. It occurs in bouts or paroxysms.
3. Accompanied by hyperalgesia.
4. Associated with reflex sympathetic dystrophy.
5. Hardly to be treated.
6. Partially responsive to opioid therapy.

Pain control system (pain analgesia system)

☒ **Def:** It is a system concerned with the inhibition of pain impulses transmission at different levels in the pain pathway and produces analgesia during stress and emotions

☒ The activity of this system differs from one person to another and from time to time in the same person.

☒ **Components of pain control system**

- **Peri-aquiductal gray area (PAG)** in midbrain
- **Raphe magnus nuclei (RMN)** and **nucleus reticularis para-giagantocellularis (NRPG)** in medulla oblongata
- **Pain inhibitory complex** located in the dorsal horn of the spinal cord

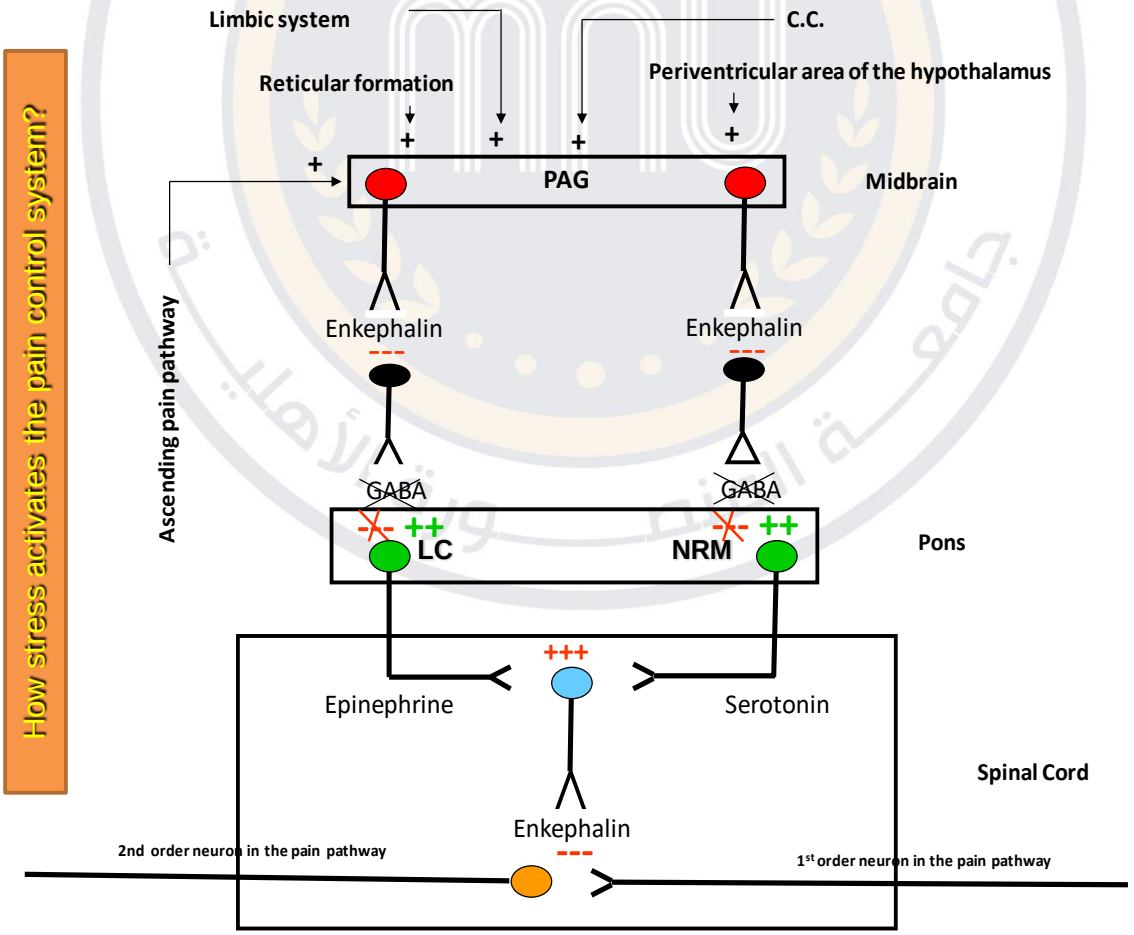
☒ **How and when this system is activated?**

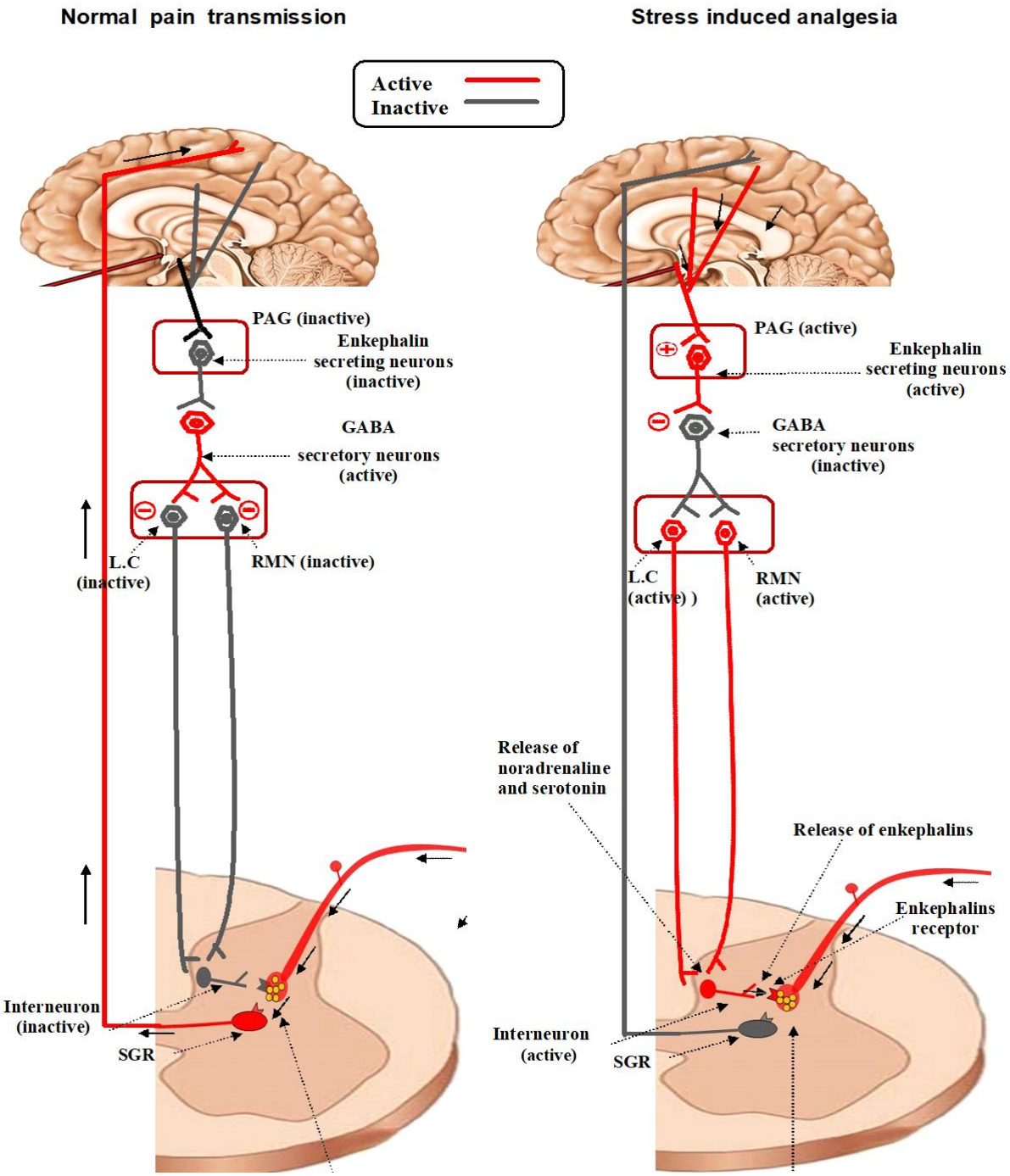
- This system is **activated by** impulses from many areas in cases of **severe stresses and strong emotions** e.g. during severe exercise, battles, fear **by impulses from many areas as**:
  - Cerebral cortex
  - Limbic system and hypothalamus.
  - Reticular formation.
  - Ascending pain pathways via collaterals (-ve feedback).

☒ **Mechanism of action:**

- **PAG** area receives stimulatory input from **hypothalamus during stress** and emotions and from other areas.
- Fibers from **PAG** release **enkephalins** that inhibit **GABA ergic neurons** (which normally inhibits both RMN and NRPG), thus **RMN and NRPG become activated**.

- The **activated RMN (serotonergic neurons)** and **NRPG (noradrenergic neurons)** release **serotonin** and **noradrenaline** at their terminals in the dorsal horn of the spinal cord.
- The released serotonin and noradrenaline excite **inhibitory interneuron** in the dorsal horn which by its turn release the inhibitory transmitter **enkephalins**.
- **Enkephalins** bind to **opioid receptors** on the terminals of the afferent pain fibers ➔ closure of Ca++ channels **(presynaptic inhibition)** ➔ stoppage of release of substance-P and glutamate ➔ stoppage of pain transmission ➔ no impulses reach the brain (analgesia).




Normal pain transmission
Stress induced analgesia
Active
Inactive
PAG (inactive)
Enkephalin secreting neurons (inactive)
GABA secretory neurons (active)
L.C (inactive)
RMN (inactive)
Interneuron (inactive)
SGR
PAG (active)
Enkephalin secreting neurons (active)
GABA secretory neurons (inactive)
L.C (active))
RMN (active)
Release of noradrenaline and serotonin
Release of enkephalins
Enkephalins receptor
Interneuron (active)
SGR

☒ Neurochemistry of pain control system:

A. Endogenous opioids:

- **Def:** Natural peptide substances produced inside the body & have the ability to bind opioid (morphine) receptors producing pain analgesia.
- **Classes:**

	1. Enkephalin:	2. Endorphin:
Derived from	proenkephalin	Pre-opio-melanocortin (POMC)
Present in	brain stem & spinal cord	Anterior pituitary & hypothalamus
Main types	leu-enkephalin & met enkephalin	β-endorphins

3. Dynorphin

- Derived from **pre-dynorphin.**
- Present in **brain stem**.

B. Opioid receptors:

Respond to opiates (exogenous opioids e.g. morphine) & endogenous opioids.

- **Types:**

Receptor	Responds to
1**. Delta** receptors (δ)	**enkephalins**.
2. **Sigma** receptors (σ)	**dynorphins**
3. **Kappa** receptors (K)	**dynorphins**
4. **Mu** receptors (μ)	**endorphins**.

- **Morpine (exogenous opoid)** binds to & stimulates **most opioid receptors** & produces profound analgesia.
- **Naloxone blocks** opioid receptors & acts as **morphine antagonist.**

☒ Other Mechanisms for Pain Control and Inhibition

- **Stimulation of the large sensory nerves (A-beta) in the area of pain produces pain relief:**
  - **Mechanism:**
    - The large sensory nerves (carrying tactile sensations); during their ascent in the dorsal column; **send collaterals** that produce **presynaptic inhibition** of pain carrying nerve fibers (at the SGR) by blocking Ca++ channels ➔ prevention of pain transmission ➔ pain suppression.
    - ***Example:*** The relief of pain sense by rubbing the skin area around the site of pain.
  - **Acupuncture:**

    Insertion of certain needles by the Chinese at certain areas may stimulate the large sensory nerves mostly type A, which by its turn:

    1. Through collaterals can inhibit pain transmission at SGR "presynaptic inhibition via enkephalins.
    2. Can stimulate PAG area at the brain stem.

☒ Gate theory of pain control

- SGR acts as gate through which pain impulses reach the antero-lateral system.
- **Pain impulses transmission to SGR can be inhibited by:**
  1. **Supra-spinal inhibition:** Pain analgesia system.
  2. **Spinal inhibition** through impulses from:

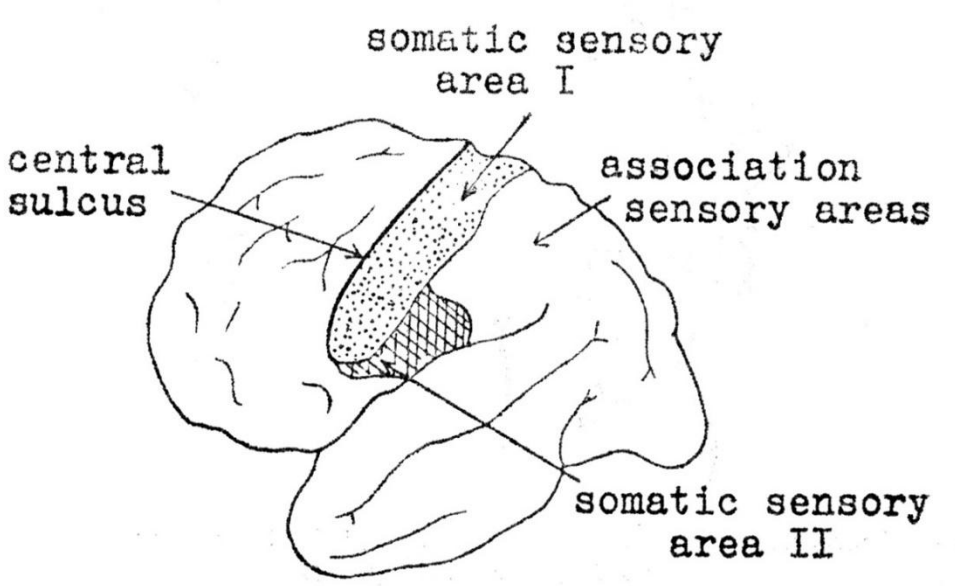
     a) A-B fibers (as during rubbing of skin) (see above).
     b) A-δ fibers (as during acupuncture) (see above).
     c) Cortico-fugal fibers (as during thinking the pain is ↓↓).

Somatic sensory cortex

☒ **Def:** It is the part of the cerebral cortex concerned with the perception and interpretation of the sensory information.

☒ **It is divided into 3 areas:**

A. **Primary sensory cortex , SI** (Broadman areas 3,1,2)
B. **Secondary somatic sensory cortex, SII** (Broadman area 40)
C. **Somatic sensory association cortex** (Broadman areas 5 & 7)



Somatic sensory areas : Somatic sensory areas I, II and association sensory areas.

	Primary somatic sensory area	Secondary somatic sensory area	Somatic sensory association area
Brodmann's classification:	Areas 3,1, and 2	Area 40	Areas 5 and 7
Location:	In the postcentral gyrus of the parietal lobe.	Lateral & posterior to face representation in SI area	Behind the upper most part of SI.
Receive signals from:	Ventral posterior nucleus of thalamus (VPNT)	• VPNT • SI area.	• VPNT • Other thalamic nuclei • SI area. • Visual cortex and auditory cortex.
Body representation	**1- Contralateral (crossed):** receive sensation from opposite side of body. **2- Inverted:** face is represented downward & the leg upward. **3-The area of representation depends on the number of receptors in the organ (not its size):** so,	• **Bilateral representation**. (in a horizontal manner) ✓ **Head ➔** anteriorly. ✓ **Leg ➔** posterioly. ✓ **Arm ➔** in between	• **Contralateral** • **Inverted** • **peripheral parts are widely represented**.

	peripheral parts of the body (as fingers) have wider area of representation than thighs.		
Functions:	1- **Perception of somatic sensation** as touch, pressure, vibration, stereognosis & kinesthetic sensations. 2-**Identify** the **shape & form** of objects **(stereognosis)** 3- **Localize the site of sensation.** 4-**Discriminate** different **intensities**.	Potentiate functions of SI	1. **Interpretation** of somatic sensory information to find their **meaning (stereognosis)**. 2. Provide **brain motor centers** by **pre-analyzed proprioceptive** information for control & coordination of movements.
Effect of lesion:	1. **Inability to localize** site of different stimuli. 2. **Inability to discriminate different intensities** of sensory stimuli. 3. **Astereognosis** i.e. inability to recognize the shapes or forms or texture of materials.	**Defect in learning based on tactile discrimination.**	1. **Astereognosis:** The patient cannot interpret sensory information. 2.**Parietal lobe neglect (amorphosynthesis):** - The sensory information from opposite side of body are ignored and neglected The brain forgets other ½ of body & forgets to use it during motor activity.

Spinal reflex arc

1. Receptor.
2. Afferent neuron.
3. Interneurons.
4. Efferent neuron.
5. Effector organ.

I. Afferent Neuron

☒ **They are monopolar neurons whose cell bodies are located in the D.R.G.**

☒ **Their axons give two branches:**

- **A peripheral branch** which terminates in sensory receptors located in tissues.
- **A central branch** which enters into the spinal cord. through dorsal root and **divide into many terminals.**

☒ **The central branch synapse with:**

1- Interneurons.
2- α motor neurons (large AHCs).
3- 2nd order neurons of sensory pathways.

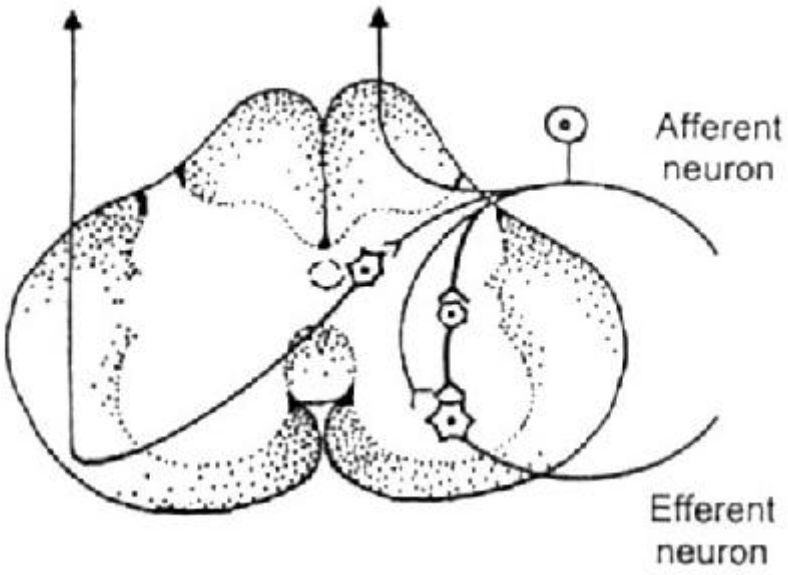
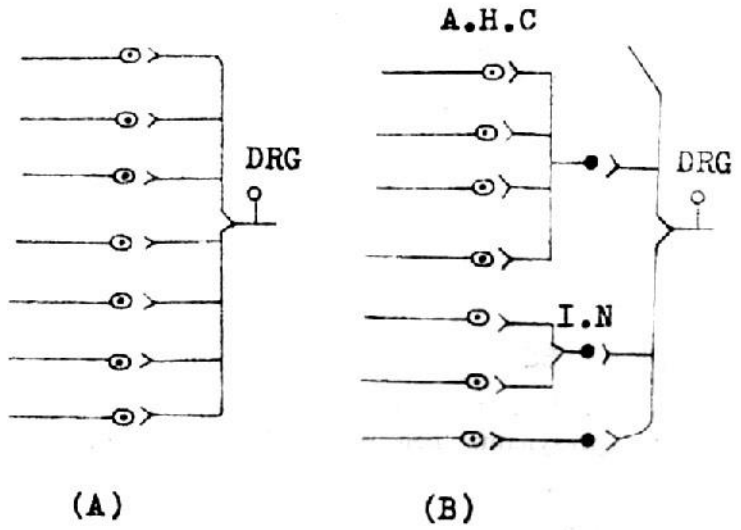


Figure: Terminals of central branch of afferent neuron

☒ Functions:

1. **Conduction** of impulses from the receptors to the centers in spinal cord.
2. **Divergence** of the sensory signals into wide areas in the nervous system via several central terminals of the afferent neurons. This makes the reflex to be multisegmental.
   - **Stimulation of single afferent (input)** ➔ stimulation of multiple efferents (outputs).
   - **Mechanism:** when the afferent enters the spinal cord, it divides into ascending & descending branches which give many collaterals that terminate on efferents (AHCs) ➔ widespread stimulation.

3. It helps the phenomenon of irradiation.



Divergence of afferent impulses in the spinal cord. Collaterals terminate on the A.H.Cs. either (A) directly or (B) through interneurones (I.N.).

4. Convergence:

- Several afferent fibers **converge** on a single efferent neuron.
- It helps the phenomenon of **spatial summation**.

II. Interneurons

☒ **Def:** They are **small** sized, highly **excitable** & **numerous** neurons

☒ **Site:** They are located in the **grey matter** of spinal cord and provide a link between the central terminals of afferent neurons & the efferent neurons.

☒ **Types:** Some of them are **excitatory** and the others are **inhibitory**

☒ **Polysynaptic and monosynaptic reflexes: All** reflex arcs include interneurons **except** the **stretch reflex**. Thus, **all** reflexes are **polysynaptic except** the **stretch reflex** which is a **monosynaptic** reflex.

☒ **Functions of interneurons:**

1. **Divergence:**
   - The interneuron divides into several collaterals and reach a larger number of efferent neurons.
   - It helps the phenomenon of **irradiation.**

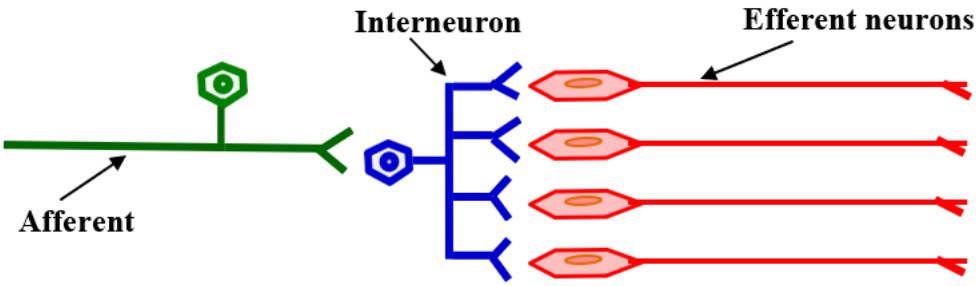


Figure 6: divergence of interneurons

2. **Convergence:**
   - Multiple collaterals from interneurons converge on a relatively fewer number of output (efferent) neurons.
   - It helps the phenomenon of **spatial summation.**

3. After discharge circuits:

- **Def:** It is prolonged discharge from an efferent neuron even after stoppage of stimulation of the afferent nerves. **i.e.** when the interneuronal circuit receives single impulse, it produces prolonged efferent discharge of several impulses which continue for some time.
- **Types:**

There are **2 types of interneuronal circuits** involved in the after discharge:

i) Open chain (= parallel) circuits.
ii) Closed chain (= Reverberating) circuits.

i. Open chain (= parallel) circuits:

- The afferent neuron stimulates the efferent neuron both **directly and indirectly through a number of interneurons**.
- **Stimulation of the afferent neuron** will excite the efferent neuron and at the same time gives collateral branch to stimulate the parallel interneurons.
- **This parallel interneuron** also stimulates the efferent neuron and gives collateral which stimulate another parallel interneuron & so on.
- The **duration of after discharge** is determined by the **number of the interneurons in the circuit**.

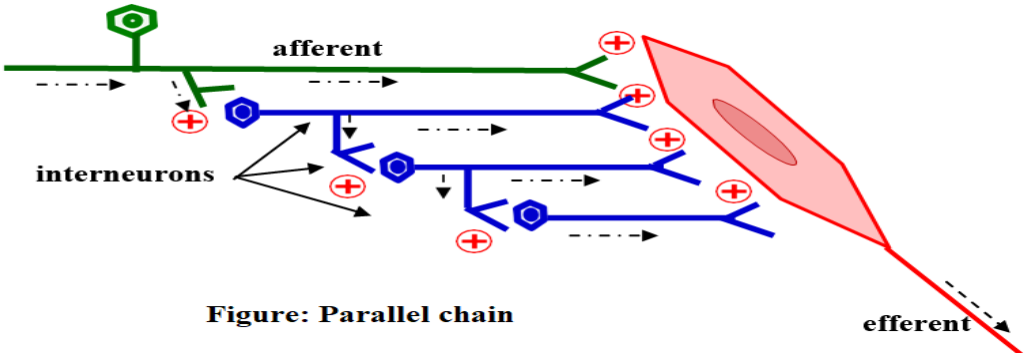


Figure: Parallel chain

ii. Closed chain or (reverberating) circuits:

- The afferent nerve is connected to the efferent neuron through **a principal interneuron**. This interneuron terminates **directly** on the efferent neuron, and at the same time it gives **branches** which return to **re-stimulate the principle interneuron** through **interneurons**.
- The entry of a brief afferent signal into these circuits causes **re-circulation (Reverberation) of the signal** in the circuit for a prolonged period ➔ repetitive excitation of the efferent neuron.

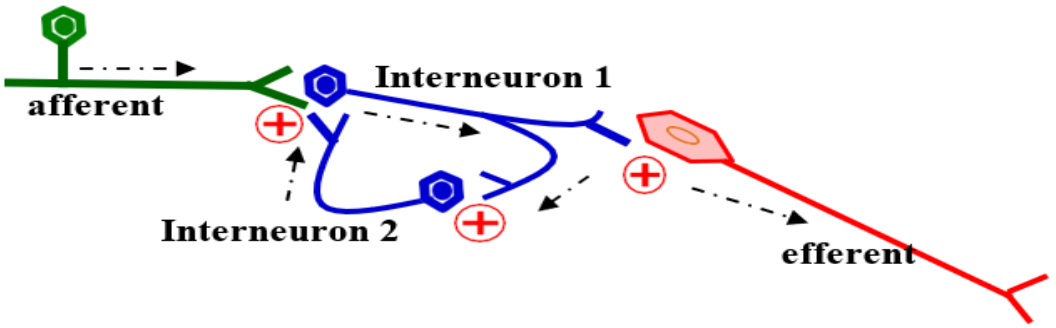


Figure: reverberating circuit

- **The activity of these circuits continue till stopped by either:**
  a. **Fatigue** in the synapse, OR
  b. **Inhibition from other neurons**.

- **Examples:**

a. Reticular activating system (RAS):

- It is present in the **brain stem**.
- It is responsible for **wakefulness**.
- This system contains many reverberating circuits. So, single sensory stimulation leads to **its activation for long time** (16-18 hours).
- This system by its turn will stimulate the **cerebral cortex** which by its turn **re-stimulate it** & so on.
- This activity continues till **fatigue** of the synaptic transmission occurs & then **sleep** occurs.

b. Apneustic & inspiratory centers:

- Continue to discharge due to reverberating circuits.
- **Inhibited by** impulses from **pneumotaxic** center

4. Inhibitory circuits:

- **Inhibitory interneuronal circuits** exist in the spinal cord and convert an excitatory afferent input into inhibitory output ➔ **modulate the response to afferent stimulation**.
- **Types of inhibitory circuits:**

i. Lateral inhibitory circuits:

- **Def:** They are inhibitory interneurons which are stimulated by collaterals from the most active central neurons to inhibit the less active surrounding neurons.
- ***Example:*** The ascending sensory tracts during their course to cerebral cortex
- ***Mechanism:***
  - When a stimulus is applied to the skin, it produces strong stimulation of the receptors and afferents of the **central part** of the receptive field.
  - During their ascent in the CNS, the central most excited neurons send collaterals that through inhibitory interneurons will inhibit the less stimulated afferents arising from the **peripheral parts** of the field.
- ***Significance:*** help in **sharpening** or focusing the sense.

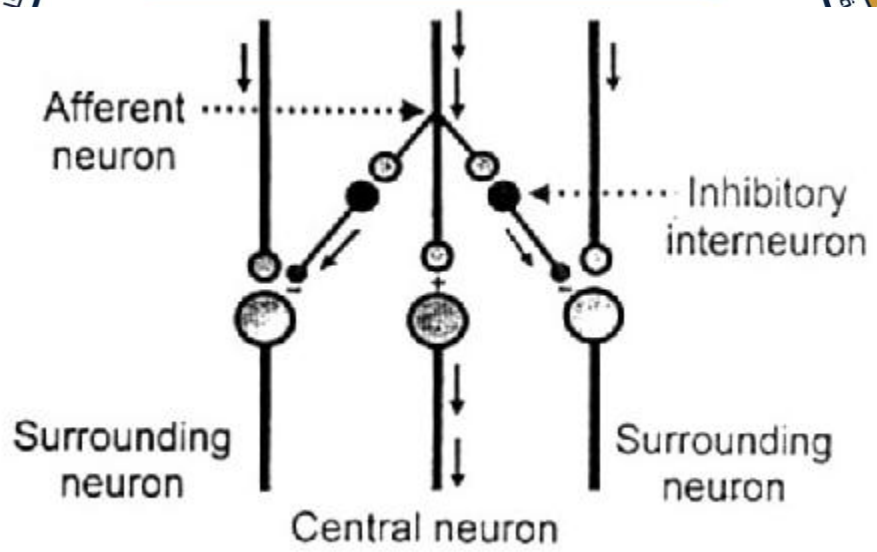


Fig.: Lateral inhibitory circuits.

ii. Recurrent (feedback) inhibitory circuits:

- Collaterals **arise** from the axon of **efferent neuron** (before leaving the spinal cord) & **synapse** with certain inhibitory interneurons called "**Renshaw cells**"
- These cells in turn project their axon terminals back on the:
  - **Surrounding α-motor neurons**
  - **Same stimulated α-motor neurons**.
- The Renshaw cells are stimulated by **Acetylcholine** and when stimulated they release **glycine** (inhibitory neurotransmitter).
- **The glycine released by Renshaw cells will inhibit:**
  - **The neighboring α-motor neurons:** ➔helps in **focusing** the motor activity to the most facilitated α-motor neurons.
  - **The originally stimulated α-motor neuron:** ➔ helps to **limit its discharge** (-ve feedback control).

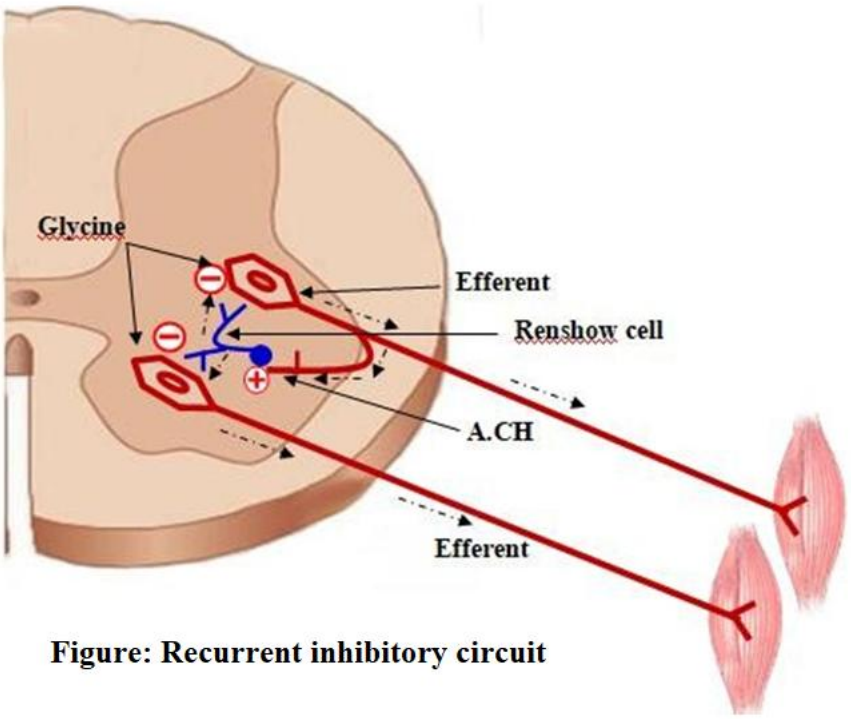
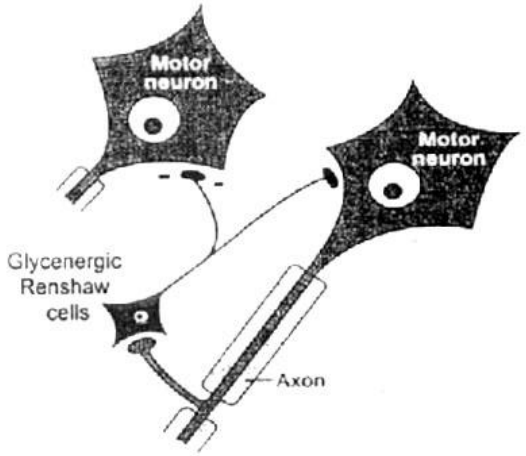


Figure: Recurrent inhibitory circuit



Recurrent inhibition of α-motor neurons by inhibitory interneurons (Renshaw cells).

Fig.: Recurrent inhibitory circuits.

III. Efferent Neurons

☒ **In the spinal reflexes the efferent neurons are of two types:**

A. **Autonomic efferent neurons (L.H.Cs):** mediate **autonomic reflexes**.

B. **Somatic efferent neurons (A.H.Cs):**

- mediate **somatic spinal reflexes**.
- **divided into:**

	α-motor neurons	**γ-motor neurons**
Size	Large AHCs	Small AHCs
Represent	70% of A.H.Cs	30% of A.H.Cs.
Axons	Aα	Aγ
Supply	extrafusal muscle fibers	intrafusal muscle fibers

☒ **Laterally situated AHCs** supply **distal** muscles & **medially situated AHCs** supply **axial** muscles.

☒ **Motor unit:**

- **Includes** one A.H.C + its efferent terminals + muscle fibers supplied by it.
- Motor unit of distal muscles contain less number of muscle fibers.

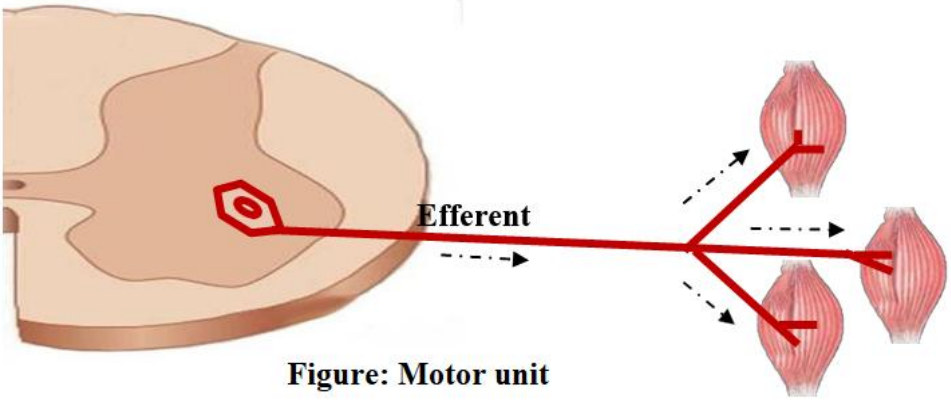
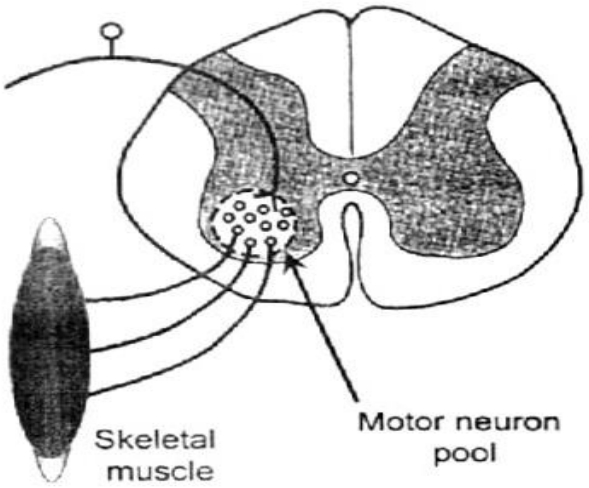


Figure: Motor unit

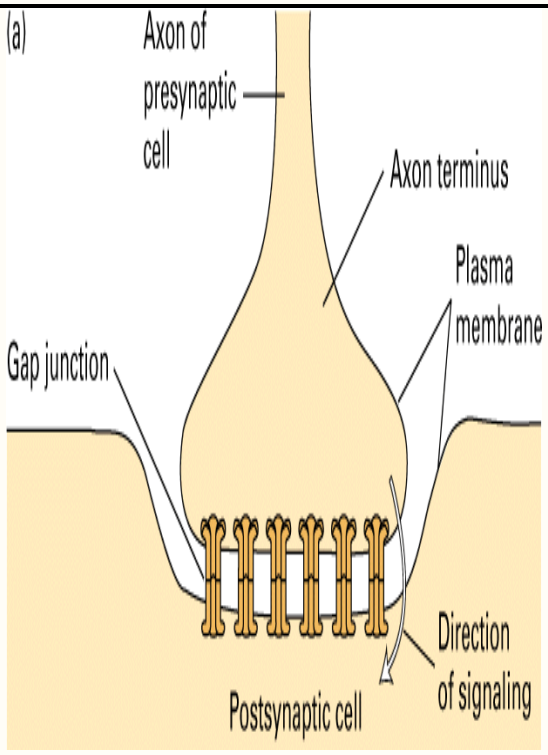
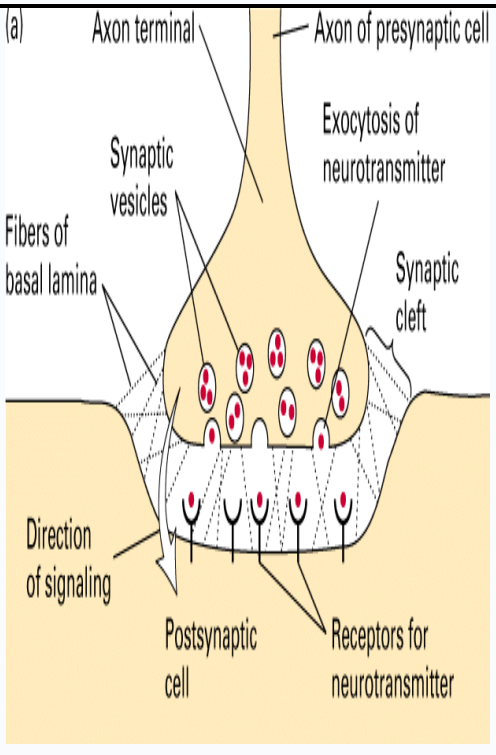
☒ **Motor neuron pool:** Number of A.H.Cs supplying certain muscle.



Synapses

☒ **Def:** areas of contact between neurons

☒ **Types:**

	Electrical Synapse	Chemical Synapses
Site	- They are extremely rare. - Present in hippocampus and retina	They represent almost all synapses in C.N.S.
Structure	- They are in the form of ***Gap junctions*** between the membranes of presynaptic and postsynaptic neurons. - These junctions are composed of proteins called ***"connexons"*** which are **highly permeable to ions**, so allow ease transmission of potential changes from one neuron to next.	These synapses consist of 2 neurons, one releasing the chemical transmitter called **(presynaptic neuron)** and one receiving the signal called **(postsynaptic neuron)**
		
Fatigue	- They **resist** fatigue.	- They **show** fatigue.
Direction	- Conduction occurs in **both** directions	**- One-way** conduction only.
Velocity	**- Faster**	**- Slower**

Chemical synapses

☒ Physiological anatomy of chemical synapses:

- **It consists of:**
  1) Presynaptic Terminal.
  2) Postsynaptic membrane.
  3) Synaptic cleft (20-30 nm).
- The presynaptic terminals are dilated forming certain swelling called **presynaptic knobs** that contain the neurotransmitter vesicles.
- **These presynaptic terminals (knobs) may synapse on:**
  - **Dendrites** of postsynaptic neuron (**Axo-dendritic synapse**) (**most common**)
  - **Soma** (**Axo-Somatic Synapse**)
  - **Axon** (**Axo-Axonic Synapse**).
- **The postsynaptic neuron** contains **receptors** for the chemical transmitter.

☒ Steps of synaptic transmission:

A. **<u>Release</u>** of neurotransmitter into synaptic cleft.
B. **<u>Action</u>** of the neurotransmitter on postsynaptic membrane.
C. **<u>Termination</u>** of synaptic transmission.

A. Release of neurotransmitter into synaptic cleft:

- **During rest**, both the synaptic knobs and the post synaptic membrane are in a **polarized state** i.e.: R.M.P is about **-70 mV**.
- When the presynaptic neuron is stimulated and an action potential reaches the synaptic knob ➔ transient opening of the **voltage sensitive Ca^{2+} channels** ➔ Ca^{2+} entry into the knob ➔ Ca^{2+} will bind the transmitter vesicles with the knob membrane ➔ vesicles open into the synaptic cleft and release the transmitter by **exocytosis**.

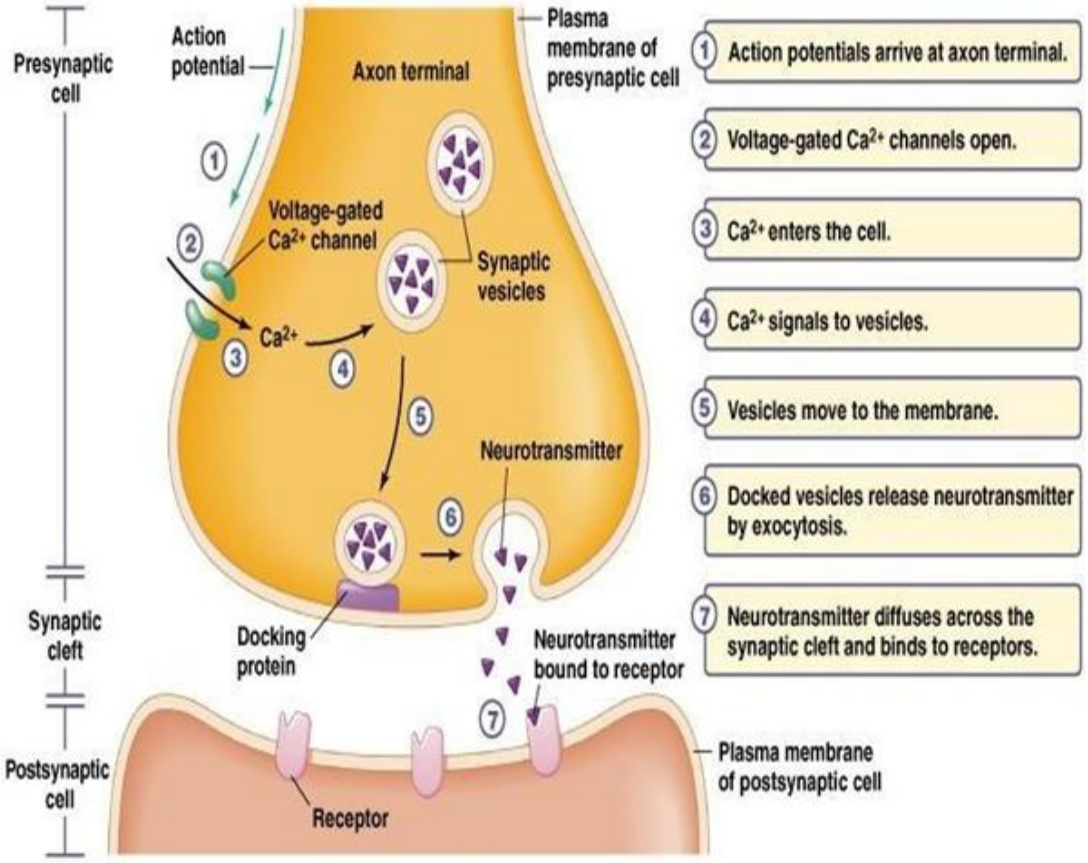


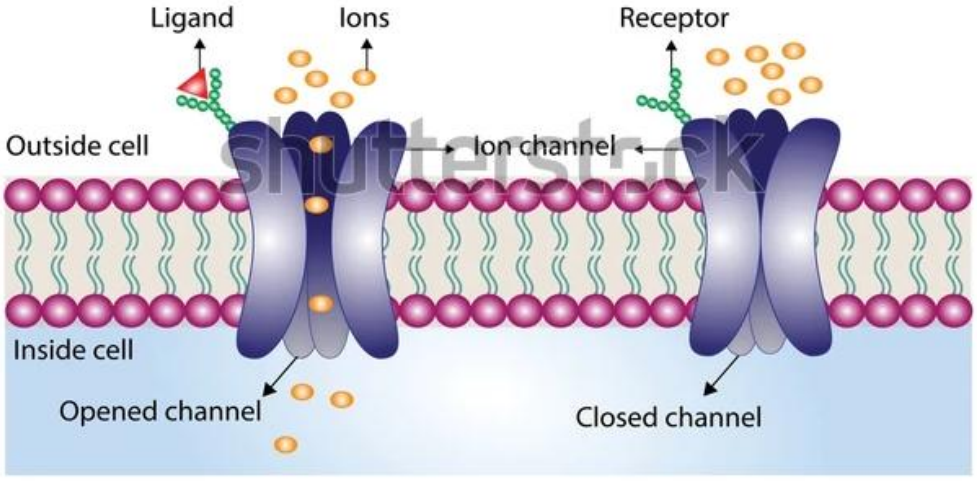
Figure: Release of the neurotransmitter

B. Action of neurotransmitter on the postsynaptic membrane:

- After a chemical transmitter is released into the cleft, it produces its effects through binding with **specific receptors** located in post-synaptic membrane.
- **Types of postsynaptic membrane receptors:**
  - **a. Ligand-gated ionic channels:**
    - Binding of these receptors to their specific neurotransmitter ➔ ↑ the channels permeability to ions.
    - **Types:**

Cation channels	Anion channels
When activated ➔ **Na^+ & Ca^{2+} influx ➔ depolarization** of postsynaptic membrane	When activated ➔ **Cl^- influx ➔ hyper-polarization** of postsynaptic membrane.
The transmitter which produces this effect is called **excitatory transmitter**.	The transmitter which produces this effect is called **inhibitory transmitter**.

Ligand-gated ion channel receptor



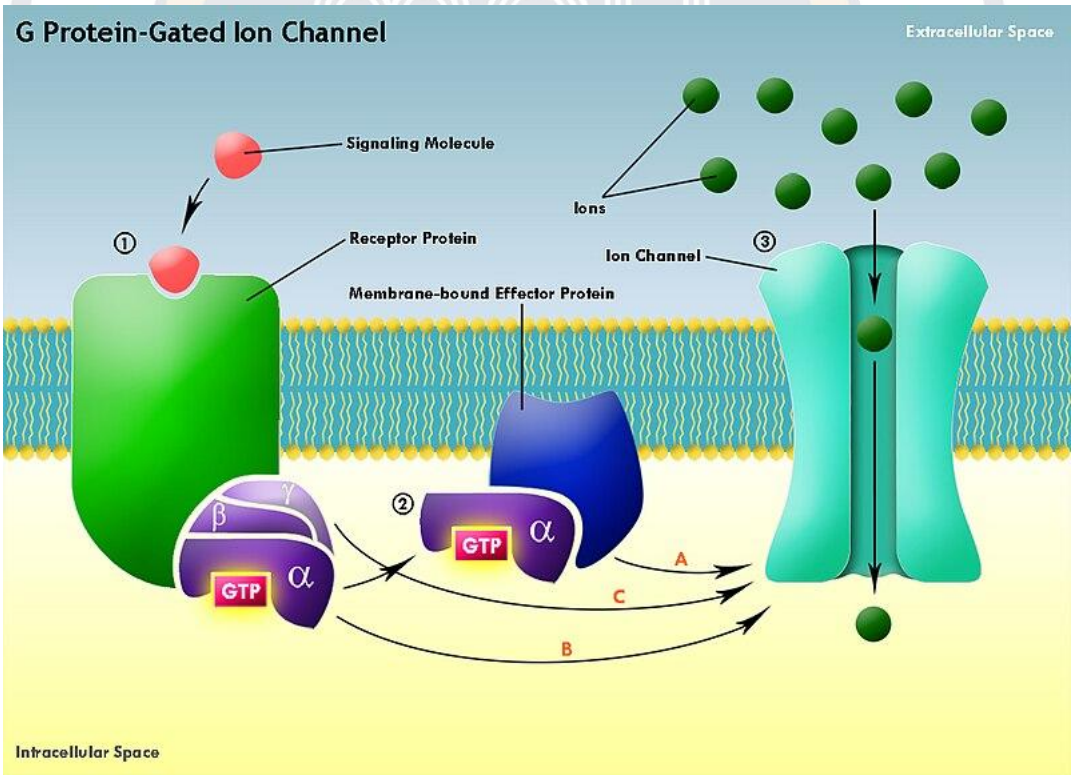
b. G-protein coupled receptors:

- Binding of these receptors to their specific neurotransmitter ➔ activation of G protein molecule (consists of α, β and γ subunits) by replacement of its GDP with GTP ➔ separation of α subunit ➔ perform these functions:

  i- Opening specific ion channels as 2nd messenger-gated K^+ channels ➔ ↑ K^+ efflux ➔ **hyperpolarization** of postsynaptic neuron membrane.

  ii- Activation of enzymes in cell membrane ➔ catalyze the formation of 2nd messengers as **cAMP** which control **metabolic pathways**.

  iii- Regulation of gene transcription ➔ produce **mRNA** molecules ➔ control synthesis of certain **proteins** that act as **receptors** & **enzymes**.



C. Termination of synaptic transmission:

It occurs when **the transmitter is removed** from the synaptic cleft by:

i) **Active reuptake of the transmitter into the presynaptic terminal**.

ii) **Enzymatic degeneration**.

iii) **Diffusion to interstitial fluid**.

☒ Nature of postsynaptic potentials (PSP):

The postsynaptic potentials are of 2 types:

1) Excitatory Post-Synaptic Potential (EPSP).

2) Inhibitory Post-Synaptic Potential (IPSP).

EPSP	IPSP
On stimulation: presynaptic terminals release ***excitatory neurotransmitter*** which open ***ligand-gated cation channels*** ➔ ↑ Na^+ influx more ➔ ***partial depolarization*** called ***EPSP.***	**On stimulation:** presynaptic knob release ***inhibitory neurotransmitter*** which open ***ligand-gated anion channel*** ➔ ↑ Cl^- influx ***or specific K^+ channels*** with ↑ in K^+ efflux ➔ ***hyper-polarization*** called ***IPSP***.
Characterized by: 1.↑ **excitability** of postsynaptic membrane. 2.**Localized** i.e. not spread. 3.**Short duration** i.e. 15 m.sec. 4.Its **amplitude** is very small (0.5 mv) & cannot reduce the membrane potential to the threshold level, so to produce action potential must be **summated**. **The summation is of 2 types:** **a) Spatial:** occurs by stimulation of several presynaptic fibers that converge on the post synaptic neuron at the same time. **b) Temporal:** occurs by stimulation of a single presynaptic neuron repetitively within very short duration (less than 15 m.sec).	**Characterized by:** 1.↓ **excitability** of postsynaptic membrane. 2. **Localized** i.e. not spread. 3. **Short duration** i.e. 15 m.sec. 4. Its **amplitude** is very small (0.5 mv).

☒ General properties of chemical synaptic transmission:

1) One-way conduction:

- At synapses, impulses are conducted only **in one direction** from the presynaptic to the post-synaptic neuron.
- Conduction ***never occurs in the opposite direction*** because no vesicles in the post-synaptic membrane & no receptors in the presynaptic membrane.

2) Synaptic delay:

- **Def:** It is the time that passes between arrival of impulse to the synaptic knob & appearance of response in the postsynaptic neuron.
- **It represents the time required for:**
  - Release and diffusion of the neurotransmitter
  - Activation of the post synaptic membrane receptors
  - Altering the membrane permeability to ions.
- **Value:** 0.5 msec.

3) Synaptic fatigue:

- **Def:** progressive ↓ and even stoppage of synaptic transmission when a synapse is stimulated rapidly and repeatedly.
- **Cause:** depletion of the neurotransmitters in the presynaptic knobs.
- The **fatigued synapse remains inactive** until the depleted transmitter is **reformed**.
- **Significance:**
  - Fatigue is a **protective mechanism** against **excessive neuronal activity**.
  - It could **suppress the activity of** reverberating circuits **during epilepsy** ➔ spontaneous ending of the epileptic fit (normal protective mechanism).

	4) Short term potentiation (post-tetanic facilitation) (post-tetanic potentiation)	5) Long-term potentiation (LTP)
Def:	Rapid repetitive stimulation of presynaptic neuron for a few seconds➔ ↑ excitability of post synaptic neuron	Brief repetitive stimulation of presynaptic neuron ➔ rapidly developed, long-term lasting enhancement of synaptic transmission
Duration	seconds or minutes	several days
Cause:	↑ Ca^{2+} inside the synaptic knob ➔ more & more vesicles release their transmitter ➔ a greater response of post synaptic neuron (↑EPSP).	↑ Ca^{2+} influx in the postsynaptic neuron (where it acts as a 2^{nd} messenger) ➔ ↑EPSP.
Significance	It may have a role in memory.	It occurs in hippocampus where it plays a role in learning & memory.

6) Effects of hypoxia on synaptic transmission

Marked hypoxia for a short period (few seconds) ➔ loss of excitability of many neurons and stoppage of synaptic transmission.

7) Effects of pH on synaptic transmission

- **Alkalosis:** increases neuronal excitability ➔ convulsions at pH 8.
- **Acidosis:** depresses neuronal excitability ➔ coma at pH 7.

8) Effects of drugs on synaptic transmission

- **Caffeine and theophylline** (in coffee and tea)**:** increase neuronal excitability.
- **Strychnine:** causes hyper-excitability of neurons.
- **Anesthetics and hypnotics:** decrease neuronal activity and thereby decrease synaptic transmission.

Polysynaptic somatic spinal reflexes

Flexion-withdrawal reflex

☒ **Def:** It is a **polysynaptic** reflex that moves the affected limb **away from** the painful stimulus. Application of injurious stimulus to a limb ➔ contraction of flexor muscles of this limb ➔ withdrawal of the limb away from the injurious stimulus.

☒ **Neural pathway:**

- **Stimulus:** Injurious agent with resultant tissue damage.
- **Receptors:** Free nerve endings.
- **Afferents:** A-δ nerve fibers.
- **Center & Response:**

  The afferents enter the spinal cord & divide into large number of terminals that synapse with interneurons in many segments of the spinal cord **leading to:**

  - **Excitation** of motor neurons of **ipsilateral flexor** muscles, thus **removing the limb** away from the injurious agent.
  - **Inhibition** of motor neurons of **ipsilateral antagonistic extensor** muscles (mediated by inhibitory interneurons).
  - **When the painful stimulus is a strong**, the response includes not only **flexion of the stimulated limb** but also increased **extension of the contralateral limb.**

☒ **Significance:**

- It is of **survival value**, because it immediately removes the exposed limb away from the injurious agent.
- It is a **prepotent reflex**; i.e. can suppress any other reflex occurring at the same time.

Crossed-extensor reflex

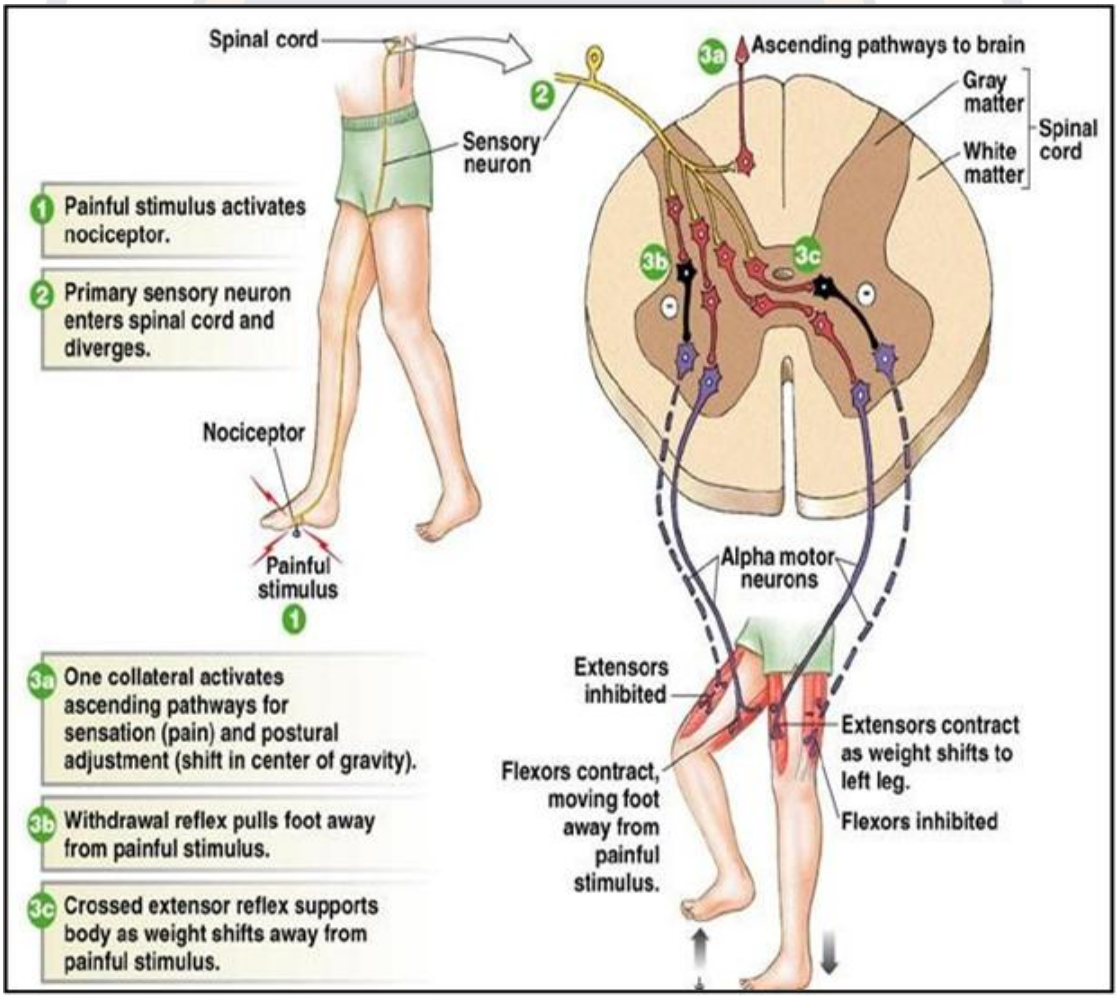
☒ **Def:** It is a reflex extension of a limb during flexion of the other limb (flexor withdrawal reflex).

☒ **Neural pathway:**

When a strong painful stimulus is applied to one limb, the afferent fibers activate interneurons which **cross** to the opposite side of spinal cord **leading to:**

- **Excitation** of the motor neurons of the **contralateral extensor muscles ➔ limb extension.**
- **Inhibition of** the motor neurons of the **contralateral flexor muscles.**

☒ **Importance: supportive reflex** that **support** the body posture.



Properties of polysynaptic somatic spinal reflexes

1. **ONE-WAY CONDUCTION:** see before.
2. **TOTAL REFLEX TIME & CENTRAL DELAY:**

☒ **Total Reflex time**

- **Def:** is the time between application of the stimulus and the onset of reflex response.
- **It represents the time needed for:**
  - Conduction of the nerve impulse through afferent & efferent.
  - Transmission through central synapses (central delay).

☒ **Central Delay** is the period needed for the transmission of impulses through central synapses in the reflex pathway, and **it mainly depends** upon the number of these synapses.

3. **SYNAPTIC FATIGUE:**

☒ When a spinal reflex is elicited **continually for a long period**, the reflex **gradually declines** or even **disappears**.

☒ This is due to **fatigue of the synapses** in its pathway.

4. **LOCALIZATION [LOCAL SIGN]**

☒ **This means** that the **site (locality)** of the stimulus determines the **nature of response**.

☒ **e.g.: In withdrawal reflex**, the pattern of flexion that occurs **varies with the site of the stimulus:**

Stimulus at the lateral aspect of the thigh ➔ adduction & **medial rotation**	**Stimulus at medial aspect of the thigh ➔ abduction** & **lateral rotation**

☒ **Mechanism:**

- It is due to different connections of the afferent fibers from the different regions of the stimulated limb e.g.
    - Afferent pain fibers from the **lateral** aspect of the thigh excite the motor neurons of the **flexors** & **adductors.**
    - Afferent pain fibers from the **medial** aspect of the thigh excite the motor neurons of the **flexors** & **abductors.**
- **Importance:** to remove the limb away from the injurious (painful) stimulus.

5. IRRADIATION:

☒ **This means** that the **extent** of the reflex response is determined by the **strength** of the stimulus

☒ **e.g.:**

* **Mild** painful stimulus at the sole of the foot ➔ dorsiflexion of ankle only.
* **Stronger** painful stimulus at the sole of the foot ➔ dorsiflexion of ankle & flexion of the knee.
* **Very strong** painful stimulus at the sole of the foot ➔ dorsiflexion of the ankle & flexion of both knee and hip (flexion-withdrawal of the stimulated limb for protection) and extension of the other limb for support (crossed extensor reflex).

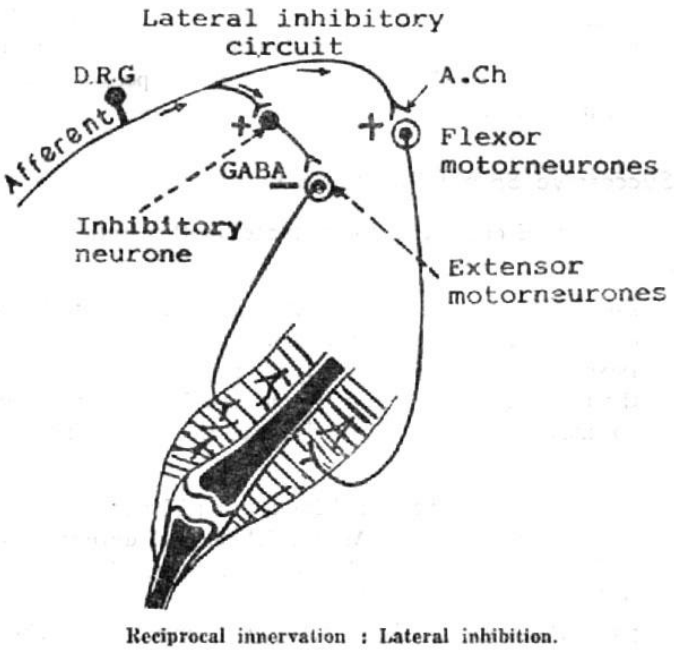
☒ **i.e. weak stimulus produces a limited response whereas a strong stimulus produces a widespread response.**

☒ **Mechanism:**

- The strong stimuli **stimulate more receptors**.
- **Divergence** of afferent neurons & interneurons.

6. RECIPROCAL INHIBITION:

- ☒ **This means** that **reflex contraction** of a group of muscles is accompanied by **reflex inhibition** of their antagonistic muscles
- ☒ **e.g.:** In **Flexion withdrawal reflex**, painful stimulus to a limb produces reflex contraction of the flexors and inhibition of the extensors.
- ☒ **Mechanism:**
  - The stimulated afferent is divided into 2 branches; **one branch stimulates** the A.H.Cs of the **flexors & the other inhibits** the A.H.Cs of the **extensor** muscles (through **inhibitory interneurons**).



Reciprocal innervation : Lateral inhibition.

- ☒ **Significance:**

It **coordinates muscular contractions around joints** & **reduces resistance** to movement performed by a contracting muscle.

N.B. Positive supporting reaction:

- **The only exception for the reciprocal inhibition is the positive supporting reaction:**
- **Deep pressure** applied to the sole of foot by the body weight during standing ➔ **reflex contraction of both flexors and extensors** of the lower limb to support the body against gravity.
- **Significance:** to convert the limb into a **rigid pillar** that provides **maximum support** of the body against gravity.

7. RECRUITMENT AND AFTER DISCHARGE:

☒ **Recruitment:**

- **Means** a **gradual ↑ in the magnitude** of the reflex response till reaching its maximum.
- The motor neurons are gradually **recruited** (activated), one after the other **i.e.** not excited at the same time.

☒ **Cause:**

1) Different **velocities** of nerve impulses due to **different thickness** of afferent neurons.
2) Presence of **different number of interneurons** in the pathway.

☒ **After discharge:**

- **Means** the **continuation of the reflex response** for sometime after stoppage of stimulation.
- **Cause:** passage of the incoming signals through the repetitive discharge interneuron circuits (see before) prolonging the stimulation of efferent neurons.

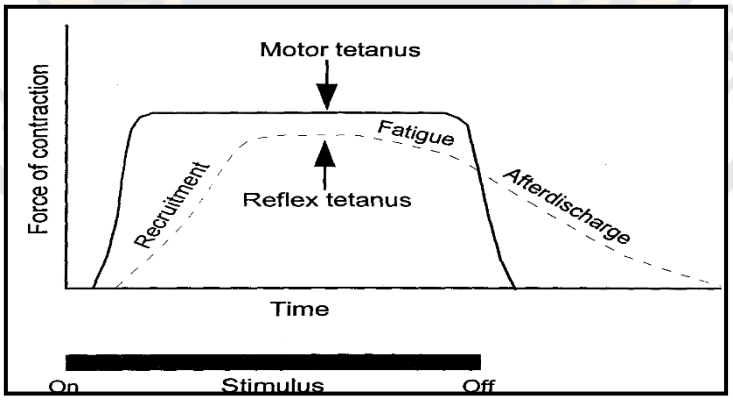


Fig. Reflex & motor tetanus

☒ **These 2 phenomena are best studied by comparing the reflex tetanus & motor tetanus:**

- **Reflex tetanus** is due to stimulation of the **afferent** neuron.
- **Motor tetanus** is due to stimulation of the **efferent** neuron.

	REFLEX TETANUS	MOTOR TETANUS
Def:	Continuous contraction of the muscles due to **repetitive** stimulation of the **afferent**.	Continuous contraction of the muscles due to **repetitive** stimulation of the **efferent**.
Latent period:	Much longer. **It is the time needed for conduction at:** - Afferent neuron - Synapse - Efferent neuron - MEP.	Shorter **It is the time needed for conduction at:** - Efferent neuron. - MEP.
Contraction:	Gradual rise in flexor contraction till reach a peak.	Sudden rise in the flexor contraction.
Relaxation:	Gradual decline in flexor contraction	Sudden decline in the flexor contraction.

Stretch reflex

☒ **Def:** It is a reflex contraction of a skeletal muscle when it is passively stretched.

☒ **Pathway:**

- **Stimulus:** Passive stretch of the skeletal muscle
- **Receptor:** Muscle spindle
- **Afferent:** A-α & A-β (type Ia & II) nerve fibers
- **Center:** A.H.Cs (α motor neurons)
- **Efferent:** -α-motor nerves
- **Response:** contraction of the muscle

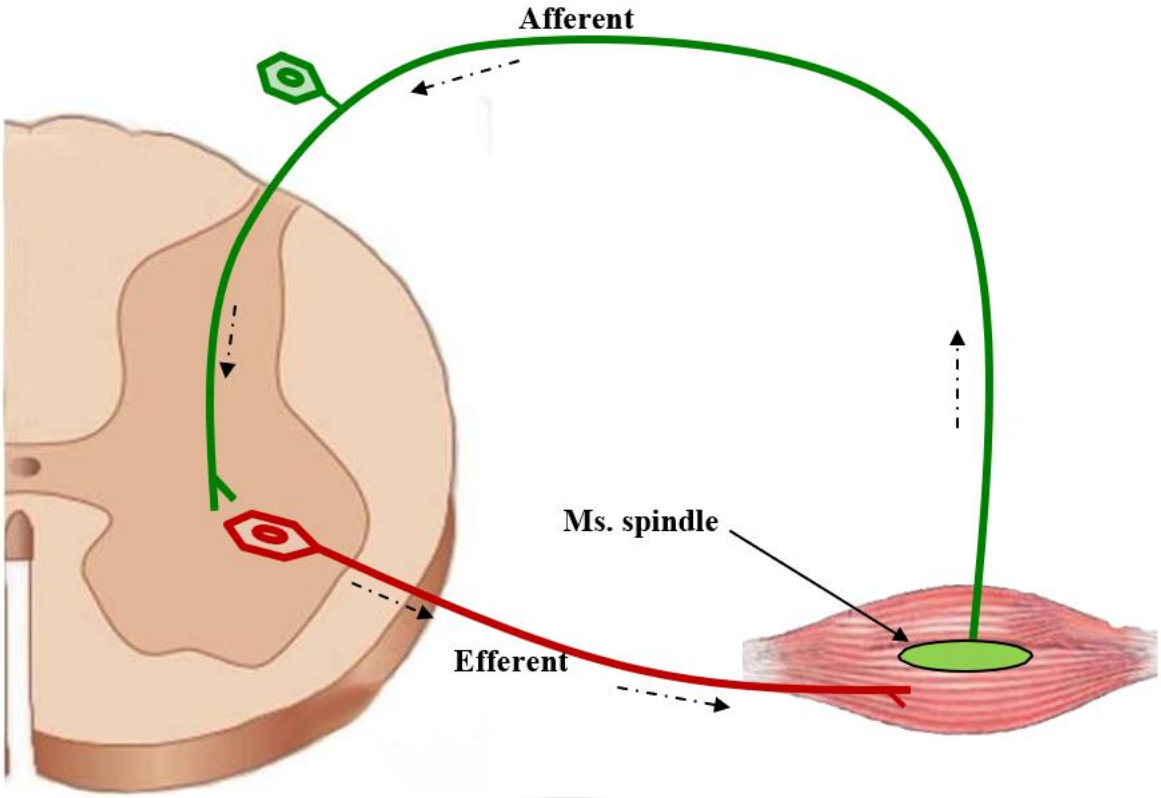


Figure: pathway of stretch reflex

☒ Receptor of stretch reflex (muscle spindle)

☒ **Def:** Specialized fusiform capsulated structures located in the fleshy part of the muscles.

- They act as **length receptors i.e.** detect the changes in the muscle length.
- They are **parallel to the extrafusal muscle fibers.**

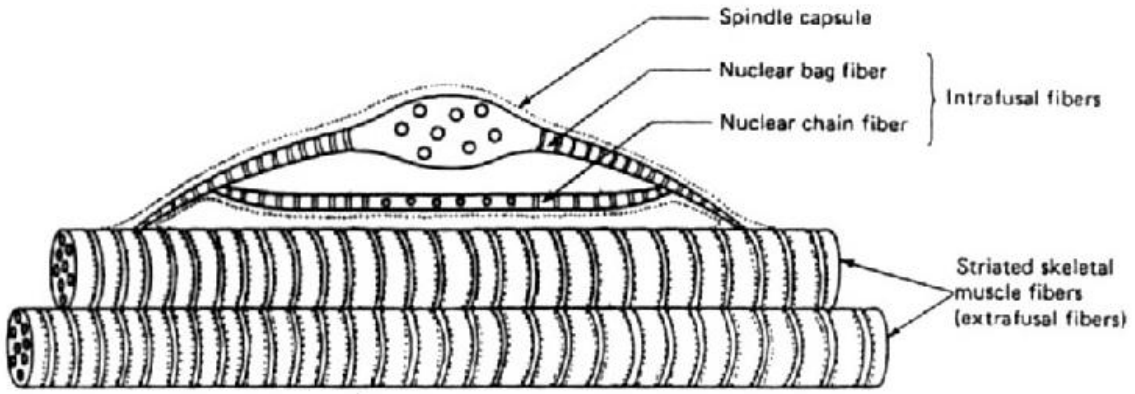
☒ **Structure of muscle spindle:**

- Each muscle spindle consists of **4-12 modified muscle fibers** called **intrafusal muscle fibers**
- **Intrafusal muscle fibers:**
- **Each intrafusal muscle fiber consists of 2 parts:**

i) central receptor area	ii) peripheral contractile parts
From which the afferent nerve endings arise	Which can contract and produce stretching of the central receptor area

▪ **Types of intrafusal fibers:**

	i) nuclear bag muscle fibers	ii) nuclear chain muscle fibers
Length	- Long.	- Short.
Central part	is dilated & contains the nuclei **i.e.** like a **bag**.	Straight & nuclei are arranged as a **chain**
Number	**1-2** in each spindle	**5-8** in each spindle



☒ Innervation of muscle spindle

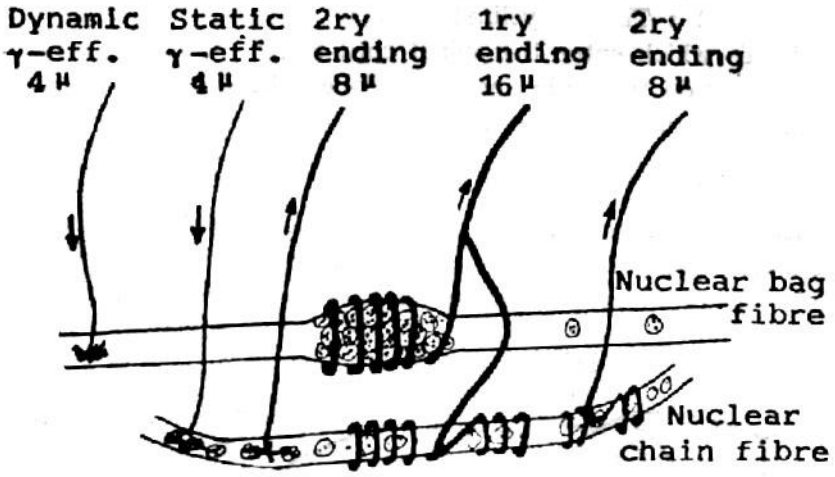
A. Afferent innervation of muscle spindle:

There are 2 types of afferent nerves:

1- 1ry afferents (Ia type)

2- 2ry afferents (II type).

	1) Primary afferents	2) Secondary afferents
Give rise to	Thick myelinated, rapidly conducting **A-α (Ia)** nerve fibers	Thin myelinated, less rapidly conducting **Aβ (II)** nerve fibers
Its endings	**-Annulospiral** **-Arise from** the central receptor area of both nuclear bag & nuclear chain muscle fibers. **-Rapidly responding & rapidly adapting**	**-Flower spray** **-Arise from** the central receptor area of nuclear chain muscle fibers on both sides of 1ry endings. **-Slowly responding & slowly adapting**
They are stimulated by **stretch of central receptor area**		



Innervation of the muscle spindle.

B. Efferent innervation of muscle spindle

- **γ -dynamic nerve fibers:**

  Supplying the peripheral contractile part of the nuclear bag fibers.

- **γ-Static nerve fibers:** Supplying the contractile part of the nuclear chain fibers.

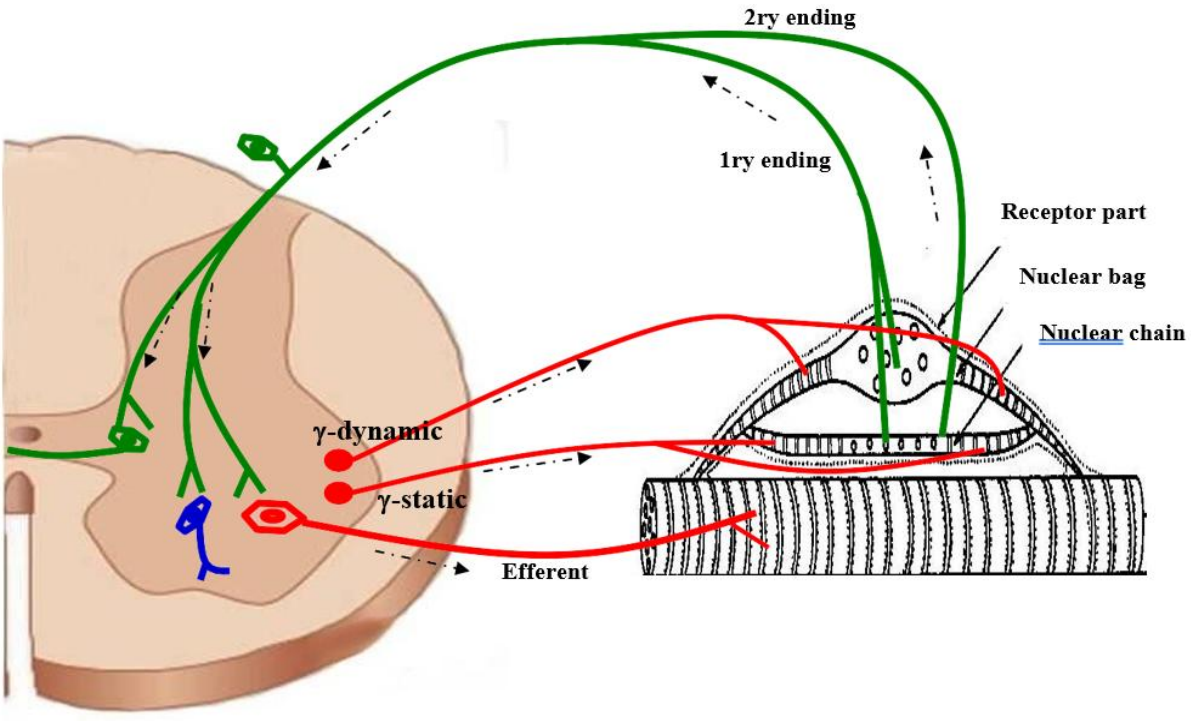


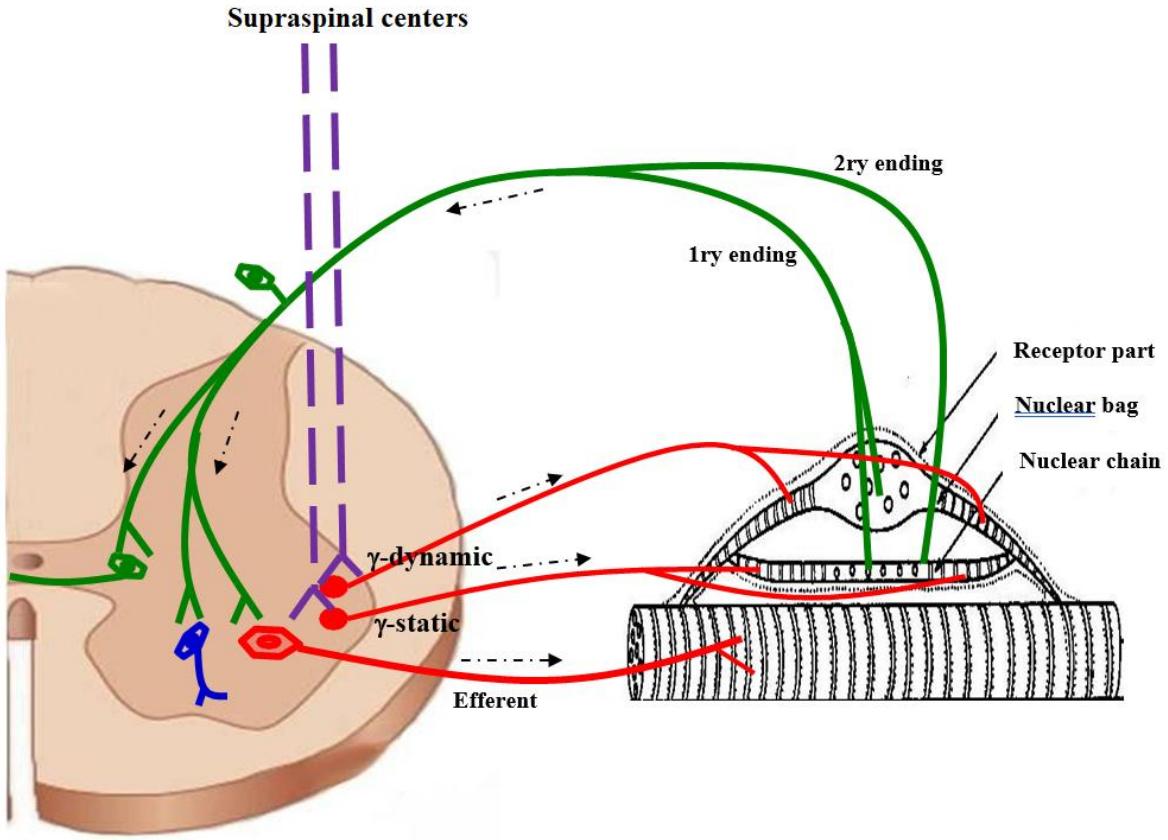
Figure: innervation of muscle spindle

☒ Methods of stimulation of muscle spindle:

1) Direct passive stretching of the muscle.

2) Stimulation of the efferent γ-motor neurons:

Stimulation of γ-motor neurons by supraspinal facilitatory impulses.➔ contraction of peripheral contractile regions of intrafusal MFs ➔ stretch of the central receptor area ➔ discharge of impulses through 1ry & 2ry endings ➔ stimulation of α MNs ➔ muscle contraction (**Gamma- spindle loop**).



☒ Types of stretch reflex:

	Dynamic stretch reflex	Static stretch reflex
Stimulus	Sudden stretch.	Maintained stretch of muscle.
Receptors	Nuclear bag muscle fibers.	Nuclear chain muscle fibers.
Afferents	A-α nerve fibers.	A-β nerve fibers.
Center	Stimulation of α-motor neurons for short duration ➔ rapid contraction followed by relaxation.	Continuous stimulation of α- motor neurons ➔ a state of continuous contraction as long as the stretch is maintained.
Example:	Tendon jerks.	Muscle Tone.

☒ Functions of stretch reflex (functions of muscle spindles):

1) Generation of muscle tone:

- Muscle spindles, through the stretch reflex, are responsible for generation of skeletal muscle tone.
- CNS adjusts muscle tone by varying the level of γ-motor neurons activity which by its turn affect the frequency of spindle sensory discharge.

2) Smoothing of muscle contraction (Damping function):

- **Def:** it is the ability of muscle spindle to prevent oscillation & jerkiness of body movements.
- The signals are sent from brain to motor neurons controlling muscles in an **unsmooth form**, (↑ in intensity for a few milliseconds, then ↓ in intensity for a few milliseconds, and so on).
- However, muscle oscillations or jerkiness does not occur due to presence of muscle spindle.

3) Load Reflex:

- **Def:** It is a reflex responsible for keeping the hand or foot in position when a moderate or heavy load is applied.
- **e.g.** when a person holding up a cup while someone is filling it with tea, as the load gets bigger and bigger, the force required to keep the hand in position must be continually increased.

4) Proprioceptive functions:

Muscle spindles provide proprioceptive information to the brain and cerebellum for keeping them continually informed about muscle length and changes in that length.

☒ Inverse stretch reflex (Golgi tendon reflex) (Lengthening reaction):

☒ **Def:** Reflex relaxation of a contracting skeletal muscle (lengthening) when it is exposed to excessive stretch (overstretch) or severely contracted.

☒ **Importance:** It is a **protective** reflex which protects against:

a) Muscle tearing.

b) Tendon avulsion

☒ **Pathway:**

- **Stimulus:** Increased tension in the tendon of the muscle due to:

  i) Severe contraction OR

  ii) Overstretch.

- **Receptors:** Golgi tendon organs (GTO):
  - Present in the **tendon of the muscle** in series of the muscle fibers.
  - Each organ consists of modified fibers mostly **elastic fibers** "number 6-20".
  - Stimulated by **increased tension** in the tendon **"Tension Receptors"**.

- **Afferent:** A-α (Ib) nerve fibers.
- **Center and response:** The impulses from GTO inhibit the A.H.Cs via interneurons ➔relaxation of the muscle.
- **Significance:** it is a **protective** reflex which prevents:
  a) Muscle tearing.
  b) Tendon avulsion

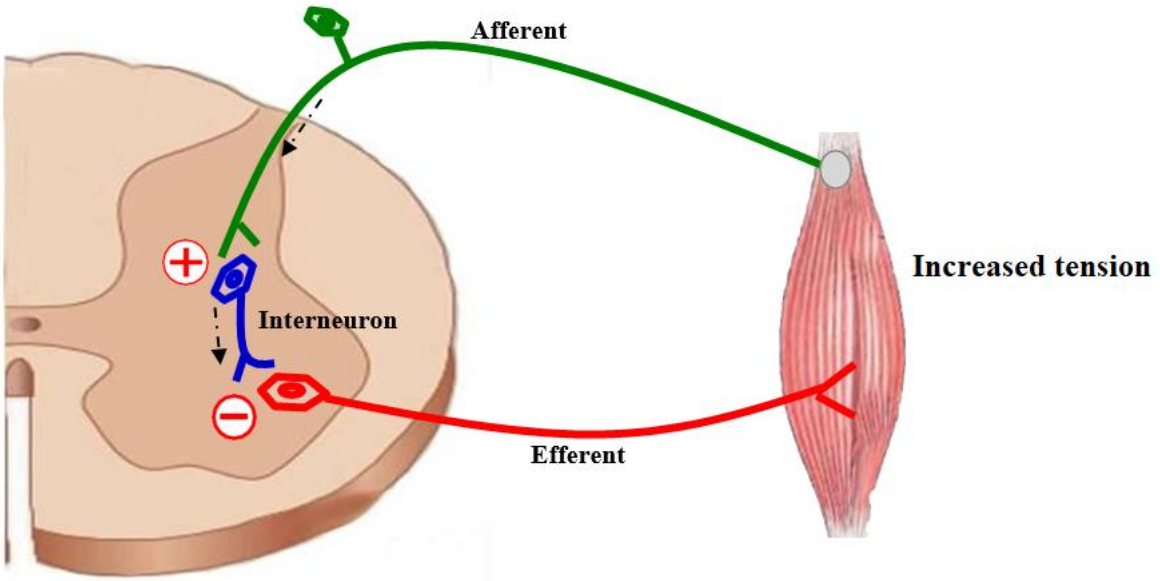


Figure : inverse stretch reflex

N.B: Differences between stretch reflex & inverse stretch reflex:

	Stretch reflex	Inverse stretch reflex
Type	Monosynaptic	Di-synaptic
Receptor	Muscle spindle	Golgi tendon organ
Stimulus	↑ muscle length (muscle stretch)	↑ muscle tension (due to severe contraction or overstretch)
Effect	Muscle contraction	Muscle relaxation
Function	1- Generation of muscle tone 2- Damping function. 3-Load reflex. 4-proprioceptive functions	Prevention of: 1-Muscle tear 2-Tendon avulsion.

N.B: Differences between muscle spindle & Golgi tendon organ:

	Muscle spindle	Golgi tendon organ
Found in	fleshy part of muscle	tendons of muscle.
Formed of	intrafusal muscle fibers.	modified fibers mostly elastic fibers “number 6-20”.
Stimulated by	muscle stretch	↑ muscle tension
Its stimulation elicits	stretch reflex (Monosynaptic reflex).	inverse stretch reflex (polysynaptic reflex).
Effect on muscle	muscle contraction.	muscle relaxation.
Afferent:	Aα (Ia) & Aβ (II) nerve fibers.	A-α (Ib) nerve fibers.

Skeletal muscle tone

☒ **Def:** It is a state of continuous partial (subtetanic) contraction present in all skeletal muscles during rest.

☒ **Mechanism: Static stretch reflex (see before)**

☒ **Distribution:** The muscle tone is more prominent in the **antigravity muscles** (extensors of the lower limb, flexors of the upper limb, extensors of the back and neck, anterior abdominal wall muscles, and elevators of the lower jaw). This occurs because these muscles are **exposed to more stretch** under the effect of **gravity**.

☒ **Functions:**

1. It is the basic mechanism for **postural reflexes which regulate the body posture and equilibrium**.
2. Helps production and maintenance of **body temperature**.
3. **Helps venous and lymphatic return**.
4. **Keeps viscera** in position and prevents visceroptosis

Somatic motor system

☒ **The somatic motor system consists of:**

- **Higher motor centers** located in the **cerebral cortex** and **brain stem**, and
- **Their axons** form **descending motor tracts** that descend to and synapse with the neurons of **lower motor centers** in the brain stem (**cranial nuclei**) and spinal cord (**A.H.Cs**) from which **peripheral somatic nerves** arise to supply the skeletal muscles.

☒ **Thus, somatic motor system is composed of two sets of neurons:**

1) **Upper motor neurons (UMN)**; whose cell bodies lie in the higher motor centers and their axons constitute the descending motor tracts.
2) **Lower motor neurons (LMN)**; whose cell bodies lie in the spinal ventral horns or the corresponding cranial nuclei, and their axons constitute the efferent motor fibers in the peripheral somatic nerves.

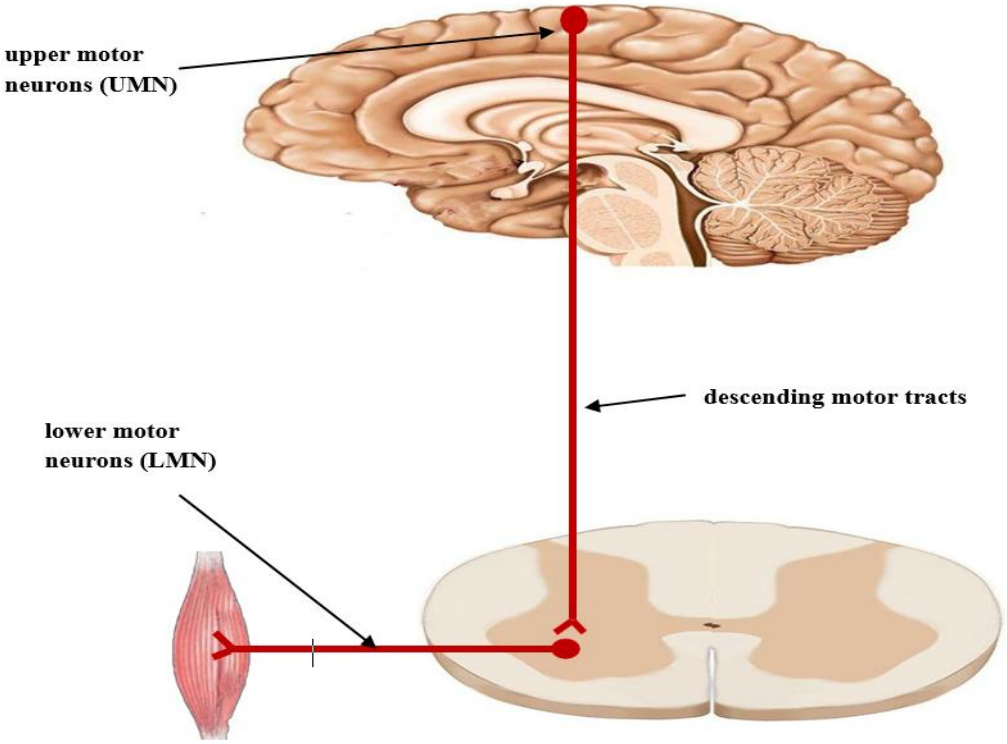


Figure: upper & lower motor neurons

Cortical motor areas

☒ **The motor cortex is located in the frontal lobe, and includes:**

I. **Primary motor area (area 4).**

II. **Premotor area (area 6).**

III. **Supplemental motor area.**

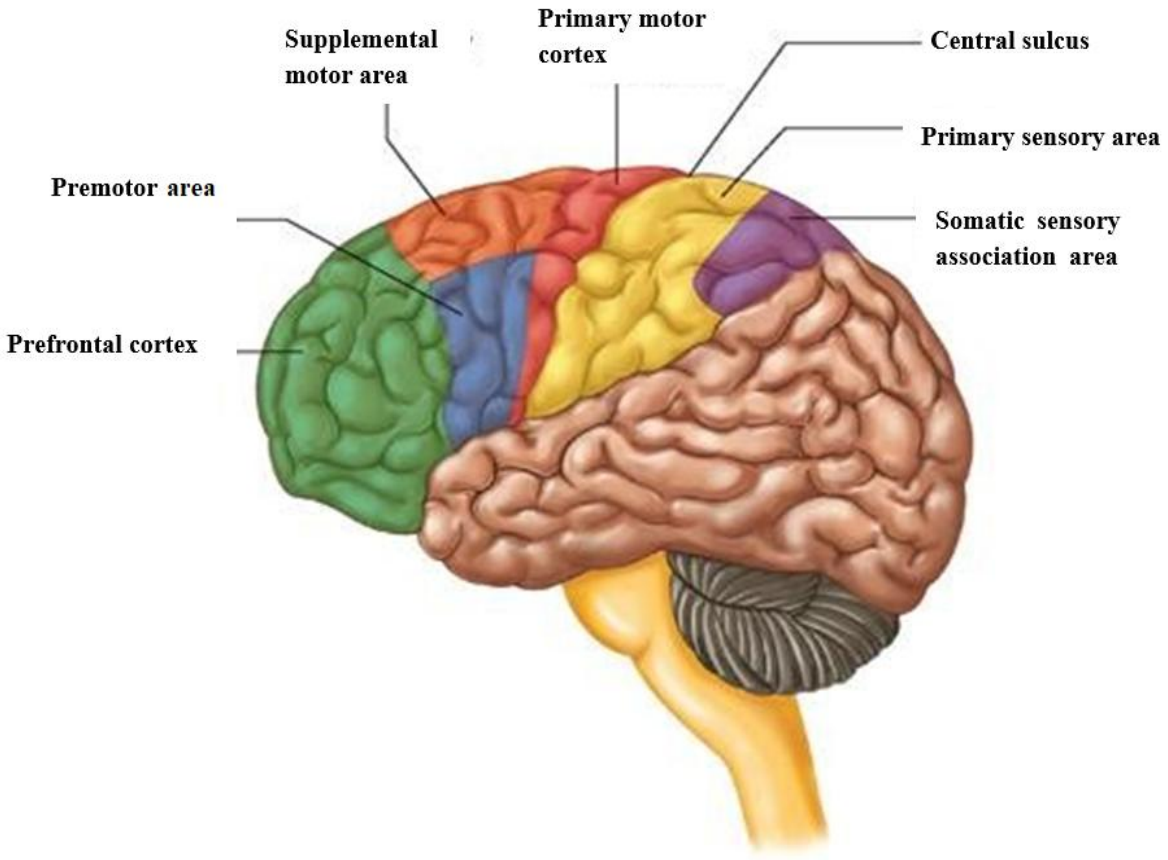


Figure: Cortical motor areas

I. Primary motor area (Area 4)

☒ **Site:** It lies in the **precentral gyrus** of the frontal lobe.

☒ **Body representation:**

- **Contralateral:** controls opposite side.
- **Inverted:** feet are represented up & face down
- **Area of representation:** is directly proportional to complexity of motor function (not to its size of the organ). So, thumb is widely represented than thigh.

☒ **Functions:**

- Initiation of **fine voluntary movements** done by distal limb muscles (fingers & hands).
- **Facilitates stretch reflex.**

II. Premotor area (Area 6)

☒ **Site:** lies immediately anterior to area 4 in area 6, bounded superiorly by supplemental area.

☒ **Body representation:**

1) **Contralateral.**
2) **Inverted.**

☒ **Functions:**

1) **Planning of complex movements** together with **supplemental motor area.**
2) **Initiation of gross movements** as those done by the trunk.
3) **Postural adjustment during voluntary distal movements,** together with **basal ganglia.**

4) **Initiation of automatic & associative movements done at subconscious level e.g.** swinging of arms during walking, together with **basal ganglia**.
5) **Inhibits stretch reflex.**
6) **Inhibits grasp reflex**
7) **Contains specialized areas:**

a) Broca's area (area 44 and 45): it produces speech

b) Eye movement area (area 8): it controls voluntary movements of eyes.

c) Exner's area=area of hand skills: it stores memory of voluntary skilled movements.

d) Head rotation area: it directs the head toward objects.

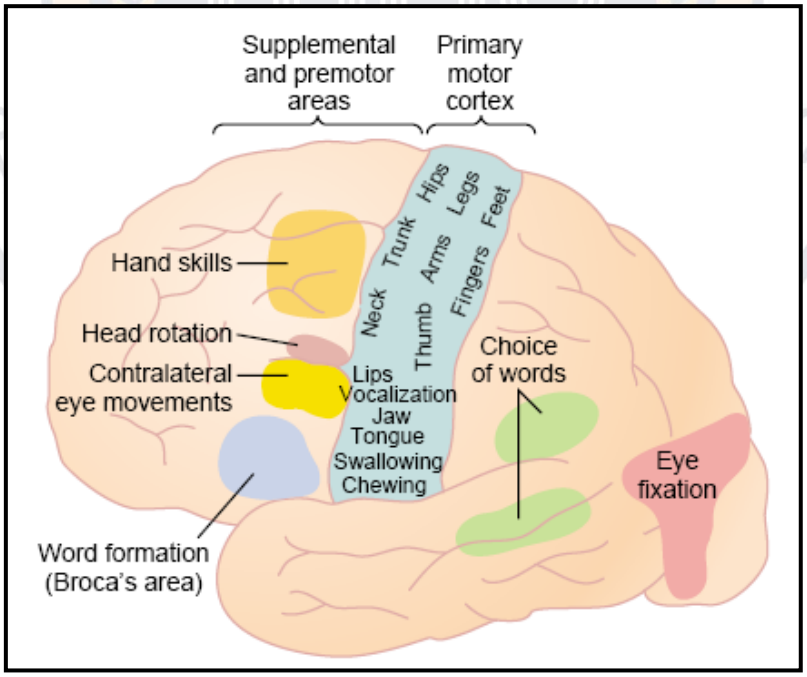


Figure: premotor area

III. Supplemental motor area

☒ **Location:** In the upper medial side of the frontal lobe just above premotor area.

☒ **Functions:**

- It **evokes complex movements** which often involve both sides of the body **e.g.:** causing both hands to perform a motor act together.
- It **functions with the premotor area (6)** in providing **suitable background for the performance of the fine skilled movements** by hands and fingers that are mediated by the C.B.S tract.
- **Planning and programming of the complex movements** with area 6.

Descending motor pathways

The motor signals are transmitted from motor cortex to lower motor neurons through **descending motor tracts which are classified into:**

A. Pyramidal and extrapyramidal tracts:

Pyramidal tract	Extrapyramidal tracts
- Its fibers **pass** through **medullary pyramid**	- Its fibers **do not pass** through **medullary pyramid**
- **Controls** most of the **voluntary movements**	- **Control involuntary movements** as posture & muscle tone.

B. Medial & lateral motor systems:

	a) Tracts of medial motor system	b) Tracts of lateral motor system
Terminate on	**Medial motor neurons** in the ventral horns of spinal cord.	**Lateral motor neurons** in the ventral horns of spinal cord.
Innervate	the antigravity muscles	distal muscles of the limbs
concerned with	control of the body posture	fine voluntary movements
Include	1-Ventral corticospinal tract. 2-Reticulospinal tract. 3-Vestibulospinal tract. 4-tectospinal tract.	1-Lateral corticospinal tract. 2-Rubrospinal tract.

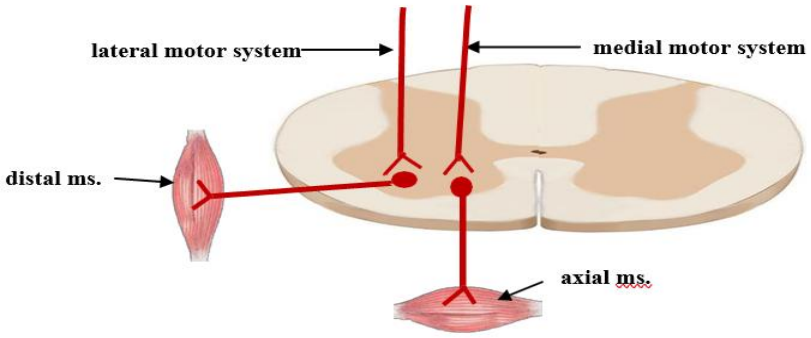


Figure: Lateral and medial motor systems

Pyramidal tract (Cortico-bulbo-spinal tract)

☒ **Origin:** CBS tract originates from:

1. Primary motor 4 cortex (30%).
2. Premotor & supplemental motor areas (30%).
3. Some fibers from the somatic sensory areas (40%).

☒ **Course and terminations:**

- The CBS tract descends through **the genu & anterior 2/3 of posterior limb of internal capsule**, then through the **brain stem** where:
  - Fibers innervating or controlling **eye muscles** cross to the **opposite side** and terminate on the cranial nuclei of **III, IV, VI** cranial nerves. This division of pyramidal tract is termed **Cortico-Nuclear Tract**.
  - Fibers innervating or controlling **facial & neck muscles** terminate **bilaterally (opposite & same sides)** on the motor nuclei of the cranial nerves **V, VII, IX, X, XI, XII.** This division of pyramidal tract is termed **Cortico-Bulbar Tract**.
  - Fibers innervating the **spinal motor neurons** descend through the **middle 3/5 of the cerebral peduncles** of **midbrain**, then collect in the **upper medulla** forming the **pyramid**. This division of pyramidal tract is termed **Cortico-Spinal Tract**.
- **At the lower part of medulla:**
  - **90% of its fibers** cross to the **opposite side** and descend in the **lateral column** of the spinal cord as **Lateral Corticospinal Tract**, its fibers terminate mainly on the **lateral motor neurons** which innervate the **distal muscles**.

- **The remaining 10%** which do not cross in the medulla descend **ipsilaterally** in the **ventral column** of the spinal cord as **Ventral Corticospinal Tract**.
  - **About 9% of these fibers cross** before their termination to synapse with the **medially located neurons** which innervate the **axial muscles** of the **opposite side.**
  - **Only 1%, (Uncrossed Corticospinal Tract)** supply **axial**, **respiratory** and **abdominal** muscles.

☒ **Functions of the CBS tract:**

1. **Mediation of voluntary motor commands:**
   - **Corticonuclear tract:** controls **eye movements**.
   - **Corticobullar tract:** controls **facial & neck movements**.
   - **Lateral corticospinal tract:** controls **distal muscles** responsible for **voluntary skilled movement**.
2. **Postural adjustment: Ventral corticospinal tract:** controls axial muscles that regulate body posture.
3. **Facilitatory** to **muscle tone** of the **distal limb** muscles.

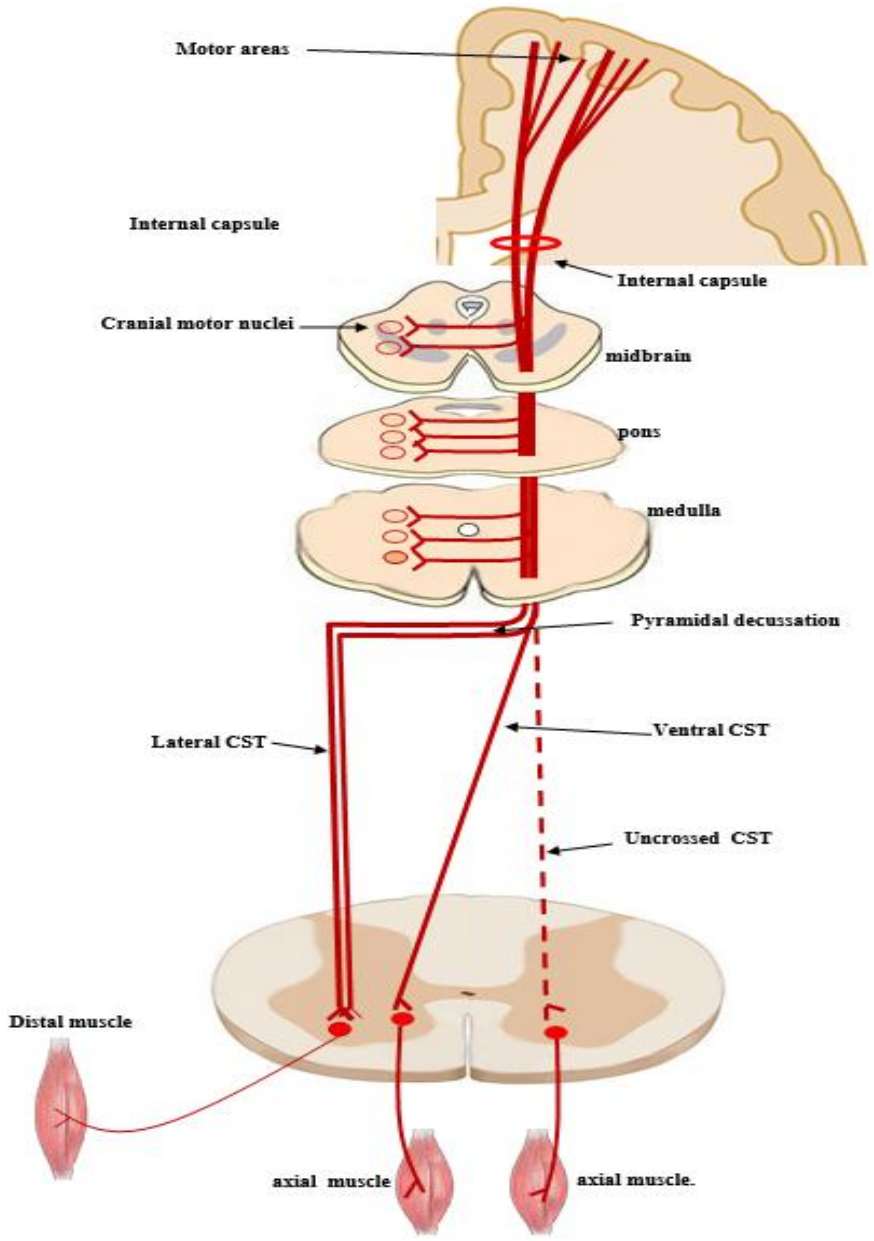


Figure: Origin, course, and termination of the corticobulbospinal tract.

Extrapyramidal tracts

Rubrospinal tract

☒ **Origin:** Red nucleus in the midbrain.

☒ **Course:** Descends contralateral.

☒ **Termination:** Terminates primarily in the cervical spinal cord, suggesting that it functions in upper limb.

☒ **Functions:**

- a role in voluntary control of distal ms. of upper limb responsible for skilled movements (together with lateral corticospinal tract).
- Facilitatory to the muscle tone of the distal limb muscles.

Medial Reticulospinal tract

☒ **Origin:** Pontine (fascilitatory) reticular formation.

☒ **Course:** Descends ipsilaterally.

☒ **Functions:** Facilitates motor neurons of antigravity muscles → support body posture against gravity

Lateral Reticulospinal tract

☒ **Origin:** Medullary (inhibitory) reticular formation.

☒ **Course:** Descends bilaterally.

☒ **Functions:** Inhibits motor neurons of antigravity muscles

Medial vestibulospinal tract

- ☒ **Origin:** Medial vestibular nucleus.
- ☒ **Course:** Descends bilaterally: on the motor neurons of neck & upper limb muscles.
- ☒ **Functions:** Facilitatory to muscles of head & upper limbs & adjust their position on exposure to acceleration

Lateral vestibulospinal tract

- ☒ **Origin:** Lateral vestibular nucleus.
- ☒ **Course:** Descends ipsilateral, on the motor neurons of the antigravity muscles.
- ☒ **Functions:** Facilitatory to the antigravity muscles to maintain overall body posture on exposure to acceleration

Tectospinal Tract

- ☒ **Origin:** Superior (Mainly) & inferior colliculi in the midbrain.
- ☒ **Course:** Descends contralateral.
- ☒ **Termination:** On the spinal motor neurons of the neck muscles only
- ☒ **Functions:** Reflex turning of the head in response to sudden visual or auditory stimuli

Upper motor neuron lesion (UMNL)

☒ **Def:** damage of **upper motor neuron** in the **higher center** or the **descending motor tract**.

☒ **Most common site** of UMNL is the **internal capsule**.

☒ **Effects of UMNL at the internal capsule:**

(I) Motor loss:

1) **Contralateral paralysis**
   - **Means** complete loss of voluntary movements.
   - **Occurs in:**
     a. **Distal limb muscles particularly those of hand & fingers** (performing voluntary skilled movements) due to **damage of lateral corticospinal tract**.
     b. **Muscles of the lower face & tongue** due to **damage of contralateral corticobulbar tract**.
2) **Contralateral paresis:** weakness (**i.e.**, incomplete loss of movements).
3) **Spasticity** (**hypertonia of skeletal muscles):** due to ↑ supraspinal facilitation by damage of **cortico-reticular tract** (which **normally inhibits** facilitatory RF and vestibular nucleus and **facilitates** the inhibitory RF).
4) **Exaggerated tendon jerk & clonus:** due to ↑ supraspinal facilitation by damage of **cortico-reticular tract** (which **normally inhibits** facilitatory RF and vestibular nucleus and **facilitates** the inhibitory RF).

5) **Positive Babiniski's sign:** Abnormal planter response characterized by **dorsiflexion of the big toe** & **fanning of the lateral 4 toes** on scratching the skin of the lateral edge of the sole of foot. It is a **withdrawal reflex** that is **normally inhibited** by impulses from area 4 & 6.

6) **No or minimal muscle atrophy because:**

- The LMN is intact and the muscle **contracts reflexely**.
- The muscle is still supplied with **trophic substance** from LMN.

(II) Sensory loss:

- **Contralateral hemianaesthesia i.e,** loss of all sensations on the opposite side of the body.

Lower motor neuron lesion (LMNL)

☒ Effects of LMNL:

1) **Atrophy of denervated muscles due to:**
   a. deprivation of the muscle from **trophic factors** secreted by the cut motor neuron.
   b. Lack of movement.
2) **Flaccid paralysis: characterized by:**
   a. **Complete loss of all types of movements:** including voluntary, postural & reflex movements.
   b. **Hypotonia of paralyzed muscles (flaccidity)** due to interruption of motor component of stretch reflex.
   c. **Lost of tendon jerk in the denervated muscle**.
   d. **Lost all reflexes in the denervated muscle.**
   e. **The extent of paralysis is limited** to a small group of muscles.
3) **Fasiculations and fibrillations:**

- **Def:** Abnormal contractions in denervated muscle.

Fasiculations	Fibrillations
Start few days after denervation.	**Start few weeks** after denervation.
Synchronous contraction of all MFs of motor unit.	**Asynchronous contraction** of different MFs of motor unit.
Visible to naked eye.	**Not Visible** but detected by EMG.

Vestibular apparatus

☒ **It consists of 2 parts:**

A) Semicircular canals:

- **3 on each side**.
- **Each S.C.C has two ends:** One of them is dilated called **ampullary end** which contains the receptors of S.C.C (Crista).
- **Each S.C.C** contains endolymph.
- **Arranged with right angles in between (represent 3 planes of the space):**
  - One **anterior vertical**.
  - One **Horizontal.**
  - One **posterior vertical**.
- **They open into** the utricle by **5 openings** only because the non ampullary ends of anterior vertical & posterior vertical open into a common opening.
- **The co-planner of the semicircular canals:**
  - Each semicircular canal on one side correspond to one SCC **on the opposite side** (lie with it in the same or parallel plane), and both act as a **functional unit** (i.e. act together).
  - **For example:**
    - Horizontal canals on both sides.
    - The anterior vertical canal on one side and posterior vertical one on the opposite side.

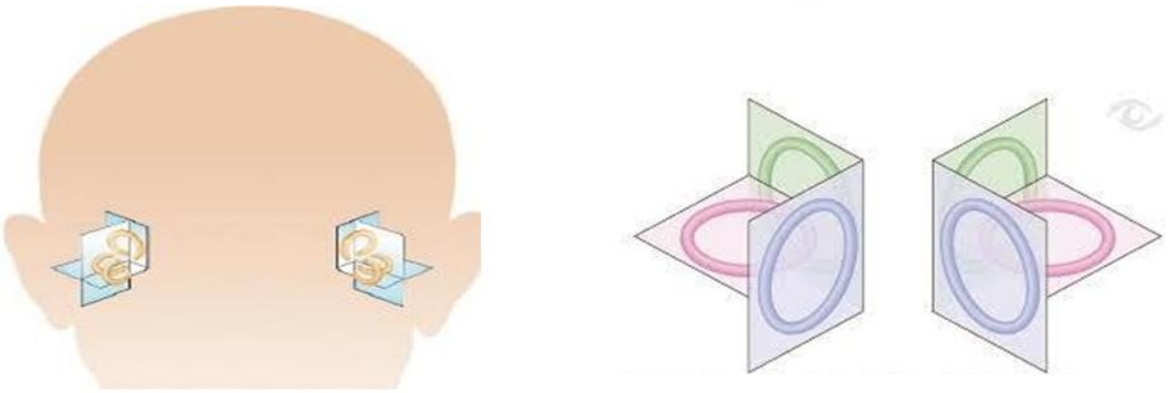
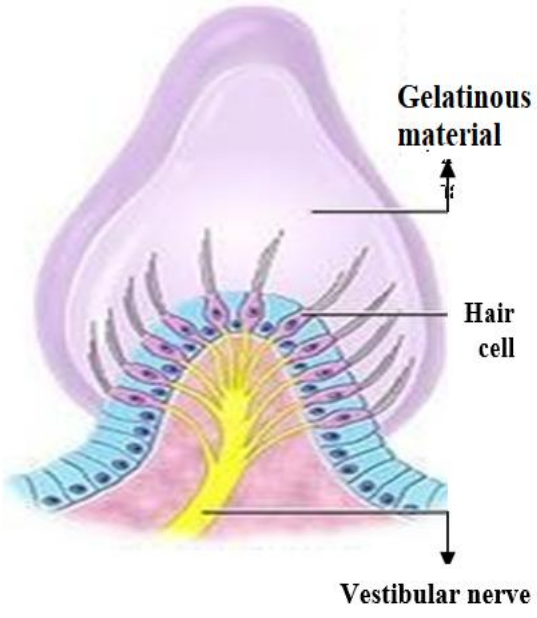
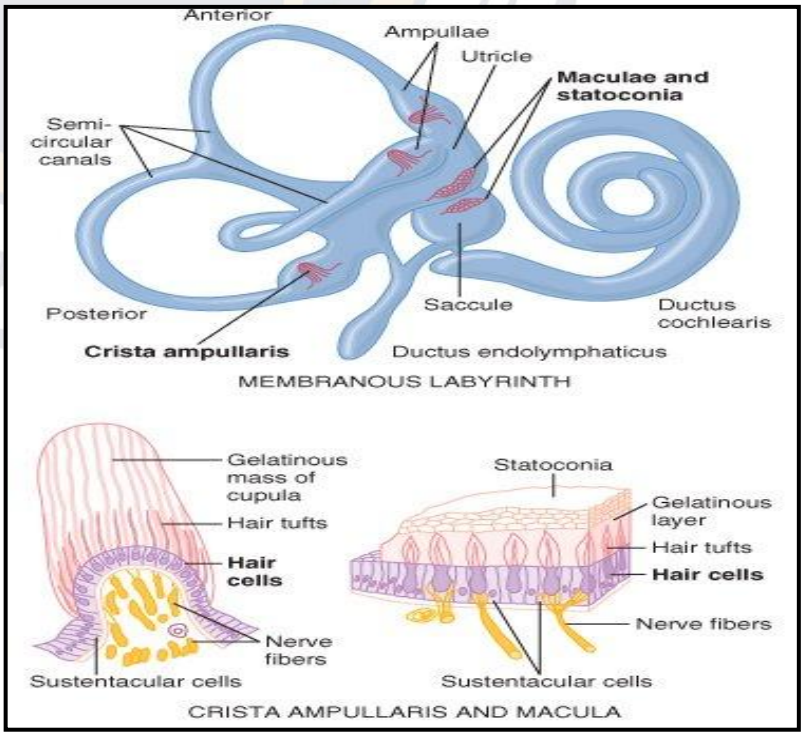


Figure : co-plannar canals

- **The structure of the crista (figure).**
  - It consists of **an elevated ridge of epithelium covered by a wedge-shaped gelatinous mass called a cupula**.
  - **Epithelium consists of 2 types of cells:**
    - **Hair cells;** its upper border show **ciliary projections** which are embedded into the **cupula**. Its base and lateral borders are surrounded by the **vestibular nerve endings**.
    - **Supporting cells (columnar in between the hair cells).**





B) Utricle and saccule:

- 2 small sacs or cavities.
- Each one contains specific receptor called **Macula.**
  - **Macula:**
    - Similar in structure to crista but the copular or gelatinous part is rich in **calcium carbonate crystals** which make it hard.
    - These crystals are called **Otoconia** and the covering is called **otolith membrane.**

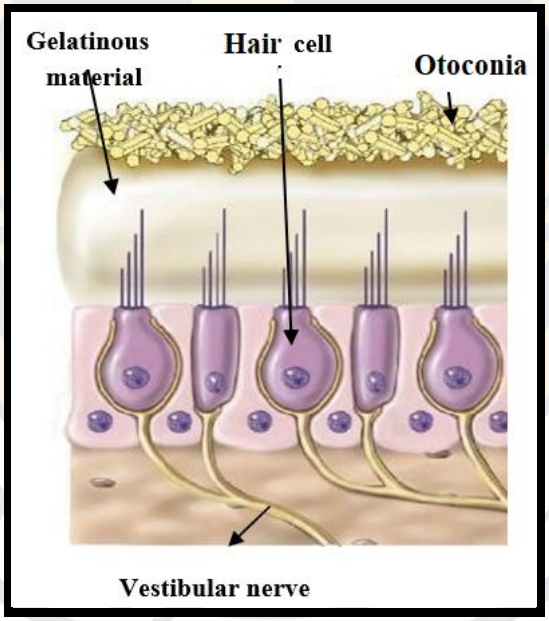


Fig: otolith organ (Macula)

Vestibular Hair cells

☒ **Has upper border show ciliary projections which are of 2 types:**

a. **Stereocilia**; short, numerous **(60-100)**, thin. and motile

b. **Kinocilium**; long, single, thick. and tough.

☒ **The kinocilium** is located at **one side** & the **stereocilia** become **progressively shorter** towards the **other side** of the cell.

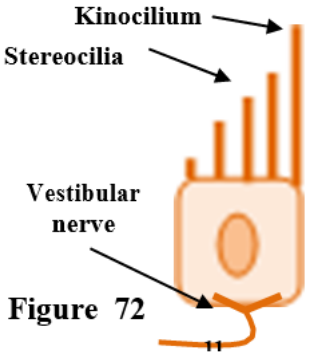
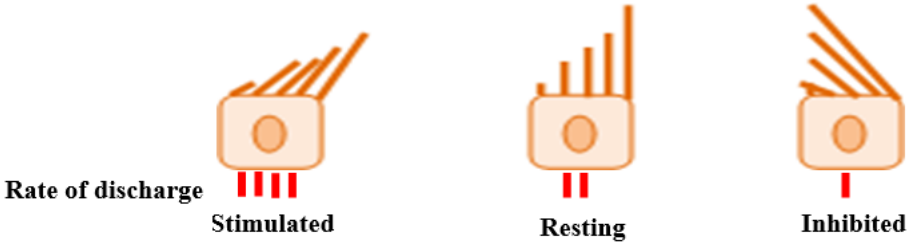


Figure 72

Stimulation of the vestibular hair cells:

- **During Rest (no deflection of cilia)**, there is a basal rate of impulse discharge from the hair cells along the vestibular nerve.
- **Bending of the stereocilia towards the kinocilium** ➔ opening of mechanosensitive K^+ channels (↑ K^+ permeability) ➔ depolarization of hair cells ➔ ↑ release of chemical transmitter ➔ ↑ impulse discharge from the hair cells.
- **Bending of stereocilia away from the kinocilium** ➔ closing of K^+ channels (↓ K^+ permeability) ➔ hyperpolarization of hair cells ➔↓ release of chemical transmitter ➔ ↓ impulse discharge.



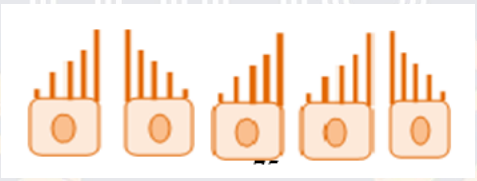
Orientation of hair cells in the Vestibular Apparatus:

In cristae

- The position and arrangement of stereocilia in relation to the kinocilium is the **same in all hair cells of the same crista**.
- In **Horizontal S.C.Cs**; the Kinocilium **towards** the utricle
- In **Vertical S.C.Cs**; the Kinocilium **away** from the utricle

In maculae

- The position of the kinocilium and stereocilia **differ from one group of hair cells to another in the same Macula.**



Functions of the Vestibular Apparatus:

A) Functions of the utricle and saccule (Maculae):

1- Detection or orientation of the absolute position of head in space:

a) When the head is in erect position, equal discharge from the maculae of both sides because both are exposed to the same gravitational force.

- The Symmetrical discharge from both maculae interpreted by the cortex that the head is in erect position.

b) If the head is tilted to one side:

- The macula on that side (otolith membrane) is pulled more under the effect of gravity and the macula on the opposite side is less exposed to

the gravitational force ➔ asymmetrical discharge from both maculae, interpreted by the cortex that the head is tilted to that side.

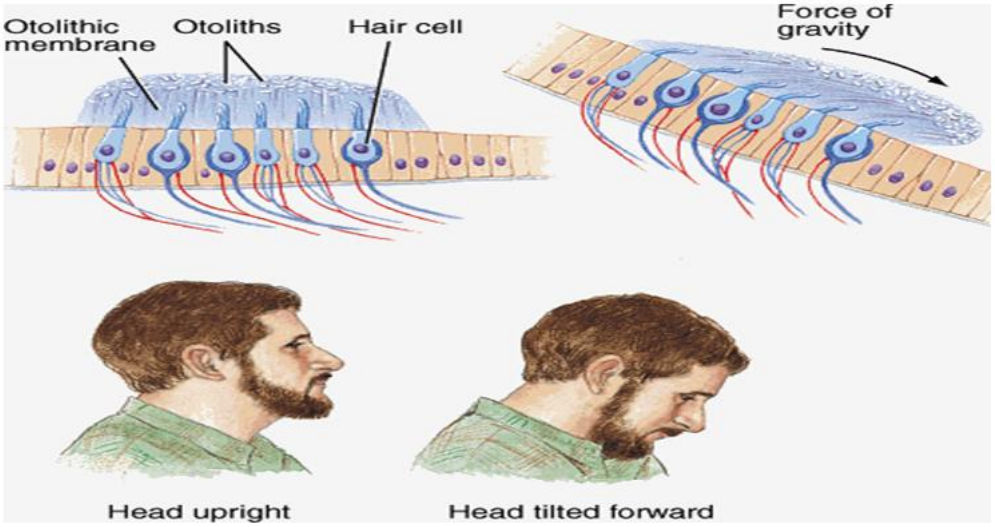


Fig.: Role of macula in detection of head position.

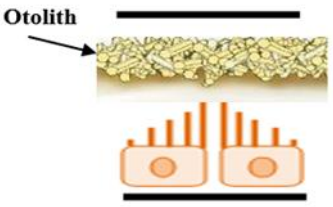
2- Detection of linear acceleration:

Responsible for perception of linear acceleration as regard:

1- Onset of acceleration.

2- Deceleration (Stoppage).

3- Change in the rate of acceleration.

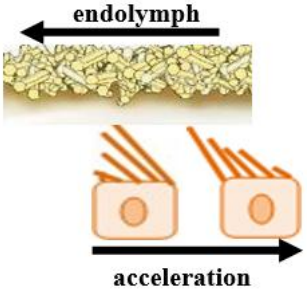


a- Before the start of acceleration (resting):

Maculae show symmetrical basal discharge.

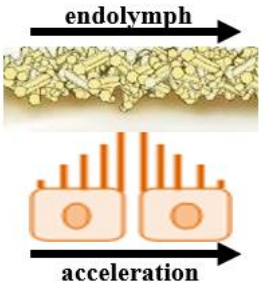
b-At the onset of acceleration:

Due to inertia, the maculae displaced in opposite direction ➔ bending of the cilia ➔ peculiar pattern of discharge ➔ when this pattern reaches the cortex, the cortex interprets it ➔ feeling of onset of acceleration.



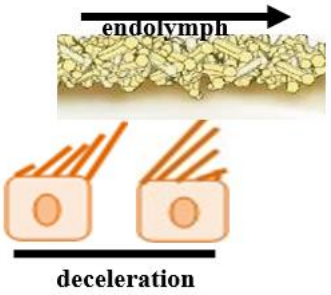
c- With constant speed:

When the linear acceleration reaches a constant speed, the otolith membrane moves with the same speed as the head ➔ cilia straighten again ➔ discharge becomes basal ➔ no feeling of movement occurs.



d- At Deceleration:

As movement stop, the otolith membrane is displaced in the same direction of previous acceleration due to **momentum** ➔ bending of the cilia ➔ peculiar pattern of discharge ➔ when this pattern reaches the cortex, the cortex interprets it ➔ feeling of stoppage of acceleration.



3- Initiation of reflexes that maintain body posture.

B) Functions of SCCs

I) Perception of angular acceleration (Rotation): as regard:

1- Onset of acceleration.

2- Stoppage of acceleration.

3- Change in velocity of rotation.

HOW? by the following mechanism of action:

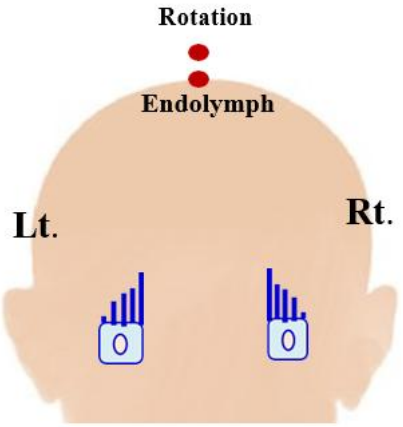
- The rotation of the body in certain plane, stimulate the 2 corresponding S.C.Cs acting on that plane.

* **For Example:**

- Rotation in the horizontal plane from the **left to right**, the 2 horizontal SCCs will act together, how?

a- Without rotation (at rest):

- The rate of discharge from both S.C.Cs is equal i.e. symmetrical ➔ no feeling of movement.



b- With onset of rotation:

e.g: from left ➔ right.

- The endolymph is displaced by its **inertia** to the opposite direction of rotation **(left side)** leading to:
  - Bending of the cupula of **right crista towards the utricle**. **i.e.** bending the stereocilia towards the kinocilium ➔ ↑ **the rate** of discharge from the **right crista**.
  - Bending of the cupula of the **left crista away from the utricle i.e.** bending the stereocilia away from the kinocilium ➔ ↓ **the rate** of discharge from the **left crista**.

-Asymmetrical discharge from both Horizontal S.C.Cs with excessive discharge from the right ➔ when this pattern of discharge reaches the **CNS,** it evokes **sense of rotation to the right side**.

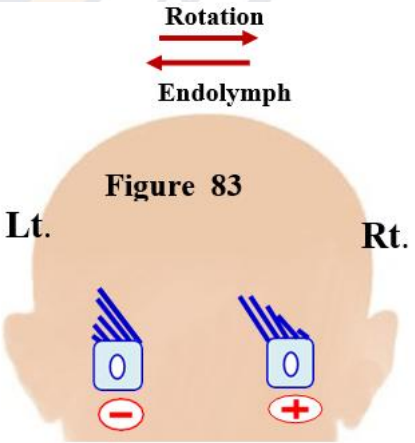
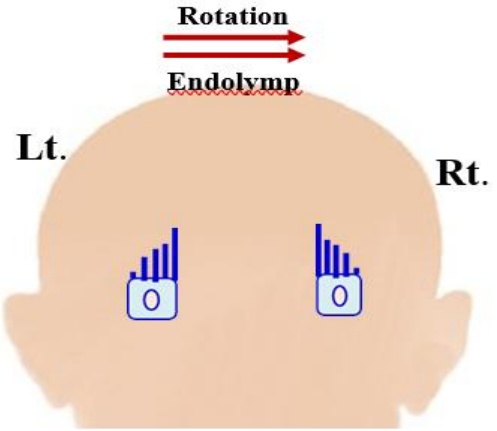


Figure 83

c- When the rotation speed become constant:

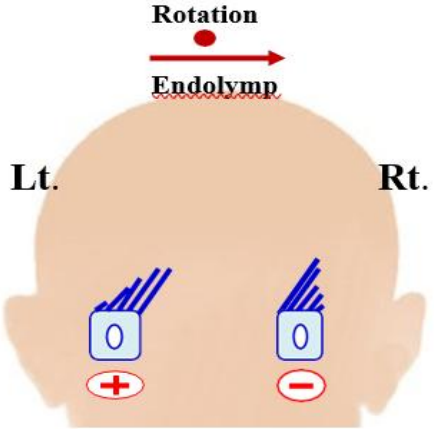
After 20 seconds, endolymph will gain the **same speed as the SCC** & the **cupulae** return to the **original position**, and the rate of discharge return to **symmetrical basal** level ➔ **no feeling of rotation**.



d- On deceleration:

- The endolymph continues to move, due to its **momentum**, in the same direction of the **original rotation (Right side)** leading to:
  - Deflection of the cupulae of the **right crista away from the utricle** ➔ bending of the stereocilia away from Kinocilium ➔ ↓ the rate of discharge from the **right crista (inhibited)**.
  - Deflection of the cupulae of the **left crista away from the utricle** ➔ bending of the stereocilia twards Kinocilium ➔ ↑ the rate of discharge from the **left crista (stimulated)**.

-Asymmetrical discharge from both Horizontal S.C.Cs with excessive discharge from the left ➔ when this pattern of discharge reaches the **CNS,** it evokes **sense of rotation to the left side** ➔ **false sensation** of **counter-rotation to the left (Vertigo)**.



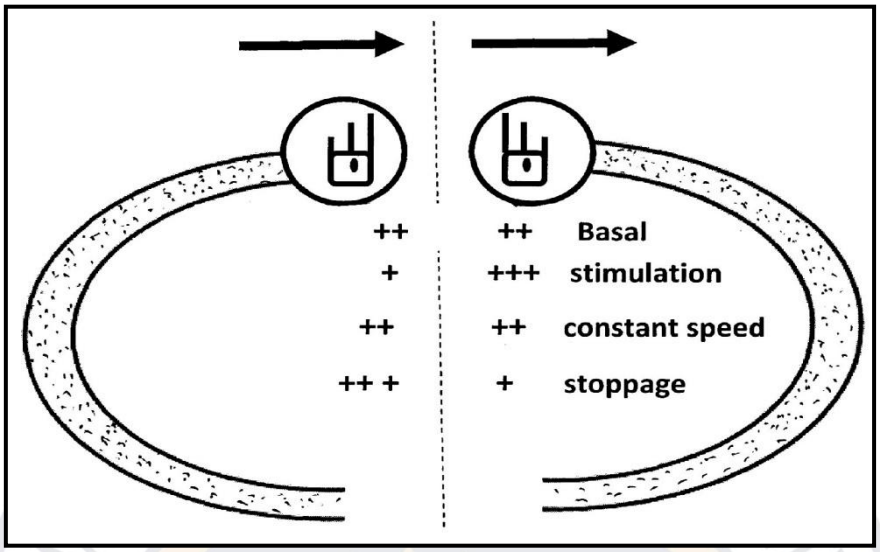


Fig.: Asymmetrical stimulation of semicircular canal

II) During acceleration or deccelaration, postural reflexes initiated from the cristae to maintain the equilibrium.

EFFECTS OF STIMULATION OF S.C.Cs

If the S.C.Cs are stimulated asymmetrically and excessive as in the following conditions: (1) when the person exposed to unusual pattern of motions e.g. after prolonged & rapid rotation, (2) in certain diseases e.g. Menier's disease, **the following manifestations will occur:**

1- Vertigo
2- Nystagmus
3 Autonomic reactions
4- Changes in the muscle tone.

1- VERTIGO

☒ **Def:** sense of rotation of either the subject or his surroundings.

☒ **Causes:**

1- **Post- rotational vertigo:**
- Remains for about 20-30 seconds.
- Disturb the equilibrium.

2- **Spontaneous (i.e without rotation)**; It may be due to:
a) Excessive irritation of S.C.Cs. e.g. in labyrinthitis
b) Irritation of pathway of vertigo (e.g by brain tumours).
c) Exposure to unusual pattern of movement.

2- NYSTAGMUS

☒ **Def:** oscillatory movement of the eye balls.

☒ **Causes:**

A. *Rotational nystagmus*:

* **Due to rotation and occurs:**
I) At the onset of rotation (for 20-30 sec.).
II) Post-Rotational nystagmus (for 20-30 sec.)
} **due to asymmetrical discharge from SCCs.**

*** Significance:**
- **At the onset of Rotation:** help in maintaining clear vision during rotation ➔ maintaining the body equilibrium.
- **Post-Rotational nystagmus:** - It may disturb the equilibrium.

B. Spontaneous nystagmus:
- **Due to:** * irritation of the labyrinth as in Minier's disease.
  * Neocerebellar Syndrome.
  * Severe defective vision (e.g. in blind)

C. Optokinetic nystagmus:
- Occurs during looking out from a moving vehicle, e.g. train.

2- AUTONOMIC REACTIONS

☒ The exposure to unusual pattern of motions leads to a group of manifestations called (**Motion Sickness**). **These manifestations include:**

1- Bradycardia.

2- Hypotension.

3- Nausea & vomiting.

4- Profuse sweating.

☒ This is due to the **effect of vestibular apparatus on the autonomic centers** in the brain stem reticular formation.

Thalamus

- ☒ It is an **ovoid gray mass located in the diencephalon**.
- ☒ The two thalami of both sides are separated by the **3rd ventricle** with interconnection by a narrow band called **interthalamic adhesion**.
- ☒ The gray matter of the thalamus is divided internally by **lamina of white matter** into many separate **nuclei.**

☒ Functionally, thalamic nuclei are divided into:

A. Specific: Receive well defined afferents and project to **specific areas** in the cerebral cortex, includes:

i- Anterior nuclei.

ii- Medial nuclei.

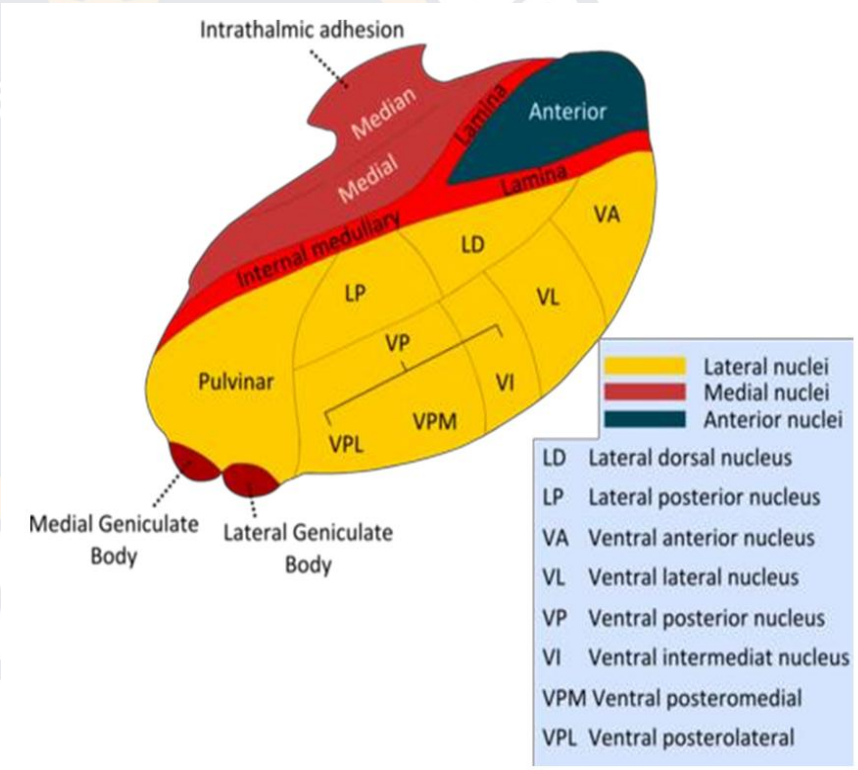
iii- Lateral nuclei

B. Non-specific: Receives input mainly from R.A.S, and project diffusely to **all parts of the neocortex**, includes:

i- Intralaminar nuclei.

ii- Midline nuclei.

iii-Reticular nuclei



☒ Thalamic functions:

1) Sensory functions

A- Thalamus acts as a sensory relay station:
All ascending sensory pathways before reaching the cerebral cortex relay in the thalamus especially those carrying fine epicretic sensations from opposite side of the body.

i) Somatic sensory pathways relay in ventral posterior (VP) nucleus of the opposite side, where those

- from body relay in lateral part of VP nucleus
- from face & taste relay in medial part of VP nucleus

ii) Special sensations:

- **Vision:** the optic fibers from both retinae reach L.G.B. and projected to the visual cortex.
- **Hearing:** auditory fibers from both ears relay in M.G.B. before reaching the auditory cortex.

B- Gating of the ascending sensory information:

- **Corticofugal impulses** are transmitted back from the cerebral cortical sensory areas to the thalamic relay nuclei which already project to these areas.
- **This cortical-feedback is inhibitory**, and it decreases transmission through these nuclei particularly when the **sensory input is very high**.

C- Thalamus as a sensory center: Discrimination of many sensory impulses occurs in the thalamus but the sensations felt are of **crude protopathic** nature e.g: diffuse pain & crude touch

2) Motor functions:

- **Ventral anterior (VA) and ventral anterior (VL) nuclei** relay motor signals from the basal ganglia and cerebellum to the motor and premotor areas of the frontal lobe to control their functions.
- **V.P.L nucleus** relays proprioceptive signals to the motor cortex. This provides sensory information about position and movements of the different parts of the body.

3) Association & integration functions:

- The **anterior and medial nuclei** together with **hypothalamus and limbic system** play a role in integrating the visceral and somatic motor responses evoked during emotions.
- The **reciprocal connection between the dorsomedial (D.M) nucleus of the thalamus and prefrontal areas** may play a role in the coding, storing and recalling of memory.

4) Arousal function:

The non-specific thalamic nuclei receive excitatory signals from the **R.A.S** of brain stem, and project it to almost all areas of the **cerebral cortex**, producing **arousal** and **wakefulness**.

Wakefulness (Arousal)

☒ **Def.:** The state of **consciousness** in which the person is aware of the various **sensory stimuli**, as well as, **his feelings, thoughts and ideas.** It also enables the person to **pay attention to external stimuli.**

☒ **Reticular activating system (RAS):**

- The RAS consists of the **facilitatory reticular formation** (in **pons**) with its upward projections to the **non-specific thalamic nuclei**, from which the excitatory signals project diffusely to all areas of the **neocortex**, causing **generalized activation of the brain**.
- This activation of the brain produces **arousal and wakefulness**.

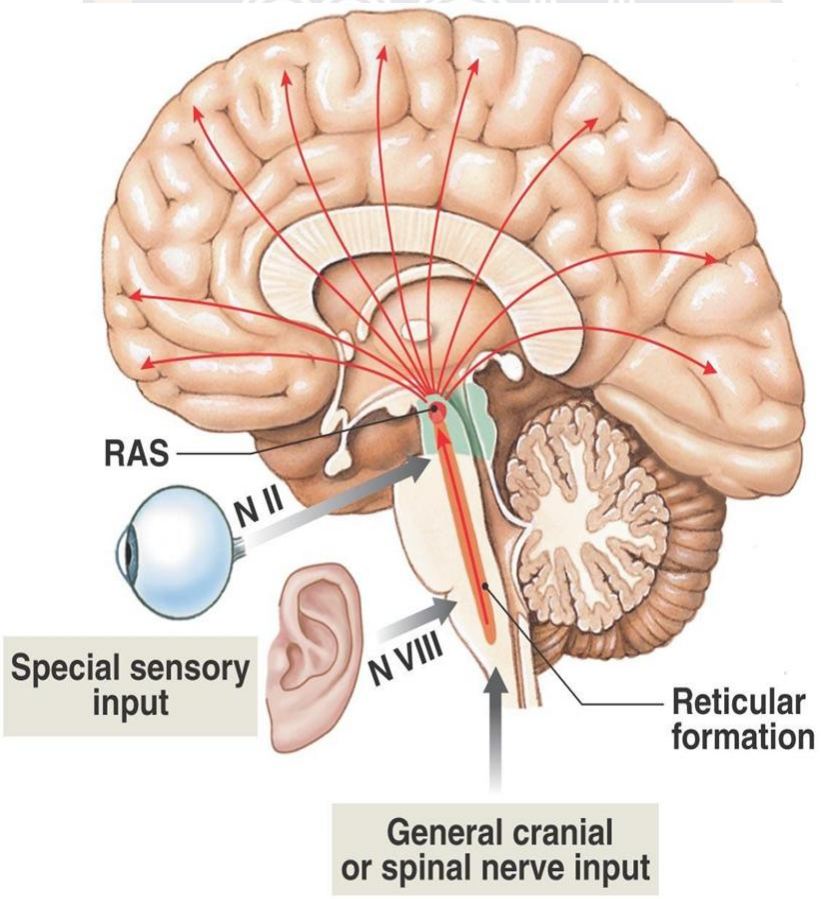


Figure: reticular activating system

☒ Factors affecting activity of R.A.S

1-Sensory signals:

- Sensory signals from every sensory system in the body produce activation of RAS neurons.
- **Pain** and **proprioceptive** signals are **stimulatory** than others.

2-Feedback signals:

- Feedback signals from the cerebral cortex are sent back to RAS, whenever the cortex becomes activated by **thinking or motor activity**.
- This corticofugal feed-back activates **R.A.S** which in turn sends more excitatory signals to the **cortex** to enhance its activity.

3-Neurotransmitters:

- **Epinephrine and norepinephrine:** Lower the threshold for excitation of neurons of the R.A.S.
- **Serotonin:** Released mainly by the neurons of raphe nuclei in medulla. It suppresses R.A.S and could play a role in sleep. Administration of anti-serotonin drugs ➔ insomnia.

4-The reticular inhibitory area (RIA):

- Located in medulla oblongata.
- When this area becomes excited, it inhibits RAS possibly by increased secretion of serotonin.
- The normal wakefulness-sleep cycles may be regulated through alternating reciprocal activity in between RAS and reticular inhibitory area.

5-Drugs:

- **Sympathetic drugs:** as amphetamine and adrenaline increase the activity of RAS (**explain alert state during emergency and stress**)..
- **Anesthetic drugs:** ↓ conduction through RAS synapses ➔ unconsciousness.

Basal ganglia (BG)

☒ BG is a **group of nuclear masses of gray matter** deep to the cerebral cortex and lateral to the thalamus "Within the cerebral hemisphere".

☒ **Functionally**, the B.G. consists of the following **nuclei**:

1. Caudate Nucleus. } **Corpus striatum**
2. Putamen.
3. The globus pallidus.
4. The subthalamic nucleus (STN).
5. The substantia Nigra (SNr) located in the mid brain.

Putamen & globus pallidus are called **lentiform nucleus.**

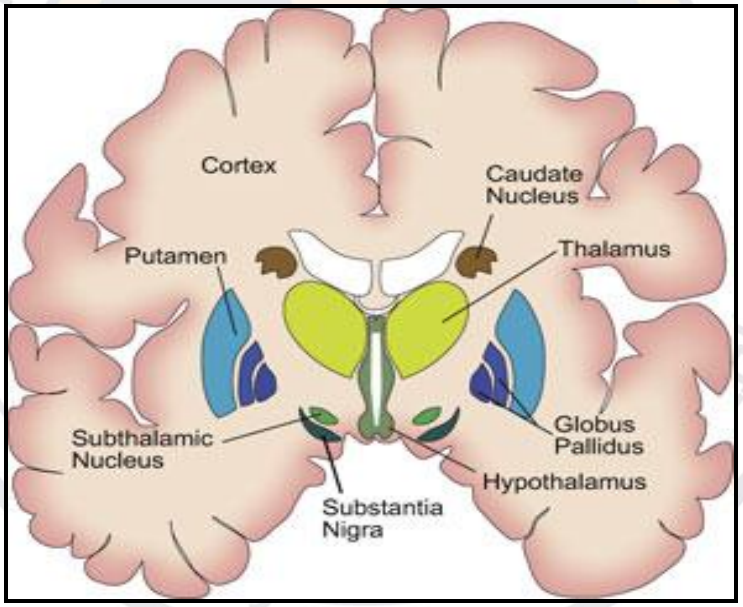
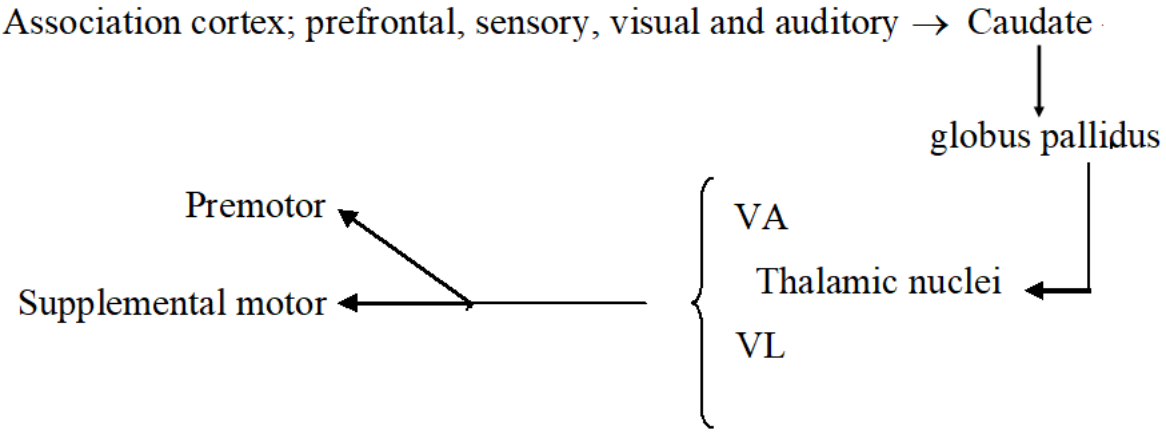


Fig.: The human basal ganglia

☒ Caudate circuit and putamen circuit:

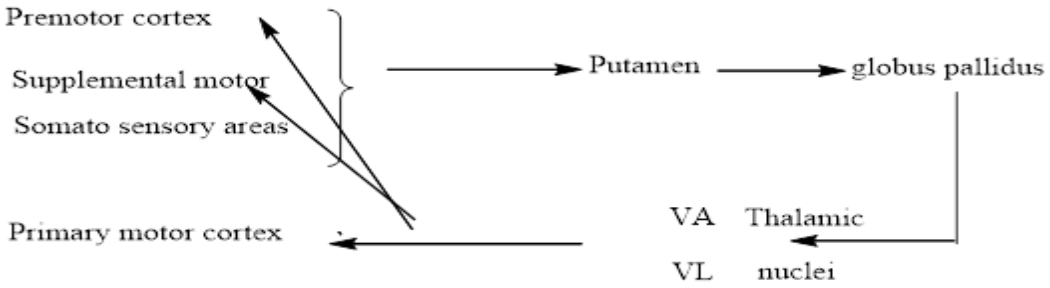
A. Caudate circuit:

-Fibers **start from association areas (sensory and prefrontal)** ➔ caudate nucleus ➔ glopus pallidus ➔ thalamus (VL&VA nuclei) ➔ finally the fibers **end mainly at** the **premotor** and **supplemental** motor areas.



B. Putamen circuit:

-Fibers start from **premotor** and **supplemental motor areas** and **somato-sensory areas** ➔ putamen ➔ glopus pallidus ➔ thalamus (VA&VL nuclei) ➔ cortical motor areas mainly the primary motor area 4.



☒ Chemical transmitters in the basal ganglia:

a. **Dopamine pathway** from substantia Nigra to the caudate nucleus and putamen (corpus striatum). It is an inhibitory pathway.
b. **GABA pathway** from the corpus striatum to the globus pallidus and substantia Nigra. It is an inhibitory pathway.
c. **Acetylcholine pathway** from the cortex to the corpus striatum. It is an excitatory pathway.
d. **Glutamate pathways** provide most of the excitatory signals that balance out the large inhibitory signals transmitted by dopamine and GABA pathways.

☒ Functions of basal ganglia:

1. Planning and programming of motor actions (Caudate circuit):

- B.G. plays a role in **cognitive control of motor activity i.e.** converting the generated thoughts in the mind into voluntary motor acts. **How? It determines when to move, and what muscles to use for moving**.
- **This function is done in close association with the motor cortex** that provide the plane of the motor act **and the cortical association areas** that provide information about the relation of different parts of the body to each other and to the surrounding environment.

2. Executing patterns of learned movements (Putamen circuit):

- The B.G. may control the **rapid and automatic repetition of certain skilled movements** as writing, & typing.
- **If damaged** the act will be done in a **crude manner** as it is done for the first time.

3. Postural regulation:

- The B.G assists in providing a **postural background**, which is necessary for the **performance of voluntary movements done by the distal muscles**.
- The B.G. **adjusts tone in the proximal muscles** through the reticular spinal tract.
- The B.G. acts as a **bridge** that links the lateral motor system (CBST) to the medial motor system.

4. Initiation of automatic associative movements:

These movements are done at subconscious level as swinging of the arms during walking and facial expressions that reflect the emotional state of the subject.

5. Regulation of muscle tone

- Caudate nucleus is excitatory to muscle tone while lentiform nucleus is inhibitory.
- The final output of B.G is inhibitory to muscle tone.

☒ Disorders of basal Ganglia

A) Parkinson's Disease:

☒ It is the **most common degenerative disease** of the brain.

☒ **Cause:** degeneration of **Dopaminergic neurons in substantia nigra** ➔ ↓ in dopamine release in corpus striatum. Most cases of parkinsonism are **idiopathic** & occur more commonly in **old age**.

☒ **Manifestations of Parkinson's disease:**

1. Tremors

- Regular rhythmic alternating contractions in the antagonistic muscles of the hands & fingers.
- It takes the characteristic: pill- rolling pattern.
- Static: occurs during rest and disappear during voluntary movements.
- Exaggerated by: emotional excitement.
- Disappear during: sleep.

2. Rigidity

- Marked increase in the muscle tone **"Hypertonia"**.
- It affects both flexors and extensors but more in flexors ➔ the patient attain flexed attitude (Gorilla-like).
- Limb shows constant resistance to bending called **(lead pipe rigidity)**, but rigidity may be of **(cog- wheel type)** when interrupted by tremors.

3. Akinesia & bradykinesia

- **Akinesia:** difficulty in initiating voluntary movements
- **Bradykinesia** voluntary movements are done slowly.
- **Manifested by:**
  - **Gait** becomes slow with short, shuffling steps.
  - **Speech** becomes slow and monotonus
  - **Loss of automatic associative movements** with loss of expressive face **"Mask face"** & loss of swinging of the arms

☒ Treatment:

1. by giving **L-DOPA which is converted to dopamine in the brain**
2. Anticholinergic drugs to decrease the effects of the un-antagonized acetylcholine.
3. **Implantation of "Dopamine secreting cells** in the B.G.

	B) Chorea	**C) Athetosis**	**D) Hemiballismus**
Lesion in:	Caudate nucleus	Globus pallidus	subthalamus
Pathology	* **Huntington's chorea:** - Degenerative. - Occurs at old age. * **Sydenham chorea**: occurs as a complication of **rheumatic fever** in children	**Wilson's disease:** Due to excessive deposition of cupper in the globus pallidus.	**Vascular lesion**
Characters	**Spontaneous rapid involuntary dancing movement** which may involve many parts of the body as face, arms, head, legs & trunk	Continuous slow **snake-like movements** of a hand, an arm, the neck or the face.	**Involuntary, intense violent movements** involving large areas of the body.
Muscle tone:	**Hypotonia**	**Hypertonia**	**Hypertonia**

Cerebellum

☒ **Anatomically,** the cerebellum (CB) is composed of an **outer cortex** surrounding a **core of white matter which consists of deep cerebellar nuclei** (Dentate nucleus – Globose & emboliform nuclei and Fastigial nucleus).

☒ **It is divided by 2 fissures** (primary fissure and posterolateral fissures) into **3 lobes:**

1- Anterior lobe. **2- Posterior lobe**. **3- Flocculo-nodular lobe**

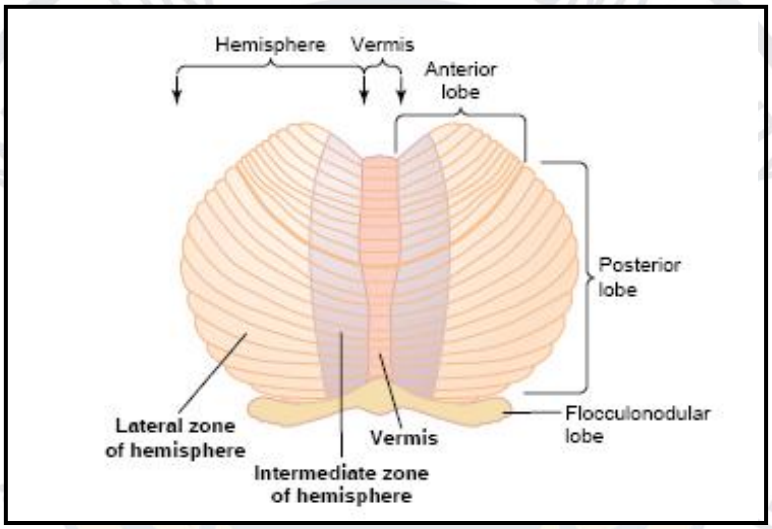


Fig.: Anatomical divisions of cerebellum

☒ **Functionally, cerebellum divided into:**

1. **Vestibulocerebellum** (floculonodular lobe; archicerebellum): Composed of the **flocculo-nodular lobe (F.N.L).** Its functions are closely related in its functions with the vestibular system
2. **Spinocerebellum** (vermis + intermediate zone; paleocerebellum): Consists of the **vermis and the intermediate zones** of the cerebellar hemispheres. Most of its sensory information comes from the spinal cord.
3. **Cerebrocerebellum** (lateral zone; neocerebellum): Composed of the **lateral zones** of the cerebellum. Almost all of its afferent signals originate from the cerebral cortex and reach it through the pons.

☒ Neural connections of the cerebellum:

I- Vestibulo-cerebellum:

a- Input or afferents:

- Vestibular apparatus ➔ vestibular nuclei ➔ inferior cerebellar peduncle ➔ cortex of F.N.L.

b- Output or efferents:

- Cortex of F.N.L ➔ Fastigial nucleus ➔ inferior cerebellar peduncle ➔ Vestibular nuclei ➔ Vestibulo-spinal and reticulospinal tracts ➔ adjust tone of postural muscles.

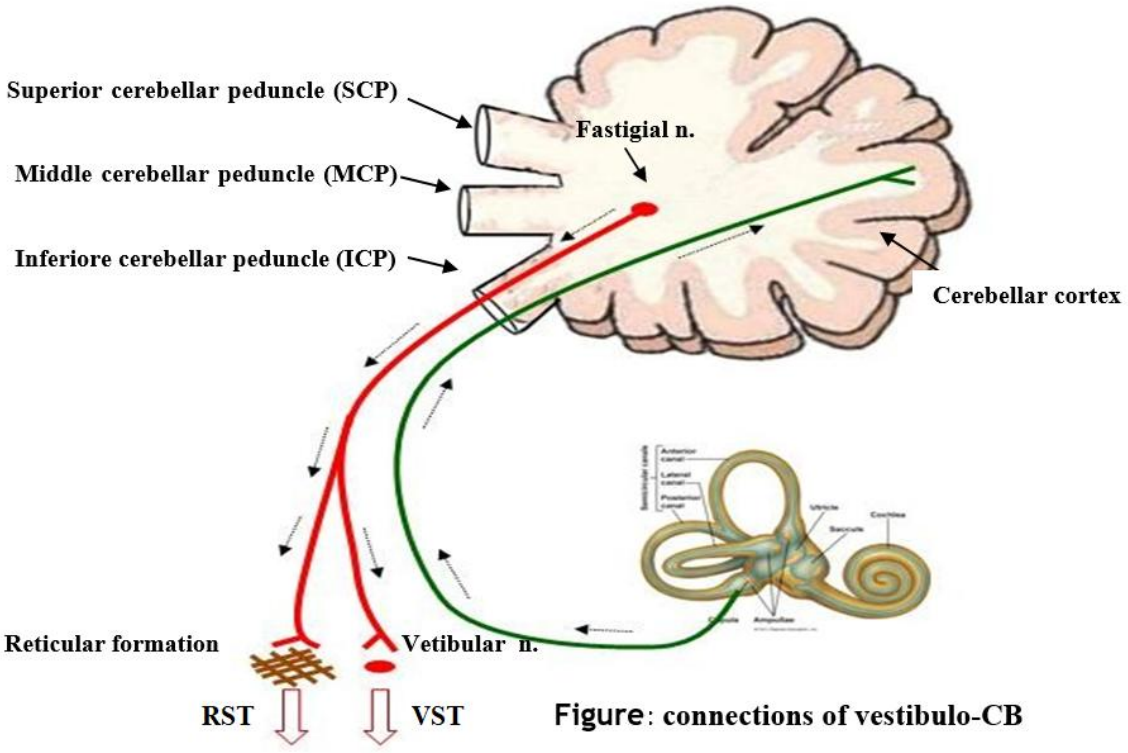


Figure: connections of vestibulo-CB

II- Spino-cerebellum:

A) Input (afferents):

a. Brain & brain stem centers:

1-Cerebral cortex.

2- Red nucleus.

3- Reticular formation

Impulses from these centers inform CB about the **plan of movement ordered by the higher centers**.

b. Proprioceptors: Ventral spinocerebellar tract (VSCT) & lateral spinocerebellar tract (LSCT) carry impulses from proprioceptors regarding the **actual performance of muscles**.

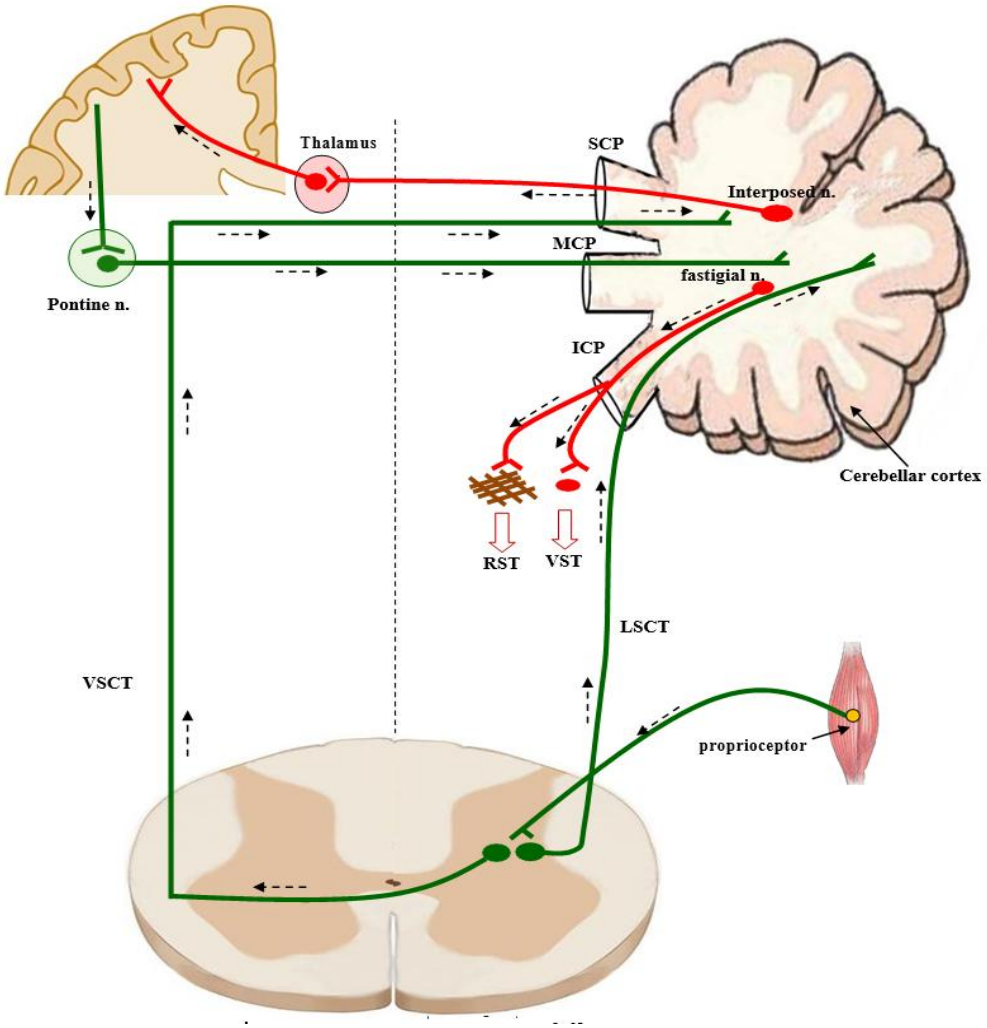


Figure: connections of spino-cerebellum

B) Output or efferents:

a. From vermis:

Neurons of vermis project to fastigial nucleus ➔ reticular formation & vestibular nuclei ➔ vestibulo-spinal (VST) & reticulo-pinal tracts (RST) ➔ antigravity muscles.

b. From intermediate zone:

Neurons of the intermediate zone project to interposed nucleus (globose and emboliform) ➔ superior cerebellar peduncle ➔

- Contra-lateral thalamus ➔ motor cortex ➔ corticospinal tract ➔ distal limb muscles.
- Contra-lateral red nucleus ➔ rubro-spinal tracts ➔ distal limb muscles.

III- Cerebro-cerebellum:

a- Input (afferents):

- Afferents originate from the cerebral cortex ➔ pontine nuclei ➔ middle cerebellar peduncle via cortico-ponto-cerebellar pathway.
- **This pathway provides the cerebellum with:**

  i) The plan of movement.

  ii) Sensory information regarding postural state of the body.

b- Output (efferents):

- Cerebellar cortex of lateral zone→ dentate nucleus→ superior cerebellar peduncle→ VL nucleus of contra-lateral thalamus → cortical motor areas.
- This pathway mediates the role of the cerebellum in **adjustment of motor commands before being discharged from cerebral cortex**.

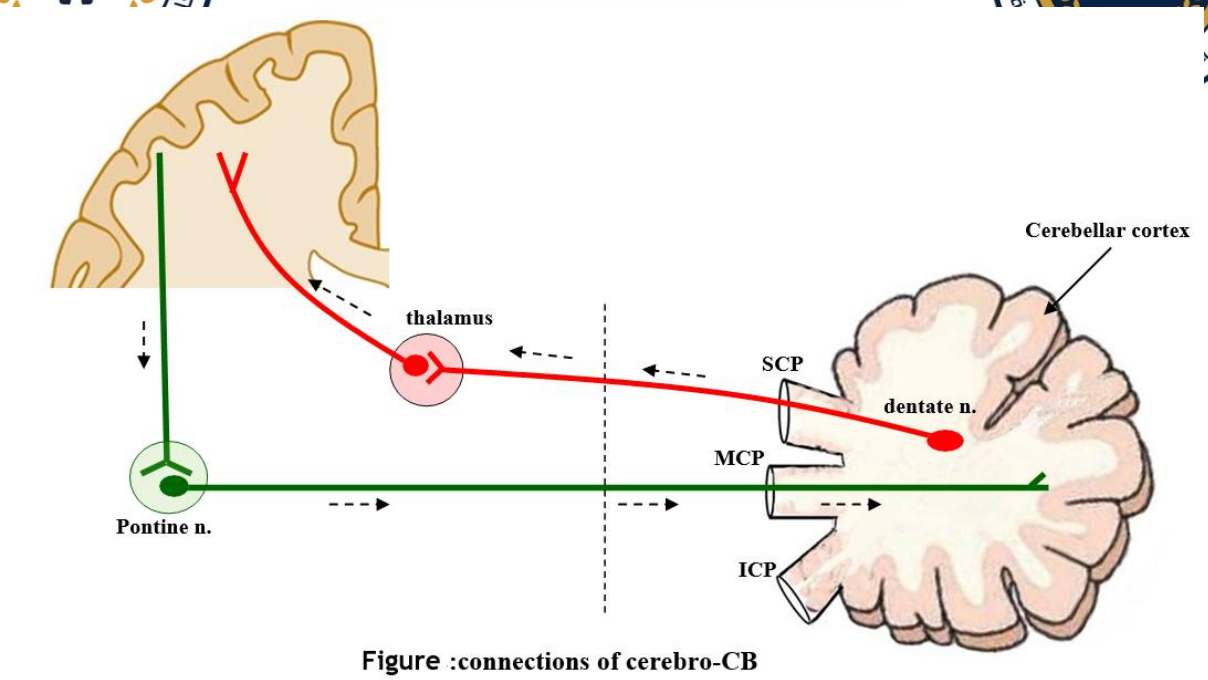


Figure :connections of cerebro-CB

☒ Functions of cerebellum:

I) Regulation of equilibrium (F.N.L):

- **Disturbed equilibrium or altered head position** ➔ stimulation of vestibular receptors ➔ vestibulo-cerebellum
- The vestibule-cerebellum **interprets** these impulses then **sends corrective impulses** ➔ Fastigial N. ➔ then **through:**
  1. **V.S.T & R.S.T** ➔ motor neurons of axial muscles & proximal limb muscles ➔ maintain body posture.
  2. **Medial longitudinal bundle** (**M.L.B) (III, IV & VI cranial nuclei)** ➔ coordinate eye movement with head movement ➔ maintain clear vision ➔ help to keep equilibrium.

II) Regulation of body posture

- This is the function of **vermal zone**.
- **It receives information** from **proprioceptors** about position and movements of every part of the body .
- **Disturbed body posture** ➔ stimulation of proprioceptors ➔ vermis.

- **CB interpretates** these impulses, then sends **correction impulses ➔ fastigial** nucleus ➔ **VST & RST ➔** adjusts the **tone of antigravity muscles**.

III) Coordination (regulation) of voluntary movements:

- **Coordination** means the ability to proceed from one movement to another smoothly, precisely & in a proper succession.
- **This is achieved through the following mechanisms (functions):**

1- Servo-comparator function (Fine-tuning):

- **The spino-cerebellum is informed about:**
  - **a) The intended plan of movement from the motor cortex** (via cortico-ponto-cerebellar tract), and
  - **b) The performance of movement from muscles** (via spino-cerebellar tracts)
- The spino-cerebellum **compares** the **intention** of the motor cortex with the **performance** of the muscles. **If not appropriate**, the spino-cerebellum sends corrective signals to motor cortex (via dentate-thalamo-cortical tract), which by its turn through descending CBS tract adjust the muscle activity

2- Predictive and damping function:

- **Damping means** ending of the movements without oscillation at the proper site.
- The cerebellum assesses the **rate of movement**, **calculates the time needed to reach the intended point** & then transmits inhibitory impulses to the motor cortex to **stop the movements at the exact intended point.**

3- Planning of the sequence and timing:

a) Sequence planning:

- The cerebro-cerebellum receives afferent impulses from the **cortical association areas** (the site of ideas for voluntary movements) about the **intension** of performing a certain voluntary movement **before** the movements starts.
- Then, the cerebro-cerebellum sends to the **motor area of cerebral cortex** (that initiate movements) the **plan of the sequential movements** required to execute the intended voluntary movement.
- The cerebro-cerebellum **plans for the next movement** while the present movement is occurring.
- Thus, it is not involved with what is happening at a given moment, but with what will occur in the subsequent moment.

b) Timing planning:

- The cerebro-cerebellum provides **proper timing for each movement**.

- Such function is necessary for **smooth transition** from one movement to the next and **joining** of sequential movements.

IV) Role of CB in motor learning:

- When a person performs a complex voluntary motor act **for the first time**, the movement will be usually **inaccurate**.
- When the CB detects this **mismatching** between the motor plan and performance, it **tries to correct it** through sending a more accurate plan to the motor cortex.
- By time, **on repetition** of this movement it becomes more & more accurate & the CB will store **"a motor program"** for this movement for future use.

☒ **Cerebellar lesions:**

I) Flocculo-nodular Lobe disorders:

- These disorders **impair equilibrium.**
- This is **manifested by** swaying during standing and unsteady wide based gait **(waddling gait)**.

II) Vermal disorders:

- These disorders cause **inability to sustain the upright posture**, due to failure to adjust the tone of antigravity muscles.

III) Neocerebellar syndrome:

- **Due to** cerebellar hemispheric (paravermal and lateral zones) lesion.
- The principal motor dysfunctions caused by cerebellar hemispheric lesions **include:**

a- Hypotonia: due to decreased supraspinal facilitation of stretch reflex (muscle tone).

b- Asthenia: leading to weakness of movements.

c- Ataxia (asynergia): refers to the incoordination of voluntary movements in absence of UMN and LMN lesions.

- **Manifestations of ataxia:**

1. **Rebound phenomenon:**
   - When the patient flexes his forearm strongly against a resistance, then the resistance is suddenly removed, the patient **cannot stop** inward movement of his forearm in proper time, and may thus strike his body.
   - This is due to **failure of the "damping" function**.
2. **Dysmetria:** The moving limb usually overshoots the intended point (**hypermetria**), reflecting **failure of "damping" functions**.
3. **Intention (Kinetic) Tremors:**
   - These tremors occur during voluntary movements, and are due to **hypermetria** of the acting muscles.

- Thus, the limb oscillates throughout the whole movement.

4. ***Nystagmus:*** represents the **kinetic tremors** of the extraocular muscles during movements of the eye.
5. ***Unsteady Gait:*** The gait is unsteady & drunken as a result of the **dysmetria and kinetic tremors** of the lower limb muscles.
6. ***Decomposition of Complex movements:*** A voluntary motor act is carried out as several successive steps, due to **failure of sequence & timing planning**.
7. ***Dysdiadochokinesia:***

- The patient is **unable to perform rapid successive opposite movements**, e.g. supination & pronation of the hands.
- Movements become slow and irregular, due to **failure of sequence & timing planning**.

8. ***Scanning speech (Dysarthria):***

- Speech becomes slow and decomposed.
- Each word is fragmented and pronounced as **several separate syllables**,
- Due to **failure of sequence & timing planning**.

Hypothalamus

☒ Hypothalamus is located at the base of brain, just above pituitary gland and below the thalamus on either side of the **3rd ventricle**.

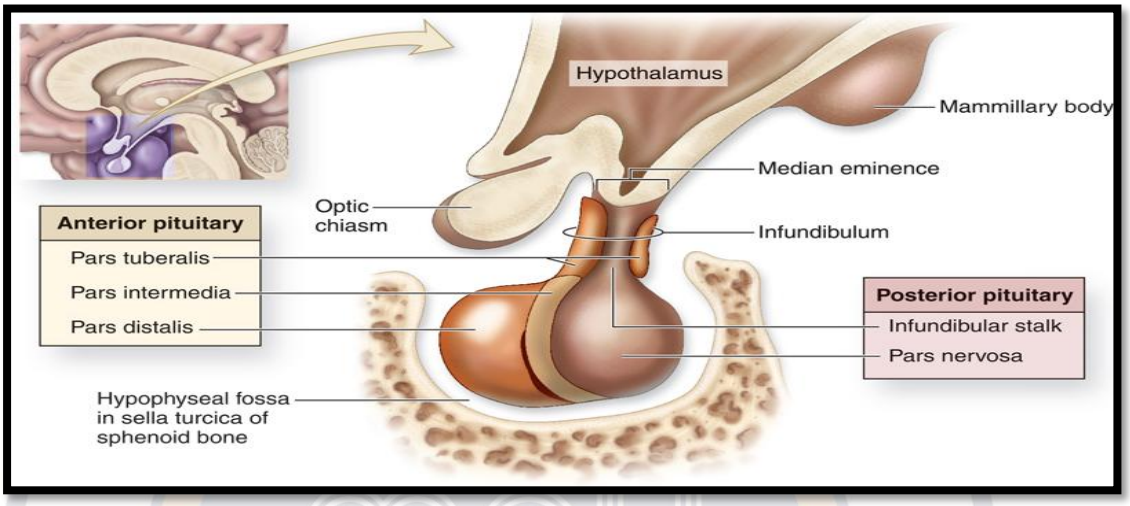


Figure (1): hypothalamus and pituitary gland

☒ **Functions of hypothalamus**

1) Regulation of autonomic nervous system

-Hypothalamus is one of the higher centers that control the autonomic functions, as evidenced by the followings:

a) **Stimulation of posterior hypothalamic area** ➔ sympathatic effects **e.g.** ↑ HR, ↑ ABP, pupillary dilatation and ↑ secretion of catecholamines from suprarenal medulla.

b) **Stimulation of anterior hypothalamic area** ➔ parasympathetic effects **e.g.** ↓ HR, ↓ABP.

2) Regulation of blood glucose level:

- Under normal conditions, glucose is the **only substrate used by the brain** for energy metabolism.
- It is supplied moment by moment due to **lack of glycogen stores**.
- Hypothalamus contains **glucoreceptors** stimulated by **hypoglycemia**.

- Hypoglycemia triggers **counter-regulatory mechanisms** to raise the blood glucose level. **These mechanisms include:**

a) **↑ secretion of adrenaline, growth hormone & cortisol hormone** ➔ ↑ glycogenolysis, ↑ gluconeogenesis ➔ ↑ blood glucose level to normal.

b) **Activation of hunger center** (in hypothalamus) ➔ person feels hungry ➔ ↑ food intake ➔ ↑ blood glucose level.

3) Regulation of body response to stress:

- **Hypothalamus integrates both the endocrinal and neural responses to stress conditions e.g:** hemorrhage, hypotension, hypoxia, hypoglycemia & muscular exercise
- Hypothalamus stimulates the secretion of **cortisol** (from adrenal cortex) and **adrenaline** (from adrenal medulla) during exposure to stress.
- **Both cortisol and adrenaline**, participate in the defense against stress by several ways.

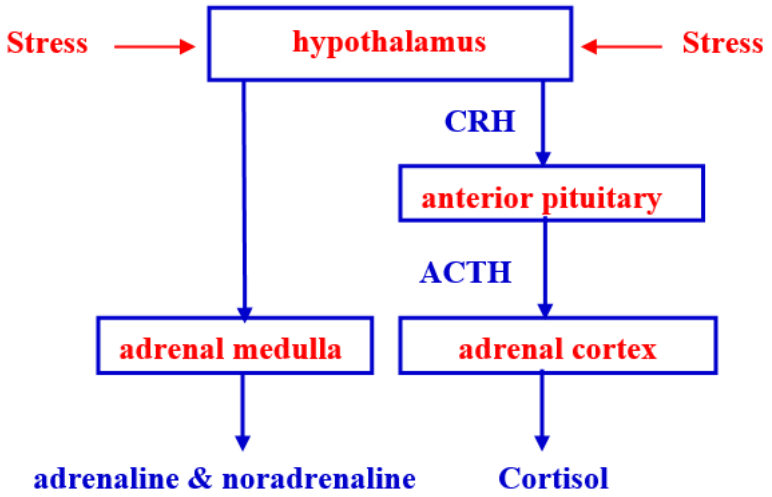


Fig: Hypothalamus and response to stress

4) Regulation of body osmolality and volume of body water:

- The hypothalamus regulates **body osmolality and volume of body water** by controlling both the **output** and the **intake of water**.

- This control is conducted by 2 mechanisms:

a) ADH

b) Thirst sensation (its center is in hypothalamus).

When osmolarity increases & blood volume decreases	**When osmolarity decreases & blood volume increases**
i- ↑ **ADH** secretion → ↑water **reabsorption** from the kidney. ii- ↑ **thirst** sensation → ↑water **intake.** - Accordingly: blood volume ↑**es** & **osmolarity** ↓**es** to normal.	i- ↓ **ADH** secretion → ↑water **loss** from the kidney. ii- ↓**thirst** sensation → ↓ water **intake.** - Accordingly blood **volume** ↓**es** & **osmolarity** ↑**es** to normal.

5) Regulation of endocrine glands:

a) Hypothalamic control of anterior pituitary gland: (**vascular control**)

- Through the **hypothalamo-hypophyseal portal circulation** between the hypothalamus and the anterior pituitary (adenohypophysis).
- The hypothalamus secretes **certain peptides** which are transported to the pituitary gland through the hypothalamic –hypophyseal portal circulation.
- **These hypothalamic peptides are of two natures:**

b) Releasing factors (hormones):

e.g.: - Thyrotropin (TSH. RF). - Corticotropin (ACTH. RF)
- Gonadotropin (GTH. RF) - Growth H. RF

c) Inhibiting factors (hormones):

e.g.: - Prolactin inhibiting factor (PIF).
- Growth inhibiting factor (GIF).

d) Hypothalamic control of posterior pituitary gland: (**Nervous control**)

- A **hypothalamo-hypophyseal tract** arises from **supra-optic (SO)** and **paraventricular (P.V) nuclei** and ends in the posterior pituitary (neurohypophysis).
- The **S.O nucleus secrets ADH** and **P.V nucleus secrets oxytocin**. These hormones are then transported along the hypothalamic-hypophyseal tract to be stored in the post pituitary. Stimulation of S.O and P.V ➔ release of these hormones from the posterior pituitary into blood stream.

e) Hypothalamic control of suprarenal medulla: (**Nervous control**)

- **Hypothalamic fibers** affect the **adrenaline-secreting center** in the medulla oblongata, which in turn affect the activity of SRM that secretes adrenaline and noradrenaline in the blood stream.

6) Role of hypothalamus in (diurnal) circadian rhythm:

- **Several body functions undergo regular variation of their level within 24 hours of day e.g.**
  a) Body temperature
  b) Blood pressure
  c) Secretion of hormones as: cortisol, growth H, melatonin.
- The **biological clock** responsible for this regulation is the **supra-chiasmatic nucleus** (SCN) of hypothalamus which receives information about light and darkness directly from the retina of the eye.

7) Regulation of body weight and food intake:

8) Regulation of body temperature.

Limbic system

☒ **The limbic system consists of parts of the brain that are important in:**

1. Initiation of emotions.
2. Regulation of emotional behavior

☒ **Components of limbic system:**

I- Limbic cortex:

- A ring of old cortex:

- Beginning in **orbitofrontal area** on the ventral surface of the frontal lobe.
- Extending upward in front and over the corpus callosum on the medial aspect of cerebral hemispheres to **cingulate gyrus**.
- Passing posteriorly to corpus callosum & downward on ventromedial surface of temporal lobe, to **para-hippocampal gyrus**, **pyriform area** & **uncus**.

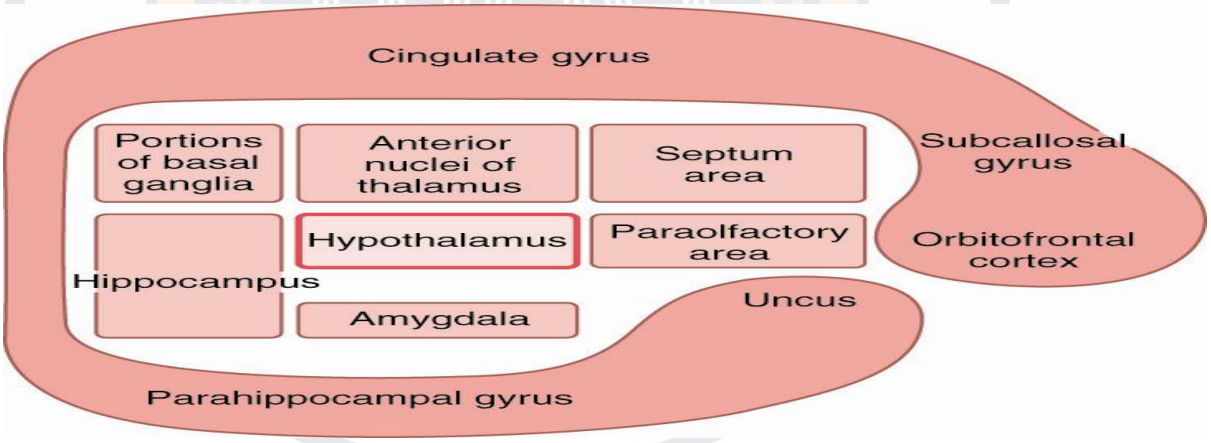


Figure: components of limbic system

II- Subcortical limbic structures:

- Hypothalamus.
- Thalamus
- Para-olfactory areas.
- Amygdala
- Hippocampus.
- Septal nucleus
- Parts of basal ganglia.

☒ Functions of limbic system:

Role of limbic system in motivation and emotional behavior:

The limbic system regulates patterns of behavior related to the following physiological functions:

1- Control of the feeding behaviour:

- This is one of the functions of the **amygdaloid nuclei**.
- The amygdaloid nuclei **differentiate food into edible and inedible** on the basis of past experience.
- The stimulation of these nuclei causes **chewing and licking movements**, while its damage leads to **hyperphagia** associated with ingestion of all kinds of food and objects.

2- Fear and rage reactions:

- The limbic system receives information from different **association areas of the cortex** about various environmental stimuli.
- During exposure to threat, many limbic centers especially the amygdale, evoke **protective emotional reactions** (**e.g. fear or rage reactions**).

Fear reaction	Rage reaction
- If an animal is threatened, it usually tries to escape.	- If a threatened animal is cornered, it attacks & fights.
Manifestations	
Autonomic responses as pupillary dilatation, sweating & somatic responses as turning the head seeking escape.	Autonomic responses as pupillary dilatation, hair erection & somatic responses as biting.

3- Control of sexual behavior and reproduction:

- **Hypothalamus** controls the **onset of puberty**, the **sexual function and activity**.
- **The behavior components** that accompany the **sexual act** are regulated by the **limbic cortex and the hypothalamus as evidenced by:**

  * ***Bilateral damage of amygdale*** ➔ hypersexuality.

  * ***Removal of limbic cortex*** ➔ loss of interest in other sex.

4- Punishment and reward response:

- Stimulation of **certain areas** in limbic system & hypothalamus, **e.g. lateral, ventromedial nuclei of hypothalamus, amygdale and septal nuclei ➔ pleasure and satisfaction** (**reward effect**). The transmitter that is responsible for this sense is **dopamine**. The **cocaine** seems to produce its euphoric effect by ↑↑ dopaminergic activity in the reward system.
- Stimulation of **certain areas** in limbic system & hypothalamus, **e.g. periaquiductal & periventricular areas ➔** displeasure, rage, fear, escape (**punishment effect**) **➔** avoidance of these punishing stimuli.

So, **there are 2 mechanisms** in hypothalamus & limbic systems:

- The one promoting pleasure, comfort and placidity called **reward or approach system** whereas
- the other one promoting anxiety, fear and rage called **punishment or avoidance system**.
- So, emotional state is determined by the balance between the two systems.

5- Role of reward and punishment in memory & learning

- **Role in learning:**

  Everything we do is related to reward and punishment. **If we do something rewarding**, we continue doing it and **if we do something punishing**, we stop doing it.

- **Role in memory:**
  - **If the stimulus causes neither reward nor punishment experience** ➔ can't be remembered easily **i.e.** no transformation into long-term memory and become hardly to be remembered.
  - **If the stimulus causes either reward or punishment** ➔ transformation of short-term memory into long-term memory and become hardly to be forgotten (remembered).
- The limbic system differentiates the sensory signals into **significant** ones which are **stored in memory** and **insignificant** ones which are **ignored**.
- **Damage of hippocampus** ➔ anterograde amnesia.

6- Olfaction:

- The limbic system is concerned with **perception and discrimination of different odours**.
- It stores the **olfactory memories** and controls the **emotional responses to olfactory stimuli**.

Cerebral cortex

Cortical Association Areas

- They **receive, analyze, and integrate signals** from many regions of cerebral cortex and subcortical centers.
- **The most important association areas are:**
  1) Parieto-occipito-temporal area.
  2) Prefrontal association area.
  3) Limbic area.

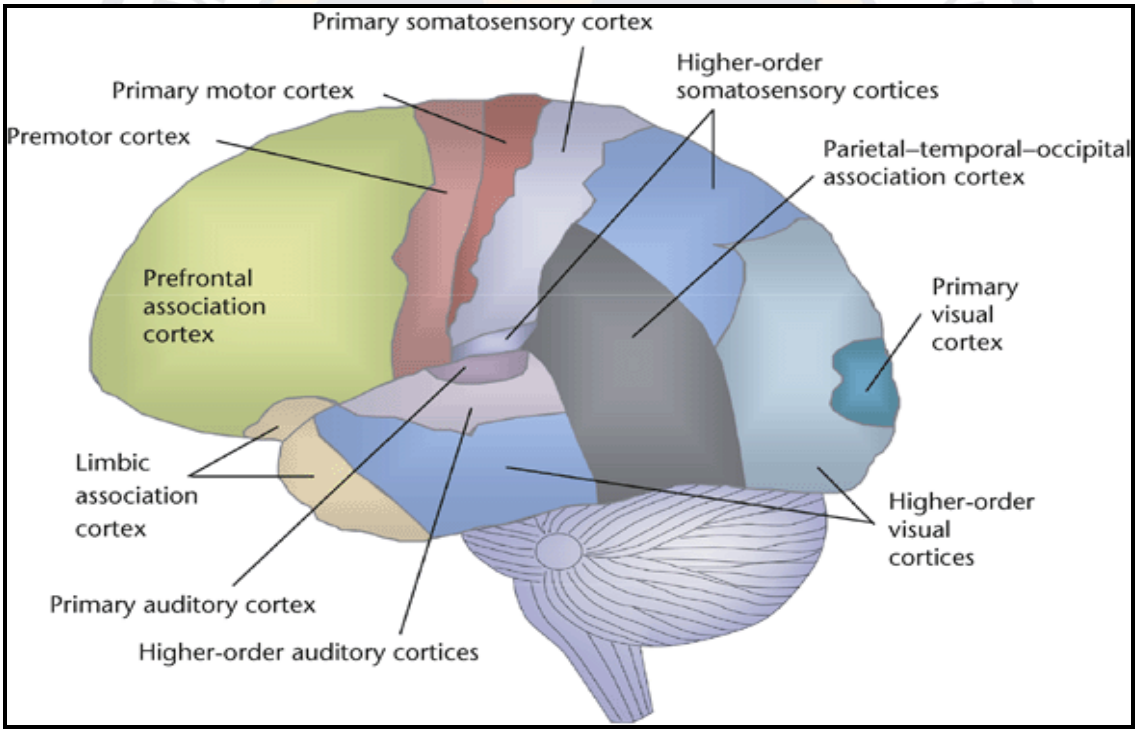


Fig.: The cortical association areas

1- Parieto-occipito-temporal association area:

- **Site:** located in the cortical region between different sensory areas of parietal, occipital and temporal lobes.
- **Functions:** It contains many functional areas as:

Area for analysis of body position	**Site**	Area between somatosensory area of parietal cortex and superior region of occipital cortex.
	Function	**It detects body position by interpretation of impulses from:** - Proprioceptors. - Visual receptors.
Area for analysis of written words (Reading area)	**Site**	Angular gyrus behind language comprehension area.
	Function	- **It recognizes** the **meaning of perceived words during reading**. - **Its damage** → word blindness **(dyslexia).**
Area for naming of objects	**Site**	Inferolateral region of parieto-occipito-temporal area
	Function	Associates **auditory input** with the **physical nature** of the object.
Area for recognition of faces	**Site**	Medioventral surfaces of occipital and temporal lobes.
	Function	- It enables the person to recognize **familiar faces** - **Its lesion → prospagnosia**
Area for language comprehension (Wernicke's area)	**Site**	Posterior part of superior temporal gyrus.
	Functions	1) Higher level of **language comprehension** and **understanding meanings of spoken and written words**.

		2) **Elaboration of thoughts** and **selection of appropriate words** → meaningful speech. 3) **processing and recall of information stored in memory**. • **Its lesion** → deterioration of intellectual functions (language, thoughts) → **i)** person is **unable to interpret** what is seen or heard **ii)** person **can't express** himself **(Aphasia).**

2- Prefrontal association area:

- **Site:** occupies anterior portion of frontal cortex.
- **Functions:**
  a. **Planning of complex pattern of voluntary movement:**

     Prefrontal association area receives **pre-analyzed sensory information** from parieto-occipito-temporal area about the position of different parts of body in relation to the surroundings → motor plan → cortical motor areas for performance of desired movement.

  b. **Sustains mental concentration.**
  c. **Elaboration of thoughts.**
  d. **A working memory:** i.e. ability of prefrontal cortex to:
     - **Collect** many bits of information simultaneously.
     - **Store** it in a readily accessible temporary memory.
     - **Recall** these information when needed.
  e. **Adjust the personal behavior:**
     - It interprets the ongoing events and makes predictions about future behavior.
     - It adjusts the behavior according to social and moral basis.
- **Damage of prefrontal area leads to:**
  - Mental distraction.
  - Inability to plan complex motor actions in proper sequence.
  - Inappropriate social behavior.

Neurological basis of language (speech)

☒ **Def:** Language is highest mental function in humans, through which they can **express their thoughts** (communicate with each others) either by **spoken or written words**.

☒ It is a complex process which requires integrity of **whole cortex** of **dominant** cerebral hemisphere (**left side in right-handed people** and vice versa) because it has both sensory and motor aspects.

☒ **The cortical areas involved in language are categorized into:**

a. **Areas for language comprehension (sensory aspect):**
   - **Wernick's area** receives input about spoken and written words from auditory and visual association areas, a pathway important in reading comprehension.
   - **Furthermore:** Wernick's area is responsible for **formulating coherent (meaningful) pattern of speech**.

b. **Areas for language expression (motor aspect):**
   - **Broca's area:**
     - **Site:** Located in **posterior part of inferior frontal gyrus** in dominant hemisphere just in front of primary motor cortex which initiates contraction of laryngeal and mouth muscles.
     - **Function:** Broca's area **integrates** language signals received from **Wernick's area** → **transmit** it into **detailed coordinated pattern of motor commands** → **specific** area in **primary** motor cortex (**area 4**) → initiation & coordination of appropriate contraction of muscles of lips, tongue and lower jaw → vocal production of speech.
   - **Exner's area:**
     - **Site:** Located in **frontal cortex in premotor cortex** immediately in front of region of primary motor cortex for hands and fingers.
     - **Function: When writing is needed**, the language signals are transmitted from Wernick's area to Exner's area → coordinates the skilled movements of hands and fingers that are necessary for writing.

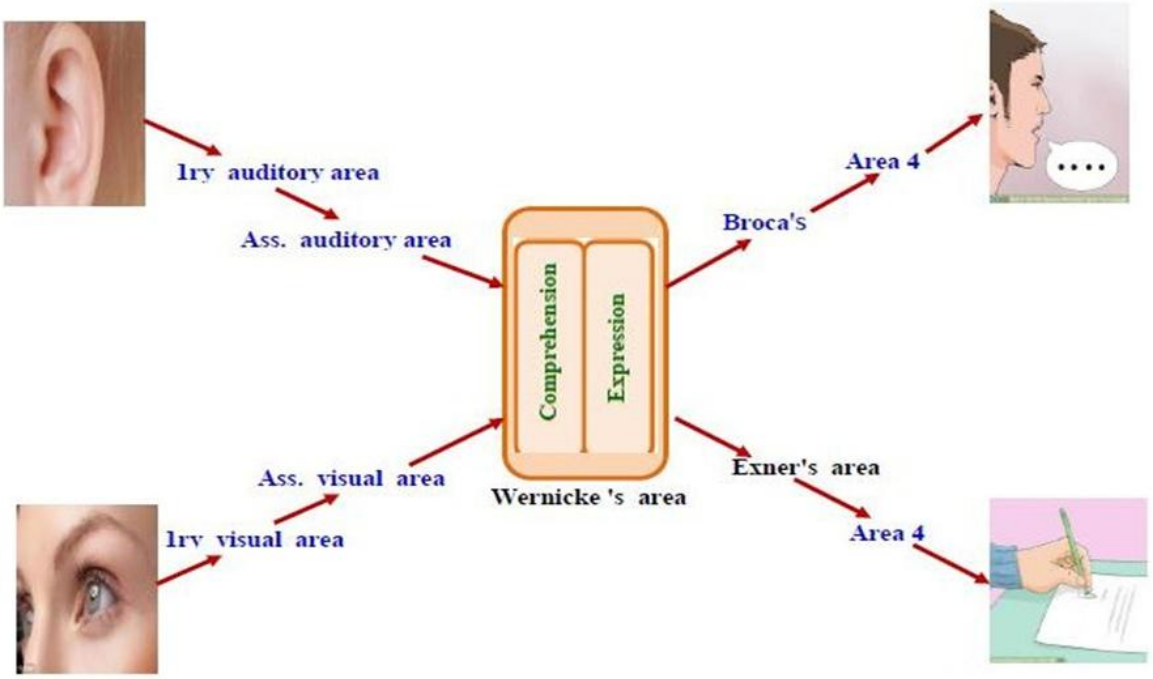


Fig.: Neural basis of spoken and written speech.

Aphasia

☒ **Def:** Speech abnormality resulting from **damage of specific language area** in dominant hemisphere, not due to defects in vision or hearing or; paralysis of the speech muscles..

☒ **Causes: vascular stroke** affecting cerebral blood vessels supplying this region.

☒ **Types:**

Type	Site of lesion	Characteristics
*** Receptive (sensory) aphasia**		
• **Auditory type**	• Auditory association area (area 22)	• Inability to understand spoken words **(auditory agnosia)**
• **Visual type**	• Visual association area (area 18-19)	• Inability to understand written words **(visual agnosia)**
• **Wernicke's type**	• Wernicke's area (39-40)	• Inability to understand both spoken and written language • Inability for proper formulation speech
*** Expressive (motor) aphasia:**		
• **Broca's area**	• Broca's area (44-45)	•Failure to articulate speech
• **Agraphia**	• Exener's area (46)	• Failure of writing
*** Global aphasia:**		
• **Global aphasia (both types)**	• Association areas • Motor areas	• Failure of understanding and expression of thoughts

Sleep

☒ **Def:** It is a state of unconsciousness from which the person can be aroused.

☒ **Duration of sleep:** inversely related to age:

- **Adults:** about 7-8 hours.
- **Infants:**18 hours.
- **Old:** about 5-6 hours.

☒ **Types of sleep:**

There are two types of sleep that alternate with each other, and are characterized by different EEG patterns.

A. **Non rapid eye movement sleep (NREM) = Slow-wave sleep (SW-sleep)** in which the brain waves are strong and of low frequency.

B. **Rapid eye movement sleep (REM sleep)** in which the eyes undergo movements.

	Slow wave sleep (SW sleep)	Non rapid eye movement sleep
Duration	90 minutes	5-20 minutes
Represent	75 % of total sleep time	25 % of total sleep time
Dreams	May be associated with dreams but not remembered	Usually associated with dreams (vivid dreams) & night mares
Muscle tone	Mild reduction	Marked reduction
Heart rate, ABP & resp rate	Mild reduction	Increase & irregular
Rest	Restful sleep	Restless sleep
EEG waves	Slow & high voltage	Rapid & low voltage
	As the stages of SWS proceed, it become deeper & restful	The brain is highly active in this stage. EEG shows a pattern similar to alert state (β rhythm).

☒ **Sleep cycles:**

- When an individual falls asleep, he **first enters** a period of **slow wave sleep** for **90 minutes.**
- This is **followed by** a phase of **REM sleep** for **5-20 minutes**.
- This completes a **sleep cycle**, which, therefore, consists of a period of NREM sleep & the following period of REM sleep.
- Usually, **normal adult** have **4-5 sleep cycles**/ night

☒ **Basic theories of sleep:**

- Sleep is caused by an **active inhibitory process** and **not simply due to fatigue of the reticular activating system** (**passive theory**).

I. Initiation of NREM sleep:

Stimulation of many areas of the brain ➔ sleep, **these areas include:**

1) Raphi nuclei in the lower half of the pons and in the medulla:

- Nerve fibers from these nuclei spread locally in the **brain stem reticular formation** and upward into the **thalamus**, **hypothalamus**, **limbic system** and even **cortex**.
- The endings of these nuclei fibers release ***serotonin*** which is the transmitter producing sleep.

2) Nucleus of the tractus solitarius.

II. Initiation of REM sleep:

- REM sleep is initiated as a result of ↑ activity of **cholinergic neurons** located in the upper brain stem reticular formation.
- These neurons **(REM-On neurons)** send excitatory signals to RAS, thalamus as well as cerebral cortex.

III. Termination of REM sleep:

- The **termination of the REM sleep** results from ↑ activity of the serotoninergic neurons in the raphi nuclei which send inhibitory projections to the cholinergic neurons in the RAS.

☒ **Physiological significance of sleep:**

- Adequate periods of sleep are essential for **restoration of normal brain activity & different functions of the CNS**.
- Prolonged periods of wakefulness or deprivation of sleep ➔ **deterioration of the higher brain functions**.

Memory

☒ **Def:** Storage of acquired knowledge or skills in brain for later recall when needed.

☒ **Classification of memory:** *according to:*

A. The nature of information stored:

1. **Explicit (Declarative memory):** about facts and events (this is a conscious recall of information).
2. **Implicit (Non-declarative) memory:** about skills & habits (e.g. writing, driving a car or playing a piano).

B. The time course of storage:

1. **Short term memory (STM)**: lasts for seconds or minutes then either fades or changed into intermediate or long-term memory.
2. **Intermediate term memory**: lasts for hours, days or even weeks.
3. **Long term memory (LTM):** can be recalled up to several years.

☒ Mechanisms of memory:

Memories are stored in the brain through facilitation of synaptic transmission. The new or facilitated pathways are called **memory traces.** Once the traces are established, they can be selectively activated by the thinking mind to reproduce the memories.

A. **In case of short-term memory;** this is achieved by either;

i. **Activation of reverberating circuits**

ii. **Post-tetanic potentiation**

iii. **Facilitation of the presynaptic terminals (synaptic sensitization):** This occurs through a facilitatory neuron which terminates on the presynaptic ending. The facilitatory neuron releases serotonin which though cAMP causes closure of K^+ channels in the presynaptic ending ➔ prolongation of action potential in the presynaptic ending ➔ prolonged activation of Ca^{2+} channels ➔ Ca^{2+} entry into the presynaptic terminal ➔ more release of the transmitter ➔ augmented PSP.

B. **In case of intermediate-term memory;** is based on **chemical changes** in the presynaptic terminal or post-synaptic neuronal membrane that increase the synaptic sensitivity.

C. **In cases of long term memory;** is generally believed to result from actual **structural changes**, instead of only chemical changes, at the synapses, and these enhance or suppress signal conduction.

These **structural changes** include:

- increase in vesicles release sites for secretion of transmitter substance.
- increase in number of transmitter vesicles released.
- increase in number of presynaptic terminals.
- changes in structures of the dendritic spines that permit transmission of stronger signals.

☒ **Consolidation and storage of memory:**

- For STM to be converted into LTM which can be remembered months or years later, it must be consolidated.
- Efficient consolidation takes 1 hour or more. This time is used for **rehearsal (recycling)** the same information again & again.
- **Hippocampus** is essential for **consolidation of memory**. It provides the principal (decision-making) which determines importance and significance of the incoming sensory information. Hippocampus provides the drive which makes mind recycles over and over the new information until permanent storage takes place.
- The different kinds of **sensory memories** are stored in appropriate sensory cortical association areas **e.g.** visual memories in visual association areas, memories of voice and spoken words are stored in auditory association area, while memories of faces are stored in face recognition area.

Amnesia

☒ **Definition:** Impairment of memory due to lesion in certain areas of brain

Retrograde amnesia	Anterograde amnesia
* Inability to recall memories from the past i.e. from LTM**.**	* Inability to store new information in LTM for later recall.
* It follows brain trauma which interferes with brain activities	* Lesion in medial portions of temporal lobe, hippocampus (essential areas for storage & consolidation).
* Patient has good recall for present	* Patient has recall for past

The Eye

The eye ball

- The eyeball is nearly spherical in shape with a diameter of 24 mm.
- It has a wall and cavity.

a) The Wall of Eyeball:

The wall of the eyeball consists of 3 layers:

1) *Outer fibrous layer:*

It protects the inner delicate structures of the eye & consists of:

- **The cornea** is the anterior transparent one –sixth.
- **The sclera** is the posterior opaque five – sixths.

2) *Middle vascular layer (Uveal tract):*

It is formed of:

- **The iris:** is a circular colored diaphragm behind the cornea.
- **The ciliary body:** consists of ciliary epithelium and muscle.
- **The choroid:** lies between the sclera & the retina.

3) *Inner nervous layer:*

- It is the retina, which contains the photosensitive receptors, rods & cones.

b) The inner cavity:

It contains:

1) The lens: It lies behind the iris & is attached to the ciliary body by the suspensory ligaments (zonules).

2) Aqueous humour: It is a clear fluid that fills the cavity anterior to the lens.

3) Vitreous humour: It is a clear gelatinous material which fills the cavity of the eyeball behind the lens.

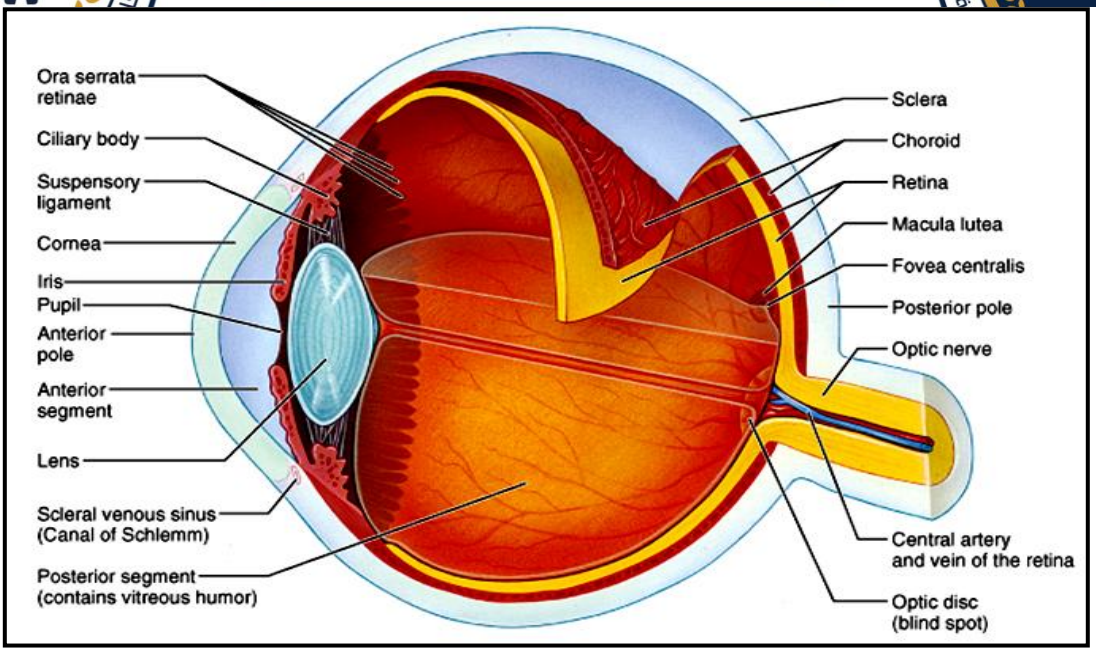


Fig: Eyeball

Extraocular structures

- Eye lids & conjunctiva
- Lacrimal apparatus & Extraocular muscles

Refractive media of the eye

- The **total refractive power of the refractive media of the eye** (cornea, aqueous humour, lens, and vitreous humour) is about **+ 59 diopters**.
- The **cornea** has a **constant refraction** and represents about **70%** of total refractive power of the eye.
- The **lens** is responsible for the other part (**30%**) of refractive power of the eye and **varies** its refractive power by ciliary muscle (from 20 to 32 diopters).

Refractive media	Refractive index	Refractive power
Cornea	1.38	+ 39 diopters
Aqueous Humour	1.33	-----
Lens	1.40	+ 20 diopters
Vitreous humour	1.34	-----

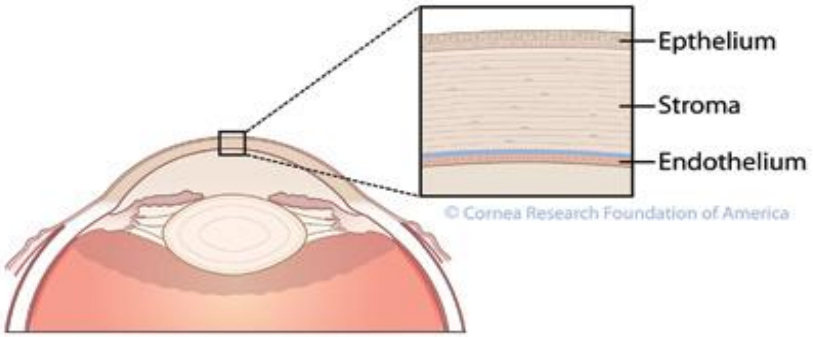
The Cornea

- The cornea is the **transparent** anterior 1/6 of outer coat of the eyeball.
- It is **11 mm** in diameter & **1.0 mm** in thickness.

Histology of the cornea:

- It consists of 5 layers from outside to inside:

1. Stratified squamous epithelium.
2. Bowman's membrane: is thin elastic membrane.
3. Substantia propria (Stroma):
   - It represents 90% of total thickness of the cornea.
   - It consists of collagenous fibres that embedded in matrix.
4. Descemet's membrane: is an elastic membrane.
5. Inner endothelium: is a single layer of flat endothelial cells.



Nutrition & metabolism:

- **Energy** of the cornea is needed for maintenance of its **dehydration** and **transparency**.
- Normally the cornea is **avascular**, so the cornea can **obtain oxygen and glucose from the following:**
  a. **Tears** → supply **O_2** from the atmosphere.
  b. **Aqueous humour** → supply **glucose**.
  c. **Capillaries** surrounding the **corneo-scleral junction** → supply both **O_2 and glucose**.

Transparency of the cornea:

- The cornea is a **transparent** structure. This is essential for passage & refraction of light entering the eye to form a sharp image on the retina.

A) Causes of transparency of the cornea:

1) Anatomic factors:

a. Regular & uniform arrangement of the epithelial cells & lamellae.
b. Absence of blood vessels & myelinated nerve fibres.

2) Physical factors:

a. The refractive index of various layers of cornea is the same.

b. Relative corneal dehydration:

- Normally the cornea is kept dehydrated by osmotic pump and metabolic pump to avoid corneal cloudiness.
- ***Mechanisms of corneal dehydration:***

i. **Osmotic pump:** The aqueous humour & tears are **hypertonic** relative to corneal tissue, so they draw water from the cornea.

ii. **Metabolic pump (Na+ pump in endothelium)** is an active process using energy produced by corneal metabolism. It pumps Na^+ from the cornea to aqueous humour followed with water.

B) Factors maintaining corneal transparency:

1) Vitamin A:

- It is essential for maintenance of **healthy corneal epithelium**.
- Its **deficiency** leads to **keratinization & opacity** of the cornea.

2) Vitamin B_2 (Riboflavin):

- It is important for **tissue respiration** especially the avascular structures as the cornea.

- Its **deficiency** leads to **hypoxia** which is compensated by **corneal vascularization** which disturbs its transparency.

3) Moistening of the corneal surface by tears: Dryness of the cornea disturbs its transparency.

4) Metabolic pump of the endothelial cells: ➔dehydration of the cornea ➔ prevents corneal cloudness.

Functions of the cornea:

1. It is **transparent** structure allowing the passage of light rays into the eye.
2. It is the most important **refractive media** of the eye. It acts as a powerful convex lens (+ 39 diopters) having (2/3) 70% of total dioptric power of the eye. Its refractive index is 1.38.
3. The **regular curvature** of the corneal surface helps the formation of sharp clear images on the retina.
4. **Protective functions of the cornea:** it protects the delicate intraocular structures because:

a) It forms with the sclera **fibrous coat** that protects the delicate intraocular structures.
b) Also it **absorbs ultraviolet rays** which are dangerous to the retina.

- **The cornea itself is protected through the following mechanisms:**
  a. The **corneal reflex**, which is initiated rapidly on touching of the cornea by any foreign body.
  b. The **precorneal film of tears**, which dilutes & washes irritant substances.

Intraocular Fluids

- The intraocular fluid is divided into:

a) **Aqueous humour:** fills the aqueous chambers.

b) **Vitreous humour:** fills the vitreous chamber.

A) The Aqueous Humour

- It is a **transparent colourless alkaline** fluid that fills the anterior and posterior chambers of the eye.

Mechanism of formation:

- It is formed continuously by the **ciliary epithelium** by **facilitated diffusion** and **active transport** mechanisms at a rate **1-2 µL/min**.
- **Sodium** is secreted actively.
- **Chloride and bicarbonate** follow Na passively.
- **Water** is pulled by osmosis.

Composition:

- In relation to plasma, the composition of the aqueous humour is:
  - Nearly **protein free** (contains about 100-200 mg/L).
  - **Na^+** concentration is higher.
  - **Bicarbonate** concentration is higher.
  - **Vitamin C** concentration is higher.

Functions of aqueous humour:

1. It is one of the important **refractive media** of the eye.
2. It **nourishes** the avascular cornea and lens.
3. It also **buffers** the acid produced by the anaerobic metabolism of the cornea and lens.
4. It has a **mechanical function** to keep the eyes rigid and to maintain its refractory power.
5. It maintains the **intraocular pressure** constant by means of its steady formation and drainage.

B) Vitreous Humour

- It is a **transparent gelatinous** material filling the space between the posterior surface of the lens and the retina.
- It is enclosed in a **membrane**.
- It is separated from the lens by a narrow space **(retrolental space).**

Functions:

1. It is one of the **refractive media** of the eye.
2. It **supports** the retina.
3. It **supports** the crystalline lens and prevents it from falling back.
4. It maintains the **spherical shape** of the eye.

Middle vascular layer

1-Iris

The Middle Layer of the Eyeball

(Uveal Tract)

- It consists of **choroid** posteriorly, **iris** anteriorly & **ciliary body** in between.
- This layer is rich in blood vessels (**vascular layer**) and supplies the eye ball with its nutrients (**nutritive layer**).

The iris

- It is the **most anterior part** of the uveal tract.
- It is a **disc like diaphragm** with a central perforation called the **pupil**.
- It divides the aqueous chamber into **anterior** and **posterior chambers**.

***Muscles of the iris:**

- The iris contains **2 smooth muscles** that control the diameter of the pupil.
- They change the diameter of the pupil from **8 mm** to about **1.5 mm**.

Sphincter pupillae muscle	*Dilator pupillae muscle*
- It has **circular fibers** that encircle pupil	- Its fibers spread **radially**
- Its **contraction** ➔ pupillary constriction (**miosis**)	- Its **contraction** ➔ pupillary dilatation (**mydriasis**).
- It is supplied by **parasympathetic fibers** from the oculomotor (III cranial) nerve	- It is supplied by **symp fibers** from 1st and 2nd thoracic segments

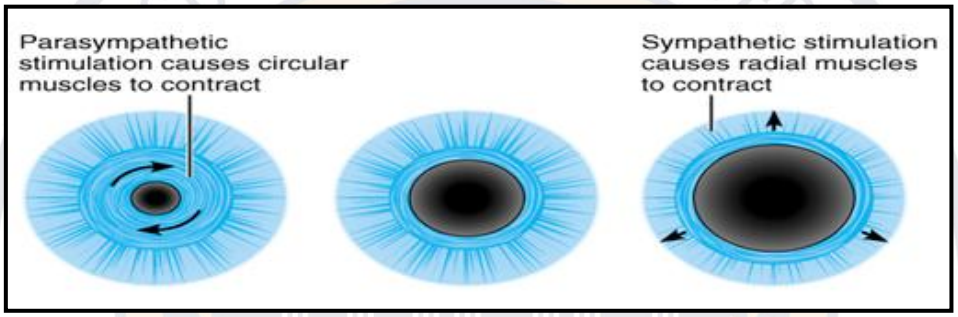


Fig: Muscles of the iris

***Functions of the iris:**

1. The pigments of iris **absorb all light rays** which enter into the eye **except though which pass through the pupil**.
2. It prevents light from falling on the **peripheral parts of the lens**. Thus it **prevents spherical and chromatic aberration**.

a. ***Spherical aberration:***

- The peripheral part of the lens has a **greater curvature** than the central part, so light rays passing through the peripheral part comes to a focus **nearer to the lens** than that of the central rays resulting in a blurred image.
- **Pupillary constriction decreases this defect** as the light rays pass only in the central part of the lens.

b. ***Chromatic aberration:***

- The peripheral part of the lens acts as a prism which **analyses the white light into the different colours** of the spectrum resulting in a blurred image surrounded by coloured halos.
- This is prevented by **constriction of the pupil**.

3. It **regulates the amount of light which enters into the eye** by regulating the size of the pupil.

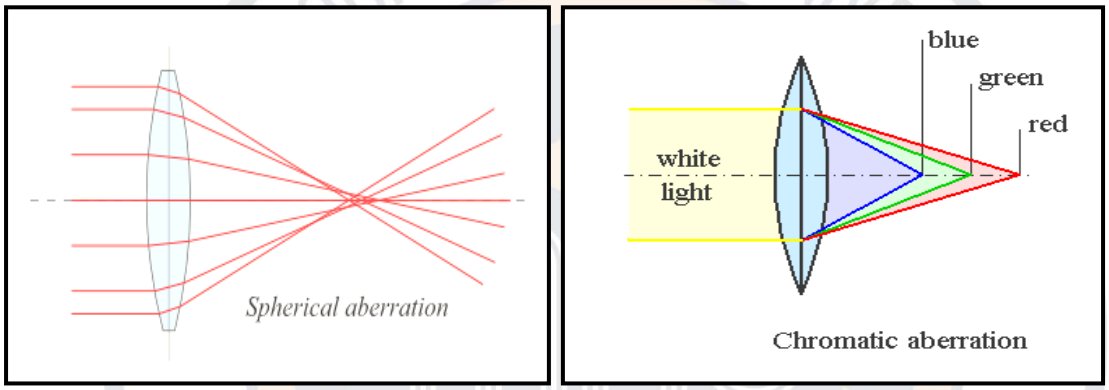


Fig: Spherical and chromatic aberrations

Functions of the choroid

1) It is a vascular layer which **provides blood supply to the eye**.
2) It contains **melanin pigments which absorb light & prevent its reflection inside the eye** which cause blurring of vision.

Functions of the ciliary body (ciliary muscle & the ciliary processes)

1) The **ciliary muscle** is essential for **accommodation**.
2) The **ciliary processes:**
   a. Secrete the **aqueous humour** into the posterior chamber
   b. Give attachment to the suspensory ligament of the lens.

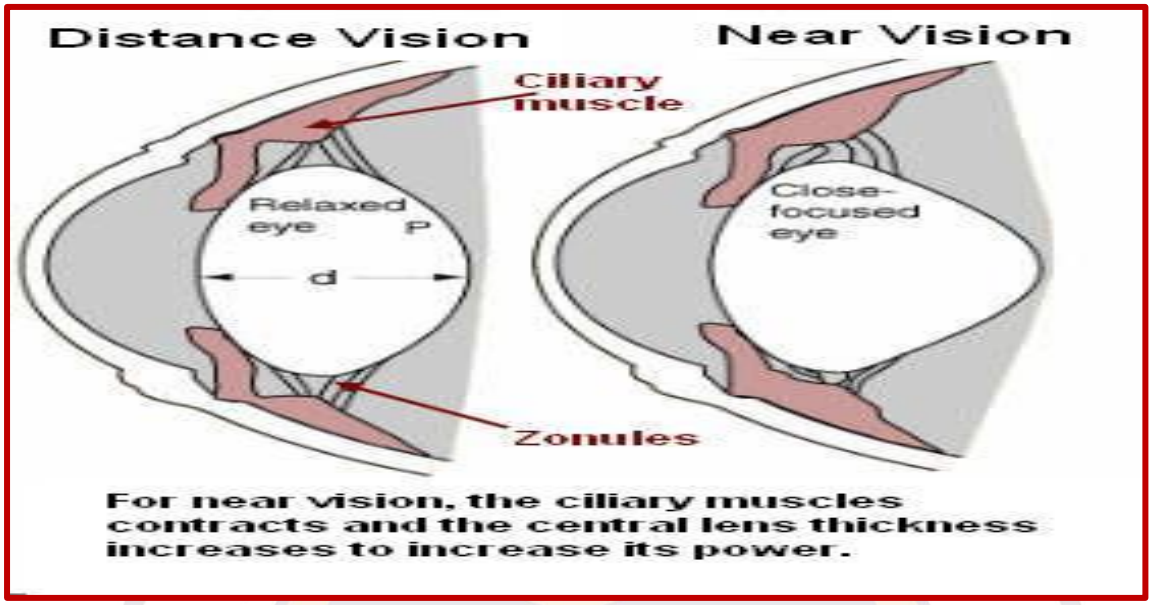


Figure (2): for near vision the ciliary muscle contracts

The Inner layer of eyeball (Retina)

- The retina is the **innermost photosensitive** layer of the eyeball.
- **Histologically**, it is formed of 10 layers.
- **Physiologically**, 4 layers have special importance.
  a. Layer of pigmented epithelium.
  b. Layer of rods and cones.
  c. Layer of bipolar cells.
  d. Layer of ganglion cells.

A) The retinal pigmented epithelium:

- It is a monolayer of **pigmented epithelial cells**; its outer side is in contact with the **choroid** and its inner side with the **rods and cones**.

Functions:

a. It contains large amounts of **melanin pigments which absorb light** and prevent its reflection inside the eyeball which cause glare.
b. It produces a **sticky extracellular matrix material** that keeps the outer segments of rods and cones straight and aligned.
c. It participates in the **breakdown and resynthesis of the photopigments**.
d. It helps the **continual renewal of the outer segment** by ingesting the old outermost tips of the rods and cones.
e. It stores large amount of **vit. A** needed for **photopigments recycling**.

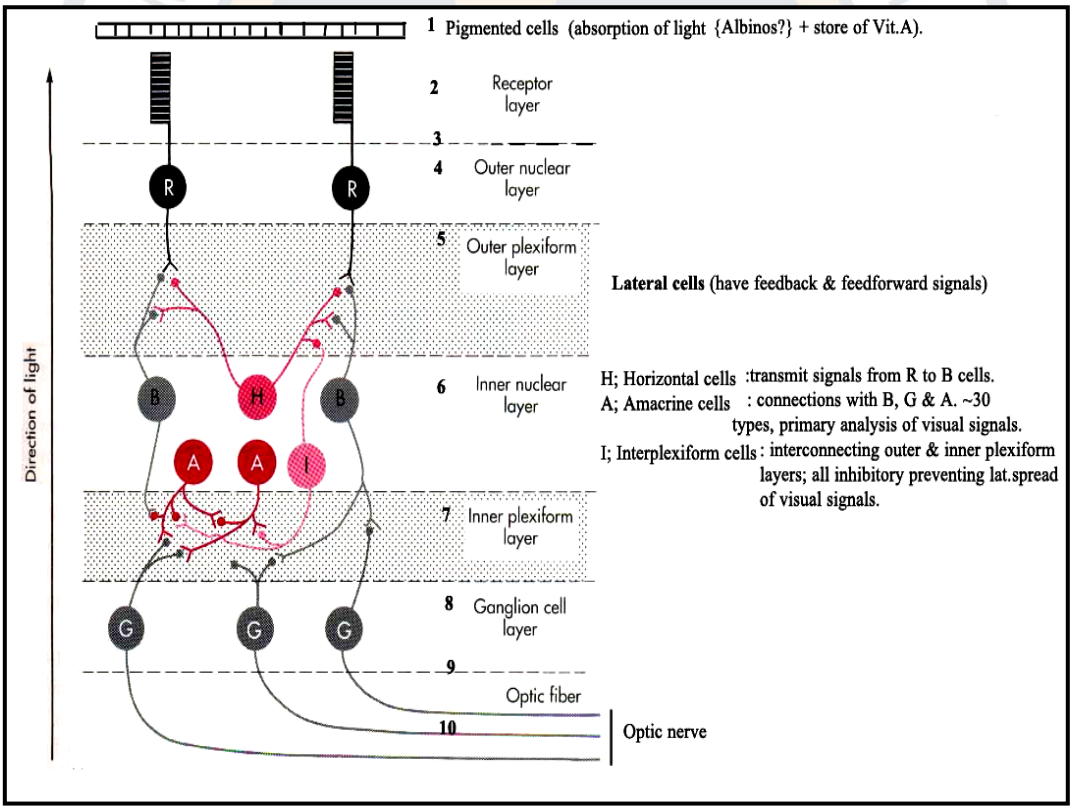


Fig: Layers of retina

B) The photoreceptors (the rods and the cones)

◊ **Structure of photoreceptors:** Each rod or cone is formed of:

(i) An outer segment

- They are **modified cilia** which are **long cylindrical** in rods and **short conical** in cones.
- They contain a great number of **disc-shaped shelves** which are composed of folds of the cell membrane.
- **The disc membrane contains**:
  - ❖ Photosensitive pigments e.g. rhodopsin.
  - ❖ G protein called transducin.
  - ❖ c GMP phosphodiestrase (PDE).
- The membrane of the outer segment of rods and cones contains **cGMP-gated ion channels** selective for Na^+, Ca^{++} and Mg^{++}.

(ii) An inner segment

- They contain **nuclei and mitochondria**.
- They have **synaptic body** that synapses with bipolar cells.
- The membrane of inner segment contains an **active Na^+-K^+ pump**.

	Cones	Rods
Number	6-7 millions	120 millions
Shape	Conical	Cylindrical
Distribution	Mainly in fovea centralis. Less in the middle part.	Mainly in peripheral part of retina Less in the middle part Absent in fovea centralis & optic disc
Photosensitive pigments	Iodopsin (3 types)	Rhodopsin (visual purple)

Connection	One cone to one bipolar cell that can be connected to one ganglion cell (1:1:1)	Many rods converge to one bipolar cell Many bipolar cell converge to one ganglion cell (300:1)
Function	1. less sensitive to light 2. more accurate i.e. can perceive fine details of subject 3. can differentiate colours 4. responsible for day vision	1. more sensitive to light 2. less accurate vision i.e. can not perceive the details of the subject 3. can not differentiate colours 4. responsible for night vision

C) Bipolar and Ganglion cells

- They constitute **1st and 2nd order neurons** in visual pathway.
- **Bipolar cells** transmit signals from photoreceptors to ganglion cells, while **ganglion cells** transmit signals from bipolar cells to brain through the optic nerve (see later).

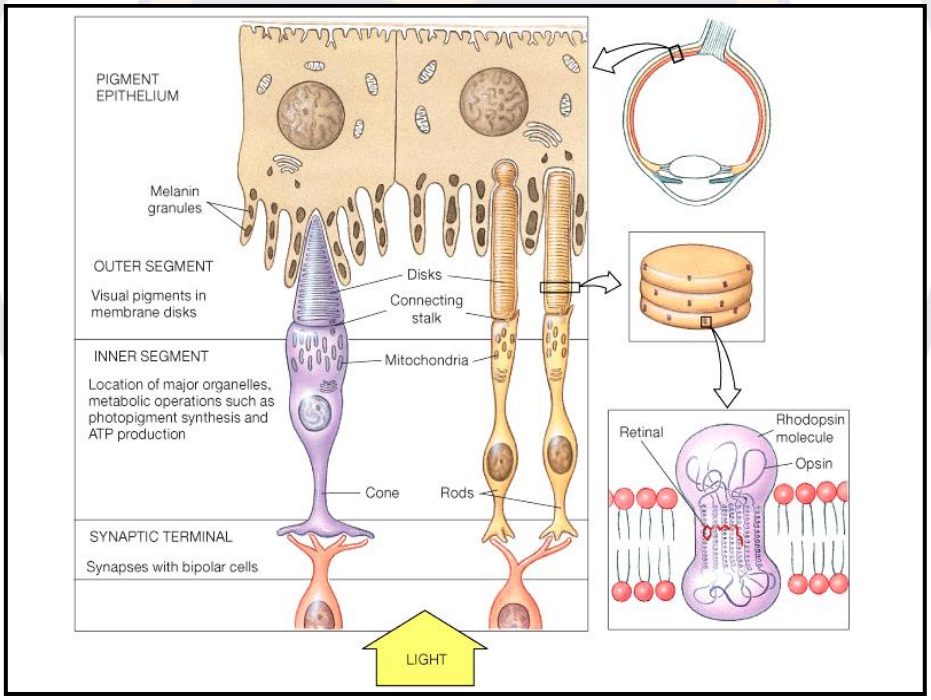


Fig: Structure of pigmented epithelium and photoreceptors (rods and cones)

Special Areas of the Retina (Fundus Oculi)

- **Fundus oculi** is the part of the retina which can be seen by ophthalmoscope.
- It is the only site in the body where arterioles are **readily visible**.
- Examination of the fundus oculi is important for the **diagnosis of diseases affecting blood vessels** (diabetes mellitus and hypertension).
- Special areas of the retina include the **fovea centralis** and **optic disc**.

	Fovea centralis (Macula Lutea)	*Optic Disc (blind spot)*
Site	At the posterior pole of the eye 4 mm lateral to optic disc	It is located 4 mm medial to fovea centralis
Size	The macula is a small yellow area (4.5 mm in diameter). It contains in its centre, an oval depression called the fovea centralis.	It is 1.5 mm in diameter
Structure	The fovea cones are very thin and densely packed	It contains no photoreceptors, so it is a blind spot
Functions	-It is the area of acute vision and it contains only cones **-Fovea is the most sensitive spot in retina because;** 1. All layers are shifted aside leaving outer segments of photoreceptors to be hit directly by light 2. High density of cones 3. 1:1 convergence (cone-bipolar cell –ganglion cell) 4. Wide presentation in occipital primary visual area	It is the site of exit and entry of blood vessels and optic nerves to the retina. **N.B.** Changes in the appearance of the optic disc are important **clinically**, the depression may be **exaggerated** due to loss of ganglion cell axons (optic atrophy) or may be **protruded** because of edema (papilledema) caused by an increase in the intracranial pressure

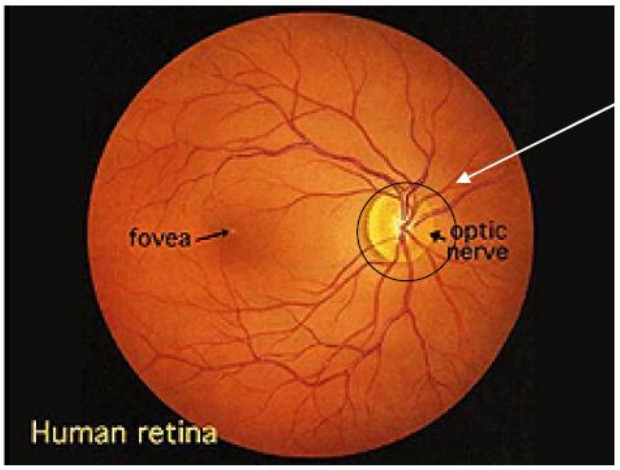


Fig: Fundus oculi shows optic disc and macula lutea.

Phototransduction (Mechanism of Vision)

- It is a process by which light is converted into signals in the rods & cone cells and photosensitive ganglion cells of the retina of the eye.
- **It consists of 4 steps:**
  1. Decomposition of photosensitive pigment in rods & cones
  2. Excitation of the photoreceptors by activated rhodopsin and generation of photoreceptor potential
  3. Termination of excitation
  4. Regeneration of photopigments.

a) Decomposition of photosensitive pigment:

- **Rhodopsin** consists of protein (**scotopsin**) and pigment (**11-cis retinal**).
- **Light** coverts the **angulated 11-cis retinal** to **straight all-trans retinal** → enhance splitting between scotopsin & all-trans retinal, thus rhodopsin is converted to **bathorhodopsin** → **lumirhodopsin** → **metarhodopsin I** → **metarhodopsin II (activated rhodopsin)**.
- **Metarhodopsin II** splits slowly (in seconds) into scotopsin and all-trans retinal by rhodopsin kinase enzyme.

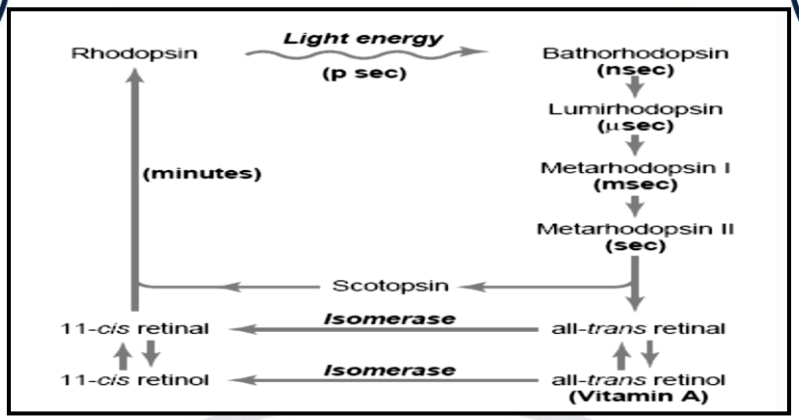


Fig: Breakdown and regeneration of rhodopsin (visual purple cycle).

b) Generation of photoreceptor potential (ionic basis):

In Dark:

- In dark, the intracellular concentration of cGMP is high → open **cGMP dependent cation channels** in the outer segment of the photoreceptor cells.
- **Na^+ (mainly) & Ca^{++} (small fraction)** enter the outer segment & diffuse into the inner segment where it is pumped out.
- The flow of Na^+ between outer and inner segments forms a current flow called **dark current** of about **– 40 mV (depolarization)** → continuous release of synaptic transmitter (**glutamate**) from the synaptic terminals → **hyper polarization of bipolar cells** by opening of **Cl- channels** → **inhibition of ganglion cells** → no action potentials in optic nerve.

In Light:

The **activated rhodopsin** activates **G- protein transducin** which in turn activates **phosphodiestrase** enzyme→ breakdown of cGMP → closure of **cGMP dependent Na^+ channels** → ↓ Na entry to outer segment (with Na^+ still pumped out of inner segment) → **hyperpolarization** of rod to **-80 mv** → ↓ transmitter (**glutamate**) release in synaptic terminal → **stimulation of bipolar cells** → **excitation of ganglion cells** that respond by generation of action potential in optic nerve → visual pathway.

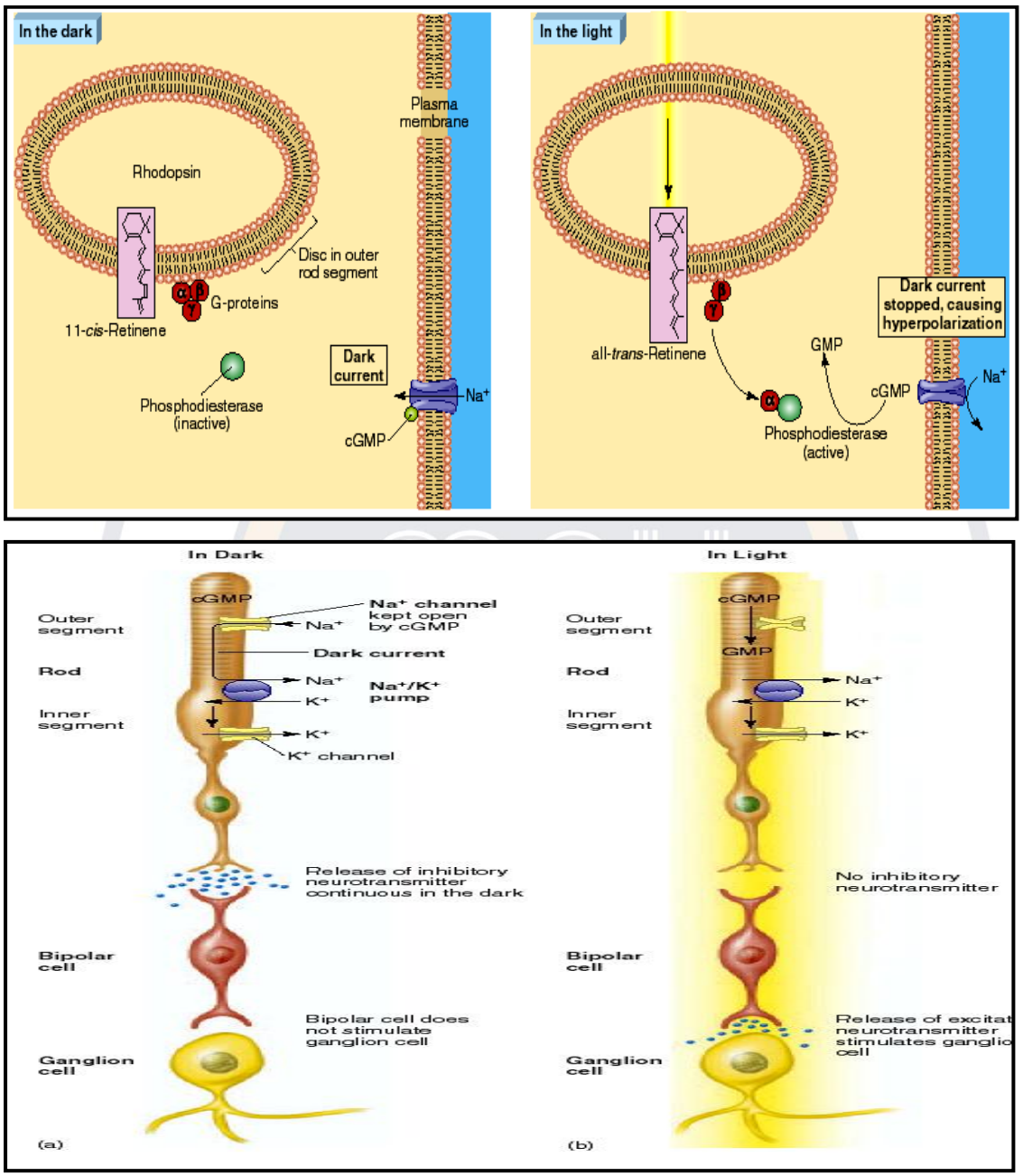


Fig: Mechanism of phototransduction. *In the dark, Na^+ channels in the outer segment are held open by cGMP. Light leads to increased conversion of cGMP to 5´-GMP, and some of the channels close. This produces hyperpolarization of the synaptic terminal of the photoreceptor and decrease in release of inhibitory chemical transmitters.*

c) Termination of excitation:

Within a second the activated rhodopsin is inactivated by the enzyme rhodopsin kinase → reversal of all reactions → regeneration of cGMP → reopening of Na^+ channels → termination of excitation.

d) Regeneration of photopigment:

- **All-trans retinal** is taken up by **pigmented epithelium** where it is converted to **11-cis retinal** by **isomeraze** then sent back to rods to recombine with **opsin**.

Duplicity Theory of Retinal Function

☒ This theory states that **retinal function is double in nature depending on the properties of its 2 photoreceptors**.

☒ It assumes the existence of **2 different inputs from the retina** (one from rods & the other from the cones) to the CNS, each input works maximally under a different condition of illumination.

☒ Cones are used for bright day light (**photopic vision**) while rods are used for dim night light (**scotopic vision**).

	Photopic Vision	Scotopic Vision
Receptors	Cones	Rods
Site	Central part of the retina	Peripheral part of the retina
Threshold	Is high	Is low
Sensitivity to light	Low	High
Accuracy	High (can perceive the fine details of the object)	Less (cannot perceive the fine details of the object)
Colour vision	Can perceive colours	Cannot perceive colours
Adaptation	Is rapid	Is slow

Retinal Adaptation

***Def:** Change in the retinal sensitivity according to the intensity of light. So, retinal sensitivity increases in dark and decreases in light.

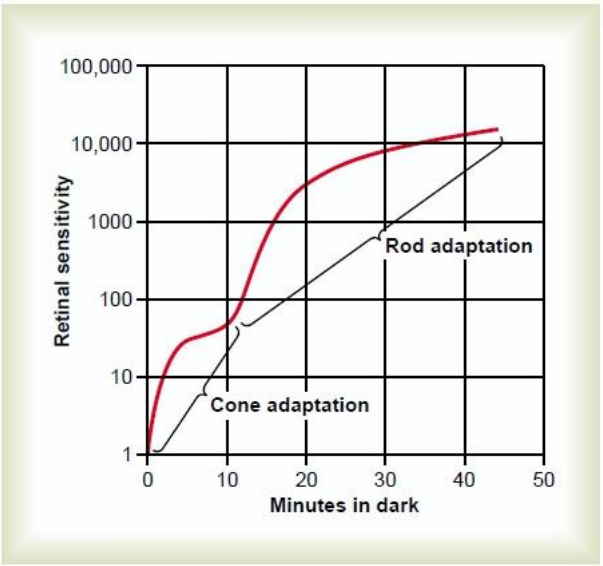
***Types:**

I- *The Dark adaptation:*

- It is the ability of the retina to become **more sensitive to faint light**.
- **When a person enters a dark room** after being previously exposed to bright light, he cannot see anything at the start in spite of the rapid pupillary dilatation. **After a few minutes**, he becomes accustomed to the dark and can see well, i.e. the retina become more sensitive to light.
- Dark adaptation is a **slow process** during which **regeneration** of the photosensitive pigments (rhodopsin and iodopsin) occurs.
- When the dark adaptation becomes complete **after about 30 minutes**, the sensitivity of the retina increases by 10,000 - 100,000 times.
- **Dark adaptation occurs in 2 phases:**

A) Cone adaptation: due to regeneration of **iodopsin** ➔ a slight increase in the retinal sensitivity and completed within **5 minutes**.

B) Rod adaptation: due to regeneration of **rhodopsin** ➔ a marked increase in the retinal sensitivity and completed within **30 minutes**.



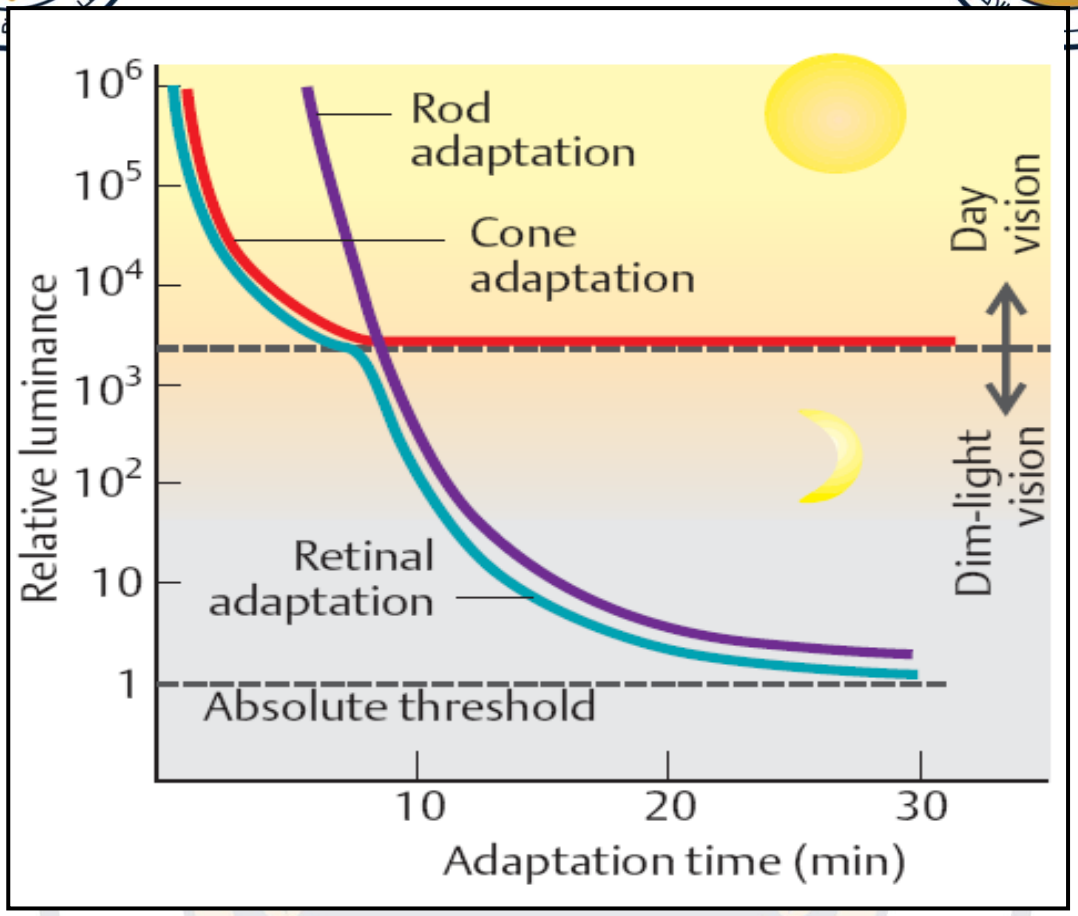


Fig: Dark adaptation.

➢ Changes occurring during the dark adaptation

1- **Dilatation of the pupils** which allows more light to enter the eye and stimulates more rods.

2- **Regeneration of the pigments** in the rods and the cones which increases the retinal sensitivity to the dim light.

3- **Decreased visual acuity** so that the fine details and colours of the object cannot be seen.

II- The Light Adaptation:

- It means a **decrease in the retinal sensitivity** which occurs in bright light.
- **When a person moves from a dark place to bright light**, at the start even moderate light seems to be very intense and uncomfortable.
- **After about 5 minutes**, this sensation disappears due to the decrease in the retinal sensitivity, which results from degeneration of the photosensitive pigments (rhodopsin and iodopsin).

➢ Changes occurring during the light adaptation

1- **Constriction of the pupils** (miosis) to reduce the amount of light entering the eye.
2- **Breakdown of the pigments** in the rods and cones, so photopigments are decreased.
3- **Decrease in the retinal sensitivity** due to a parallel decrease in the amounts of the photosensitive pigments of the rods and cones.

Binocular Vision

***Def:** It is the ability to see an object with 2 eyes without double vision (diplopia).

*Requirements of binocular vision:

a. The visual fields must **overlap** to a great extent.
b. A nearly **normal refractive power** in both eyes.
c. Intact neuromuscular apparatus that allow the eyeball to move so that both images of the object fall at the **corresponding points** of both retinae.
d. **Intact visual cortex** where fusion of images occur.

*Fusion and corresponding points:

- The 2 images of an object (one from each retina) are **fused at the level of 1ry visual area** (17) into a single image.
- The retinal points at which the images of an object must fall to be seen as a single image are called the **corresponding points**. They are located at the **nasal side** of one retina and the **temporal side** of the other retina.
- The **foveae centralis** of both eyes are the **normal corresponding points**.

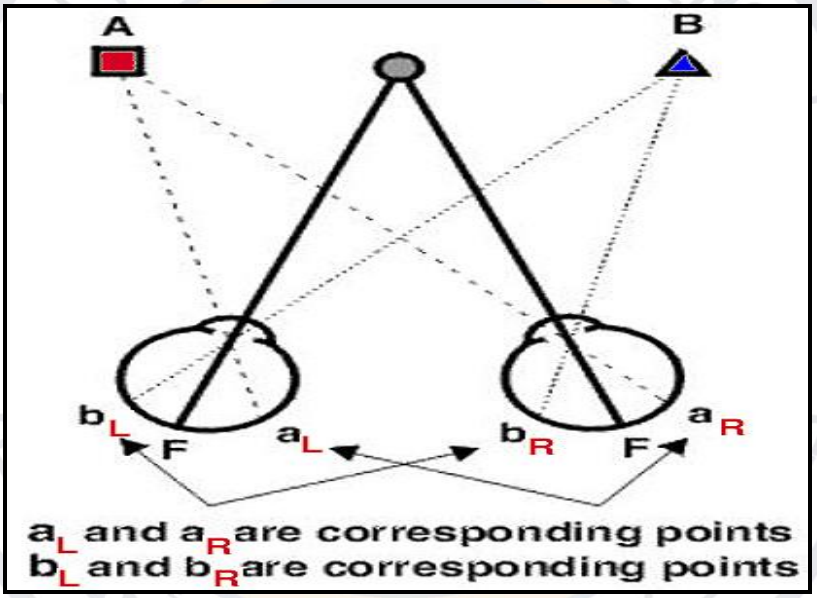


Fig: Corresponding points on retina on both sides. F means fovea centralis

*Advantages of binocular vision:

1. It **increases the visual field horizontally** from 160 to 200 degrees.
2. It **corrects the minor defects** in one eye by the other eye **e.g.** blind spot of one eye is corrected by the other eye.
3. **Stereoscopic vision** (3 dimensions of object height, width, and depth). It can be perceived by **monocular vision** but it is better recognized by **binocular vision** (due to the more accurate perception of depth).
4. It **improves the depth perception**.

Depth Perception

***Def:** It is the ability to known the **relative distance of the objects** from the eyes. It is principally a **monocular property** but it becomes more accurate by **binocular vision**.

***Monocular depth perception:**

- The perception of depth depends on the following factors

1. The relative **sizes** of objects.
2. The **occlusion of part of a distant object** by a nearer one.
3. The **fade of the colours and details of distant objects** as their distances from the eyes are increased.
4. **Parallel lines** appear to **converge with distance**.
5. **Movement parallax:** the nearer objects appear to move in the opposite direction and distant objects move in the same direction.

The Visual Pathway

The **photoreceptors** (rods and cones) stimulate **bipolar cells** (**1st order neuron**) which, in turn, stimulate the **ganglion cells** (**2nd order neuron**), the axons of which form the **optic nerve**. The optic nerve reaches the **optic chiasma**, where the nasal fibers cross to the opposite side while the temporal fibers pass in the same side to form the optic tract (ipsilateral temporal fibers + contralateral nasal fibers of retina). The fibers of optic tract terminate on **lateral geniculate body** in the thalamus from which the fibers of the **optic radiations** (**3rd order neuron**) arise and terminate on the **visual cortex** in the occipital lobe (1ry and 2ry visual areas).

N.B.

The optic tract fibers terminate on:

a. ***Lateral geniculate body*** ***(LGB)***

b. ***Pretectal nucleus*** in the midbrain (center of pupillary light reflex).

c. ***Superior colliculus*** in midbrain (center of visuo-spinal reflex).

d. ***Suprachismatic hypothalamic nucleus*** for control of circadian rhythm.

Role of Different Parts of Visual Pathway in Visual Perception

1) Retinal cells: They start the **analysis of the visual image**.

a. Photoreceptors (rods and cones): transmit signals to the **bipolar cells**.

b. Role of Bipolar cells:

- They constitute direct pathway between **photoreceptors** and **ganglion cells**.
- They release excitatory chemical transmitter **glutamate**.

c. Role of Ganglion cells:

- They are about **1.6 millions cells**.
- They are the only retinal neurons that respond to stimulation by a full action potential i.e. depolarization which is conducted by optic nerve to brain.

- **Types:**

	1- Magnocellular (M) (10%):	2- Parvocellular (P) (80%):	3- Coniocellular (10%):
Size	large	small	medium
Responsible for	gross analysis of visual image & location of objects in visual field and motion	fine detailed vision (shape & texture) and colour vision	controlling pupillary reflexes

- **Functions of ganglion cells:**

1. Detection of 2 point discrimination in the visual scene
2. Detection of the contrast in the visual scene
3. Detection of the movement and its orientation in the visual scene
4. Colour analysis

2) Lateral Geniculate Body (LGB)

- It is a thalamic relay nucleus that present at the dorsal end of thalamus
- It consists of C-shaped **6 defined layers**.
- **Layers 1, 2** receive from large M ganglion cells → magnocellular division.
- **Layers 3, 4, 5 & 6** from small P ganglion cells → parvocellular division.
- **Layers 2, 3, 5** → receive signals from ipsilateral retina.
- **Layers 1, 4, 6** → receive signals from contralateral retina.

Functions of LGB:

1. It plays a part in **fusion of retinal images** from the 2 eyes.
2. It plays a part in **stereoscopic vision** by comparing the visual images from both eyes and detection of minimal differences.
3. **Magnocellular neurons** are concerned with **perception of white and black shape and motion**.
4. **Parvocellular neurons** are concerned with **perception of color vision and accurate point-point spatial information**.

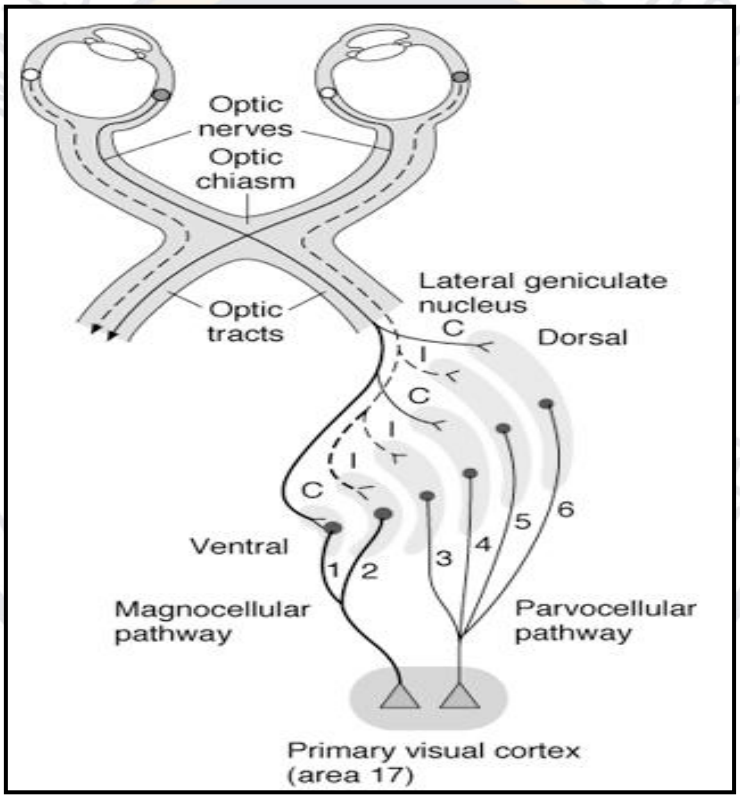


Fig: Ganglion cell projections from the right hemiretina of each eye to the right LGB and from LGB to the right primary visual cortex. *Note the six layers of the geniculate. P ganglion cells project to layers 3-6, and M ganglion cells project to layers 1 and 2.*

3) Visual cortical areas

• They are present in the occipital lobe and include areas 17,18, and 19;

1ry Visual Area (area 17)

***Site:**

- It surrounds the calcarine fissure on the occipital lobe
- Its neurons arranged in the form of columns forming 6 distinct layers.

***Representation of retina in area 17:**

- **Peripheral part of retina** is represented in **anterior** part
- **Macula** is represented in **posterior** part
- **Upper part** of retina is resented **above** calcarine fissure
- **Lower part** of retina is represented **below** the calcarine fissure

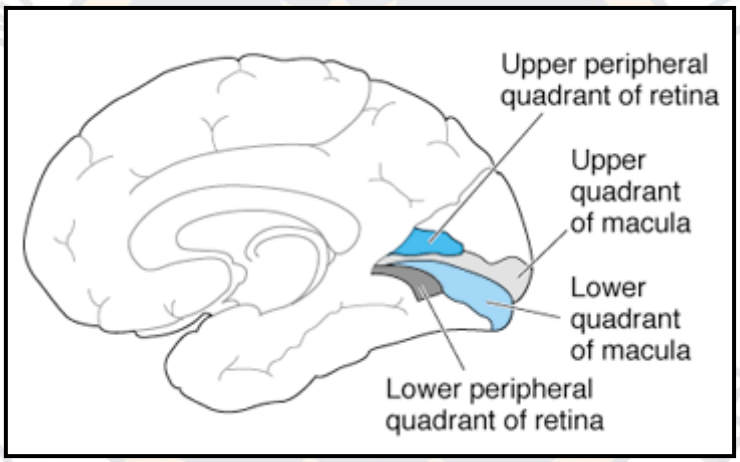


Fig: Primary visual area

***Functions of area 17:**

1. Perception of the visual sensations without understanding the meaning of the images.
2. Perception of the colours.
3. Fusion of the 2 images formed on both retinae.
4. Perception of luminosity.

2ry Visual Areas (areas 18 and 19)

***Site:**

- They lie on the occipital lobe around 1ry visual area and extend to the parietal & temporal lobes

***Functions:**

Area 18: (visuopsychic area) which is concerned with;

a. Recognition the nature of the objects and correlates their colours
b. Interpretation of visual sensations
c. Localization of object in space i.e. depth perception

Area 19: (occipital eye field area).

a. It shares area 18 its functions.
b. It controls the different types of eyeball movements.

Lesions in visual pathway:

- **Lesion in optic nerve:** ***Blindness*** of the corresponding eye.
- **Lesion in optic chiasma:**
  - **Central lesion: Bitemporal hemianopia** (loss of temporal halves of visual fields) due to injury of the nasal fibers in the centre of optic chiasma.
  - **Peripheral lesion: Binasal hemianopia** (loss of nasal halves of visual fields) due to injury of temporal fibres in the periphery of optic chiasma.

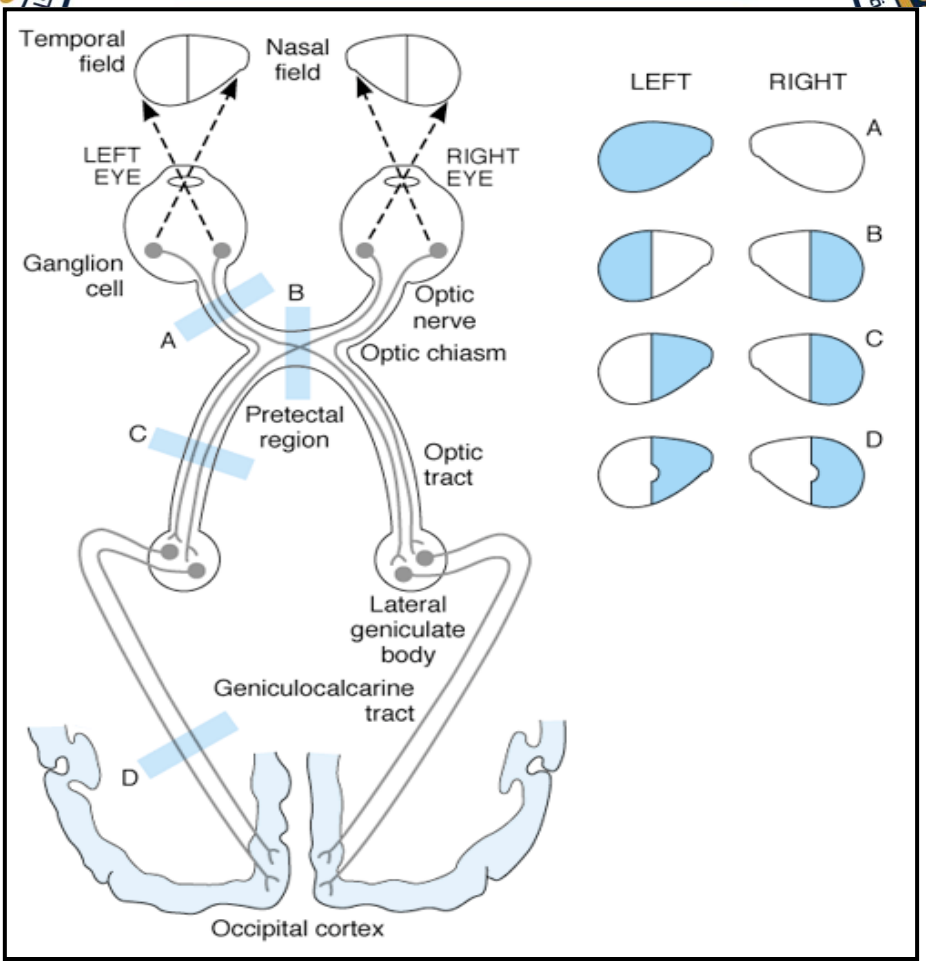


Fig: Visual pathway and its lesions.

- **Lesion in optic tract:** ***Contralateral homonymous hemianopia*** (loss of corresponding halves of visual fields in the opposite side of the lesion) due to injury of same side temporal fibers and opposite side nasal fibers in the optic tract.
- **Lesion in LGB and optic radiation:** ***Contralateral homonymous hemianopia***.
- **Lesion in 1ry visual cortex:** ***Contralateral homonymous hemianopia with macular sparing.***
- **Lesion in 2ry visual cortex :** ***Visual agnosia*** or word blindness i.e. inability to understanding the meaning of seen object.

Hearing

- The human ear consists of 3 parts:
    a. External ear.
    b. Middle ear.
    c. Inner ear.

A) The External Ear

- The external ear consists of:
    a. Ear pinna.
    b. External auditory meatus.

a. The Ear Pinna (Auricle)

- It is the cartilaginous external flap.

Functions:

a. It **collects and directs** sound waves into the external auditory meatus.
b. **Sound localization**.

b. The External Auditory Meatus

- It is an **oblique tortuous** skin-lined canal of about **2.5cm** length in the **temporal bone**.
- The **tympanic membrane** (**ear drum**) exists at the end of the canal and completely **separates** the external ear from the middle ear.

Functions:

1. It **conducts and concentrates the sound waves** to the tympanic membrane.
2. It produces **resonance** which **amplifies the sound** and increases its pressure at the ear drum.
3. **It protects the tympanic membrane:**
    a) From external trauma by being **long and tortuous**.
    b) From entrance of foreign bodies or insects by **hairs and the wax**.
    c) From growth of microorganisms because the **wax is of acidic pH and contains**

lysozymes and immunoglobulins.

4. It **<u>maintains the proper temperature and humidity of the air inside</u>**, which is essential for the proper function of the ear drum.

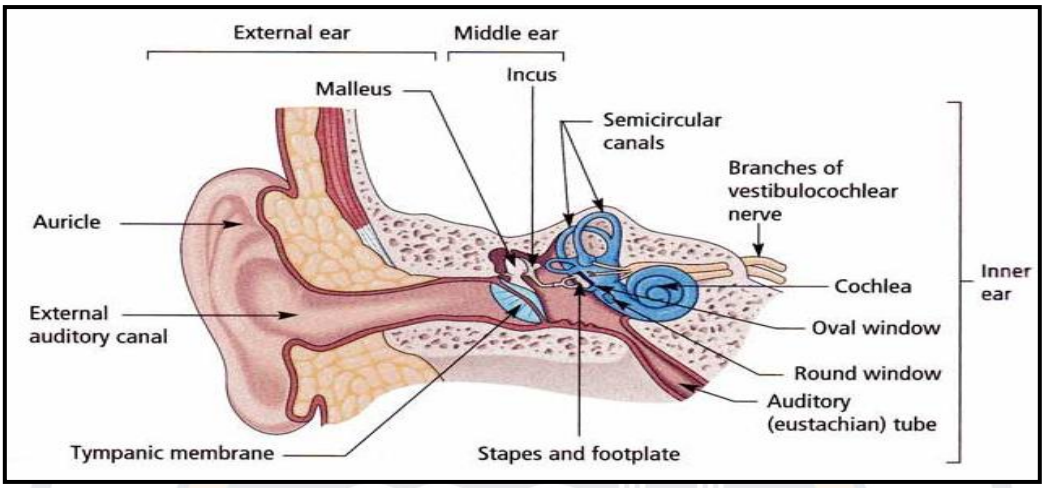


Fig: External ear, middle ear and inner ear.

B) The Middle Ear

*Anatomy of Middle Ear:

- It is an **<u>air-filled cavity in the temporal bone</u>**.
- **<u>It contains</u>**;
  - ❖ **<u>3 bony ossicles</u>**; the malleus (hammer), incus (anvil), and the stapes (stirrup).
  - ❖ **<u>2 skeletal muscles</u>**; the tensor tympani muscle (supplied by the 5th cranial nerve) and the stapedius muscle (supplied by the 7th cranial nerve).
- It is **<u>bounded by the tympanic membrane</u>** on lateral side and the **<u>oval and round windows</u>** on the medial side.
- It is connected with the naso-pharynx by the **<u>Eustachian tube</u>**.

<u>*Functions of Middle Ear:</u> Transfer sound from the external ear to inner ear.

1) The Tympanic Membrane

- It is a **thin semi-translucent** membrane, **conical** in shape with its **concavity** directed **laterally**.
- Its surface area is about **55 mm^2** and its thickness is about **0.1 mm**.

Functions:

1. It **acts as a resonator** that reproduces the vibrations of the sound source i.e. vibrates in and out according to the frequency and intensity of the sound introduced.
2. It is **highly damped** i.e. its vibration stops when the applied sounds stop, this prevents the unnecessary sound prolongation.
3. It is **aperiodic** i.e. it has no natural frequency, but takes up the characteristics of the vibrations applied on it.

2) Function of the Ossicular System (Amplification and Impedance Matching)

- The **transmission** of sound waves from **air** in the external ear to **endolymph** in the inner ear results in a **great loss of energy**.
- **More than 97% of a sound's energy** would be reflected at the surface of water (i.e. sound of loud speaker would be lowered to just whisper).
- **This impedance sound transmission can be matched by 2 mechanisms:**

1) The areal ratio of the tympanic membrane and the oval window:

- The surface area of the **drum (55 mm^2)** is about **17 times** greater than that of the **foot plate of the stapes (3.2 mm^2)**.
- This areal ratio produces an amplification sound waves about **20-fold** at the oval window.

2) The lever system of the bony ossicles:

- The bony ossicles are arranged in such a manner that they function as a **series of levers**. The **handle of the malleus is about 1.3 times that of long process of the incus**. This lever action of the malleus and incus increases the force of movement

of the stapes about **1.3 times**.

- ***The lever action of ossicles and areal ratio of the tympanic membrane and oval window*** amplify the sound pressure at the oval window about ***22 times***.

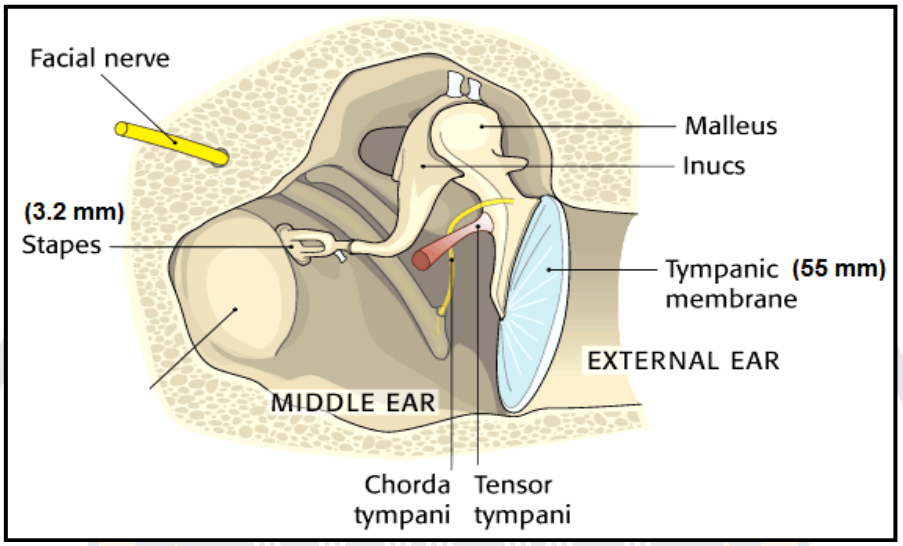


Fig: The bony ossicles of the middle ear act as a lever system.

3) Role of the round window in sound transmission

- The **oval window** opens into the **scala vestibuli** and the **round window opens into the scala tympani.**
- **If sound waves strike the two windows simultaneously** (as that occur when the transformer action of the middle ear is not present) ➔ the effect could be the same as that produced by making equal pressure on the two ends of an open U tube filled with water **i.e**. there would be no displacement of fluid, this is called **cancellation effect**.
- In intact ear, sound energy is applied to the **ear drum** whose vibrations are transmitted to the **ossicular bones** to the oval window then through the **scala vestibuli** and **scala tympani** to the **round window**.
- Therefore, when there is **condensation phase**, at the oval window there will be **rarefaction phase** at the round window i.e. the two windows vibrate reciprocally in

response to sound energy.

- So the round window serves as **a relief hole** in the bony cochlea.

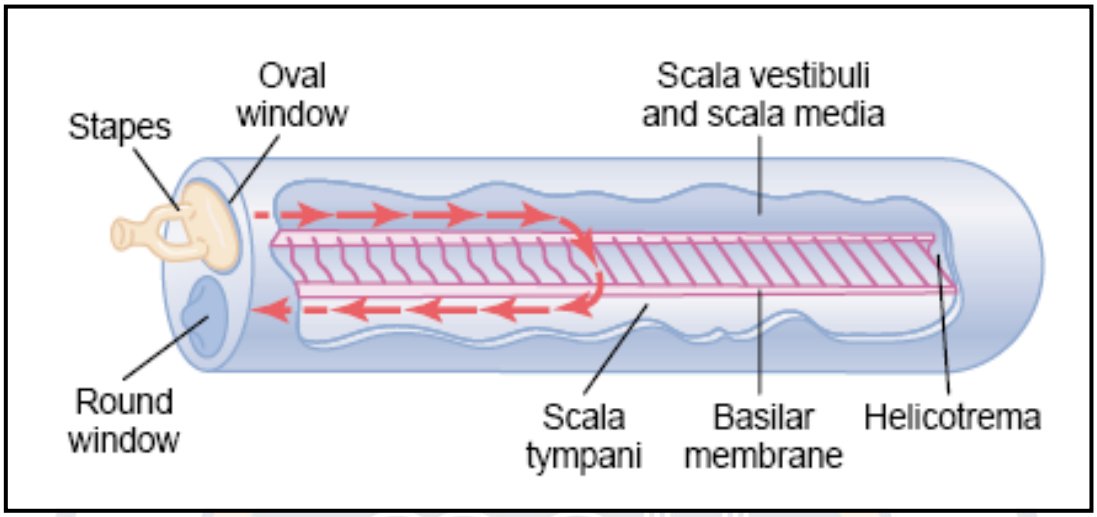


Fig: The round window acts as a relief hole in the bony cochlea.

4) Eustachian Tube

- It connects the **middle ear** with the **nasopharynx**.

Functions:

1. It **equalizes the pressure on both sides of the tympanic membrane**.

- **Normally** the tube is **closed** but it opens during swallowing, chewing, yawing, blowing the nose, and sneezing.
- **If the tube is continuously opened➔** the sounds of breathing and talking will produce noise and interfere with normal hearing.
- **If the tube is continuously closed** (as in common cold)➔ the air in the middle ear will be absorbed ➔ a negative pressure in the middle ear ➔ sucking of the tympanic membrane inwards ➔ limitation of its movement and ↓ hearing.

2. **Continual renewal of air in the middle ear**.

Otitic Barotrauma:

- ✓ ***During ascent of an airplane****, the external pressure ↓ & the Eustachian tube is closed to equalize the pressure on both sides of the drum.*
- ✓ ***During rapid descent of an airplane****, the external pressure ↑ and pushes the drum inwards and may rupture it unless the person swallows.*

5) Tympanic (attenuation) reflex

(Functions of middle ear muscles)

***Def:** This is a reflex contraction of both tensor tympani and stapedius muscles in response to sounds of high intensity and low frequency (above 80 dB and below 1000 Hz).

***Mechanism:**

- The **tensor tympani** muscle pulls the **handle of the malleus inward** while the **stapedius muscle** pulls the **stapes outward**.
- These two forces cause the entire ossicular system to develop a **high degree of rigidity** and **greatly reduce the transmission of loud sound**.
- This reflex has a **long latent period** (about **40 m.sec**).

***Importance of attenuation reflex:**

1. It **protects the cochlea from the damaging vibrations caused by very loud sound** which is usually of low frequency. The effect of the reflex is **not complete** because of its **long latent period**.
2. It **masks low frequency sounds in loud environments i.e**. it provides selective attenuation of low frequency sounds so ***removes a major part of the background***

noise and allows a person to ***concentrate on sounds above 1000 Hz***.

3. It **decreases the person's hearing sensitivity to his own speech**, (this effect is activated by collateral signals transmitted to these muscles during speech).

C) The Inner Ear

- It is situated in the **petrous portion of the temporal bone**.
- **It consists of 2 parts:**
  a. **The cochlea**, which is the organ of hearing.
  b. **The vestibular apparatus**, which is concerned with posture & equilibrium.

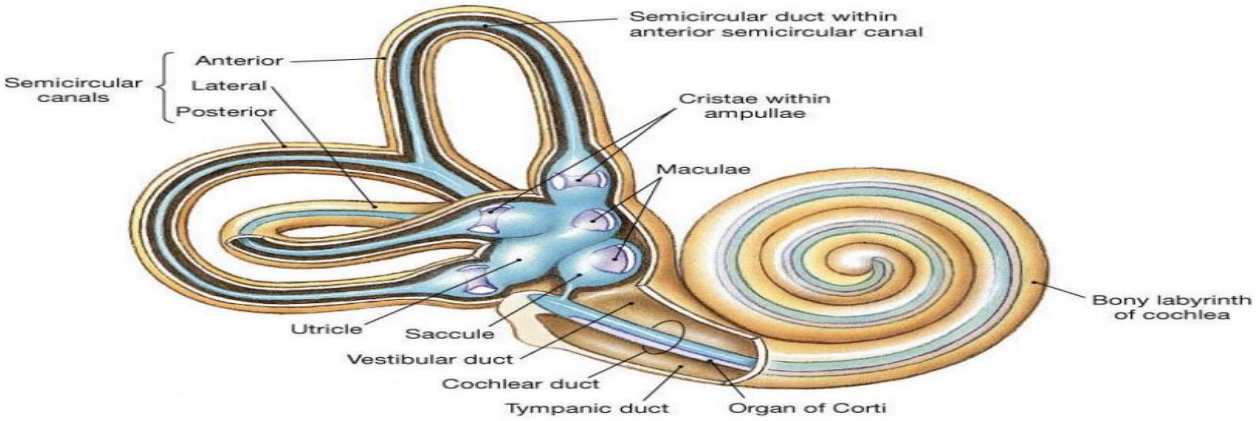


Fig: inner ear

The Cochlea

- The cochlea is a **coiled bony tube** about **3.5 cm long** that makes **2 and half turns** around bony axis called **modiolus**.
- It starts by a **broad base** to a **narrow apex**.
- **The cavity of the cochlea is divided by 2 membranes**, vestibular and basilar **into 3 compartments (or scalae):** scala vestibuli, scala media, and scala tympani.
- **The scala media or endocochlear duct** is filled with **endolymph** which is similar

to **intracellular fluid** and it ***ends at the apex*** of the cochlea as a blind sac.

- **Both scala vestibuli and scala tympani** contain perilymph which is similar to **extracellular fluid** and ***communicate with each other at the apex*** of the cochlea.
- **At the base of the cochlea**, the scala vestibuli ends at the **oval window** which is sealed by the **footplate of the stapes** while the scala tympani ends at the **round window** which is closed by a flexible membrane called **"2ry tympanic membrane"**.
- **The vestibular membrane** is a thin membrane, moves easily and transmits the vibrations from scala vestibuli to scala media.
- **The basilar membrane** is a fibrous membrane and carries the "Organ of Corti".
- **It contains** about ***25.000 basilar fibers*** that project from the ***modiolus*** toward the ***outer wall of the cochlea***.
- **The basilar membrane** fibers have special **gradual change in length, diameter and stiffness** as they go from base to apex. **At the base**, they are short, thick a stiff whereas **at the apex**, they are long, thin and lax with gradual change in between.

The Organ of Corti

*** Def:** It is the sense organ of hearing.

*** Site:** It lies on the basilar membrane, extending in a spiral shape from the base to the apex of the cochlea.

*** Structure:** It consists of:

1) Receptor cells (hair cells): are of 2 types

a. Outer hair cells:

- They are about **20000 cells** and form **3-4 rows**.

- They control the **sensitivity of inner ear for different sound pitches**.

b. Inner hair cells:

- They are about ***3500 cells*** and form ***single row.***
- They are important for the ***detection of sound***.

✓ ***Both types*** are separated by the ***arches of the tunnel of Corti*** (***rods of Corti***).
✓ The ***hair-bearing end of the hair cells*** are held firmly together by a rigid membrane called the reticular lamina which by its turn is ***supported on the rods of Corti***.
✓ The ***bases and sides of the hair cells*** are surrounded by a network of ***cochlear nerve endings***.

2) Supporting cells (phalangeal cells).

3) Tectorial membrane: a flap of gelatinous elastic tissue which rests on the top of the cilia of the hair cells.

4) Nerve fibers: the peripheral branches of cochlear nerve synapse with the hair cells.

The nerve fibers cross the tunnel of Corti to reach the spiral ganglion which lies in the modiolus of the cochlea.

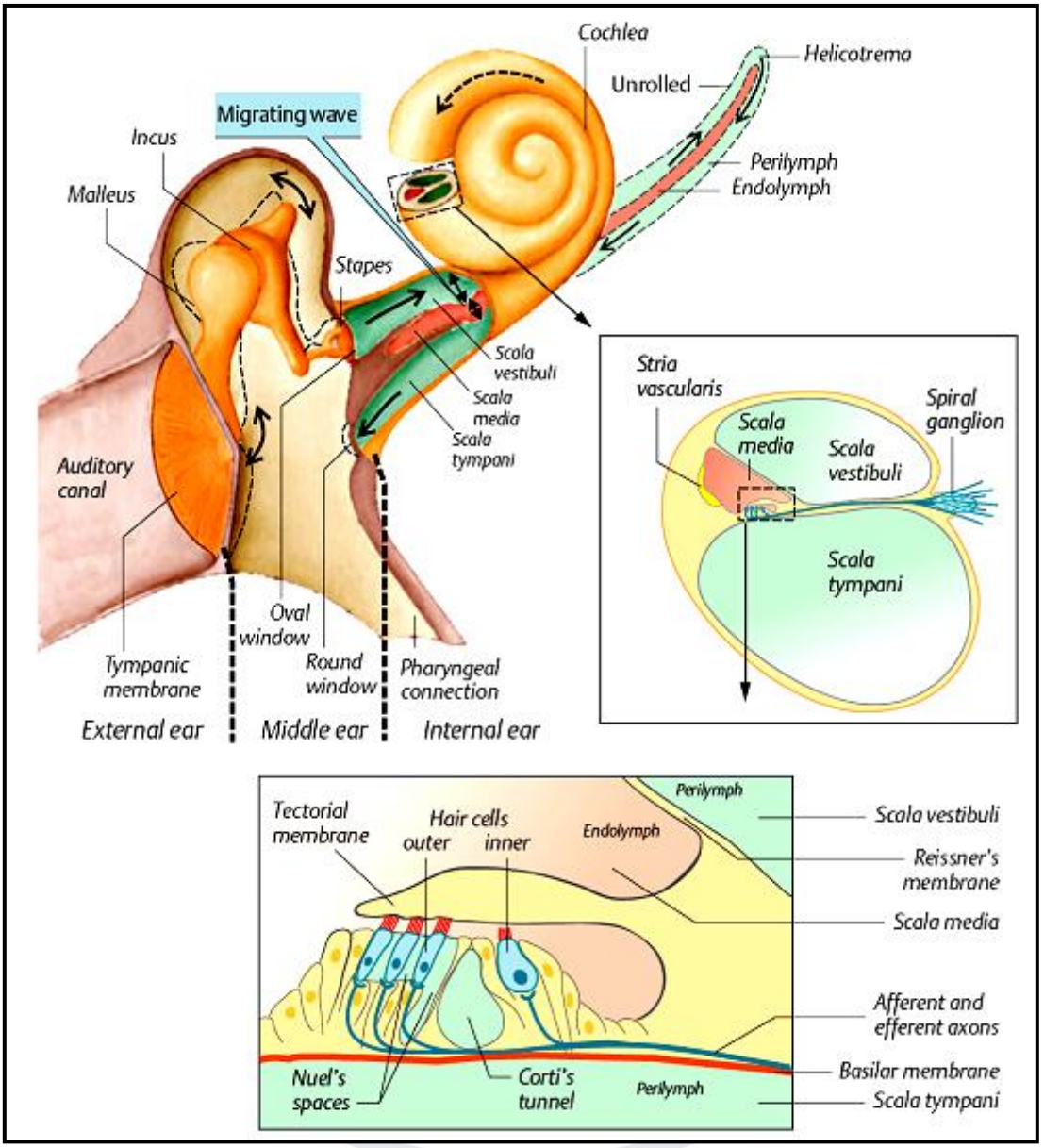


Fig: Structure of Cochlea and organ of Corti

Auditory Hair Cells

* They are **mechanoreceptors** that are specialized to **detect movement**.

* Structure:

- The cells have a **hair bundle** projecting from the apical end and **synaptic contacts** with cochlear nerve fibers at their basal ends.
- The **hair bundle** consists of a **large one** on one side of the bundle (**kinocilium**) while the **others** are falling away in height to the opposite side (called **stereocilia**).
- Within the bundle, **stereocilia are connected** one to the next with very fine elastic **protein filaments** called **"tip links"**, but they can slide with respect to each other as the bundle is deflected side to side.

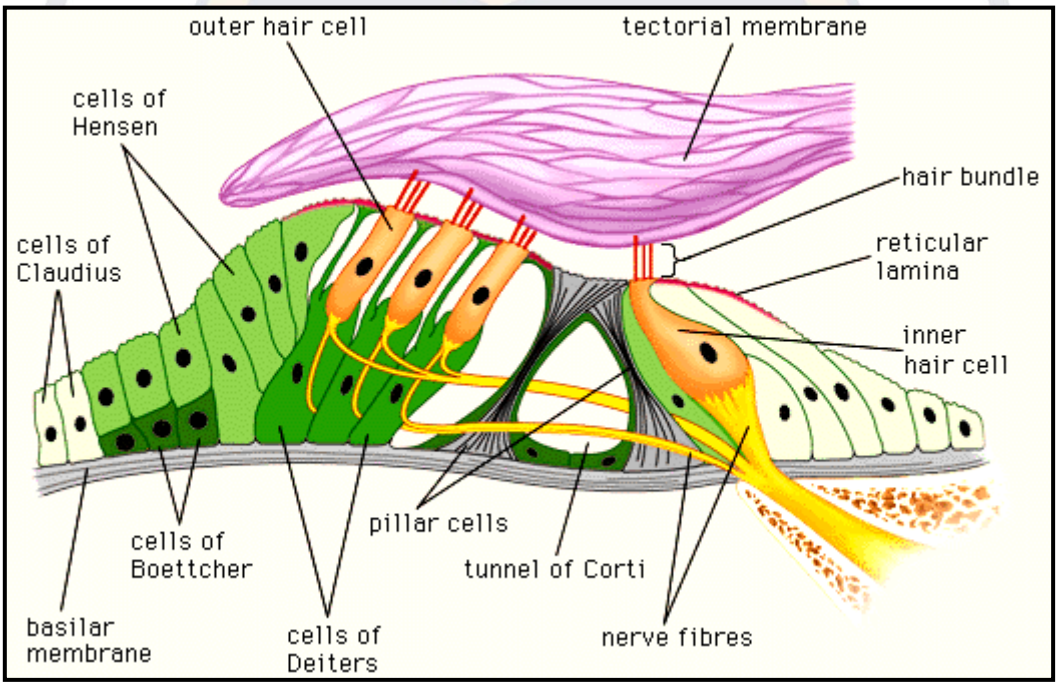


Fig: Structure of the organ of Corti, (in the basal turn of the cochlea).

*** Mechanism of stimulation of hair cells:** (See later; generation of receptor potential in hair cells).

Mechanism of Hearing

Hearing occurs in the following steps:

1) Transmission of sound waves in the outer and middle ear:

- The ear pinna **collects and directs** the sound waves toward the external auditory canal.
- Sound waves cause **vibrations of the tympanic membrane** at the same frequency.
- Movements of the **tympanic membrane** are transmitted and amplified by the **bony ossicles** of the middle ear to the **oval window** via the footplate of the stapes.

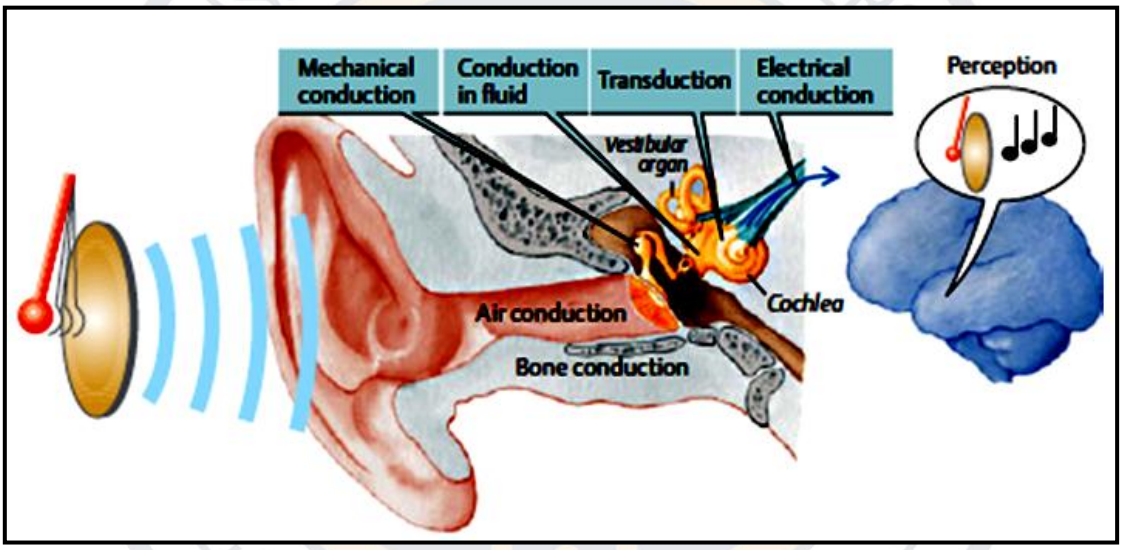


Fig: Conduction of sound waves in the ear.

2) Transmission of sound waves in the cochlea (the traveling wave):

- This occurs in the form of **traveling wave** in the basilar membrane.
- **Inward movement of the footplate** of stapes increases the pressure in the scala vestibuli.
- This results in **displacement of the cochlear membranes** (vestibular and basilar) towards the scala tympani increasing its pressure and causing the round window to bulge in the middle ear.
- Rapid movements of the tympanic membrane in response to sound waves ➔ **traveling waves** that move in the basilar membrane from base to apex.

3) Receptor potential and generation of cochlear nerve impulse:

- **Up and down movements of the basilar membrane** create a shearing force in the tectorial membrane ➔ **depolarization or hyperpolarization** of the receptor cells.
- Because **endolymph** which surrounds the **apex of the hair cells** has a higher concentration of K^+ than that inside the hair cells, the opening of **K^+ channels at the apex** of the hair cells causes **depolarization** whereas its **closure** causes **hyperpolarization**.
- **Bending of the stereocilia toward the kinocilium** opens the apical channels ➔ K^+ influx ➔ cellular depolarization ➔ activation of Ca^{2+} channels, opening them ➔ Ca^{2+} influx ➔ release of an excitatory transmitter, probably glutamate ➔ stimulation of the postsynaptic terminals of the sensory neurons.
- **Bending of the stereocilia away from the kinocilium** closes the apical channels ➔ cellular hyperpolarization ➔ inhibition of Ca^{2+} channels and release of chemical transmitter.
- **Thus**, **hyperpolarization and depolarization** of hair cells alter the rate of impulse discharge along the cochlear nerve.

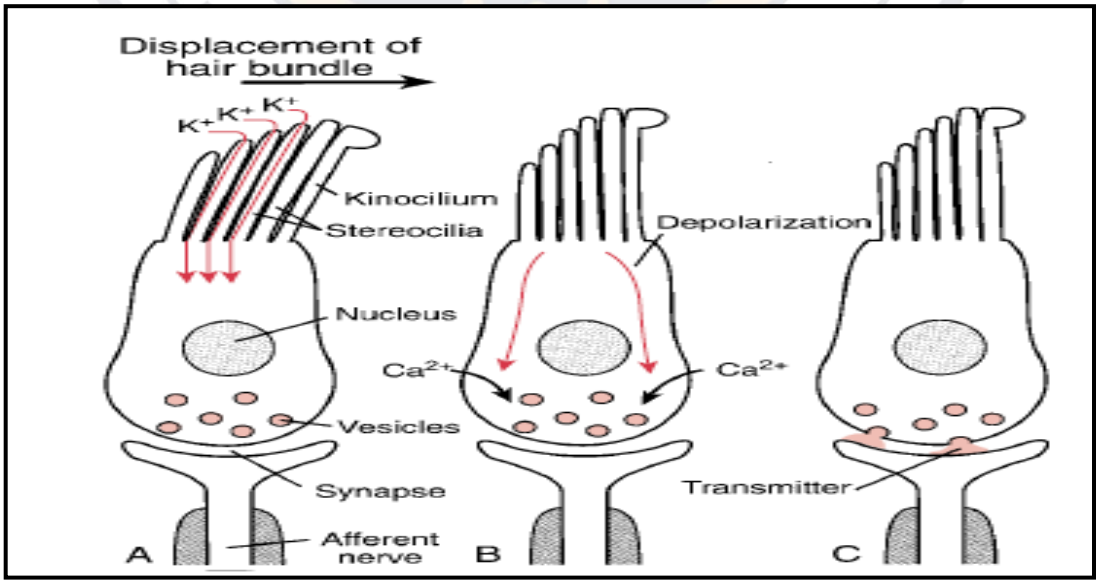


Fig: Mechanism of activation of cochlear hair cells.

The Auditory Cortex

	A) Primary auditory area (areas 41 & 42):	B) Secondary (associated) auditory area (area 22):
Site:	The upper part of temporal lobe.	Surrounds the primary area.
Receive impulses from:	-Both ears through fibers from the ipsilateral MGB. - **Anterolateral part** receives impulses from **apex** of cochlea (**low pitched** sounds) and **posteromedial part** receives impulses from **base** of the cochlea (**high pitched** sounds).	the primary auditory area
Functions:	-Perception of pitch, amplitude, and sound pattern without understanding its meaning. -Perception of the source of the sound.	-Interpreting& understanding the meaning of sounds.
Lesion:	- Bilateral damage ➔ greatly reduces the capacity for hearing -Unilateral damage ➔ slightly reduces hearing of the opposite ear	-The person will be unable to interpret the meaning of the heard sound **(auditory aphasia or word deafness).**

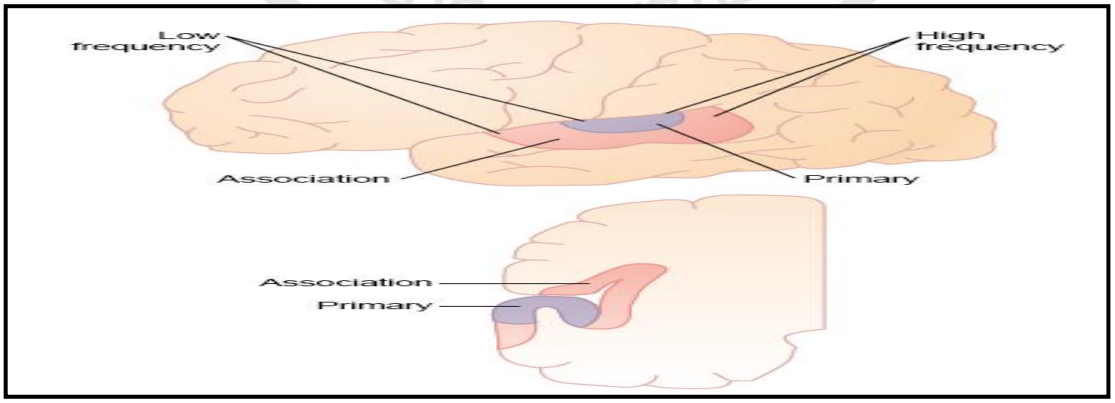


Fig: Auditory cortex

Taste Sense (Gustation)

*Basic Taste Modalities:

There are **five basic tastes:** sweet, sour, bitter, salt, and umami. Further tastes are due to **combination of these 5 basic modalities**.

1) Sour Taste:

- It is **caused by** acids, and the intensity of this taste sensation is proportional to the H ion concentration.
- It is **tasted by** edges of the tongue.

2) Salty Taste:

- It is **elicited by** ionized salts, mainly by the sodium ion and to less extent by Cl ions.
- It is **tasted by** anterior part of the dorsum of the tongue.

3) Sweet Taste:

- It is **elicited by** organic chemicals e.g. sugars, alcohols, aldehydes and ketones.
- It is **tasted by** the tip of the tongue

4) Bitter Taste:

- ❖ It is **caused by** alkaloids e.g. quinine, caffeine, strychnine, and nicotine.
- It is **tasted by** the back of the tongue

5) Umami Taste:

- Umami (=delicious) designate a pleasant taste sensation that is different from sour, salty, sweet, or bitter.
- Umami is the dominant taste of food containing **L-glutamate** (particularly monosodium glutamate, MSG), such as meat extracts and aging cheese.
- It is tasted by all parts of the tongue.

*Gustatory Receptors (Taste Buds):

- Site of taste buds:

- Taste buds are **oval structures** present in:

a) Lateral walls of :

- ✓ ***Fungiform papillae*** which are present in **tip and edges of tongue**
- ✓ ***Circumvallate papillae*** which are present in **V-shaped area** in the back of the tongue

b) Mucosa of palate, epiglottis and pharynx

- **Filliform papillae** which present on the dorsum of the tongue **do not contain taste buds**.
- The adult man has about **10,000** taste buds that start to **decrease after the age of 45years**.

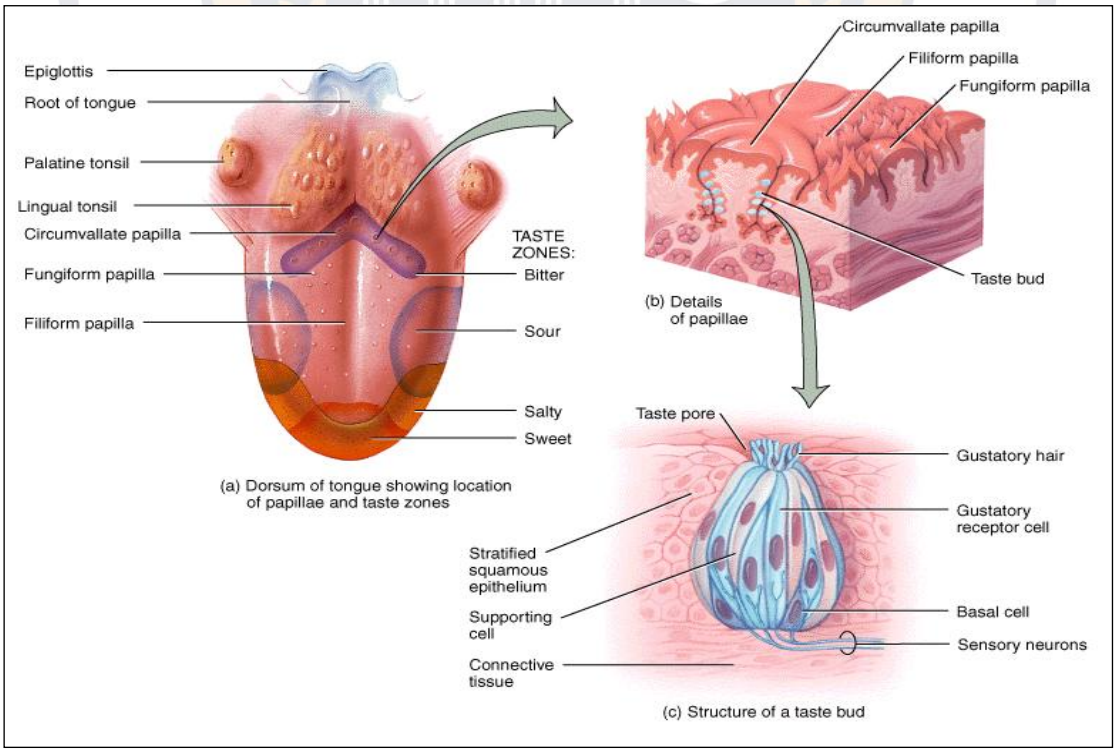


Fig: Different taste modalities and different areas of the tongue receiving them.

- Structure of taste buds:

- **Each bud is formed of 3 types of cells:**

a. ***Supporting cells.***

b. ***Gustatory receptor cells:***

  - They are **modified epithelial cells**.
  - Each taste bud contains **50-150 receptor cells**.
  - They are **long cells** with their upper poles containing cilia that project from the taste pore.
  - **Sensory nerve endings** synapse with their lower poles.
  - Their life span is **1-2 week** (**10 days**), and then they are **degenerated and continuously regenerated from the basal cells**.

c. ***Basal cells:*** They are **stem cells** for production of new receptor cells.

- Mechanism of stimulation of taste buds:

- For a chemical substance (**tastant**) to bind to the taste receptor, it must be in a **solution or dissolved in saliva**.
- **Taste binding protein (TBP)** (produced by **Ebner's glands**) transports the tastant and concentrates it at taste buds.
- Then the tastant binds to its **specific receptors** in the microvilli of gustatory cells ➔ opens or closes ion channels ➔ potential changes in the taste receptor cell and release of the chemical transmitter **e.g**. glutamate which excite the nerve fibers to generate nerve impulses.
- **For each tastant, there is a different mechanism:**

a) Salty taste:

✓ Nacl in food activates epithelial Na channels **(ENaC)** ➔ Na^+ influx (down the electrochemical gradient) ➔ cell depolarization ➔ opening of voltage-gated Ca^{2+} channels allowing Ca^{2+} to enter the cell ➔ triggers the release of the transmitter.

b) Sour tastes:

- ✓ H^+ ions in the food bind to K^+ channels, blocking them, and preventing K^+ from leaving the cell ➔ depolarization➔ opening of voltage-gated Ca^{2+} channels allowing Ca^{2+} to enter the cell ➔ trigger the release of the transmitter.

c) Sweet tastes:

- They bind with a plasma membrane receptor that activates a G-protein called ***"gustatin"***, which stimulates the production of cAMP ➔ phosphorylation of K^+ channels decreasing K^+ leakage out of the cell causing depolarization; which opens Ca^{2+} channels that trigger release of transmitter.

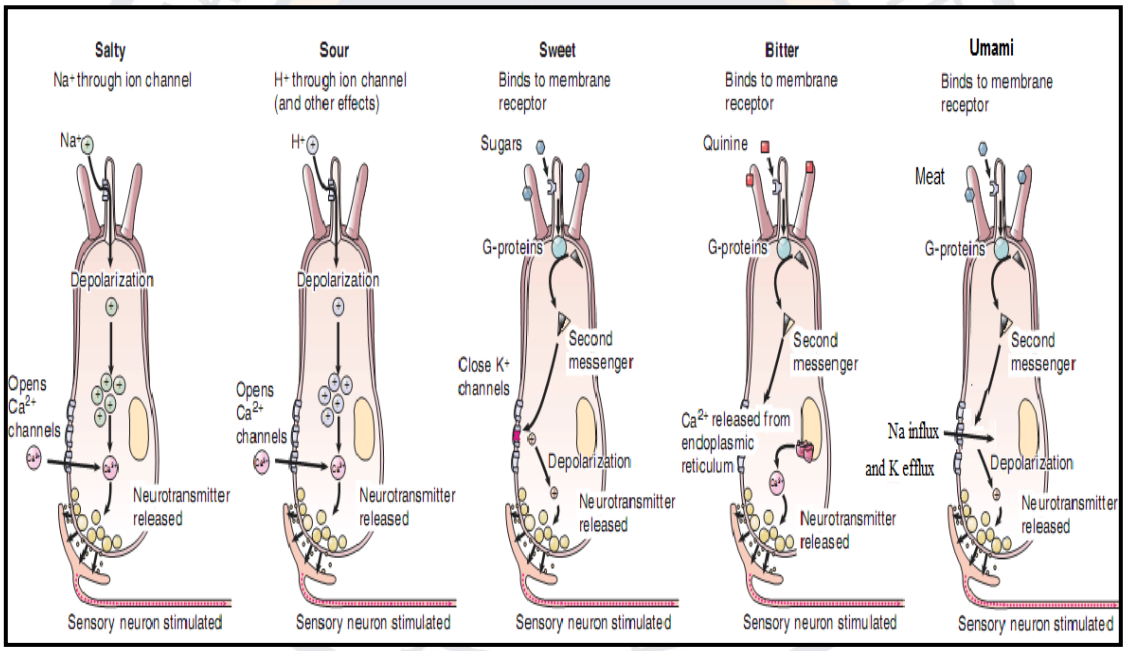


Fig: Mechanism of stimulation of taste receptors by different taste modalities.

d) Bitter tastes:

1- Some compounds (Ca^{2+} & quinine) decrease conductance of K^+ selective channels.

2- Others increase intracellular messenger inositol triphosphate (IP_3) which causes the release of Ca^{2+} from internal storage sites which in turn directly stimulates the release of the neurotransmitter.

e) Umami taste:

It is due to activation of a truncated metabotropic glutamate receptor, **mGluR4.** These receptors allow Na^+ influx & K^+ efflux with the net effect is depolarization which releases the neurotransmitter.

***Taste intensity discrimination:**

- The ability to **discriminate differences in intensity** of taste is **limited.**
- A **30%** change in the intensity of the substance being tasted is necessary before an **intensity difference** can be detected.

*** Specificity of taste receptors:**

- Each taste bud responds to **only one of the 5 primary taste modalities** when the **concentration of tastant is low** (adequate stimulus).
- But **at high concentration**, most taste buds can be excited by **2 or more taste stimuli**. This explains the **great number of tastes** that a person can perceive.

***Adaptation of taste:**

- Taste sensations adapt **rapidly within minutes** in spite of continuous stimulation.
- It occurs in the **CNS itself**. This is **different from most other sensory systems which adapt mainly at the receptors**.

***Significance of Taste:**

1. **Stimulation of GIT secretions** e.g. salivary secretion through unconditioned reflexes.
2. **Prevention of ingestion of most poisons** which have strong bitter taste.
3. **Determination of the flavor of food**.

***Taste Preference:**

- This means the **selection of certain types of food in preference to others**.
- Usually, these types are **needed to the body**.
- In experimental animals it has been found that **adrenalectomised** animals show great preference to **salty water** (containing Nacl) while **parathyroidectomised** animals prefer **Ca^{++} containing water**.
- Taste preference occurs in the **CNS** by unknown mechanism.

***Disturbance of taste sensation:**

1- **Ageusia (taste blindness):** absence of taste sensation for certain substance.
2- **Hypogeusia:** diminished taste sensation
3- **Gustatory hallucination:** False sensation of certain tastes
4- **Dysgeusia:** disturbed taste sensation.

Smell (Olfactory) Sensation

- The olfactory (smell) sensation is a **chemical sense** involving receptors which are sensitive to volatile chemical substances.

Olfactory Mucosa:

- **It is located on** the superior nasal concha and the upper third of the nasal septum.
- **The total area of the olfactory mucosa** in both sides is about 5 cm^2.
- **The olfactory mucosa is distinguished from the surrounding respiratory mucosa by:**
  - Its distinctive yellow-brown pigments
  - The presence of many tubular Bowman's glands
  - The absence of rhythmic ciliary movements that characterize the respiratory mucosa

- **The olfactory mucosa is innervated by:**

a. **Olfactory (cranial I) nerves** which are stimulated by the odorant substances

b. **Branches of the trigeminal (cranial V) nerve** which are stimulated by the **irritative effect of some odors** as peppermint, menthol, and chlorine. They are responsible for **initiating sneezing, lacrimation, respiratory inhibition, and other reflex responses to nasal irritants**.

Structure of olfactory mucosa:

- Histologically olfactory mucosa consists of 3 types of cells and great number of mucus secreting glands (Bowman's glands):

a) Olfactory receptor cells;

- They are **bipolar neurons** which have:

❖ A short thick dendrite with an expanded end called **olfactory rod**. From these rods, **cilia** (**10-20 cilia per neuron**) project to the surface of mucus.

❖ The axons of the olfactory receptor neurons pierce the **cribriform plate of the ethmoid bone** and enter the **olfactory bulbs**.

- Each olfactory mucosa contains **100 million olfactory cells.**
- These olfactory neurons are **continually regenerated throughout life** (their life span is about **60 days**).

b) Supporting cells.

c) Basal cells: They are the stem cells for the production of new receptor cells.

Bowman's glands

They are **small mucus secreting glands** which are interspersed among the cells of olfactory epithelium and secrete a layer of mucus covering the surface of the olfactory membrane.

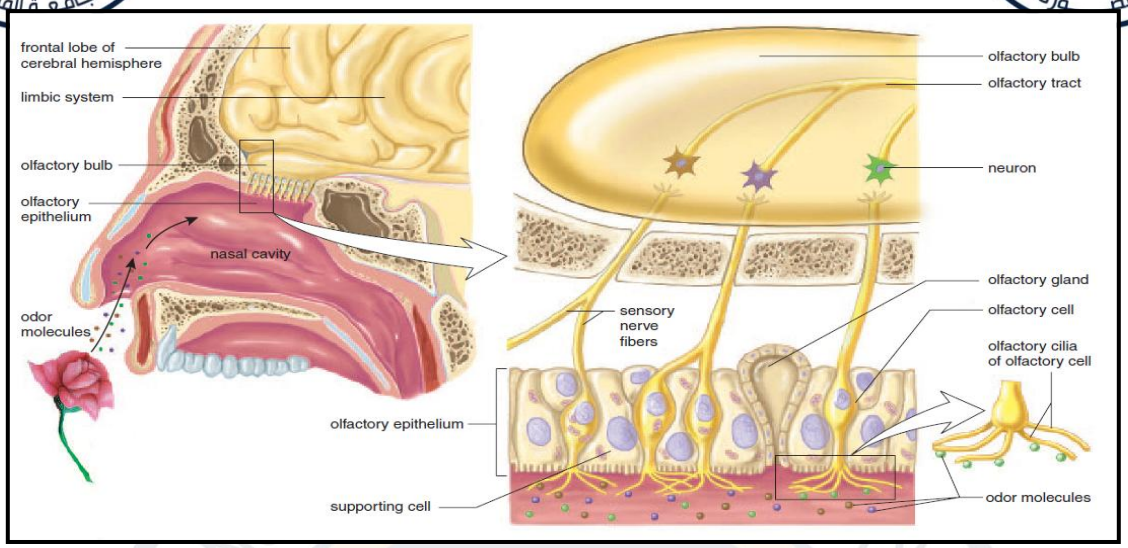


Fig: Organization of the olfactory mucous membrane.

Stimulation of the olfactory receptor:

- ***The odorant substance* must be:**

1. **Volatile** in order to be sniffed into the nose to reach the olfactory receptors.
2. **Sufficiently water soluble** in order to pass through mucous layer coating the mucosa to reach the olfactory cells
3. **Lipid soluble** in order to penetrate the cells membrane of the olfactory cells.

- The olfactory cells are stimulated when **air blasts upwards into the superior region of the nose**. The amount of air reaching this region is greatly increased by **sniffing**.

Mechanism of stimulation of olfactory receptors:

- The odorant substance, on coming in contact with the olfactory mucosa, ➔ first **diffuses into the mucus** that covers the cilia, ➔ then binds with **odorant-binding proteins** (OBP) that trap and concentrate the substances and transfer them to the olfactory receptors.

- The odorant receptors are **G-protein coupled receptors**. The specific G-protein in olfactory receptors is called **Golf** (G-protein in olfactory receptor). Binding the odour to the receptor ➔ activates Golf ➔ stimulates **adenylate cyclase ➔ ↑cAMP ➔ opens Na, Ca channels ➔ depolarization** and generation of receptor potential which at threshold levels will fire an action potential.

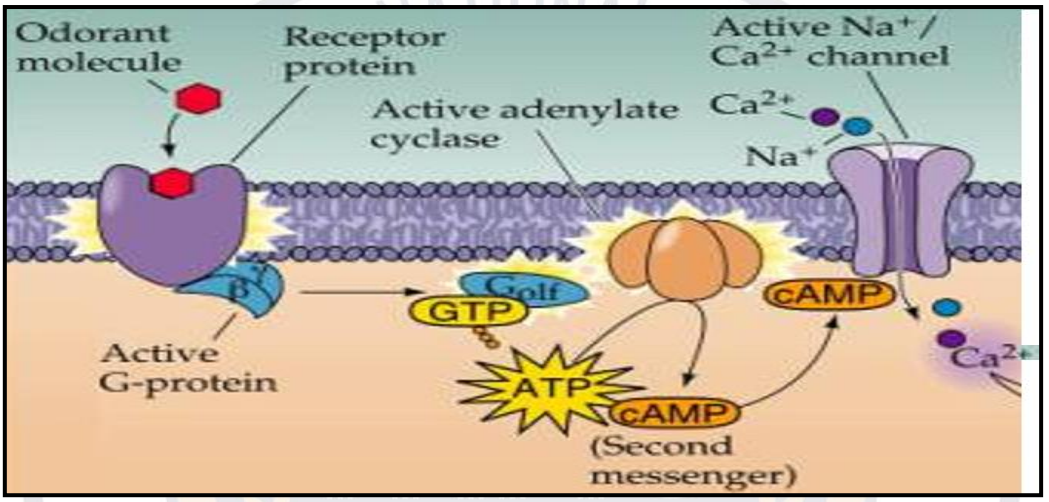


Fig: Mechanism of stimulation of olfactory receptors

Olfactory Cortex:

A) The medial olfactory area:

- The medial olfactory area **consists of** a group of nuclei located in the immediately anterior to the hypothalamus e.g. *septal nuclei*, and portions of limbic system.
- This olfactory area is **concerned with:**

a. **Primitive responses to olfaction**, such as licking the lips, salivation caused by the smell of food.

b. **Primitive emotional drives** associated with smell.

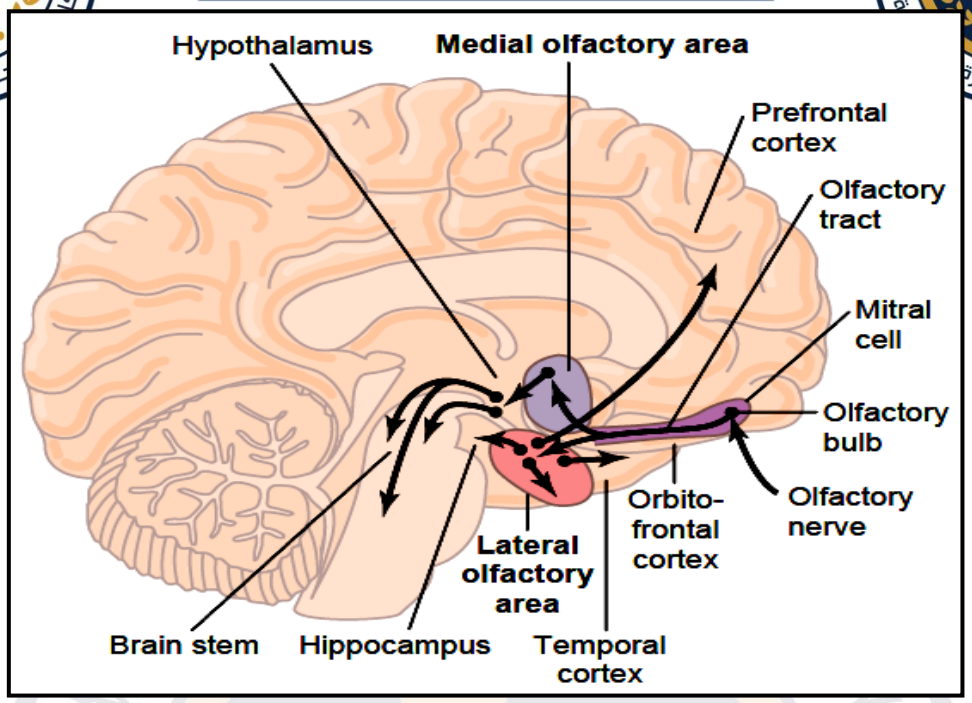


Fig: Neural connection of olfactory pathway

B) The Lateral Olfactory Area:

In the lateral olfactory area, fibers may take one of **2 pathways:**

1) To Prepyriform and pyriform cortex plus the cortical portion of the amygdaloid nuclei.

- From these areas, signal pathways pass into all portions of **limbic system**, especially the **hippocampus**. It is **concerned with:**

a. ***Learning to like or dislike certain foods***.

b. ***Behavioral responses to food*** e.g. development of absolute aversion to foods that have caused nausea and vomiting

c. ***Olfactory conditioned reflexes***.

2) To dorsomedial thalamic nucleus and then project to **orbitofrontal cortex**.

- This system is responsible for the **conscious perception of olfaction** i.e. analysis, interpretation and significance of the odour.

Adaptation of olfaction:

- Adaptation of olfactory receptors is:

❖ **Specific** i.e. it occurs for this odour only and not for the other odours

❖ **Rapid** i.e. occurs within few minutes.

❖ **It is mainly central**.

❖ **Peripheral mechanism** of adaptation is also present and believed to be due to an odorant eating enzymes in the mucus layer

Significance of Smell:

1. **Stimulation of all GIT secretions** e.g. salivary secretion through conditioned reflexes
2. **Determination of the flavor of food** with taste
3. **Selection of the type of food**.
4. **Control of sexual functions** particularly in animals.

Olfactory discrimination:

- The olfactory receptors in man can recognize more than **10,000 different odors**.
- However the determination of **differences in the intensity of any given odor is poor**. The concentration of an odor-producing substance must be changed by about **30%** before a difference can be detected. So the olfactory receptors are concerned mainly with **detection of the presence or absence of the odours** rather than with detection of their intensities.

Disturbance of olfaction:

1) **Anosmia:** means complete absence of the sense of smell
2) **Hyposmia:** means diminished olfactory sensitivity.
3) **Dysosmia:** means distorted sense of smell e.g.
   a. Olfactory hallucinations due to lesion in the prepyriform cortex.
   b. Hypersensitivity for both smell and taste as in Addison disease.

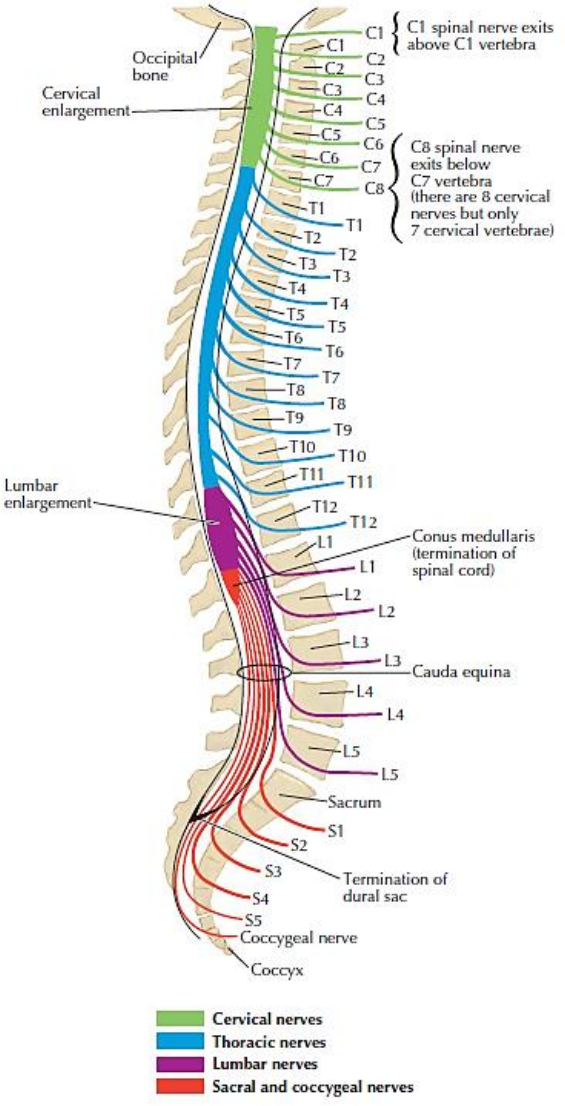
FACULTY OF MEDICINE
MANSOURA NATIONAL UNIVERSITY

ANATOMY

Spinal cord

External features:

- **Length:** 45 cm in the adult male and 42 cm in the adult female.
- **Location:** in the upper two-thirds of the vertebral canal.
- **Begins:** as the continuation of the medulla oblongata just below the foramen magnum at
- the level of the first cervical nerve.
- **Ends:** the lower end of the cord is called the **conus medullaris. It ends at:**
    1. **In the newborn:** at the level of the third lumbar vertebra.
    2. **In the adult:** at the level of the lower border of the first lumbar vertebra. The cause is the differential growth of the vertebral column and the spinal cord.



Enlargements: two

1. **Cervical enlargement: (C5-T1)** in the cervical region & gives origin to brachial plexus.
2. **Lumbar enlargement: (L1-S2)** in the lumbar region & gives origin to lumbosacral plexus.

Fissures and Sulci:

1. **Anterior median fissure:** is a deep fissure on the anterior surface.
2. **Posterior median sulcus:** is a shallow midline groove on the posterior surface.
3. **Anterior lateral sulcus:** one on each side. It marks the attachment of the ventral root.
4. **Posterior lateral sulcus:** one on each side. It marks the attachment of the dorsal root.
5. **Posterior intermediate sulcus:** it separates the gracile tract from the cuneate tract.

Spinal Meninges: dura, arachnoid and pia mater

1. **The dura mater:** is the outer layer and **ends at** the level of the 2nd sacral vertebra (**S2**).
2. **The arachnoid mater:** is the middle layer and **ends at** the level of the 2nd sacral vertebra.
3. **The pia mater:** It is inner layer and **forms two types of ligaments:**

A. Filum terminale:

- ☒ It extends from the conus medullaris to the back of the coccyx.
- ☒ It is divided by the lumbar cistern into filum terminale interna inside the cistern and filum terminale externa outside the cistern.

B. Two denticulate ligaments:

- ☒ They extend from the pia mater between the dorsal and ventral nerve roots to anchor the spinal cord to the dura.
- ☒ The lateral edge is serrated and has 21 processes attached to the dura.
- ☒ They support the spinal cord.

Lumbar Cistern:

- It is the lower part of the **subarachnoid space**.
- It extends from **L2 to S2**.
- It is used for **lumbar puncture**.
- **Contents:**
  - ☒ The CSF.
  - ☒ Cauda equina: roots of lumbar and sacral nerves (dorsal and ventral).
  - ☒ Filum terminale interna.

Arterial supply of the spinal cord

1. **Anterior Spinal Artery:**
   - Is a single artery formed by the union of the two anterior spinal branches of the vertebral arteries. It descends in the anterior median fissure of the spinal cord.
   - It supplies the anterior 2/3 of the spinal cord.
   - It becomes very small below the cervical region & reinforced by radicular arteries
2. **Two Posterior Spinal Arteries:**
   - Each is a branch of the vertebral artery or usually from the PICA.
   - They descend along the dorsal nerve roots (posterolateral fissure).
   - They supply the posterior 1/3 of the spinal cord (dorsal funiculus and horn).
3. **Radicular Arteries:**
   - They are the major source of blood to the lower two-thirds of the spinal cord.
   - They enter the vertebral canal through the intervertebral foramina and divide into anterior and posterior branches which join the anterior & posterior spinal arteries.
   - They are branches from:
     - ☒ In the neck: from the vertebral & ascending cervical arteries.
     - ☒ In the thorax: from the intercostal arteries.
     - ☒ In the abdomen: from the lumbar arteries.
     - ☒ In the pelvis: from the lateral sacral arteries.

Venous drainage of the spinal cord:

- The veins correspond to the arteries and drain into the internal vertebral venous plexus present in the epidural space.

Spinal cord segments

- The spinal cord has **31 segments** corresponding to the number of the spinal nerves: 8 cervical, 12 thoracic, 5 lumbar, 5 sacral and 1 coccygeal segment.
- **Each segment** has a pair of dorsal and ventral nerve roots.
- **The dorsal and ventral roots** join at the intervertebral foramen forming the spinal nerve.

Relation of the spinal nerves to the vertebrae

- Each cervical nerve emerges above its corresponding vertebra: example: C1 nerve emerges above the atlas and C4 nerve emerges above C4 vertebra.
- C8 nerve emerges above T1 and below C7 vertebra.
- All other spinal nerves from T1 downward emerge below the corresponding vertebra.

Internal structure of the spinal cord

- The spinal cord is divided into two halves by the anterior median fissure and posterior median septum.
- Each half is composed of an inner gray matter and outer white matter.
- The two halves are connected by 3 commissures:
  - ☒ White commissure.
  - ☒ Anterior gray commissure
  - ☒ In front of the central canal.
  - ☒ Posterior gray commissure behind the central canal.

Spinal cord white matter

- The white matter is formed primarily of the axons of the nerve cells called tracts.
- It is organized into three funiculi: dorsal, lateral and ventral.
- The name of the tract denotes its origin and termination such as:
  - ☒ Spinocerebellar tract: from the spinal cord to the cerebellum.
  - ☒ Corticospinal tract: from the cerebral cortex to the spinal cord.

Spinal cord gray matter

- The gray matter is H-shaped and contains the nerve cell bodies.
- It is formed of 3 horns on each side:

A. Ventral horns (motor): contains motor neurons.

B. Dorsal horns (sensory): contains four nuclear groups:

- ☒ **Posteromarginal nucleus:** at the tip of the dorsal horn and mediates pain and temperature sensations.
- ☒ **Substantia gelatinosa of Rolandi:** at the apex of the dorsal horn. It is associated with pain & temperature sensation.

- **Nucleus proprius:** in the center of the dorsal horn. It mediates pain, temperature, touch and pressure sensations.
- **Nucleus dorsalis (Clarke's nucleus):** at the base of the dorsal horn and extends from C8 to L2 segments. It is associated with unconscious proprioception.

C. **Lateral horns (sympathetic):** present only in the thoracic & upper lumbar segments from T1 to L2 or L3 segment. It contains the preganglionic sympathetic nerve cells.

Laminae of Rexed

Rexed divided the gray matter into 10 zones called **laminae of Rexed** (lamina I to X):

- **Lamina I:** is the posteromarginal nucleus.
- **Lamina II:** is the substantia gelatinosa.
- **Lamina III & IV:** is the nucleus proprius.
- **Lamina V:** is the neck of the dorsal horn.
- **Lamina VI:** is the base of the dorsal horn.
- **Lamina VII:** Clarke's nucleus and the lateral horn.
- **Lamina VIII:** Commissural nucleus **Lamina IX:** the ventral horn.
- **Lamina X:** Grisea centralis (Glial cells around the central canal).

Brain stem

Medulla oblongata

- The medulla is the lower part of the brainstem and continues downwards as the spinal cord.

Features of the ventral surface

A. 3 Elevations:

on each side of the midline. From the medial to the lateral side:

1. **Pyramid:** contains the corticospinal tract. In the lower part, 85% of the corticospinal fibers cross to the opposite side forming the pyramidal decussation.
2. **Olive:** oval elevation formed by the underlying inferior olivary nucleus.
3. **Inferior cerebellar peduncle:** it connects the medulla with the cerebellum.

B. 3 Fissures:

1. **Anterior medial sulcus:** in the midline.
2. **Preolivary fissure:** between the pyramid and olive.
3. **Postolivary fissure:** between the olive and inferior cerebellar peduncle.

C. Exit of the last 4 cranial nerves:

1. **Glossopharyngeal, vagus and cranial accessory nerves:** in the postolivary fissure.
2. **Hypoglossal nerve:** exits in the preolivary fissure.

Features of the dorsal surface

A. Lower part of the medulla: it shows 3 elevations on each side of the midline**:**

1. **Gracile tubercle (clava):** medial and formed by the gracile nucleus.
2. **Cuneate tubercle:** middle and formed by the cuneate nucleus.
3. **Tuberculum cinereum:** lateral and formed by the spinal trigeminal nucleus.

B. Upper part of the medulla: lower part of the floor of the 4th ventricle

1. **It is divided into 3 trigones by sulcus limitans (inferior fovea):**
   - ☒ **Hypoglossal trigone:** medial, formed by the hypoglossal nucleus.
   - ☒ **Vagal trigone: middle, formed by the dorsal motor nucleus of the vagus.**

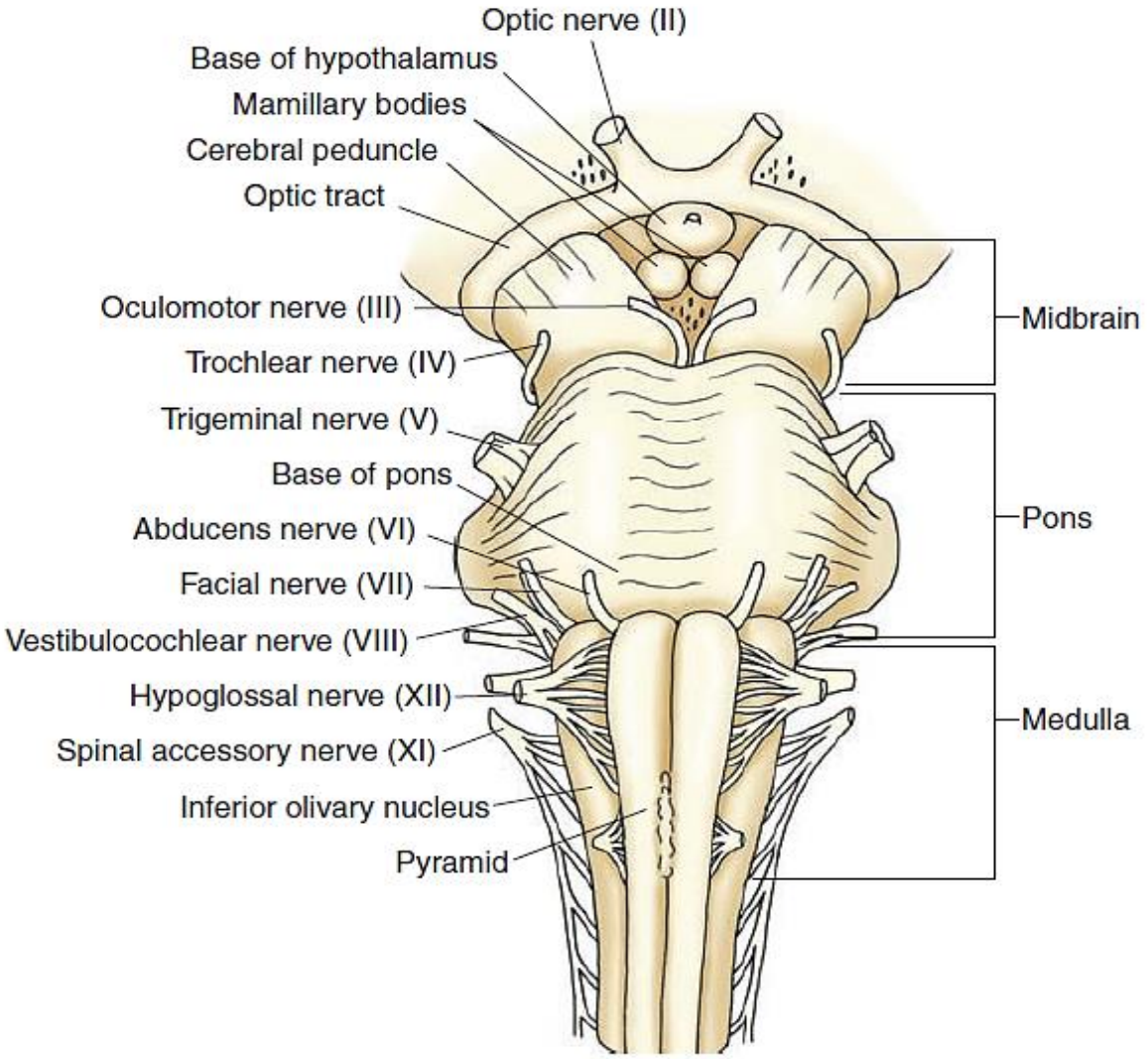
- **Vestibular trigone:** lateral, formed by the medial & inferior vestibular nuclei.

2. **Area postrema (vomiting center):** at the lower angle of the 4th ventricle (obex).
3. **Stria medullaris of the 4th ventricle:** band of fibers at the upper end of the medulla.

Arterial supply:

The medulla is supplied by branches of the vertebral artery:

1. **Medial part:** by the anterior spinal artery.
2. **Intermediate part:** by small medullary branches from the vertebral artery.
3. **Posterolateral part:** by the posterior inferior cerebellar artery (pica).
4. **Gracile and cuneate tracts and their nuclei:** by the posterior spinal artery.



The pons

- The pons is the **middle** part of the brainstem.
- It lies between the midbrain and medulla.
- It is divided into anterior part called **basis pontis** and posterior part called **tegmentum**.

Features of the ventral surface

A. Basilar groove: in the middle. It lodges the basilar artery.

B. Transverse pontine fibers: they form the middle cerebellar peduncle, which connects the pons with the cerebellum.

C. Exit of the middle four cranial nerves:

1. **Trigeminal nerve:** exits midway between the upper and lower borders of the pons near the middle cerebellar peduncle. It consists of two roots:
   - ☒ Small medial motor root
   - ☒ Large lateral sensory root.
2. **Abducent nerve:** exits in the groove between the pyramid and the pons.
3. **Facial nerve:** exits in the cerebellopontine angle. It consists of 2 roots:
   - ☒ Medial motor root: is large
   - ☒ Lateral sensory root: is small and called nervus intermedius.
4. **Vestibulocochlear nerve:** exits in the cerebellopontine angle lateral to the facial nerve.

D. Cerebellopontine angle: junction of the medulla, pons and cerebellum. It contains:

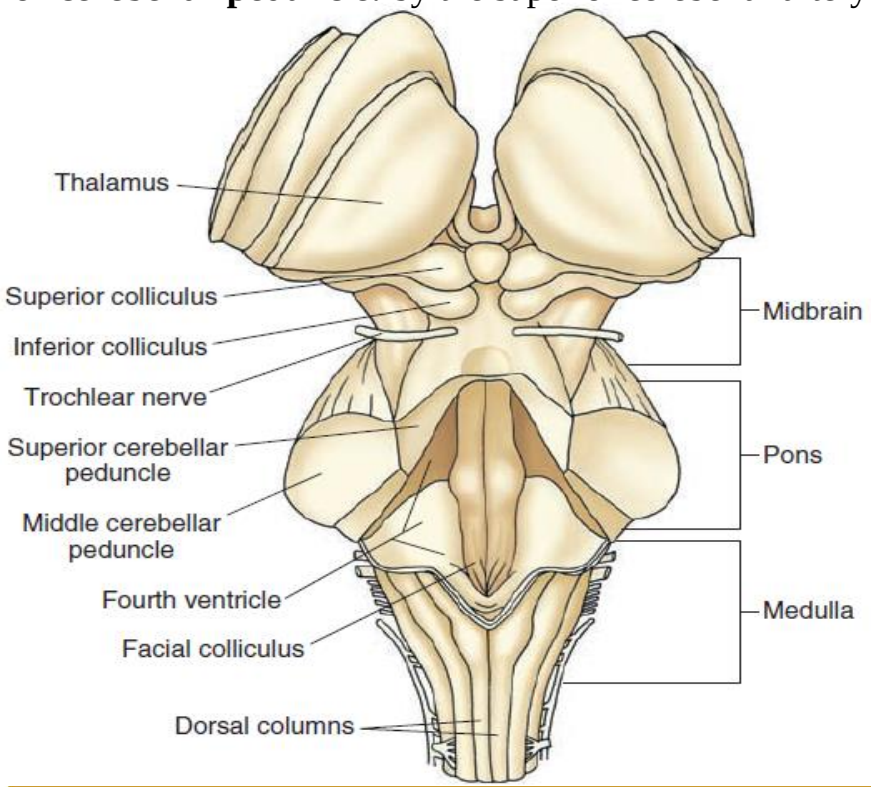
1. **Cranial nerves:** facial, vestibulocochlear, and glossopharyngeal nerves.
2. **Lateral recess and foramen of luschka of the 4th ventricle.**
3. **Choroid plexus** of the 4th ventricle protruding into foramen of luschka.
4. **Aica** (anterior inferior cerebellar artery).

Features of the dorsal surface

- It forms the upper part of the floor of the 4th ventricle.
- It is bounded on each side by the superior cerebellar peduncle.
- It contains:
  - **A. Medial eminence:** medial. It contains the facial colliculus at its lower end, which is produced by the abducent nucleus and the encircling facial nerve fibers.
  - **B. Sulcus limitans (superior fovea):** middle. It contains a small, pigmented area at its upper end called locus ceruleus, which is a noradrenaline-secreting center.
  - **C. Vestibular area:** lateral. It is produced by the superior and lateral vestibular nuclei.

Arterial supply: by pontine branches of the basilar artery:

1. **Anterior part (basis pontis):** by the paramedian and the short circumferential branches
2. **Posterior part (tegmentum):** By the long circumferential branches.
3. **Middle cerebellar peduncle:** by the anterior inferior cerebellar artery **(aica).**
4. **Superior cerebellar peduncle:** by the superior cerebellar artery.



The midbrain

- The midbrain is the **upper** part of the brainstem.
- It lies between the pons and the diencephalon.
- It is connected with the cerebellum by **the superior cerebellar peduncle**.
- It contains a **cavity** called the **cerebral aqueduct of Sylvius** which divides the midbrain into 2 parts:
  - **Anterior part:** called cerebral peduncle.
  - **Posterior part:** called tectum.

Features of the ventral surface:

A. two cerebral peduncles: Each is divided into 3 parts:

1. **Crus cerebri:** the anterior part.
2. **Substantia nigra:**
   - The middle-pigmented part.
   - It contains melanin pigment.
   - It secretes dopamine.
3. **Tegmentum:** the posterior part.

B. Interpeduncular fossa: a depression Between the two cerebral peduncles.

C. Occulomotor nerve exits from the interpeduncular fossa medial to the crus cerebri.

Features of the dorsal surface (tectum)

A. Four colliculi (corpora quadrigemina): are 4 rounded elevations:

1. **Two superior colliculi:**
   - Are visual reflex centers.
   - Are connected with the **lateral geniculate body** by the superior brachium.
2. **Two inferior colliculi:**
   - Are auditory reflex centers.
   - Are connected with the **medial geniculate** body by the inferior brachium.

B. Trochlear nerve: exits from the tectum just below the inferior colliculus.

Features of the lateral surface

A. **Superior brachium (brachium of the superior colliculus):** connects the superior colliculus with the optic tract and the lateral geniculate body **(part of the thalamus).**
B. **Inferior brachium (brachium of the inferior colliculus):** connects the inferior colliculus with the medial geniculate body **(part of the thalamus).**
C. **It is related to 5 structures around the crus cerebri:** 2 arteries, 2 nerves, 1 vein
   1. Posterior cerebral artery.
   2. Superior cerebellar artery.
   3. Trochlear nerve.
   4. Optic tract.
   5. Basal vein (Rosenthal's vein).

Arterial supply:

- **Mainly by:** the posterior cerebral artery
- **Assisted by:** the superior cerebellar artery and the posterior communicating artery.

Clinical note:

- **Obstruction of the cerebral aqueduct:** causes hydrocephalus.
- **Lesion of the substantia nigra:** causes Parkinson's disease.
- **Occlusion of the posterior cerebral artery causes:**
  - ☒ weber s syndrome or
  - ☒ Benedikt s syndrome.

The cerebellum

- It is separated from the cerebrum by the tentorium cerebelli.
- It is separated from the pons and medulla by the cavity of the 4th ventricle.

Gross features:

- It consists of a central part called **vermis** and **two cerebellar hemispheres.**
- The cerebellar hemisphere has many gyri called **folia** separated by deep fissures.
- The vermis: is divided into superior and inferior vermis:

A. **The superior vermis** is present on the superior surface**.**

B. **The inferior vermis:** present on the inferior surface in a groove called **the vallecula.**

- ☒ Formed of **4 lobules**: nodule, uvula, pyramid and tuber, from before backward.
- ☒ The nodule is continuous with the flocculus.
- ☒ The uvula is continuous with the cerebellar tonsil.

Notches: the cerebellum has 2 notches:

A. **Anterior notch:** surrounds the brainstem**.**

B. **Posterior notch:** contains the falx cerebelli**.**

Peduncles: 3 cerebellar peduncles:

A. **Superior cerebellar peduncle:** between the midbrain and the cerebellum.
B. **Middle cerebellar peduncle:** between the pons and the cerebellum.
C. **Inferior cerebellar peduncle:** between the medulla and the cerebellum.

Fissures: the 3 important fissures are:

A. **Horizontal fissure:** divides the cerebellum into superior and inferior surfaces.
B. **Primary fissure:** on the superior surface at the junction of its anterior third and posterior two-thirds. It separates the anterior lobe from the posterior lobe.
C. **Posterolateral fissure (uvulo-nodular fissure):** on the inferior surface separating the nodule from the uvula, and the posterior lobe from the flocculonodular lobe.

Deep cerebellar nuclei: 4 in number. From the medial to the lateral side they are:

1. Fastigial nucleus
2. Globose nucleus
3. Emboliform nucleus
4. Dentate nucleus (the largest).

Divisions of the cerebellum

A. Anatomical divisions: 3 lobes

The cerebellum is divided by the **primary fissure and the posterolateral fissure** into:

1. **Anterior lobe:** lies cranial to the primary fissure.
2. **Posterior lobe:** lies between the primary fissure and the posterolateral fissure.
3. **Flocculonodular lobe:** is formed of the nodule and the two flocculi.

B. Longitudinal divisions: 3 longitudinal zones

According to the connections of the deep cerebellar nuclei:

1. **Vermal zone:** the cerebellar cortex projects to the fastigial nucleus.
2. **Paravermal zone:** the cerebellar cortex projects to the interposed nuclei.
3. **Lateral zone**: the cerebellar cortex projects to the dentate nucleus.

C. Functional divisions: 3 functional zones

1. **Archicerebellum (vestibulocerebellum):**
   - ☒ Consists of the flocculonodular lobe.
   - ☒ Connected with the vestibular system
   - ☒ Concerned with equilibrium.
2. **Paleocerebellum (spinocerebellum):**
   - ☒ Consists of the vermal & paravermal zones of the anterior and posterior lobes.
   - ☒ Connected with spinal cord.
   - ☒ Concerned with regulation of muscle tone and muscle coordination.
3. **Neocerebellum (cerebrocerebellum):**
   - ☒ Consists of the lateral zone of the cerebellar hemisphere.
   - ☒ Connected with the cerebral cortex.
   - ☒ Concerned with automatic control of movement.

Arterial supply of the cerebellum: the cerebellum is supplied by:

A. Superior cerebellar artery:

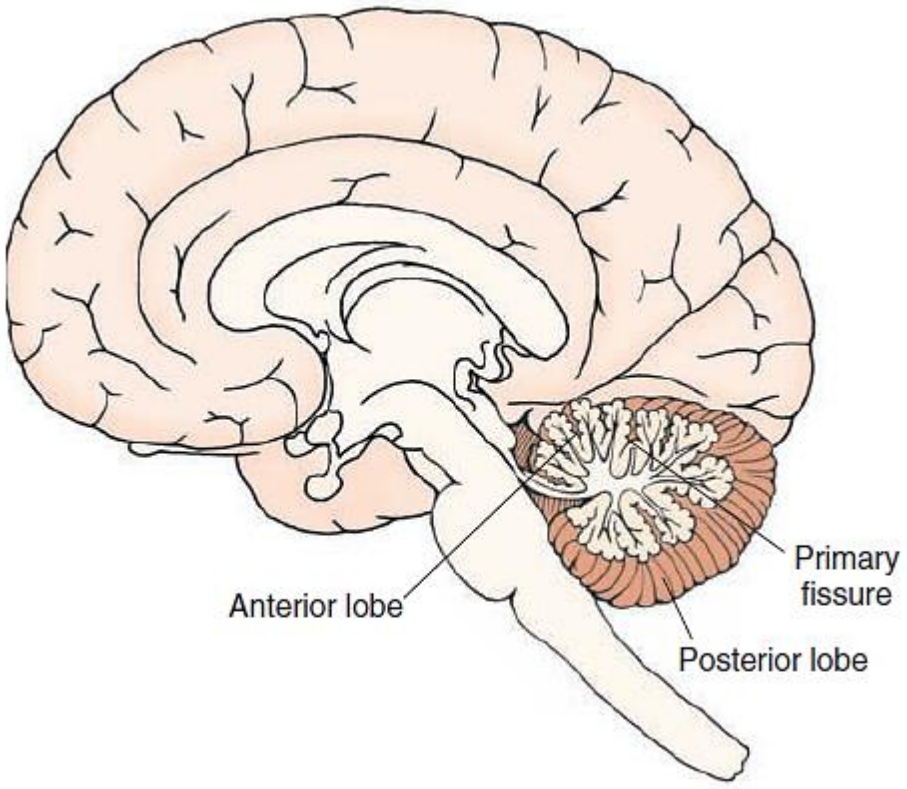
- ☒ Branch of the basilar artery.
- ☒ It supplies the superior surface of the cerebellum and the superior cerebellar peduncle.

B. Anterior inferior cerebellar artery (Aica):

- ☒ Branch of the basilar artery.
- ☒ It supplies the anterior part of the inferior surface and the middle cerebellar peduncle.

C. Posterior inferior cerebellar artery (Pica):

- ☒ Branch of the vertebral artery.
- ☒ It supplies the posterior part of the inferior surface and the inferior cerebellar peduncle.



Blood supply of the brain stem

Vertebral artery

- **Origin:** it is a branch of the first part of the subclavian artery.
- **Course:** **4 parts**
  - **A. First part:** from the origin to foramen transversarium of c6.
  - **B. Second part:** ascends through foramina transversaria of the upper six cervical vertebrae.
  - **C. Third part:** on the posterior arch of atlas.
  - **D. Forth part:** enters the cranial cavity through foramen magnum. Ascends upward on the medulla to reach the lower border of the pons.
- **Termination**: at the lower border of the pons where the 2 vertebral arteries unite to form the basilar artery.
- **Branches in the cranial cavity:**
  1. **Anterior spinal artery:**
     ☒ It unites with the opposite one to form a single anterior spinal artery. It supplies:
     - Anterior two-thirds of the spinal cord.
     - Medial zone of the medulla.

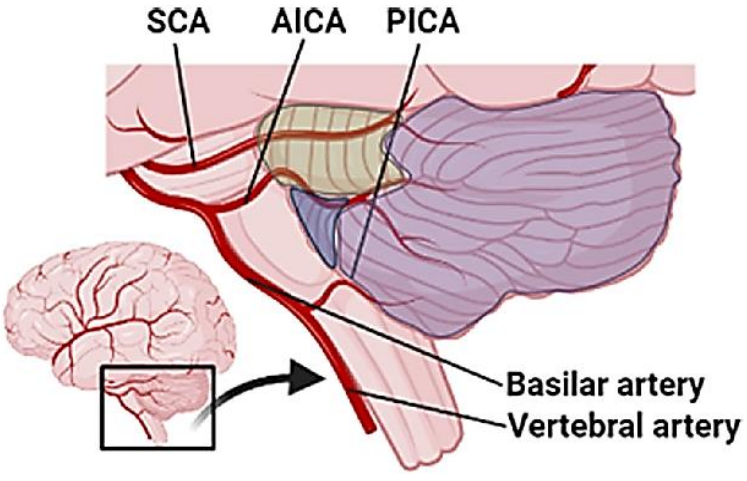
     ☒ Occlusion of the anterior spinal artery causes **medial medullary syndrome**.
  2. **Posterior spinal artery:**
     Usually arises from the **PICA**. It supplies:
     ☒ Posterior third of the spinal cord.
     ☒ Gracile and cuneate tracts and nuclei.
  3. **Medullary branches:** supply the middle zone of the medulla including the olive.
  4. **Posterior inferior cerebellar artery (PICA): it supplies:**
     a. Porsolateral zone of the medulla.
     b. Inferior cerebellar peduncle.
     c. Posterior part of the inferior surface of the cerebellum.
     d. Choroid plexus of the 4th ventricle.

     ☒ It usually gives the posterior spinal artery.
     ☒ Occlusion of the pica causes **lateral medullary syndrome.**
  5. **Posterior meningeal artery**: supplies the meninges of the posterior cranial fossa.

Basilar artery

- **Origin**: at the lower border of the pons by the union of the two vertebral arteries.
- **Course:** ascends in the basilar groove of the pons.
- **Termination:** at the upper border of the pons by dividing into 2 posterior cerebral arteries.
- **Branches:**

1. **Pontine branches: 3 groups**
   - **Paramedian branches**: to the medial zone of basis pontis.
   - **Short circumferential branches**: to the lateral zone of basis pontis.
   - **Long circumferential branches**: to the pontine tegmentum.
2. **Anterior inferior cerebellar artery (AICA):** supplies:
   - Anterior part of the inferior surface of the cerebellum.
   - Middle cerebellar peduncle.
   - It gives the labyrinthine artery in 85%.
3. **Labyrinthine (internal auditory) artery (in 15%):**
   - It accompanies the vestibulocochlear nerve and the facial nerve in the internal acoustic meatus
   - It supplies the internal ear.
   - It is separated from the Aica by the abducent nerve.
4. **Superior cerebellar artery (SCA):**
   It winds around the midbrain and supplies:
   - Superior surface of the cerebellum.
   - Superior cerebellar peduncle and the superior medullary velum.
   - Inferior colliculus of the midbrain.
5. **Two terminal branches (posterior cerebral arteries):**
   - They wind around the midbrain.
   - It is connected with the internal carotid artery by the posterior communicating artery.
   - It supplies the midbrain, thalamus, hypothalamus and occipital lobe.
   - It is separated from the superior cerebellar artery by the oculomotor & trochlear nerves.



The fourth ventricle

- **Definition:** it is the cavity of the hindbrain (rhombencephalon)
- **Boundaries of the 4th ventricle:**

A. Lateral borders:

- **Superiorly**: the superior cerebellar peduncle.
- **Inferiorly**: the inferior cerebellar peduncle and the gracile and cuneate tubercles.
- **In the middle:** the lateral angle forming the lateral recess.

B. Roof (posterior wall):

- **Superiorly:** superior medullary velum connecting the two superior cerebellar peduncles.
- **Inferiorly:** inferior medullary velum connecting the two inferior cerebellar peduncles.
- **In the middle:** the cerebellum.

C. Floor (anterior wall):

- The floor is divided into two similar halves by the **median sulcus**.
- It is divided by the **stria medullaris into** upper pontine part & lower medullary part:

1. Upper pontine part: contains the following from the medial to the lateral side:

- **Medial eminence:** on each side of the median sulcus. The facial colliculus is a small swelling at the lower end of the medial eminence and is produced by the abducent nucleus and the encircling facial nerve fibers.
- **Sulcus limitans (superior fovea):** contains a pigmented area called locus ceruleus at its upper end, which secretes noradrenaline.
- **Vestibular area:** overlying the superior and lateral vestibular nuclei.

2. Lower medullary part: contains:

- **Sulcus limitans dividing the medullary part into 3 trigones:**
  a. **Hypoglossal trigone:** medial, overlying the hypoglossal nucleus.
  b. **Vagal trigone:** middle, overlying the dorsal motor nucleus of the vagus.
  c. **Vestibular trigone:** formed by the medial & inferior vestibular nuclei.
- **Area postrema:** is a narrow area at the obex between the vagal trigone and the margin of the ventricle. It is the vomiting center.

3. Intermediate zone: Formed by the stria medullaris of the 4th ventricle. These transverse fibers are arcuatocerebellar fibers connecting the arcuate nucleus with the cerebellum.

- **Cranial nerve nuclei in the floor of the 4th ventricle:**
  - **A. Abducent nucleus:** opposite the facial colliculus in the pons.
  - **B. Hypoglossal nucleus:** in the hypoglossal trigone in the medulla.
  - **C. Dorsal motor nucleus of the vagus:** in the vagal trigone in the medulla.
  - **D. Vestibular nuclei:** in the vestibular trigone in both the pons and medulla.
- **Foramina of the 4th ventricle: 3 foramina**
  - **A. Median aperture (foramen of Magendie):** present in the inferior medullary velum.
  - **B. Two lateral apertures (foramina of Luschka):** in the lateral recess at the cerebellopontine angle.
- **Communications:**
  - **A.** With the **3rd ventricle** through the cerebral aqueduct of Sylvius.
  - **B.** With **the central canal** of the medulla and spinal cord.
  - **C.** With the **subarachnoid space** through foramen of Magendie & foramina of Luschka.
- **Choroid plexus:** It has a T-shaped plexus. It has a stem and 2 lateral arms. Each arm extends laterally into the lateral recess and is supplied by the PICA.

Base of the brain

Interpeduncular fossa

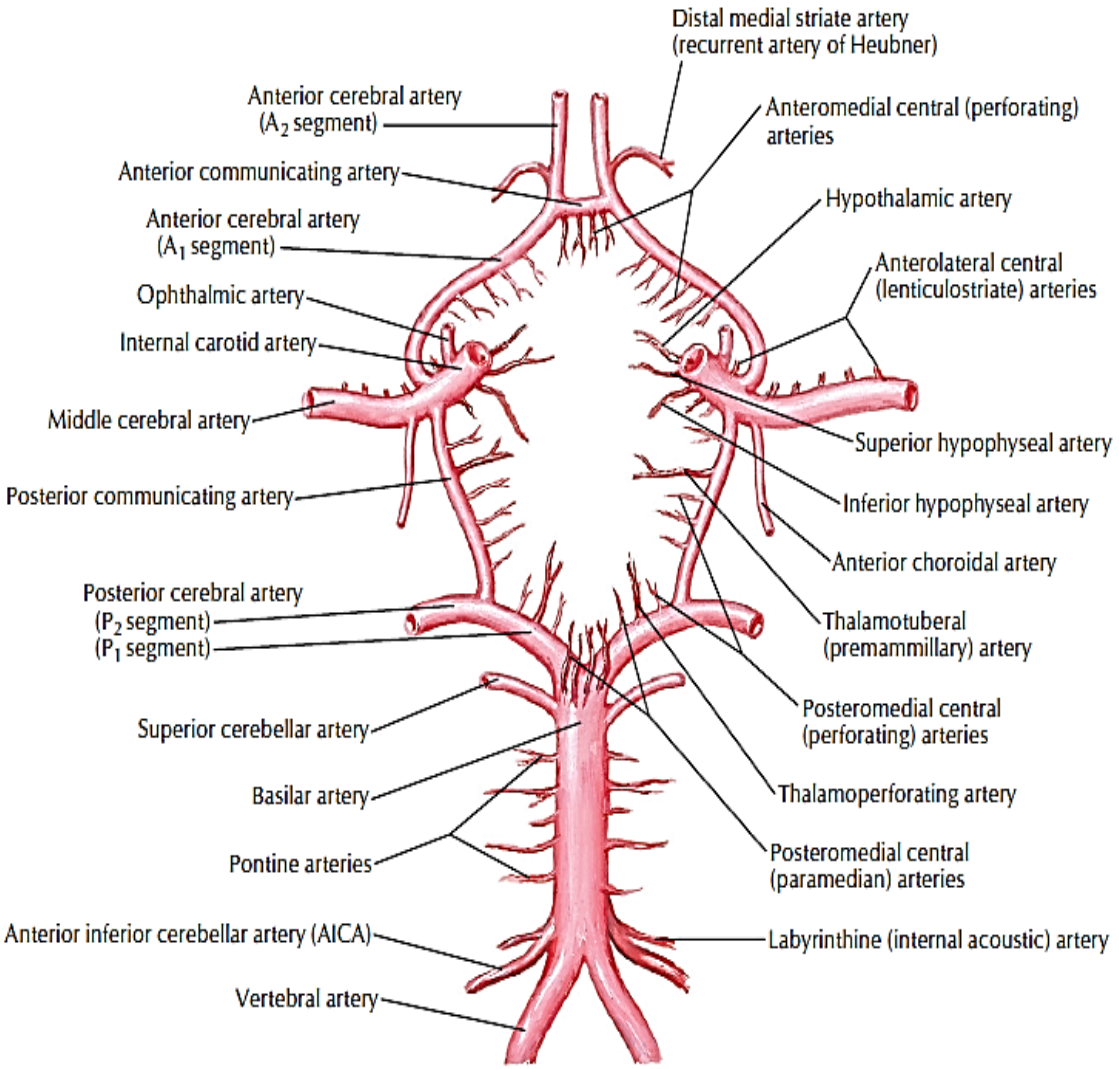
- **Location**: between the two cerebral peduncles.
- **Boundaries:**
  - **A. Anteriorly:** optic chiasma.
  - **B. Posteriorly:** upper border of the pons.
  - **C. On each side:**
    1. Optic tract anteriorly.
    2. Crus cerebri posteriorly.
- **Contents:** from before backward:
  1. **Tuber cinereum and infundibulum of pituitary gland:** parts of the hypothalamus.
  2. **Two mamillary bodies:** one on each side. They are parts of the hypothalamus.
  3. **Posterior perforated substance:** part of the hypothalamus. It is perforated by the central branches of the posterior cerebral and the posterior communicating arteries.
  4. **Two oculomotor nerves:** each exits from the medial side of the crus cerebri.
  5. **Circulus arteriosus (circle of Willis):** along the margins of the interpeduncular fossa.

Circulus arteriosus (circle of Willis)

- **Location**: in the interpeduncular fossa at the base of the brain.
- **Formation**: it is formed by the following arteries:
  - **A. Anteriorly:** anterior communicating artery connecting the two anterior cerebral arteries.
  - **B. Posteriorly:** two posterior cerebral arteries.
  - **C. On each side:** from before backward:
    - ☒ **Anterior cerebral artery:** the smaller terminal branch of the internal carotid artery.
    - ☒ **Internal carotid artery.**
    - ☒ **Posterior communicating artery** connecting the internal carotid artery with the posterior cerebral artery.

Anatomical and clinical importance:

1. It connects the vertebrobasilar system with the internal carotid arteries.
2. It connects the arteries of the two sides (right and left).
3. Normally, mixing of blood does not occur in the basilar and the communicating arteries because blood pressure is equal in the arteries of the circle.
4. It provides a collateral circulation in case of occlusion of any artery in the circle.
5. It acts as a safety valve to equalize pressure between the major arteries.
6. The circle is a common site of arterial aneurysm (local dilatation of the artery).



The diencephalon

- The diencephalon is located between the midbrain and the cerebral hemisphere.
- It has a single midline cavity called the third ventricle.
- **Boundaries:**
  1. **Anteriorly**: lamina terminalis and anterior commissure.
  2. **Posteriorly**: posterior commissure, pineal gland and habenular trigone.
  3. **Superiorly**: tela choroidea of the third ventricle, body of the fornix and lateral ventricle.
  4. **Inferiorly**: optic chiasma, tuber cinereum & infundibulum, mamillary bodies and posterior perforated substance.
  5. **Medially**: the 3rd ventricle. The medial wall is divided by the hypothalamic sulcus into upper part called thalamus and lower part called hypothalamus.
  6. **Laterally**: posterior limb of the internal capsule.
- **Divisions**
  1. Thalamus
  2. Hypothalamus
  3. Epithalamus
  4. Subthalamus

Thalamus

- The thalamus is the largest part (four-fifth) of the diencephalon.
- It receives all sensations except olfaction and projects them to sensory areas of the brain.
- **The thalamus has two ends and four surfaces:**
  1. **Anterior end:** is related to the interventricular foramen.
  2. **Posterior end:** called pulvinar and is related superiorly to the splenium of the corpus callosum and inferiorly to the tectum of the midbrain.
  3. **Superior surface:** is related to the tela choroidea, fornix and lateral ventricle.

4. **Inferior surface:** is related to:

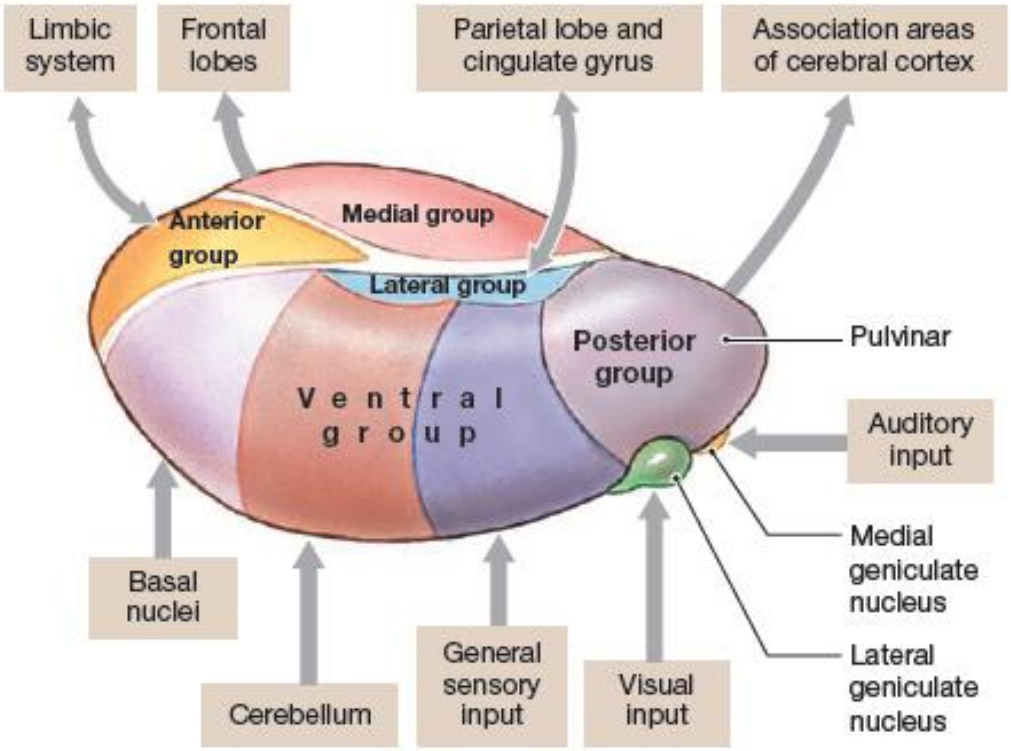
   ☒ The hypothalamus and the subthalamus.
   ☒ The metathalamus projects downward from the pulvinar.
   ☒ It is formed of the medial geniculate body & lateral geniculate body.

5. **Medial surface:** is related to the third ventricle. It is connected with the opposite one in 70% of humans by the interthalamic adhesion (massa intermedia).

6. **Lateral surface:** is related to the posterior limb of the internal capsule.

Arterial supply:

1. Posterior cerebral artery: from the basilar artery. It is the main arterial supply.
2. Posterior communicating artery: from the internal carotid artery.
3. Anterior choroidal artery: from the internal carotid artery to the lateral geniculate body



Hypothalamus

- The hypothalamus is the principal autonomic and endocrine center.
- **Relations:**
  A. **Related Anteriorly** to lamina terminalis and anterior commissure.
  B. **Related Superiorly to** the hypothalamic sulcus separating it from the thalamus.
  C. **Related Inferiorly to** the interpeduncular fossa.
- **Arterial supply: from circulus arteriosus**
  A. **Anterior part:** Anterior cerebral & anterior communicating arteries.
  B. **Posterior part:** Posterior cerebral & posterior communicating arteries
  C. **Lateral part: middle cerebral artery.**

Subthalamus

- **Site:** it lies lateral to the hypothalamus between the thalamus and the midbrain.
- It contains subthalamic nucleus (motor nucleus) which regulates movement of muscles.
- **Lesion in the subthalamic nucleus** causes **hemiballismus** (involuntary movement).

Epithalamus

- **The epithalamus is formed of 4 structures:**
  A. **Posterior commissure: is a band of fibers connecting the following structures:**
     ☒ The two superior colliculi.
     ☒ The pretectal nuclei with the Edinger-Westphal nuclei for bilateral light reflex.
     ☒ The two oculomotor nuclei for the upward gaze (moving the two eyes upward).
  B. **Pineal gland:**
     ☒ It is an endocrine gland located above the posterior commissure.
     ☒ It doesn't contain nerve cells. It contains cells called pinealocytes.
     ☒ It secretes melatonin (hormone of darkness). It regulates the sleep-wake cycle.
  C. **Habenular nucleus:**
     ☒ It is lies above the pineal gland.
     ☒ It is connected with the opposite one by the habenular commissure.
     ☒ It is part of the limbic system, which is concerned with emotion & behavior.
  D. **Stria medullaris thalami:**
     ☒ It is a band of fibers connecting the septal area with the habenular nucleus.
     ☒ It is part of the limbic system.

The third ventricle

- **Definition:** the third ventricle is the cavity of the diencephalon.
- **Boundaries:**

A. Anterior wall:

- ☒ Lamina terminalis: the cranial end of the neural tube.
- ☒ Anterior commissure connecting the two temporal lobes.
- ☒ Anterior column of the fornix.

B. Posterior wall:

- ☒ Posterior commissure.
- ☒ Pineal gland.
- ☒ Habenular trigone and the habenular commissure.

C. Lateral wall:

- ☒ Thalamus. The 2 thalami are connected in 70% by interthalamic adhesion.
- ☒ Hypothalamus. It is separated from the thalamus by the hypothalamic sulcus.

D. Roof:

- ☒ Ependymal layer between the two stria medullaris thalami.
- ☒ Tela choroidea of the third ventricle above the ependymal layer.
- ☒ Two internal cerebral veins inside the tela choroidea.

E. Floor: hypothalamic structures

- ☒ Optic chiasma, tuber cinereum, infundibulum and mamillary bodies
- ☒ Posterior perforated substance and the tegmentum of the midbrain.

- **Communications**

- ☒ **With the lateral ventricles**: through the interventricular foramina of Monro.
- ☒ **With the fourth ventricle**: through the cerebral aqueduct of Sylvius.

- **Recesses:**

- ☒ Optic recess: above the optic chiasma.
- ☒ Infundibular recess: extends into the infundibulum.
- ☒ Pineal recess: extends into the stalk of the pineal gland.
- ☒ Suprapineal recess: above the pineal gland.

- **Choroid plexus:**

- ☒ **Site**: projects downward from roof of the 3rd ventricle.
- ☒ **Shape**: 2 vascular ridges, one on each side of midline.
- ☒ **Supplied by** the posterior choroidal artery (branch from the posterior cerebral artery).

General sensory system

Ascending sensory pathways

- **Ascending sensations pass in 3 main components which are:** Receptor, 3 order neurons to the sensory areas of the brain.
- **The 3 order neurons are:**
  - **A. First order neuron:** dorsal root ganglia
  - **B. Second order neuron:** spinal cord or brainstem
  - **C. Third order neuron:** ventral posterior lateral nucleus of thalamus
    - ☒ Axons of 1st and 3rd order neurons never cross
    - ☒ Axons of the 2nd order neuron always cross

Sensations from the body ascending tracts of the spinal cord

A. Tracts in the posterior column (dorsal fasciculus) of the spinal cord:

1. **Gracile tract:** medial in position and conveys sensations from below t6 segment.
2. **Cuneate tract:** lateral in position and conveys sensations from above t6 segment.

They convey the following sensations from the same side of the body:

- ☒ Conscious proprioception (sense of position and sense of movement).
- ☒ Discriminative touch (localization, 2 point-discrimination and stereognosis)
- ☒ Sense of vibration.

B. Tracts in the lateral funiculus:

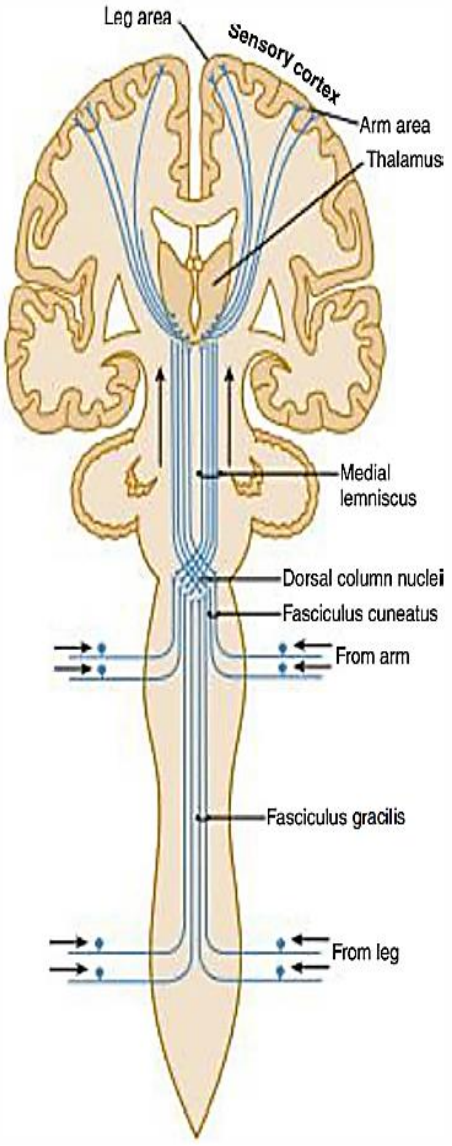
1. Posterior (dorsal) spinocerebellar tract.
2. Anterior (ventral) spinocerebellar tract.
3. Spinoolivary tract: The 3 tracts convey unconscious proprioception from the muscles to the cerebellum for coordination of the movements of the limbs
4. Lateral spinothalamic tract: conveys pain and temperature sensations from the opposite side of the body to the thalamus.
5. Spinotectal tract: conveys information to the superior colliculus for spinovisual reflexes.
6. Lissauer's tract: is a short tract at the tip of the dorsal horn.

C. Tracts in the ventral funiculus:

Anterior (ventral) spinothalamic tract. It mediates simple touch and pressure sensations from the opposite side of the body to the thalamus.

Conscious proprioception (kinesthesia), discriminative touch and vibration sense

- **Receptors:**
  - **A. Proprioception**: muscle and tendon spindles.
  - **B. Discriminative** touch: Meissner's corpuscles.
  - **C. Vibration**: Pacinian corpuscles.
- **Tracts:**
  - **A. Gracile** tract: carries sensations from below t6.
  - **B. Cuneate** tract: carries sensations from above t6.
- **Pathway:**
  - **A. First-order neuron:** dorsal root ganglia
  - **B. Second-order neuron**: gracile and cuneate nuclei.
  - **C.** Axons cross and form the medial lemniscus.
  - **D. Third-order neuron:** ventral posterior lateral nucleus of the thalamus (**VPLNT**). Axons of the VPLNT pass in the posterior limb of the internal capsule to end in the general sensory area in the postcentral gyrus.



- **Lesions:**

Loss of proprioception, discriminative touch, and sense of vibration:

- **A.** In the dorsal funiculus: on the same side of the body below the level of the lesion.
- **B.** In the medial lemniscus: on the opposite side of the body.

Unconscious proprioception (pathway to the cerebellum)

- **Receptors**: muscle spindles, tendon spindles and joint receptors.
- **Tracts:**
  - **A. Dorsal spinocerebellar tract:** from the trunk and lower limb.
  - **B. Ventral spinocerebellar tract:** from the lower limb.
  - **C. Cuneocerebellar tract:** from the upper limb.

A. Dorsal spinocerebellar tract:

- ☒ **Origin**: from clarke's nucleus (lamina vii).
- ☒ It **extends** from c8 to l2 or l3.
- ☒ It does **not cross**; ascends on the same side.
- ☒ **Sensation from** the trunk and lower limb reach cerebellum via the inferior cerebellar peduncle.

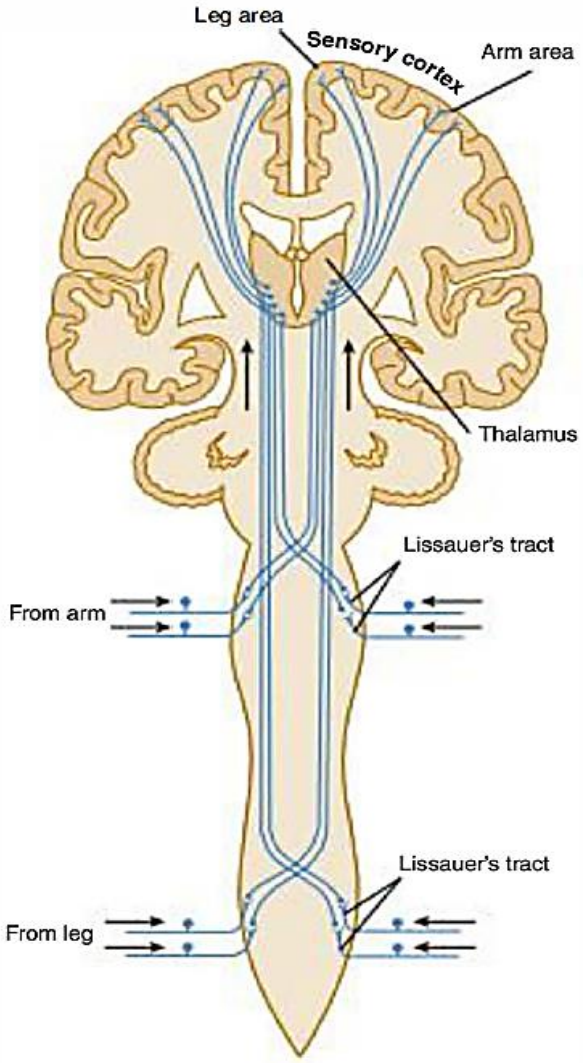
B. Ventral spinocerebellar tract:

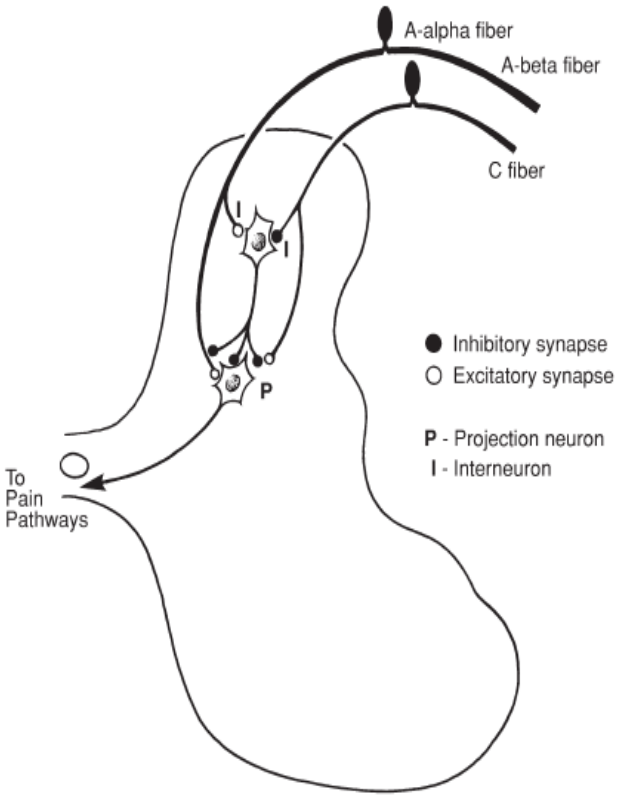
- ☒ **Origin**: from the spinal border cells. They extend from l2 to s2 (in lamina vii)
- ☒ It **crosses** in the spinal cord then in the cerebellum.
- ☒ **Sensation from** the lower limb
- ☒ Reach cerebellum via the sup cerebellar peduncle.

C. Cuneocerebellar tract:

- ☒ **Origin**: accessory cuneate nucleus in the medulla.
- ☒ It does **not cross**; ascends on the same side.
- ☒ **Sensation from** the upper limb.
- ☒ Reach cerebellum via the inferior cerebellar peduncle.

- **Function of the spinocerebellar and cuneocerebellar tracts:**
  - ☒ They convey proprioceptive information from the muscles, tendons and joints to the cerebellum for coordination of movement and for maintenance of muscle tone.
- **Lesion: ataxia** (loss of muscle coordination).


Leg area
Sensory cortex
Arm area
Thalamus
Lissauer's tract
From arm
Lissauer's tract
From leg


A-alpha fiber
A-beta fiber
C fiber
I
I
P
Inhibitory synapse
Excitatory synapse
P - Projection neuron
I - Interneuron
To
Pain
Pathways

Pain and temperature sensations

- **Receptors:** free nerve endings.
- **Tract:** lateral spinothalamic tract.
- **Afferent pain fibers:**
  1. A-delta fibers (myelinated): fast pain.
  2. C-fibers (unmyelinated): slow pain.
- **Pathway:**
  1. First-order neuron: dorsal root ganglia
  2. Second-order neuron: laminae I to IV of Rexed
  3. Third-order neuron: VPLNT
- **Lesion in the lateral spinothalamic tract:**

  Loss of pain and temperature sensations on the **opposite** side of the body two segments **below** the level of the lesion.

Simple (light) touch and pressure sensations

- **Receptors:**
  1. **Touch**: free nerve endings, Merkel's disc and Meissner's corpuscles.
  2. **Pressure**: Pacinian corpuscles.
- **Tracts:**
  1. **Ventral spinothalamic tract.**
  2. **Gracile and cuneate tracts.**
- **Lesions in the ventral spinothalamic tract:**

  Signs are not detected clinically because touch is also carried by gracile & cuneate tracts.

Sensations from the face (trigeminal sensory system)

Trigeminal sensory nuclei:

A. Spinal trigeminal nucleus:

- **Site**: in the medulla and descends in the upper three segments of the spinal cord to become continuous with the substantia gelatinosa.
- **Function**: is the second-order neuron for pain and temperature sensations from the same side of the face.

B. Main sensory nucleus:

- **Site**: in the pons.
- **Function**: is the second-order neuron for discriminative touch sensation from the same side of the face.

C. Mesencephalic nucleus:

- **Site:** in the midbrain.
- **Function:** is the first-order neuron for proprioception from the muscles of the head and from the teeth and the temporomandibular joint.
- It contains pseudounipolar cells like those of the dorsal root ganglia.

Pain & temperature sensations from the face

Receptors: free nerve endings.

First-order neuron: trigeminal ganglion

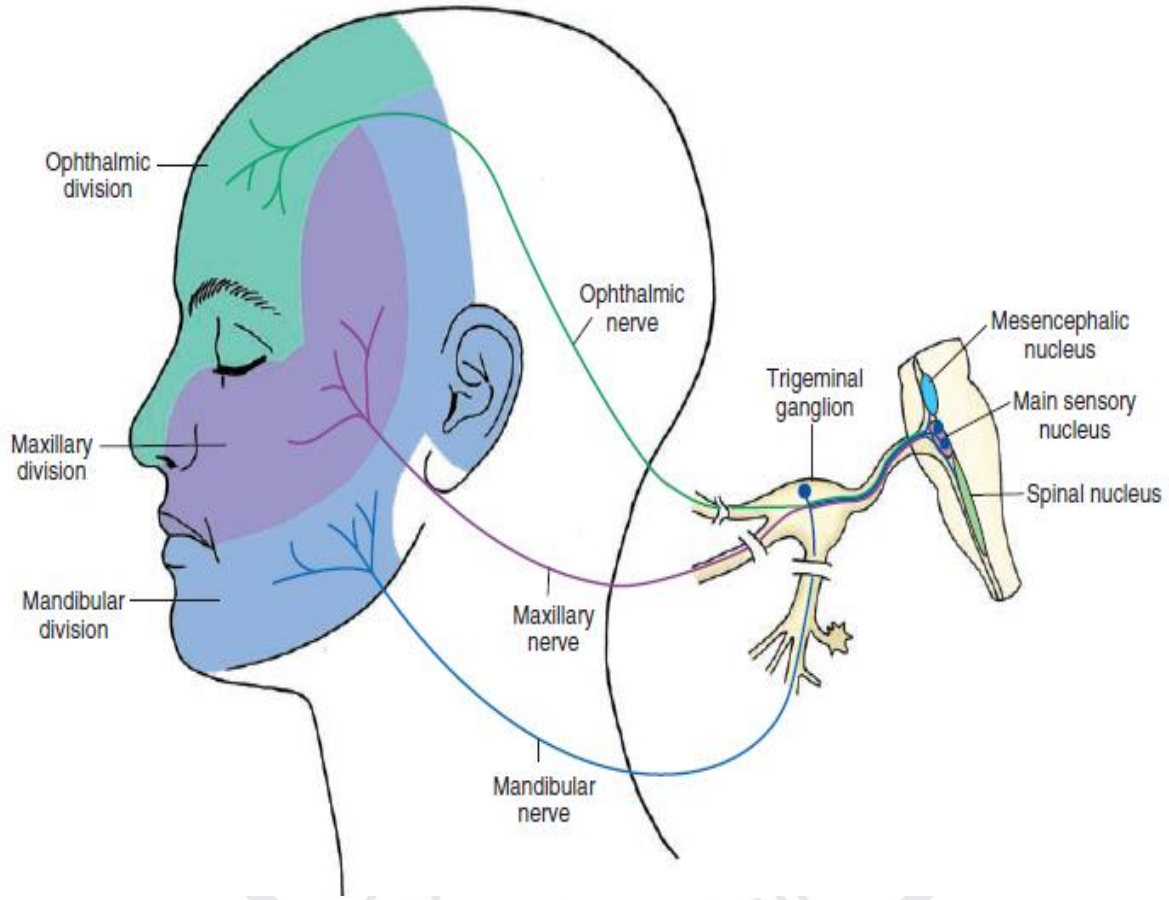
- **The peripheral branches of the nerve cells in the trigeminal ganglion** form the three divisions of the trigeminal nerve and terminate in the receptors.
- **The central branches form the sensory root of the trigeminal nerve,** which enters the pons and divides into ascending (touch fibers) and descending (pain fibers) divisions.
- **The descending division carries pain and temperature fibers,** forms the spinal trigeminal tract and terminates in the spinal trigeminal nucleus.

Second-order neuron: spinal trigeminal nucleus

Axons of the spinal trigeminal nucleus **cross** to the opposite side to form the **trigeminal lemniscus**. It terminates in the ventral posterior medial nucleus of thalamus (**VPMNT**).

- **<u>Third-order neuron</u>: ventral posterior medial nucleus of the thalamus**

Axons of the VPMNT ascend in the posterior limb of the internal capsule to end in the lower third of the postcentral gyrus.



Discriminative touch sensation from the face

- **Receptors:**
  - Meissners corpuscles for discriminative touch sensation.
  - Pacinian corpuscles for sense of deep pressure.
- **First-order neuron: trigeminal ganglion**
  - **The peripheral branches** of the trigeminal ganglion terminate in the receptors.
  - **The central branches** divides into ascending (touch fibers) and descending divisions.
  - **The ascending division** terminates in the main sensory nucleus in the pons.
- **Second-order neuron: main sensory nucleus in the pons**
  - **Some axons cross to the opposite side** and join the trigeminal lemniscus and end in the contralateral VPMNT.
  - **Other axons ascend on the same side** in the dorsal trigeminothalamic tract to end in the ipsilateral VPMNT.

  Therefore, touch from one side of the face terminates in the 2 sensory areas. Damage of one thalamus or sensory area causes contralateral loss of pain & temperature sensations only.
- **Third-order neuron: ventral posterior medial (VPMNT) nucleus of the thalamus**

  Axons of the **VPMNT** ascend in the posterior limb of the internal capsule to end in the lower third of the postcentral gyrus.

Pathway of proprioception from the head

- **The first-order neuron** is the mesencephalic nucleus of the trigeminal nerve in the midbrain. It contains pseudounipolar cells.
- **The peripheral branches end in** muscle spindles of the muscles of head.
- **The central branches cross** to the opposite side to join the trigeminal lemniscus and end in the contralateral VPMNT.
- **Axons of the VPMNT** reach the general sensory area of the face in the lower 1/3 of the postcentral gyrus.

Motor system

There are three different descending motor systems:

- **Pyramidal system:**

  Forms a direct link between the cerebral cortex and the spinal cord and brainstem.

  It forms:

  - **Corticospinal tract:** descends to anterior horn cells (ahcs) of the spinal cord.
  - **Corticobulbar tract:** descends to the cranial nerve motor nuclei in the brainstem.

- **Extrapyramidal system:**

  - Forms an indirect link between the cerebral cortex and spinal cord through the brainstem.
  - The tracts reach the spinal cord outside the pyramid of the medulla.

- **Motor pathway to the cerebellum:** cortico-ponto-cerebellar system.

Descending tracts of the spinal cord

A. Pyramidal tracts (2 corticospinal tracts): originate from the cerebral cortex:

- **Lateral corticospinal tract (crossed).**
- **Ventral corticospinal tract (uncrossed).**

B. Extrapyramidal tracts: originate from the brainstem:

- **2 from the midbrain:** rubrospinal tract and tectospinal tract (are crossed).
- **2 from the vestibular nuclei:** lateral & medial vestibulospinal tracts.
- **2 from the reticular formation:** lateral and medial reticulospinal tracts.
- **2 others:** raphe-spinal tract & descending autonomic fibers (hypothalamospinal tract).

Pyramidal system

Corticospinal tract

- **Origin:** it is formed of the axons of pyramidal and fusiform cells:
  1. **40% of the fibers:** from the upper two-thirds of the primary motor area (area 4). 3% of the fibers are large and arise from the giant pyramidal cells (betz cells).
  2. **40% of the fibers:** from the premotor area (area 6).
  3. **20% of the fibers:** from the general sensory area (area 3, 1 & 2).
- **Course**: descend in:
  1. **Medullary center of cerebral hemisphere:** the fibers converge toward the internal capsule forming corona radiata.
  2. **Posterior limb of internal capsule**: in the anterior 1/2 of the lenticulothalamic part.
  3. **Midbrain**: in the middle three-fifths of the crus cerebri.
  4. **Pons:** in the basis pontis forming bundles.
  5. **Medulla:** in the pyramid of the medulla.
  6. **In the lower part of the medulla:**
     a. **85% of the fibers cross to the opposite side** forming the lateral corticospinal tract and the pyramidal decussation.
     b. **15% of the fibers remain uncrossed** and form the ventral corticospinal tract. They cross in the cervical and upper thoracic regions of the spinal cord.
- **Termination:**
  1. About 95% terminate on the opposite side.
  2. About 5% terminate on the same side.
  3. About 95% of the fibers terminate on interneurons in the ventral horn, which synapses with alpha motor neurons.
  4. About 5% terminate directly on alpha motor neurons.
- **Functions:**
  1. Facilitation of the flexor muscle tone.
  2. Initiation of the highly skilled fine movements.
  3. Fibers originating in the sensory area modulate sensory input to the spinal cord.

- **Lesion:** upper motor neuron lesion (UMNL)
  1. **Above the decussation:** contralateral hemiplegia (paralysis of the opposite ½ of the body).
  2. **Below the decussation:** ipsilateral paralysis.
- **Signs of the UMNL**: after the stage of shock:
  1. **Hypertonia:** exaggerated muscle tone.
  2. **Hyper-reflexia:** hyperactive deep tendon reflexes.
  3. **Spasticity:** resistance to passive movements.
  4. **Babinski sign:** extension of the big toe upon stroking the sole of the foot.
  5. **Clonus:** alternating flexion and extension of the foot upon strong dorsiflexion of the foot.
  6. **Loss of the superficial abdominal reflexes and cremasteric reflex.**

Corticobulbar tract

- **Origin:**
  1. Lower one-third of the primary motor area.
  2. Adjacent premotor area and sensory area.
- **Course:** the tract descends through the:
  1. Corona radiata of the medullary center.
  2. Genu of the internal capsule.
  3. Crus cerebri of the midbrain with the corticospinal fibers.
  4. Basis pontis of the pons.
  5. Pyramid of the medulla.
- **Termination:**
  - ☒ It terminates on the cranial nerve motor nuclei of the two sides mainly on the opposite side.
  - ☒ All the cranial nerve motor nuclei receive bilateral corticobulbar fibers except the lower part of the facial nucleus, which receives fibers from the opposite side only.
- **Lesion:**
  - ☒ **UMN** paralysis of the lower part of the contralateral facial nucleus and weakness of the muscles supplied by the cranial nerves.

Extrapyramidal tracts

- **Function:**

All the pyramidal and extrapyramidal tracts facilitate the flexor muscle tone **except** the 2 tracts which arise from the pons which facilitate the extensor muscle tone:

- ☒ Lateral vestibulospinal tract.
- ☒ Pontine (medial) reticulospinal tract.

Rubrospinal tract:

- **Origin:** from the red nucleus of the opposite side.
- **Function:** carries information from the cerebellum and cerebral cortex to the spinal cord

Tectospinal tract:

- **Origin:** from the superior colliculus of the opposite side.
- **Function:** reflexes associated with vision and hearing.

Lateral vestibulospinal tract (vestibulospinal tract):

- **Origin:** lateral vestibular nucleus in the pons.
- **Function:** facilitation of the extensor muscle tone.

Medial vestibulospinal tract (sulcomarginal tract):

- **Origin:** medial vestibular nucleus in the medulla.
- **Function:** facilitation of the flexor muscle tone.

Pontine reticulospinal tract (medial reticulospinal tract)

- **Origin:** pontine reticular formation.
- **Function:** facilitation of the extensor muscle tone.

Medullary reticulospinal tract (lateral reticulospinal tract)

- **Origin:** medullary reticular formation.
- **Function:** facilitation of the flexor muscle tone.

Descending autonomic fibers

- **Origin**: hypothalamus and autonomic centers in the reticular formation.
- **Termination:** sympathetic nucleus (lateral horn) and sacral parasympathetic nucleus.
- **Lesion:** autonomic disturbances. Lesion above t1 will cause Horner's syndrome.

Horner's syndrome:

1. **Ptosis**: drooping of the upper eyelid due to paralysis of muller،s muscle.
2. **Miosis**: constriction of the pupil due to paralysis of the dilator pupillae.
3. **Anhidrosis**: dry face due to paralysis of the sweat glands.
4. **Enophthalmos**: retraction of the eyeball.
5. **Flushing**: the face is red and warm due to vasodilation of skin blood vessels.

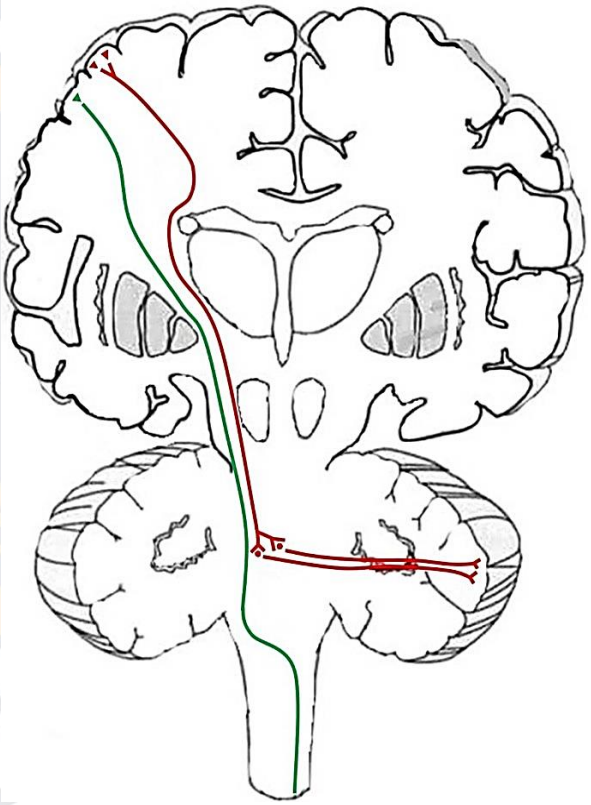
Cortico-ponto-cerebellar pathway

- **The cortico-ponto-cerebellar pathway is divided into 2 neurons:**
  1. **Corticopontine fibers.**
  2. **Pontocerebellar fibers.**

A. Corticopontine fibers:

Arise from the cerebral cortex. They are divided into 2 types:

a. **Frontopontine fibers:** from the frontal lobe.
b. **Non frontopontine fibers:** from the other 3 lobes (temporo-parieto-occipito-pontine).



a. Frontopontine fibers:

- ☒ They arise from the frontal lobe.
- ☒ They transmit motor information to the neocerebellum.
- ☒ They descend in the:
  1. Anterior limb of the internal capsule.
  2. Medial one-fifth of the crus cerebri.
  3. Basis pontis to synapse with the pontine nuclei.

b. Non frontopontine fibers: (parieto-occipito-temporo-pontine fibers):

- ☒ They arise from the cortex of the parietal, temporal and occipital lobes
- ☒ They transmit sensory information to the neocerebellum.
- ☒ They descend in the:
  1. Sublenticular part of the internal capsule.
  2. Lateral one-fifth of the crus cerebri.
  3. Basis pontis to synapse with the lateral group of the pontine nuclei.

B. Pontocerebellar fibers: axons of the pontine nuclei

Axons of the pontine nuclei cross to the opposite side and enter the cerebellum through the middle cerebellar peduncle. They terminate in the cortex of the neocerebellum.

Function:

1. Transmit motor and sensory information from the cerebral cortex to the neocerebellum.
2. The pathway brings the cerebellum under the control of the cerebral cortex for precise correction of movements.

Spinal cord lesions

Causes:

1. Trauma: by fracture of the vertebral column, stab or by bullet.

2. Compression: by tumor or herniated disc.

3. Vascular: by occlusion of an artery such as the anterior spinal artery.

4. Infection: as in poliomyelitis and Tabes dorsalis (syphilis).

5. Degenerative: as in vitamin b12 deficiency and lateral sclerosis.

Signs: are motor and sensory

A. Motor signs: are either of upper motor or of lower motor neuron lesion:

1. Upper motor neuron lesion (UMNL):

- ☒ It is due to a lesion in the pyramidal and the extrapyramidal tracts.
- ☒ Signs of the upper motor neuron lesion:
  - **a. Spastic paralysis.** The spasticity of muscles is due to increased muscle tone of the antigravity muscles (flexors of the arm and extensors of the leg).
  - **b.** Increase of the muscle tone (**hypertonia**)
  - **c. Exaggerated deep tendon reflexes (hyper-reflexia):** extension of the big toe upon stroking of the sole of the foot.
  - **d. Clonus**: alternating flexion and extension of the foot upon sudden and strong dorsiflexion of the foot

2. Lower motor neuron lesion (LMNL):

- ☒ It is due to a lesion in the anterior horn cells or their axons.
- ☒ Signs of the lower motor neuron lesion:
  - **a. Flaccid paralysis.** The flaccidity of muscles is due to loss of muscle tone.
  - **b.** Decrease or loss of muscle tone **(hypotonia).**
  - **c.** Absence of deep tendon reflexes **(areflexia).**
  - **d. Fibrillation or fasciculation** due to spontaneous contraction of muscle fibers.
  - **e. Muscle atrophy.**

B. <u>Sensory signs: are due to</u>

1. **Lesion in the gracile and cuneate tracts:** causes loss of kinesthesia (sense of position and sense of movement), discriminative touch and sense of vibration below the level of the lesion and on the same side.
2. **Lesion in the lateral spinothalamic tract:** causes loss of pain & temperature sensations on the opposite side of the lesion and 2 segments below the level of the lesion.
3. **Lesion in the anterior gray and white commissure (syringomyelia):** causes bilateral loss of pain and temperature sensations in the affected dermatomes, two segments below the lesion due to damage to the crossing fibers of the lateral spinothalamic tracts.

Complete cut of the spinal cord

A. <u>In the cervical region:</u>

1. **Above the origin of the phrenic nerve:** causes immediate death from respiratory failure.
2. **Below the origin of the phrenic nerve:** causes quadriplegia (paralysis of the four limbs) with loss of the bladder and bowl voluntary control (incontinence).

B. <u>Above the lumbar plexus:</u> causes paraplegia (paralysis of the two lower limbs) With loss of the bladder and bowl voluntary control.

Hemisection of the spinal cord (Brown-Sequard syndrome)

A. <u>Signs below the level of the lesion:</u>

1. **On the same side:**
   - **a.** Loss of kinesthesia, discriminative touch and sense of vibration due to damage of the dorsal column tracts (gracile and/or cuneate tracts).
   - **b.** UMN paralysis due to damage of the pyramidal and extrapyramidal tracts producing spasticity, hypertonia, hyperreflexia, Babinski sign & clonus.
   - **c.** Horner,s syndrome if the lesions is above t1 due to damage of the sympathetic fibers descending to t1. It causes ptosis, miosis, anhidrosis and enophthalmos.
2. **On the opposite side:** loss of pain and temperature sensations two segments below the level of the lesion due to damage of the lateral spinothalamic tract.

B. <u>Signs at the level of the lesion:</u>

The signs are present on the same side in the segment of the lesion due to damage of the anterior horn, the dorsal horn and the entering dorsal root fibers:

1. **Ipsilateral LMN paralysis** of the muscles supplied by the damaged anterior horn cells.
2. **Ipsilateral loss of all sensations** in the dermatomes of the damaged dorsal nerve roots.

Common diseases of the spinal cord

1. Poliomyelitis:

- ☒ It is a viral infection of the anterior horn cells.
- ☒ It causes LMN paralysis of the affected muscles. (flaccidity, hypotonia, areflexia and muscle atrophy).

2. Lateral sclerosis (LS or MS):

- ☒ It is a degenerative disease affecting the anterior horn cells and the lateral corticospinal tract.
- ☒ It causes a combination of UMNl and LMNL.

3. Tabes dorsalis:

- ☒ It is a syphilitic infection of the spinal cord.
- ☒ It causes destruction of the DRG neurons, dorsal roots and dorsal column tracts.
- ☒ Therefore, it causes bilateral loss of sense of position and sense of movement associated with ataxia.

4. Subacute combined degeneration:

- ☒ It is due to pernicious anemia.
- ☒ It causes demyelination of the gracile & cuneate tracts, corticospinal and spinocerebellar tracts.

5. Syringomyelia:

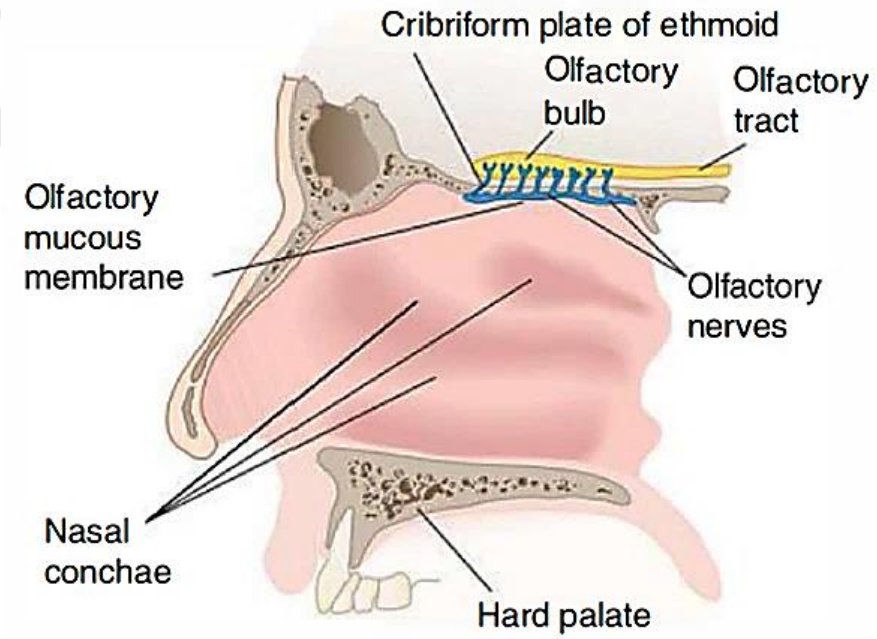
- ☒ It is abnormal dilatation of the central canal.
- ☒ It causes destruction of the crossing fibers of the lateral spinothalamic tract in the anterior gray and white commissures with bilateral loss of pain & temperature sensation in the affected dermatomes.

Cranial nerves and special senses

- The 12 pairs of cranial nerves are referred to by either name or Roman numeral named according to their order in exist from the brain and from the skull.
- The optic nerve are not true nerves but rather fiber tracts of the brain, whereas nerve XI (the spinal accessory nerve) is derived, in part, from the upper cervical segments of the spinal cord. The remaining nine pairs relate to the brain stem.
- Cranial nerve fibers with motor functions arise from the motor nuclei that lie deep within the brain stem; they are homologous to the anterior horn cells of the spinal cord.
- Cranial nerve fibers with sensory functions have their cells of origin (first-orde r nuclei) outside the brain stem, usually in ganglia that are homologous to the dorsal root ganglia of the spinal nerves.
- Nerves **I, II, and VIII** are the special sensory input.
- Nerves **III, IV, and VI** control eye movements and pupillary constriction.
- Nerves **XI and XII** are pure motor.
- Nerves **V, VII, IX, and X** are mixed.
- Nerves **III, VII, IX, and X** carry parasympathetic fibers.

I. Olfactory nerve

- There are 9 to 15 olfactory nerves that are short connections that project from the olfactory mucosa within the nose to the olfactory bulb within the cranial cavity on each side of the brain.
- They arise from the olfactory receptor cells in the nose.
- The olfactory bulb lies just above the cribriform plate and below the frontal lobe (nestled within the olfactory sulcus).
- Axons from the olfactory bulb run within the olfactory stalk, synapse in the anterior olfactory nucleus, and terminate in the:
  1. **Primary olfactory area:** located in the uncus.
  2. **Olfactory association area (area 28):** in the anterior part of the parahippocampal gyrus.
- **Effect of lesion:** partial or complete loss of smell.

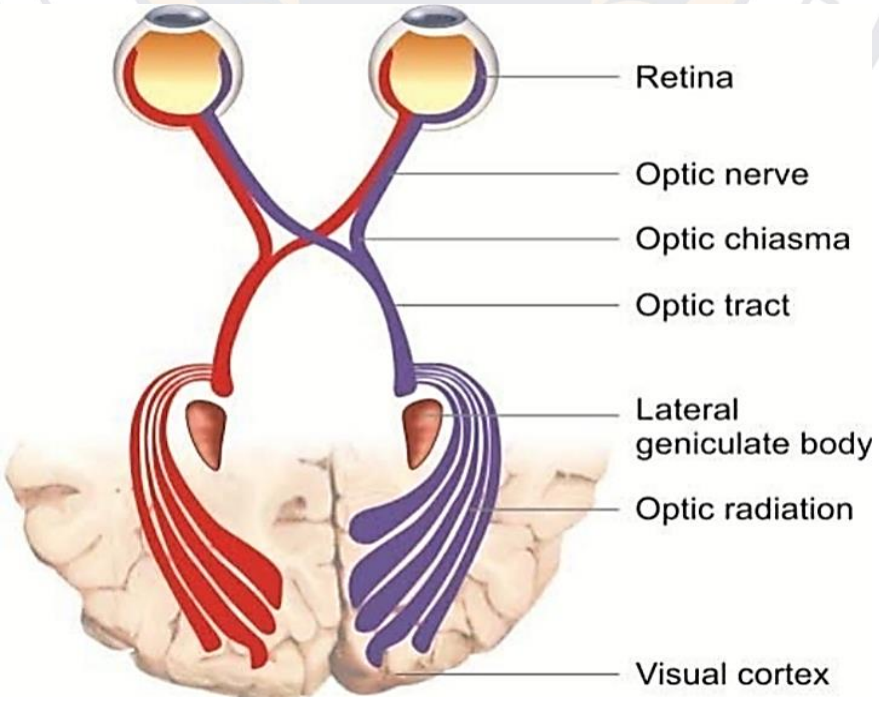


II. Optic nerve & Visual pathway

- The optic nerve contains myelinated axons that arise from the ganglion cells in the retina.
- The axons within the optic nerve are myelinated by oligodendrocytes.
- It contains a central retinal artery and vein.
- It is covered by the brain meninges and CSF.
- The optic nerve passes through the optic papilla to the orbit.

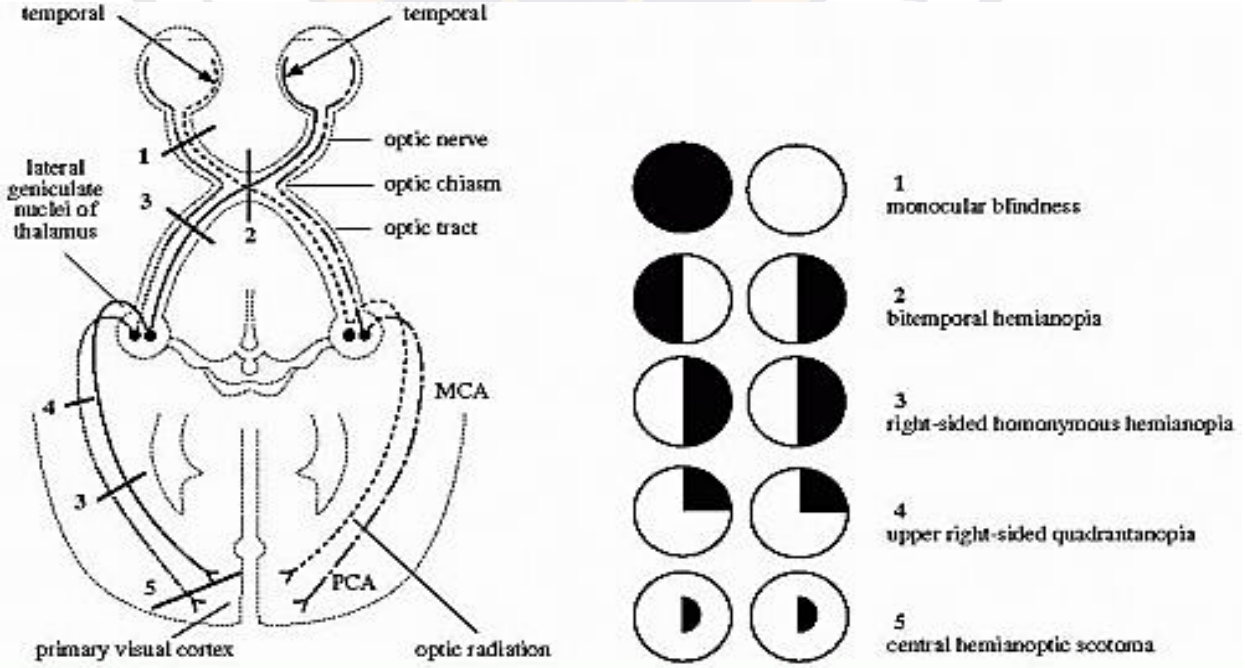
Visual pathway

- Retina to optic nerve → optic chiasma.
- In the optic chiasma, the temporal fibers enter the ipsilateral optic tract, while the nasal fibers cross the midline and enter the contralateral optic tract → lateral geniculate body.
- From the lateral geniculate body axons form the optic radiation →to the retrolenticular part of the internal capsule → the primary visual area (area 17) → the visual association areas (areas 18 & 19) for recognition of what we see.



Lesions of the Visual Pathway

1. **Optic nerve:** total blindness of the same eye.
2. **Optic chiasma:**
   - ☒ **Midline (central) lesion:** bitemporal hemianopia. It is usually due to a pituitary tumor.
   - ☒ **Peripheral lesion on the two sides:** binasal hemianopia.
3. **Optic tract:** contralateral homonymous hemianopia.
4. **Lateral geniculate body & optic radiation:** contralateral homonymous hemianopia.
5. **Visual area:**
   - ☒ **Total lesion:** contralateral homonymous hemianopia with macular sparing. The sparing is due the anastomoses between branches of the middle and posterior cerebral arteries.
   - ☒ **Above calcarine sulcus (cuneus):** contralateral homonymous lower quadrantic anopia.
   - ☒ **Below calcarine sulcus (lingual gyrus):** contralateral homonymous upper quadrantic anopia.



III. Oculomotor nerve

- **Type:** it is a motor nerve.
- **Deep origin: it has a nuclear complex at the level of the superior colliculus.**

1. Somatic motor nucleus:

- ☒ It supplies the levator palpebrae superioris and all the extraocular muscles except the lateral rectus and the superior oblique.

2. Parasympathetic nucleus (Edinger-Westphal nucleus): medial.

- ☒ The fibers synapse in the ciliary ganglion and supply the sphincter pupillae muscle and the ciliary muscle.

3. Accessory oculomotor nuclei:

- ☒ Interstitial nucleus of Cajal: for the vertical movements of the two eyes. It connects:
  - **a.** The oculomotor nuclei of the 2 sides for the upward eye movement.
  - **b.** Oculomotor and trochlear nuclei of the 2 sides for the downward eye movement.
- ☒ Pretectal nucleus: for the pupillary light reflex.

- **Lesions:**

1. Paralysis of levator palpebrae superioris: ptosis (drooping of the upper eyelid).
2. Paralysis of the medial rectus muscle: external strabismus (by the lateral rectus).
3. Paralysis of the sphincter pupillae muscle: mydriasis (dilatation of the pupil).
4. Loss of light and accommodation reflex of the same eye.

IV. Trochlear nerve

- **Type**: it is a motor nerve.
- **Deep origin**: The motor nucleus located at the level of the inferior colliculus.
  - ☒ The axons cross to the opposite side to supply the opposite superior oblique muscle.
  - ☒ It is the only cranial nerve which appears from the back of the brain stem.
- **Lesion:** paralysis of the superior oblique muscle. It causes inability to depress the adducted eye causing difficulty in walking downstairs.

V. Trigeminal nerve

- The trigeminal nerve is the largest cranial nerve.
- **Type**: mixed (sensory, motor & parasympathetic).
- **Deep origin**: It has 4 nuclei, one motor and 3 sensory:

A. Motor nucleus:

- Lies in the pons and forms the motor root of the trigeminal nerve.
- It supplies muscles of the 1st pharyngeal arch (4 muscles of mastication, anterior belly of the digastric and mylohyoid, tensor palate and tensor tympani).

B. 3 Sensory nuclei:

- **Main sensory nucleus:** lies in the pons. It mediates discriminative touch sensation from the same side of the face.
- **Spinal trigeminal nucleus:** lies in the medulla and upper 3 segments of the spinal cord. It mediates pain and temperature sensations from the same side of the face.
- **Mesencephalic nucleus:** lies in midbrain. It is the first-order neuron for proprioception from the muscles of the head and from the temporomandibular joint.

- **Course:**
  - It leaves the pons as 2 roots (small motor and a large sensory). The large sensory root expands to form the trigeminal ganglion.
  - The trigeminal ganglion lies within a pouch of dura mater called cavum trigeminal.
  - The motor root of the trigeminal nerve is situated below the sensory ganglion and is separate from it.
- **Branches:**
  - The ophthalmic (V1), maxillary (V2), and mandibular(V3) nerves arise from the anterior border of the ganglion.
  - The motor root joins the mandibular nerve.

- Distribution:
  1. **Ophthalmic (V1):** General sensory from bridge nose, upper eyelid, forehead and cornea.
  2. **Maxillary (V2):** General sensory from lateral nose, lower eyelid, upper lip, cheek, upper teeth, and gingiva.
  3. **Mandibular (V3):** Motor t:o muscles of mastication, tensor tympani, tensor palati. General sensory from lower lip, chin, lower teeth and gingiva, and anterior 2/3 of tongue (not taste).

- **Lesion:**
  - Paralysis of muscles of mastication on the **same** side of the head.
  - Loss of all sensations on the **same** side of the face.

VI. Abducent nerve

- **Deep origin**: it is a pure motor nerve.
- **The abducent nucleus is formed of 2 parts:**
  - **Abducent motor nucleus:** forms with the encircling facial nerve fibers the facial colliculus of the 4th ventricle. It supplies the lateral rectus muscle.
  - **Paraabducent nucleus (horizontal gaze center):** it connects the abducent nucleus of the same side with the oculomotor nucleus of the opposite side through the MLF for the ipsilateral lateral gaze (lateral rectus of the same side and medial rectus of the opposite side).
- **Lesion:**
  - **Abducent nerve lesion** causes paralysis of the lateral rectus muscle producing **internal strabismus (squint).**

VII. Facial nerve

- **Type**: it is a mixed nerve.
- **Roots**: it has two roots:
  - **A. Motor root:** large and medial and is the facial nerve proper.
  - **B. Sensory root:** small and lateral. It is called nervus intermedius. It contains both sensory & parasympathetic fibers.
- **Deep origin**: it has 4 nuclei:

A. Motor nucleus:

- ☒ lies in the lower part of the pons. It supplies muscles of the 2nd pharyngeal arch. The upper half of the nucleus receives bilateral corticobulbar fibers.
- ☒ The lower half of the nucleus receives corticobulbar fibers from the opposite side only.

B. Parasympathetic nucleus (superior salivatory nucleus): it innervates:

- ☒ Submandibular & sublingual salivary glands through the chorda tympani nerve.
- ☒ Lacrimal, nasal & palatine glands through the greater superficial petrosal nerve.

C. Two sensory nuclei:

- ☒ **Nucleus solitarius:** receives taste fibers from the anterior two-thirds of the tongue through the chorda tympani nerve.
- ☒ **Spinal trigeminal nucleus:** receives somatic sensory fibers from the external ear via the posterior auricular nerve and small branches that join the tympanic plexus.

- **lesions of the facial nerve**

A. Upper motor neuron lesion: lesion in the corticobulbar tract

- ☒ It causes paralysis of the lower half of the opposite facial nucleus and paralysis of the muscles of the lower half of the opposite side of the face.

B. Lower motor neuron lesion: lesion in the facial nerve or the facial nucleus

☒ It causes flaccid paralysis of all muscles of facial expression on the same side of the face. The lesion may be located at any level:

1. In the facial colliculus, where it is accompanied by abducent nuclear lesion.
2. In the basis pontis: accompanied by hemiplegia (paralysis of one 1/2 of the body).
3. At the cerebellopontine angle, where it is accompanied by VIII lesion.
4. At the facial canal or the stylomastoid foramen (Bell's palsy).

☒ Signs of the Lower Motor Neuron Lesion of Facial Nerve:

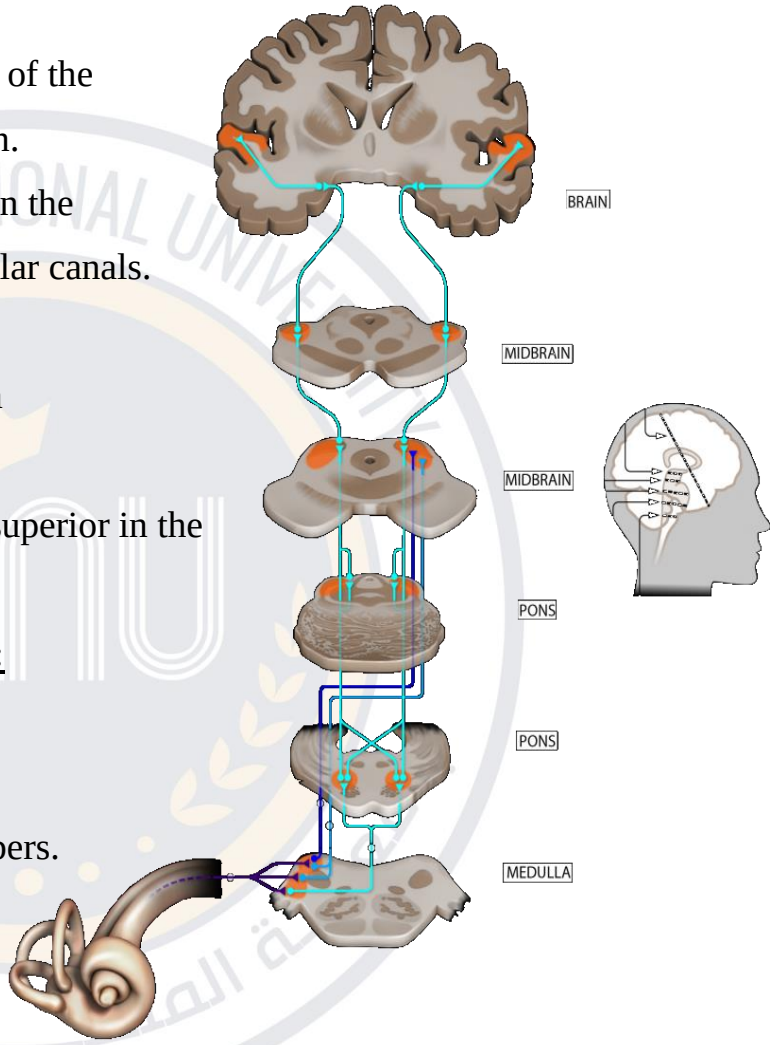
The signs are present on the **same** side of the face:

1. **Paralysis of the frontalis:** inability to raise the eyebrow.
2. **Paralysis of the orbicularis oculi:** inability to close the eye, which remains open and loss of the corneal reflex.
3. **Paralysis of the orbicularis oris:** inability to whistle.
4. **Paralysis of the levators of the angle of the mouth:** drooping of the angle of the mouth.
5. **Paralysis of the buccinator:** accumulation of food in vestibule of the mouth.
6. **Paralysis of the stapedius:** hyperacusis (hypersensitivity to sounds).
7. **Paralysis of the chorda tympani:** loss of taste sensation from the anterior two-thirds of the tongue and decreased salivation.
8. **Paralysis of the greater superficial petrosal nerve:** loss of lacrimation.

VIII. Vestibulocochlear nerve

Vestibular nerve

- **Type**: It is a pure sensory nerve concerned with equilibrium.
- **Origin**:
  - ☒ It is formed by the central processes of the bipolar cells of the Scarpa's ganglion.
  - ☒ The peripheral processes terminate in the vestibular receptors in the semicircular canals.
- **Termination:**
  - **A. Cerebellum:** in the archicerebellum (flocculonodular lobe).
  - **B. The 4 vestibular nuclei:** lateral & superior in the pons. Medial & inferior in medulla.
- **Connections of the vestibular nuclei:**
  - **A. Input: from the:**
    - ☒ Vestibular nerve
    - ☒ Cerebellum: cerebellovestibular fibers.
  - **B. Output: they send fibers to:**
    1. Cerebellum (archicerebellum): through the inferior cerebellar peduncle.
    2. Spinal cord: via the lateral and medial vestibulospinal tracts.
    3. Nuclei that move the extraocular muscles: of the two sides (III, IV, VI) via the MLF to coordinate movements of the two eyes.
    4. Thalamus (VPMN) and cerebral cortex: (vestibular area) for conscious awareness of the position of the head in space.



Cochlear Nerve

- **Type:** It is a pure sensory nerve concerned with hearing.
- **Origin**:
  - ☒ It is formed by the central processes (axons) of the bipolar cells of the spiral ganglion (cochlear ganglion).
  - ☒ The peripheral processes terminate in the organ of Corti in the cochlea.
- **Termination:** in the dorsal and ventral cochlear nuclei at the pontomedullary junction.
- **Auditory Pathway:**
  - ☒ Organ of Corti → spiral ganglion cochlear nerve → dorsal & ventral cochlear nuclei → trapezoid body → lateral lemniscus inferior colliculus→ medial geniculate body →auditory radiation →primary auditory area (41 & 42) →auditory association area (22).
- **Lesions of the auditory pathway**
  - ☒ Lesion in the cochlea, cochlear nerve or cochlear nuclei: complete ipsilateral deafness.
  - ☒ Lesion in the lateral lemniscus MGB or auditory area: partial deafness on the 2 sides mainly on the opposite side (bilateral diminution of hearing).

IX. Glossopharyngeal nerve

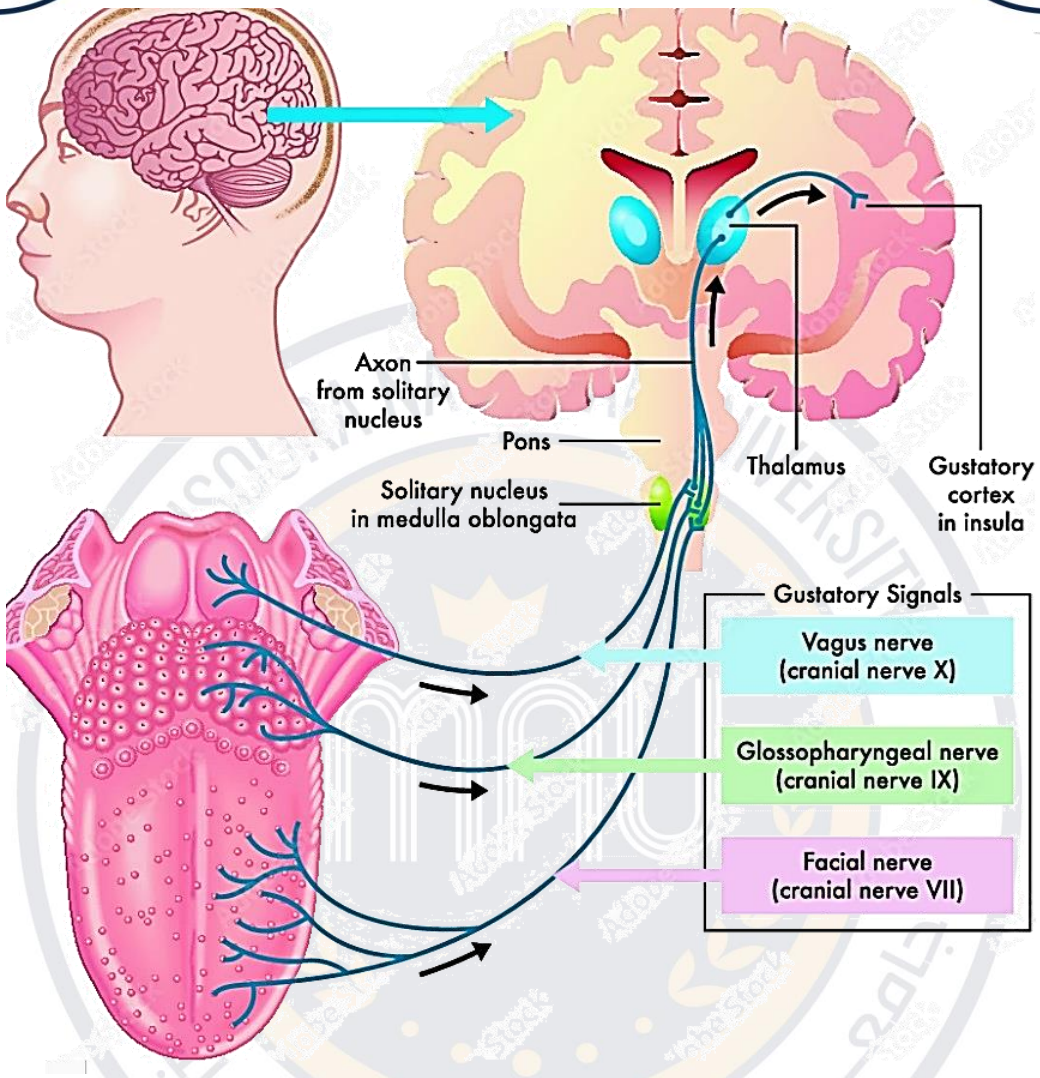
- **Type**: it is a mixed nerve.
- **Deep origin**: it has 4 nuclei:
  1. Motor nucleus: upper part of nucleus ambiguous. It supplies the stylopharyngeus muscle.
  2. Parasympathetic nucleus: inferior salivatory nucleus. It supplies the parotid gland.
  3. Two sensory nuclei:
     - ☒ Nucleus solitarius: it receives taste fibers from the posterior third of the tongue.
     - ☒ Spinal trigeminal nucleus: it receives sensory fibers from a small area behind the ear.
- **Lesion:**
  1. Loss of taste sensation from the posterior third of the tongue.
  2. Loss of the pharyngeal gag reflex.
  3. Loss of the carotid sinus reflex.

X. Vagus Nerve

- **Type:** it is a mixed nerve.
- **Deep origin:** it has 4 nuclei:
  1. Motor nucleus: middle part of nucleus ambiguous. It supplies muscles of the pharynx except the stylopharyngeus, larynx and palate except the tensor palati muscle.
  2. Parasympathetic nucleus: dorsal motor nucleus of the vagus. It supplies the thoracic and the abdominal organs as far as the left colic flexure.
  3. Two sensory nuclei:
     - ☒ **Nucleus solitarius:** it receives taste fibers from the most posterior part of the tongue and epiglottis. They terminate in the upper third of the nucleus.
     - ☒ **Spinal trigeminal nucleus:** it receives sensory fibers from the external auditory meatus and tympanic membrane.
- **Lesion:**
  1. Paralysis of muscles of the pharynx causes dysphagia & loss of the pharyngeal gag reflex.
  2. Paralysis of muscles of the larynx causes hoarseness of voice.
  3. Paralysis of muscles of the palate causes regurgitation of food from the nose and deviation of the uvula to the normal side.
  4. Anesthesia of the larynx causes loss of the cough reflex.

Taste pathway

- **Receptors:** Taste buds of the tongue, epiglottis, soft palate and oropharynx.
- **Nerves:**
  1. **Chorda tympani:** branch of the facial nerve, anterior 2/3 of the tongue.
  2. **Glossophryngeal nerve:** posterior 1/3 of the tongue, the vallate papillae, soft palate and oropharynx.
  3. **Internal laryngeal branch of vagus:** epiglottis and most posterior part of the tongue.
- **First-order neuron: ganglia**
  1. **Anterior two-thirds of the tongue:** geniculate ganglion of the facial nerve.
  2. **Posterior one-third of the tongue:** inferior ganglion of the glossopharyngeal nerve.
  3. **Epiglottis and most posterior part of the tongue:** inferior ganglion of the vagus nerve.
     - ☒ The peripheral branches of the ganglia end in the taste buds.
     - ☒ The central branches enter the brainstem and end in the nucleus solitarius.
- **Second-order neuron: upper 1/3 of nucleus solitarius**
  - ☒ Axons of nucleus solitarius cross to the opposite side and ascend in the central tegmental tract dorsal to the medial lemniscus to end in the ventral posterior medial nucleus of the thalamus (VPMNT).
  - ☒ Collateral branches reach the salivatory nuclei for reflex activity.
- **Third-order neuron: VPMNT**
  - ☒ Axons of the VPMNT pass through the posterior limb of the internal capsule and terminate in the taste area (area 43) (gustatory area) in the lower part of the postcentral gyrus.


Axon from solitary nucleus
Pons
Solitary nucleus in medulla oblongata
Thalamus
Gustatory cortex in insula
Gustatory Signals
Vagus nerve (cranial nerve X)
Glossopharyngeal nerve (cranial nerve IX)
Facial nerve (cranial nerve VII)

XI. Accessory Nerve (CN XI)

- **Type**: pure nerve.
- **Roots**: It is pure motor nerve and has two roots:

A. Cranial root:

- ☒ It arises from the lower part of the nucleus ambiguous.
- ☒ It leaves cranial cavity through the jugular foramen and joins the vagus nerve.
- ☒ It is distributed with the recurrent laryngeal nerve to all muscles of the larynx except the cricothyroid muscle.

B. Spinal root:

- ☒ It arises from the upper five or six cervical segments of the spinal cord.
- ☒ It supplies the sternomastoid and trapezius muscles. Lesion of the spinal accessory nerve:

1. Paralysis of sternomastoid: causes inability to rotate the head to the opposite side.
2. Paralysis of trapezius: causes inability to shrug (up and down) the shoulder.

XII. Hypoglossal Nerve (CN XII)

- **Type:** It is a pure motor nerve.
  - ☒ It arises from the hypoglossal nucleus of the medulla in the floor of the 4th ventricle.
  - ☒ It exits from the preolivary fissure.
  - ☒ It supplies all muscles of the tongue except palatoglossus muscle.
- **Lesion:**
  - ☒ LMN paralysis of the same side of the tongue (hemiparalysis).
  - ☒ Deviation of the protruded tongue toward the affected side.

Internal features of the brain stem

I. Medulla oblongata

A. Gracile and cuneate nuclei.

B. Cerebellar relay nuclei.

C. Cranial nerve nuclei.

Gracile and Cuneate Nuclei

- They receive gracile and cuneate tracts. They are the second-order neuron for kinesthesia, discriminative touch and sense of vibration from the same side of the body.
- Their axons cross to the opposite side in the sensory decussation and form medial lemniscus.

Cerebellar Relay Nuclei

1. Accessory (lateral) cuneate nucleus:

- It receives proprioceptive information from the upper limb via the cuneate tract.
- The axons form the cuneocerebellar tract (dorsal external arcuate fibers) to ICP.

2. Arcuate nucleus:

- It is considered a misplaced pontine nucleus anterior to the pyramid.
- It receives fibers from the cerebral cortex via the pyramidal tract.
- Their axons form arcuatocerebellar fibers. They reach the cerebellum via ICP by:
  - Ventral external arcuate fibers: from the same side.
  - Stria medullaris of the fourth ventricle: from the opposite side.

3. Inferior olivary nuclear complex:

- **Input**: They receive
  - Motor data from the cerebral cortex, basal ganglia and red nucleus.
  - Sensory data from the spinal cord via the spinoolivary tract.

- **Output**: olivocerebellar tract which cross to the opposite side and enter the cerebellum through the inferior cerebellar peduncle.
- **Function**: cerebellar control of movement.
- **Lesion**: cerebellar dysfunction (ataxia).

4. Reticular formation:

- Input: The reticular formation receives:
  - Motor data from the motor areas of the cerebral cortex.
  - Sensory data from the spinal cord and the special sense organs.
- Output: it projects these data to the cerebellum via the reticulocerebellar tracts.
- Functions of the Brainstem Reticular Formation:
  - Reticular Activating System (RAS): responsible for the electrical activity of the cerebral cortex. It is important for alertness & arousal from sleep.
  - Motor Function: it influences the muscle tone. The medullary and pontine reticulospinal tracts facilitate the flexor and extensor muscles, respectively.
  - Autonomic Function: it contains respiratory and cardiovascular centers.

5. Vestibular nuclei:

- They project vestibulocerebellar fibers by 2 routes:
  - Direct: from the vestibular nerve.
  - Indirect: from the vestibular nuclei

Cranial nerve nuclei

1. Spinal trigeminal nucleus: sensory

- It ascends in the pons and descends in the spinal cord to the level of C3 to become continuous with the substantia gelatinosa.
- It mediates pain and temperature sensations from the same side of the face.
- The axons cross to the opposite side, form the trigeminal lemniscus, which terminates in the VPM nucleus of the thalamus.

2. Nucleus solitarius: sensory

- ☒ It is divided into two parts:
  a. Upper one-third: receives taste fibers from the tongue and epiglottis via the:
     - Facial nerve: anterior 2/3
     - Glossopharyngeal nerve: posterior 1/3
     - Vagus nerve: epiglottis and the most posterior part of tongue.
  b. Lower 2/3: receive general sensation from the viscera by the vagus and the glossopharyngeal nerves.

3. Hypoglossal nucleus: motor nucleus

- ☒ It is located in the floor of the fourth ventricle (hypoglossal trigone).
- ☒ It supplies all muscles of the tongue except the palatoglossus muscle.

4. Nucleus ambiguous: motor nucleus

- ☒ It supplies all muscles of the pharynx, all muscles of the larynx and all muscles of the palate except tensor palati muscle. It is divided into three parts

5. Inferior salivatory nucleus: parasympathetic

- ☒ It supplies the parotid gland via the glossopharyngeal nerve.

6. Dorsal motor nucleus of the vagus: parasympathetic

- ☒ It lies in the floor of the fourth ventricle.
- ☒ It supplies the glands, smooth muscles and blood vessels of the thoracic and abdominal viscera till the left colic flexure through the vagus nerve.

7. Medial and inferior vestibular nuclei:

- ☒ They are located in the vestibular trigone in the floor of the fourth ventricle.

II. Pons

- **The pons is divided into:**
  1. Anterior part called basis pontis.
  2. Posterior part called tegmentum.
- **The basis pontis contains:**
  1. Bundles of the pyramidal tract fibers forming:
     - ☒ Corticospinal fibers to the spinal cord.
     - ☒ Corticobulbar fibers to the cranial nerve motor nuclei.
  2. Pontine nuclei: are the second-order neurons for the cortico-ponto-cerebellar pathway.
  3. Transverse pontine fibers: are the axons of the pontine nuclei.
  4. Fibers of the middle 4 cranial nerves on their way outside the pons.
- **Tegmentum: contains tracts and nuclei:**

A. Tracts:

1. Four lemnisci: medial, trigeminal, spinal and lateral lemniscus.
2. Medial longitudinal fasciculus (MLF): it connects the vestibular nuclei with the motor nuclei that move the eyes (III, IV & VI) to coordinate eye movements.
3. Other tracts: tectospinal, rubrospinal, central tegmental tract and other tracts.

B. Nuclei:

1. Of the middle 4 cranial nerves: V, VI, VII and VIII (vestibular & cochlear nerves).
2. Pontine reticular formation

III. Midbrain

- **The midbrain is divided by the cerebral aqueduct into two parts:**

A. Ventral part (cerebral peduncle): divided into:

1. Crus cerebri: anterior part.
2. Substantia nigra: middle part, formed of:
   - ☒ Pars compacta: posterior, secrete dopamine.
   - ☒ Pars reticularis: anterior, secrete GABA.
3. Tegmentum: posterior part.

B. Dorsal part (tectum): formed of two superior colliculi and two inferior colliculi.

- **Crus Cerebri:**
  - ☒ it is the most anterior part of the cerebral peduncle with the interpeduncular fossa in between.
  - ☒ Contents: it contains the following fibers:
    1. Medial one-fifth: Frontopontine fibers.
    2. Lateral one-fifth: Nonfrontopontine fibers.
    3. Middle three-fifths: Corticospinal and corticobulbar fibers.
- **Substantia Nigra**:
  - ☒ it is extrapyramidal motor nucleus and is divided into 2 parts:
    - **A. Pars compacta (posterior):** the nerve cells contain melanin and secrete dopamine.
    - **B. Pars reticularis (anterior):** the nerve cells secrete gamma aminobutyric acid (GABA).
  - ☒ **It projects two types of inhibitory fibers:**
    1. Nigrostriate fibers: They convey dopamine to the corpus striatum to inhibit the activity of the caudate nucleus.
    2. Nigrothalamic fibers: They convey GABA to the thalamus to inhibit the activity of the ventral anterior and ventral lateral thalamic nuclei.

- **Lesion of the substantia nigra**: Parkinson's disease

Tegmentum: contains tracts and nuclei

- **Tracts:** such as the 4 lemnisci and other tracts.
  1. **Medial lemniscus:** (kinesthesia, discriminative touch and vibration sense).
  2. **Trigeminal lemniscus:** conveys sensations from the opposite side of the face.
  3. **Spinal lemniscus:** (pain, temperature, simple touch and pressure sensations).
  4. **Lateral lemniscus:** (auditory sensation to the inferior colliculus).

Nuclei:

A. Cranial nerve nuclei:

1. Oculomotor nuclei: at the level of the superior colliculus.
2. Trochlear nucleus: at the level of the inferior colliculus.
3. Mesencephalic nucleus of the trigeminal nerve.

B. Other nuclei:

a. Red nucleus: at the level of the superior colliculus.

b. Nuclei of the reticular formation.

c. Locus ceruleus: it is a pigmented area in the upper part of the pons and the lower part of the midbrain. The cells secrete norepinephrine.

Red nucleus

- It is an extrapyramidal motor nucleus. It relays motor impulses from the cerebral cortex and cerebellum to the thalamus & the spinal cord (cortico-rubro-spinal and dentato-rubro-spinal).
- **Input:**
  - **A. Corticorubral tract:** from the motor and premotor areas of the cerebral cortex.
  - **B. Dentatorubral tract:** from the opposite dentate nucleus of the cerebellum.
- **Output:**
  - **A. Rubrospinal tract**: to the spinal cord
  - **B. Rubrothalamic tract:** to the motor nuclei of the thalamus (VA and VL nuclei).
- **Lesion**: results in signs of cerebellar damage (contralateral tremor and ataxia).
- **Tectum**

The tectum is formed of four colliculi called corpora quadrigemina: 2 superior and 2 inferior.

Inferior Colliculus:	Superior Colliculus:
• **It is connected with** the opposite one by the commissure of the inferior colliculus. • **It is connected with** the medial geniculate body by brachium of the inferior colliculus.	• It is connected with the opposite one by the posterior commissure. • It is connected with the lateral geniculate body by brachium of the superior colliculus.
Function: • A relay nucleus in the auditory pathway: It receives the lateral lemniscus and projects to the medial geniculate body. • An auditory reflex center for reflexes associated with sound.	A visual reflex center for reflexes associated with vision. It projects to: • Tectospinal tract: to the spinal cord to move the neck toward the stimulus. • Tectobulbar tract: to the motor nuclei that move the eye. • It Establishes the auditory reflexes through connection with the inferior colliculus.

External features of the cerebral hemisphere

Each cerebral hemisphere has:

3 poles, 3 borders and 3 surfaces, 4 major sulci and 4 lobes.

A. Poles:

1. **Frontal pole: is the anterior end.**
2. **Occipital pole: is the posterior end.**
3. **Temporal pole: anterior end of the temporal lobe.**

B. 3 Borders:

1. **Superior border: related to superior sagittal sinus.**
2. **Inferomedial border: divided into 3 parts:**
   - **a.** Medial orbital border: from the frontal pole to the optic chiasma.
   - **b.** Hippocampal border: around the midbrain.
   - **c.** Medial occipital border: from the splenium to the occipital pole.
3. **Inferolateral border:** from the occipital pole to the temporal pole. It has a notch called the preoccipital notch 4 cm from the occipital pole.

C. 3 Surfaces:

1. **Lateral surface (superolateral):** is convex.
2. **Medial surface:** is separated from the opposite one by the falx cerebri.
3. **Inferior surface:** is divided into two parts by the lateral sulcus:
   - **a.** Orbital part: lies on the roof of the orbit.
   - **b.** Tentorial part: lies on the tentorium cerebelli.

D. 4 Major sulci of the cerebral hemisphere:

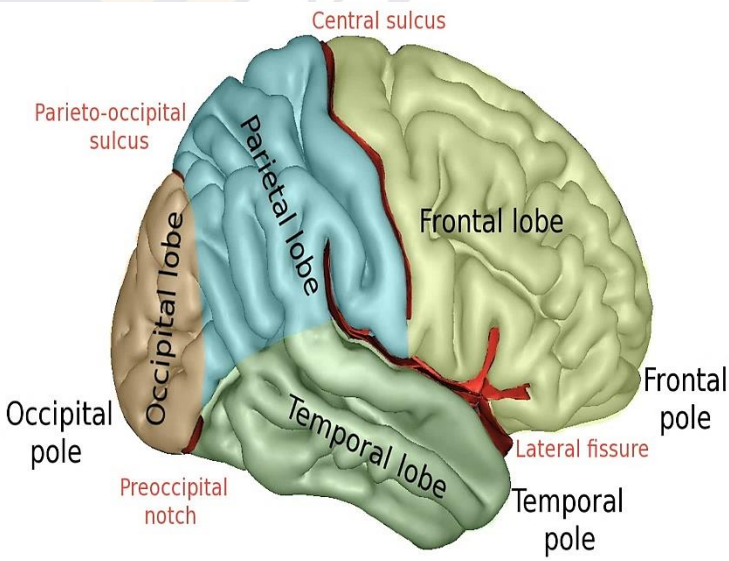
1. **Central sulcus:**
   - ☒ it runs downward across the lateral surface 1cm behind the midpoint between the frontal and occipital poles. It ends just above the lateral sulcus.

2. **Lateral sulcus:**
   - ☒ consists of a short stem and 3 rami: anterior ramus, ascending ramus and posterior ramus.
   - ☒ The area of the cortex that lies at the bottom of the lateral sulcus is called the insula.
3. **Calcarine sulcus:**
   - ☒ begins below the splenium of corpus callosum and extends to the occipital pole.
   - ☒ It is joined at its midpoint by the parieto-occipital sulcus.
4. **Parieto-occipital sulcus:**
   - ☒ it extends from middle of the calcarine sulcus to the superior border and continues on the lateral surface.

E. 4 Lobes of the cerebral hemisphere:

Each hemisphere is divided into 4 lobes by the central sulcus, the lateral sulcus and a vertical line between the parieto-occipital sulcus and the preoccipital notch:

1. **Frontal lobe:** in front of the central sulcus and above the lateral sulcus.
2. **Parietal lobe:** behind the central sulcus, above the lateral sulcus and in front of the vertical line between the parieto-occipital sulcus and the preoccipital notch.



3. **Occipital lobe:** behind the vertical line.
4. **Temporal lobe:** below the lateral sulcus and in front of the vertical line.

The superolateral surface

A. Sulci:

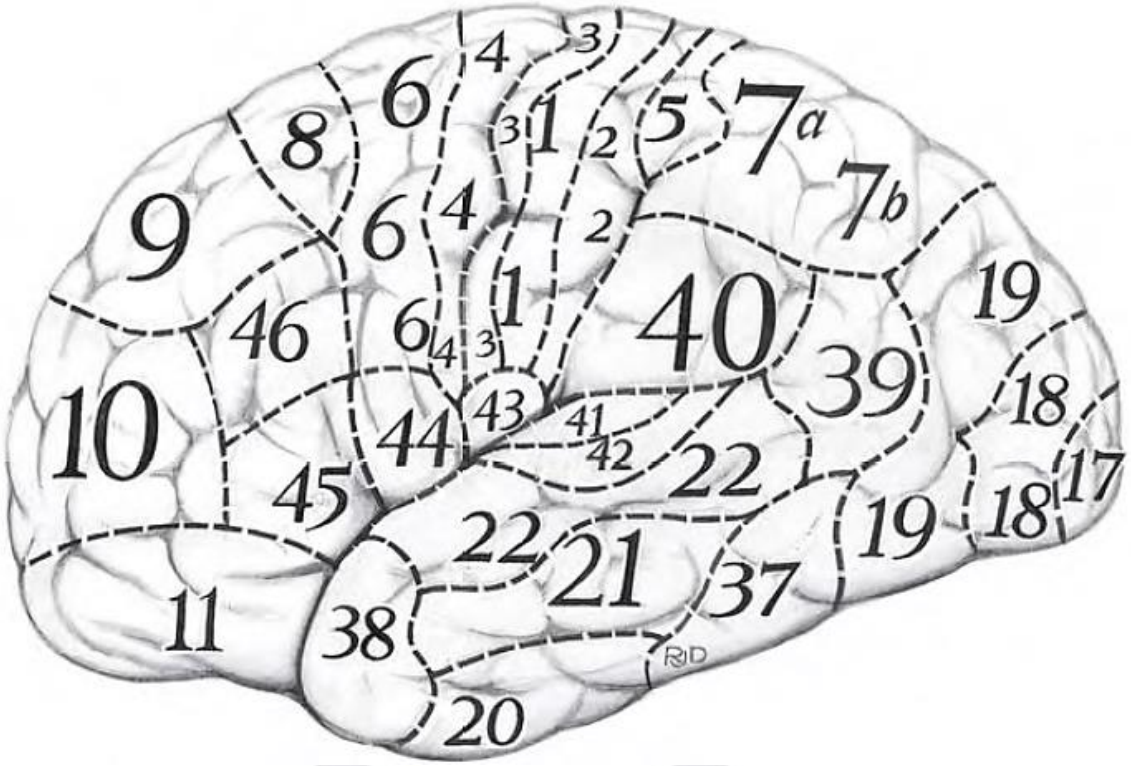
1. Central sulcus: 1cm behind the midpoint between the frontal and occipital poles.
2. Precentral sulcus: in front and parallel to the central sulcus.
3. Postcentral sulcus: behind and parallel to the central sulcus.
4. Three rami of the lateral sulcus: anterior ramus, ascending ramus and posterior ramus.
5. Two frontal horizontal sulci: superior and inferior frontal sulci.
6. Two temporal horizontal sulci: superior and inferior temporal sulci.
7. Intraparietal sulcus: extends posteriorly from the middle of the postcentral sulcus.
8. Parieto-occipital sulcus and calcarine sulcus: extend from the medial surface.
9. Sulcus lunatus: curved sulcus surrounding the end of the calcarine sulcus.

B. Gyri:

1. Precentral gyrus: lies between the central and precentral sulci.
2. Postcentral gyrus: lies between the central and postcentral sulci.
3. Three frontal gyri:
   - ☒ Superior frontal gyrus: lies above the superior frontal sulcus.
   - ☒ Middle frontal gyrus: lies between the superior and inferior frontal sulci.
   - ☒ Inferior frontal gyrus: lies below the inferior frontal sulcus. It is divided into 3 parts by the anterior and ascending rami of the lateral sulcus:
   - ☒ Opercular part: behind the ascending ramus.
   - ☒ Triangular part: between the ascending ramus and the anterior ramus.
   - ☒ Orbital part: below the anterior ramus.
4. Three temporal gyri:
   - ☒ Superior temporal gyrus: above the superior temporal sulcus.
   - ☒ Middle temporal gyrus: between the superior and inferior temporal sulci.

- ☒ Inferior temporal gyrus: below the inferior temporal sulcus.

5. Superior parietal lobule: above the intraparietal sulcus.
6. Inferior parietal lobule: below the intraparietal sulcus. It is divided into:
   - ☒ Supramarginal gyrus: surrounds the posterior end of the lateral sulcus.
   - ☒ Angular gyrus: surrounds the posterior end of the superior temporal sulcus.



Cortical areas on the lateral surface

Frontal Lobe: all the motor areas

1. **Primary motor area (area 4):** in the precentral gyrus, anterior wall of the central sulcus and extends into the anterior part of the paracentral lobule.
2. **Premotor area (area 6):** lies anterior to the primary motor area.
3. **Frontal eye field area (area 8):** in the posterior part of the middle frontal gyrus.
4. **Motor speech area (Broca s area):** in the posterior part of the inferior frontal gyrus of the dominant hemisphere. It lies in the opercular (# 44) & triangular gyri (# 45).
5. **Prefrontal cortex (personality center)** (areas 9, 10, 11 & 12): in the frontal pole.

Temporal Lobe:

1. **1. Primary auditory area (Heschl s area) (areas 41 & 42):** in the middle of the upper surface of the superior temporal gyrus.
2. **2. Auditory association area (Wernicke s area) (area 22):** in the posterior part of the superior temporal gyrus. It is a sensory speech area, it recognizes what you hear. It understands spoken language.

Parietal Lobe:

1. **General sensory area (areas 3, 1 & 2):** lies in the postcentral gyrus, posterior wall of the central sulcus and the posterior part of the paracentral lobule.
2. **Somatosensory association areas:**
   - ☒ Superior parietal lobule: areas 5 & 7.
   - ☒ Supramarginal gyrus: area 40.
3. **Primary taste area (area 43):** present in the lower end of the postcentral gyrus.
4. **Primary vestibular area**: present in the face area of the general sensory area.

5. **Two sensory speech areas:** in the dominant hemisphere in the following gyri:
   - ☒ Angular gyrus (area 39): understands written language.
   - ☒ Supramarginal gyrus (area 40): understands sizes, shapes, weights and texture.

- **Occipital Lobe:**

  Extension of the primary visual area (area 17) & visual association areas (# 18 & 19): around calcarine sulcus.

Insula (island of Reil)

- The insula is the area of the cerebral cortex present at the bottom of the lateral sulcus.
- It is hidden by the lips of the lateral sulcus, which form the opercula of the insula.
- **Opercula:**
  1. **Frontal operculum:** upper lip of the posterior ramus in the frontal lobe
  2. **Parietal operculum:** upper lip of the posterior ramus in the parietal lobe.
  3. **Temporal operculum:** lower lip of the posterior ramus in the temporal lobe.
  4. **Orbital operculum:** formed by the orbital part of the inferior frontal gyrus.
- **Relations:**

  A. Superficial Relation:
  1. **Middle cerebral artery:** at the bottom of the lateral sulcus.
  2. **Deep middle cerebral vein:** at the bottom of the lateral sulcus.
  3. **Superficial middle cerebral vein:** at the lips of the lateral sulcus.

  B. Deep Relation: from outside inward:
  1. Extreme capsule
  2. Claustrum
  3. External capsule
  4. Lentiform nucleus.

The medial surface

Sulci:

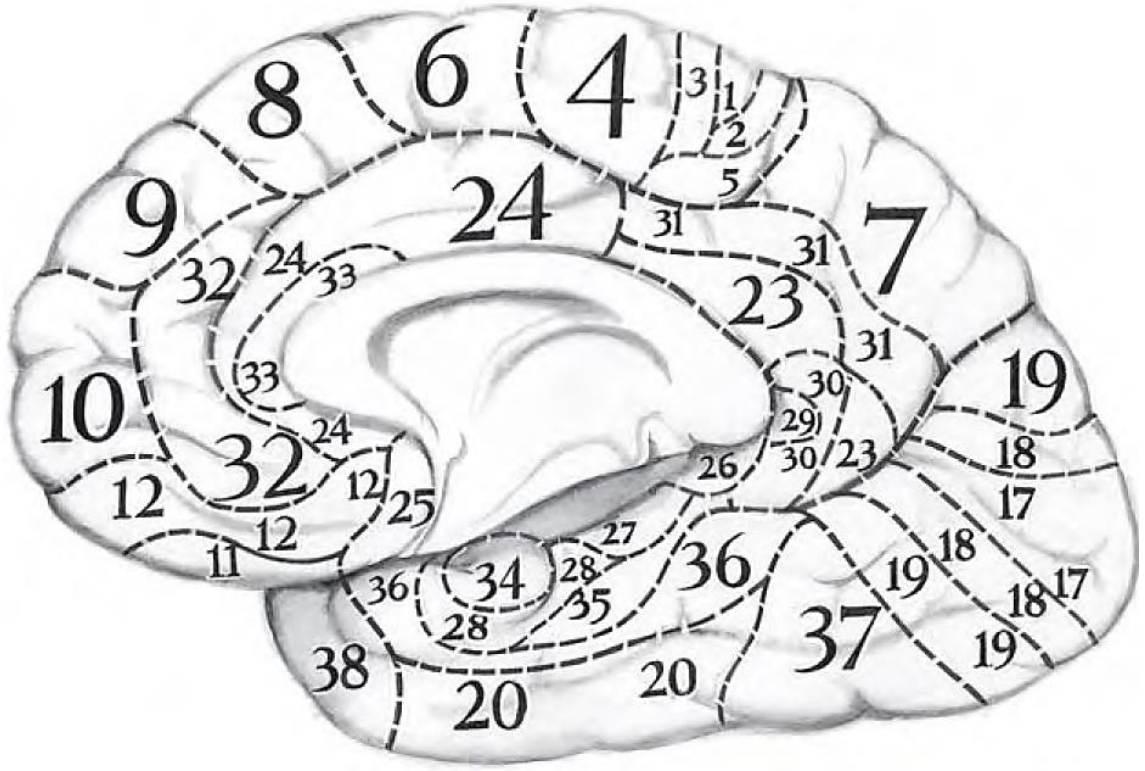
1. **Callosal sulcus:** lies above the corpus callosum.
2. **Cingulate sulcus:** extends parallel to the callosal sulcus.
3. **Marginal sulcus**: extends from the cingulate sulcus to lie behind the central sulcus.
4. **Subparietal sulcus:** extends from the cingulate sulcus toward the calcarine sulcus
5. **Calcarine sulcus.**
6. **Parieto-occipital sulcus:** extends from the calcarine sulcus to the superior border.
7. **Collateral sulcus:** is mainly present on the inferior surface.

Gyri:

1. **Cingulate gyrus:** lies above the corpus callosum, between the callosal sulcus and cingulate sulcus. It curves around the splenium of corpus callosum to form the isthmus and continues anteriorly in the temporal lobe as the parahippocampal gyrus.
2. **Lingual gyrus:** lies below the calcarine sulcus.
3. **Cuneus:** lies between the calcarine sulcus, superior border and parieto-occipital sulcus.
4. **Precuneus:** lies between the parieto-occipital sulcus, marginal sulcus, subparietal sulcus and superior border.
5. **Paracentral lobule:** the area surrounding the upper end of the central sulcus.
6. **Superior (medial) frontal gyrus:** lies between the cingulate sulcus and the upper border.

Cortical areas of the medial surface

1. **Primary visual area (area 17):** present above and below the calcarine sulcus.
2. **Visual association areas (areas 18 & 19):** on either side of the primary visual area.
3. **Extension of the primary motor & general sensory areas:** in the paracentral lobule.
4. **Prefrontal cortex (personality center):** in the frontal pole.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The inferior surface

- **Orbital surface:**
  1. **Olfactory sulcus:** contains the olfactory bulb and tract. The olfactory tract divides into medial and lateral olfactory striae, which bound the anterior perforated substance.
  2. **Orbital sulcus:** is H-shaped sulcus.
  3. **Gyrus rectus:** lies medial to the olfactory sulcus.
  4. **Four orbital gyri**: lie around the orbital sulcus (anterior, posterior, medial & lateral gyri).
- **Tentorial surface:**
  1. **Collateral sulcus:** extends from below the calcarine sulcus to the rhinal sulcus.
  2. **Rhinal sulcus:** curved sulcus at the anterior end of the collateral sulcus.
  3. **Occipitotemporal sulcus:** lies lateral and parallel to the collateral sulcus.
  4. **Parahippocampal gyrus:** lies medial to the collateral and rhinal sulci. The anterior end of the parahippocampal gyrus hooks backward forming the uncus.
  5. **Uncus:** is the anterior hooklike end of the parahippocampal gyrus.
  6. **Occipitotemporal (fusiform) gyrus:** between the collateral and occipitotemporal sulcus.

Cortical areas of the inferior surface

1. **Primary olfactory area:** located in the uncus.
2. **Olfactory association area (area 28):** in the anterior part of the parahippocampal gyrus.

Internal structure of the cerebral hemispheres

The basal ganglia

- **Components: they are composed of:**

A. Corpus Striatum: formed of:

1. Caudate nucleus.
2. Lentiform nucleus.

B. Amygdaloid nucleus: functionally, it is a part of the limbic system.

C. Claustrum: controversial function.

- **Caudate nucleus**

A. Shape: is a C-shaped nucleus.

B. Parts: it is formed of 3 parts: head, body and tail.

1. **Head:**
   - ☒ It forms the lateral wall of the anterior horn of the lateral ventricle
   - ☒ It is separated from the lentiform nucleus by the anterior limb of the internal capsule.
2. **Body:**
   - ☒ It lies in the floor of the central part of the lateral ventricle
   - ☒ It is separated from the thalamus by the thalamostriate vein and the stria terminalis (fibers connecting the amygdaloid nucleus with the hypothalamus and septal area).
3. **Tail:**
   - ☒ Extends into the temporal lobe in the roof of the inferior horn of the lateral ventricle.
   - ☒ It ends anteriorly at the amygdaloid nucleus.

Lentiform nucleus

A. Shape: wedge-shaped. Its apex is directed medially.

B. Parts: It is divided into two parts:

1. **Putamen:** is the lateral part.
2. **Globus pallidus:** is the medial part.

C. Relation:

1. **Medially: related to the internal capsule.**
   - ☒ Anterior limb separates it from caudate nucleus.
   - ☒ Posterior limb separates it from the thalamus.
2. **Laterally: related to the external capsule, which separates it from the claustrum.**
3. **Inferiorly: related to the amygdaloid nucleus and the anterior commissure.**

Claustrum

Relation: deep to the insula

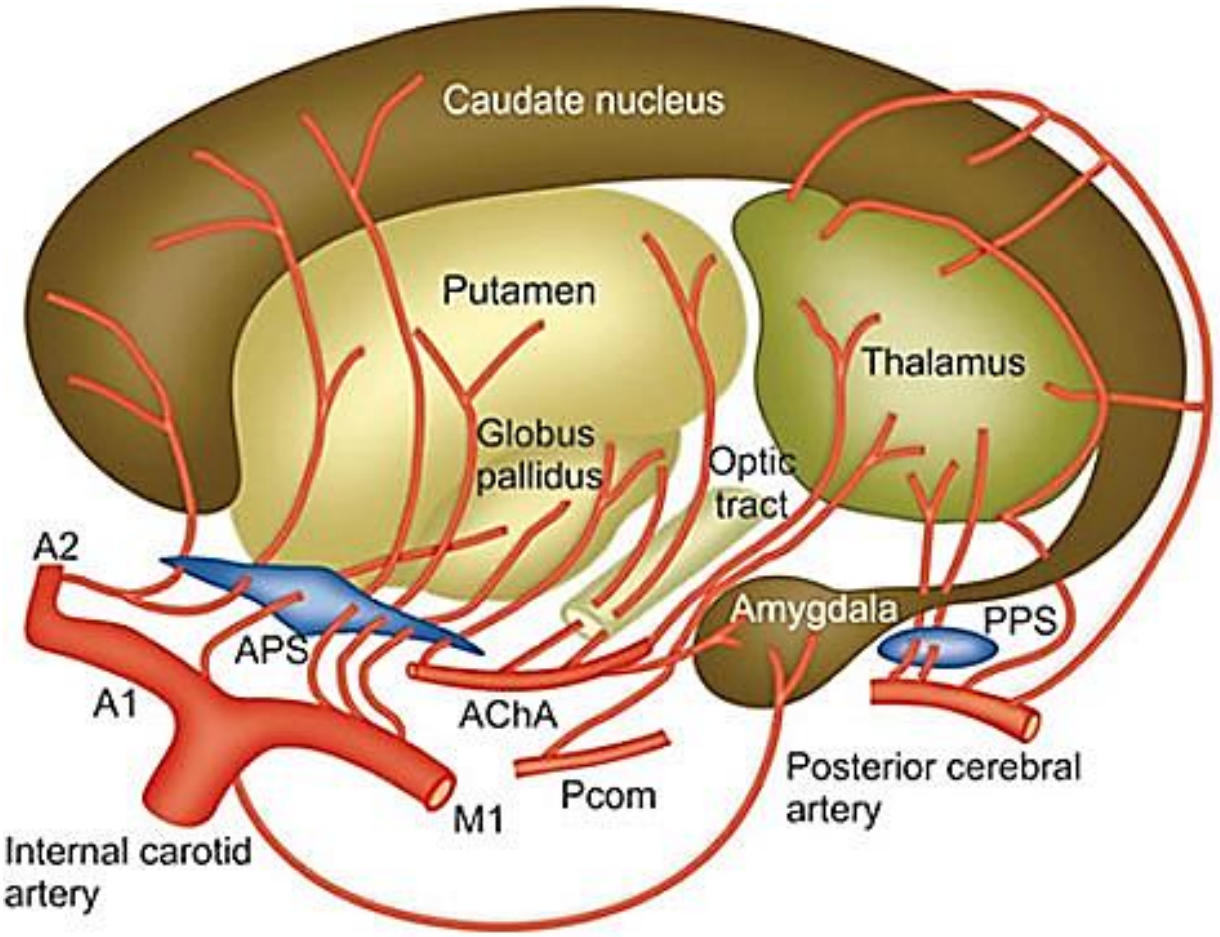
- ☒ External capsule: separating it from the lentiform nucleus.
- ☒ Extreme capsule: separating it from the insula.

Amygdaloid nucleus

- ☒ It lies in the anterior part of the temporal lobe in the roof and in front of the tip of the inferior horn of the lateral ventricle.
- ☒ **Function:** It is a part of the limbic and olfactory systems.

Arterial supply of the Basal Ganglia

1. **Anterior part of corpus striatum:** by the anterior cerebral artery (medial striate artery).
2. **Remaining parts of corpus striatum except tail of the caudate nucleus:** by the middle cerebral artery (lateral striate arteries).
3. **Tail of the caudate nucleus & amygdaloid nucleus:** anterior choroidal artery from the ICA


Caudate nucleus
Putamen
Thalamus
Globus pallidus
Optic tract
A2
APS
Amygdala
PPS
A1
AChA
Posterior cerebral artery
Pcom
M1
Internal carotid artery

Nerve fibers of the white matter

Types: the white matter contains 3 types of nerve fibers:

1. **Commissural fibers:** connect the same cortical areas of the two cerebral hemispheres.
2. **Association fibers:** connect cortical areas in the same cerebral hemisphere.
3. **Projection fibers:** connect the cerebral cortex with the subcortical areas.

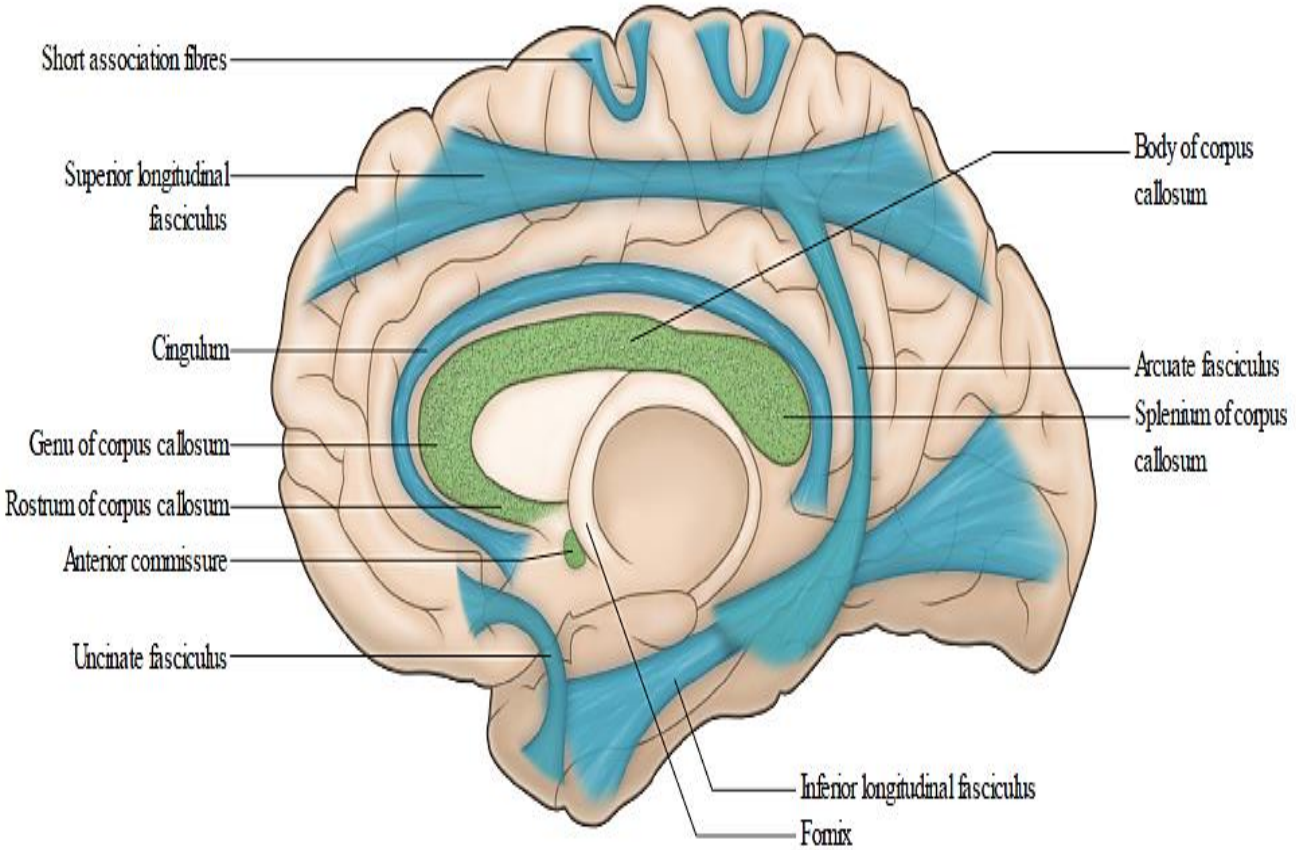
Commissural fibers

- **Definition:** They connect the same cortical areas of the two cerebral hemispheres.
- **Types: 5**
  1. **Corpus callosum.**
  2. **Anterior commissure.**
  3. **Posterior commissure.**
  4. **Hippocampal commissure.**
  5. **Habenular commissures.**

Corpus Callosum:

- **Parts: it is divided into 4 parts:**
  - **Rostrum:** it is continuous with the lamina terminalis.
  - **Genu:** is the anterior end of the corpus callosum. Its fibers form the forceps minor, which connects the two frontal lobes.
  - **Splenium:** is the posterior end of the corpus callosum. Its fibers form the forceps major, which connects the two occipital lobes.
  - **Body (trunk):** is the central part of the corpus callosum. Its fibers form the radiation of corpus callosum. The posterior fibers form the tapetum, which connects the 2 temporal lobes.
- **Function:** transfer of information (memory and language) between the 2 hemispheres.
- **Lesion:** Callosal apraxia. The memory and language processes will not be accessible to the nondominant hemisphere causing left side disorders.

- **Anterior Commissure:** It connects the two temporal lobes.
- **Posterior Commissure: It connects:**
  1. The two superior colliculi.
  2. The pretectal nucleus and the Edinger-Westphal nuclei for the bilateral light reflex.
  3. The two-occulomotor nuclei for the upward gaze.
- **Hippocampal Commissure**: connects the 2 fornices and the 2 hippocampi.
- **Habenular Commissure**: connects the habenular nuclei of the two sides.



Association fibers

- **Definition:** they connect one cortical area with another cortical area in the same hemisphere.
- **Types**: They are divided into short and long fibers:

  A. Short Association Fibers: they connect adjacent cortical areas.

  B. Long Association Fibers: they connect distant cortical areas. They include:

  1. Superior longitudinal fasciculus (arcuate fasciculus): connects the 4 lobes together.
  2. Inferior longitudinal fasciculus: connects the occipital lobe with the temporal lobe.
  3. Uncinate fasciculus: forms an arch around the stem of the lateral sulcus and connects the frontal lobe with the temporal lobe.
  4. Cingulum: lies in the cingulate gyrus. It is the fiber bundle of the limbic lobe. It connects the cingulate gyrus with the parahippocampal gyrus and ends in the uncus.
- **Function:** processing of information (such as language) in the same hemisphere.

Projection fibers

- **Definition**: they connect the cerebral cortex with the subcortical areas and form a compact bundle called the internal capsule.
- **Types:** they are divided into ascending and descending fibers:
  1. Ascending projection fibers: are mainly thalamocortical fibers.
  2. Descending projection fibers: such as corticospinal and corticobulbar fibers.

The internal capsule

- **Definition:** It is a band of projection fibers
- **Divisions: It is divided into 3 parts:**

A. **Anterior limb:** between the lentiform nucleus and the head of the caudate nucleus.

B. **Genu:** opposite the apex of the lentiform nucleus.

C. **Posterior limb: is divided into:**

1. Lenticulothalamic part: between the lentiform nucleus and the thalamus.
2. Retolenticular part: behind the lentiform nucleus.
3. Sublenticular part: below the lentiform nucleus.

The lateral ventricle

- **Definition:** is the cavity of the cerebral hemisphere.
- **Shape**: it is a C-shaped cavity filled with the CSF.
- **Divisions:** It is divided into central part and 3 horns: anterior, posterior and inferior

A. Anterior Horn:

- ☒ Extension: extends into the frontal lobe anterior to the interventricular foramen.
- ☒ Relations:
  1. Anterior end: genu of the corpus callosum.
  2. Roof: body of the corpus callosum.
  3. Floor: rostrum of the corpus callosum.
  4. Medial wall: septum pellucidum.
  5. Lateral wall: head of the caudate nucleus.

B. Central Part (Body):

- ☒ Extension: In the parietal lobe from the interventricular foramen to the splenium of the corpus callosum.

☒ Relations:

- Roof: body of the corpus callosum.
- Medial wall: the septum pellucidum.
- Floor: from the lateral to the medial side:

1. Body of the caudate nucleus.
2. Thalamostriate vein.
3. Stria terminalis.
4. Thalamus.
5. Choroid plexus in the choroid fissure.
6. Body of the fornix.

- Lateral wall: meeting the roof with the floor.

C. Posterior Horn:

☒ Extension: extends in the occipital lobe behind the splenium of the corpus callosum.

☒ Relations:

- Roof: tapetum of the corpus callosum.
- Floor: collateral trigone produced by the collateral sulcus.
- Medial wall: has two elevations:

1. Bulb of the posterior horn: superior and produced by the forceps major.
2. Calcar avis: inferior and produced by the calcarine sulcus.

- Lateral wall: from medial to lateral:

1. Tapetum of the corpus callosum.
2. Optic radiation.
3. Inferior longitudinal fasciculus.

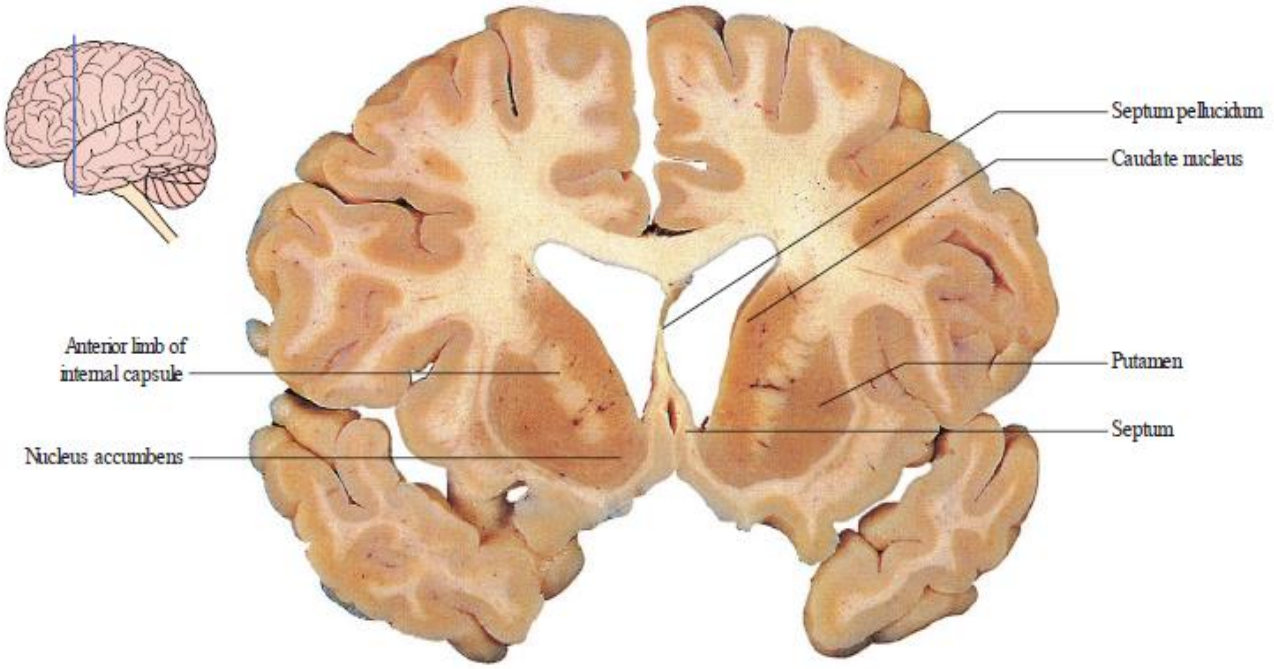
D. Inferior Horn:

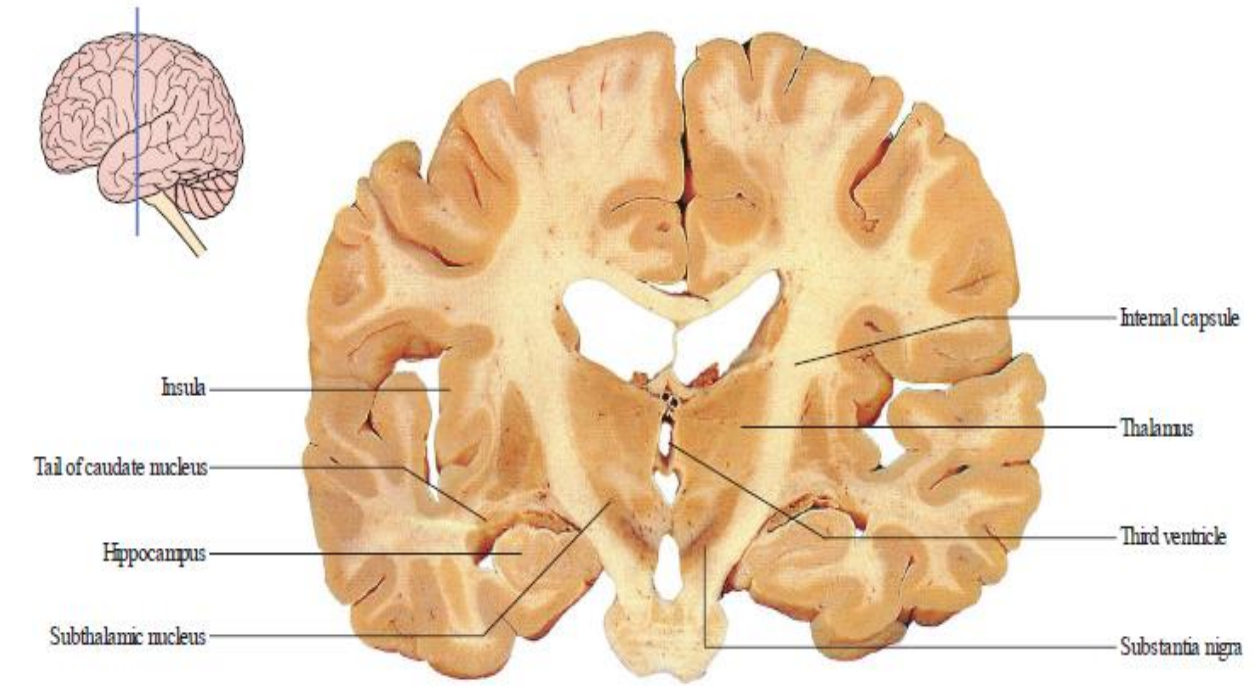
- ☒ Extension: it winds around thalamus and extends anteriorly into the temporal lobe.
- ☒ Relations:
  - Roof: 3
    1. Tail of the caudate nucleus and amygdaloid nucleus.
    2. Thalamostriate vein.
    3. Stria terminalis
  - Floor: 3, from the medial to the lateral side:
    1. Fimbria: arises from the hippocampus and continues backward as the fornix.
    2. Hippocampus: its anterior end is enlarged to form the pes hippocampi.
    3. Collateral eminence: is produced by the collateral sulcus.
  - Medial wall: the choroid plexus of the inferior horn.
  - Lateral wall: tapetum of the corpus callosum.
- ☒ Communication:

  With the third ventricle through the interventricular foramen of Monro.

Choroid Plexus:

- ☒ **Site:** in the body and the inferior horn of the lateral ventricle.
- ☒ **Arterial supply:** supplied by the anterior & posterior choroidal arteries:


Septum pellucidum
Caudate nucleus
Anterior limb of internal capsule
Putamen
Nucleus accumbens
Septum


Internal capsule
Insula
Thalamus
Tail of caudate nucleus
Third ventricle
Hippocampus
Substantia nigra
Subthalamic nucleus

The limbic system

- **Components**: The limbic system is formed of:
  - **A. Nuclei.**
  - **B. Fiber bundles connecting the nuclei.**
- **Nuclei of the Limbic System**
  1. Limbic lobe: formed of the cingulate gyrus, parahippocampal gyrus and the uncus.
  2. Hippocampus: is continuous externally with the parahippocampal gyrus.
  3. Hypothalamus: the mammillary bodies.
  4. Anterior and medial thalamic nuclei.
  5. The prefrontal cortex (personality center).
  6. Amygdaloid nucleus (amygdala).
  7. Septal area (medial olfactory area):below the rostrum.
  8. Habenular nucleus.
- **Fiber Bundles of the Limbic System**
  1. Cingulum: fiber bundle of the limbic lobe.
  2. Fornix: Arises from the hippocampus and terminates in the mamillary body. Formed of 4 parts:
     - ☒ Fimbria: nerve fibers on the medial border of the hippocampus.
     - ☒ Crus of the fornix: is the continuation of the fimbria.
     - ☒ Body of the fornix: the two crura fuse to form the body of the fornix.
     - ☒ Anterior column of the fornix: each one terminates in the mamillary body.
  3. Mamillothalamic tract: connects the mamillary body with the anterior thalamic nucleus.
  4. Anterior thalamic radiation: connects the medial thalamic nucleus with personality center

5. Stria terminalis: it begins in the amygdaloid nucleus and ends in the septal area.
6. Stria medullaris thalami: begins in the septal area and in the habenular nucleus.

Functions of the Limbic System:

1. Recent memory: the hippocampus has a role in remembering recent events.
2. Emotional behavior: it plays a role in feeling, feeding, aggression, anger, fear, sadness, pleasure and emotions associated with sexual behavior.
3. Olfaction: the uncus is a primary olfactory area.
4. Clinical Problems:
   - ☒ Lesion in the hippocampus causes loss of the recent memory.
   - ☒ In Alzheimer s disease, there is extensive degeneration in the hippocampus.
   - ☒ Lesions in the amygdaloid nucleus cause loss of aggressive behavior, fear and anger.

Cerebrospinal fluid (CSF)

- **Definition**: it is the fluid that fills the ventricles of the brain and the subarachnoid space.
- **Volume**: about 130 ml (30 ml in the ventricles and 100 ml in the subarachnoid space).
- **Formation**: formed by active secretion and by diffusion from:
  1. Choroid plexus: is the main source of the CSF (70%). Mostly in the lateral ventricle.
  2. Ependymal lining of the ventricles: add CSF to the ventricles.
  3. Cells of the pia mater: add CSF to the subarachnoid space.
- **Circulation:**
  1. It flows from the lateral ventricles to the third ventricle through the interventricular foramina of Monro, then to the fourth ventricle through the aqueduct of Sylvius.
  2. More CSF is added in each ventricle.
  3. It leaves the fourth ventricle to the subarachnoid space through the median foramen of Magendie and the lateral foramina of Luschka.
  4. A small amount flows to the central canal of the spinal cord.
  5. The CSF flows in the subarachnoid space around the brain and the spinal cord.
  6. The following factors facilitate the CSF circulation:
     - ☒ Pulsations of the arteries in the subarachnoid space.
     - ☒ Movements of the cilia of the ependymal cells.
     - ☒ Positive and negative pressure created by continuous production and absorption.

Absorption:

1. Main site for drainage: arachnoid villi & granulations. They drain the CSF into the venous blood of the dural sinuses especially the superior sagittal sinus.
2. Gap junctions between ependymal cells & between pial cells back to the brain tissue.
3. Into the venous blood through small veins in the subarachnoid space.
4. Into the perineural lymph vessels around the cranial and spinal nerves.

Functions of the CSF:

1. Reduces the brain weight 60 folds (from 1400 gm to 25 gm).
2. Protects the brain and the spinal cord.
3. Substitutes the lymphatic system in the CNS and provides a drainage system
4. Maintains the chemical environment for the CNS through communication with the brain extracellular space.
5. Regulation of the intracranial pressure.

Clinical Conditions Associated with the CSF

☒ Hydrocephalus

- Definition: It is an abnormal increase in the volume of the CSF with dilatation of the ventricles and increase in size of the head.
- Causes:

1. Obstruction to its circulation: It is the commonest cause. The commonest site of obstruction is the aqueduct of Sylvius . Other sites are interventricular foramina.
2. Overproduction of the CSF: by choroid plexus tumor (rare).
3. Inadequate drainage of the CSF: by thrombosis of the superior sagittal sinus.

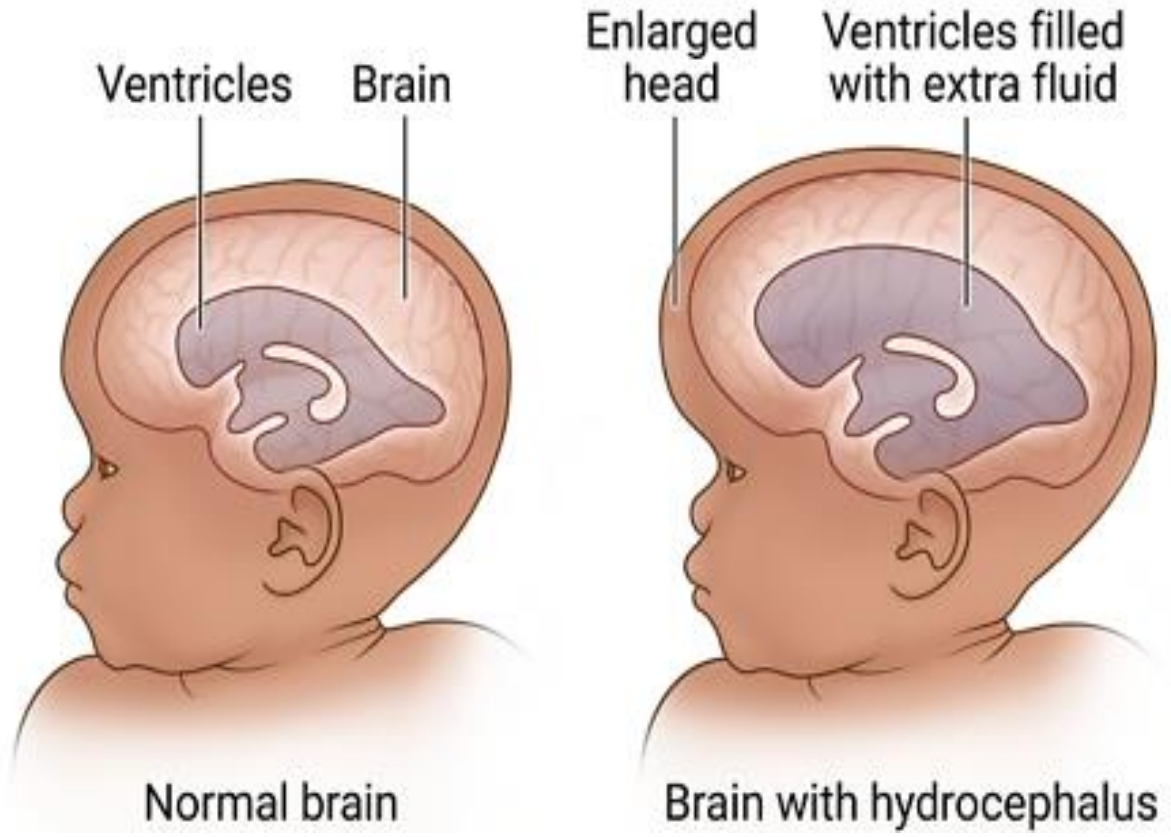
☒ **Lumbar puncture**

It means introducing a needle into the subarachnoid space for:

1. Injecting drugs into the CSF such as anaethetics and antibiotics.
2. Obtaining a sample of CSF for analysis.
3. Measuring the CSF pressure by attaching a manometer to the needle.

☒ **Papilledema:** edema of the optic disc

The subarachnoid space extends around the optic nerve and the other cranial nerves. Elevation of the CSF pressure compresses the optic nerve and the central retinal vein causing edema of the optic disc.



Blood supply of the brain

Arterial supply

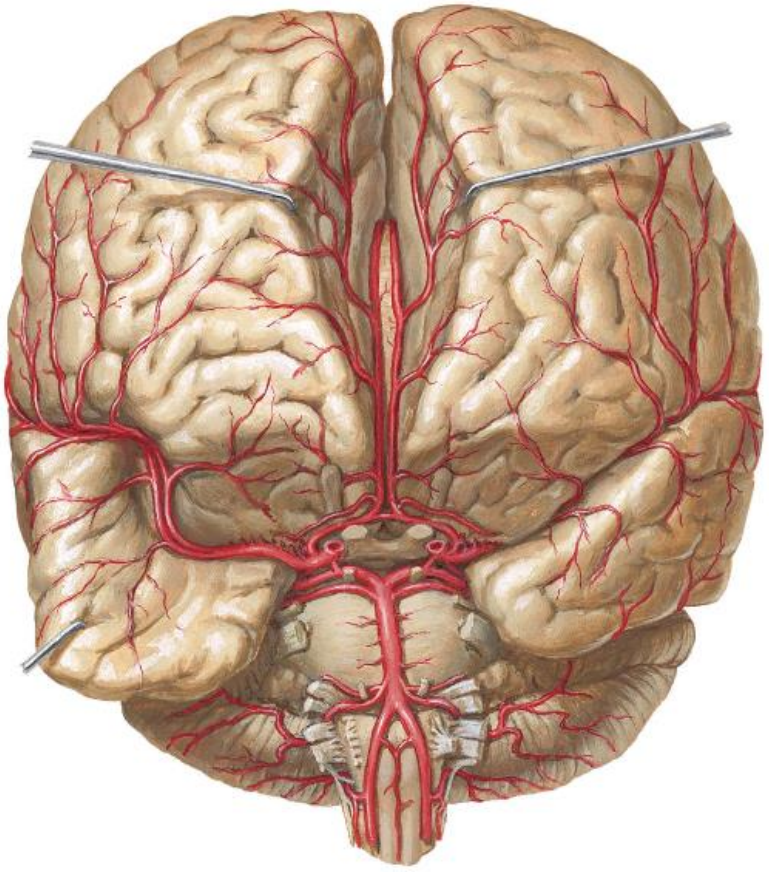
☒ **The brain is supplied by two systems:**

1. **Vertebrobasilar system:** the two vertebral arteries and the basilar artery.
2. **Internal carotid system:** the two internal carotid arteries.

Internal carotid artery

- **Origin:** one of the two terminal branches of the common carotid artery at the upper border of the thyroid cartilage (disc between C3 and C4).
- **Course:** the course of the internal carotid artery is divided into 4 parts:
  1. **Cervical part:** inside the carotid sheath with the internal jugular vein & the vagus nerve.
  2. **Petrous part:** in the carotid canal in the petrous part of the temporal bone.
  3. **Cavernous part:** passes forward inside the cavernous sinus, then pierces its roof to form the supracavernous part.
  4. **Supracavernous part:** passes backward above the cavernous sinus. The cavernous and supracavernous parts form the carotid siphon (U-shaped in the angiogram)
- **Termination:** lateral to optic chiasma by dividing into anterior & middle cerebral arteries.
- **Branches:**
  1. **Hypophyseal branches:** superior and inferior. They supply the pituitary gland.
  2. **Ophthalmic artery:** enters the orbit through the optic canal.
  3. **Posterior communicating artery:** joins the posterior cerebral artery and supplies the:
     - ☒ Midbrain, thalamus and hypothalamus.
     - ☒ Internal capsule: posterior part of the genu & anterior third of the posterior limb.

4. **Anterior choroidal artery: supplies the:**
   - ☒ Posterior two-thirds of the posterior limb of the internal capsule.
   - ☒ Choroid plexus of the inferior horn of the lateral ventricle.
   - ☒ Optic tract and lateral geniculate body.
   - ☒ Tail of the caudate nucleus and amygdaloid nucleus.
5. **Two terminal branches: anterior cerebral artery and middle cerebral artery.**



Anterior cerebral artery (ACA)

- **Origin:** one of the two terminal branches of the internal carotid artery (it is the smaller one).
- **Course:**
  - ☒ It is joined with the opposite one by the anterior communicating artery.
  - ☒ It passes around the genu of the corpus callosum and continues backward on the upper surface of the corpus callosum in the callosal sulcus.
  - ☒ It ends at the splenium by anastomosing with branches of the posterior cerebral artery.
- **Branches:**
  1. **Cortical branches: supply:**
     - ☒ Upper one inch of the lateral surface of the frontal and parietal lobes. It supplies the leg area of the motor and sensory cortical areas.
     - ☒ Medial surface of the frontal and parietal lobes.
     - ☒ Medial half of the orbital surface.
  2. **Central branches: supply: (4 anterior)**
     - ☒ Anterior limb of the internal capsule.
     - ☒ Anterior part of the genu of the internal capsule.
     - ☒ Anterior part of corpus striatum: lentiform nucleus & head of caudate nucleus.
     - ☒ Anterior part of the hypothalamus.
  3. **Callosal branches: to the entire corpus callosum.**
- **Clinical Note: Occlusion of the anterior cerebral artery causes:**
  1. **Affection of the paracentral lobule:**
     - ☒ Contralateral paralysis of the leg muscles.
     - ☒ Contralateral somatosensory loss in the leg.
  2. **Affection of the corpus callosum: callosal apraxia.**

Posterior cerebral artery (PCA)

- **Origin**: by the bifurcation of the basilar artery at the upper border of the pons.
- **Course:**
  - ☒ It passes backward around the lateral side of the midbrain to reach the splenium of the corpus callosum where it divides into temporal, calcarine and parietooccipital branches.
  - ☒ The temporal branches are distributed over the inferior surface of the temporal lobe.
  - ☒ The other branches run in the corresponding sulci and anastomose with branches of the anterior cerebral artery.
  - ☒ It is joined with the internal carotid artery by the posterior communicating artery.
  - ☒ It is separated from the superior cerebellar artery by the oculomotor and trochlear nerves.
- **Branches:**
  1. **Cortical branches: supply:**
     - ☒ Lower inch of the lateral surface (inferior temporal gyrus).
     - ☒ All aspects of the occipital lobe. It supplies the primary visual area (area 17) and the visual association areas (areas 18 & 19).
     - ☒ Medial and inferior surfaces of the temporal lobe except the temporal pole.
  2. **Central branches**: enter through the posterior perforated substance and supply:
     - ☒ Thalamus and the hypothalamus.
     - ☒ Midbrain.
  3. **Posterior choroidal artery: supplies:**
     - ☒ Choroid plexus of the third and lateral ventricles.
     - ☒ Thalamus
     - ☒ Midbrain.

4. **Splenial artery:** it may be present and supplies the splenium of the corpus callosum.

- **Clinical Note:**
  - ☒ Occlusion of the posterior cerebral artery causes contralateral homonymous hemianopia with macular sparing.

Middle cerebral artery (MCA)

- **Origin:** one of the two terminal branches of the internal carotid artery (it is the larger one).
- **Course:**
  - ☒ Passes in the lateral sulcus
  - ☒ Ends on the surface of the insula by dividing into terminal branches.
- **Branches:**

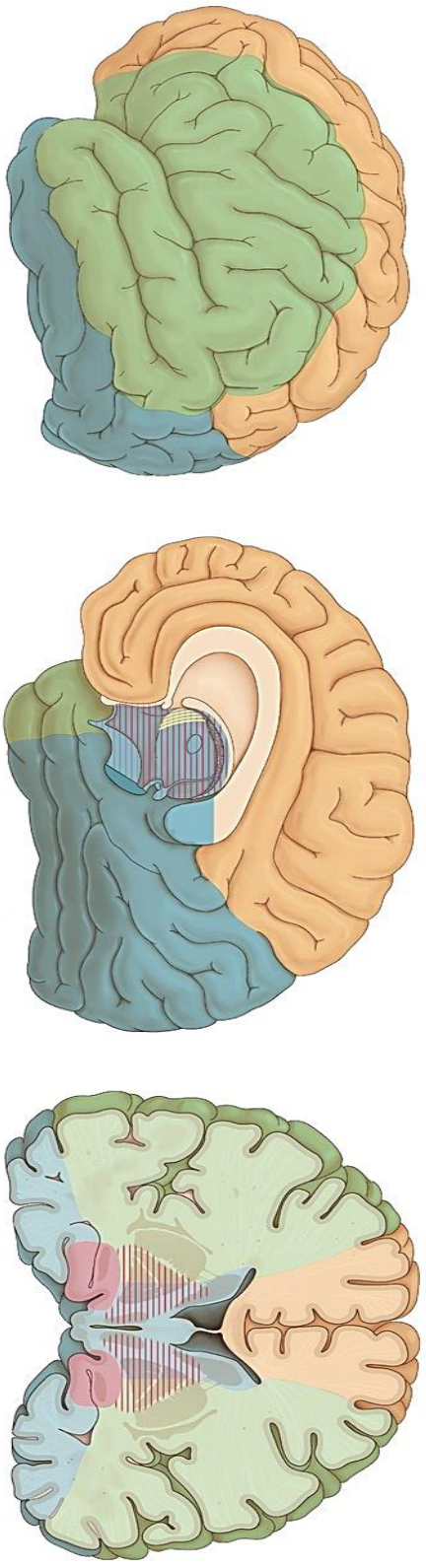
1. **Cortical branches: supply:**
   - ☒ Lateral half of the orbital surface.
   - ☒ All aspects of the temporal pole.
   - ☒ Lateral surface of the hemisphere **except**:
     a. Upper one inch (by anterior cerebral).
     b. Lower one inch (inferior temporal gyrus) (by the posterior cerebral).
     c. Occipital lobe (supplied by the posterior cerebral).

2. **Central branches (lateral striate arteries):**
   - ☒ One of these arteries is large, liable to rupture and called artery of cerebral hemorrhage
   - ☒ The central branches pierce the anterior perforated substance and supply the:
     a. Anterior and posterior limbs of the internal capsule.
     b. Posterior part of the corpus striatum except the tail of the caudate nucleus.

- **Important Cortical Areas Supplied by the MCA:**
  1. Motor, premotor and general sensory areas except the leg area (upper inch).
  2. Auditory and auditory association areas.
  3. Motor speech area (Broca s area) and sensory speech areas.
- **Clinical Note: occlusion of the middle cerebral artery causes:**
  1. Contralateral hemiplegia, most marked in the upper limb and face.
  2. Contralateral sensory loss of proprioception and discriominative touch.
  3. Bilateral diminution of hearing but mainly on the opposite side.
  4. Aphasia (paralysis of the speech) if the dominant hemisphere is affected.

Arterial supply of the cerebral cortex

- **Lateral surface:**
  1. Upper inch of the frontal and parietal lobes: by the anterior cerebral artery.
  2. Occipital lobe and lower inch (inferior temporal gyrus): by the posterior cerebral artery.
  3. The rest of the lateral surface: by the middle cerebral artery.
- **Medial surface:**
  1. Frontal and parietal lobes: by the anterior cerebral artery.
  2. Occipital and temporal lobes except the temporal pole: by the posterior cerebral artery.
  3. Temporal pole: by the middle cerebral artery.
- **Inferior surface:**
  1. Medial half of the orbital surface: by the anterior cerebral artery.
  2. Lateral half of the orbital surface and the temporal pole: by the middle cerebral artery.
  3. Tentorial surface except the temporal pole: by the posterior cerebral artery.


Anterior cerebral artery
Middle cerebral artery
Partially supplied by posterior communicating artery
Posterior cerebral artery
Anterior choroidal artery
Partially supplied by anterior choroidal artery

Arterial supply of the internal capsule

- **Anterior Limb:**
  - ☒ Dorsal 1/2: middle cerebral artery.
  - ☒ Ventral 1/2: anterior cerebral artery.
- **Genu:**
  - ☒ Anterior part: anterior cerebral artery.
  - ☒ Posterior part: post communicating artery.
- **Posterior Limb:**
  - ☒ Dorsal half: middle cerebral artery.
  - ☒ Ventral half:
    1. Anterior 1/3: posterior communicating artery.
    2. Posterior 2/3: Anterior choroidal artery.

Venous drainage of the brain

The brain is drained by two venous systems:

1. Superficial cerebral veins.
2. Deep cerebral veins.

Superficial cerebral veins

- ☒ They drain the superficial structures into the dural venous sinuses.
- ☒ They are divided into: superior, middle and inferior cerebral veins.

1. Superior cerebral veins (8-12): they drain into the superior sagittal sinus.
2. Middle cerebral veins: are divided into:
   a. Superficial middle cerebral vein: in the lateral sulcus. Drains into cavernous sinus.
   b. Deep middle cerebral vein: in the bottom of the lateral sulcus and drains the insula. It unites with the anterior cerebral vein to form the basal vein.
3. Inferior cerebral veins: they drain into the cavernous and transverse sinuses.

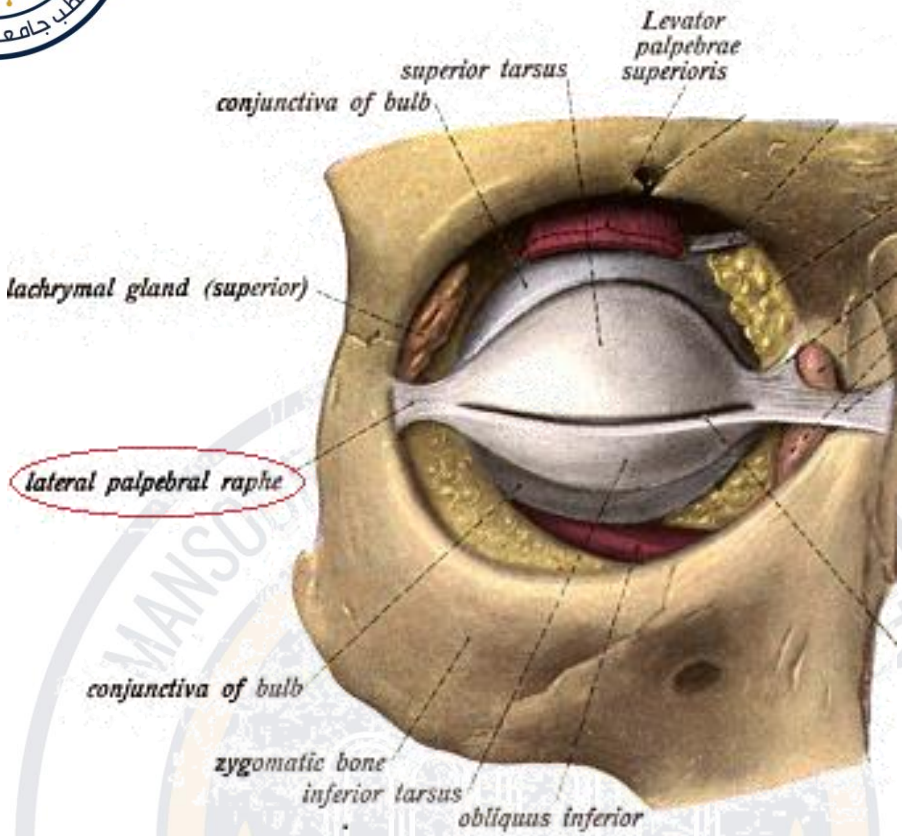
Deep cerebral veins:

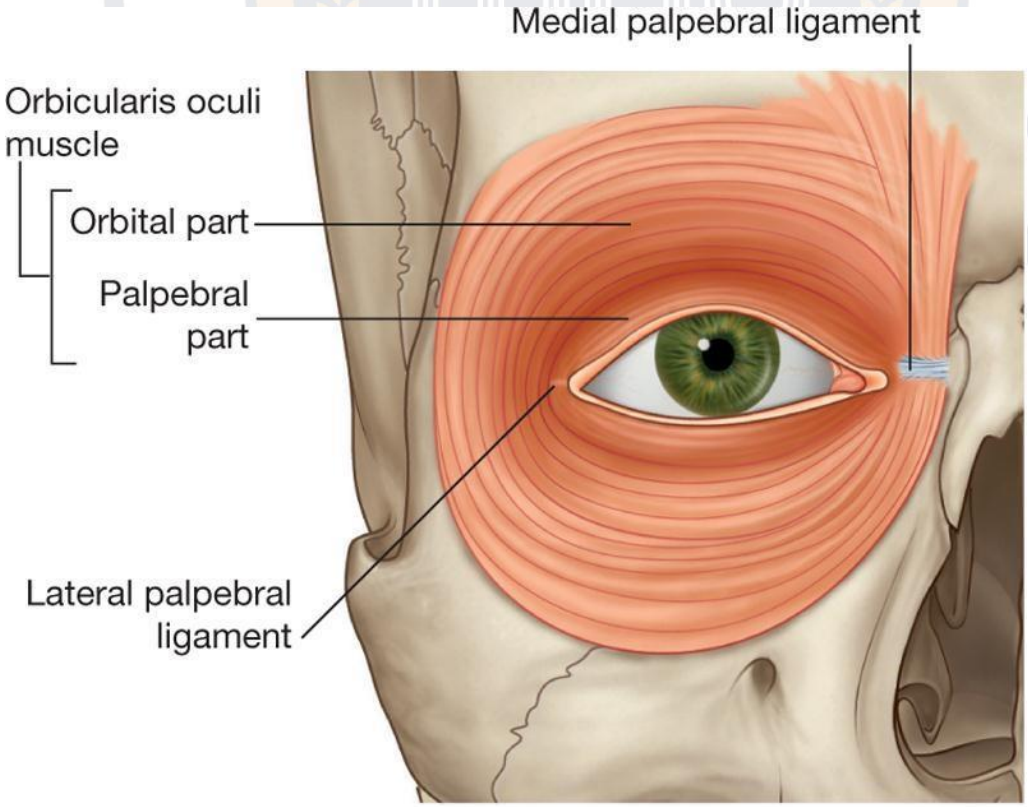
They drain the deep subcortical structures and form three large veins:

1. **Two internal cerebral veins:**
   - ☒ Each is formed at the interventricular foramen of Monro by the union of the thalamostriate vein and the choroidal vein.
   - ☒ The two internal cerebral veins unite below the splenium of the corpus callosum to form the great cerebral vein.
2. **Great cerebral vein:**
   - ☒ Formed by the union of the two internal cerebral veins.
   - ☒ It unites with the inferior sagittal sinus to form the straight sinus.
3. **Two basal veins:**
   - ☒ Formed by the union of the deep middle cerebral vein and anterior cerebral vein at the anterior perforated substance.
   - ☒ It ends in the great cerebral vein

	Anterior cerebral artery	Middle cerebral artery	Posterior cerebral artery
Origin	Smaller terminal branch of internal carotid.	Larger terminal branch of internal carotid.	Bifurcation of basilar artery.
Course	• Pass upward and medially in the longitudinal fissure • Joined with the other anterior cerebral artery by the anterior communicating, artery. • Pass upward on genu of corpus callosum to continue backwards in callosal sulcus • Ends at the splenium by anastomosing with branches of posterior cerebral artery.	• Enters the lateral sulcus • Ends on the surface of the insula by terminal branches over the lateral surface of the brain.	• Curves around the lateral side of the midbrain to reach the splenium of corpus callosum where it divides into: 1. **Temporal branches** supply the surface of the temporal lobe & anastomose with branches of middle cerebral artery: **2. Calcarine & parieto-occipital branches** Run in the corresponding sulci to anastomose with anterior cerebral artery at the parieto-occipital sulcus
Branches	**1. Cortical branches: supply:** **a.** Upper one inch of the lateral surface of the frontal and parietal lobes. It supplies the leg area of the motor and sensory cortical areas. **b.** Medial surface of the frontal and parietal lobes. **c.** Medial half of the orbital surface. **2. Central branches: supply: (4 anterior)** **a.** Anterior limb of the internal capsule. **b.** Anterior part of the genu of the internal capsule. **c.** Anterior part of corpus striatum: lentiform nucleus & head of caudate nucleus. **d.** Anterior part of the hypothalamus. **3. Callosal branches: to the entire corpus callosum.**	**1. Cortical branches:** supply: **a.** Lateral half of the orbital surface. **b.** All aspects of the temporal pole. **c.** Lateral surface of the hemisphere except: o Upper one inch. o Lower one inch. o Occipital lobe. **2. Central branches (lateral striate arteries):** One of these arteries is large, liable to rupture and called artery of cerebral hemorrhage **The central branches** pierce the anterior perforated substance and **supply the:** **a.** Anterior and posterior limbs of the internal capsule. **b.** Posterior part of the corpus striatum except the tail of the caudate nucleus.	**1. Cortical branches:** supply: **a.** Lower inch of the lateral surface. **b.** All aspects of the occipital lobe. It supplies the primary visual area (area 17) and the visual association areas (areas 18 & 19). **c.** Medial and inferior surfaces of the temporal lobe except the temporal pole. **2. Central branches:** enter through the posterior perforated substance and supply: **a.** Thalamus and hypothalamus. **b.** Midbrain. **3. Posterior choroidal artery:** supplies: **a.** Choroid plexus of the third and lateral ventricles. **b.** Thalamus **c.** Midbrain. **4. Splenial artery:** supplies the splenium of the corpus callosum.

Lesion	**<u>Paracentral lobule:</u>** Contralateral somatosensory loss in the leg & contralateral paralysis of leg muscles. **<u>Corpus callosum:</u>** o Callosal apraxia o Tactile agnosia	**<u>Motor area:</u> Contralateral hemiplegia marked in the upper limb & face.** **<u>Sensory area:</u>** Contralateral sensory loss. **<u>Auditory area:</u>** Bilateral diminution of hearing but mainly on the opposite side**.** **<u>Broca's area:</u>** Aphasia when the dominant hemisphere is affected.	**<u>Primary visual area & visual association area:</u> (17,18 & 19):** Contralateral homonymous hemianopia with macular sparing. **The macular vision is spared due** to anastomosis between branches of middle & posterior cerebral arteries


Levator palpebrae superioris
superior tarsus
conjunctiva of bulb
lachrymal gland (superior)
lateral palpebral raphe
conjunctiva of bulb
zygomatic bone
inferior tarsus
obliquus inferior


Medial palpebral ligament
Orbicularis oculi muscle
Orbital part
Palpebral part
Lateral palpebral ligament

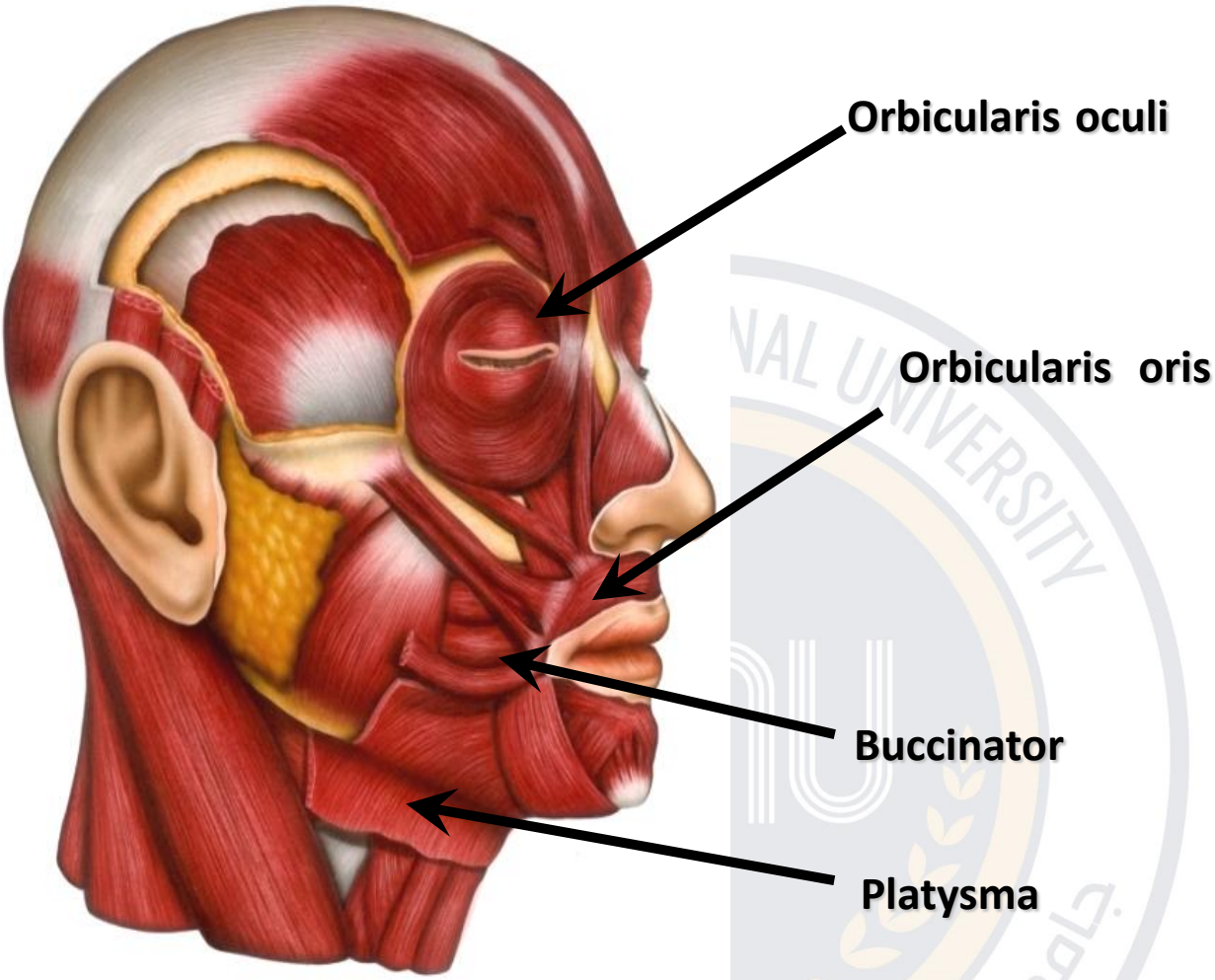
The face

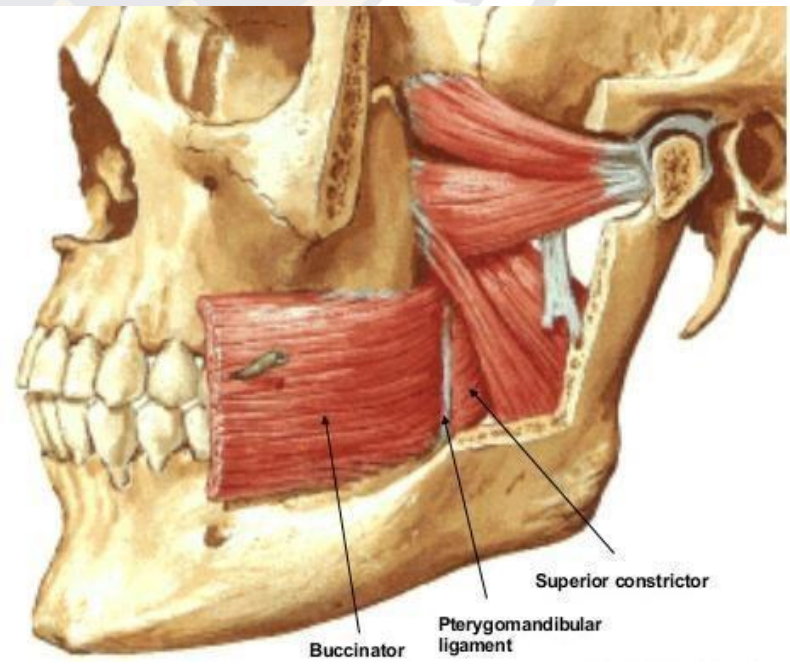
- **Definition:** it is the part between the ears and from the eyebrows to the chin.
- **Extent:**
  - **Superiorly**: the eyebrows and inferiorly: the chin.
  - **Laterally** to the external auditory meatus.
  - NB: The forehead is common to both scalp and face
- **Layers:**
  - **Skin:** contains hairs, sweat and sebaceous glands.
  - **Muscles:**
- **Muscles of the face have these criteria:**
  - They take origin from the bones surrounding the openings of the face (eye, ear, nose, and mouth).
  - They are inserted in the skin.
  - Their action appears directly on the face hence named muscles of facial expression.
  - They develop from the 2nd pharyngeal arch.
  - They are supplied by the facial nerve (VII cranial nerve).
  - Many muscles are responsible for every minute movement of the face, however only 3 have especial importance.

Orbicularis oculi

It is formed of 3 parts: orbital, palpebral and lacrimal.

- **Origin and insertion:**
  - **Orbital part:**
    Arises from the medial palpebral ligament and the adjoining bone. The fibers form a circle around the eye to insert in the same ligament.
  - **Palpebral part:**
    Arises from the medial palpebral ligament. The fibers run above and below the eye inside the eye lids and interlace at the lateral angle of the eye forming the lateral palpebral raphe.
  - **Lacrimal part:**
    Arises from the lacrimal bone and the fascia covering the lacrimal sac. The fibers pass in both lids.
- **Nerve supply:** Temporal and upper Zygomatic branches of facial nerve.
- **Action:**
  - The orbital part wrinkles the skin around the orbital margins.
  - The palpebral part closes the eye gently.
  - The whole muscle closes the eye firmly to protect the eye (sphincter to the eye).
  - Contraction of the lacrimal part help drainage of the tears.


Orbicularis oculi
Orbicularis oris
Buccinator
Platysma


Superior constrictor
Pterygomandibular ligament
Buccinator

Buccinator

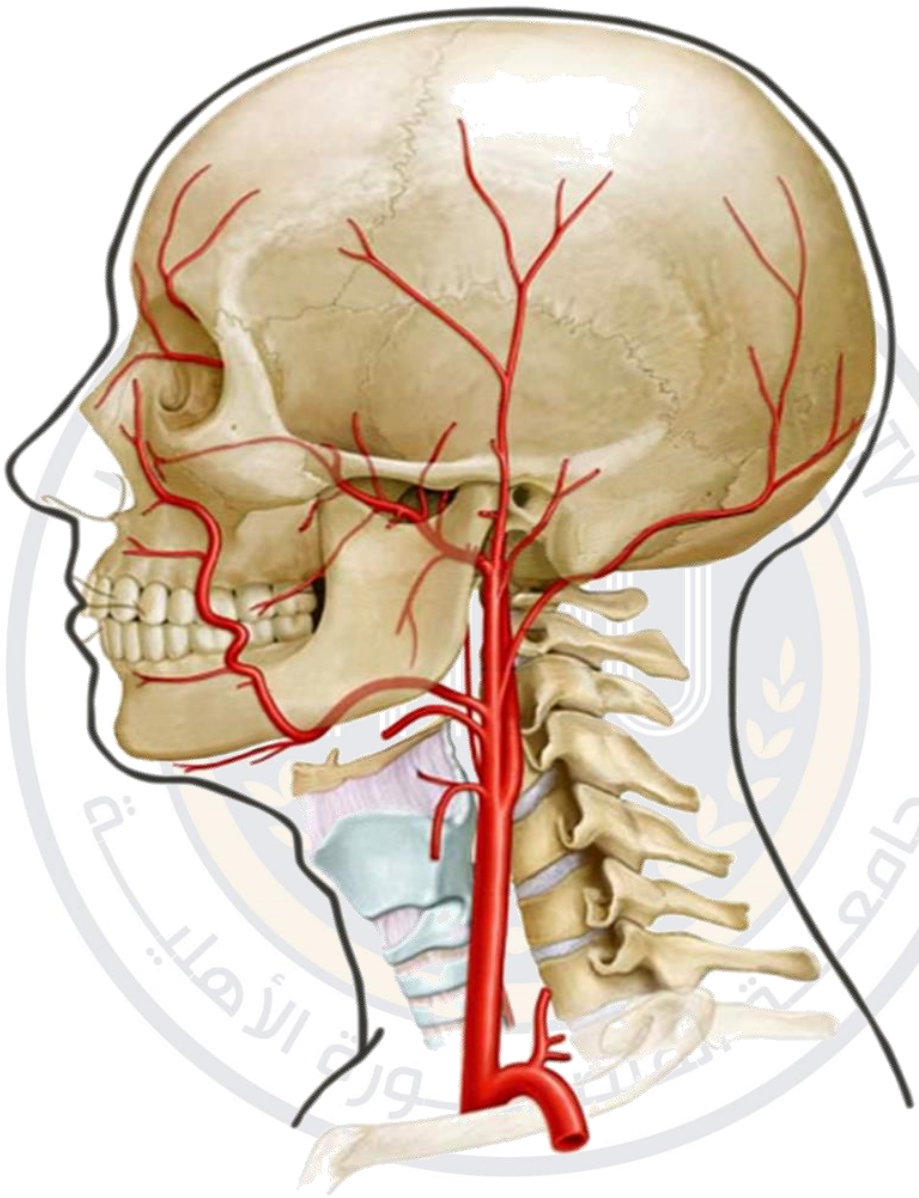
- **Origin:**
  - Upper fibers: Maxilla opposite upper molars.
  - Lower fibers: Mandible opposite lower molars.
  - Middle fibers: from the ligament connecting the skull to the mandible (Pterygomandibular ligament).
- **Insertion:**
  - The upper and lower fibers pass to the lips.
  - The middle fibers decussate at the modulus.
- **Nerve supply:** Buccal branch of facial nerve.
- **Action:**
  - Presses the cheek against the gums to close the vestibule of the mouth and prevent accumulation of food in the vestibule.
- **Its paralysis** leads to accumulation of food in the vestibule of the mouth and dribbling of saliva.

Orbicularis oris

- **Origin:** maxilla above incisor teeth.
- **Insertion:** skin of lip.
- **Nerve supply:** Buccal branch of facial nerve.
- **Action:** Close the mouth (sphincter to the mouth).

Platysma:

- **Origin**: fascia of the chest
- **Insertion:** base of mandible, skin of lower face and lip
- **Action:**
  - Releases the atmospheric pressure of skin on neck veins.
  - Depress mandible and pulls angle of mouth downwards.



Vessels of the face and scalp

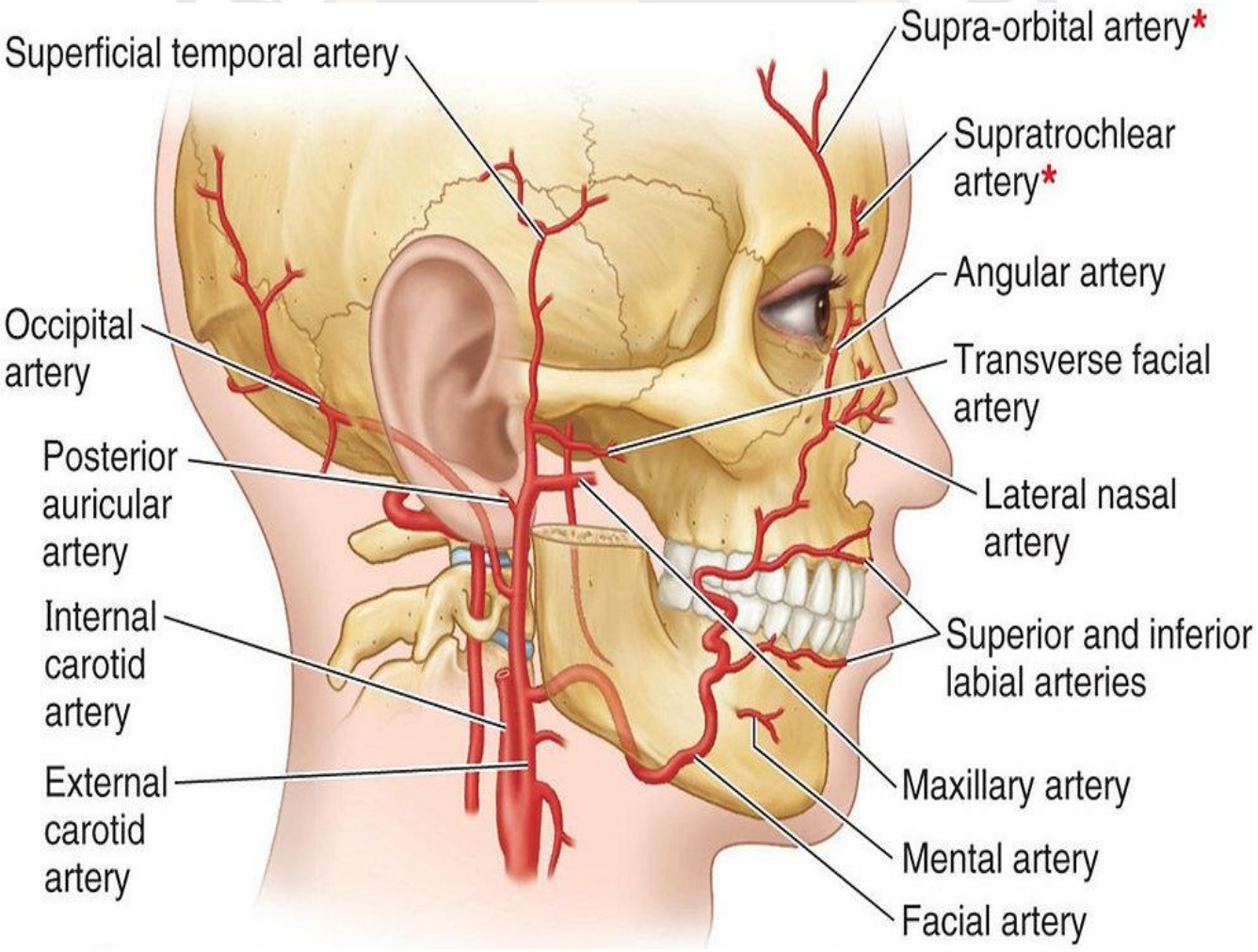
Both face and scalp get their arterial supply from the common carotid artery and its 2 terminal branches: External and Internal carotid arteries.

Internal carotid artery

- **Beginning: It is one of the two terminal branches of the common carotid artery.**
- **Course:**
  - ☒ Ascends in the neck to reach the base of the skull.
  - ☒ Enters the skull to supply the brain.
- **Branches:**
  - ☒ Branches to the brain.
  - ☒ Branches to the pituitary gland.
  - ☒ Ophthalmic artery to the eye and orbit. Their terminals reach the scalp and face. They are:
    a. Supratrochlear artery: Appear at the medial angel of the eye close to the midline.
    b. Supraorbital artery: Appear at the supraorbital foramen lateral to the midline.
  - ☒ It has no branches in the neck.

External carotid artery

- **Beginning**: It is one of the two terminal branches of the common carotid artery.
- **Course:**
  - ☒ Ascends in the neck to reach the parotid gland.
- **Branches:**
  1. Posterior auricular artery to scalp.
  2. Occipital artery to the scalp.
  3. Facial artery to the face.
  4. Superficial temporal artery to the face
  5. Multiple arteries to the neck.



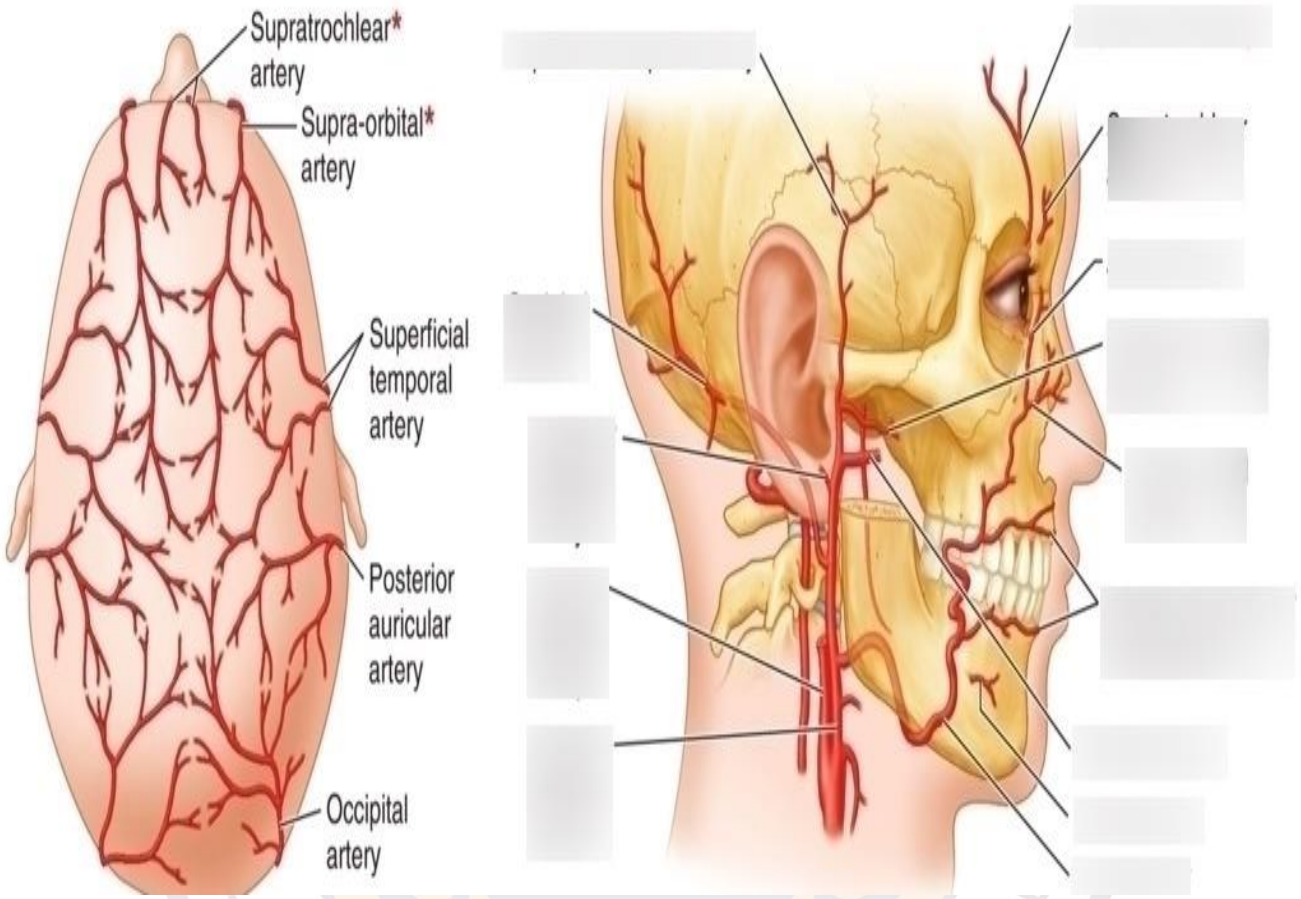
Arteries of the face

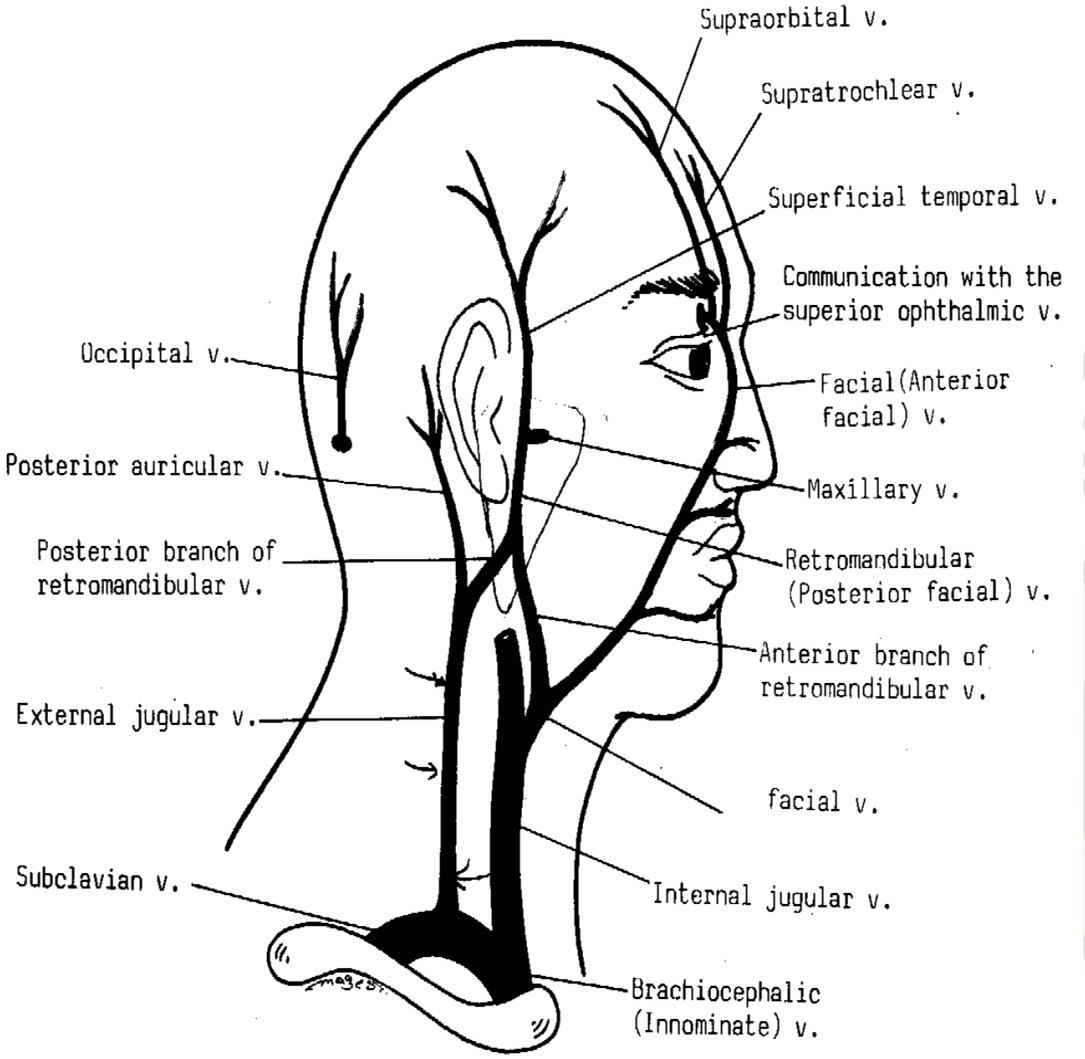
Facial artery

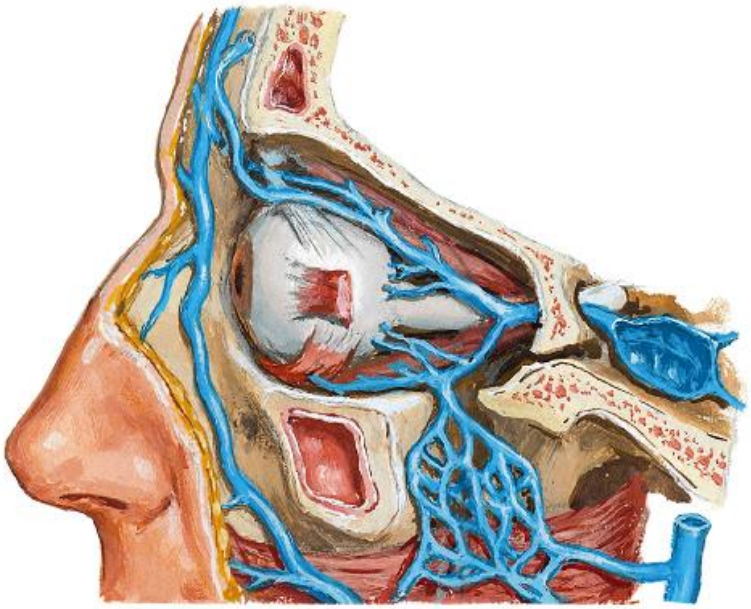
- **Beginning:** It is one of the branches of the external carotid artery.
- **Course:** begins in the neck and turns around the lower border of the mandible in a tortious course to permit free movement of mandible, lips, and cheeks.
- **It runs close to 3 angles:**
    a. Anteroinferior angel of masseter muscle.
    b. Angel of the mouth,
    c. Medial angel of the eye.
- **Supply the face by 3 branches:**
    a. Inferior labial to the lower lip.
    b. Superior labial to the upper lip.
    c. Nasal to the nose.

Superficial temporal artery

- **Beginning**: one of the two terminal branches of the external carotid artery.
- **Course**: ascend inside the parotid gland to exist from its upper border.
- **Supplies the face and scalp by 3 branches:**
    a. Transverse facial artery to the face.
    b. Anterior temporal branch to the side of the scalp (temple).
    c. Posterior temporal branch to the side of the scalp (temple).
    - The face and scalp receive multibed minute arteries accompany nerves supplying them.
    - The face and scalp are richly supplied with blood. Wounds of the face and scalp bleed profusely and heal fast.
    - Face wounds are suture by thin surgical threads.
    - Scalp wounds are sutured by thick surgical threads.


Supratrochlear* artery
Supra-orbital* artery
Superficial temporal artery
Posterior auricular artery
Occipital artery


Supraorbital v.
Supratrochlear v.
Superficial temporal v.
Communication with the superior ophthalmic v.
Occipital v.
Facial (Anterior facial) v.
Posterior auricular v.
Maxillary v.
Posterior branch of retromandibular v.
Retromandibular (Posterior facial) v.
Anterior branch of retromandibular v.
External jugular v.
facial v.
Subclavian v.
Internal jugular v.
Brachiocephalic (Innominate) v.



Veins of the face

Both face and scalp drain their venous blood in a number of veins which form a network that ends in the main veins passing to the heart.

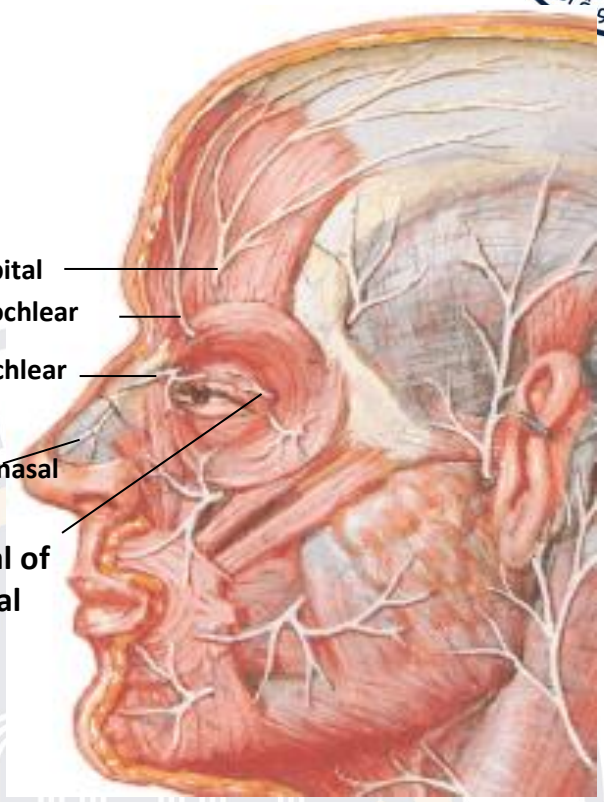
1. **Anterior facial vein:**
   Formed by union of supratrochlear & supraorbital veins at the medial angle of eye.
2. **Posterior facial vein (retromandibular vein):**
   Formed by union of superficial temporal vein with maxillary vein. It ends by dividing into anterior and posterior divisions.
3. **Common facial vein:**
   Formed by union of the anterior facial with anterior division of the posterior facial veins. It ends in the internal jagular vein.
4. **External Jagular vein:**
   Formed by union of the posterior division of retromandibular with posterior auricular veins. It ends in the subclavian vein.
5. **Deep facial vein:**
   Connects the anterior facial vein with the pyrgotid plexus of veins.
6. **Posterior auricular and occipital veins:**
   End in the external jagular vein.

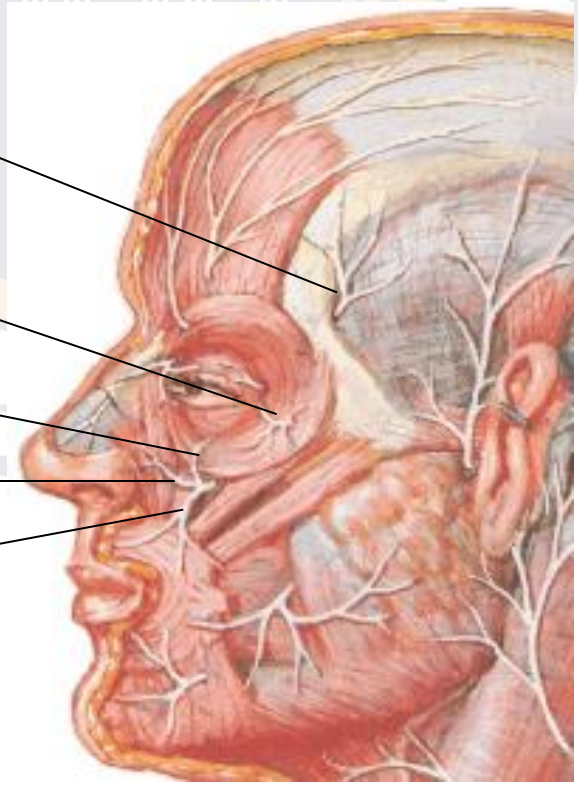
Communications of the anterior facial vein:

- ☒ At its beginning it receives the ophthalmic veins which are connected to the cavernous sinus (inside the skull) through the orbit.
- ☒ It is connected to the pterygoid venous plexus through the deep facial vein. The pterygoid venous plexus is connected to the cavernous sinus through emissary veins passing through foramen ovale.

The dangerous area of the face

- ☒ Infections from face (mainly from upper lip & nose) can go to cavernous sinus inside the skull.
- ☒ The dangerous area of the face is a triangular area involves the upper lip & nose between the two anterior facial veins can lead to cavernous sinus thrombosis by two roots:
  1. Anterior facial vein, to ophthalmic veins, to cavernous sinus.
  2. Anterior facial vein to deep facial vein to pterygoid venous plexus to emissary veins through ovale to cavernous sinus.


Supraorbital
Supratrochlear
Infratrochlear
Branches from
ophthalmic n
External nasal
Palpebral of
lacrimal


Zygomatico-temporal
Zygomatico-facial
Palpebral
Infraorbital
Nasal
Labial

Nerves of the face

- Skin of the face and scalp is supplied by sensory nerves.
- Muscles of the face and scalp are supplied by a motor nerve (Facial nerve)

Sensory nerves of the face

Trigeminal nerve

- It is the 5th cranial nerve. It is a mixed nerve (has motor and sensory supply)
- **It has 3 branches:**
  - ☒ Ophthalmic
  - ☒ Maxillary
  - ☒ Mandibular

Branches of ophthalmic nerve in face and scalp

1. **Supratrochlear nerve:**
   - ☒ Appear at the medial angel of the eye close to the midline. Accompanying the supraorbital nerve.
   - ☒ Supplies the medial 1/3 of the upper eyelid in face and front of scalp close to the midline.
2. **Supraorbital nerve:**
   - ☒ Appear at the supraorbital foramen lateral to the midline. Accompanying the supratrochlear nerve.
   - ☒ Supplies the middle 1/3 of the upper eyelid in face and front of scalp lateral to the midline.
3. **Palpebral of lacrimal:** Supplies the lateral 1/3 of the upper eyelid in the face.
4. **External nasal nerve:** Supplies the lower 1/2 of the dorsum of the nose.
5. **Infratrochlear nerve:** Supplies the upper 1/2 of the dorsum of the nose and the adjoining part of the lower eyelid.

From the maxillary division of trigeminal

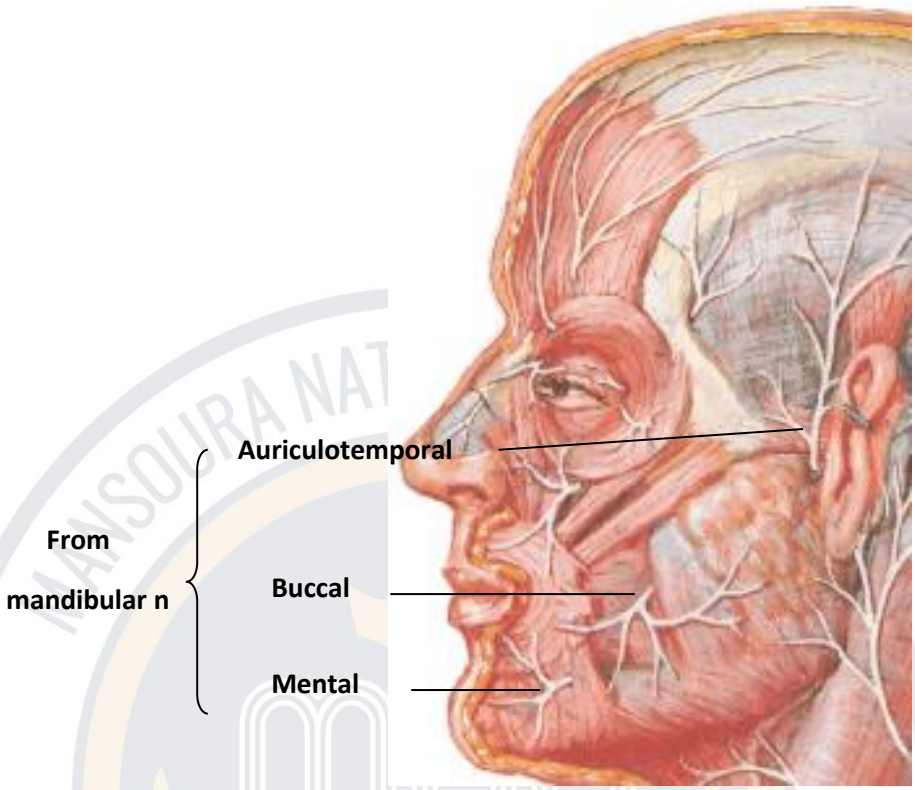
1. **Zygomaticofacial nerve:** Supplies the skin over the bony cheek in the face.
2. **Zygomaticotemporal nerve:** Supplies the skin of the anterior part of the lateral side of the scalp (temple).
3. **Infraorbital nerve: gives 3 branches in the face:**
   - ☒ Palpebral branch: Supplies the skin of the lower eyelid.
   - ☒ Nasal branch: Supplies the skin of the side of the nose.
   - ☒ Labial branch: Supplies the skin of the upper lip.

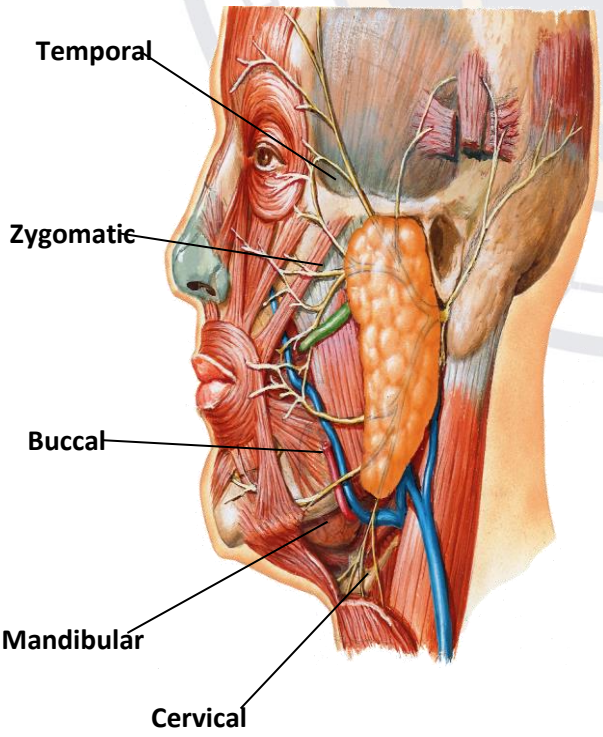
From the mandibular division of trigeminal

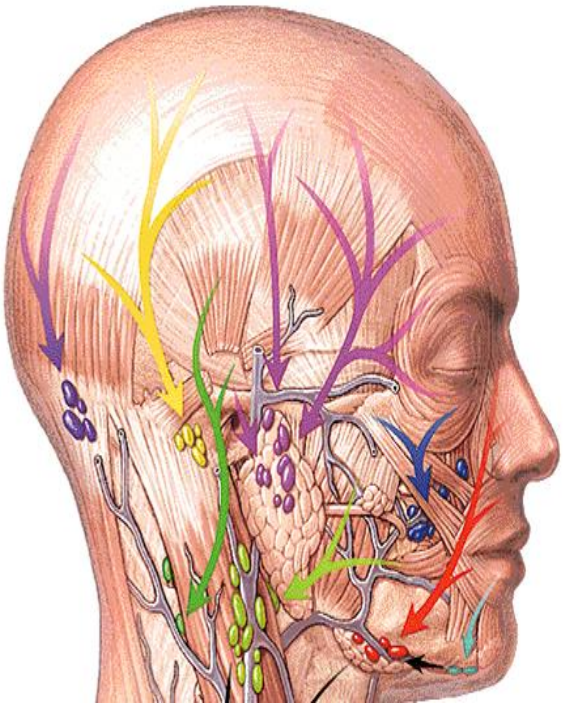
1. **Auriculotemporal nerve:** Supplies the skin of the anterior part of the lateral side of the scalp (temple).
2. **Buccal nerve:** Supplies the skin of the cheek (skin over buccinator).
3. **Mental nerve:** Supplies the skin of the lower lip.

Branches of the trigeminal nerve receives sensations from:

1. The whole face except the skin over the angel of the mandible (through the great auricular branch of the cervical plexus).
2. The anterior part of the scalp.
   - ☒ Trigeminal nerve receives sensations from the whole face except the skin over the mandibular angle is supplied by greater auricular nerve.
   - ☒ Trigeminal neuralgia: pain (usually of unknown cause) in the region of distribution of ophthalmic, maxillary and mandibular branches of trigeminal nerve.


Auriculotemporal
From
mandibular n
Buccal
Mental


Temporal
Zygomatic
Buccal
Mandibular
Cervical



Motor nerves of the face and scalp

The muscle of the face gets their motor nerve supply through the facial nerve (7th cranial nerve).

Facial nerve in face and scalp

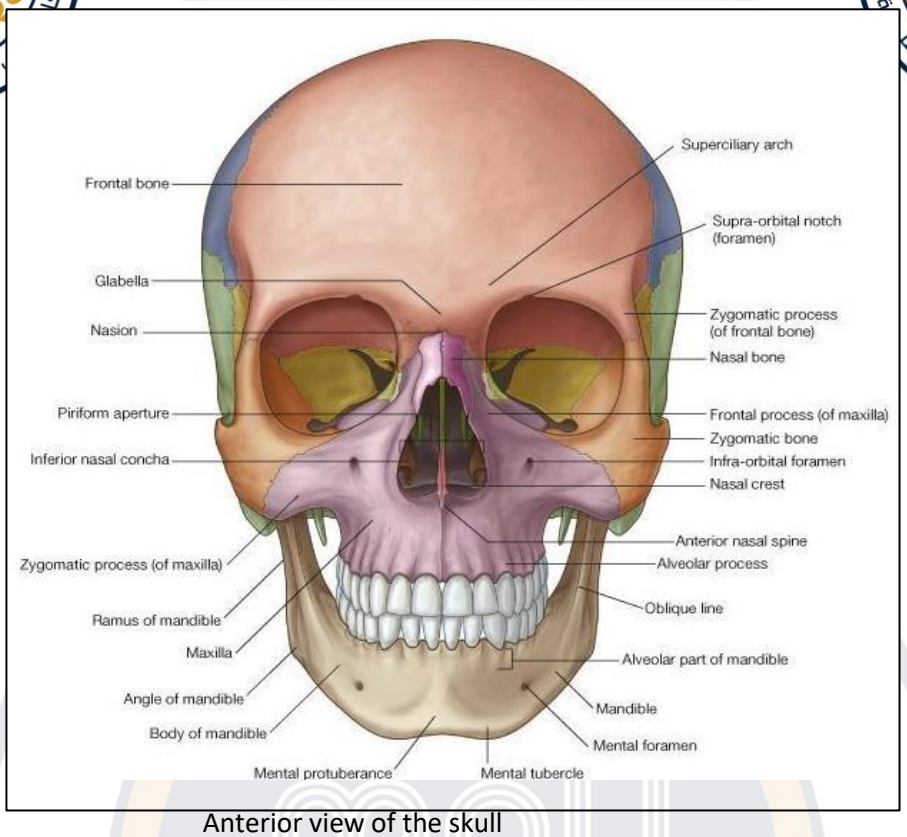
- **Course:** after exit from the skull (stylomastoid foramen) it enters the parotid gland.
- **Branches:** has fine branches to all muscle of face and scalp. From above downward are:
  1. Temporal: supplies frontal belly of occipitofrontalis and orbicularis oculi.
  2. Zygomatic: supplies orbicularis oculi.
  3. Buccal: (upper and lower) to buccinator and orbicularis oris.
  4. Mandibular: supplies muscles of the lower lip.
  5. Cervical: supplies the platysma.

- **Lesions of the terminal part of the facial nerve (eg, bell's palsy) results in:**
  1. The affected side is motionless.
  2. Loss of wrinkles of the skin.
  3. Eye cannot be closed.
  4. In smiling the mouth is drawn to normal side.
  5. During mastication food accumulates in vestibule of mouth.

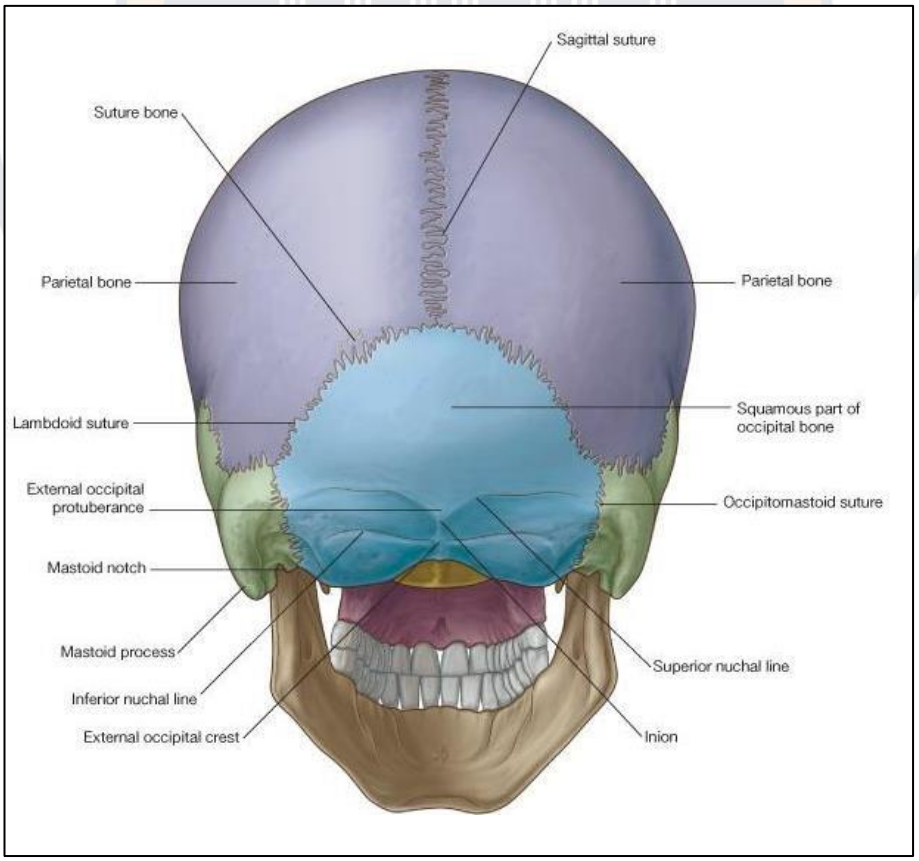
Lymph drainage of the scalp and face

The face drains their lymph into 5 groups of lymph nodes :

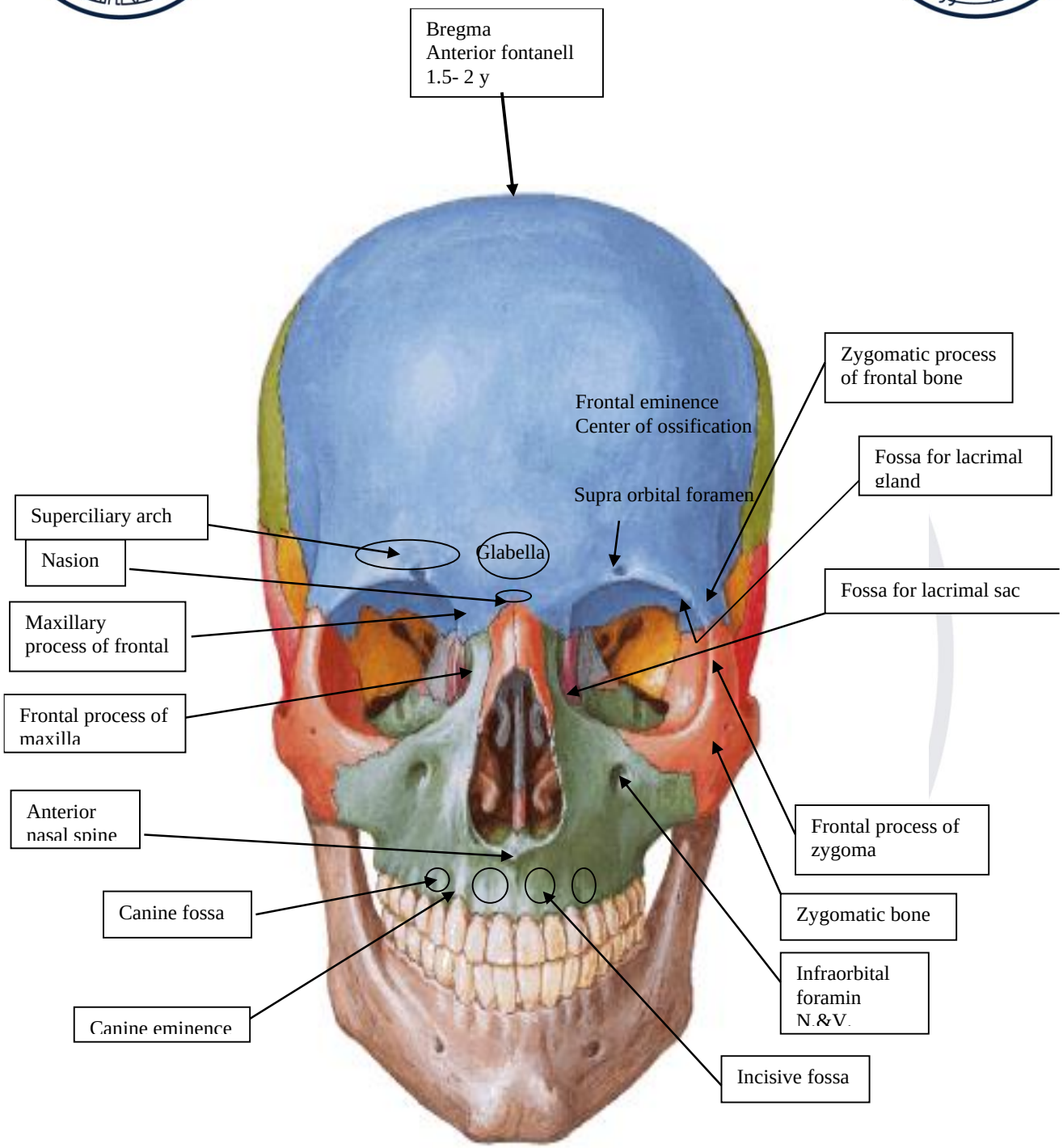
1. Submental lymph nodes receives from lower lip and chin.
2. Submandibular lymph nodes receives from the external nose and upper lip.
3. Preauricular receives from the forehead, lateral ½ of eye lid, cheek and parotid area.

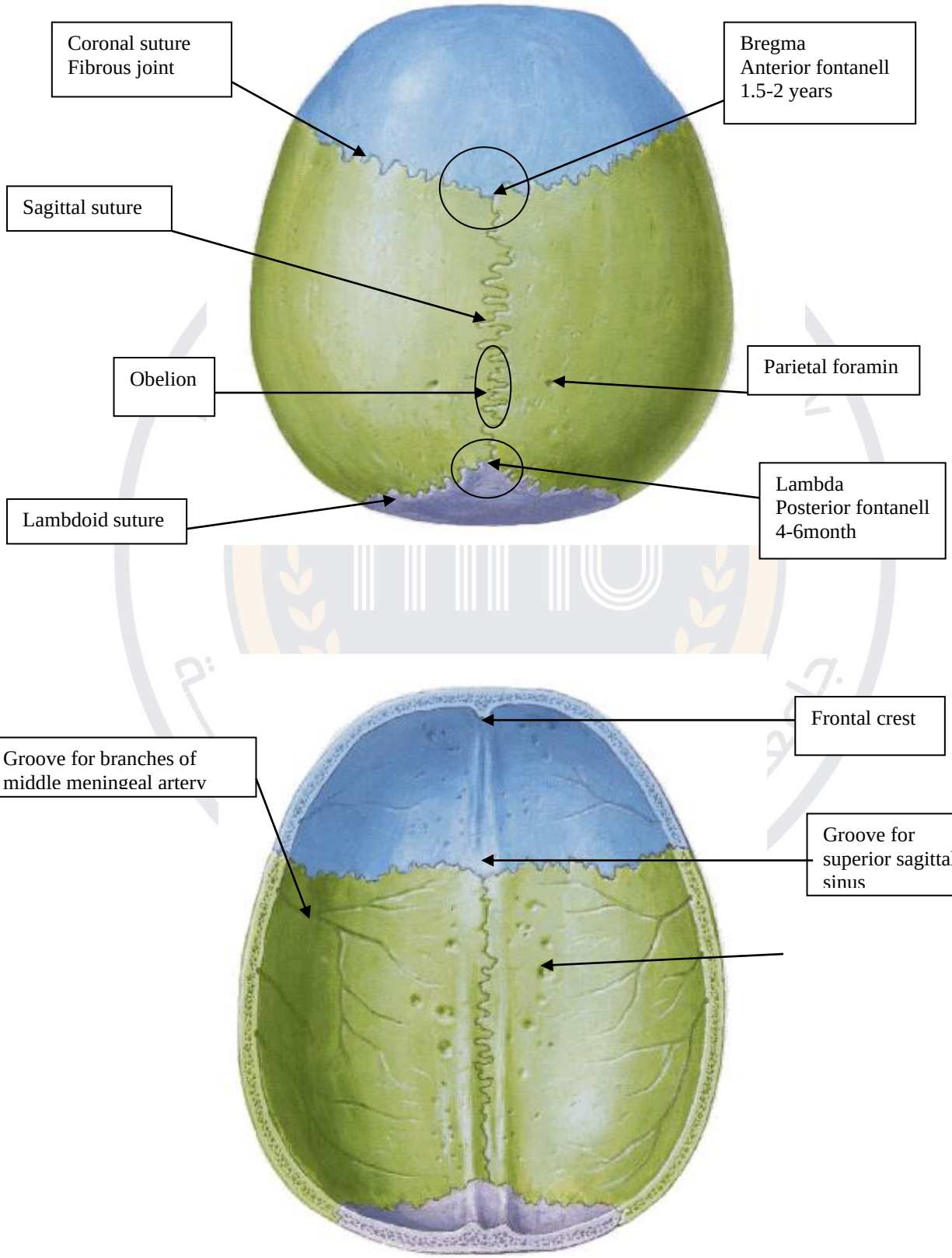


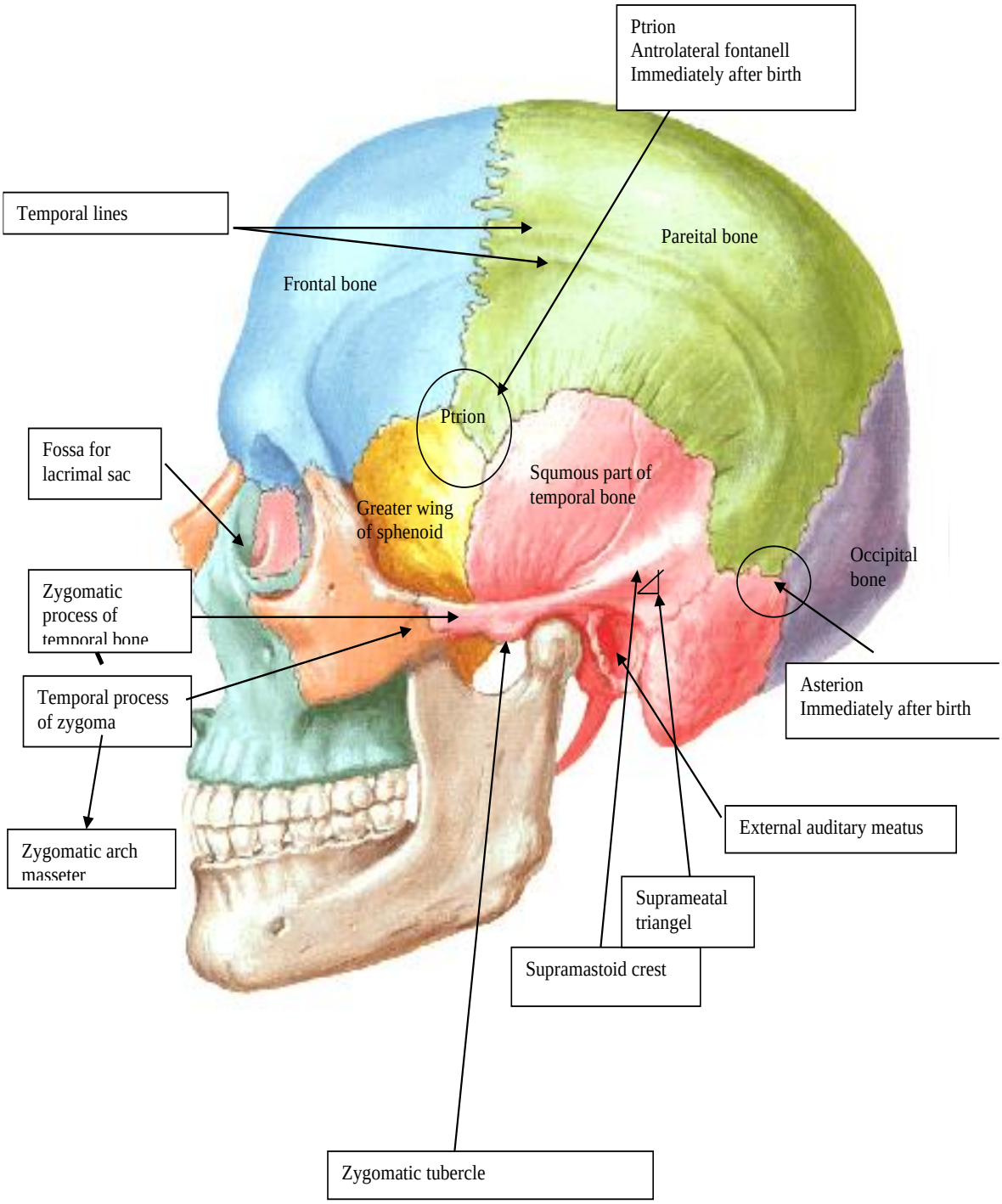
Anterior view of the skull

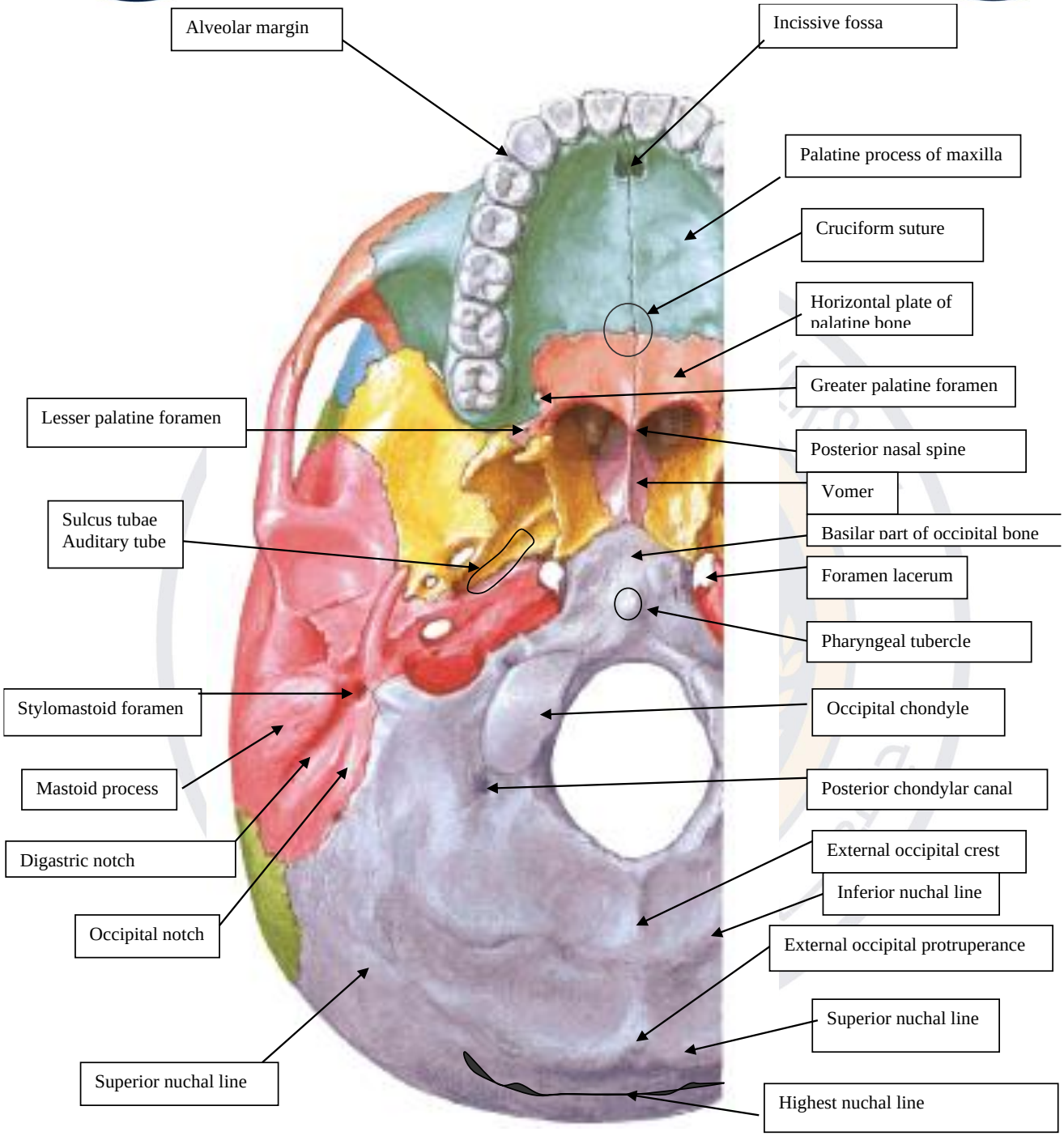


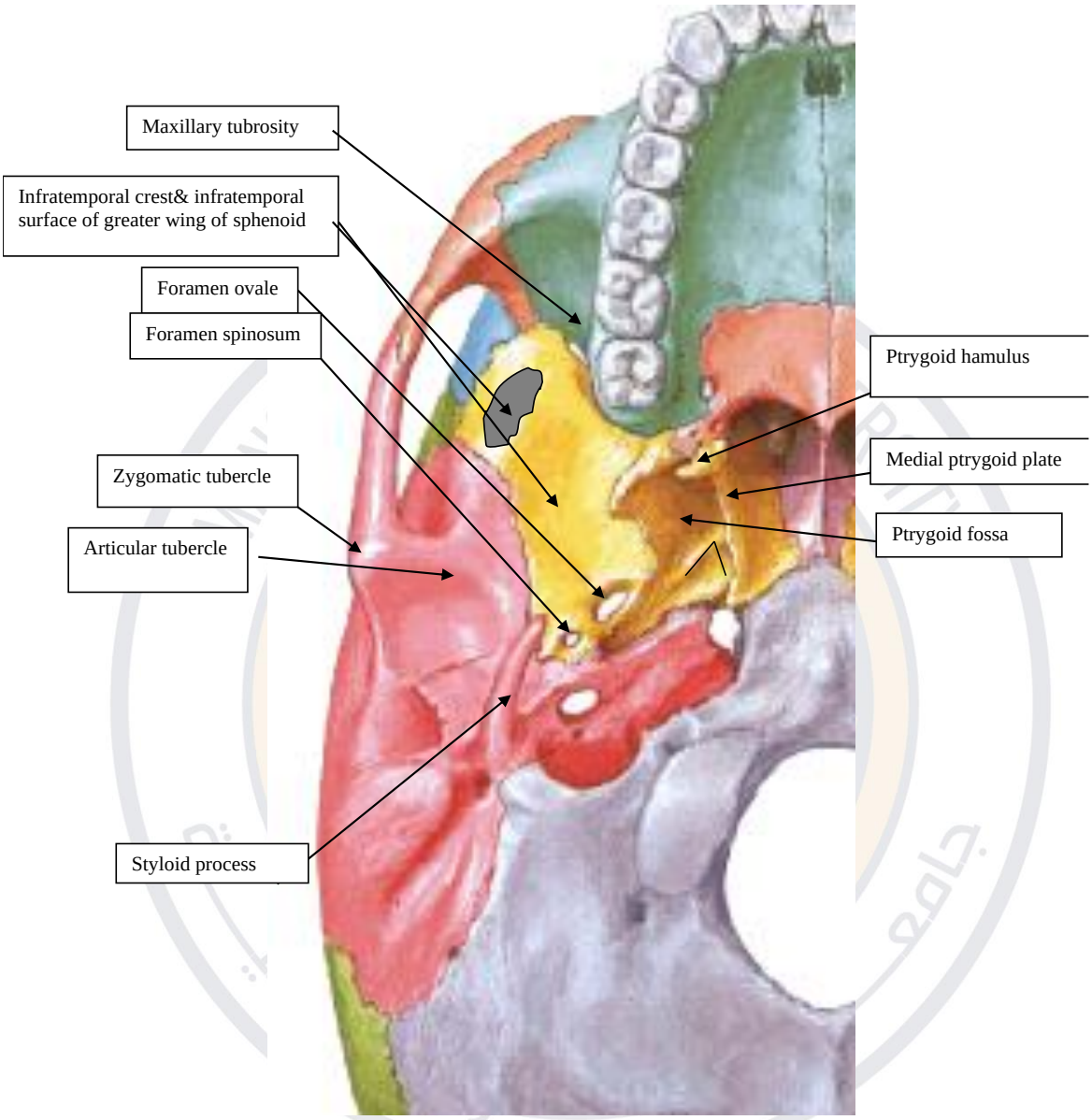
Posterior view of the skull


Bregma
Anterior fontanell
1.5- 2 y
Zygomatic process of frontal bone
Frontal eminence
Center of ossification
Fossa for lacrimal gland
Supra orbital foramen
Superciliary arch
Glabella
Nasion
Fossa for lacrimal sac
Maxillary process of frontal
Frontal process of maxilla
Anterior nasal spine
Frontal process of zygoma
Canine fossa
Zygomatic bone
Infraorbital foramin N.&V.
Canine eminence
Incisive fossa


Coronal suture
Fibrous joint
Bregma
Anterior fontanell
1.5-2 years
Sagittal suture
Obelion
Parietal foramin
Lambda
Posterior fontanell
4-6month
Lambdoid suture
Frontal crest
Groove for branches of
middle meningeal artery
Groove for
superior sagittal
sinus


Ptrion
Antrolateral fontanell
Immediately after birth
Temporal lines
Pareital bone
Frontal bone
Ptrion
Fossa for lacrimal sac
Squmous part of temporal bone
Greater wing of sphenoid
Occipital bone
Zygomatic process of temporal bone
Temporal process of zygoma
Asterion
Immediately after birth
External auditary meatus
Zygomatic arch masseter
Suprameatal triangel
Supramastoid crest
Zygomatic tubercle


Alveolar margin
Incissive fossa
Palatine process of maxilla
Cruciform suture
Horizontal plate of palatine bone
Greater palatine foramen
Lesser palatine foramen
Posterior nasal spine
Vomer
Sulcus tubae Auditary tube
Basilar part of occipital bone
Foramen lacerum
Pharyngeal tubercle
Stylomastoid foramen
Occipital chondyle
Mastoid process
Posterior chondylar canal
Digastric notch
External occipital crest
Inferior nuchal line
Occipital notch
External occipital protruperance
Superior nuchal line
Superior nuchal line
Highest nuchal line


Maxillary tubrosity
Infratemporal crest& infratemporal surface of greater wing of sphenoid
Foramen ovale
Foramen spinosum
Zygomatic tubercle
Articular tubercle
Styloid process
Ptrygoid hamulus
Medial ptrygoid plate
Ptrygoid fossa

FACULTY OF MEDICINE
MANSOURA NATIONAL UNIVERSITY

HISTOLOGY

THE NERVOUS TISSUE

- The nervous system is classified into:
  1. Central nervous system (C.N.S): brain and spinal cord.
  2. Peripheral nervous system (P.N.S):
     a) Peripheral nerves → Cranial
     → Spinal
     b) Ganglia → Cerebro–spinal
     → Autonomic → Sympathetic
     → Parasympathetic

THE NEURON

- **Definition:**

  Is the structural and functional unit of the nervous tissue.

- **Structure:**

  The neuron or the nerve cell consists of:

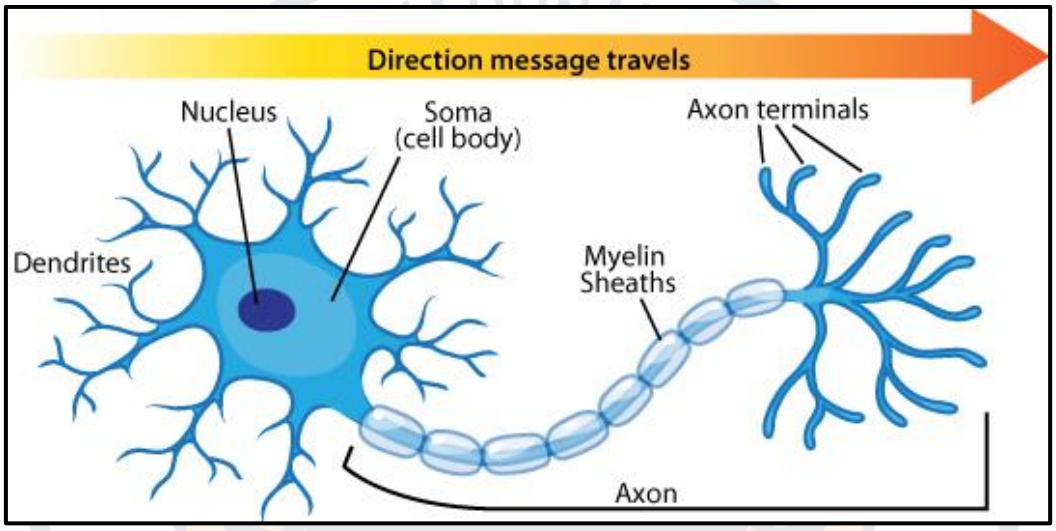
  1- Cell body (perikaryon): (Peri = around, karyon = nut)
  It contains the nucleus and surrounding cytoplasm.

  2- Processes: axon and dendrites.

- **THE CELL BODY:**

  - **The Cell membrane:** very thin.
  - **The nucleus:** Large, rounded, usually central and vesicular (open – face type) with a prominent nucleolus.
  - **The cytoplasm:**
    a. Organelles: → Nissl granules
    → Neurofibrils
    → Golgi apparatus
    → Mitochondria (Are the power house of the cell and scattered allover the neuron).

b- Inclusions:
- → Melanin pigments: in some nerve cells e.g. cells of substania nigra.
- → Lipofuscin pigments: yellow pigments increase in old age.
- → Glycogen granules. } for energy of neurons
- → Fat droplets. }



The Cytoplasmic Organelles

☒ Nissl granules or bodies

LM:

Basophilic bodies or granules scattered in the cytoplasm.

Distribution:

Allover the neuron except in:

i- Periphery of the nerve cell.
ii- Around the nucleus.
iii- Axon.
iv- Axon hillock (conical expansion at the beginning of the axon).

Staining:

Nissl granules are known as "***chromophil substance***" as they like certain stains e.g. haematoxylin, toluidine blue.

EM:

Free and attached ribosomes (i.e. rough endoplasmic reticulum)

Function:

Synthesis of protein for nerve cells.

☒ Neurofibrils

LM:

Thin fibrils or threads which cross one another in the cell body but run parallel in the axon and dendrites.

Distribution:

Scattered allover the neuron (cell body, dendrites and axon).

Staining:

Only with silver stain ⟶ black or deep brown.

EM:

- fine neurofilaments, microfilaments and microtubules.

Function:

1- They are transmitters of nerve impulses.
2- They are supporting elements i.e. maintenance of the shape of the nerve cells.

☒ Golgi apparatus

- Is well-developed and completely surrounds the nucleus "***perinuclear***".
- Demonstrated only by silver.

PROCESSES:

		The axon	The dendrites
1	**Number:**	Single.	Multiple.
2	**Thickness and Length:**	Thin & long.	Thick & short.
3	**Diameter:**	It has a constant diameter along its length.	Their diameter decrease gradually towards their ends i.e. tapering.
4	**Contour:**	Smooth.	Irregular.
5	**Branching:**	It branches at its terminal end only i.e. ***"terminal arborization"*** but it may give collateral branches which arise at right angles.	They give ***extensive branching*** along their course. The branches arise at acute angles and may show spines.
6	**Content:**	Contains mitochondria and neurofibrils only (no Nissl granules).	Contain neurofibrils and Nissl granules.
7	**Conduction of nerve impulses:**	It carries nerve impulses away from the cell body ***(centrifugal conduction)***	They carry the impulses to the cell body ***(Centripetal conduction).***

Classification of the neurons (nerve cells)

I) According to the number of processes (Polarity):

1- Unipolar nerve cells:

- **Site**: mesencephalic nucleus of the trigeminal nerve.

2- Pseudounipolar nerve cells:

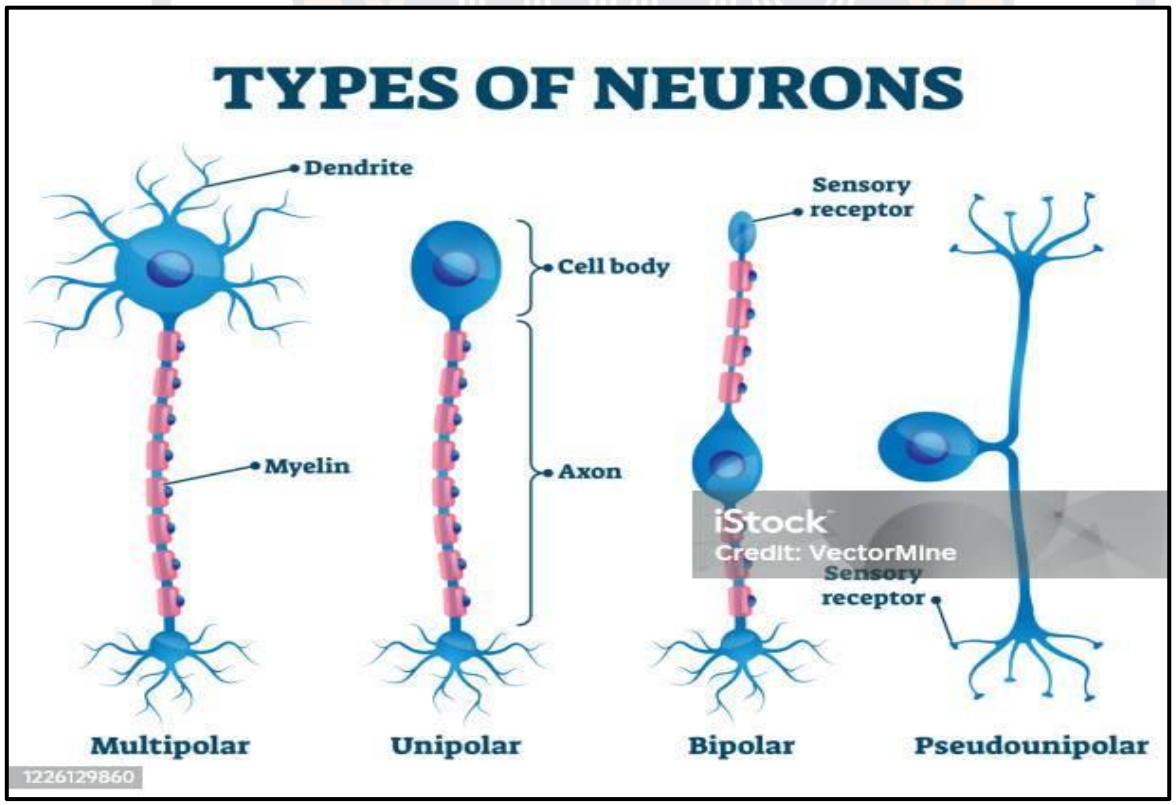
- **Site*:*** spinal ganglia.

3- Bipolar nerve cells:

- **Site:** ⟶ Retina of the eye.
  ⟶ Spiral ganglia and vestibular ganglia in the ear.
  ⟶ Olfactory epithelium of the nose.

4- Multipolar nerve cells:

- Have many dendrites and one axon.
  - ☒ ***Polygonal or stellate shaped:***
    Site: Sympathetic ganglia.
  - ☒ ***Pyramidal:***
    Site: cerebral cortex.
  - ☒ ***Pyriform:***
    Site: Purkinje cells of the cerebellum.



II) According to the size of cells and the length of their axons:

☒ ***Golgi type I neurons (Large cells):***
Have long axons e.g. pyramidal cells of the cerebrum (up to 150 µm).

☒ ***Golgi type II neurons (Small cells):***
Have short axons e.g. granular cells of the cerebellum (about 5 µm).

III) According to the function:

1- **Motor neurons:** e.g. anterior horn cells of spinal cord.
2- **Sensory neurons:** e.g. cells of spinal ganglia.
3- **Interneurons (connecting neurons):** e.g. neurons of reflex arc in spinal cord.

THE NERVE FIBER

- **Definition:** It is the axon of a nerve cell.
- The axon may be naked or ensheathed (with myelin sheath, neurolemma or both).

The axon (Axis Cylinder)

- **Structure :**

  The axon is surrounded by a membrane called **"*axolemma*"** and its cytoplasm is known as **"*axoplasm*"**. It contains neurofilaments, neurotubules and mitochondria but no Nissl granules.

- **Length:**

  May be very long (***Golgi type I***) or very short (***Golgi type II***).

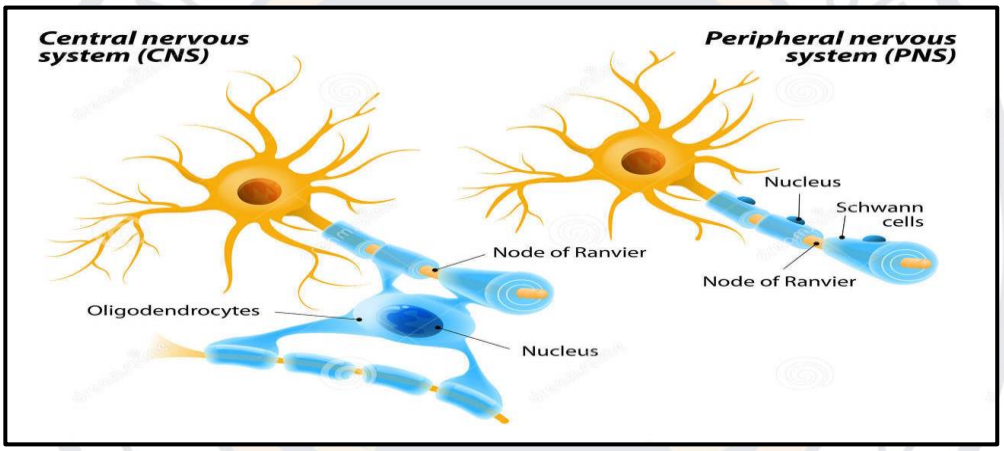
- **Diameter:**

  May be thick (of large diameter) conducting impulses rapidly or thin (of small diameter) conducting impulses slowly.

The myelin Sheath

Histological appearance:

- It is a white tubular covering for the axon.
- It is interrupted at intervals by constrictions called **"*nodes of Ranvier*"**. The segment between two successive nodes is called **"*internodal segment*"**.
- It appears in the form of concentric layers derived mainly from the lipid middle layer of the cell membrane of Schwann cell (in peripheral nerves) and oligodendroglia (in CNS).



Staining:

- In H & E preparation: the fat of myelin dissolves in fat solvent (xylol) and appears as an empty space.
- It is stained black by osmic acid.

Function:

Insulation of the nerve impulses.

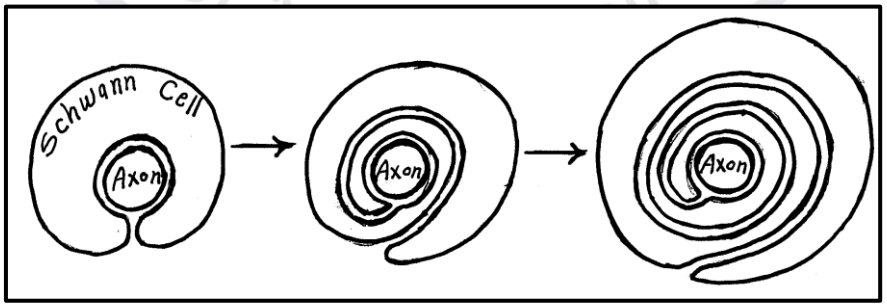
The Neurolemmal Sheath (Schwann Cells)

Histological appearance:

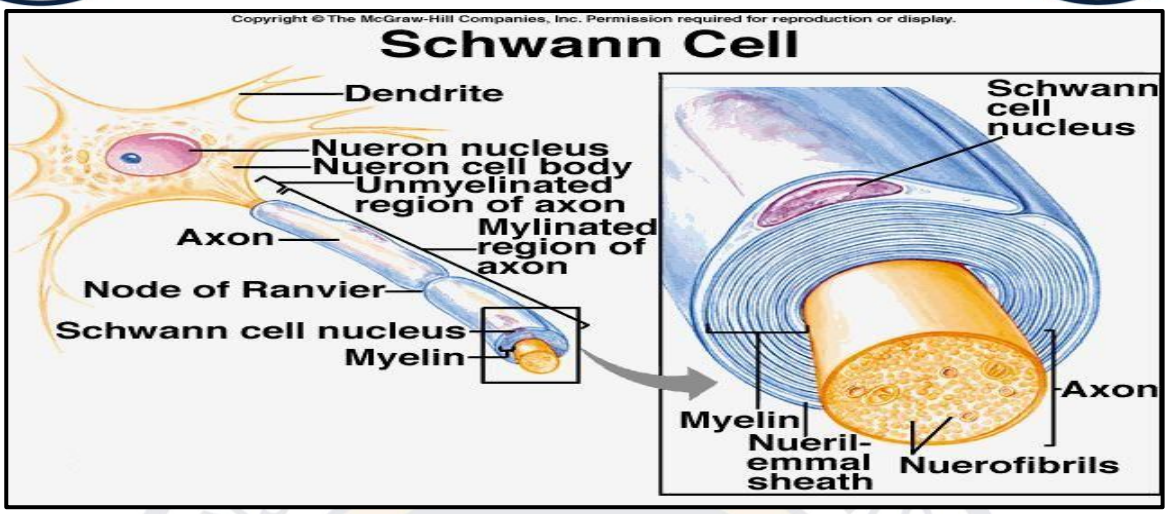
- It is formed of a chain of cells forming a tube around myelin sheath.
- Each Schwann cell has a flat oval nucleus and corresponds to an internodal segment.
- The cells come in contact with the axon at the nodes of Ranvier.

Function:

1. Insulation of nerve impulses in nonmyelinated nerve fibers.
2. Important role in regeneration of peripheral nerve after injury. (No regeneration of nerve fibers occurs in the CNS where the fibers are myelinated without neurolemma).
3. Formation of myelin sheath:
   a. The Schwann cell encircles a near- by axon.
   b. The cell rotates several times around the axon forming series of rings which are formed of two layers of cell membrane.
   c. The cytoplasm between the rings is squeezed out gradually.
   d. The lipid layers of the two fused cell membranes ⟶ lipid component of myelin.
   e. The protein layers ⟶ framework of neurokeratin.



Stages of formation of myelin sheath



Types of Nerve Fibers:

1. Naked Fibers: (non myelinated without neurolemma) e.g.

- Termination of peripheral nerves.
- Fibers in the gray matter.

2. Ensheathed Fibers:

i) Myelinated with neurolemma:
e.g. peripheral nerves.

ii) Myelinated without neurolemma:
e. g. nerve fibers in the white matter and optic nerve.

iii) Non- myelinated with neurolemma:
e.g. sympathetic nerve fibers.

Structure of a peripheral Nerve Trunk:

(I) Nervous component:

Groups of nerve fibers (myelinated axons with neurolemma) arranged in bundles.

- ***In Hx. & E. stained section:***

  Each fiber shows a centrally stained acidophilic axon, surrounded by an empty space of the dissolved myelin and a thin outer pink rim of Schwann cell cytoplasm. The nuclei of these cells may be seen if they are cut in the section.

- ***In osmic acid-stained section:***

  The myelin sheath of the nerve fibers appears as rounded black circles.

(II) C. T. component:

- **Epineurium:**

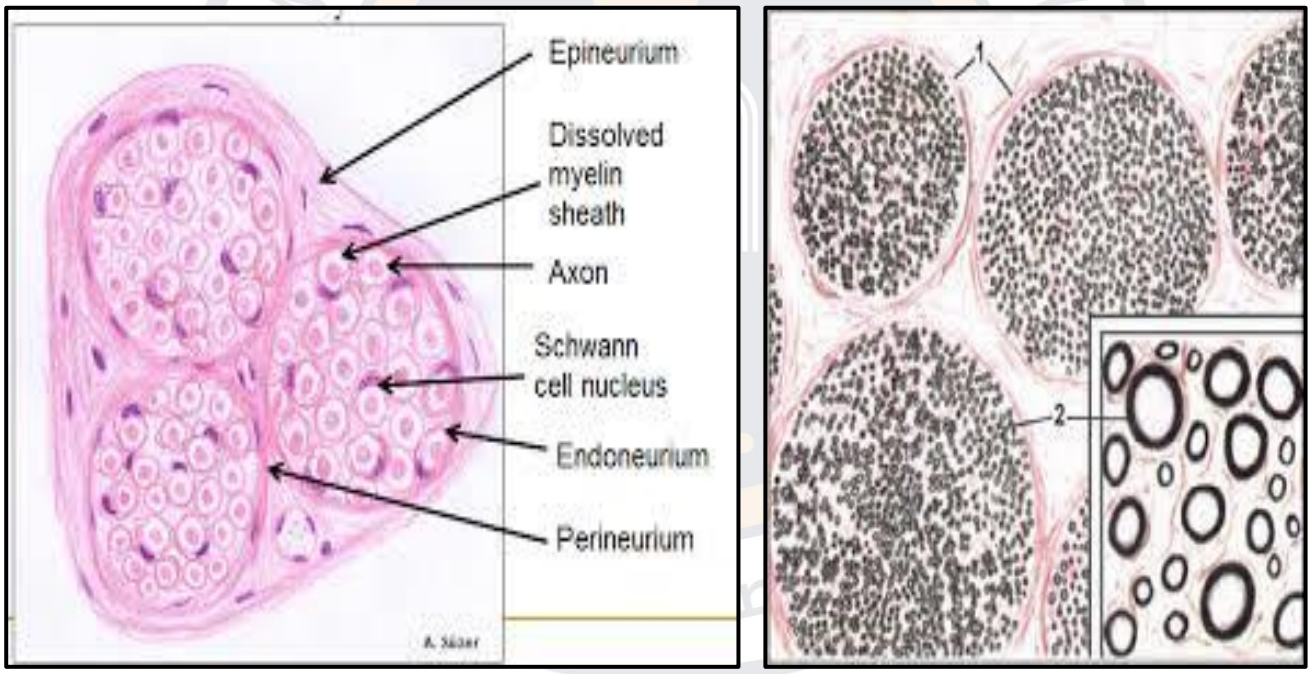
  It is a dense C. T., which surrounds the whole nerve trunk.

- **Perineurium:**

  It is a dense C. T., which surrounds the bundles of nerve fibers.

- **Endoneurium:** (Henle's sheath)

  It is a delicate loose C. T. between the individual nerve fibers.



Nerve trunk With HE and osmic acid

NERVE GANGLIA

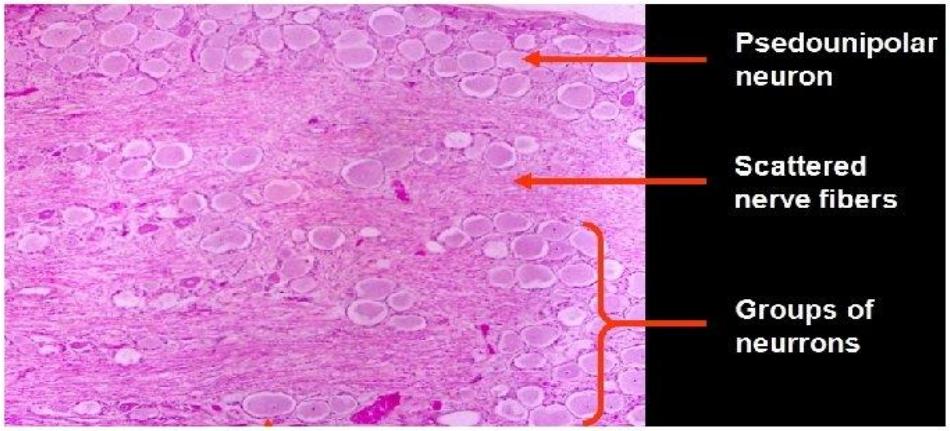
Definition:

- ☒ A nerve ganglion is a collection of nerve cells and nerve fibers, covered by a C. T. capsule, outside the C. N. S.
- ☒ NB: a collection of nerve cells **inside** the C. N. S is called **nucleus.**

	Spinal (Dorsal root) ganglion	*Sympathetic ganglion*
Site :	Dorsal roots of spinal nerves.	Sympathetic chain
C.T. Capsule:	Thick and usually present.	Thin and may be absent
Nerve cells:	**A. Type:** Pseudounipolar.	Multipolar
	B. Size: Large or small (20-120 µm). • Large pale cells: have fine Nissl granules. • Small dark cells: have coarse Nissl granules.	Mostly of the small uniform size (30 µm) and have similar appearance.
	C. Arrangement: In groups or rows.	Scattered irregularly.
	D. Number: Few.	Numerous.
	E. Nuclei: Central	Eccentric.
	F. Satellite or capsule cells: Numerous and form distinct layer i.e. complete capsule. NB: these cells are supportive and nutritive to the nerve cells.	Few and less distinct i.e. incomplete capsule.
	G. Glomerulus: Present.	Absent.

Nerve Fibers:	i) Thickly myelinated. ii) Widely separated from each other iii) Parallel to the capsule. Synapse: absent (as the fibers are the peripheral processes of the nerve cells whose axons enter the C.N.S)	Thinly or non myelinated Close to each other. Irregularly distributed. Present (preganglionic fibers synapse with the ganglion cells whose axons form the postganglionic fibers).
Blood supply:	Poor.	Rich.
Function:	Acts as relay for different ***sensations*** before their entrance into the spinal cord.	Acts as relay for different ***motor functions*** arising from the spinal cord.

Dorsal root ganglion (MICROSCOPE)



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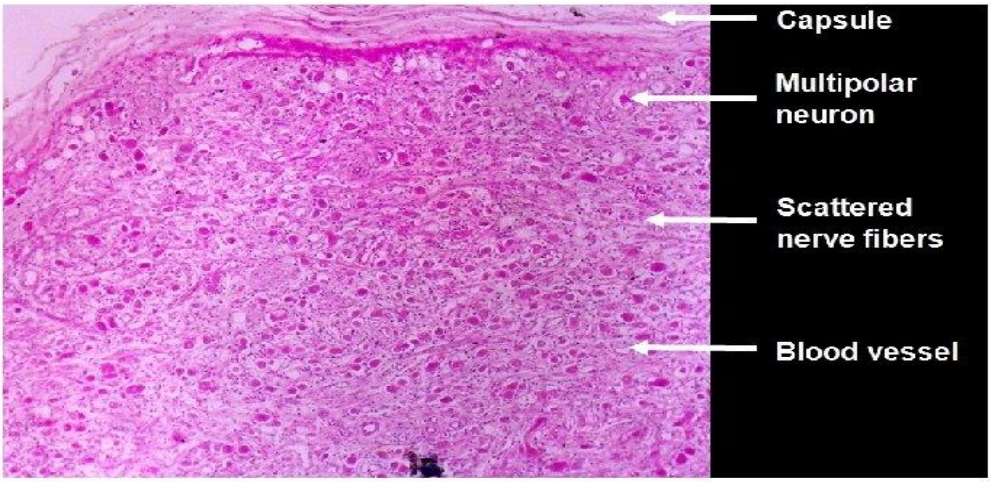
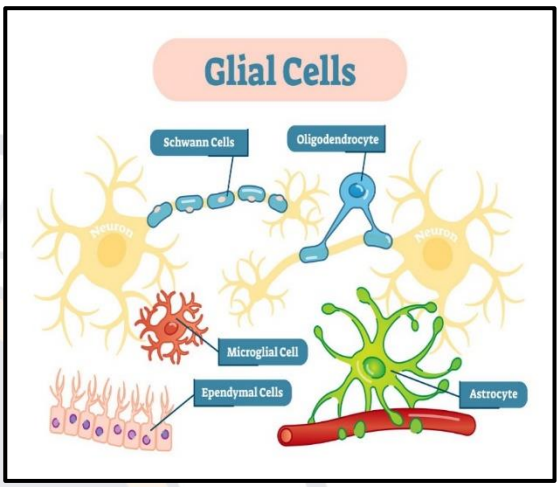
Sympathetic ganglion



THE NEUROGLIA

Definition:

It is the interstitial supporting tissue of the nervous system (similar in function to the C.T. proper of other organs).



Classification:

I. Neuroglia proper:

- ☒ Astrocytes (macroglia)
  - Protoplasmic
  - Fibrous
- ☒ Oligodendroglia
- ☒ Microglia (Mesoglia)

II. Other types of neuroglia (Neuroglia – like cells):

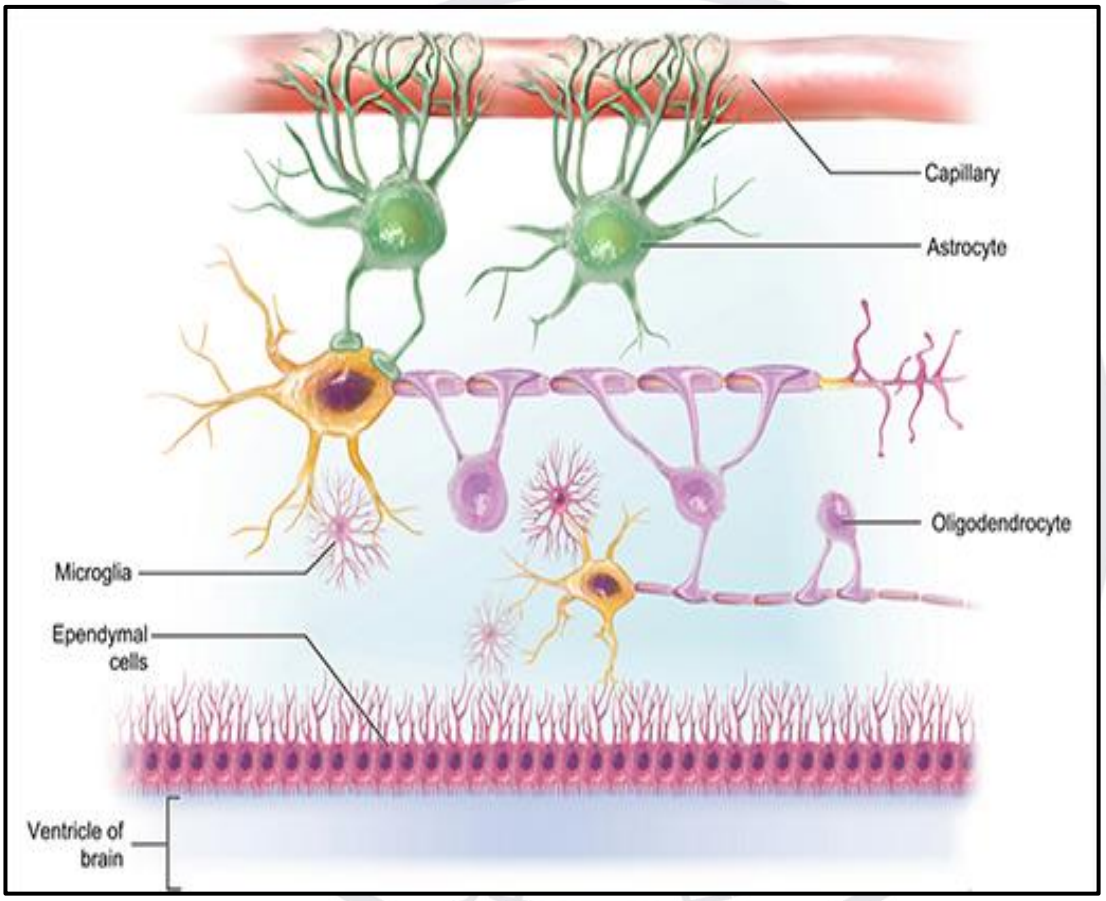
- ☒ Spongioblasts: lining the neural tube.
- ☒ Ependymal cells:
  - line the central canal of spinal cord and brain ventricles.
  - They form the C.S.F.
- ☒ Satellite cells: around the nerve cells of the ganglia.
- ☒ Schwann cells.
- ☒ Tanycyte cells: surround the neurons of hypothalamus.

Staining of neuroglia proper:

- ☒ **By H. & E:** only their nuclei appear.
- ☒ **By silver:** appear as black structures on clear background.

General functions of neuroglia proper:

- ☒ Support: by forming a network in the meshes of which the nerve cells and fibers are supported.
- ☒ Insulation: they act as insulators for nerve impulses.

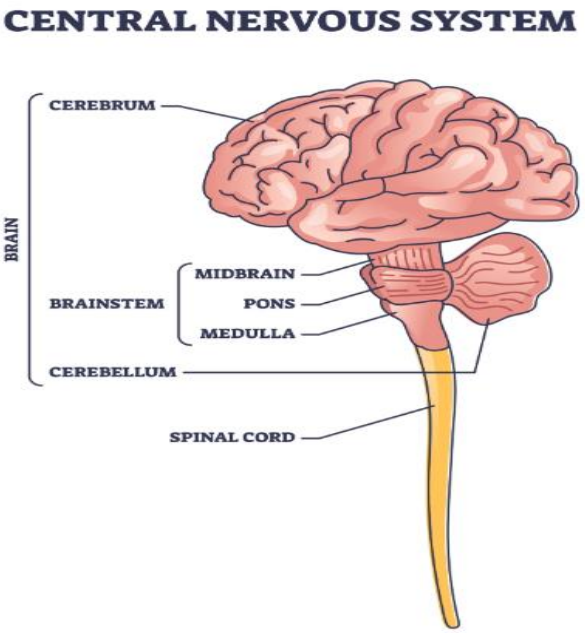


THE CENTRAL NERVOUS SYSTEM

- **The Central nervous system consists of:**

  The brain and the spinal cord.

- **The brain consists of the following parts:**



  - ☒ Cerebrum.
  - ☒ Cerebellum.
  - ☒ Brainstem which is formed of 3 midline structures:
    - Midbrain (Upper part).
    - Pons (middle part).
    - Medulla oblongata (lower part).

- **The spinal cord:**
  - ☒ It is divided into 31 segments; 8 cervical, 12 thoracic, 5 lumbar, 5 sacral and one coccygeal → give origin to the corresponding 31 pairs of spinal nerves.
  - ☒ Each spinal nerve is attached to the spinal cord by 2 roots; a posterior sensory root and an anterior motor root.
  - ☒ Each sensory root has a spinal (sensory) ganglion.
  - ☒ the anterior and posterior roots unite to form the spinal nerve
  - ☒ The spinal cord is divided into two similar halves. Each half consists of an inner core of grey matter and outer white matter.
  - ☒ The grey matter is formed mainly of nerve cell bodies. The white matter is formed mainly of the axons of nerve cells which form tracts.

- **The white matter of each half of the spinal cord is divided into:**
  1. Dorsal white column
  2. Ventral white column
  3. Lateral white column
- **Histologically, the grey matter is formed of:**
  1. Nerve cells.
  2. Non-myelinated nerve fibers
  3. Neuroglial cells and fibers.
  4. Blood capillaries.
- **The nerve cells present in the grey matter are of two types:**

A. <u>Golgi type I</u>: cells with long axons. They are grouped in little aggregations called nuclei.

B. <u>Golgi type II</u>: cells with short axons. They may be interneurons, associative, or commissural neurons. Their axons end in the same segment or in adjacent segments.

- **The grey matter of each half of the spinal cord is formed of:**

A. <u>Posterior (dorsal) horn:</u>

☒ Present in all spinal cord segments.

☒ It contains sensory neurons which receive different body sensations.

B. <u>Anterior (ventral) horn:</u>

☒ Present in all spinal cord segments.

☒ It contains the lower motor neurons which supply skeletal muscles.

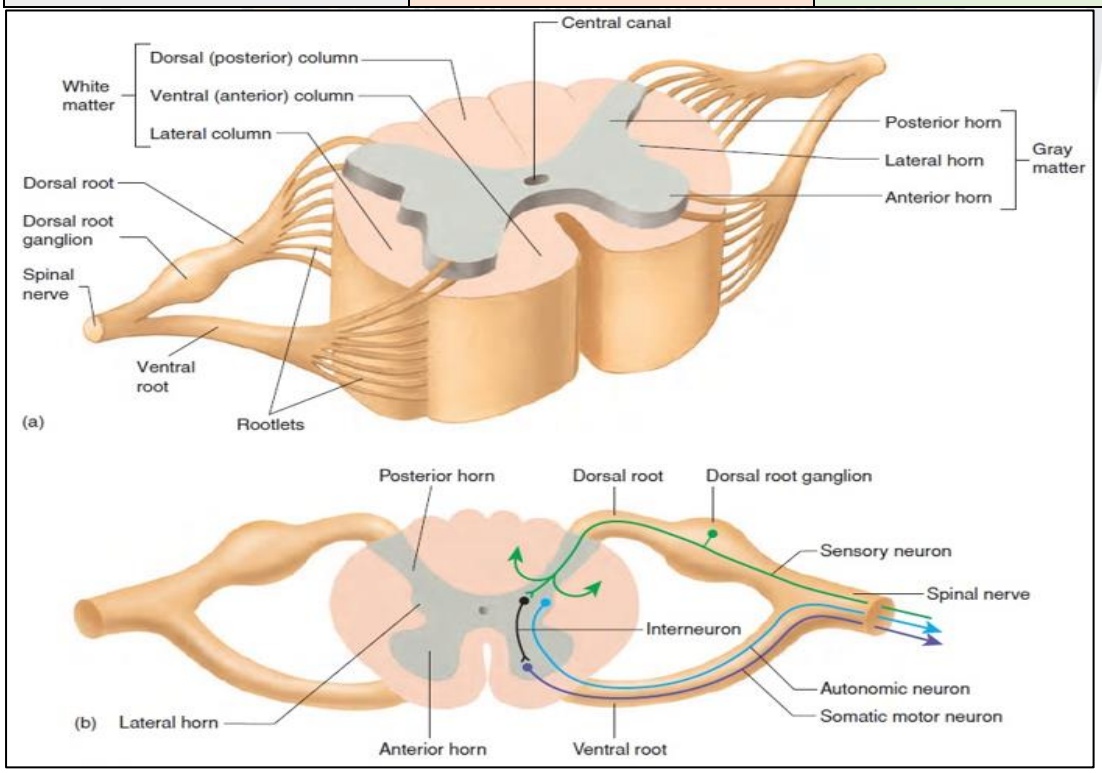
C. <u>Lateral horn:</u>

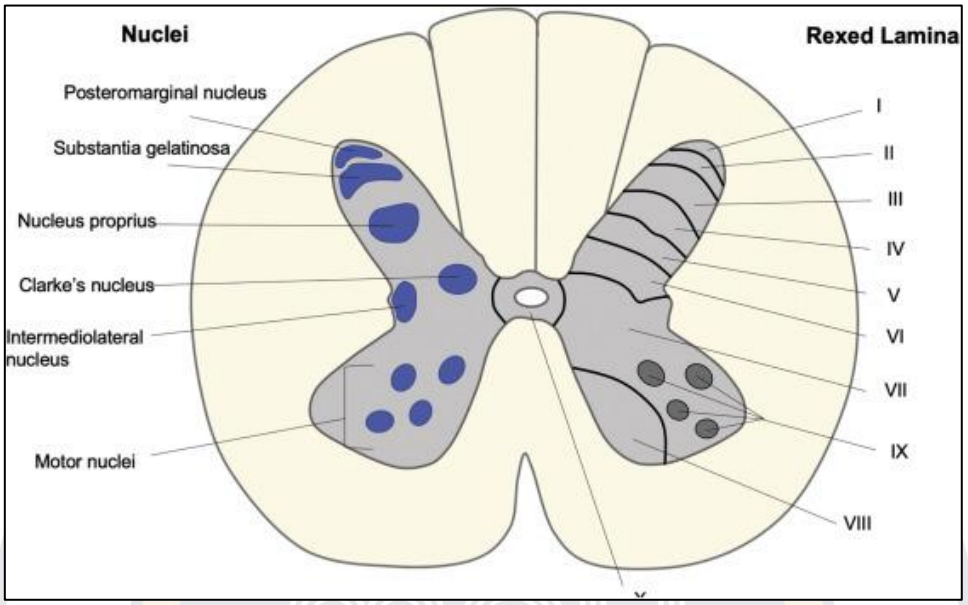
☒ Present only in the thoracic and upper lumbar segments (T1- L2 or L3).

☒ It contains the nerve cells of preganglionic sympathetic nerve fibers.

☒ Similar nerve cells are present in S2, 3, 4 segments, but they merge with the anterior horn and do not project as a separate horn. Their axons form the preganglionic parasympathetic nerve fibers.

DORSAL HORN NUCLEI	LATERAL HORN NUCLEI	VENTRAL HORN NUCLEI
4 sensory nuclei: • Posteromarginal nucleus • Substantia gelatinosa of Rolandi • Main sensory nucleus • Clarke's nucleus	• Sympathetic nucleus: • Parasympathetic nucleus	• Alpha motor neurons • Gama motor neurons • they are divided into medial, lateral and central group)




Nuclei
Rexed Lamina
Posteromarginal nucleus
Substantia gelatinosa
Nucleus proprius
Clarke's nucleus
Intermediolateral nucleus
Motor nuclei
I
II
III
IV
V
VI
VII
IX
VIII

TRACTS OF THE SPINAL CORD

There are two types of tracts in the spinal cord:

(A) <u>Short associative tracts:</u>

- They are ascending or descending tracts.
- They coordinate the different movements of the body with each other.

(B) <u>Long tracts:</u> two types:

a- Ascending tracts, which carry different sensations to the brain.

b- Descending tracts which carry motor orders to AHCs.

- **<u>Short associative tracts</u>: Four types:**

1. **Fasciculi proprii tracts.**
   - Short associative tracts that coordinate the function of the different segments of the spinal cord
2. **Comma – shaped tract.**
   - Carry proprioceptive information to the anterior horn cells to complete the stretch reflex arc of the upper limb.
3. **Septomarginal tract.**
   - They carry proprioceptive information to the anterior horn cells to complete the stretch reflex arc of the lower limb.
4. **Lissauer's tract.**
   - It carries pain and temperature sensation.

- **<u>Long Tracts of the Spinal Cord:</u>** They are of two types:

1. **Ascending sensory tracts:**
   - They arise from either the dorsal root ganglia or the dorsal horn nuclei.
   - They end in the high sensory centers in the brain.
2. **Descending motor tracts:**
   - They arise from the higher motor centers in the brain.
   - They end on the anterior horn cells of the spinal cord.

THE ASCENDING TRACTS OF THE SPINAL CORD

- **Four tracts carry sensations which are felt:**
  - ☒ Sensations which reach the sensory area of the cerebral cortex.
  - ☒ Cutting these tracts → loss of sensation.
  - ☒ These 4 tracts are:
    1. **Lateral spinothalamic tract:** pain and temperature from the opposite side of the body below the head.
    2. **Ventral spinothalamic tract:** simple (crude) touch from the opposite side of the body below the head.
    3. **Gracile tract:** proprioception, fine touch and vibration from the lower half of the body on the same side.
    4. **Cuneate tract:** proprioception, fine touch and vibration from the upper half of the body on the same side.
- **Four tracts carry sensations which are not felt:**
  - ☒ Sensations which don't reach the cerebral cortex.
  - ☒ Cutting these tracts → no loss of sensation.
  - ☒ These are 4 tracts are:
    1. **Dorsal spinocerebellar tract:** unconscious proprioception from the trunk and lower limb to the cerebellum.
    2. **Ventral spinocerebellar tract:** unconscious proprioception from the lower limb to the cerebellum.
    3. **Spinoolivary tract:** unconscious proprioception to the cerebellum as part of the spino-olivo-cerebellar pathway.
    4. **Spinotectal tract:** sensory information from the spinal cord to the superior colliculus for spinovisual reflexes.

PROPRIOCEPTIVE PATHWAYS

There are two types of proprioceptive sensation:

A. Conscious proprioceptive sensation:

☒ Carried from the body to the cerebral cortex by:

a. **Gracile tract** (from below T_6 ; the lower half of the body).

b. **Cuneate tract** (from above T_6 ; the upper half of the body).

☒ The same tracts carry also fine touch and vibration.

B. Unconscious proprioceptive sensation:

☒ Carried from the body to the cerebellum by:

a. **Dorsal Spinocerebellar tract** (from the trunk and lower limb).

b. **Ventral spinocerebellar tract** (from the lower limb).

c. **Spinoolivary tract** (from the body).

d. **Cuneocerebellar tract** (from the upper limb).

THE DESCENDING TRACTS OF THE SPINAL CORD

- All voluntary movements are done by nerve impulses, which start from the cerebral cortex and descend to reach the anterior horn cells (A. H. Cs) of the spinal cord.
- The axons of A. H. Cs. carry the nerve impulses to the striated muscles.
- The pathway from the cerebral cortex to the striated muscles is formed of two neurons; upper and lower.

A. <u>The upper motor neurons (UMN):</u>

- ☒ Present in cerebral cortex and subcortical supraspinal centers e.g. basal ganglia, subthalamus and brainstem.
- ☒ Axons of UMN reach the LMN through the descending tracts.
- ☒ The descending tracts are of two types:

1. Pyramidal tract (the main descending tract):

- It originates from the cerebral cortex.
- It occupies the pyramid on the ventral surface of the medulla.

2. Extrapyramidal tracts:

- They originate from the cerebral cortex and subcortical nuclei e.g. basal ganglia, subthalamus and brainstem.
- They descend to the spinal cord outside the pyramid of the medulla.

B. <u>The lower motor neurons (LMN): they are:</u>

- ☒ The anterior horn cells of the spinal cord.
- ☒ The motor nuclei of cranial nerves in brainstem
- ☒ Axons of anterior horn cells → peripheral nerves to striated muscles.
- ☒ Axons of cells of cranial nerve motor nuclei → motor fibers of cranial nerves to striated muscles of head and neck.

PYRAMIDAL TRACT

(PYRAMIDAL SYSTEM)

- **Definition:**

It is the motor pathway which arises from the cerebral cortex and descends to reach the motor nuclei of the cranial nerves and the anterior horn cells of the spinal cord and while descending it forms the pyramid in the medulla.

- **Divisions: It is formed of:**

1. **Corticospinal fibers** or pyramidal tract proper which terminates on the anterior horn cells of the spinal cord.
2. **Corticobulbar fibers** which terminate on the motor nuclei of cranial nerves in the brainstem.

EXTRAPYRAMIDAL TRACTS

- **Definition:**

They are the descending motor tracts which descend outside the pyramid of the medulla.

- **Origin:**

They are divided into 2 main groups:

A. The extrapyramidal tracts which start from the **cerebral cortex and descend to the brainstem.**
B. The Extra pyramidal tracts which start from the **brainstem (the midbrain, pons and medulla) and descend to the spinal cord.**

- **The extrapyramidal tracts in the spinal cord:**

There are 6 extrapyramidal tracts in the spinal cord based on origin:

A. Two tracts arise from the midbrain:

1. Rubo-spinal tract
2. Tecto- spinal tract

B. Two tracts arise from the pons:

3. Vestibulo-spinal tract.
4. Medial reticulo-spinal tract

} Both are **direct**

C. One tract arises from the medulla:

Lateral reticulo –spinal tract→ direct

D. One tract arises from the brainstem as a whole:

Sulcomarginal tract → direct.

THE CEREBELLUM

It Consists of

A. Gray matter:

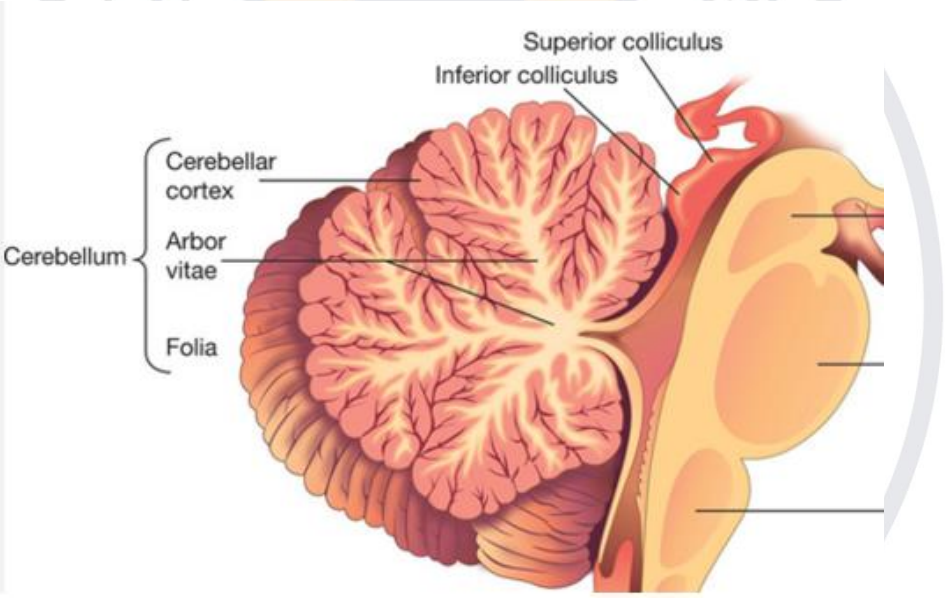
1- Cerebellar cortex.

2- Cerebellar nuclei.

B. White matter (Medulla).

The cerebellar folia

are tree like arborizations formed of outer cortex and inner medulla.



CEREBELLAR CORTEX

Formed of three layers from outside inwards:

☒ Molecular layer:

- Composed mainly of fibers and few cells.
- **Cells:**
  1. Molecular (stellate) neurons → They synapse with dendrites of Purkinje cells
  2. Basket cells
  3. Neuroglia cells

- **Fibers:**
  - **a.** Axons & dendrites of molecular & basket cells.
  - **b.** Dendrites of Purkinje cells.
  - **c.** Axons of granular cells.
  - **d.** Dendrites of Golgi II cells.
  - **e.** Climbing Fibers & recurrent collateral fibers.

☒ **Purkinje cell layer: composed of Purkinje cells only.**

- **Purkinje cells (Golgi I cells):**
  - **Body:** Large, pyriform, arranged in one row away from each other
  - **Dendrites:** Fan out in the molecular layer to synapse with axons of molecular & granular cells and climbing Fibers.
  - **Axon:** Enter the white matter to end in deep cerebellar nuclei & Vestibular nuclei.

☒ **Granular (nuclear) layer: mainly cells & few fibers.**

- **Granular cells**
  - **Body:** Very small & closely packed.
  - **Dendrites:** Synapse with a **ROSETTE** of Mossy fibers to form **CEREBELLAR GLOMERULI**.
  - **Axon:** Pass to the molecular layer.
- **Golgi II cells:**
  - **Body:** Like that of Purkinje cells.
  - **Dendrites:** Fan out in various planes.
  - **Axon:** Short, much branched, synapse with dendrites of granular cells.
- **Fibers:**
  - Axons of Purkinje cells
  - Climbing & Mossy fibers.

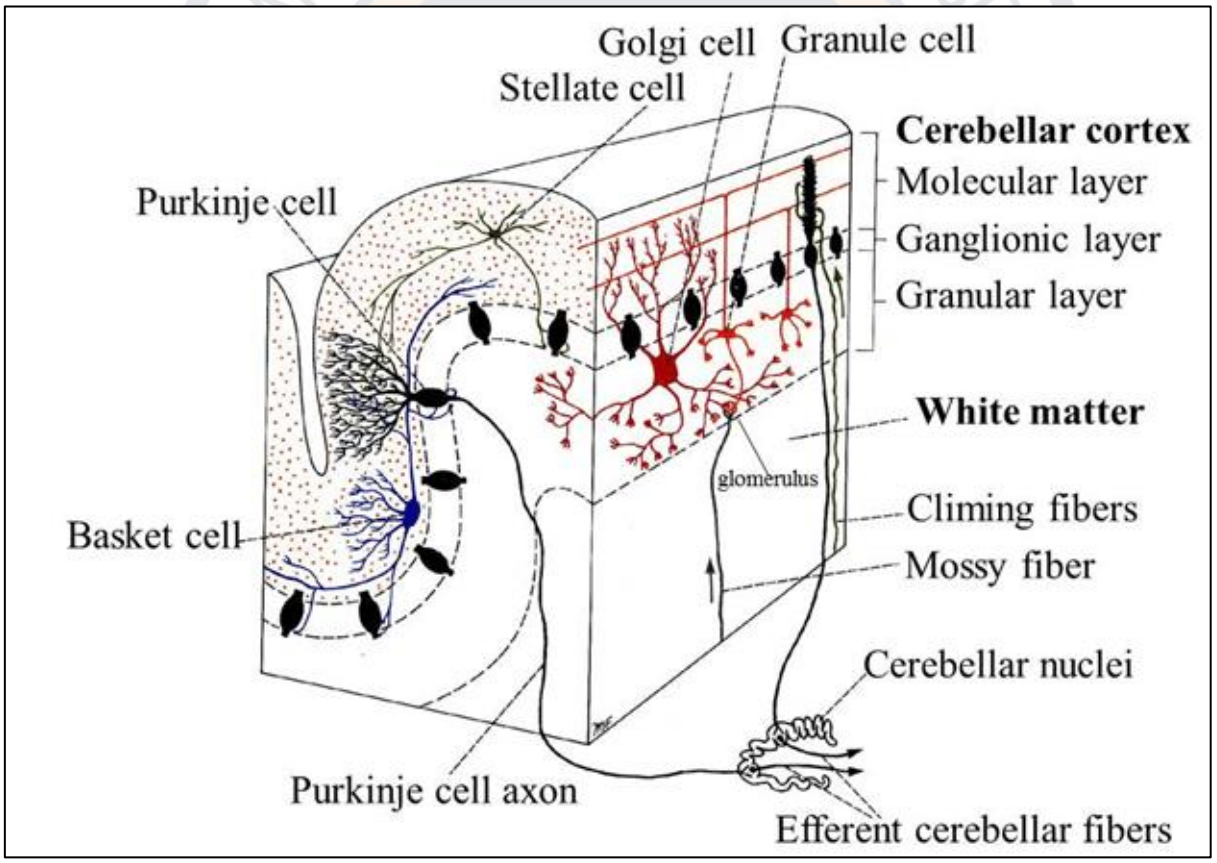
CEREBELLAR WHITE MATTER

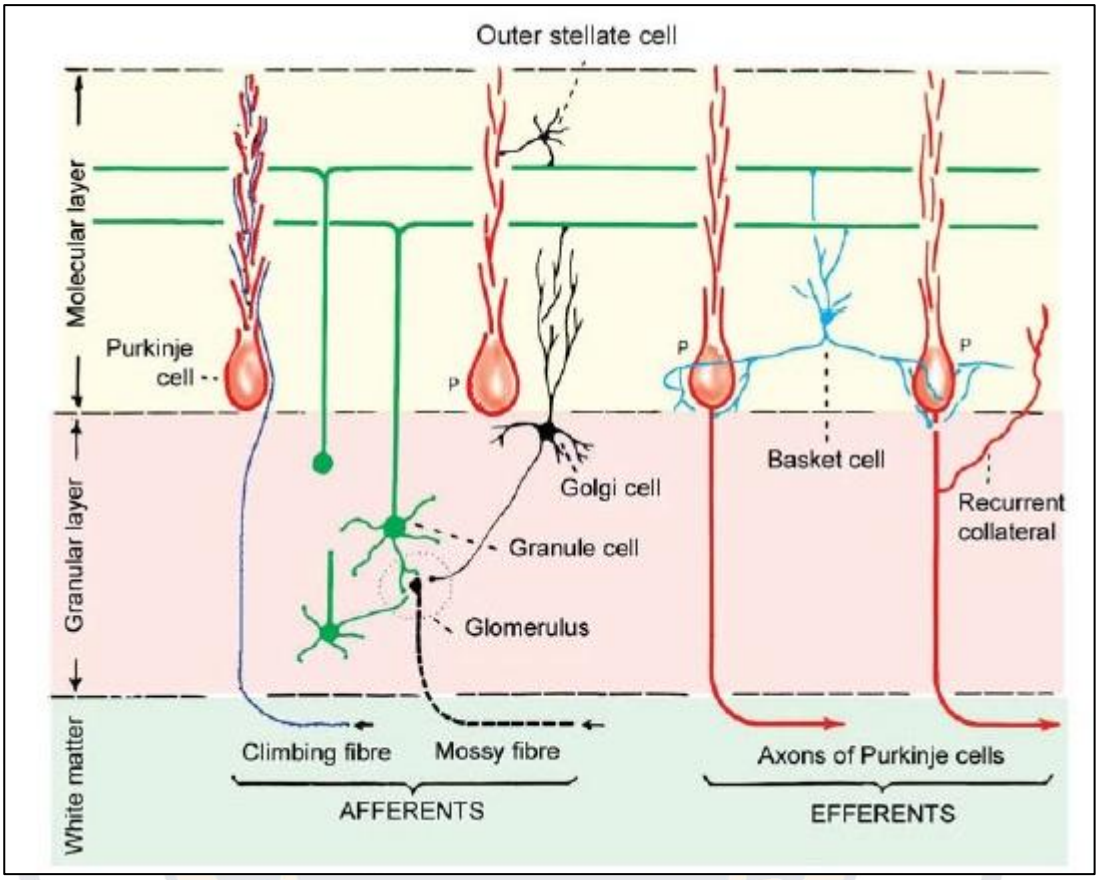
☒ **Projection fibers.**

Efferent → axons of Purkinje cells.

Afferent → **Climbing Fibers**
Afferent → **Mossy Fibers**
Afferent → **Recurrent collateral Fibers**

☒ **Commissural & association fibers.**




Outer stellate cell
Molecular layer
Purkinje cell
P
P
P
Granular layer
Golgi cell
Granule cell
Glomerulus
Basket cell
Recurrent collateral
White matter
Climbing fibre
Mossy fibre
AFFERENTS
Axons of Purkinje cells
EFFERENTS

THE CEREBRUM

Consists of:

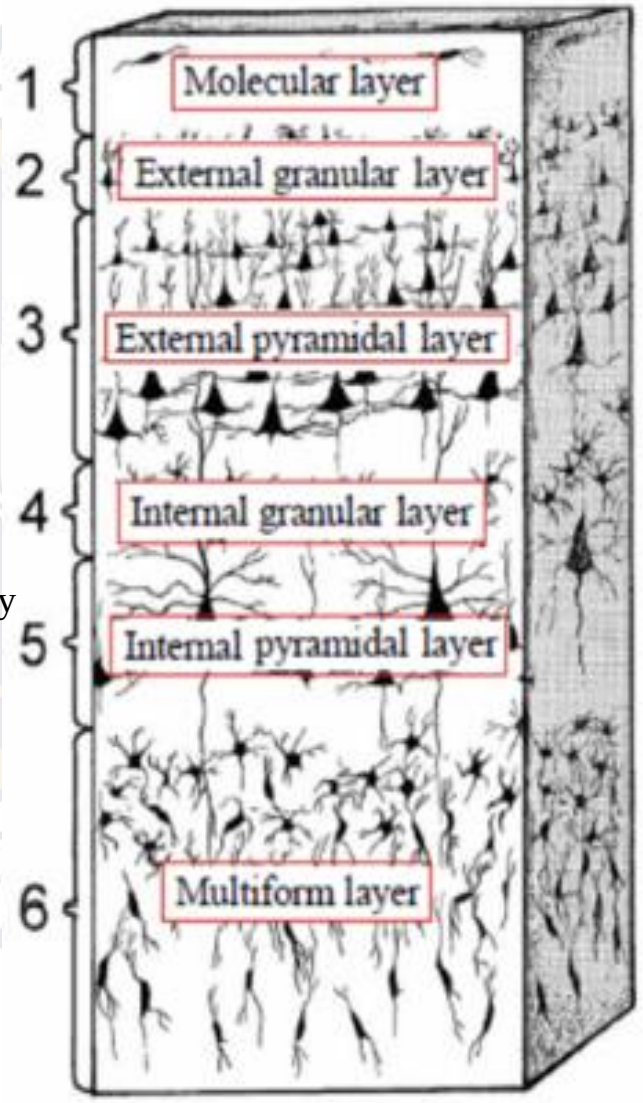
A. Grey matter

1- Cerebral cortex. 2- Basal ganglia

B. White matter (cerebral white matter).

CEREBRAL CORTEX

I. Cyto- architecture of the cerebral cortex. (from outside-inward)



☒ **Molecular layer:**

Contains few scattered horizontal cells of Cajal.

☒ **Outer granular layer:**

Contains small pyramidal (pyramidal with large vesicular nucleus) & stellate (granular) cells (polygonal or triangular with large vesicular nucleus).

☒ **Outer pyramidal layer:** contains predominantly medium sized pyramidal cells with the same characters as small pyramidal cells but larger

☒ **Inner granular layer:** contains predominantly stellate (granular) cells.

☒ **Inner pyramidal [ganglionic] layer:** predominantly large pyramidal cells with the same characters as small cells but larger.

☒ **Pleomorphic (multiform) layer:** contains fusiform & stellate (granular) cells.

II. CEREBRAL WHITE MATTER

1. Projection fibers:
2. Association fibers (on the same side)
3. Commissural fibers (between two hemispheres)

Plexiform or molecular		Transverse fibres and some scattered neurons
External granular		Mainly stellate neurons
Pyramidal		Mainly pyramidal neurons Some stellate cells and basket cells
Internal granular		Stellate neurons Outer band of Baillarger
Ganglionic		Giant pyramidal cells Inner band of Baillarger
Multiform or polymorphous		Neurons of various sizes and shapes Merges with white matter

THE EYE

Definition:

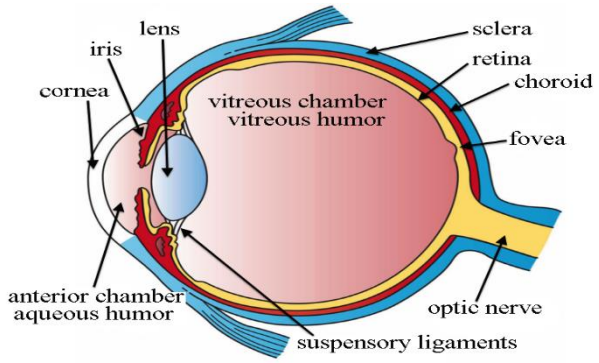
The eyes are photosensitive organs that provide us with the sense of sight.

Site:

☒ The eyes are located in a protective bony structure of the skull, the orbit.

☒ The wall of the eyeball consists of 3 coats (layers):

1. Outer fibrous layer → cornea and sclera.
2. Middle vascular or uveal layer → choroid, ciliary body and iris.
3. Inner nervous layer → retina.



A. THE OUTER FIBROUS COAT

1. The Cornea:

Definition:

It is the anterior 1/6 of the outer fibrous coat. It is colourless, non vascular and transparent.

Thickness: about 0.5 mm at its center and about 1 mm at its periphery.

L.M:

A transverse section shows that it consists of 5 layers from outside inwards:

A. Epithelium:

☒ it is a thin layer of stratified squamous non keratinized epithelium formed of 5-6 layers of cells:

- The basal layer: a single layer of cubical cells lying on a straight basement membrane.
- The intermediate layers: are 3-4 layers of polyhedral cells with numerous free nerve ending in between.

- The top layer: squamous cells provided with microvilli which retain a film of tears, a protective layer of lipid and glycoprotein, which keeps the cornea wet all the time.

B. Bowman's membrane:

☒ **LM:** it is a transparent homogenous a cellular layer.

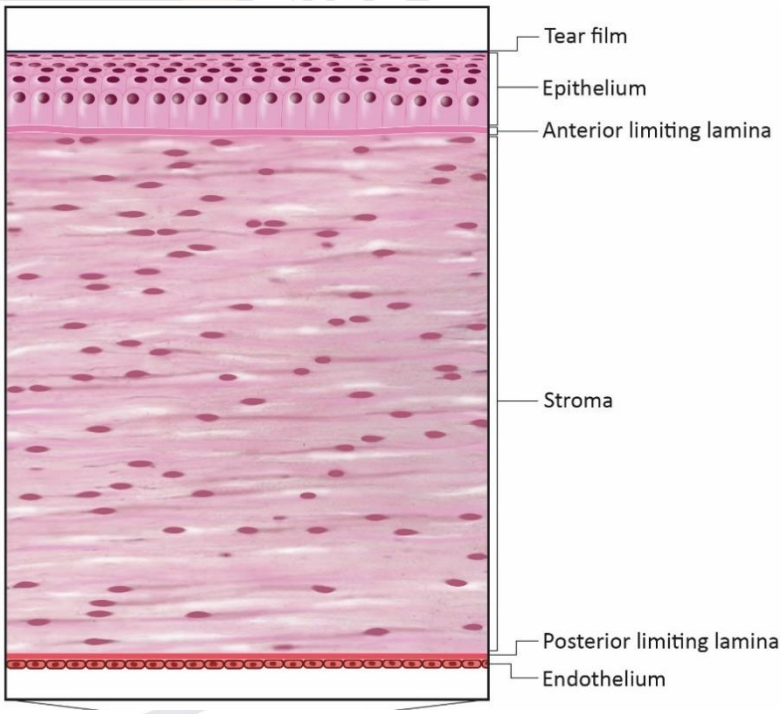
☒ **Function:**

- It acts as a protective barrier against trauma and bacterial invasion. Once destroyed, it is not regenerated and healing from the underlying C.T. always leaves a scar causing corneal opacity.

C. Substantia propria

☒ It comprises about 90% of the thickness of the cornea

☒ It is formed of about 20-25 regular lamellae of type I collagen bundles separated from each other by flattened fibroblasts (corneal corpuscles).



D. Descemet's membrane:

☒ It is a homogenous, non cellular membrane formed of fine collagenous filaments and basement membrane materials. It is thinner than the Bowman's membrane.

E. Descemet's endothelium:

☒ It is a simple squamous epithelium covering the posterior surface of the cornea facing the anterior chamber. This layer is responsible for the synthesis and maintenance of Descemet's membrane.

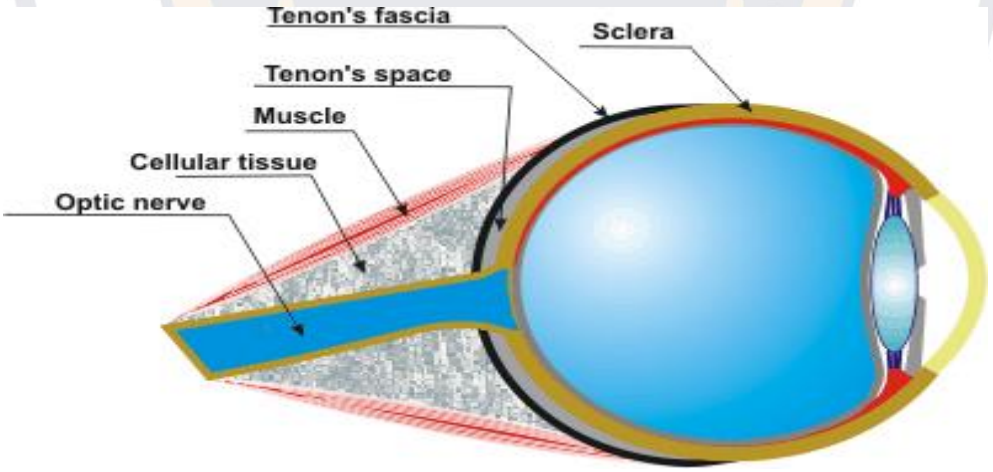
Causes of corneal transparency:

1. The continuous evaporation of water from its surface.
2. The absence of blood vessels.
3. The cells, fibers and matrix have the same refractive indices.
4. The regular arrangement of the fibers and cells of the substantia propria.
5. The regular arrangement of the cells of the covering epithelium.

2. The Sclera:

Definition:

It is the white opaque posterior 5/6 of the eye. It forms a segment of a sphere about 22 mm in diameter.



L.M.:

☒ Its external surface which gives attachment to the tendons of the eye muscles "The episclera".Surrounded by a dense layer of C.T. called tenon's capsule (Fascia) between this capsule and the sclera is "Tenon's space"

☒ Its middle part formed of irregular white dense C.T.

☒ Its inner most layer (the lamina fusca) faces the choroid is a thin layer of loose CT rich in melanocytes fibroblast and elastic fibers.

N.B.:

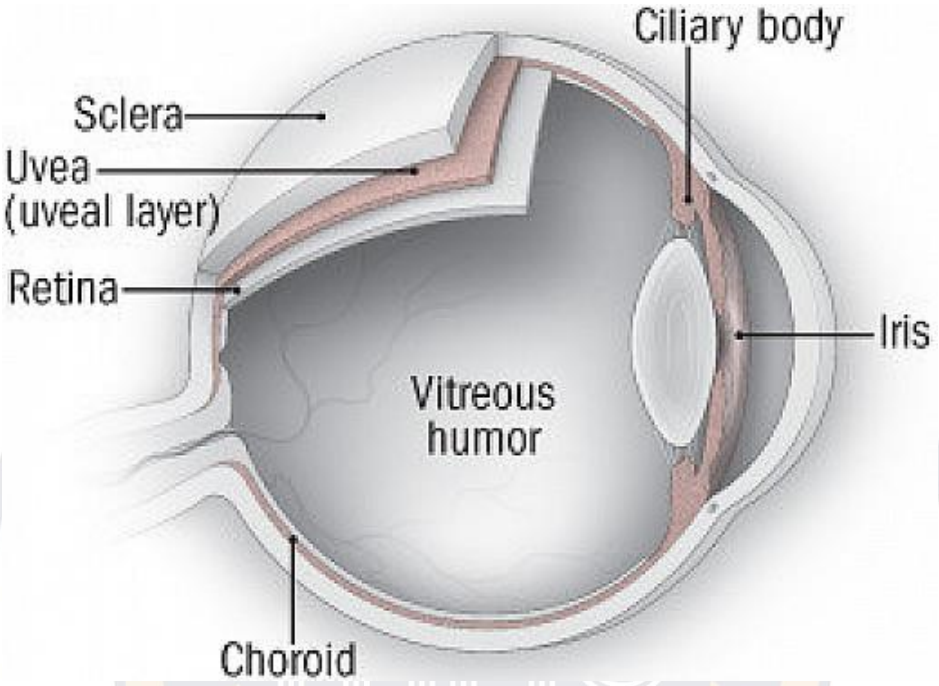
- Posteriorly the sclera is pierced by the optic nerve and is continuous with its dural sheath. This perforated part of the sclera is called "***lamina cribrosa***".

The sclera is opaque because:

1. The refractive indices of all its elements is not equal.
2. The irregular arrangement of its C.T. fibers.
3. The presence of great amount of water.

3. THE MIDDLE VASCULAR COAT

(Uvea)



A. Choroid:

- **Definition:**

  This is the pigmented vascular C.T. layer which lies between the retina and the sclera. It covers the posterior half of the eye.

- **LM.:** It is made up of 4 layers:

1. **Epichoroid or suprachoroid.**

   It is the most outer layer. It consists of a loose C.T. layer rich in melanocytes fibroblast, macrophages, nerve fibers and ganglion cells.

2. **The vessel layer:**

   A highly vascular C.T. rich in elastic fibers and pigment cells.

3. **The choriocapillaries**:

   It is formed of a single layer of fenestrated blood capillaries.

4. **Bruch's membrane:** formed of 5 layers by E.M.

   - The central layer is composed of a network of elastic fibers which is lined on its two surfaces with layers of collagen fibers its outer most and inner most collagen layers are covered by basal lamina .

Function:

1. The choriocapillary layer has an important function in the nutrition of the retina.
2. It supports the retina and absorbs excess light.
3. Bruch's membrane plays an important role in limiting access of inappropriate macromolecules from the fenestrated capillaries to the retina.

B. Ciliary body:

Definition:

- It is the thickened anterior part of the choroid. It appears as a thickened ring at the inner aspect of the sclera.
- In transverse section, it has a triangular shape, one of its faces is in contact with the vitreous body, one with the sclera and the third with the lens and posterior chamber of the eye. Its apex is continuous posteriorly with the choroid.

Histological Structure:

☒ Made of loose C.T. rich in blood vessels and melanocytes in which the ciliary muscles (smooth muscles fibers) are embedded.

Ciliary Processes:

☒ Irregular processes arising from the medial side of the ciliary body extending toward the lens.

☒ Formed of loose C.T. core contains fenestrated capillaries covered by the ciliary epithelium.

☒ ciliary epithelium is formed of 2 layers of cubical cells the inner is nonpigmented while the outer layer is pigmented rich in melanin pigment.

- **Function:**

1. Formation of the aqueous humor by the ciliary processes.
2. The ciliary body are responsible for the processes of accommodation of the lens to near and far objects → as the ciliary muscles are attached to the suspensory ligament of the lens.
   - Contraction of the ciliary muscle fibers pulls → the lens becomes more convex → change the focus for near vision.
   - Relaxation of these muscle fibers → flattening of the lens → focusing on distant vision.

C. Iris:

- **Definition:**

The iris is a disk shaped coloured diaphragm with a central adjustable aperture named the pupil.

- **Site:**

The iris is present between the anterior and posterior chambers of the eye.

- **Histological structure:**

1. The anterior surface is lined with a discontinuous layer of fibroblasts, melanocytes and collagen.
2. The stroma of the iris contains loose C.T. that differentiates into 2 layers:
   a. Anterior stromal layer more pigmented but less vascular.
   b. Posterior vessel layer is more vascular but less pigmented. It contains the muscles of the iris which are arranged as follows:
   - The dilator pupillae muscles, which are myoepithelial cells, radially arranged lie near the back of the iris they dilate the pupil.

- The constrictor pupillae muscle is a circular band of smooth muscle fibres that is situated at the pupillary margin of the iris they constrict the pupil.

3. The posterior surface is covered by two layers of heavily pigmented cuboidal epithelial cells "pars iridis retina".

Function:

1. Changes the pupillary size.
2. Shares in the formation of aqueous humor.
3. Gives the color of the eye.

THE REFRACTIVE MEDIA OF THE EYE

1. The cornea.
2. The aqueous humor.
3. The lens.
4. The vitreous body or vitreous humor.

The aqueous humor:

- **Composition:**
  - ☒ It is a watery fluid has an inorganic ion composition similar to that of plasma but with less protein content. It is hypertonic and contains high hyaluronic acid content.
- **Formation:**
  - ☒ It is produced mainly by the ciliary processes and partly by the posterior surface of the iris.
- **Circulation and absorption:**
  - ☒ The fluid passes from the posterior chamber to the anterior chamber through the pupil, then to the spaces of Fontana → to the canal of schlemm → absorbed through small channels across the sclera to → aqueous veins in the subconjunctival tissue → venous circulation.

N.B.: If there is an obstruction to the drainage and the secretion continues, intraocular pressure rises. This condition is called glaucoma and may result in damage to the eye and blindness if left untreated.

The Lens

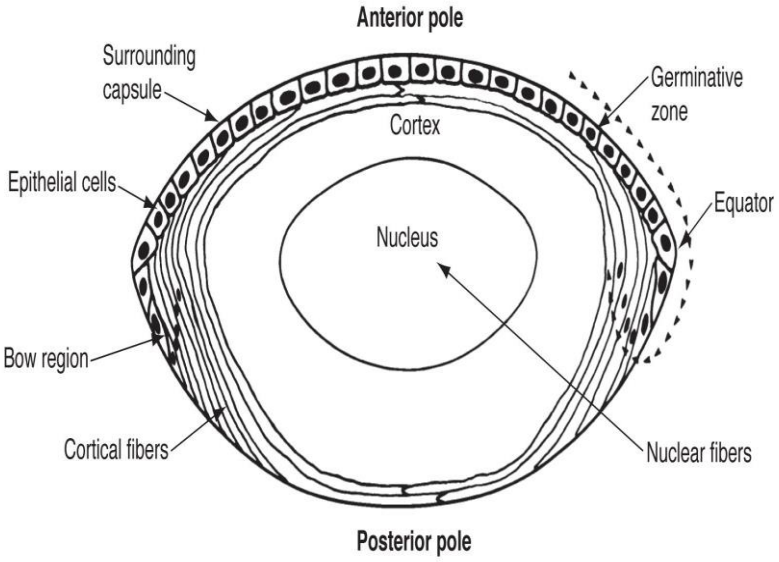
Definition:

☒ The lens is an elastic, transparent biconvex structure of epithelial origin.

Position:

☒ It is situated in the posterior chamber behind the pupil and in front of the vitreous body. It is encircled by the suspensory ligament and ciliary processes.

Histological structure:



a) Lens capsule:

b) Lens epithelium:

- It consists of cuboidal cells.
- At the equator these cells are high columnar.

c) Lens fibers

The suspensory ligament of the lens (the zonules):

Is an annular ligament extending from the periphery of the lens to the ciliary processes. Zonular fibers are similar to the microfibrils of elastic fibers

Function:

The lens is important for accommodation → contraction and relaxation of the ciliary muscles can change the curvature of the lens. Thus the image of near and far objects can be focused on the retina.

N.B.:

- *Presbyopia:* Is a normal aging process occurring after age of 40 in which the ability of the lens to change its curvature is lost, It can be corrected by wearing glasses with convex lenses.

- *In persons exposed to excessive amount of ultraviolet radiation and in diabetic patient especially elderly individuals. Their lens become gray and opaque leading to impairment of vision a condition called "**cataract**". Surgical removal of the clouded lens and replace it by a clear artificial one must be done to restores vision.*

The vitreous body (Vitreous Humor)

Definition:

Transparent jelly-like amorphous substances harder in the periphery and softer in the center.

Composition:

- ☒ Consists of about 99% water.
- ☒ A small amount of type II collagen fibrils.
- ☒ Hyaluronic acid.

Function:

1. Transmits light.
2. It helps to hold the lens in its place.
3. Prevents retinal detachment.

THE INNER NERVOUS COAT

(RETINA)

The pigmented epithelium:

☒ **LM:**

Consists of high cubical cells with rounded nuclei. The cytoplasm contains melanin granules

The neural part of the retina: The retinal layers are 9 layers:

1. **The rods and cones layer:**

☒ It contains the dendritic processes of the rods & cones.

☒ These processes are photoreceptors (see the table).

The following table shows the differences between the rods & cones cells

	Rods	Cones
(A) Number:	120 millions	6-7 millions
(B) Function:	- Adapted to function in dim light	- Adapted to function in bright light.
(C) Site:	Not present at the fovea centralis	The only receptors found in the fovea centralis.

2. **The outer limiting membrane: (dark line)**
3. **The outer nuclear layer:**

☒ Contains the cell bodies of rod and cone cells (the 1st order neurons).

4. **Outer plexiform (reticular) layer:**

☒ It contains the synapses between the axons (synaptic processes) of rod and cone cells and the dendrites of the bipolar and the horizontal cells.

5. **The inner nuclear layer:**

It contains the cell bodies of:

a. The bipolar cells (the 2nd order neurons)

b. Horizontal cells

c. Amacrine cells

d. Muller Cells

6. **The inner plexiform (reticular layer):**

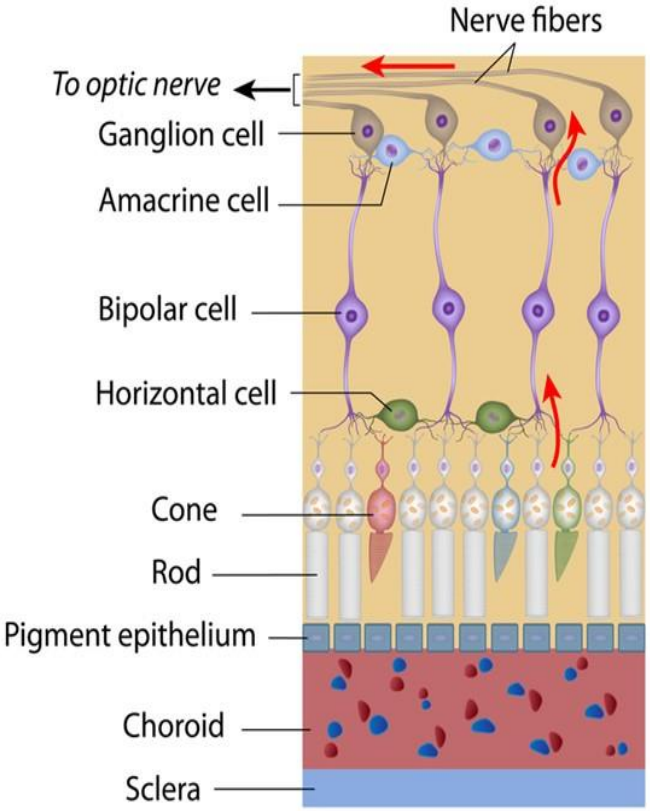
   ☒ It contains the synapse between the axon of the bipolar nerve cells and the dendrites of ganglion cells, It contains the synapses of amacrine cells.

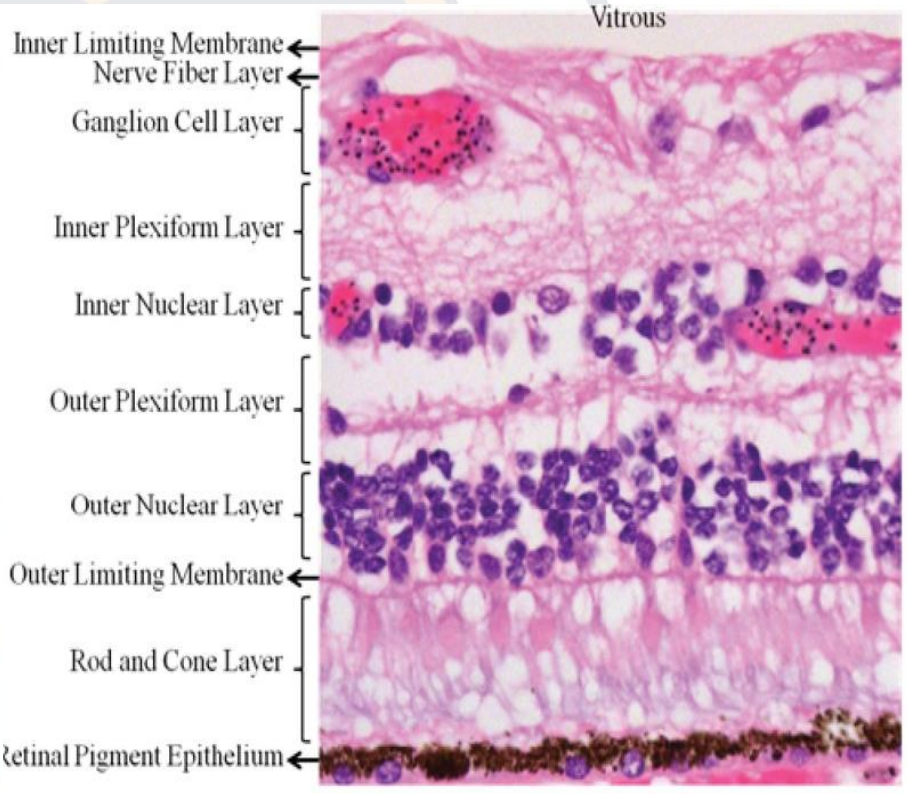
7. **The ganglion cell layer (the 3rd order neuron):**

   ☒ It contains the ganglion cells, their dendrites synapse with the axons of the bipolar nerve cells. Their axons form the fibers of the optic nerve.

8. **The nerve fiber layer:** It contains the axons of the ganglion cells which pass at right angle to form the optic nerve which is not covered by myelin sheath except after traversing the sclera.

9. **The inner limiting membrane: (dark line)**





Fovea Centralis

- **Definition:** it is an area of the retina that provides the highest visual acuity.
- **Site:** it lies in the bottom of a depression in the retina named the macula lutea (yellow spot).
- **Type of receptors present**: cone cells only.

THE ACCESSORY STRUCTURES OF THE EYE

(1) The Conjunctiva:

- **Site**: It covers the anterior portion of the eye up to the cornea. It also lines the internal surface of the eyelids.
- **Parts:**

1- Bulbar conjunctiva which covers the anterior part of the sclera.
2- Palepebral conjunctiva which lines the skin of the eyelid from its inside.
3- Fornix of conjunctiva: at junction between part (1) & (2).

- **Histological structure:**

1. **Epithelium:**
   a- At the fornix: stratified columnar with few goblet cells.
   b- At the bulbar part near the limbus it changes to stratified squamous.
   c- At the palbebral part: it changes to stratified squamous
2. **Corium:**
   loose connective tissue

(2) The Eyelids:

Histological structure:

A perpendicular section shows the following layers from front backwards:

1. Skin:
2. Skeletal muscles: bundles of the orbicularis occuli.
3. The tarsus
4. Palpebral Conjunctiva
5. The Eye lashes

The three types of glands in lid are:

a) **The meibomian glands**: are sebaceous glands in the tarsal plate.

- "**Chalazion**" is a swelling as a result of the infection of the meibomian glands.

b) **Gland of Moll**: are modified sweat glands.

c) **Gland of Zeis**: Are modified sebaceous glands which are present at the roots of the hair follicles of the eye lashes.

- **"A sty"** is produced as a result of infection of either the gland of moll or the gland of Zeis.

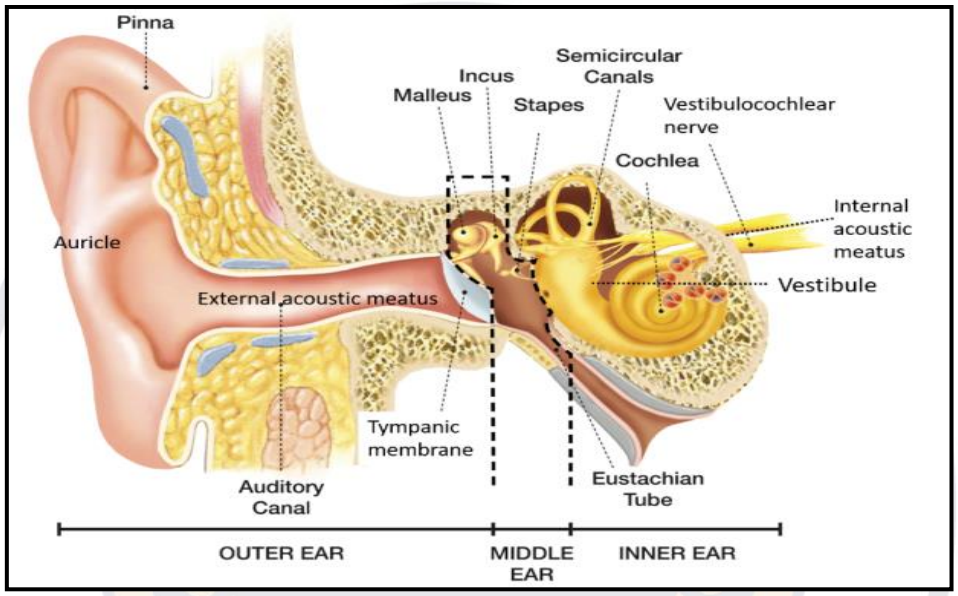
(3) Lacrimal Apparatus:

It includes the lacrimal gland, accessory lacrimal gland, lacrimal sac and nasolacrimal duct.

THE EAR

The ear is formed of:

1. The external ear.
2. The middle ear (the tympanic cavity).
3. The inner ear (the labyrinth).



I) The external ear

- **It consists of three parts:**

1. The auricle
2. The external auditory meatus
3. The tympanic membrane (Ear drum)

1. The auricle (ear pinna):

- **Structure:**

☒ Yellow elastic fibro-cartilage.
☒ Thin skin on both sides.
☒ The lobule of the ear is formed of adipose C.T.

- **Function:**

☒ It collects the sound waves and directs them towards the external auditory meatus.

2. The external auditory meatus:

- **This canal leads to the middle ear. Its wall is formed of:**
  - ☒ Outer 1/3 cartilaginous (yellow elastic)
  - ☒ inner 2/3 bony (spongy bone)
- **It is lined by thin skin which contains:**
  - ☒ Stiff hairs (outer part)
  - ☒ Sebaceous gland.
  - ☒ Ceruminous gland
  - ☒ The secretion of both glands forms the cerumen or the wax of the ear.

3. The tympanic membrane (the ear drum):

- **It separates the external auditory meatus from the middle ear cavity.**
- **It consists of 2 layers of collagenous fibers:**
  - ☒ Outer radial collagenous fibers.
  - ☒ Inner circular collagenous fibers.

    Both layers are covered externally by skin and internally by simple cuboidal epithelium.
  - ☒ The tympanic membrane transmits the vibrations of sound to the middle ear.

II) The middle ear

- It is a cavity present in the temporal bone.
- It is **bounded by** the tympanic membrane (laterally) and the bony wall of the inner ear (medially).
- It is lined with **simple cuboidal epithelium.**
- It is connected to the pharynx through the auditory tube (Eustachian tube).
- **It Contains:**
  - ☒ 3 ossicles
  - ☒ 2 muscles
  - ☒ 2 windows
  - ☒ Chorda tympani nerve

- **The wall of the eustachian tube:**

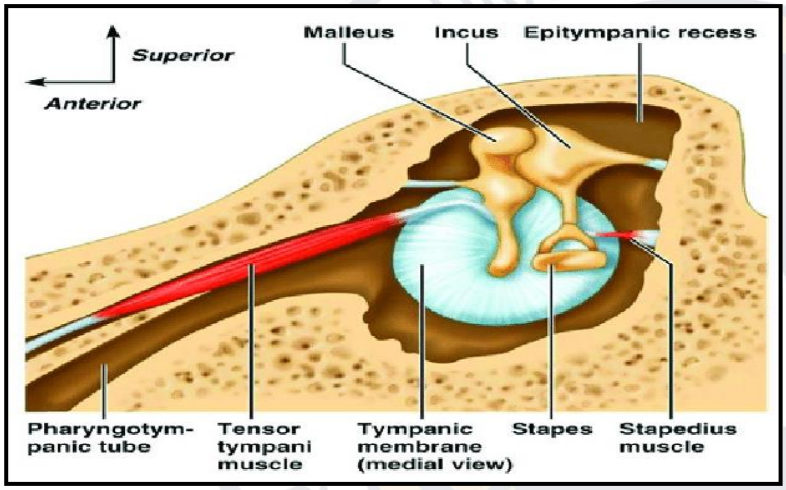
Anterior 2/3	Posterior 1/3
Yellow elastic cartilage	Spongy bone
Lined by pseudostratified columnar ciliated epithelium.	Lined by simple columnar ciliated epithelium

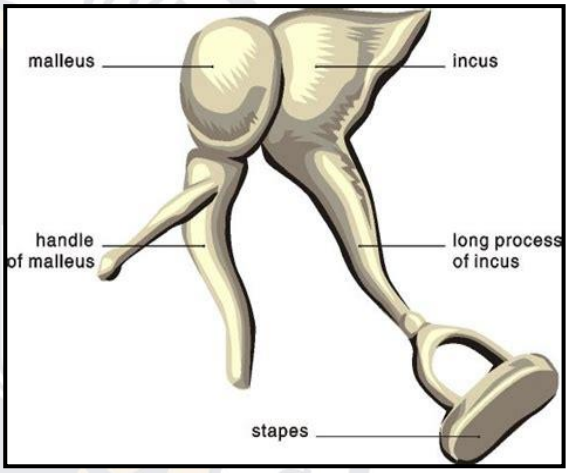
- **The function of the eustachian tube** is to equalize the air pressure in the middle ear and the naso-pharynx.
- **The three bony ossicles:**
  - ☒ Spongy bone, articulate with each other by synovial joint lined with simple squamous epithelium.
  - ☒ From lateral to medial:
    1. **Malleus:**
       Its handle is attached to the tympanic membrane.

2. **Incus:**
   present between malleus and stapes.
3. **Stapes:**
   Its foot closes the oval window.

The two muscles are:

1. **Tensor tympani** (attached to malleus).
2. **Stapedius** (attached to stapes).





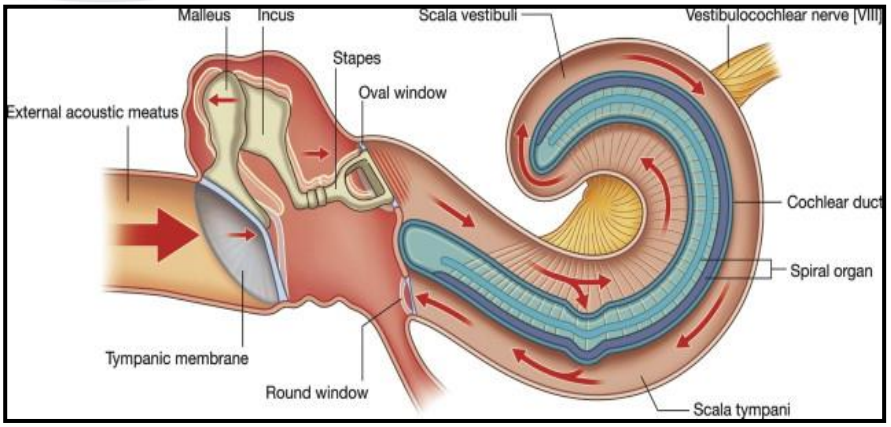
The two windows in the medial wall of the middle ear are:

A. Oval window:

- ☒ Closed by annular ligament which is attached to the foot of stapes.
- ☒ Transmit waves to perilymph in internal ear.

B. Round window:

- ☒ Closed by elastic membrane (2ry tympanic membrane).
- ☒ Dissipates the sound waves after they have stimulated the sensory receptors in the inner ear.



III) The inner ear (the labyrinth)

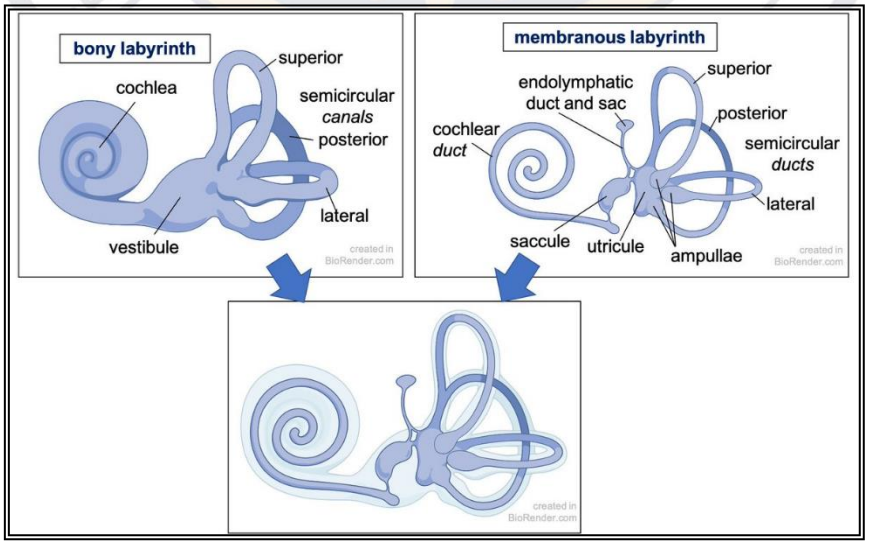
It is formed of:

1. The membranous labyrinth:

- ☒ It contains the receptors of hearing and equilibrium (neuro-epithelial structures).
- ☒ The membranous labyrinth is filled with the endolymph **(↑K & ↓Na)**.
- ☒ It is present inside the bony labyrinth.

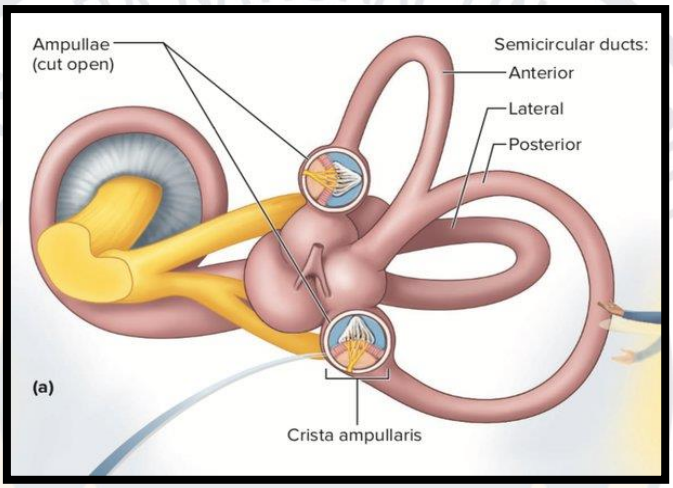
2. The bony labyrinth:

- ☒ It consists of bony spaces and cavities in the petrous part of the temporal bone in which membranous labyrinth is present.
- ☒ It is filled with perilymph (↑Na).
- ☒ The bony labyrinth consists of:
  - The cochlea.
  - The semicircular canals.
  - The vestibule.



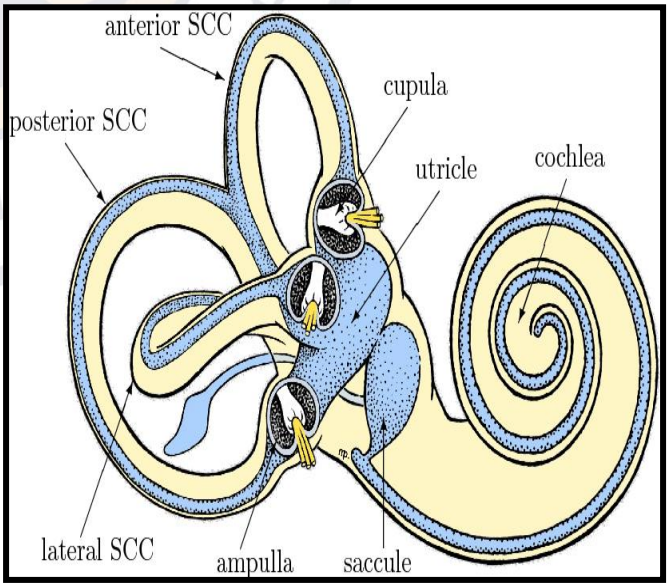
The semicircular canals

- Three bony semi-circular canals arranged in 3 different planes at right angles to each other.
- They have 5 openings on the vestibule.
- Each bony semicircular canal contains a membranous canal which is filled with endolymph.
- Each membranous semicircular canal has an expanded end called crista ampullaris which regulate the body position in relation to the movements of the head.



The vestibule

- The vestibule contains two membranous structures which are the **utricle** and the **saccule**.
- The utricle and the saccule are filled with endo-lymph.
- Each of the utricle and the saccule contains a neuro-epithelial structure. That of the utricle is known as the macula utriculi while that of the saccule is known as the macula sacculi.
- **The function of the maculae** is to maintain the body equilibrium in relation to gravity.

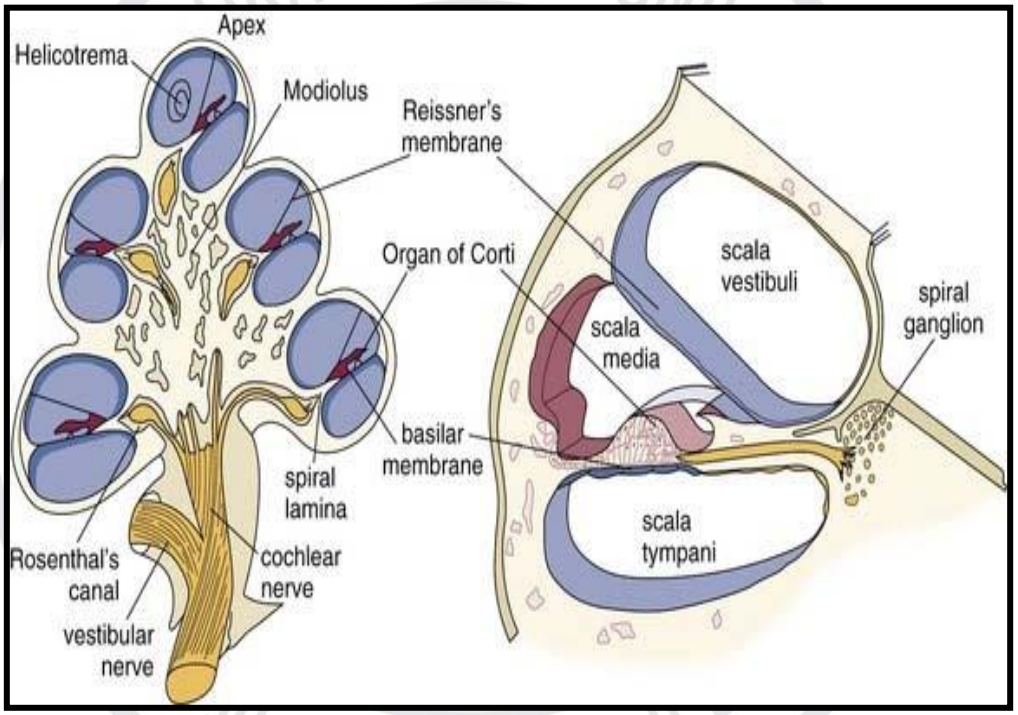


The cochlea

☒ It is a hollow bony spiral tubule that turns upon itself 2½ turns around a central bony axis called the modiolus.

☒ The modiolus is formed of spongy bone and has a cavity in its center contains the fibers of the cochlear nerve.

☒ In section; it appears as 5 cavities because the 2 complete turns are cut twice.



☒ The cochlea is divided by basilar and vestibular membranes into three compartments:

- The scala vestibuli.
- The cochlear duct.
- The scala tympani.

The cochlear duct:

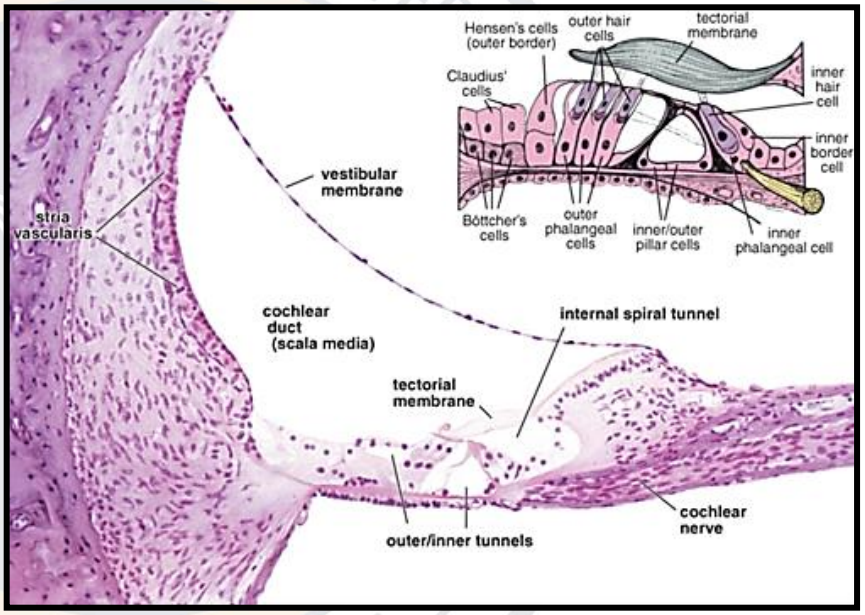
☒ **Triangular** in cross section.

☒ **Boundaries:**

- **Vestibular membrane** which is lined by simple squamous epithelium.
- **Basilar membrane**
- **Stria vascularis** which is in direct contact with the bony cochlea and is formed of vascular C.T. covered with pseudostratified columnar epithelium.

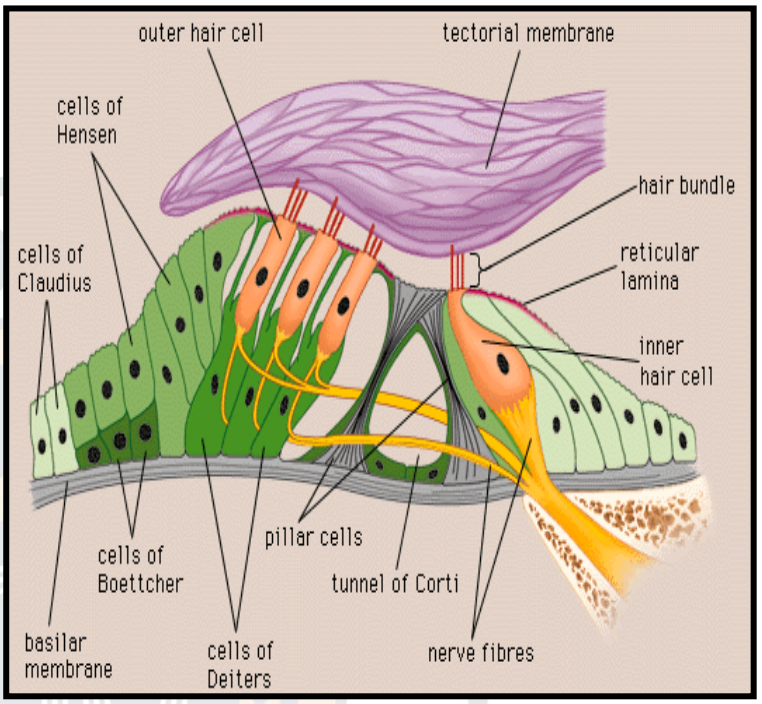
☒ **Contents:**

- Endolymph
- Organ of Corti



The organ of Corti

- It is a neuro-epithelial structure present in the cochlear duct, on the upper surface of basilar membrane.
- **It is formed of:**
  1. Supporting cells.
  2. Hair cells.



The supporting cells are:

☒ **The inner and outer pillar cells:**

The cytoplasm of pillar cells contains bundles of microtubules. Pillar cells form with the basilar membrane a triangular space called the tunnel of Corti.

☒ **The inner and outer phalangeal cells:**

- They support the hair cells. The inner phalangeal cells are arranged in one row while the outer ones are arranged in 3-5 rows.
- The cytoplasm of phalangeal cells contains 2 groups of bundles of microtubules.

☒ **Cells of Claudius:** are cubical cells.

☒ **The Hensen's cells:** are tall cells with narrow bases and enlarged upper ends.

☒ **The border cells:** which form the innermost supporting cells of the organ of Corti.

The hair cells are:

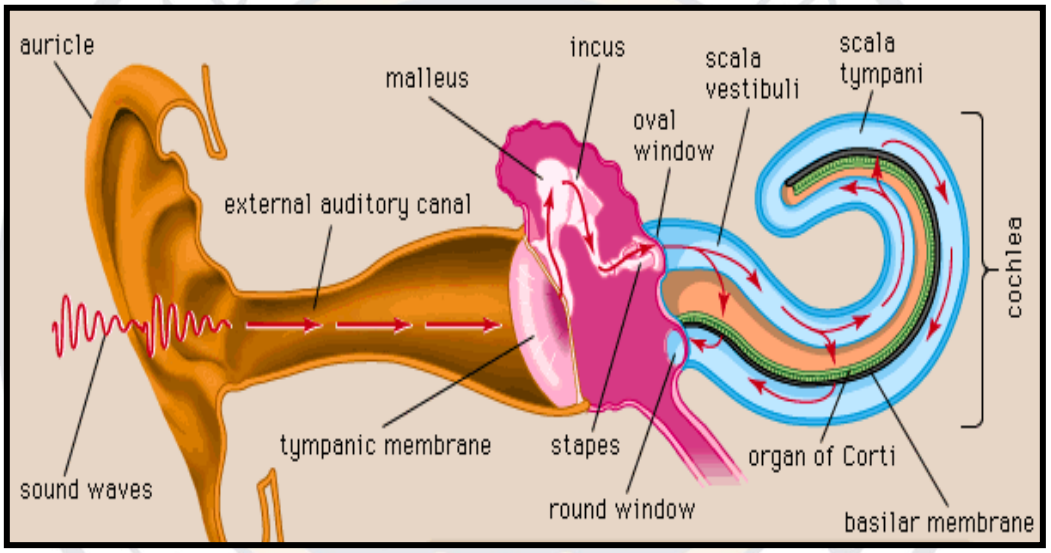
☒ **The inner hair cells:** which are arranged in one row lying on the inner phalangeal cells.

☒ **The outer hair cells:** which are arranged in 3-5 rows lying on the outer phalangeal cells.

- The free surface of each hair cell is provided with stereocilia (non-motile cilia).
- The basal part of each cell is surrounded by the terminal ends of the dendrites of the bipolar nerve cells of the spiral ganglia.

The mechanism of hearing:

- ☒ Sound waves vibrates → ear drum → 3 ossicles (foot of stapes) → peri-lymph in scala tympani → basilar membrane.
- ☒ Vibrations stimulate hair cells in organ of Corti → cochlear nerve → auditory area of the brain.
- ☒ The brain will translate these stimuli into their specific meanings.



NERVE ENDINGS

A. RECEPTORS

1. **Receptors for special sense:**

   A- Eye: Vision → ***Retina.***

   B- Ear: Hearing → ***Organ of Corti***.

   Head position & movement → ***Crista ampullaris***, ***maculae utriculi*** & ***sacculi.***

   C- Smell: ***Olfactory epithelium***.

   D- Taste: ***Taste buds.***

2. **Receptors for cutaneous sensation (extroceptors):**

   A- Pain (nocireceptors) → ***Free nerve endings***.

   B- Temperature (thermoreceptors) → ***Free nerve endings***.

   C- Touch (mechanoreceptors):

   * Epidermal: ***Merkel's complex and peritrichial free nerve endings.***
   * Dermal: Papillary Layer → ***Meissner's corpuscles***.

     Reticular Layer → ***Pacinian***, ***Ruffini corpuscles*** and ***Krause end bulbs***.

3. **Receptors for deep sensation:**

   A- Proprioceptors: ***Pacinian corpuscles.***

   B- Kinesthesia (motion sensation)**:** ***Pacinian corpuscle, muscle spindles, Tendon spindles*** & ***joint receptors.***

4. **Receptors for visceral sensation (visceroceptors):**

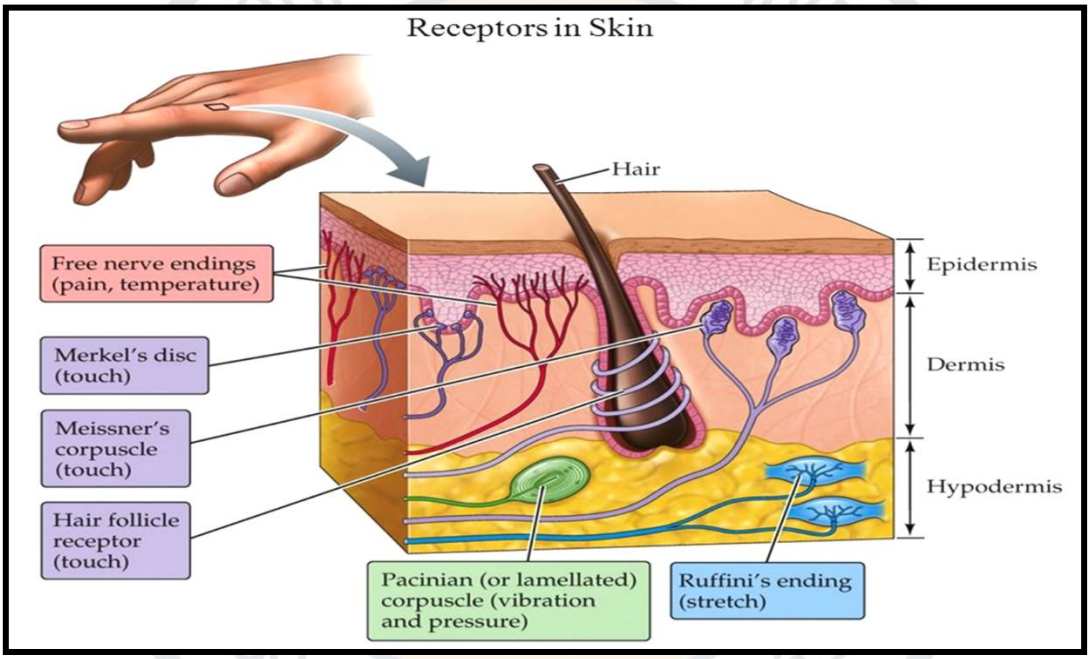
   Via the autonomic nervous system.

B. EFFECTORS

1) **Motor end plates (M.E.Ps) (Myo-neural junction)** → motor to striated muscles.

2) **Autonomic motor endings** → motor to smooth muscle fibers and myoepithelial cells.

3) **Autonomic secretory endings** → secretory to epithelial secretory cells.



Pain and temperature receptors

	Nocireceptors	Thermoreceptors
Site	Epithelium ✓ Epidermis up to granular cell layer ✓ epithelium of: • Corneal surface. • oral cavity • Respiratory tract. Connective tissue	Papillary layer of dermis (dermo-epidermal border)
Shape	Fine Tortuous fibers.	• More tortuous than nocireceptors. • Thin with bulbous termination.
Structure	• No capsule or Axial core. • Non–myelinated nerve fibers (Nerve fibers penetrate the basement membrane, some lose neurolemma to end freely between epithelial cells).	• No capsule or axial core. • Non–myelinated nerve fibers • End freely.
Direction of fibers	Perpendicular to skin surface.	Parallel to skin surface.

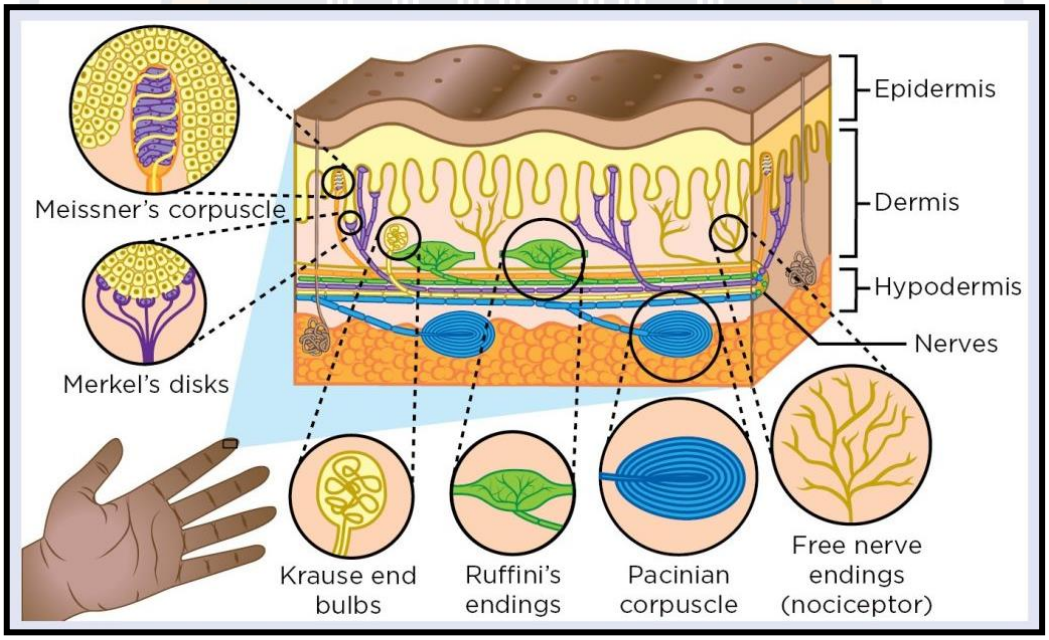
Touch (Mechanoreceptors) in epidermis

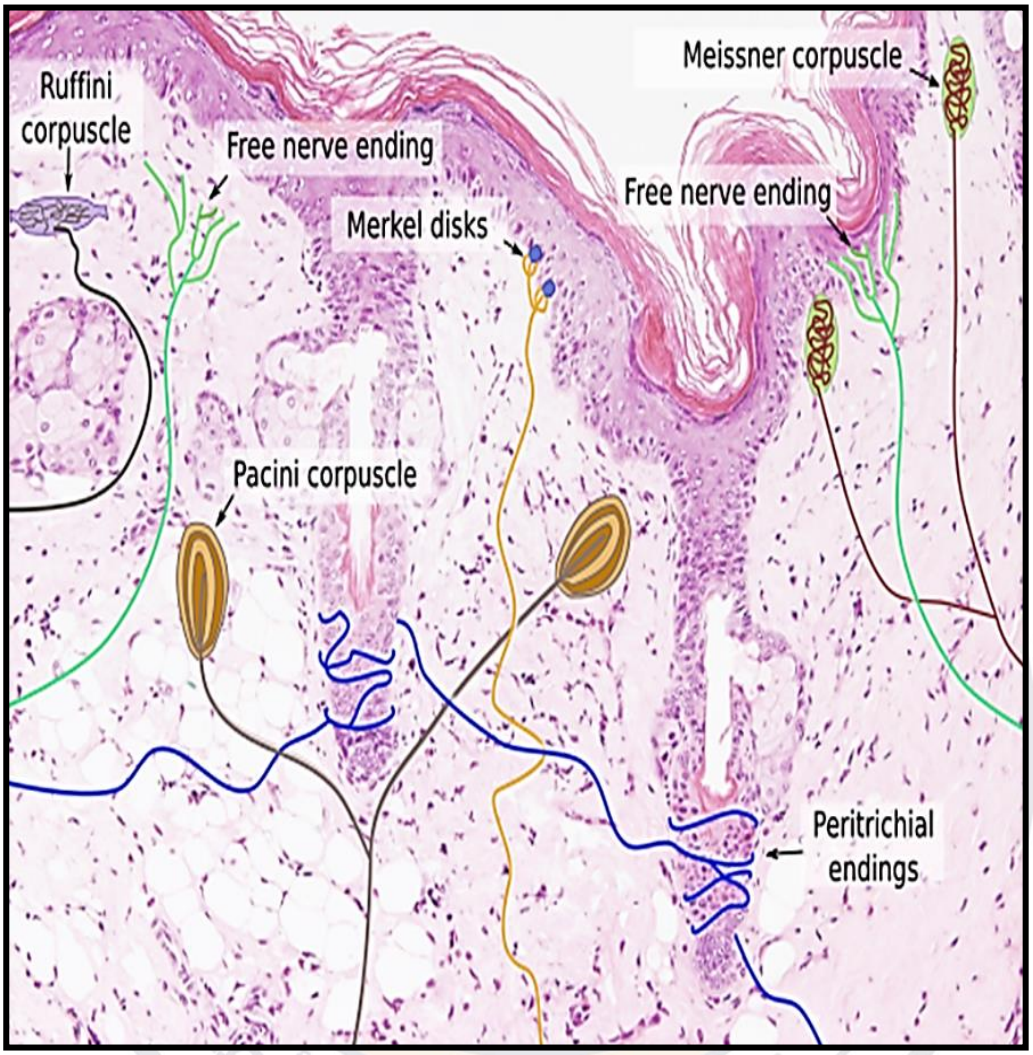
	Merkel's complex	Peritrichial free nerve endings
Site	Deep layer of epidermis of sole and palm.	C.T sheath around bases of hair follicles.
Shape	Fine fibers end by terminal expansions	A basket like plexus of fine fibers
Capsule	No	No
Axial core	No	No
Nerve fibers	loses myelin & neurolemma • Penetrates BM • End as terminal disc under Merkel's cells.	• End around C.T sheath at bases of hair follicles. • Some fibers enter the outer root sheath to end around tactile cells.

Touch (Mechanoreceptors) in dermis

	Meissner's corpuscle	Pacinian corpuscle	Ruffini corpuscle	Krause end bulb
Site	In dermal papillae. Numerous in Fingers, soles lips, eyelids, nipples, external genitalia	Deep in the dermis and hypodermis: Numerous in Fingers, external genitalia and breast sites subjected to pressure: inter-muscular septa, joint capsules, interosseous membranes, wall of UB & mesentery.	Deep in dermis & hypodermis Numerous in the sole.	C.T of: - Conjunctiva - Tongue - Dermis of external genitalia
Shape	- Oval - 100 µm long X 50 µm wide. - Long axis perpendicular to the surface	- Oval - 1-4 m.m long X 1m.m wide	- Elongated, fusiform - 1m.m long X 0.1m.m wide	- Round corpuscle
Capsule	- Thick. - Anchored to dermo-epidermal junction by bundles of C.T fibers.	Thin separated from the corpuscle by a subcapsular space	Thin	Poor capsule
Axial core	Transversally arranged modified Schwann cells and some intercellular collagenous fibers.	20 – 80 concentric layers of flat modified Schwann cells joined together by desmosomes and separated by intercellular spaces containing collagen	Axially arranged collagen fibers.	

		fibers and tissue fluid. Thus in L.S it exhibits an onion like appearance.		
Nerve fiber	Myelinated, penetrates the corpuscle base giving 2- 9 non myelinated spirally running branches that end between collagenous fibers.	Myelinated, penetrates the corpuscle at one pole to become non myelinated, then run to the opposite pole to terminate by an expanded terminal	Myelinated, penetrates the corpuscle side to give numerous non myelinated branches which end between the collagenous fibers by knob like bulb.	Myelinated, penetrates the side to give numerous non myelinated branches that end by bulbous terminals.

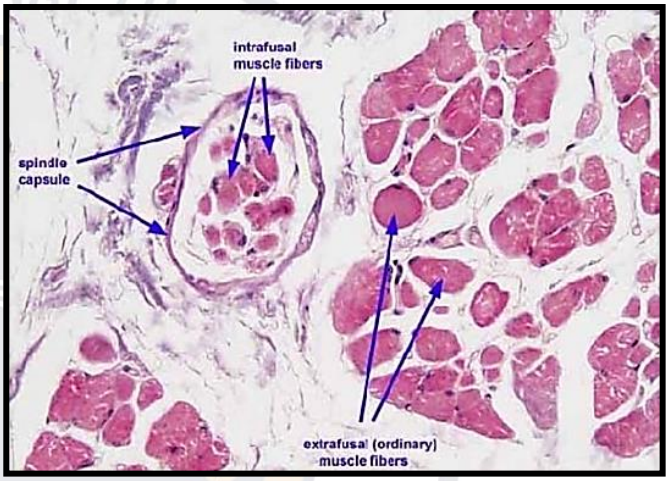



Ruffini corpuscle
Free nerve ending
Merkel disks
Meissner corpuscle
Free nerve ending
Pacini corpuscle
Peritrichial endings

MUSCLE SPINDLE

(NEURO-MUSCULAR SPINDLE)

- **Function:**
  - A stretch receptor for kinesthesia
  - Reflex control of muscle tone, movement and posture.
- **Site:**
  1) Between the striated muscle fibers specially near their insertion.
  2) Numerous in small muscles doing fine work e.g. Hand muscles.



- **Size**: 3– 5 m.m × 0.2 m.m.
- **Shape**: fusiform.
- **Structure:**

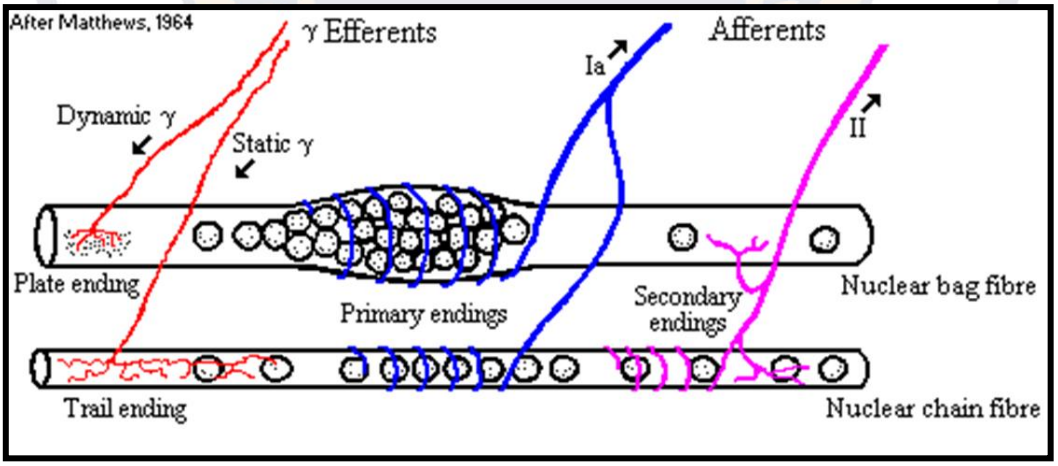
1) Capsule: stretchable connective tissue.

2) Intrafusal muscle fibres: 2 – 12 bag and chain fibers bathed in tissue fluid. Each fiber is formed of a non-contractile central part and contractile two poles.

	Nuclear bag fibers	Nuclear chain fibers
Size:	Thicker - longer	Thinner - shorter
No:	Fewer	Numerous
Central Part:	1) Expanded. 2) Contains a bag of nuclei.	1) Not expanded 2) Contains a chain of nuclei

3) Innervations:

Afferents:	*** 1ry (annulo – spiral) ending** → thick myelinated fiber end around the central part. *** 2 ry (flower spray) ending** → thin myelinated fibers end around the sides of the 1ry afferents. *The bags have only 1ry endings while the chains have 1ry & 2ry endings.
Efferent:	γ- fibers (fine fibers from anterior horn) supply the contractile poles of the intrafusal muscle fibers → more stretch and more firing of **AFFERENT** fibers.

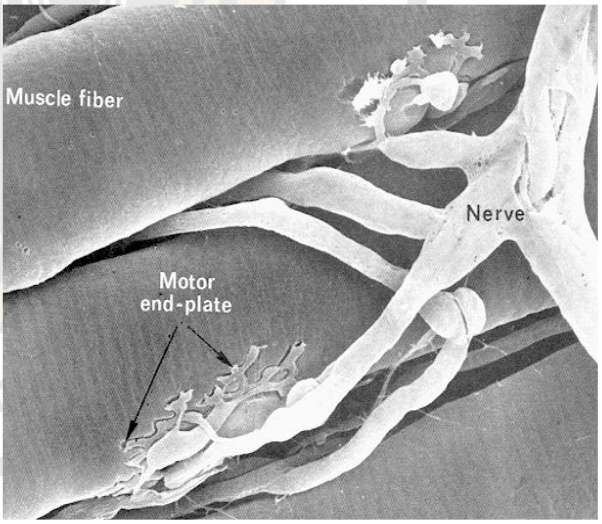


THE MOTOR END PLATES

1) The motor nerve fiber approaches the middle of the muscle fiber at an angle. It loses its myelin while the neurolemma makes a roof for the junction. Then the axon branches into axon terminals which lie in grooves in the sarcolemma and contain plenty ***mitochondria*** and ***vesicles containing acetyl choline.***

2) The 1ry synaptic cleft is a 20 – 60 n.m. gap between the axon & the muscle fiber. Its surface area is increased by enfolding of the sarcolemma called the junctional folds. The spaces between folds are called 2 ry synaptic clefts or sub- neural clefts. The cleft contains glycosaminoglycans and cholinesterase.

3) The sole plate is the sarcoplasm under the myoneural junction. It is rich in nuclei & mitochondria.



- Arrival of nerve impulse → axolemmal depolarization → Ca^{++} enter the presynaptic terminal → acetyl choline discharge into the cleft → affect receptors on the junctional folds→ sarcolemmal depolarization → muscle contraction.

FACULTY OF MEDICINE
MANSOURA NATIONAL UNIVERSITY

PATHOLOGY

CNS Congenital Anomalies

Congenital Malformations

☒ **Causes:**

- Unknown,
- Genetic factors,
- Environmental factors: Teratogens (e.g. chemicals, infectious agents)
- Maternal conditions: Folic acid deficiency early in pregnancy, alcoholism.

☒ **Classification:**

- Neural tube defects
- Forebrain malformations
- Posterior fossa malformations
- Spinal cord malformations

Neural tube defects

☒ Failure of a part of the neural tube to close →malformations involving neural tissue, meninges, and overlying bone or soft tissues.

☒ Maternal serum level of alpha-fetoprotein (MSAFP) is used to screen neural tube defects (elevated).

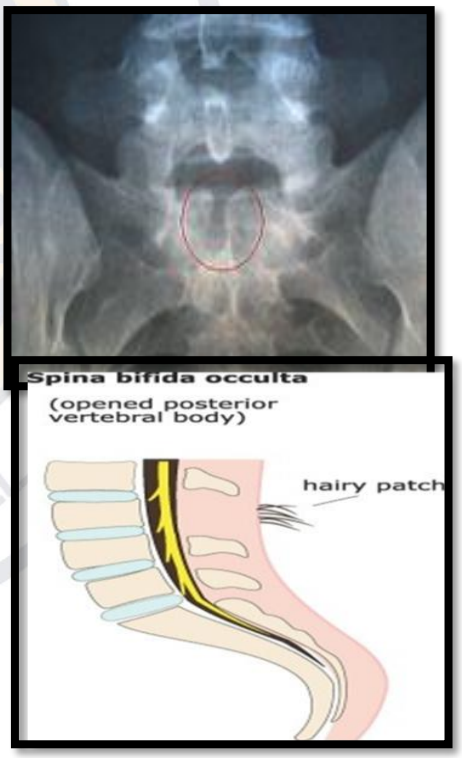
☒ **Classification:**

- **Spinal neural tube defects**
  - Spina bifida occulta
  - Meningocele
  - Myelomeningocele
- **Cranial neural tube defects**
  - Anencephaly
  - Encephalocele

A. Spinal neural tube defects

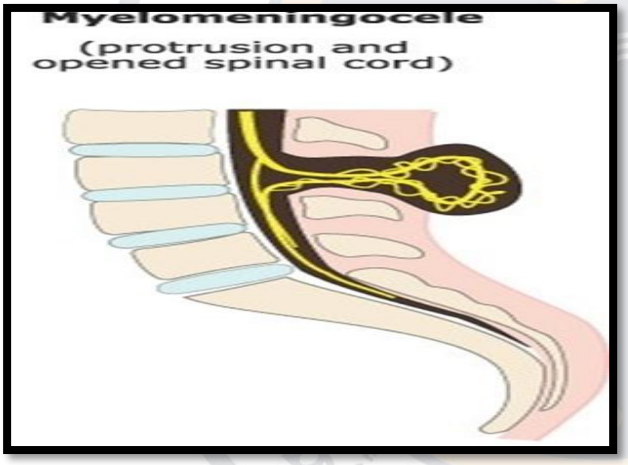
☒ Site: lumbo-sacral region (mostly S1 to S2).

1. ***Spina bifida occulta***: (least severe type)
   - A bone gap of the vertebral spine.
   - Other layers are normal.
   - No opening on the back.
   - Associated with moles, angioma, lipoma, and a hair
   - patch over the affected area.
   - Clinically: Very few cases have symptoms as:
     - back pain, scoliosis, leg weakness
     - and bowel or bladder dysfunction.



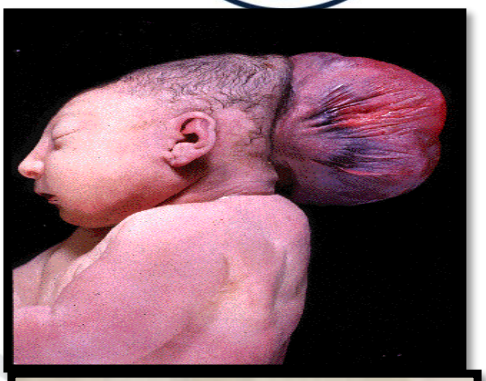
2. **Meningocele:**
    - The meninges are protruded through the bone opening forming a CSF-filled sac.
    - The rarest type of spinal defects.

3. **Myelomeningocele**: (most severe type)
    - Protrusion of a segment of spinal cord and nerves within a meningeal sac through the back, leads to:
    - Bowel and bladder dysfunction, or total paralysis of the lower limbs.
    - Risk of infections.



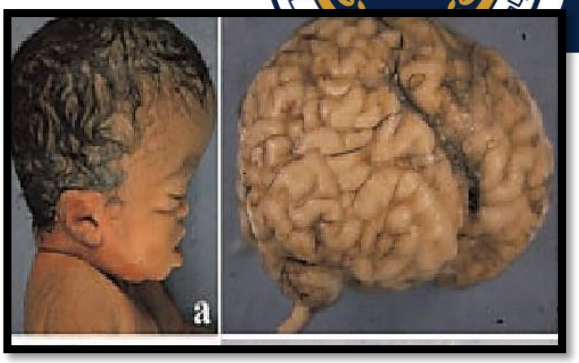
B. Cranial neural tube defects

1. **Encephalocele:**
   - Cranial defect with a sac-like protrusion
   - of malformed brain tissue and membranes.
   - It most often occurs in the occipital region.



2. **Anencephaly:**
   - Absence of most of the brain and calvarium.
   - Incompatible with postnatal life.

3. **Microencephaly:(more common)**
   - Small brain volume, with a small head circumfer
   - Caused by:
     - Chromosomal abnormalities,
     - Fetal alcohol syndrome
     - Intrauterine human immunodeficiency virus 1 (HIV-1) infection.

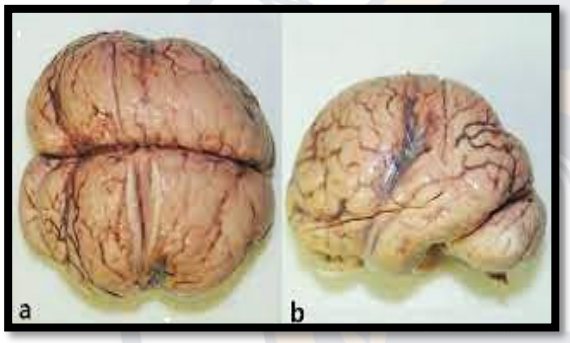


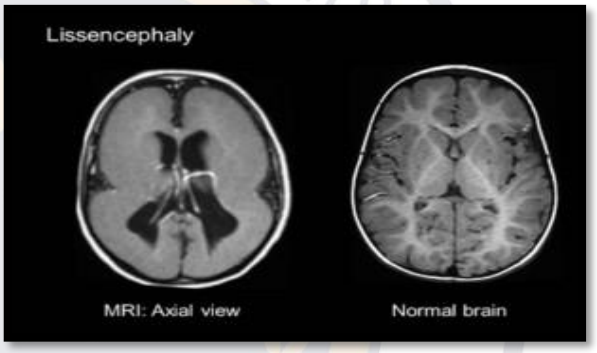
4. **Megalencephaly:**
   - Large brain volume (less common).

Forebrain malformations

A. Lissencephaly:

☒ Reduction in the number of gyri, or no gyral pattern (agyria).

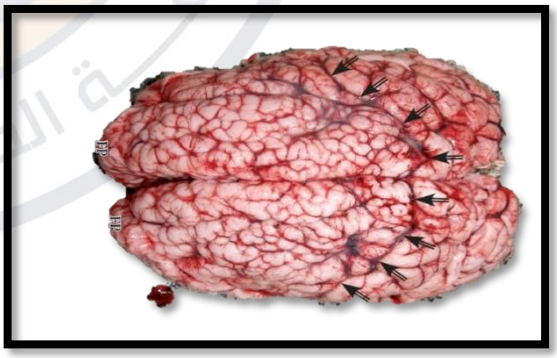




B. Polymicrogyria:

☒ Increased number of abnormal gyri

☒ with altered cortical structure.



C. Neuronal heterotopia:

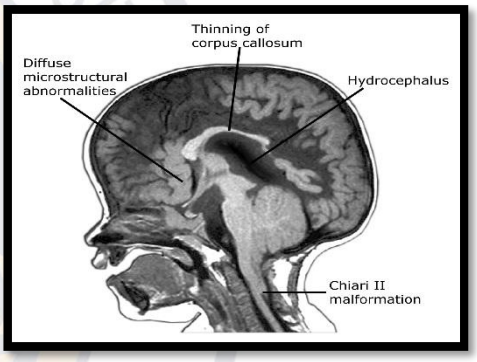
☒ A collection of neurons in inappropriate locations (defect in migration) →epilepsy.

Posterior fossa malformations

A. Chiari malformations:

☒ **Type I:**

- Low-lying cerebellar tonsils into the vertebral canal →medullary compression.
- Associated with syringomyelia.



☒ **Type II:**

- Extension of cerebellar vermis through the foramen magnum→ hydrocephalus.
- Associated with myelomeningocele.

B. Dandy-Walker malformation:

☒ Enlarged posterior fossa, absent cerebellar vermis with a large midline cyst

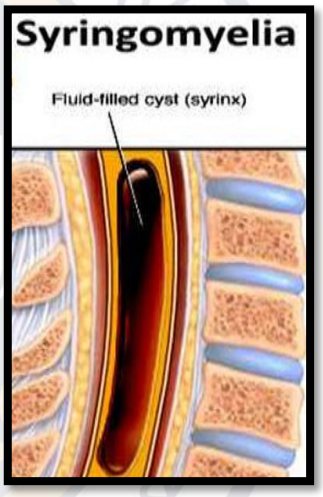
C. Aqueductal stenosis → hydrocephalus.

Spinal cord malformations

A. Hydromyelia: Expansion of the central canal of the cord.

B. Syringomyelia (syrinx):

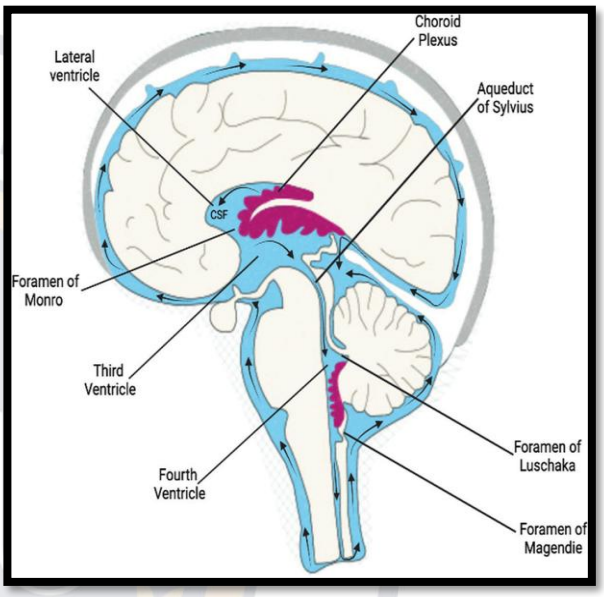
A central fluid-filled cleft-like cavity in the cord →loss of pain and temperature sensation in the upper extremities.



Hydrocephalus & CNS Infections

CSF Circulation

1. CSF is produced by choroid plexus in the lateral ventricles →
2. 3rd ventricle →
3. Aqueduct of Sylvius →
4. 4th ventricle →
5. Foramina of Magendie→
6. Resorbed by arachnoid granulations in subarachnoid space →
7. The dural venous sinuses →
8. Blood stream.

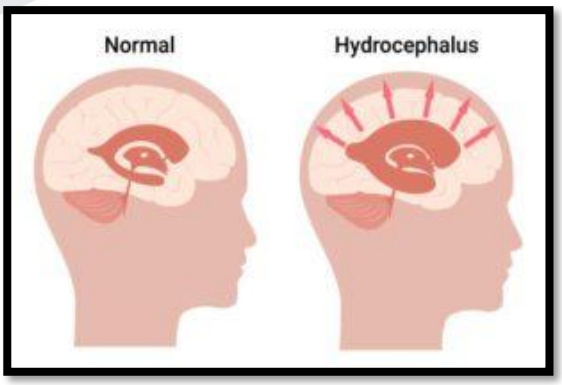


The balance between CSF production and resorption regulates its volume.

Hydrocephalus

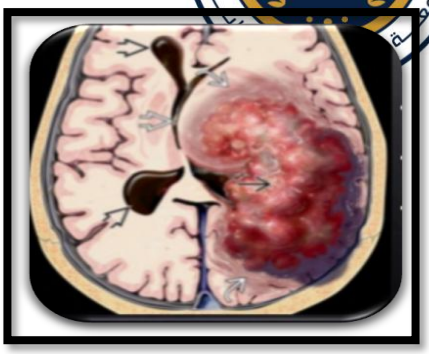
Definition:

Abnormal dilatation of the ventricles of the brain due to increased C.S.F volume associated with pressure atrophy of the brain tissue.



Pathogenesis, causes: 3 mechanisms

1. Increased CSF production
2. Decreased CSF resorption
3. CSF flow obstruction



Choroid plexus carcinoma

1. Increased CSF production

• Choroid plexus neoplasms (papilloma, carcinoma)

• Choroiditis.

2. Decreased CSF resorption

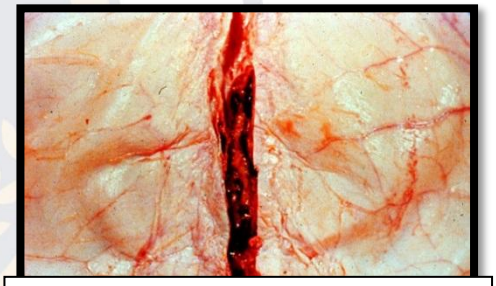
• **Congenital**: Agenesis, aplasia or hypoplasia of arachnoid granulations.

• **Acquired**:

- Fibrosis of arachnoid granulations (after meningitis or subarachnoid hemorrhage).

-Space occupying lesions (abscess, hematoma, tumor → compress the brain against the skull compromising the arachnoid granulations).

- Superior sagittal sinus thrombosis.



Superior sagittal sinus thrombosis

3. CSF flow obstruction

☒ **Congenital**:

• Stenosis of aqueduct of Sylvius.

• Obstruction or stenosis of foramina of Luschka and Magendie.

• Chiari type II malformation.

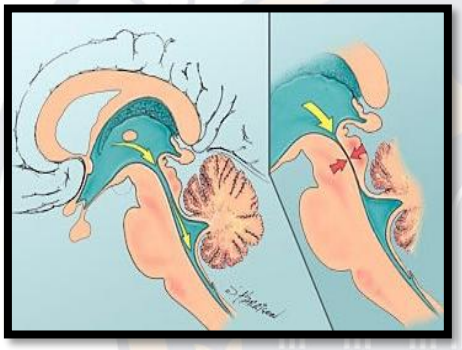
☒ **Acquired:**

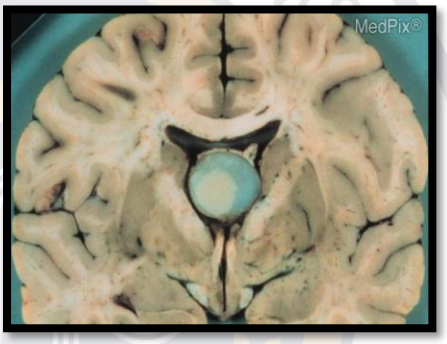
• 3rd ventricle cyst or glioma.

• Adhesions of 4th ventricle foramina (post meningitis, post-subarachnoid hemorrhage).

• Adhesions of arachnoid space (post-meningitis, post- subarachnoid hemorrhage).

• Space occupying lesions (abscess, hematoma or tumor compress the brain to the skull compromising the subarachnoid space). Third ventricle cyst





Stenosis of aqueduct of Sylvius ***3rd ventricle cyst***

Types of hydrocephalus:

➢ **Communicating**:

The ventricles communicate with the subarachnoid space (mainly increased production).

➢ **Non-communicating**:

The ventricles are not communicating with the subarachnoid space (mainly obstruction to CSF flow).

➢ **Compensatory hydrocephalus**:

Increased amount of CSF to compensate loss of brain tissue (atrophy, infarcts, surgery).

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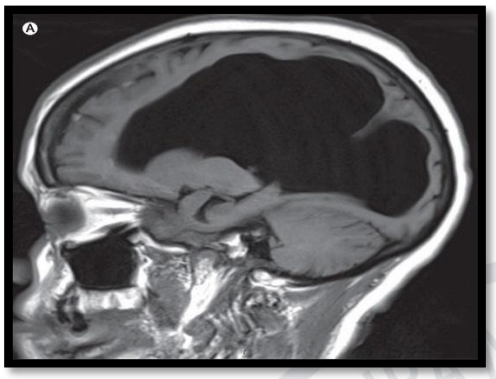
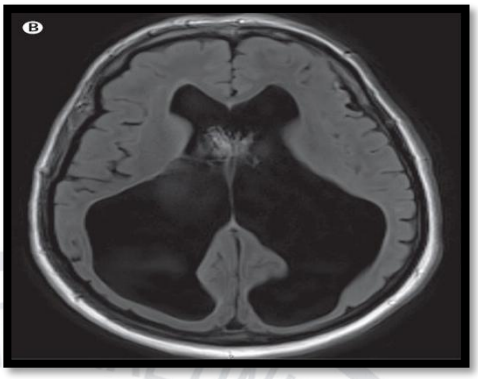




Communicating hydrocephalus ***Non-Communicating hydrocephalus***

Pathological effects of hydrocephalus:

• Permanent dilation of the ventricular systems proximal to the site of obstruction.

• Raised ventricular C.S.F pressure.

• Pressure atrophy of brain tissue.

• Skull changes:

- **In children:**
  - ☒ Separated Sutures
  - ☒ Mental deficiency.
- **In adults:**
  - ☒ Head does not enlarge (sutures and fontanels are closed)
  - ☒ Skull bone show varying degrees of convolutional markings.

Permanent dilation of the ventricular systems

Skull changes in child

Cerebrovascular diseases

Brain disorders involving blood vessels.

1. Hypoxia, Ischemia, and Infarction

A. Global cerebral ischemia

B. Focal cerebral ischemia & infarction

2. Intracranial Hemorrhage

A. Intra-parenchymal

B. Subarachnoid,

C. Subdural

D. Extradural

3. Hypertensive Cerebrovascular Diseases

4. Other Vascular Diseases:

A. Aneurysms

B. Vascular malformations

C. Cerebral amyloid angiopathy

D. Vasculitis

I. Hypoxia, Ischemia, and Infarction

A. Global cerebral ischemia:

Widespread ischemic-hypoxic brain injury.

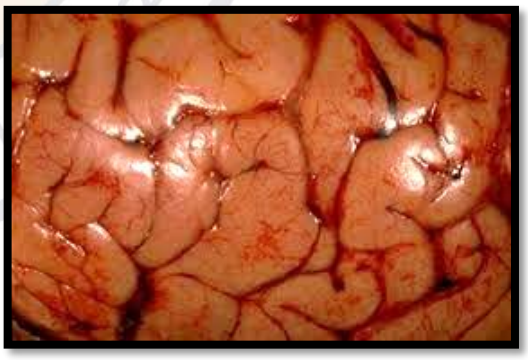
☒ **Cause:**

- Severe systemic hypotension (systolic pressure below 50 mm Hg) as in cardiac arrest and shock.

☒ **Clinical outcome: Varies with severity and duration.**

- Mild, transient → complete recovery.
- Moderate→ damage to vulnerable areas.
- Severe, long-standing → widespread neuronal death.
- Neurons are more liable to hypoxic injury than glial cells. (most susceptible neurons are the pyramidal cells of the hippocampus and neocortex and Purkinje cells of the cerebellum.)
- Patients who survive suffer severe neurologic impairment.

☒ **N/E:**

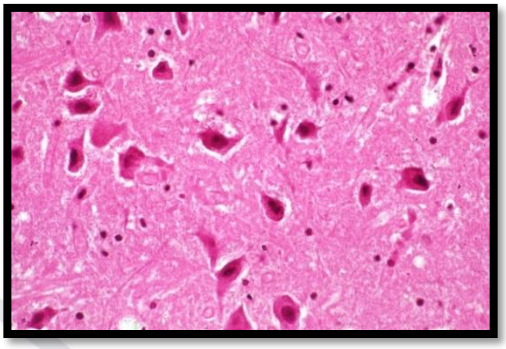


- Brain swelling, wide gyri & narrow sulci.
- Poor grey /white matter demarcation.

☒ **M/E:**

- **Early changes:**
  - Red neurons (cytoplasmic eosinophilia, nuclear dissolution).
  - Similar changes occur in astrocytes and oligodendroglia.

- **Subacute changes:**
  - Necrosis,
  - Phagocytic cells remove necrotic tissue.
- **Repair:**
  - Loss of organized CNS structure.
  - Gliosis.
  - Hypoxia, Ischemia, and Infarction



B. Focal Cerebral Ischemia

☒ Leads to infarction (cerebral stroke) in the distribution of the occluded vessel by embolus or thrombus.

☒ The presence of collaterals protects against infarction:

- Thalamus, basal ganglia and deep white matter are more affected due to deficient collaterals.
- Circle of Willis and cortical leptomeningeal surface are protected by collaterals.

☒ Clinically: Neurologic deficit according to the area supplied by the affected vessel.

☒ **Embolic infarcts: More common.**

- Source of emboli:
  - Cardiac mural thrombi.
  - Valvular vegetations.
  - Atheromatous plaques within the carotid arteries or aortic arch.

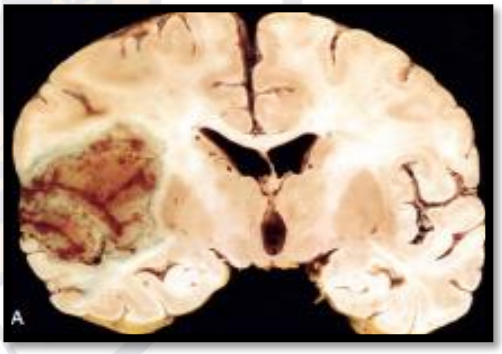
☒ **Thrombotic infarcts: Less common.**

- Sources of thrombi:
  - Thrombosis on top of atherosclerosis of the origin of the middle cerebral artery, and end of the basilar artery.
  - Thrombi of dural venous sinuses or deep cerebral veins (less common).

☒ **NE: Types and morphology of infarcts:**

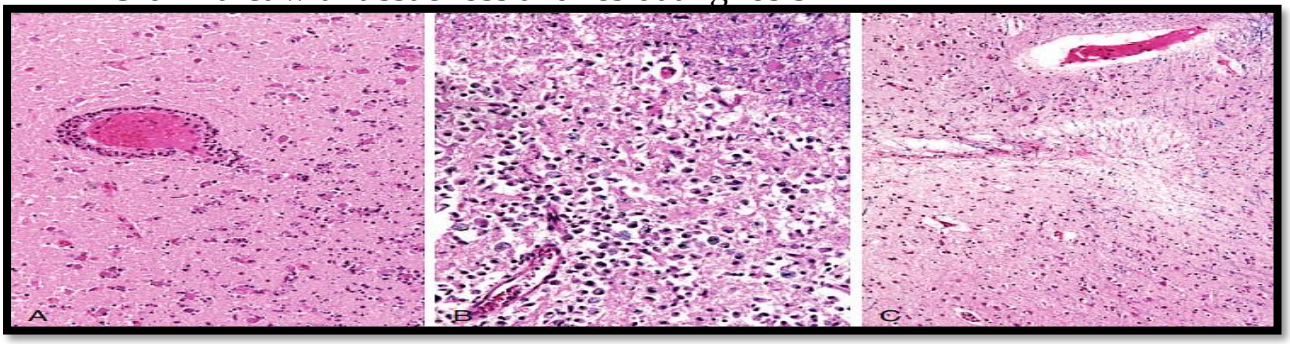
- **Non-hemorrhagic Infarct:**
  - Early: Pale, opaque.
  - Liquefactive necrosis → creamy fluid-filled cavity.
  - Healing → destruction of cortex + gliosis.

- **Hemorrhagic infarct: Due to:**
  - Reperfusion of ischemic tissue (collaterals or therapeutic/spontaneous dissolution of emboli).
  - Infarcts caused by venous occlusion.



☒ **ME: Cerebral infarction stages:**

- Early infarct (red neurons) with neutrophil infiltration
- By day 10, influx of phagocytic cells
- Old infarct with tissue loss and residual gliosis

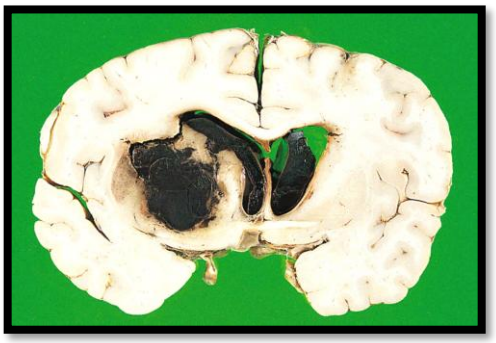


ME of cerebral infarction

II. Intracranial Hemorrhage

A. Intra-parenchymal hemorrhage:

- Most common in hypertension.
- Atherosclerosis.
- Tumors.
- Cerebral contusions (trauma).
- Clotting disorders.
- Cerebral amyloid angiopathy.
- Vascular malformations.



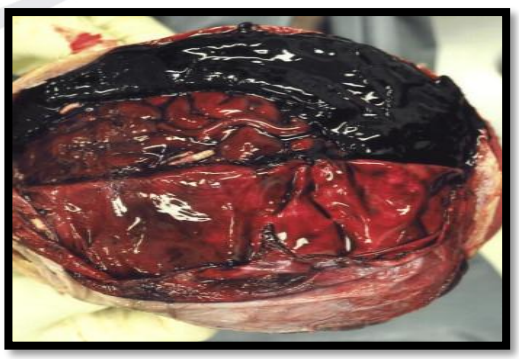
Intra-parenchymal hemorrhage

B. Subarachnoid hemorrhage:

- Ruptured aneurysms
- Vascular malformations
- Brain trauma.

C. Subdural hemorrhage (hematoma):

- Caused by rupture of venous sinuses or bridging subduralcerebral veins.
- Common in old patients with
- brain atrophy, alcoholics.



D. Epidural (Extradural) hemorrhage:

• Caused by traumatic skull fracture, especially temporal or parietal bones (tear of middle meningeal artery).

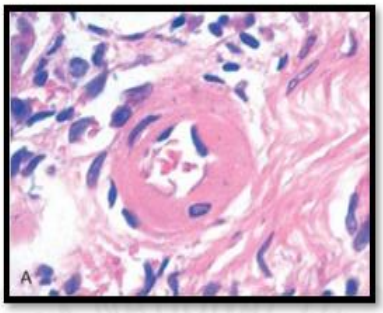
• Expands rapidly (arterial bleeding) with rapid increase of ICP

• It is a neurosurgical emergency (drainage and repair to prevent death).

III. Hypertensive Cerebrovascular Diseases

☒ **Sites**: Thalamus, basal ganglia, deep white mater, internal capsule and pons.

☒ **Lesions:**



Hyaline arterio-sclerosis

1. Hyaline arterio-sclerosis of cerebral arterioles,
2. Charcot-Bouchard microaneurysms,
3. Lacunar infarcts: few millimeters in size,
4. Slit hemorrhages: Rupture of the small penetrating vessels,
5. Massive intra-parenchymal hemorrhage: arterial
6. Cerebral edema
7. Acute hypertensive encephalopathy: if diastolic blood pressure exceeds 130 mm Hg. (mostly) → cerebral dysfunction, headaches, confusion, vomiting, convulsions, and sometimes coma.

IV. Other Vascular Diseases:

A. Cerebral Aneurysms

☒ **Types:**

1. Congenital berry aneurysms:
2. Microaneurysms of essential hypertension (Charcot Bouchard).
3. Atheromatous aneurysms.
4. Traumatic aneurysms.
5. Mycotic aneurysms: emboli of bacterial endocarditis.

☒ **Clinical effects:**

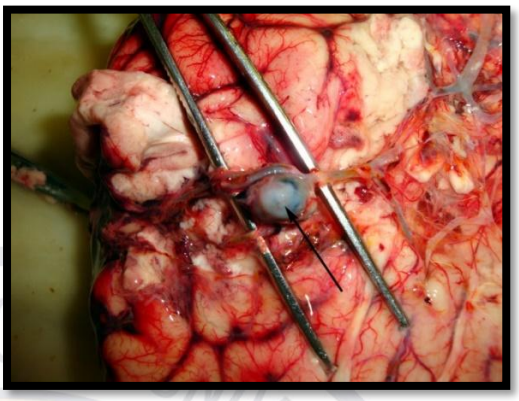
• Pressure on the surrounding,

• Rupture and subarachnoid or intraparenchymal hemorrhage.

• Thrombosis and calcifications lead to acute ischemia (Infarction) or chronic ischemia (brain atrophy).

☒ **Congenital saccular berry aneurysms:**

- Site: circle of Willis (small, multiple).
- Pathology: internal elastic lamina & medial weakness at bifurcation of arteries causing saccular aneurysm.
- Most frequent cause of spontaneous subarachnoid hemorrhage (sudden severe headache and loss of consciousness).
- Rupture associates straining (increase intracranial pressure. e.g. constipation, severe cough…..).



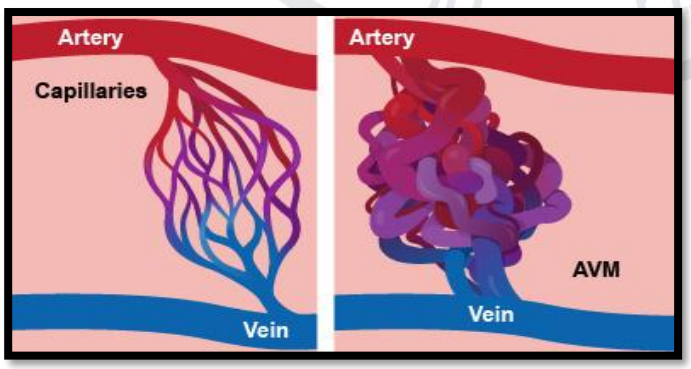
Congenital saccular berry aneurysms

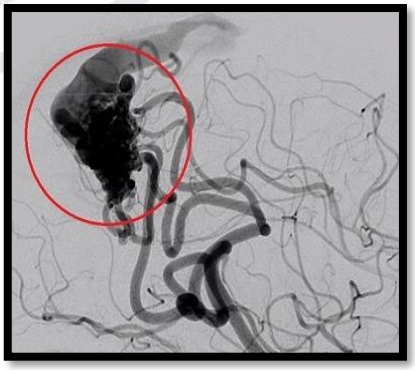
B. Vascular Malformations

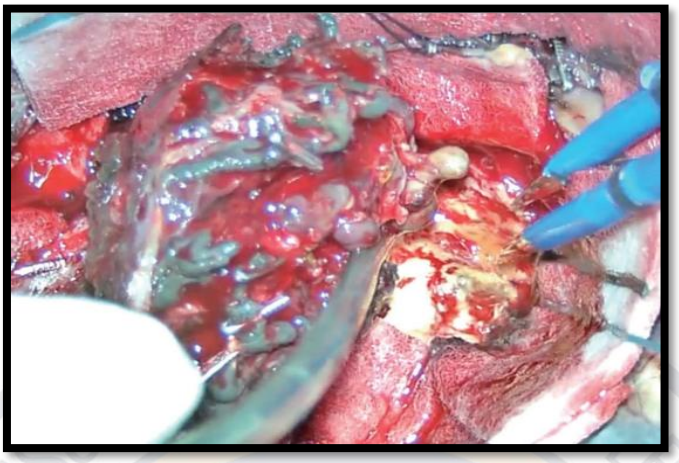
Variants:

1. Arterio-venous malformations (AVMs)
2. Cavernous malformations (hemangiomas)
3. Capillary telangiectasias
4. Venous angiomas.

- The most dangerous malformation is AVM.
- Appears as tangled network of wormlike vascular channels.
- Leads to mixed intra-parenchymal or subarachnoid hemorrhages







Vascular Malformations

CNS Infections

Routes of Infection:

1. Hematogenous: most common; by arterial circulation, or retrograde venous spread from veins of the face.
2. Direct implantation: traumatic, iatrogenic (e.g. lumbar puncture) or with congenital malformations (e.g. meningomyelocele).
3. Local spread: from adjacent structures, such as: air sinuses, teeth, skull, or vertebrae.
4. Nerve spread: Viruses transported along the peripheral nerves as in rabies and herpes zoster viruses.

Classification:

☒ **Bacterial:**

- Acute suppurative (bacterial or pyogenic) meningitis
- Focal suppurative infections: Brain abscess, Extradural Abscess, Subdural empyema.
- Chronic bacterial meningoencephalitis: (TB, Syphilis).

☒ **Viral:**

- Viral (aseptic) meningitis.
- Viral encephalitis and meningoencephalitis:

  Herpes Simplex Virus Type 1 and 2, Varicella-Zoster Virus, Cytomegalovirus (CMV), JC polyomavirus and Human Immunodeficiency Virus (HIV).
- Brainstem and Spinal cord infection: Rabies and Polio Viruses.

☒ **Parasitic:** Toxoplasmosis, Cysticercosis, Malaria, Amoebiasis.

☒ **Fungal:** Candida, Aspergillus, Mucor-mycosis,

☒ **Prion Diseases.**

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Acute Pyogenic Meningitis

☒ Acute suppurative inflammation of leptomeninges involving the subarachnoid space.

☒ **Organisms:**

- In neonates: Escherichia coli and group B streptococci.
- Young children: Haemophilus influenzae.
- In adolescents and young adults: Neisseria meningitidis.
- In older adults, Streptococcus pneumoniae and Listeria monocytogenes.

☒ **Routes of infection:**

- Blood born
- Direct spread
- Penetrating wounds

☒ **Clinical features:**

- Signs of systemic infection (e.g. fever)
- Signs of meningeal irritation (headache, irritability, neck stiffness, confusion)

☒ **CSF changes (lumbar puncture):**

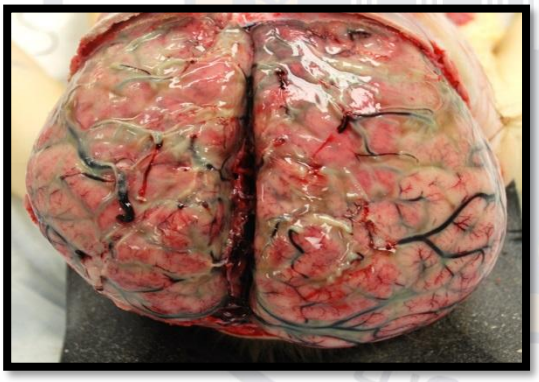
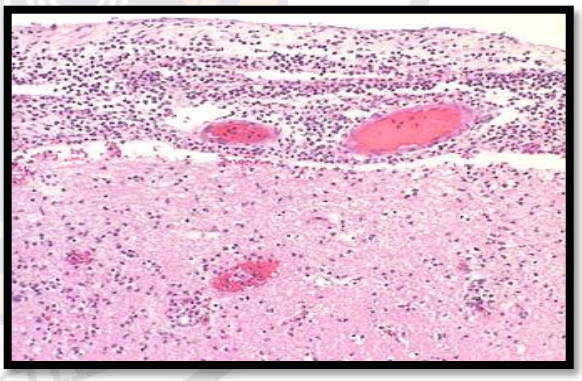
- Turbid,
- Increased pressure,
- Increased protein,
- Low glucose,
- Excess neutrophils,
- Bacteria detected in smear or by culture.

☒ **Gross:**

1. **The leptomeninges:**
   - Hyperaemic (dilated leptomeningeal vessels), thick opaque, tense
   - The subarachnoid space is filled with yellow pus more apparent at the base of the brain
2. **The brain:** is edematous
3. **The ventricles:** are moderately dilated, contain turbid CSF

☒ **Microscopic:**

- Neutrophils and pus cells fill the subarachnoid space and the leptomeninges.
- Edema around the congested blood vessels.
- Brain underneath show oedema and cellular degeneration.

Gross and ME of acute Pyogenic Meningitis

☒ **Complications:**

- Spread of infection:
  - Meningo- encephalitis and small brain infarcts.
  - Subdural abscess and sinus thrombophlebitis.
  - Meningococcal speticaemia may occur when big number of meningocci reach the blood. This can cause bilateral suprarenal hemorrhage and acute suprarenal failure (water- house Friedricksen syndrome).

- Nerve paresis especially 3,4,6. caused by Pressure of the exudates and late Fibrous adhesions
- Hydrocephalus (Increased intracrainal pressure), caused by Pressure of the exudates and late Fibrous adhesions

Brain Abscess

☒ Causes:

- Pyogenic bacteria, (strept. and staph.)

☒ Routes of infection:

- External from opened injury, mastoiditis or otitis media, frontal' sinusitis.
- Blood spread from suppuration or septic emboli.

☒ Acute abscess:

- Cavity filled with pus, surrounded by area of congestion and has irregular shreddy lining.

☒ Chronic abscess:

- Develops after 3-6 weeks.
- Has fibrous wall of fibrogliosis and the lining is smooth.

☒ Complications:

- Direct spread produces suppurative encephalitis, subdural abscess, sinus thrombophlebitis and extradural abscess.
- Rupture into ventricular system (ventriculitis) or subarachnoid space producing meningitis.

Acute Viral (Aseptic) Meningitis

Acute inflammation of leptomeninges in absence of bacteria by culture.

☒ **Cause:**

- Most commonly enteroviruses (polio-, echo-, coxackie-).

☒ **C/P:**

- Signs of meningeal irritation, fever, and alterations of consciousness of relatively acute onset.

☒ **CSF changes:**

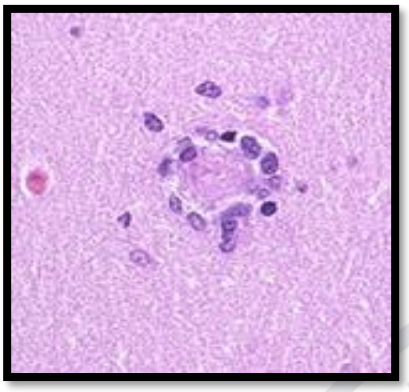
- Lymphocytosis,
- Mild to moderate increase in protein,
- Normal glucose.

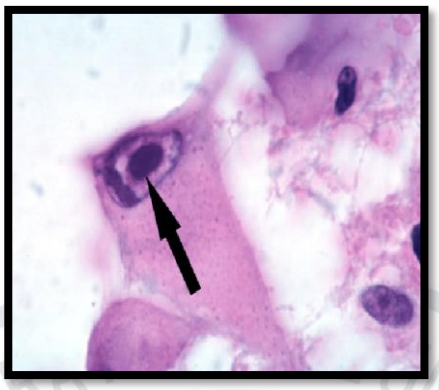
☒ **Fate:** Usually self-limited.

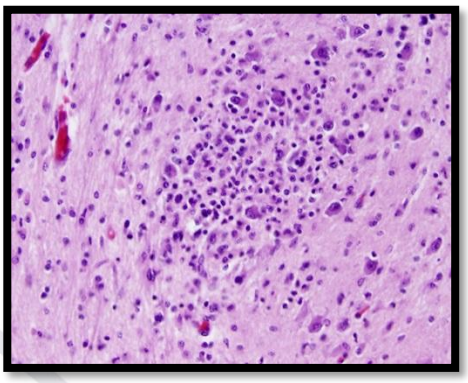
Viral Encephalitis / Meningoencephalitis

☒ **General Features:**

- generalized viraemia which in a proportion of cases is followed by localization in the C.N.S
- virus multiply within the nerve cells:
- Nissel degeneration
- inclusion bodies (virus particles)
- Nerve cell necrosis, which are removed by microglia (neuronophagia).
- hyperemia and mononuclear cell inflammatory response with collection of macrophage (Microglial nodules).
- Healing occur by glial scar (gliosis).







Neuronophagia ***Nissel degeneration*** ***Microglial nodules***

1. Herpes Simplex Virus (HSV):

☒ **Type 1:**

- Affects children in the temporal and inferior frontal lobes.
- Acute viral infection of sensory nerve ganglia, its nerve and its area of supply
- (skin or mucous membrane). It produces redness and vesicles which ulcerate without scar
- Cowdry type A bodies are intranuclear inclusion bodies.

☒ **Type 2:** Affects immunocompromised adults and neonates born by vaginal delivery of actively infected mother.

2. Varicella-Zoster Virus:

☒ **An acute viral infection of adults, immune deficient individuals**

☒ **It is due to recurrence of latent variclla (chicken pox) infection**

☒ **Common Sites:**

- Posterior root ganglia of lower cervical and upper thoracic and Gasserian ganglia (Fifth nerve)
- Traverse from the affected ganglia along the sensory nerves to skin

- In the skin it causes pain, redness and vesicles (shingle) containing serous or hemorrhagic exudate
- The vesicles occur in the dermatome supplied by the affected sensory neuron.

☒ The virus may spread to brain causing encephalitis

3. Cytomegalovirus (CMV):

☒ **Age:** Adult infection and intrauterine infection:

☒ **Site:** Periventricular region.

☒ Microcephaly & periventricular calcification in newborn.

☒ M/E: Large cells with cytomegalic intranuclear inclusions.

4. Human Immunodeficiency Virus (HIV; AIDS):

☒ **Pathological lesions:**

1. Acute aseptic meningitis.
2. Subacute HIV encephalitis.
3. Opportunistic infections (Fungal, parasitic, viral).
4. Leukoencephalopathy (myelinopahty).
5. Tumors as cerebral lymphoma.

☒ Congenital HIV encephalitis is more severe than the adult and may result in microcephaly.

5. Rabbies:

☒ **Cause:** Rabies virus

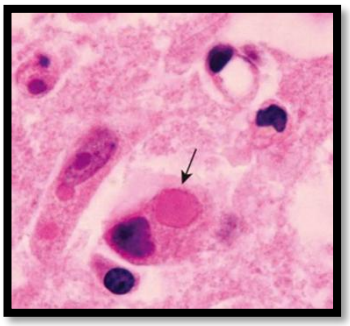
☒ **Method of infection:** Bites of rabid animals, spread along the peripheral nerves to the C.N.S.

☒ **Site of affection:** brain stem, hypothalamus, hippocampus cerebellum and dorsal root ganglia

☒ **N/E:** Swelling and hyperemia of the affected tissue

☒ **M/E:**

- Diffuse encephalomyelitis of nerve cells.
- Swelling and necrosis, vascular dilation, perivascular infiltration by plasma cells and lymphocytes
- Negri bodies (esinophilic intracytoplasmic inclusions) are more common in hippocampus and cerebellum



Negri bodies

☒ **Clinically:**

- Hyperexcitability, hydrophobia caused by spasm of Pharynx, usually fatal.

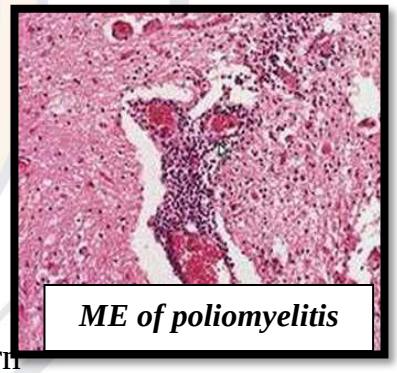
6. Poliomyelitis

☒ Acute viral infection of the anterior horn cells by Polio virus; an enterovirus transmitted by ingestion

☒ **Incubation periods** 1-3 weeks

☒ **Stage of diseases:**

- Intestinal stage 5 days
- Viraemia stage 5 days
- Neural stage at which the virus attaches the anterior horn cells of the spinal cord (rarely brain stem)



ME of poliomyelitis

☒ **N/E:** Swelling, hyperemia of the cervical and lumbar anterior horn gray matter.

☒ **M/E:** Degeneration and necrosis of anterior horn cells, Perivascular mononuclear inflammatory cells and neuronophagia.

☒ **Fate:** Healing by gliosis is-followed by:

- Degeneration and thinning of the related peripheral nerves
- Neuropathic muscular atrophy and replacement by fibrofatty tissue of the related muscles.

☒ **C/P:**

- Permanent flaccid paralysis (about 1% of cases): muscle wasting and hyporeflexia in the corresponding region of the body mostly lower limbs.
- Post-polio syndrome: progressive weakness, decrease in muscle mass and pain (affects polio survivors many years after recovery from an initial acute attack of the poliomyelitis virus).

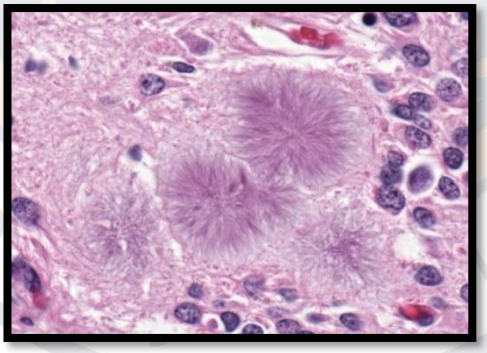
7. Prion Disease

☒ Very rare diseases (forms: sporadic, familial, iatrogenic, and mad cow disease).

☒ Infective agent is an abnormal misfolded cellular protein called prion.

☒ It causes fatal and transmissible neurodegenerative diseases in humans and many other animals.

☒ The primary method of infection is through ingestion (infected meat products) or less commonly inoculation (e.g. medical instrument).



ME of prion disease

Tumors of the Nervous System

Classification of Nervous System Tumors

1- Gliomas:
- Astrocytoma
- Oligodendroglioma
- Ependymoma

2- Embryonal tumors:
- Medulloblastoma.

3- Tumors of Meninges:
- Meningioma
- Mesenchymal Nonmeningothelial tumors

4-Tumors of peripheral nerves.
- Shwannoma
- Neurofibroma
- Malignant nerve sheath tm

5- Hemopoietic tumors
- Plasmacytoma
- Lymphoma

6- Germ cell tumors

7- Tumors of seller region
- Pituitary tumors
- Craniopharyngioma

8- Choroid plexus tumors:
- Choroid plexus papilloma.
- Choroid plexus carcinoma.

9-Pineal body tumors
- Pinealoma
- Pineoblastoma

10- Metastatic tumors

I. Gliomas

Astrocytomas

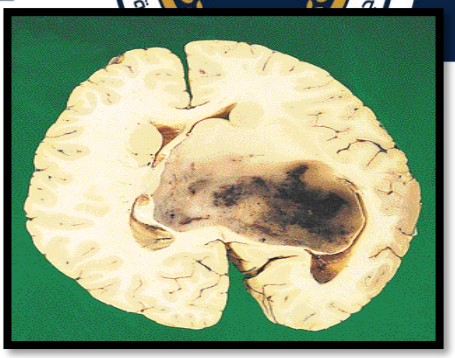
☒ Tumors of astrocytes are the commonest glioma.

☒ **Site:**

- Cerebellum of children.
- Cerebrum of adults.

☒ **N/E:**

- Soft grey mass with ill-defined outline. The cut surface shows areas of cystic degeneration.
- In high grade forms it shows necrosis and hemorrhages.



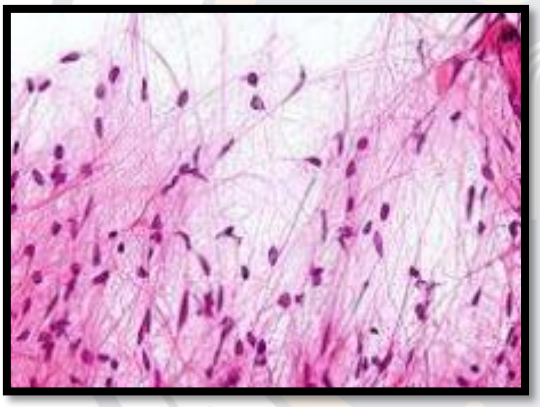
Hemorrhage and necrosis in high grade astrocytoma

☒ **M/E:**

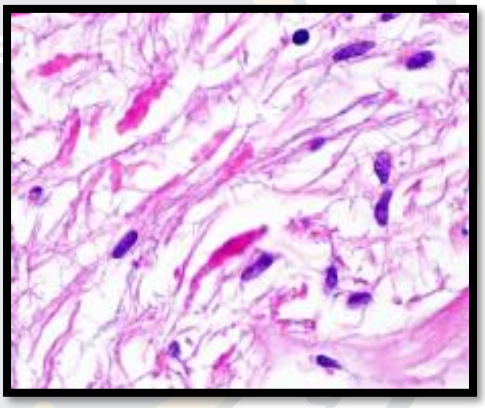
- Neoplastic Astrocytes, branched cells with fibrillary background it may be of variable grades of differentiation.

A. Localized astrocytomas:

- Pilocytic astrocytoma ---grade I
- Mildly cellular, formed of mature astrocytes within excess fibrillary back ground, cells are bipolar with stroma of eosinophilic elongated and coma shaped fibers (Rosenthal fibers).



ME of pilocytic astrocytoma



Rosenthal fibers

B. Diffuse astrocytomas:

a. Diffuse fibrillary astrocytoma ---grade II:

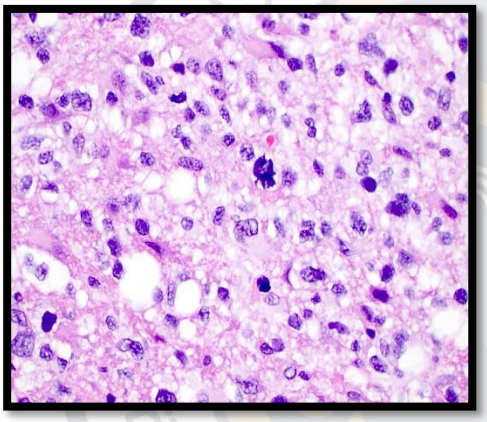
- Hypercellular, formed of pleomorphic astrocytes within excess fibrillary background. A subtype of Grade II diffuse astrocytoma show Large astrocytes with excess esinophilic cytoplasm and eccentric nuclei ; called gemistocytic astrocytoma.

b. Anaplastic astrocytoma---- grade III:

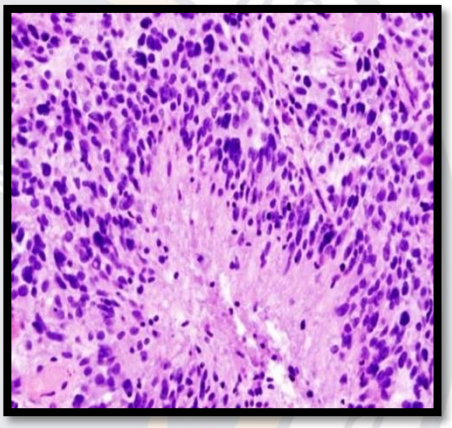
- Formed of pleomorphic less mature astrocytes with excess mitosis without necrosis

c. Glioblastoma Multiforme -----grade IV:

- Formed of primitive astrocytes with marked pleomorphism, Giant cells, mitosis, necrosis (palisaded), vascular endothelial proliferation (glomeruloid).



ME of anaplastic astrocytoma



ME of glioblastoma multiforme

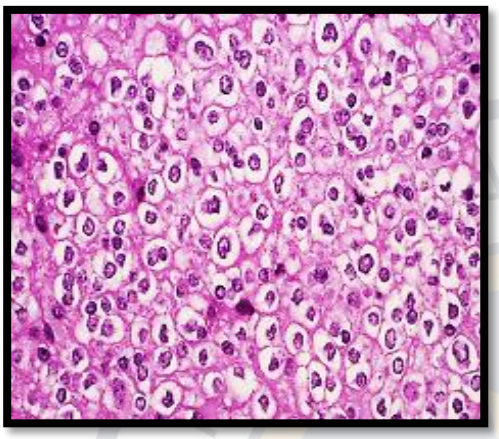
Oligodendroglioma

- ☒ From oligodendroglia cells of cerebrum.
- ☒ Middle age.
- ☒ **N/E:** pink, Firm with cyst formations and calcification.
- ☒ **M/E:** Rounded cells, with uniform round nuclei and clear cytoplasm with focal of calcification.

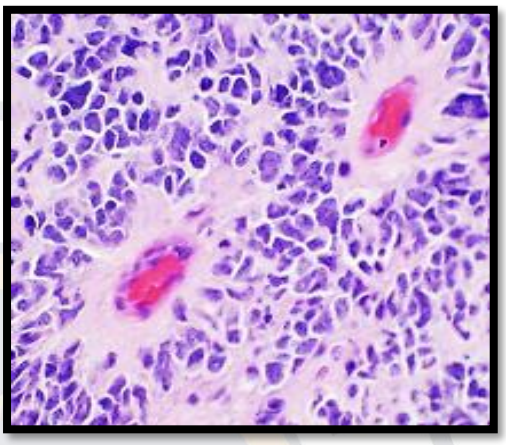
Ependymoma

- ☒ From ependymal cells lining the ventricles,
- ☒ commonly the 4th ventricle and Lower part of the spinal cord
- ☒ Children and young adults.

- **N/E:** Fleshy vascular mass with calcification.
- **M/E:** Elongated cells arranged perivascular in pseudorosettes.



ME of oligodendroglioma

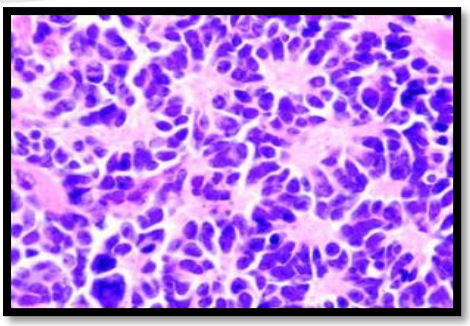


ME of ependymoma

II. Embryonal tumors

Medulloblastoma

- Common childhood brain tumor
- At the roof of 4th ventricle
- **N/E:** Fleshy soft grey mass projections in the 4th ventricle may penetrate the brain to reach the subarachnoid space.
- **M/E:** Small dark stained cells arranged in rosettes.

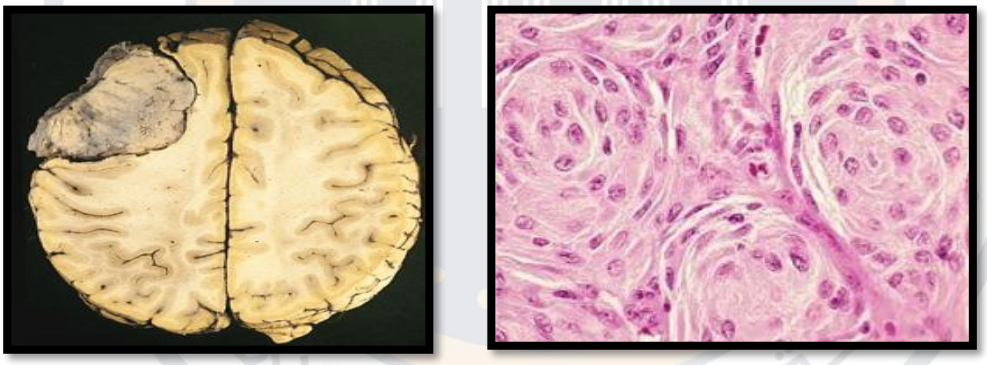


NE and ME of medulloblastoma

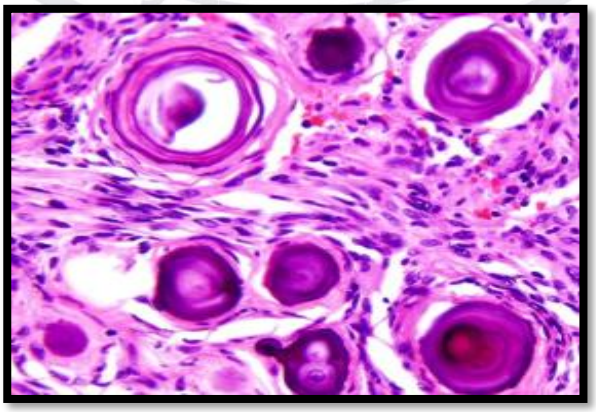
III. Tumors of Meninges

Meningioma

- In adults common in females.
- Originates from the endothelial cells of the arachnoid villi
- **N/E:** Rounded firm capsulated tumor attached externally to the dura and imbedded in the brain tissue internally.
- **Cut surface:** greyish white and often show whorly appearance.
- **M/E:** Formed of spindle shaped cells arranged in concentric layers with calcifications in the center (Psammoma bodies).
- Meningioma may turn **malignant**.



NE & ME of meningioma

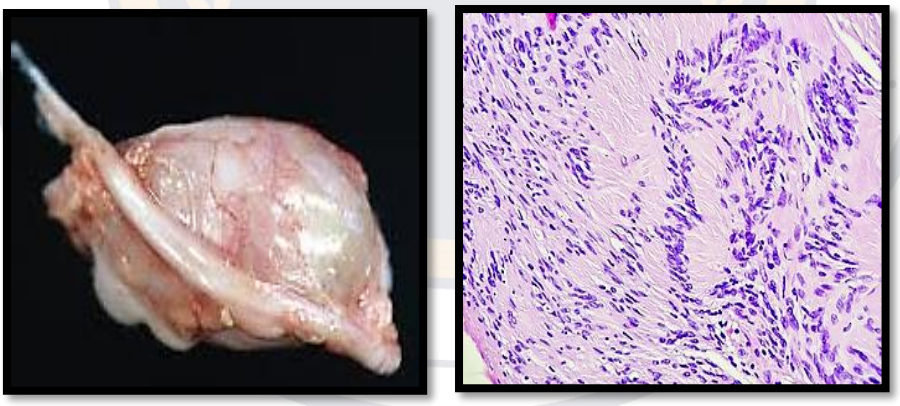


Psamomma bodies in meningioma

IV. Tumors of peripheral nerves

Schwannoma

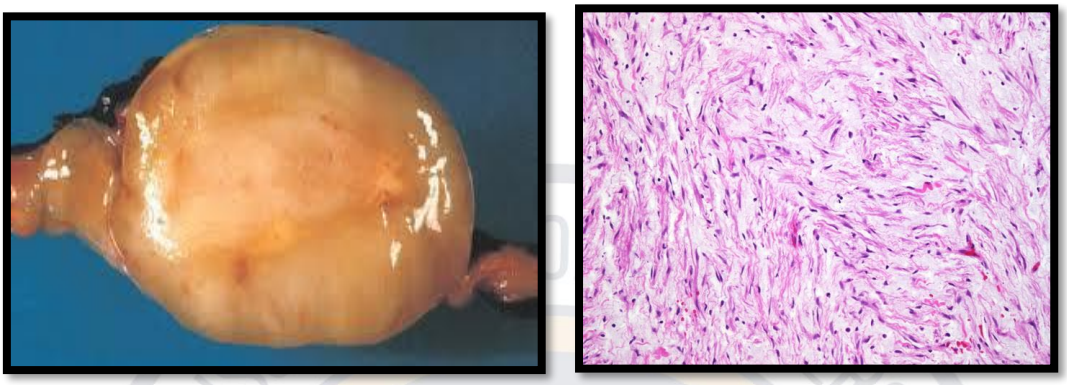
- ☒ It is a benign tumor of cranial and spinal nerves, originate from schwann cells which cover the peripheral nerves.
- ☒ **Age:** 50-60 years.
- ☒ **N/E:**
  - Acoustic neuroma of 8th cranial nerve at the base of the brain (cerebello- pontine angle)
  - Solitary mass, capsulated, firm round or fusiform with the related nerve at one side
  - **Cut surface** is grey white and may show cysts
- ☒ **M/E:** Spindles shaped cells arranged in bundles, with rod- shaped nuclei side by side in palisademanner with reticular and collagen fibers in between.



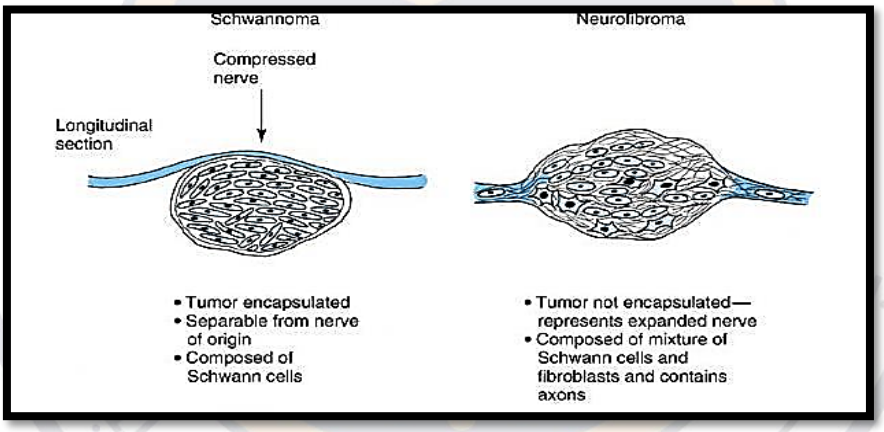
NE & ME of schwannoma

Neurofibroma

- ☒ **N/E:** Fusiform mass through which the nerve pass Firm grey uncapsulated.
- ☒ **M/E:** Spindle shaped cells in bindles with fibrous stroma and neurofibres.



NE & ME of neurofibroma



Schwannoma vs neurofibroma

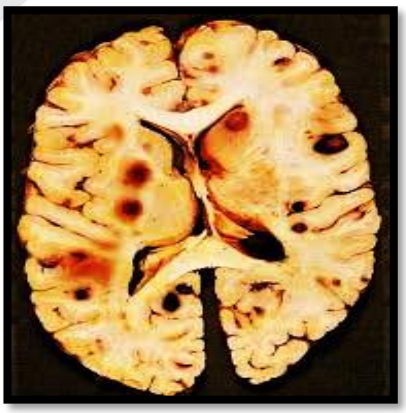
Multiple neurofibromatosis. (Von-Reckling Hausen disease).

- ☒ Hereditary autosomal dominant hamartoma.
- ☒ Multiple neurofibromas of cutaneous nerves.
- ☒ Cafe au lait skin patches of skin hyperpigmentation.
- ☒ Localized or diffuse overgrowth of fibrous tissue of overlying skin (Elephantiasis neuromatosa).
- ☒ **Prognosis:** Malignant transformation is common than in schwannoma. (10%)

Multiple neurofibromatosis

V. Metastatic tumors

- ☒ The most common malignant tumor in the brain representing 30% of brain tumors.
- ☒ Majority is carcinomas.
- ☒ Occur mostly in older people.
- ☒ They reach the C.N.S. through arteries or vertebral system of veins.
- ☒ Common sources: carcinomas of lungs, breast and kidney
- ☒ **N/E:** Multiple nodules of variable size in the cerebrum at junction of grey and white matter surrounded by oedema, show hemorrhage, necrosis and cyst formation
- ☒ **M/E:** As primary tumor and in relation to blood vessels.



NE of brain metastasis

Effect of intracranial tumors

☒ Local effects:

- Compression and destruction of the affected site lead to neurologic deficit such as hemiplegia.
- Hydrocephalous.
- Increased intracranial tension caused by increased intracranial contents by:
- Tumor mass
- Cerebral oedema due to compression of the veins by tumour obstruction of C.S.F. pathway.

☒ Manifestations:

- Headache
- Papilloedma (blurring of vision) oedema of optic disc due to compression of retinal veins.
- Brain herniation.

Special sense

Infections

Blepharitis

☒ **Def:** Inflammation of eye lid

☒ **Causes:**

- Allergies
- Dandruff (seborrheic dermatitis)
- Parasitic as lice or mites in eyelashes
- Meibomian gland dysfunction (MGD)

☒ **Symptoms:**

- Redness & swelling
- Itching.
- Pain
- Discharge that forms a crust at the

lid margin during night that may prevent eyes from opening in the morning.

☒ Complications:

Stye:

- Acute suppurative inflammation of sebaceous glands or follicles (Boil) of eyelid
- very painful. At the eyelid's edge
- Chalazion:
- Granulomatous inflammation of obstructed meibomian glands.
- Slowly growing lid nodule.
- M/E: Lipogranuloma (empty spaces surrounded by epithelioid with multinucleated giant cells, fibrosis)

Conjunctivitis

☒ **Inflammation of the conjunctiva.**

☒ **Causes:**

- Viral infection (Adenovirus, Herpes simples and herpes zoster)
- Bacterial infection
- Allergic reaction.

☒ **Symptoms:**

- Redness
- Itching.
- Gritty feeling
- Discharge that may form a crust
- Lacrimation.
- Sensitivity to light, called photophobia

Keratitis

☒ **Inflammation of the cornea.**

☒ **Causes:**

A. Infectious keratitis

- Bacterial
- Viral
- Fungal
- Parasitic (Acanthamoeba)

B. Non infectious keratitis

- Injury
- Eyelid disorders
- Dry eye syndrome
- Exposure to intense ultraviolet (UV) light (photokeratitis)

Bacterial keratitis:

Common in contact lenses wearer from contaminated eye drops or contact lens solution.

Viral keratitis:

- Herpes simplex virus, Chicken pox virus.

The repeated infections are triggered by stress, an impaired immune system, or exposure to sunlight.

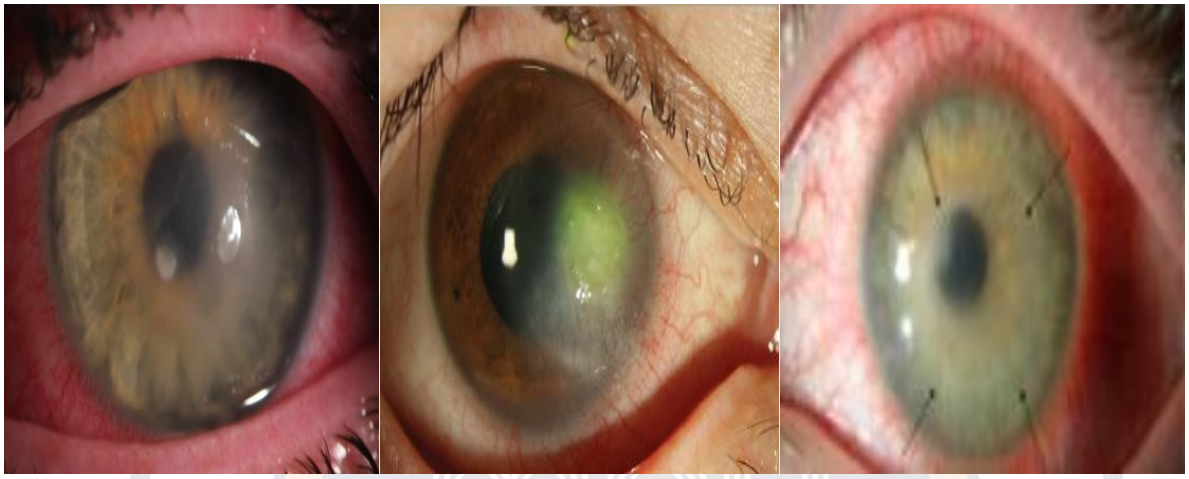
Parasitic keratitis:

- Acanthamoeba

Poor contact lens hygiene, Exposure to water (like swimming pools) while wearing contact lenses.

Eyelid disorders:

If the eyelid does not close properly, the cornea can dry out, and keratitis can develop



☒ Pathologic features:

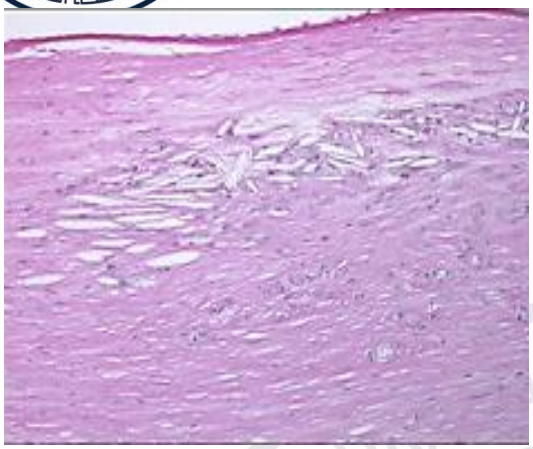
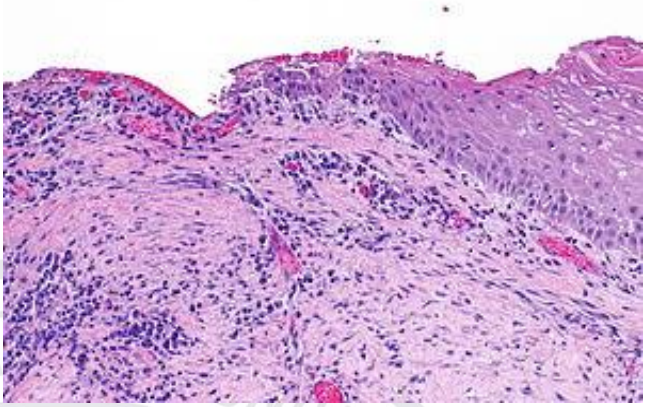
- Stromal edema.
- Corneal ulceration may lead to fibrosis

with final fibrosis and opacity.

- Rapid neovascularization.
- Stromal mixed inflammatory infiltrates could be focal, or diffuse.

☒ Clinical features:

- Eye redness.
- Eye pain.
- Excess tears or other discharge.
- Blurred vision due to edema or opacities.
- Photophobia.
- Foreign body sensation

Eye Tumors

Eyelid:
1. Squamous cell papilloma.
2. Basal cell papilloma.
3. Sebaceous adenoma.
4. Nevi.

Conjunctiva & cornea:
1. Squamous cell papilloma.
2. Nevi

Intraocular:
1. Nevus.

Eyelid:
1. Squamous cell carcinoma.
2. Basal cell carcinoma.
3. Sebaceous adenocarcinoma.
4. Malignant melanoma.

Conjunctiva & cornea:
1. Squamous cell carcinoma.
2. Malignant melanoma.

Intraocular:
1. Melanoma.
2. Lymphoma
3.Retinoblastoma.

Intraorbital:
lymphoma.
Rhabdomyosarcoma.

Activate Windows

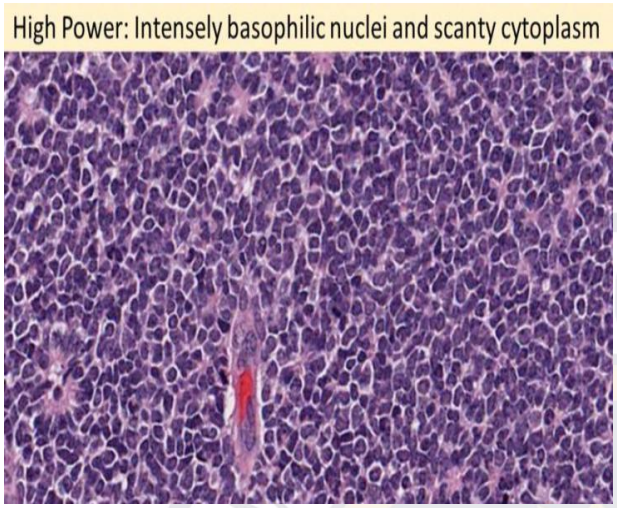
* The most common malignant tumor of the eye lid is Basal cell carcinoma followed by Sebaceous adenocarcinoma.
* The most common primary ocular malignancy in the adults is Uveal Melanoma.
* The most common malignant ocular tumor in Children is Retinoblastoma.
* The most common malignant orbital tumor in Children is rhabdomyosarcoma

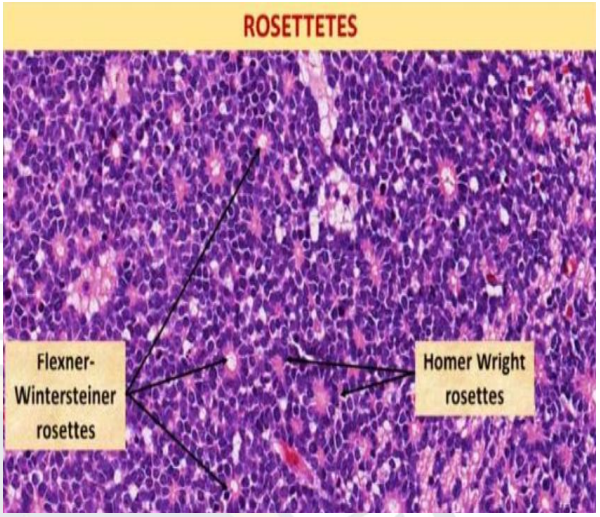
Retinoblastoma

- ☒ The most common malignant ocular tumor in children.
- ☒ Present at birth or in early childhood (<4 years old).
- ☒ 40% of cases are familial; carrying mutation in Rb1 gene; with tendency of bilateral tumors
- ☒ Tumor occurs when both alleles of the retinoblastoma 1 gene (RB1) are inactive
- ☒ **NE:** Greyish white mass within the retina with areas of calcification and yellow necrosis.

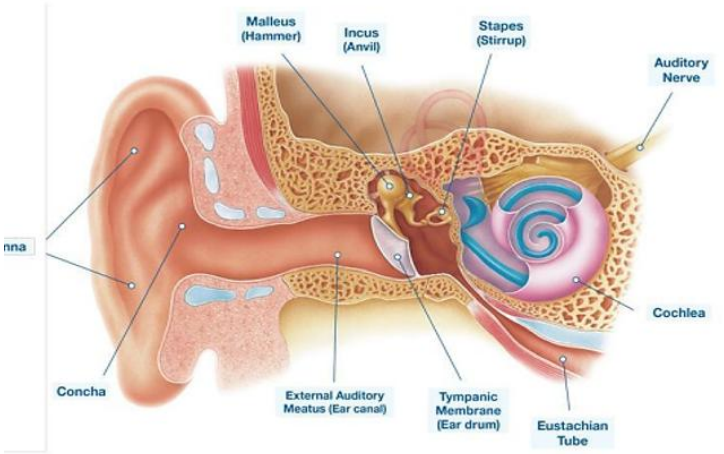
- ☒ **M/E:**

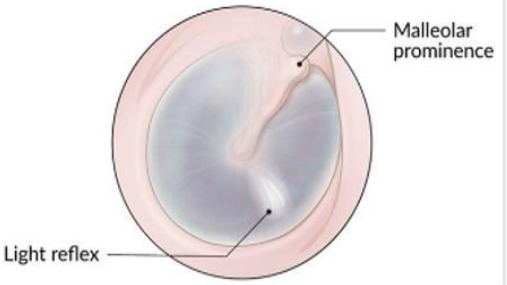
- Embryonal tumor consists of small round blue cells with hyperchromatic nuclei and scant cytoplasm arranged in sheets.
- The tumor cells show characteristic rosettes (tends to form photo-receptor elements) where the tumor cells are arranged around a lumen or around neurofibrillary structure.


High Power: Intensely basophilic nuclei and scanty cytoplasm


ROSETTETES
Flexner-Wintersteiner rosettes
Homer Wright rosettes

Ear



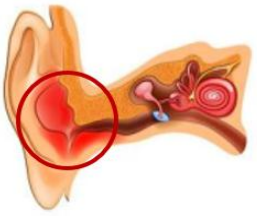


- Glistening, transparent
- Light reflex
- Pearly gray to pale pink.
- Mobile (to the air pulses).
- Handle and short process of malleus well identified

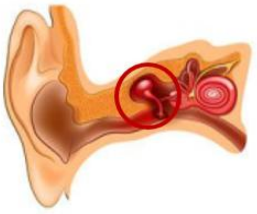
Activate Windows

Diseases of Ear

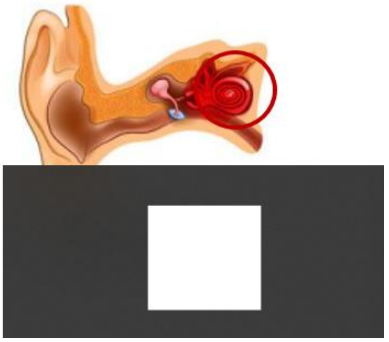
Otitis



otitis externa



otitis media

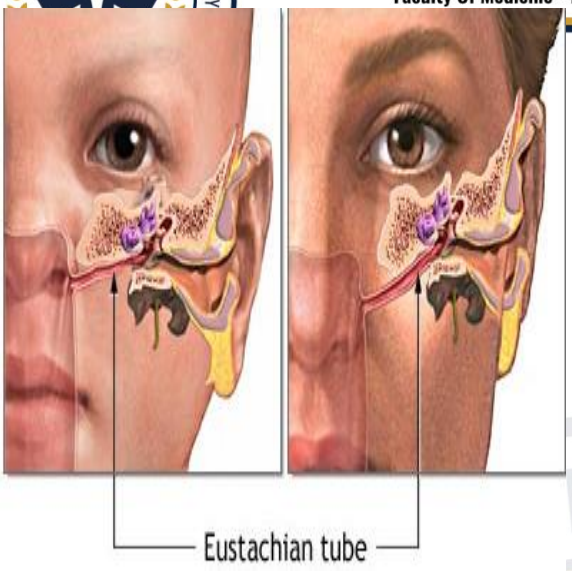


Otitis Media

☒ Inflammation of the middle ear.

☒ Risk factors:

- Children in first 2-4 years of life ???
  - Immune system not fully developed
  - Eustachian tube is easier to get blocked as it is shorter, more horizontal with narrower opening
  - Adenoids show infection or hyperplasia
- Bottle feeding (in supine position)
- Day care (kid-to-kid)
- Craniofacial anomalies as cleft palate
- Ciliary dysfunction as in exposure to cigarette



☒ **Etiology:**

- *S. pneumoniae - 40-45%
- *H. influenzae - 30-35%
- Others:
  - Moraxella catarrhalis,
  - Group A strep, staph,
  - Viral

☒ **Routes:**

- Via eustachian tube: the most common.
- Via external ear: tympanic membrane perforation.
- Direct spread from mastoiditis.
- Blood-born: very rare.

☒ **Classification:**

- Acute Otitis media:
- Otitis Media with effusion (OME):
- Chronic otitis media:
  - OM lasting 6 weeks or more
  - -Chronic suppurative
  - -Cholesteatoma

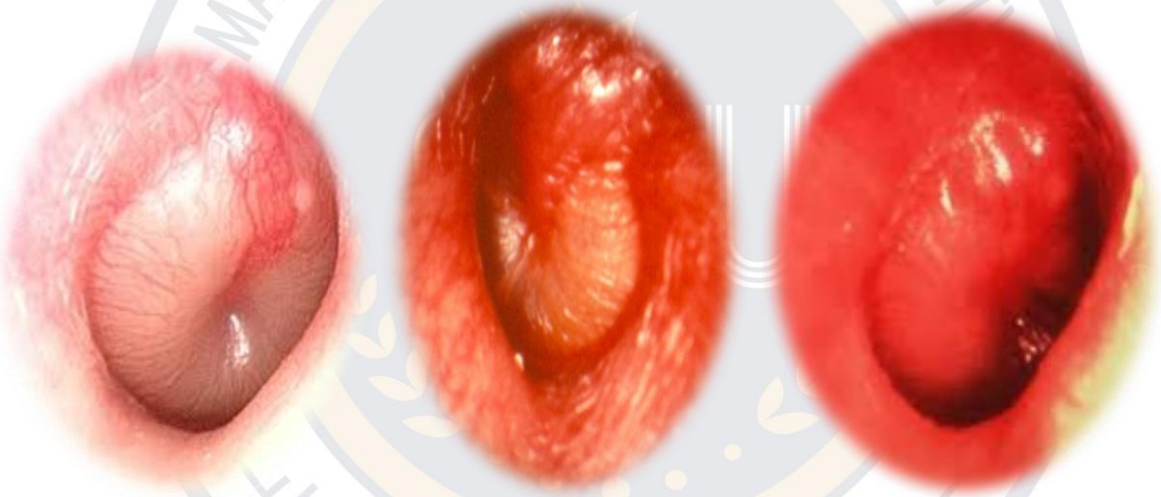
☒ Complications:

- Hearing loss;conductive, temporary
- Facial nerve Paralysis
- Spread of infection:
  - Labyrinthitis, Mastoiditis
  - Intracranial as meningitis & brain abscess

Acute otitis media:

Tympanic membrane:

- Opaque, thick
- Bulging/injected (erythematous)
- Loss of anatomic landmarks
- Reduced mobility
- Purulent effusion

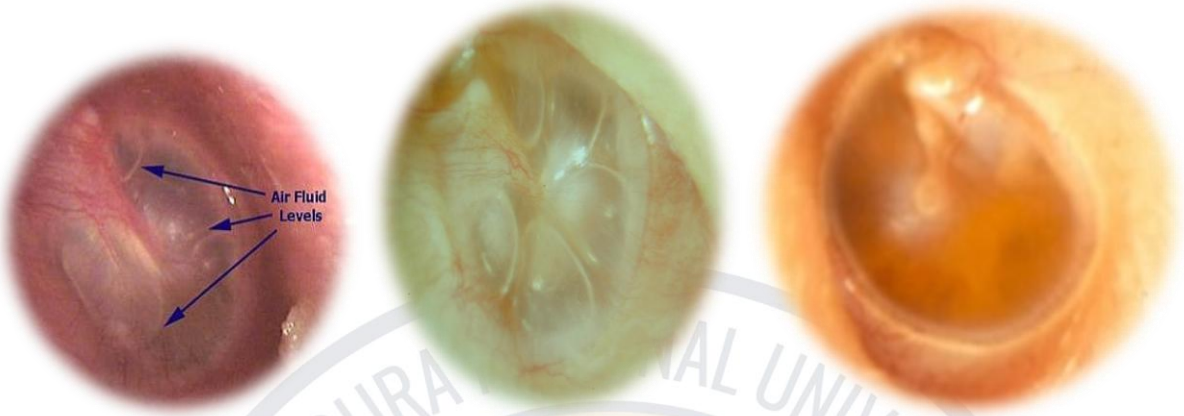


Otitis media with effusion:

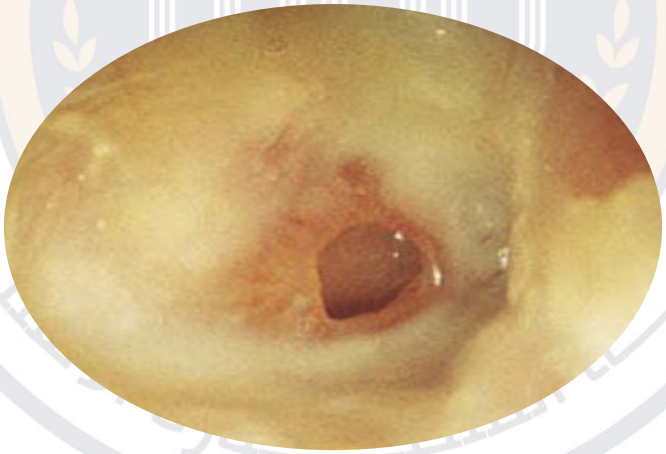
☒ Effusion with intact tympanic membrane, not associated with acute inflammatory symptoms & signs.

☒ Tympanic membrane:

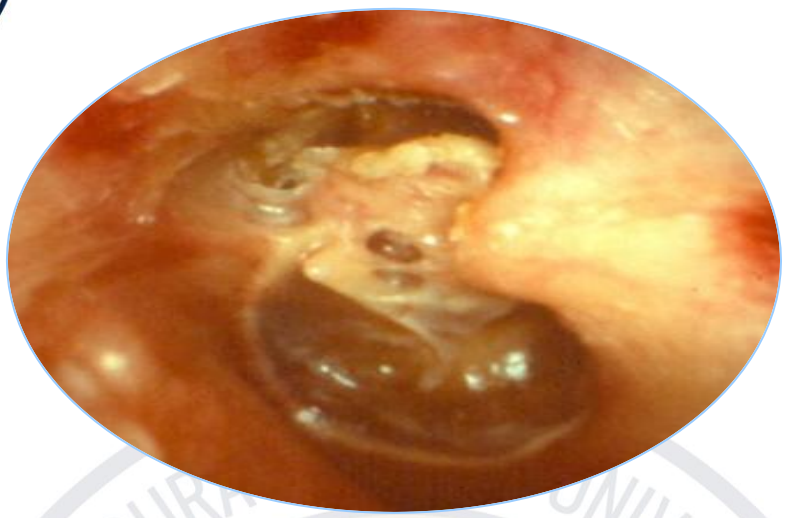
- Translucent or opaque
- Gray/pink
- Reduced mobility
- Effusion (thick mucoid) +/- airEffusion (thick mucoid) +/- air



- **Chronic suppurative otitis media:**
  - Chronic tympanic membrane perforation, fibrosis, calcification
  - Purulent discharge (mucopurulent otorrhea)
  - Conductive hearing loss



- **Chronic otitis media with cholesteatoma:**
  - Accumulation of squamous epithelium with keratin +cholesterol clefts + large number of histiocytes. in middle ear & mastoid
  - Osteolytic (osteoclastic inflammation)
  - Often accompanied by chronic otorrhea
  - Adult disease



Otitis Externa

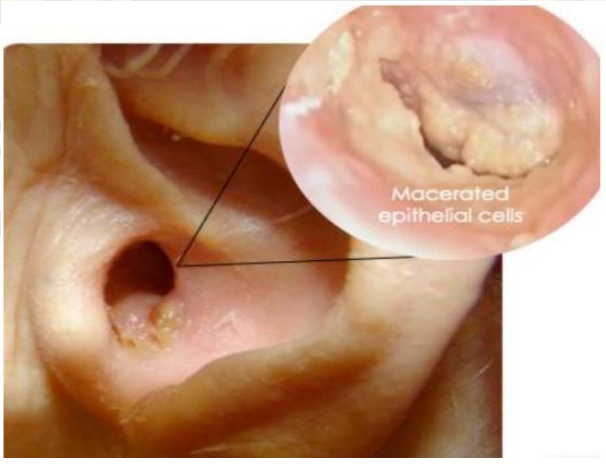
- ☒ Infection of the skin and subcutis of the external auditory canal
- ☒ Types:

1- Acute diffuse otitis externa

2- Circumscribed otitis externa.

3- Chronic otitis externa.

4- Malignant (Necrotizing) otitis externa



Otitis Interna

Commonly known as labyrinthitis or vestibular neuritis.

Caused mainly by viral infection.

• Symptoms include vertigo, dizziness, a ringing sound in your ears

Ear Tumors

- Tumors of external ear: Cerumen-gland tumors
- Tumors of middle ear: Jugular paraganglioma (glomus tumor).
- Tumors of inner ear: Acoustic neuroma.

Schwannoma

☒ It is a benign tumor called Acoustic neuroma of 8th cranial nerve

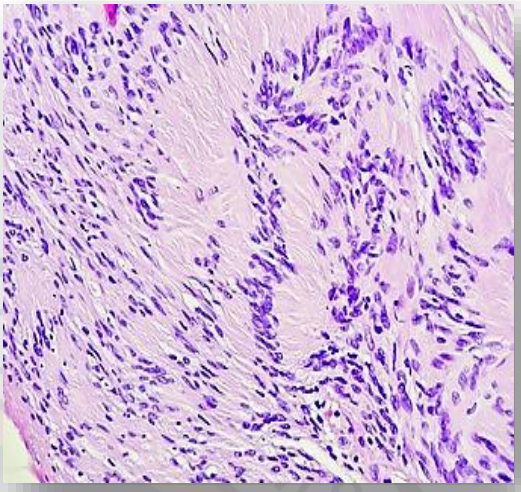
☒ Age: 50-60 years.

☒ **N/E:**

- Solitary mass, capsulated, firm round or fusiform with the related nerve at one side
- Cut surface is grey white and may show cysts

☒ **M/E:**

- Spindles shaped cells arranged in bundles, with rod- shaped nuclei side by side in palisade manner with reticular and collagen fibers in between.



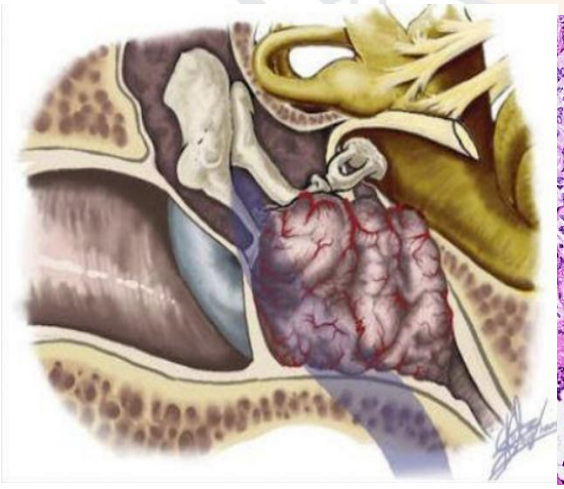
Jugular para-ganglioma

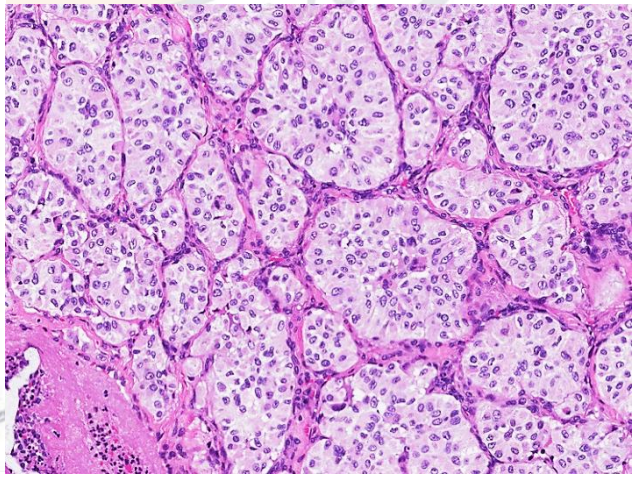
☒ The most common benign tumor of the middle ear. Called Glomus jugular- Arise from parasympathetic ganglia.

☒ **M/E:**

Classic organoid/nested pattern called “zellballen”; with fibrovascular stroma separates the nests

- the central cells are rounded/ovoid chief cells with abundant eosinophilic granular cytoplasm.
- Spindle cells present at the periphery of the nests.





FACULTY OF MEDICINE
MANSOURA NATIONAL UNIVERSITY

PHARMACOLOGY

Parkinsonism

- A progressive neurological disorder of muscle movement characterized by Muscle rigidity, tremors, bradykinesia and postural instability
- This is due to loss of dopaminergic neurons in substantia nigra resulting in imbalance of dopaminergic (inhibitory) and cholinergic (excitatory) influences on the extrapyramidal system.

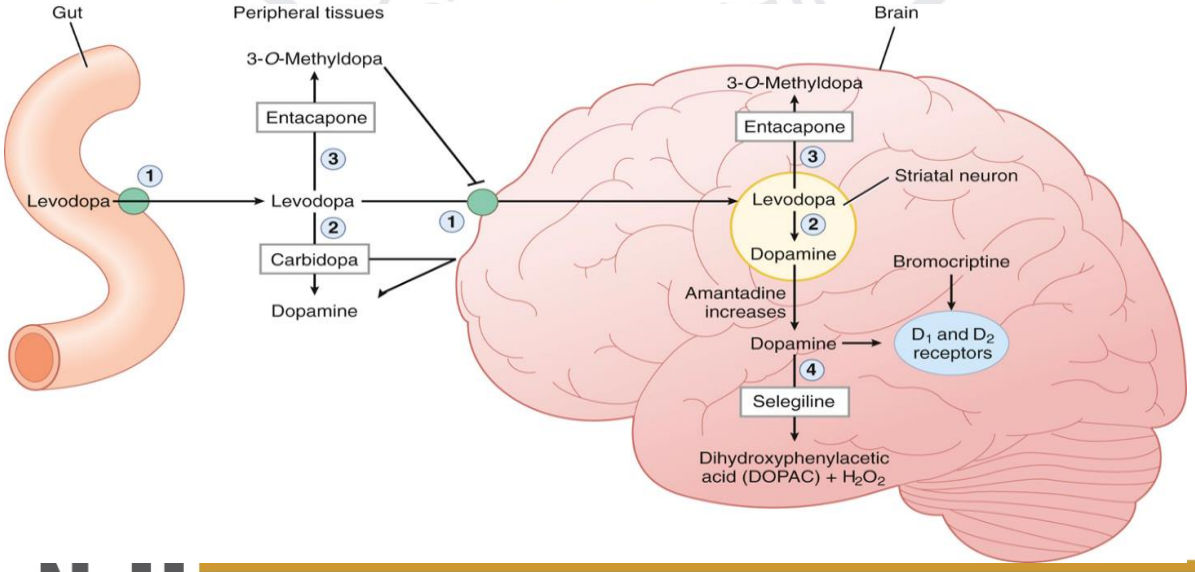
Classification of antiparkinsonian drugs

Dopaminergic drugs:

- Dopamine précurseurs: Levodopa (L-dopa).
- COMT inhibitors: Tolcapone – Entacapone
- Selective MAO-B inhibitors: Selegiline
- Dopamine agonists: Bromocriptine
- Releaser of dopamine : Amantadine

Anticholinergic drugs:

- Synthetic atropine substitutes (M1): Benztropine –Trihexyphenidyl



1. Levodopa (L-dopa)

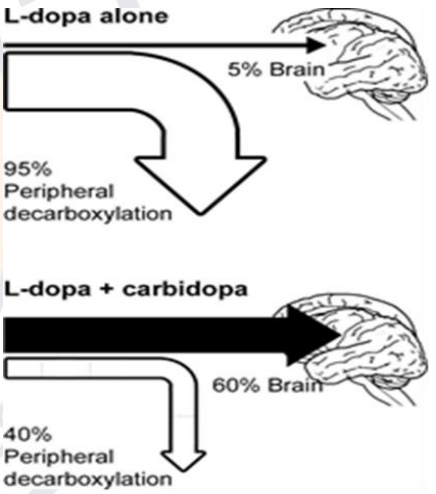
Pharmacokinetics

- Absorbed rapidly from the small intestine.
- Short t1/2 (1-2 h).

This short t1/2 may produce "on-off phenomenon"

Means: rapid fluctuation of the clinical state in the form of sudden tremors & immobility after short period of recovery.

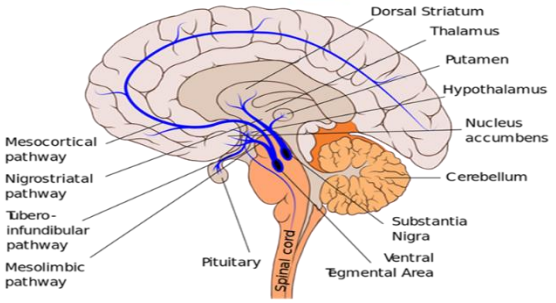
- Amino acids (e.g. leucine& isoleucine) compete with L-dopa absorption from the gut so it should be taken on an empty stomach.



Mechanism of action

- Dopamine can't cross BBB but L-dopa can pass.
- It is considered the 1st line treatment of Parkinsonism.
- More than 95% of the administered dose is rapidly decarboxylated into dopamine in the peripheral tissues.
- Only a small fraction escapes and crosses BBB.
- Peripheral decarboxylation can be minimized by administration of a decarboxylase inhibitor which can't cross BBB e.g. **carbidopa,** Such a combination helps to reduce the dose of L-dopa and hence the adverse effects

Adverse effects



Sites of dopamine in the brain

1. GIT:

   Nausea & vomiting
2. CNS:

   Mood changes, hallucinations and nightmares.
3. On-off phenomenon:

   Rapid **fluctuation** of the clinical state in the form of sudden tremors and immobility after a short period of recovery due to the **short t1/2**.
4. Dyskinesia:

   Involuntary movements of the head, lips, and tongue.
5. Autonomic:

   Postural hypotension, arrhythmias, mydriasis (peripheral effect)
6. Brownish body secretions& red urine due to the metabolite homovanilic acid.

2. COMT inhibitors
(Tolcapone- Entacapone)

Mechanism of action

- Reversibly inhibit COMT enzyme that converts L-dopa to 3-O-methyldopa (3OMD) in the gut and liver.
- Increases the efficacy of L-dopa and stabilizes dopamine levels in the striatum and improves motor function.

Adverse effects

Hepatic necrosis and same side effects of L-dopa

3. MAO inhibitors

Selegiline

Mechanism of action

Selective MAO-B inhibitor decreasing breakdown of dopamine in the brain.

Adverse effects

1. GIT upset.
2. Hallucinations& mood changes
3. **Insomnia.**

4. Dopamine agonists

Bromocriptine

- Dopamine (D2) agonist derived from ergot alkaloids.
- It differs from L-dopa in: Faster onset, longer duration, No on-off effect.

Adverse effects

1. GIT upset.
2. Hallucinations & mood changes in large doses.
3. Postural hypotension.
4. **Pulmonary fibrosis& vasospasm** (ergot alkaloids).

Pramipexole and Ropinirole

- Not ergot alkaloids.
- Both act as selective D 2 -receptor agonists.

- Pramipexole or ropinirole can delay the need for levodopa when used in early stages of parkinsonian disease. In advanced stages, these agents can reduce the "off" period and decrease the levodopa dosage requirement

Apomorphine

- Chemically related to morphine, does not bind to opioid receptors but rather is a dopamine receptor agonist.
- Approved for the treatment of acute intermittent hypomobility (freezing) episodes associated with advanced parkinsonian disease.

5. Amantadine

- An antiviral drug for influenza A2 virus.

Mechanism: (Not clear)

1. Amantadine is believed to act in Parkinson's disease as a weak glutamate N -methyl- d -aspartate (NMDA) receptor antagonist, reducing glutamatergic over activity.
2. It also stimulates release of dopamine stored in nerve terminals.
3. Reduces reuptake of released dopamine by the presynaptic neuron.

Adverse effects

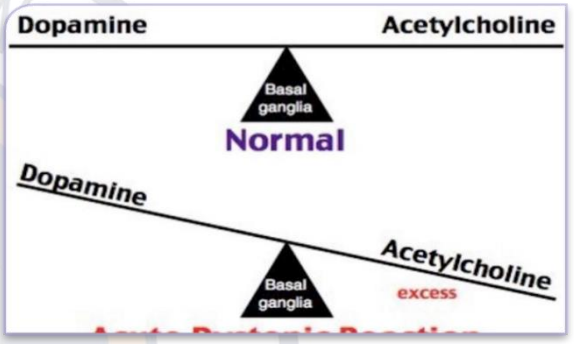
1. GIT upset.
2. Hallucinations& mood changes.
3. Postural hypotension.
4. **Skin pigmentation** (moteld skin) dilatation of capillaries (Livedoreticularis).

6. Anticholinergic drugs

Benztropine –Trihexyphenidyl

Mechanism of action:

1. Selectivity block central than peripheral muscarinic receptors (M1).
2. Improve tremors & little effect on muscle rigidity.



Uses

1. Parkinsonism
2. Drug-induced extrapyramidal side effects.

Adverse effects

1. In patients suffering from Parkinsonism, there is some degree of dementia associated with atrophy of cortical neurons. Anticholinergic drugs may aggravate dementia and memory loss.
2. Urine retention, glaucoma

Sedative hypnotics

Classification of sedative-hypnotic drugs

1-Benzodiazepines: Diazepam

2-Barbiturates: Phenobarbital

3-Other anxiolytic Drugs: Buspirone

4-Other newer hypnotic drugs:

Zolpidem, Zaleplon, Eszopiclone, Ramelteon

5-Antihistamines: Diphenhydramine

Benzodiazepines

Classification

- Short acting (t½ < 5h): **midazolam** – triazolam
- Intermediate acting (t½ 5-24 h): alprazolam – **lorazepam** – clonazepam
- Long acting (t½ > 24 h): **diazepam** – clorazepate - flurazepam

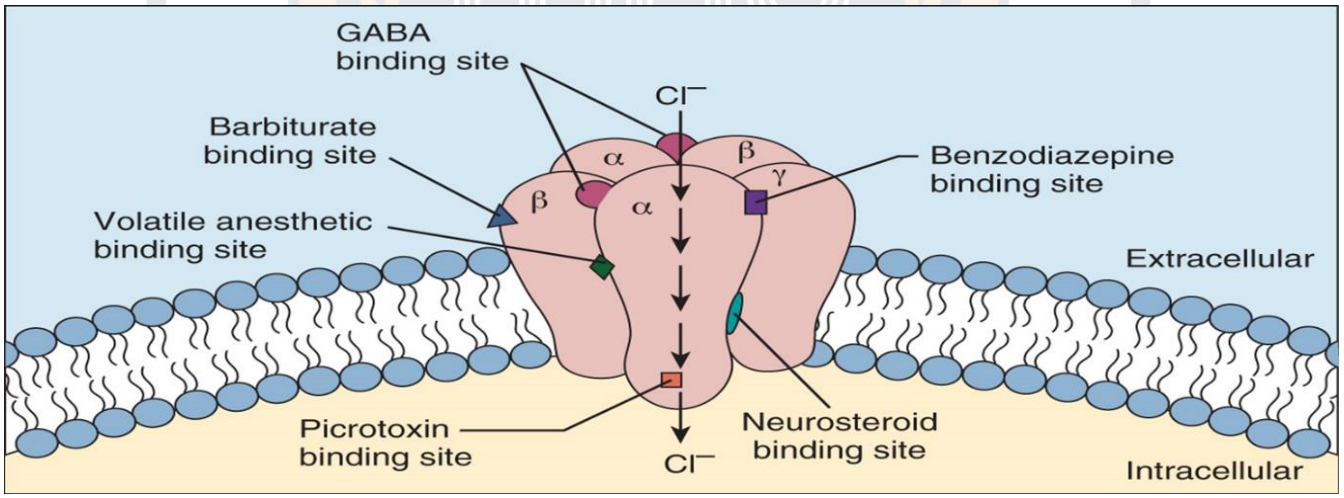
Pharmacokinetics

- Oral absorption →rapid.
- Distributed to all tissues including the brain, cross placenta & breast milk
- As the plasma concentration of a benzodiazepine decrease, the drug is redistributed from the brain to the blood, and this contributes significantly to the termination of its effects on the CNS.
- All benzodiazepines are extensively metabolized in the liver
- Long acting drugs are metabolized by oxidation (CYP450) into active metabolites giving them long duration of action (diazepam, and flurazepam).

- Short acting drugs are metabolized by conjugation into inactive metabolites followed by renal clearance (alprazolam, midazolam).

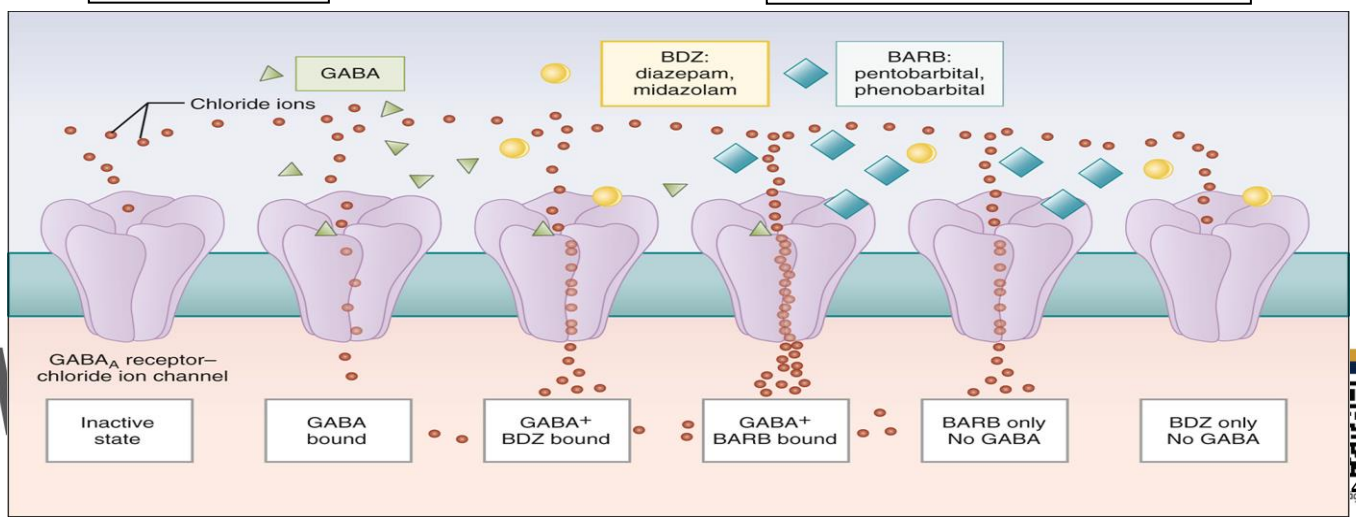
Mechanism of action

- By acting on its receptors, BDZ cause allosteric modulation of GABA action on GABA A receptors resulting in ↑Cl- conductance and hyperpolarization. (Benzodiazepines increase the frequency with which the channel opens)
- This receptor-ion channel complex is made up of five subunits with the major form of the complex containing alpha (α), beta (β), and gamma (γ) subunits.
- There are at least 16 types of these protein subunits GABA A receptors mediate the clinical and adverse effects of drugs that bind to them.



GABA receptor

Mechanism of action of benzodiazepine



Pharmacological effects

1. Reduction of anxiety (limited depression of the CNS) Lower doses have a sedative and anxiolytic effect.
2. Hypnosis (higher doses).
3. Central skeletal muscle relaxation
4. Anticonvulsant effect.
5. Amnesia. Anterograde amnesia, which means that an individual will not remember what happens from the time that the drug is administered to the time that the drug effects dissipate.

- Benzodiazepines produce anterograde amnesia because they interfere with the formation of new memory
- The amnesic property of benzodiazepines is often useful when patients are undergoing stressful procedures, such as endoscopy or outpatient surgery.

Therapeutic uses

1-Anxiety disorders:

Generalized anxiety disorders (GAD), phobia and panic attacks

N.B. Antidepressants (SSRIs) are effective in the treatment of chronic anxiety disorders and should be considered as first-line agents, especially in patients with concerns for addiction or dependence.

2-Insomnia (e.g., temazepam).

3-Anticonvulsants: diazepam, given i.v. used for treatment of status epilepticus and drug-induced seizures.

4-Anasthetic drug in short surgical procedures: Short acting benzodiazepines (e.g., midazolam) are preferred before during surgery or endoscopy.

5-Treatment of muscle spasm and spasticity: Diazepam

Adverse effects

1. Sedation, memory disturbance, dull attention (interfere with learning ability).
2. Tolerance and physical dependence (decrease GABA sensitivity & increased excitatory glutamate).
3. Rebound insomnia after discontinuation.
4. Hangover: a state of psychomotor depression occurs in the day following the use of long acting drugs (residual).
5. Apnea after rapid i.v. injection (flumazenil is the antidote)

Flumazenil

- Competitive antagonist at benzodiazepine receptors.
- Used to reverse the CNS effects from benzodiazepine overdose.
- Speed recovery from benzodiazepines effects in anesthetic & diagnostic

Barbiturates

- Phenobarbital a long acting barbiturate (6-8h)
- Thiopental is ultrashort agent (15-20 min).

Mechanism of action

- Barbiturates have either GABA-like action OR enhance the effects of GABA at GABAA receptors resulting in ↑Cl- conductance and hyperpolarization (barbiturates increase the length of time that the channel remains open).

- The action of barbiturates is non-selective i.e. High doses → generalized CNS and medullary depression.

Pharmacokinetics

- Oral absorption → rapid
- Thiopental IV.
- Distributed to all tissues including the brain, cross placenta & breast milk
- The onset and duration of action of barbiturates are determined by their lipid solubility and rate of metabolic inactivation.
- Thiopental (short acting) highly lipid-soluble are well absorbed from the gut, rapidly **redistributed** from the brain to tissues and extensively metabolized to inactive compounds.
- Phenobarbital (long acting) less lipid-soluble is slowly absorbed from the gut and more slowly redistributed from the brain
- Barbiturates induce cytochrome P450 (CYP450) microsomal enzymes in the liver.

Pharmacological effects

1. Reduction of anxiety
2. Hypnosis +++
3. Anesthetic effect thiopental
4. Skeletal muscle relaxation
5. Anticonvulsant effect phenobarbital in tonic colonic convulsion
6. Generalized CNS depression

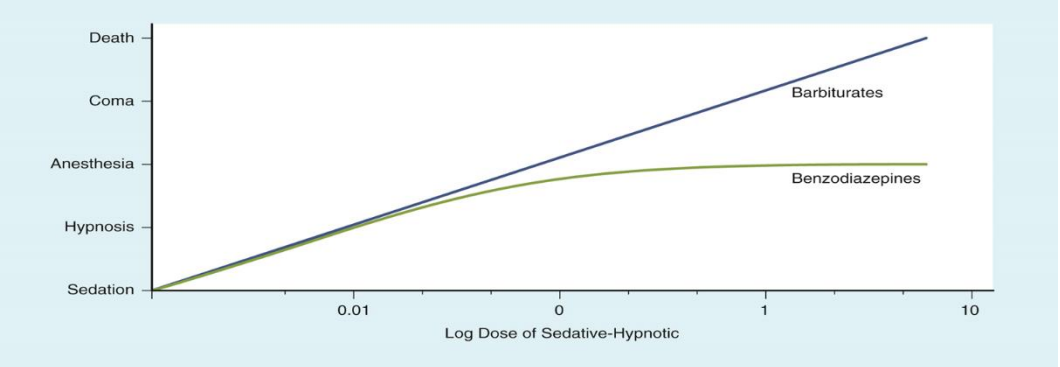
Therapeutic uses

1. Phenobarbital is used in the treatment of grand mal epilepsy.
2. Thiopental is used as short i.v. anesthetic in short procedures.

3. Phenobarbital is microsomal enzyme inducer. It is used in the treatment of hyperbilirubinemia in neonates (physiological jaundice) to activate liver enzymes (glucurony-ltransferase) and fasten metabolism of bilirubin.

Barbiturates vs benzodiazepine

- Because benzodiazepines work only in the presence of GABA released by neurons, the depth of CNS depression is limited. Therefore, the benzodiazepines exhibit a ceiling effect whereby greater doses do not produce significantly greater effects and do not depress the brain to the point of anesthesia and death.
- In contrast to the benzodiazepines, the barbiturates also act to directly increase chloride influx **in the absence of GABA**. For this reason, barbiturates do not exhibit a ceiling effect
- Barbiturates do not exhibit this ceiling effect and can produce severe respiratory depression and death after administration of a large dose.



Barbiturates vs benzodiazepine

Adverse effects

1. Drowsiness, impaired concentration, and mental and physical sluggishness
2. Physical dependence.
3. Respiratory and myocardial depression
4. Phenobarbital is hepatic microsomal enzyme inducer.

Other anxiolytic drugs

Buspirone

- It is partial agonist on 5-HT1A receptors in the midbrain.
- Selective anxiolytic without hypnotic or muscle relaxant effect.
- No liability for drug dependence
- It suppresses anxiety after a long delay (2 or more weeks) useful for the chronic treatment of GAD.
- It is the anxiolytic of choice in the elderly.
- Adverse effects Headache, tachycardia and nervousness.

Other hypnotic drugs

Zolpidem, Zaleplon, and Eszopiclone

- The newer agents have largely replaced older benzodiazepines for the treatment of insomnia.
- Mechanism of action : the same as benzodiazepine but have a different allosteric binding site
- **Advantage of newer drugs as hypnotics**

1. These agents cause fewer adverse effects than the older benzodiazepine
2. Have less potential for tolerance and dependence.

3. Shorter duration of action usually decrease daytime sedation and hangover effects.
4. Greater selectivity at targeting only GABA A receptors composed of particular subunit combinations, in particular those receptors composed of α 1 subunits. The older benzodiazepines are less selective and bind to a more widespread distribution of receptor, producing a greater degree of adverse effects on sleep, cognitive performance, and memory

Ramelteon

- Prescribed for patients who have difficulty falling asleep.
- It is a selective agonist at melatonin MT1 and MT2 receptors that are involved in the promotion of sleep and that maintain the normal circadian rhythm.
- Adverse effects: dizziness and fatigue.

Antihistamines

- Antihistaminic (diphenhydramine and Doxepin) are most widely available over –the-counter preparations for insomnia
- Antihistaminic that cross the blood-brain barrier (first generation) can produce varying degrees of sedation and used to treat mild insomnia.

Mechanism of action

1. Inhibition of H 1 receptors.

Histamine-containing neurons in the posterior hypothalamus promote wakefulness through interactions with ascending cholinergic nuclei and cholinergic projections to the thalamus and cortex, so inhibition of H 1 receptors lead to decrease alertness and sedation

2-In addition to action on H 1 receptors these drugs have anticholinergic effect

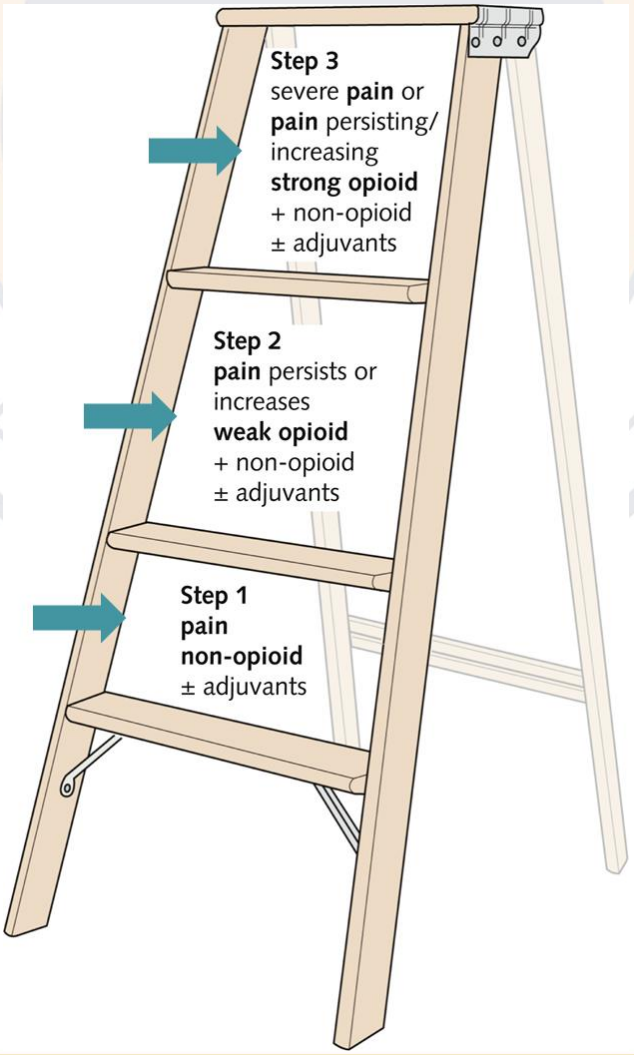
Side effects

Anticholinergic effects make them less useful than the benzodiazepines and the non-benzodiazepines

Opioid (narcotic) analgesics

Basic concepts

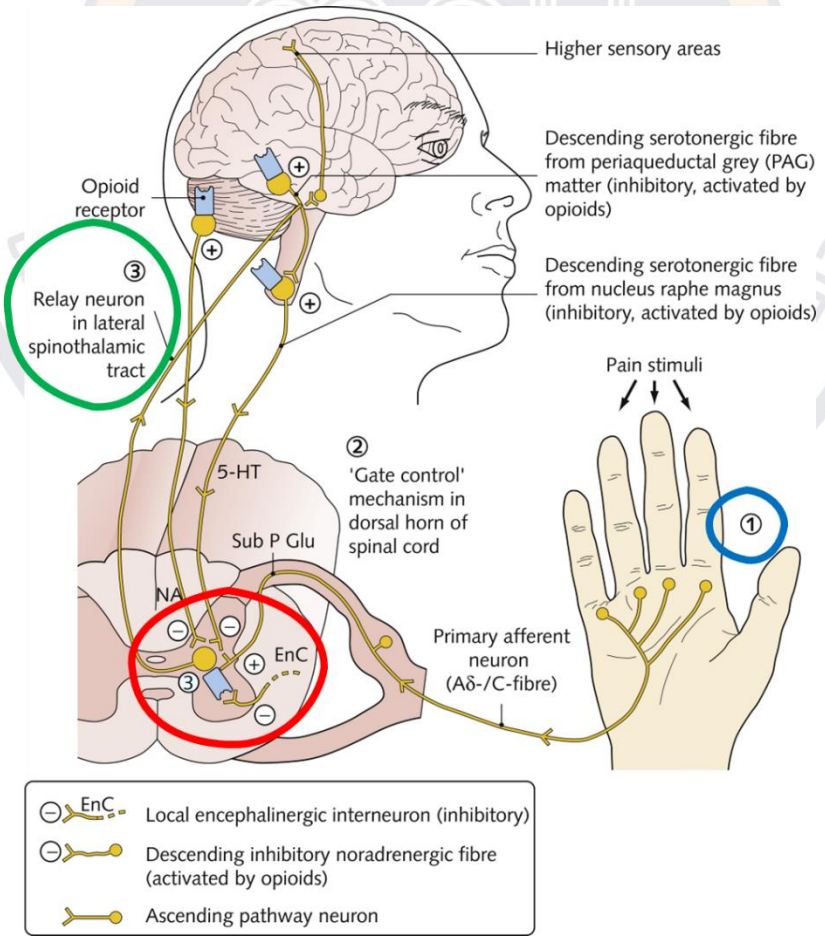
- ☒ Pain, which may be acute or chronic, is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage.
- ☒ Pain is a subjective experience.
- ☒ An analgesic drug is one that effectively removes (or at least lessens) the sensation of pain.
- ☒ Analgesics should be use of in accordance with the analgesic ladder (patients with pain should be treated with the least potent analgesic that will control their pain)



Pain perception

Pain perception is simply a three-stage process:

- Activation of nociceptors (pain-specific receptors) in the peripheral tissues.
- Transmission of pain information from the periphery to the dorsal horn of the spinal cord
    - Pain signals in the spinal dorsal horn are modulated by descending inhibitory noradrenergic/serotonergic tracts from higher brain centers. → "Gate-control mechanism".
    - Theses inhibitory tracts are activated by endogenous opioids.
- Upward passage of pain information via the spinothalamic tract, to the higher centers of the brain.



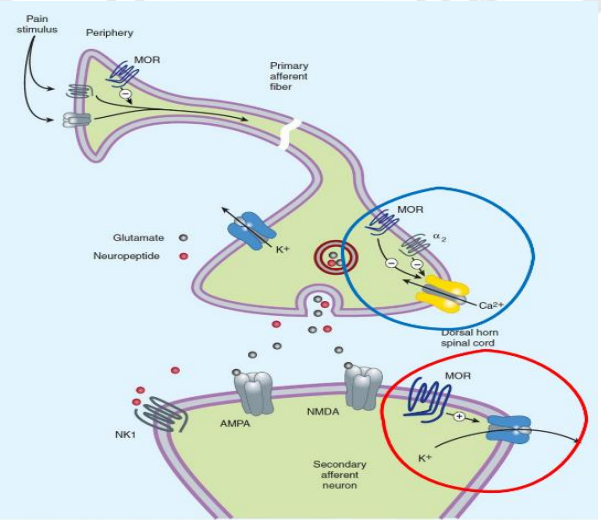
Opioid (narcotic) analgesics

- Gold standard for strong pain relief
- Natural or synthetic opioid analgesics relieve moderate to severe visceral or somatic pain by activating (agonists) a specific family of receptors known as opioid receptors.
- There are three major opioid receptor subtypes: μ (MOP), δ (DOP) and κ (KOP).
    - μ receptors → responsible for most of the analgesic effects of opioids & for the major adverse effects e.g., respiratory depression
    - δ receptors
    - κ receptors → contribute to analgesia at the spinal level

MOA:

- Opioid analgesics are mainly μ receptor agonists → either full agonists or partial agonists/mixed agonist-antagonists (agonists on one opioid receptor but antagonists or partial agonists on another)
    1. Opioid receptors localized at presynaptic neurons ↓ release of pain neurotransmitters (substance P & glutamate) mainly through ↓ in Ca^{++} influx.
    2. Opioid receptors localized at postsynaptic neurons decrease firing through increase in K^+ efflux → hyperpolarization.

    The net effect of μ receptor activation is to **inhibit neuronal activity** → so pain transmission is either blocked or diminished.



Classification of opioid analgesics

Opioid analgesics can be classified as full μ agonists, partial μ agonists/mixed agonist-antagonists.

Based on their analgesic potency, full μ agonists can be further subdivided into strong or weak/moderate agonists.

N.B. Pure opioid antagonists have no analgesic effects. They are used to counteract the adverse effects of opioid analgesics taken in overdose and for the treatment of opioid dependence (e.g., naloxone & naltrexone).

Strong μ agonists	Weak/moderate μ agonists	Partial μ agonists Mixed agonist-antagonists
• Morphine • Meperidine • Methadone • Fentanyl	• Codeine • Oxycodone Hydrocodone	• Pentazocine → partial μ agonist & κ agonist • Buprenorphine → partial μ agonist & κ antagonist

Pharmacological effects of opioid analgesics

1. **CNS**
   - Analgesia
     - Supra spinal → Activation of the descending inhibitory tracts
     - Spinal → Decrease substance P & glutamate release from presynaptic neuron. Hyperpolarization of the post synaptic neuron
   - Euphoria
   - Inhibition of cough reflex (codeine)
   - Tolerance and dependence
   - Respiratory depression
   - Sedation
   - Miosis (pinpoint pupil)

2. **GIT**
    - Constipation
    - Increased biliary sphincter tone and pressure.
    - Nausea and vomiting
3. **CVS:**
    - Vasodilation and hypotension
4. **Flushing & pruritis**
5. **Prolongation of labor (except meperidine)**
6. **Urine retention**

Uses of opioid analgesics

- Analgesia → Gold standard for strong pain relief
- Anesthesia → as adjunct with general anesthetics
- Antitussive → codeine suppresses cough reflex.
- Antidiarrheal → loperamide & diphenoxylate
- Euphoria → major cause of illicit drug use.

Adverse effects of opioid analgesics (Opioid intoxication)

- Respiratory depression (as they reduce the hypercapnic drive) → the cause of death in overdose.
- ↑ intracranial tension (due to CO2-induced dilation of in cerebral blood vessels) → CI in patients with closed-head injury
- Nausea and vomiting → direct stimulation of the chemoreceptor trigger zone.
- Miosis (pupil constriction) → direct stimulation of the Edinger-Westphal nucleus of the oculomotor nerve.
- Constipation → increase smooth muscle tone & decrease peristalsis.
- Exacerbation of pain in patients with biliary dysfunction or a gallbladder attack. Why??
- Pruritis, flushing & bronchospasm → due to histamine release from mast cells.
- Tolerance and Dependence

- **How to treat acute opioid intoxication?**
  - ☒ Cases of opioid overdose need to be rapidly treated, due to respiratory depression,
  - ☒ Naloxone is a pure competitive antagonist that quickly (in seconds to minutes) displaces opioids already bound to receptors and reverses respiratory depression.
- **Tolerance and dependence to opioid analgesics** (chronic opioid intoxication, opioid use disorder; OUD)

I. *Tolerance to opioid analgesics*

Tolerance → a decrease in the pharmacologic effect of opioid analgesics observed after chronic/long-term/repeated drug administration.

Mechanism:

- Pharmacodynamic tolerance to all opioid analgesics (cross-tolerance).
- Primarily results from down-regulation of opioid μ receptors with repeated opioid administration.
- Tolerance develops to most of the effects of opioids but not to miosis and constipation.
- Tolerance also develops to respiratory depression, still a sufficiently high dose of an opioid analgesic can still be fatal to highly opioid-tolerant individuals.

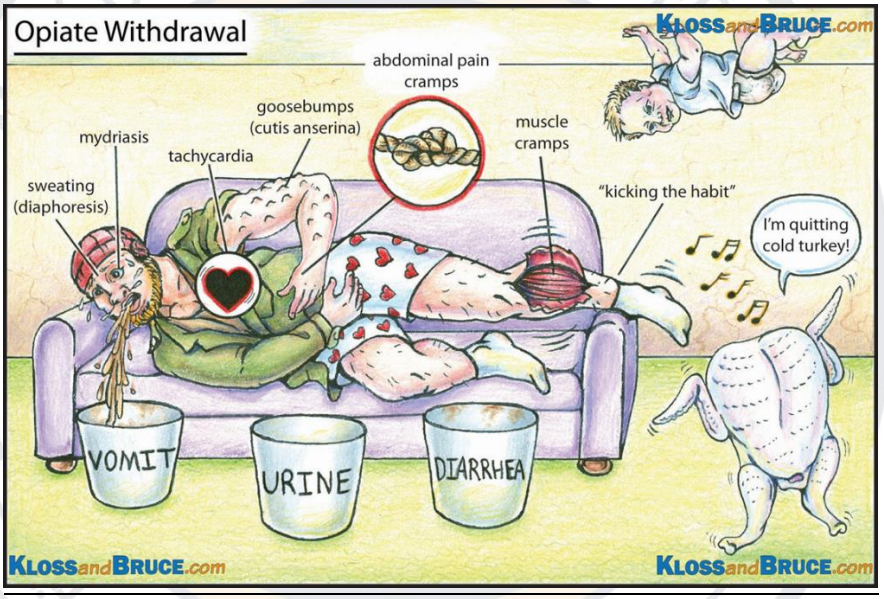
II. *Physical dependence on opioid analgesics*

- Opioid tolerance is accompanied by a similar degree of opioid physical dependence.
- **Physical dependence** → a physiologic state in which a person's continued use of an opioid analgesic is required for his or her well-being.
- Tolerance and physical dependence represent a newer situation wherein the neuron progressively becomes less responsive to the opioid, and yet requiring continued opioid use to maintain normal functions.
- **Opioid withdrawal syndrome** → If the chronically used opioid analgesic is abruptly withdrawn (or e.g., after administration of an opioid antagonist), the equilibrium is disturbed and a rebound hyperexcitability state occurs.

☒ Def: A state of irritable and sometimes aggressive behavior, plus:

- Fever and sweating
- Tachycardia.
- Nausea and vomiting.
- Pupillary dilation is an important sign of opioid withdrawal (X opioid intoxication causes pinpoint pupils).
- Piloerection.
- Abdominal cramps and diarrhea.

☒ Opioid withdrawal is not life-threatening.



III. *Psychological dependance on opioids*

- Drug dependence → a condition in which individual feels compelled to repeatedly administer a psychoactive drug (a drug that changes mood or perception).
- When this is done to avoid physical withdrawal symptoms → physical dependence.
- When this is done for a psychological reason (the need for stimulation, feeling high, pleasure, euphoria or to escape reality) → psychological dependence.

Treatment of opioid dependence (OUD)

☒ Aim: help the patient experience reduced symptoms of opioid withdrawal, reduced cravings, and maintain abstinence from other illicit opioid use.

I. Phase 1 → Medically supervised opioid withdrawal (detoxification)

- Def: administration of a drug to reduce the severity of withdrawal Symptoms
- Drugs used:
  1. **Longer acting opioid agonists**: methadone and buprenorphine
  2. **Alpha-2 adrenergic agonists**: clonidine.

II. Phase 2 → Opioid replacement, maintenance, or substitution therapy

- *Def:* Replacing an opioid with a longer acting but less euphoric and less addicting opioid.
- The commonly used drugs are:
  1. **Agonists**: buprenorphine and methadone.
  2. **Antagonists**: naltrexone (N.B. as opioid antagonists precipitate withdrawal in patients actively using opioids, medically supervised withdrawal is necessary prior to initiation of naltrexone).
- **Adjunct drugs:**
  1. Alpha-2 adrenergic agonists (clonidine) → to decrease anxiety associated with opioid withdrawal.
  2. Benzodiazepines or other sedating drugs → to treat anxiety and insomnia associated with opioid withdrawal.
  3. Anti-diarrheal and antiemetic drugs
  4. NSAIDs (naproxen) → to relieve pain.

Specific opioid analgesics

Morphine

- The standard opioid analgesic.
- It undergoes significant first-pass metabolism in the liver → less effective orally → as larger doses are required when the drug is administered orally.
- The 6-glucuronide active metabolite → is more active and has longer t1/2 than morphine → contributes significantly to the analgesic effectiveness of morphine.
- It is primarily used to treat severe pain associated with trauma, MI, and cancer.
- Other use: acute pulmonary edema

Diamorphine (heroin)

- Twice as potent as morphine
- The most abused illicit opioid drug.
- Highly addictive → as it rapidly enters the brain after injection, and produce an intense euphoric sensation called a rush.

Fentanyl and its derivatives

- The most potent opioid agonists available
- A long-acting transdermal skin patch (Duragesic) is available to provide continuous pain relief for patients with severe chronic pain.

Methadone

- Longer duration of action and milder withdrawal symptoms
- Administered orally to treat opioid dependence.

Codeine

- 1/12 of the analgesic potency of morphine → used in mild to moderate pain → Commonly given in combination with aspirin or acetaminophen.
- Also used for its antitussive effects.
- The most constipating opioid.
- Less addictive

- Metabolized by CYP2D6 → liable to genetic polymorphism → variable responses in different individuals.

Tramadol

- MOA →
  - Agonist at μ receptors
  - Inhibits the neuronal reuptake of 5HT and NE.
- Used for neuropathic pain.
- Seizures are the main side effects.

Antidepressant drugs

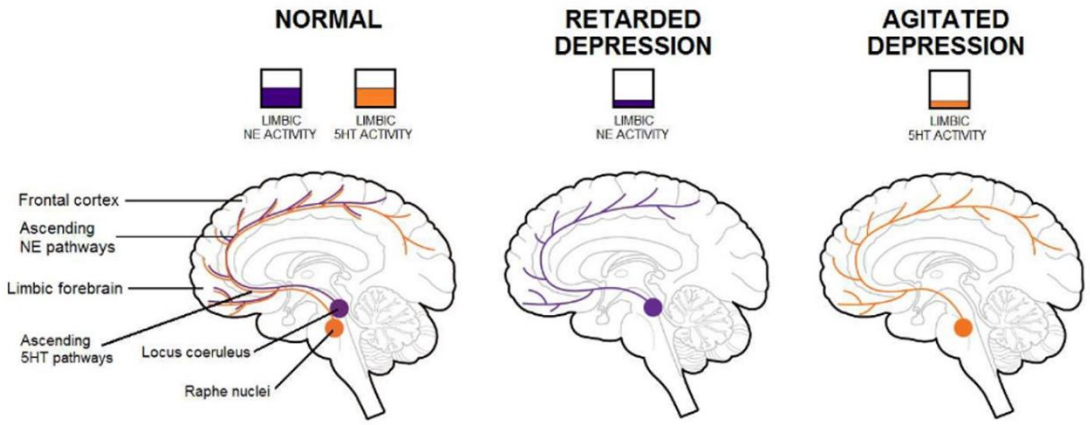
Major depressive disorder (unipolar depression) is characterized by:

- Depressed mood
- Loss of interest or pleasure in life
- Sleep disturbances
- Feelings of worthlessness
- Diminished ability to think or concentrate.
- Recurrent thoughts of suicide.

Biogenic amine hypothesis of depression

Mood disorders result from abnormalities in 5HT, NE, or DA neurotransmission. Serotonergic (5HT) fibers originating from the raphe nuclei in the midbrain to limbic structures are important in regulating mood.

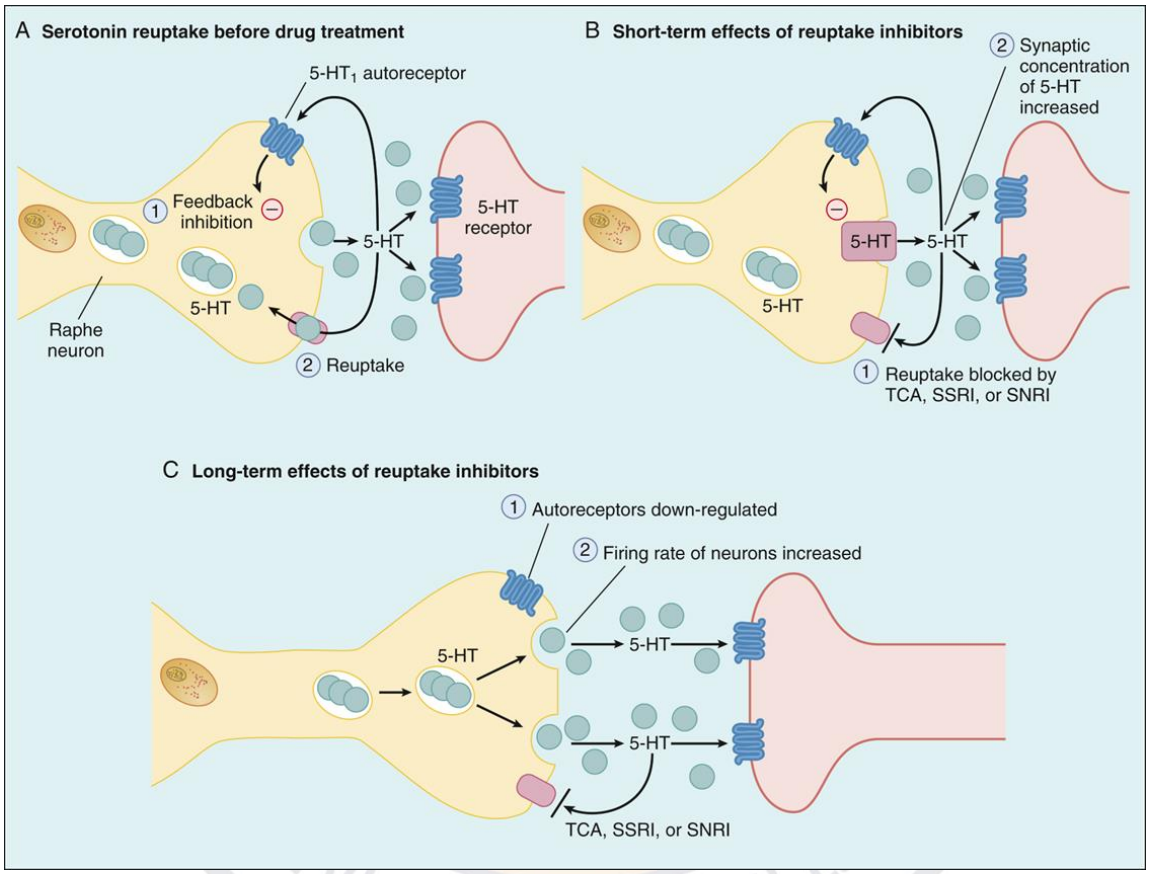
- Normally, 5HT system is activated during behavioral arousal and increases emotional reactions to environmental events.
- Impaired 5HT neurotransmission can decrease cortical responsiveness to emotional activation → depression.



Noradrenergic (NE) fibers that project from the locus ceruleus to the cerebral cortex also play a similar role in depression, as dopaminergic (DA) fibers innervating the nucleus accumbens.

The biogenic amine hypothesis is supported by the fact that all antidepressant drugs act to ↑ 5HT, NE, and/or DA neurotransmission in the brain.

Most importantly, antidepressant drugs ↑ concentration of 5HT in the synaptic clefts → leading to down-regulation of presynaptic autoreceptors → which in turn, increases the firing rate of serotonergic neurons → producing the delayed therapeutic effect of antidepressant drugs.



Antidepressant drugs

I. **The amine reuptake inhibitors**
   - Tricyclic antidepressants (TCAs)
   - **Selective serotonin reuptake inhibitors (SSRIs)**
   - Serotonin and norepinephrine reuptake inhibitors (SNRIs)
   - Norepinephrine reuptake inhibitors (NRIs) → maprotiline

II. **The multi-action drugs (atypical antidepressants)**

III. Last option → **monoamine oxidase inhibitors (MAOIs)**

The amine reuptake inhibitors

1. Tricyclic antidepressants (TCAs)

Examples → amitriptyline, imipramine, clomipramine, desipramine, and nortriptyline

Mechanism of Action

- TCAs block the reuptake transporter proteins, the norepinephrine transporter [NET] and serotonin transporter [SERT] → ↓ neuronal reuptake of NE and 5HT → causing immediate ↑ in the synaptic concentration of 5HT and NE.

Pharmacologic Effect

- TCAs antidepressant effect becomes apparent 2 - 4 weeks after drug therapy is started. Over time, the increased synaptic concentration of 5HT and NE causes down-regulation of presynaptic autoreceptors → thereby increasing the firing rate of serotonergic and noradrenergic neurons.

Adverse Effects

1. TCAs produce *autonomic side effects:*
    - Block muscarinic receptors → anticholinergic effects, such as dry mouth, blurred vision & urine retention.
    - Block α_1 -adrenergic receptor → orthostatic hypotension
2. Sedation → due to blockade of histamine H_1 receptors → should be administered at bedtime.
3. Weight gain
4. Overdose is associated with:
    - Cardiac arrythmias → increased QTc interval and widened QRS (treated with sodium bicarbonate)
    - Seizures (treated with diazepam)

Drug interactions

Strong—and predictable—interactions with many other drugs.

1. Synergistic effects with Inhibitors of biogenic amine metabolism (MOAIs) → a potentially fatal ↑ in 5HT (serotonergic syndrome) → agitation,

confusion, muscle rigidity, severe hypertension, hyperthermia, and cardiovascular collapse.

2. Additive adverse effects with:
   - Other sedative drugs
   - Drugs that increase QTc interval → ↑ risk of cardiac arrythmias
3. TCAs are metabolized by CYP2D hepatic enzymes.
   - Inhibitors of CYP2D → ↑ TCA serum levels
   - Inducers of CYP2D → ↓ TCA serum levels

Uses

1. Depression
2. Obsessive-compulsive disorder (OCD) → clomipramine
3. Eating disorders (Bulimia nervosa & anorexia nervosa)
4. Panic disorders
5. Neuropathic pain → Amitriptyline.
6. Nocturnal enuresis (bed-wetting in children) → imipramine

II. Selective serotonin reuptake inhibitors (SSRIs)

Examples → fluoxetine, citalopram, and sertraline, escitalopram, fluvoxamine, paroxetine, and vortioxetine

Mechanism of Action

- SSRIs selectively block the neuronal reuptake of 5HT → causing immediate ↑ in the synaptic concentration of 5HT.

Pharmacologic Effect

- Their antidepressant effect becomes apparent 2 - 4 weeks after drug therapy is started. Over time, the increased synaptic concentration of 5HT causes down-regulation of presynaptic autoreceptors → thereby increasing the firing rate of serotonergic neurons.

Adverse effects:

SSRIs produce fewer sedative, autonomic, and cardiovascular side effects than TCAs.

Unlike TCAs, SSRIs are usually administered in the morning because they increase alertness in patients.

1. Nervousness, dizziness, and insomnia → decrease with continued use
2. Occasionally cause male sexual dysfunction → priapism and impotence → major cause of discontinuation.
3. SSRIs should not be used with MAOIs → the combination can cause a potentially fatal ↑ in 5HT conc. in synapses (serotonergic syndrome).

Uses

- Depression → 1st-line treatment for depression → they are as effective as TCAs but with fewer autonomic side effects and less sedation.
  They are also much safer than TCAs regarding overdose → they seldom cause cardiac arrhythmia or seizures.
- Obsessive-compulsive disorder (OCD) → fluoxetine & fluvoxamine
- Eating disorders → Bulimia nervosa & anorexia nervosa → fluoxetine
- Panic disorders
- Premenstrual dysphoric disorders (PMDD)

III. Serotonin and norepinephrine reuptake inhibitors (SNRIs)

Examples → duloxetine, and venlafaxine

Mechanism of Action

- SNRIs block the neuronal reuptake of 5HT & NE → causing immediate ↑ in the synaptic concentration of 5HT & NE.

Pharmacologic Effect

- As opposed to older TCA drugs, SNRIs do not antagonize muscarinic, adrenergic, or histamine receptors and produce few autonomic, sedative, or cardiovascular side effects.

Adverse effects → like that of SSRIs

Uses

1. Depression → effective in patients in whom SSRIs are ineffective.
2. Generalized anxiety disorder → duloxetine.
3. Neuropathic pain → diabetic peripheral neuropathy, fibromyalgia → duloxetine

The multi-action drugs 'Atypical antidepressants'

I. Bupropion

Mechanism of Action

- A weak inhibitor of the neuronal reuptake of DA and NE.
- a noncompetitive antagonist at nicotinic cholinergic receptors.

Bupropion produces few anticholinergic side effects, causes very little sedation, and rarely produces cardiovascular effects or sexual dysfunction.

Adverse effects

- Agitation and insomnia
- Increased risk for seizures

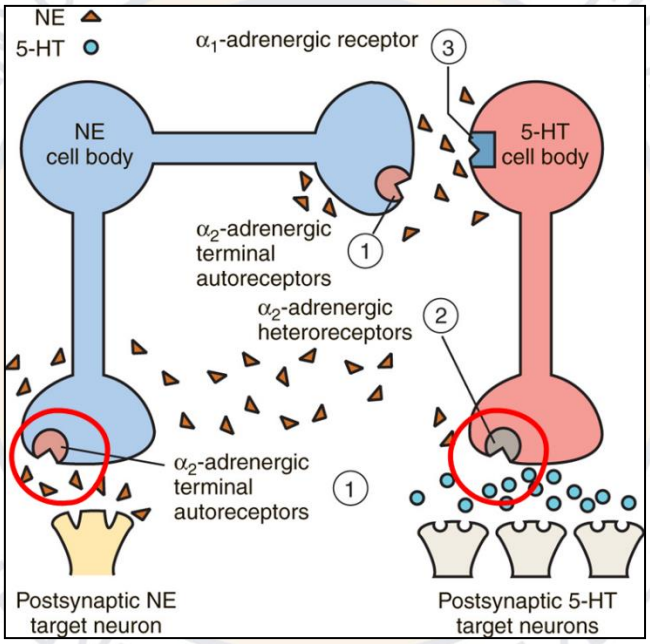
Uses:

- Depression
- Help patients who are attempting to quit smoking cigarettes.
- Bupropion + the opioid antagonist, naltrexone → indicated for weight reduction.

II. Mirtazapine

Stimulation of α_2 -autoreceptors on noradrenergic neurons decreases NE release, whereas stimulation of α_2 -receptors on serotonergic neurons inhibits 5-HT release.

- Mirtazapine *blocks α_2-adrenergic receptors* on noradrenergic and serotonergic nerve terminals → ↑ NE & 5HT release
- Blocks 5-HT $_{2A}$ receptors.



Adverse effects

- Sedation
- Weight gain
- Elevation of hepatic enzyme levels
- Rare agranulocytosis

Uses:

- Depression

III. Trazodone & Nefazodone

	Trazodone	Nefazodone
Mechanism of Action	Both inhibit biogenic amine reuptake	
	more selective for 5HT	more selective for NE
	Block 5-HT 2A receptors	
	Very strong H_1 receptor blocker → sedation	Less sedating than trazodone
Adverse effects	Priapism (prolonged, painful erection of the penis), which can lead to impotence.	
Uses	• Depression	
	• Insomnia (low doses, which causes sedation)	

The monoamine oxidase inhibitors (MAOIs)

Mechanism of Action & examples →

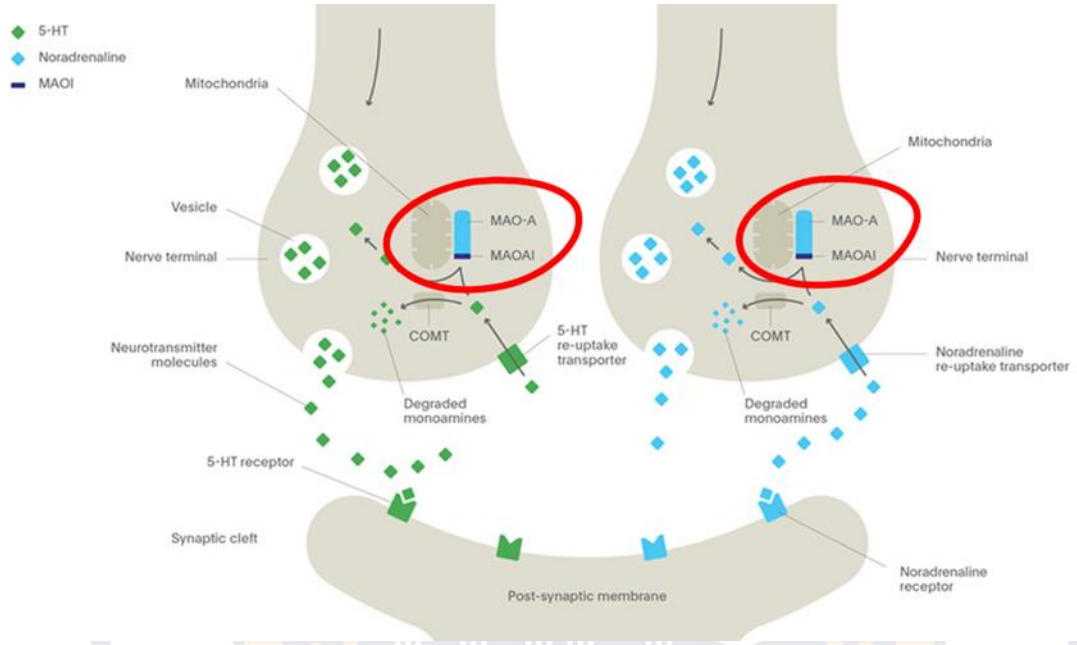
MAOs are enzymes responsible for degradation of the biogenic amine neurotransmitters (NE, DA, and 5HT).

- MAO-A → preferentially metabolizes 5HT but also metabolize NE and DA.
- MAO-B → preferentially metabolizes DA.

MAOIs are classified according to their selectivity into:

1. 1st-generation MAOIs → Phenelzine, isocarboxazid, and tranylcypromine → irreversible inhibitors of both MAO-A and MAO-B.

2. 2nd-generation MAOIs → moclobemide → reversible inhibitors of MAO-A
3. 3rd generation MAOIs → Selegiline → selectively inhibits MAO-B → approved for treatment of depression in a transdermal patch formulation.



Pharmacological effects:

- MAO-A inhibitors → ↑ 5HT levels >> NE levels in the synapses → downregulation of presynaptic autoreceptors → subsequently increased firing of serotonergic neurons.
- MAOIs have many potentially serious interactions with other drugs and with food → they are not considered drugs of choice in the treatment of depression → generally used as alternative therapy when patients have failed to respond to other drugs.
- As with other antidepressants, the clinical effects of MAOIs are delayed for 3-4 weeks after therapy begins.

Adverse effects:

1. MAOIs interact with SSRIs & TCAs → potential to cause 'serotonin syndrome.'
   At least 2 weeks should pass between discontinuation of either an MAOI or an SSRI and the start of the other.

2. ‘Cheese reaction’ → MAOIs can cause severe hypertension when administered with foods containing tyramines (aged cheeses, wines, canned meat, liver, sardines & herring, some fruits and vegetables, avocados & canned figs, chocolate and coffee)
   Mechanism: Tyramine is an indirect sympathomimetic present in some food and normally metabolized by MAO-A in the liver & intestine → causes release of NE from noradrenergic nerve fibers.

   If the patient is treated with MAO-A inhibitor or non-selective MAOIs + eating tyramine-rich food → severe hypertension

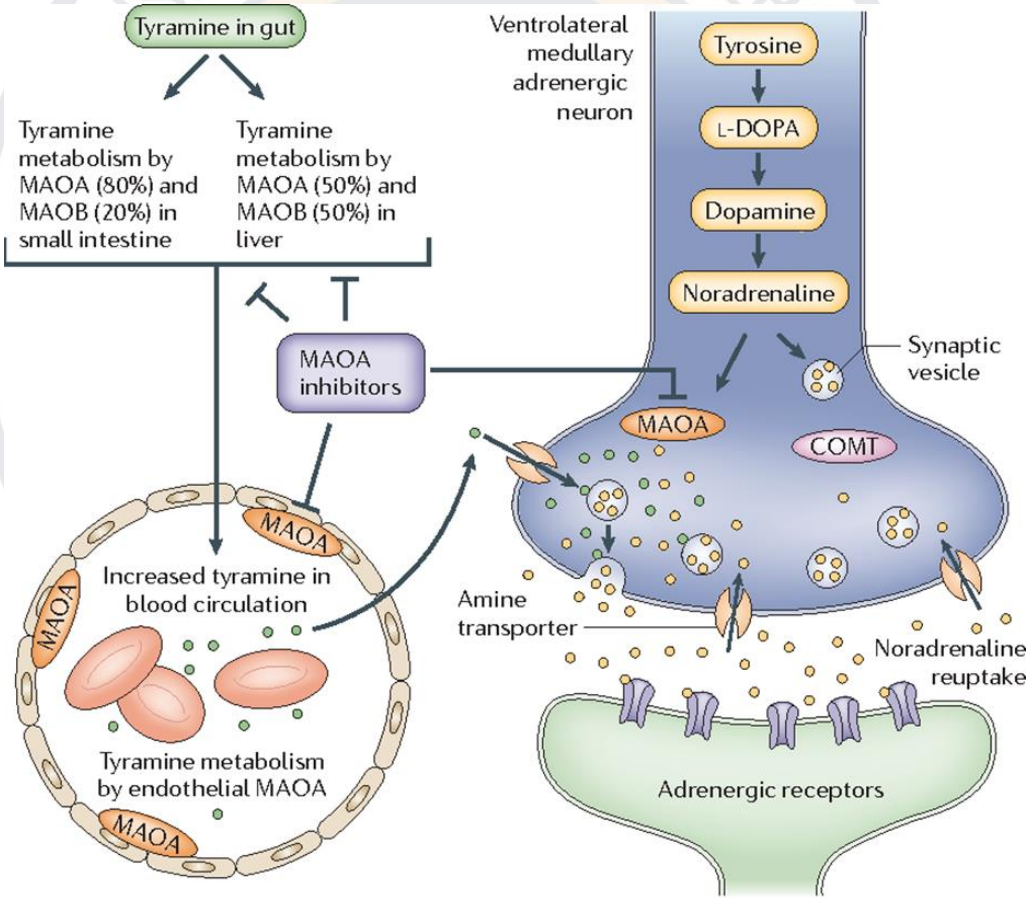


Figure 5 | **The mechanism of potentiation of cardiovascular effects of tyramine:**

Anticonvulsant Drugs

Seizures

Episodes of abnormal electrical activity in the brain that may lead to involuntary movements and sensations, which are accompanied by characteristic changes on electroencephalography (EEG).

Classification of seizures

According to the focus and spread of discharges, seizures may be classified into ways.

- Partial (focal), which originate at a specific focus and do not spread to involve other cortical areas.
- Generalized, which arise in both cerebral hemispheres, and accompanied by loss of consciousness.

International classification of partial and generalized seizures.

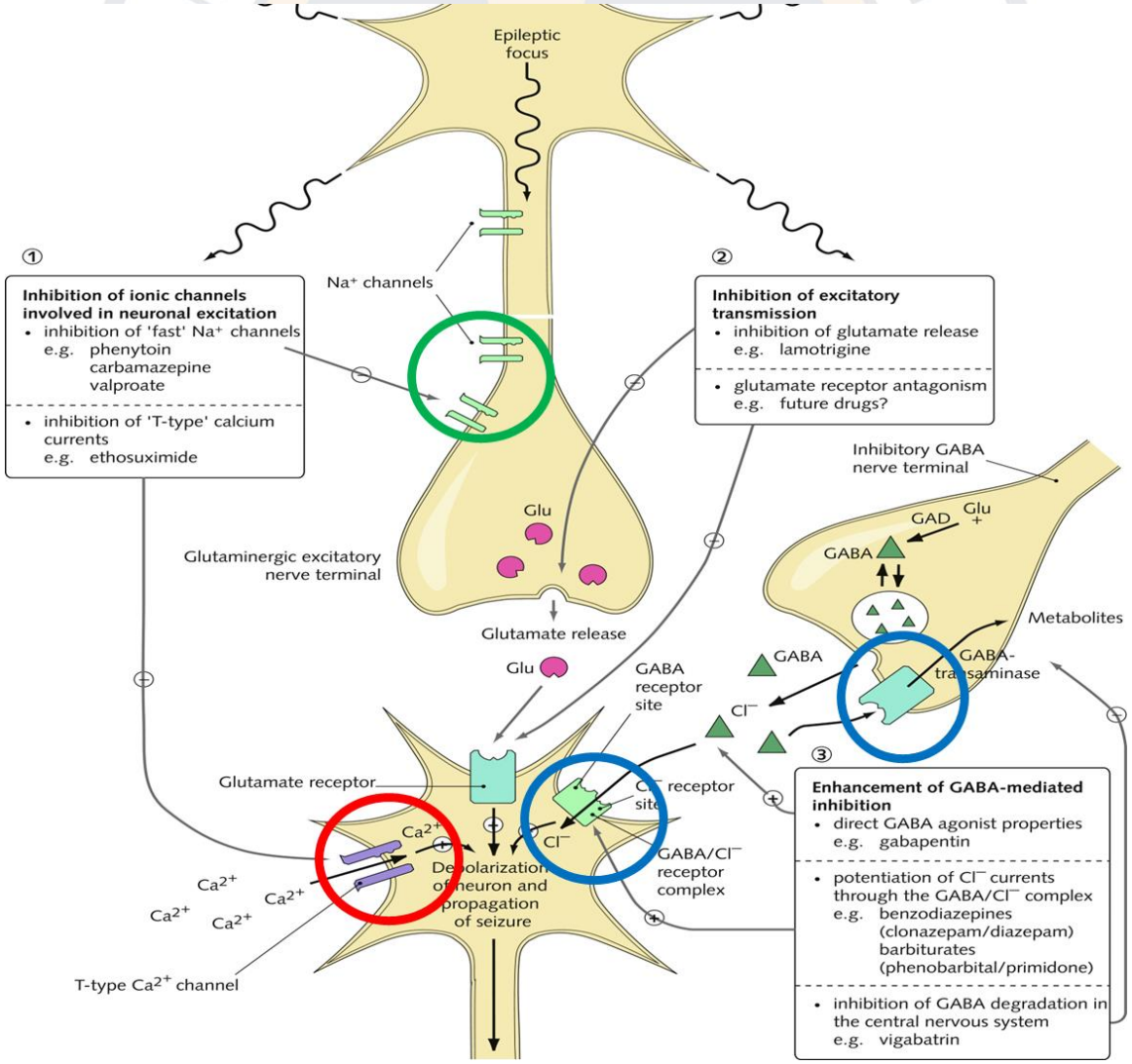
Partial (focal)	
Simple partial seizure	No alteration of consciousness
Complex partial seizure	Altered consciousness, automatisms, and behavioral changes

Secondarily generalized seizure	
Focal seizure becoming generalized and accompanied by loss of consciousness	
Generalized seizures	
Tonic-clonic (grand mal) seizure	Increased muscle tone followed by spasms of muscle contraction and relaxation
Tonic seizure	Increased muscle tone
Clonic seizure	Spasms of muscle contraction and relaxation
Myoclonic seizure	Rhythmic, jerking spasms
Atonic seizure	Sudden loss of all muscle tone
Absence (petit mal) seizure	Brief loss of consciousness (less than 10s), with minor muscle twitches and eye blinking

Treatment of epilepsy

- The etiology of the abnormal neuronal discharges in epilepsy is unknown in 60% to 70% of cases, but a family history is an important factor.
- Damage to the brain, e.g., by tumors, head injury or infections, may subsequently cause epilepsy.
- Antiepileptic drugs limit the propagation of this abnormal discharge (inhibit the rapid, repetitive neuronal firing) → so they prevent the development of seizures.
- The aim of drug treatment of epilepsy is → To minimize the seizure frequency, without producing adverse drug effects.

Classification of anticonvulsant drugs



I. **Drugs that inhibit Voltage-gated Na^+ channels:**
- Phenytoin & Fosphenytoin
- Carbamazepine & Oxcarbazepine
- Valproic acid
- Lamotrigine
- Topiramate
- Zonisamide

II. **Drugs that inhibit T-type Ca^{++} channels**
- Ethosuximide

III. **Drugs that potentiate GABA activity**:
- Stimulate GABA/Cl^- receptor complex.
  - ✓ Phenobarbital & Primidone
  - ✓ Clonazepam, Diazepam & Lorazepam
- Block GABA reuptake
  - ✓ Tiagabine
- GABA-mimetics
  - ✓ Gabapentin
  - ✓ Pregabalin
- Decrease GABA degradation.
  - ✓ Vigabatrin

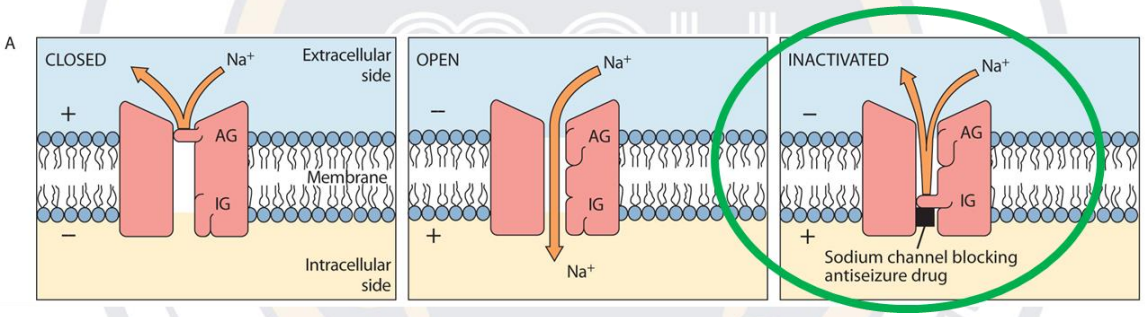
Clinical uses of anti-convulsant drugs

Seizure type	1st choice	2nd choice
Partial and generalized tonic-clonic seizures	• Carbamazepine • Sodium valproate	• Lamotrigine • Phenytoin • Gabapentin • Vigabatrin • Phenobarbital
Absence seizures	• Ethosuximide (children) • Sodium valproate (adults) • Lamotrigine	
Status epilepticus	• Lorazepam • Diazepam	• Phenytoin or fosphenytoin • Phenobarbital

Drugs that inhibit voltage-gated Na^+ channels

Mech. of action

- They block the voltage-gated "fast" Na^+ channels.
- They bind preferentially to inactivated Na^+ channels, preventing them from reopening.
- Use-dependent
  - The highly repetitive depolarization of neurons during a seizure increases the number of Na^+ channels in the inactivated state → more channels are susceptible to the blockade by drugs.
  - Neuronal transmission at normal low frequencies is relatively unaffected because a much smaller number of the Na^+ channels are in the inactivated state.



I. Phenytoin

Indications

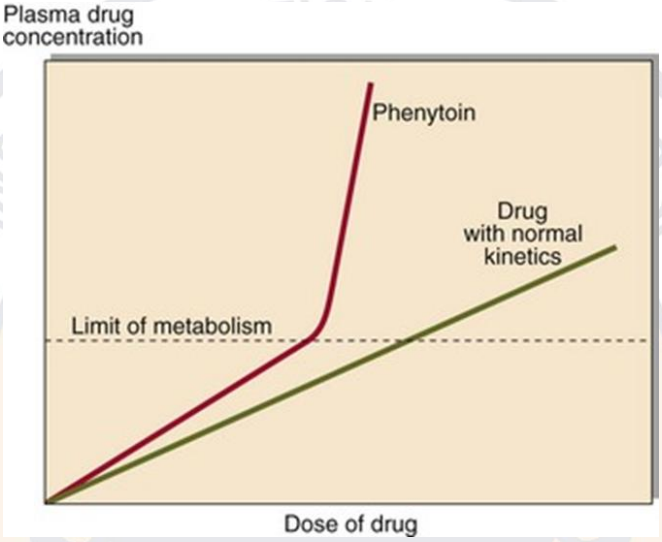
Partial and generalized tonic-clonic seizures.

Adverse effects

- *Dose-related*: Nystagmus, ataxia, diplopia - sedation and confusion (acute toxicity).
- *Non-dose-related:*
  - ✓ *Gum hypertrophy* and *coarsening of facial features.*
  - ✓ *Allergic reactions*, e.g., rash, hepatitis, and *lymphadenopathy*
  - ✓ Hematological effects, e.g., *megaloblastic anemia (folic acid deficiency)*
  - ✓ Endocrine effects, e.g., *hirsutism* (hair growth)
  - ✓ *Teratogenic* effects (it may cause congenital malformations).

Pharmacokinetics

- Phenytoin is no longer a 1st-line treatment for any of the seizures, why?
- Phenytoin has zero-order pharmacokinetics → it is metabolized by hepatic enzymes saturated at therapeutic levels → the relationship between dose and plasma concentration is nonlinear → Small increase in dosage may produce large rises in plasma concentrations.



- Phenytoin has a narrow therapeutic index → needs continuous monitoring of its plasma concentration (total plasma concentrations should not exceed 20 µg/mL)

Drug interactions:

- Phenytoin induces the hepatic CYP450 oxidase system, increasing the metabolism of oral contraceptives, anticoagulants, and dexamethasone.

II. Carbamazepine

Indications

- Partial and generalized tonic-clonic seizures
- Also used in:
  - ✓ Trigeminal neuralgia & neuropathic pain
  - ✓ Bipolar disorder

Adverse effects

- Nystagmus, ataxia, diplopia - sedation and vertigo.
- *Allergic* reactions, e.g., *rash*
- Hematological effects, e.g., *aplastic anemia*
- Endocrine effects, e.g., ↑ ADH secretion → water retention and *hyponatremia*
- *Teratogenic* effects.

Drug interactions:

- Phenytoin induces the hepatic CYP450 oxidase system.
  It accelerates its own metabolism and the metabolism of other drugs.

III. Oxcarbazepine

It is a derivative of carbamazepine and has the same mechanism of action.

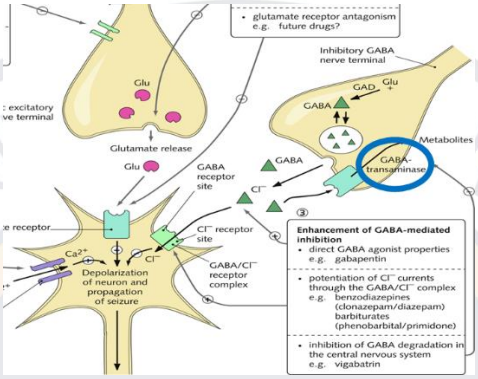
It differs from carbamazepine in:

- Less hepatic CYP450 enzyme induction.
- Lower incidence of aplastic anemia.
- Higher incidence of hyponatremia.

IV. Sodium valproate

Mech. Of action

- Blocks voltage-gated Na+ channels +
- Potentiates GABA action via inhibition of GABA transaminase → decrease GABA metabolism.



Indications

- Partial and generalized tonic-clonic seizures.
- Absence seizures
- Also used in migraine prophylaxis.

Adverse effects

Sodium valproate has fewer side effects.

- Gastrointestinal upset
- Importantly, liver failure, especially if used in combination with other antiepileptics.
- Teratogenic effects (neural tube defects & autism)

Contraindications

- Should not be given to people with liver disease.

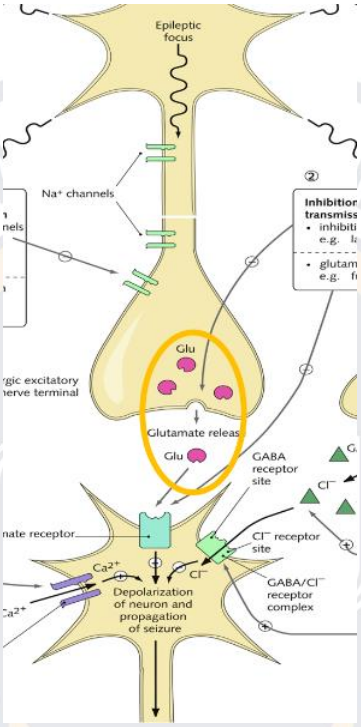
Drug interactions:

- Valproic acid inhibits the hepatic CYP450 oxidase system.

V. Lamotrigine

Mech. Of action

- Blocks voltage-gated Na+ channels +
- Inhibits the release of excitatory glutamate.



Indications

- Partial and generalized tonic-clonic seizures.
- Absence seizures, although it is not as effective as ethosuximide or valproate.
- Also used in bipolar disorder.

Adverse effects

- CNS depression: dizziness, diplopia and sleepiness.
- Rash → may progress to Stevens-Johnson syndrome, toxic epidermal necrolysis, or angioedema, which can be life-threatening.
    - Slow dose titration is essential to reduce the risk of developing a rash.
- Rarely, hepatotoxicity

Contraindications

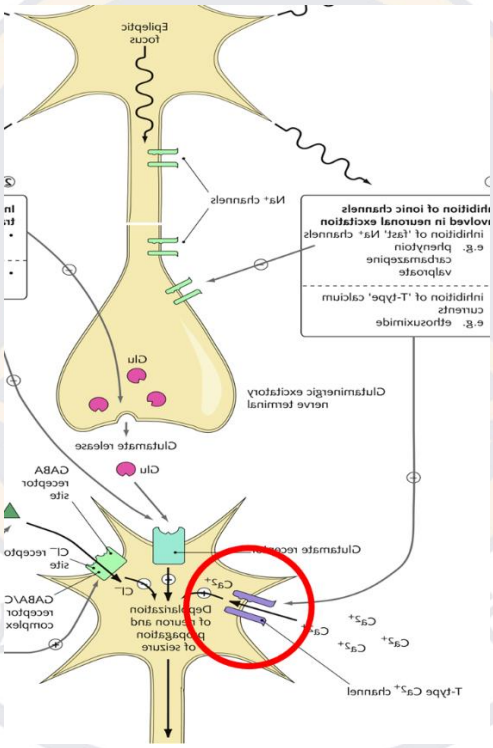
- Should not be given to people with liver failure.

Drugs that inhibit T-type Ca^{++} channels

Ethosuximide

Mech. Of action

Blocks the low-threshold T-Type Ca^{++} channels in the thalamus.



Indications

The drug of choice in simple absence seizures and is particularly well tolerated in children.

Contraindications

CI in tonic-clonic generalized seizures → make them worse.

Adverse effects

- Gastrointestinal upset,
- Drowsiness and mood swings
- Rarely, it causes serious bone marrow depression.

Drugs that potentiate GABA activity:

I. Stimulate GABA/Cl^- receptor complex.

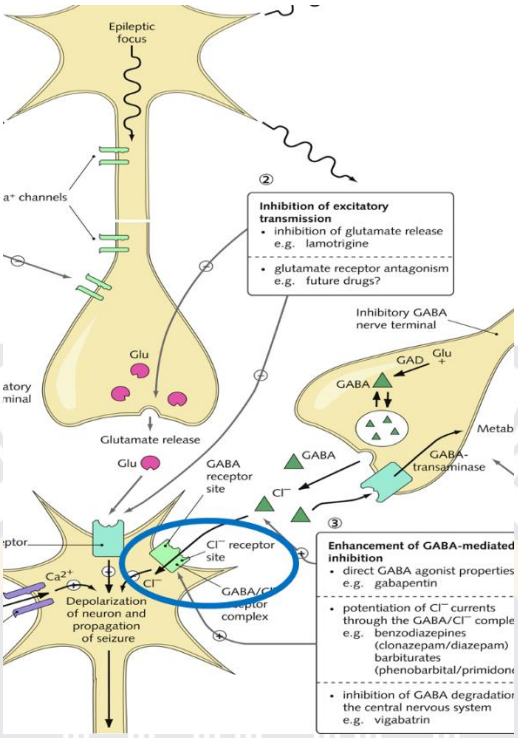
Mech. of action

- Barbiturates, e.g., phenobarbital and primidone
- Benzodiazepines, e.g., lorazepam, diazepam, and clonazepam.

GABA is the major inhibitory neurotransmitter in the brain → it causes fast inhibition through its action on $GABA_A$ receptors.

Barbiturates → act as allosteric activators of $GABA_A$ receptors → prolong the duration of Cl^- channel openings after activation by GABA → neuronal hyperpolarization.

Benzodiazepines → are also allosteric activators of $GABA_A$ receptors, acting at a different site than that of the barbiturates → increase the frequency of Cl-channel openings after activation by GABA → neuronal hyperpolarization.



Phenobarbital

Indications

- Partial and generalized tonic-clonic seizures.
- Status epilepticus

Adverse effects

- Sedation is the main side effect → limits its use clinically,
- Potentially fatal CNS and respiratory depression in overdose.
- Phenobarbital is an inducer of CYP450 → interacts with many medications.

Contraindications

- Should not be used in children, elderly, and people with respiratory depression.

Benzodiazepines

Indications

- Clonazepam → Partial and generalized tonic-clonic seizures.
- Lorazepam (IV) and diazepam (rectal or iv) → Status epilepticus

Adverse effects

- Sedation is the main side effect.
- Respiratory depression

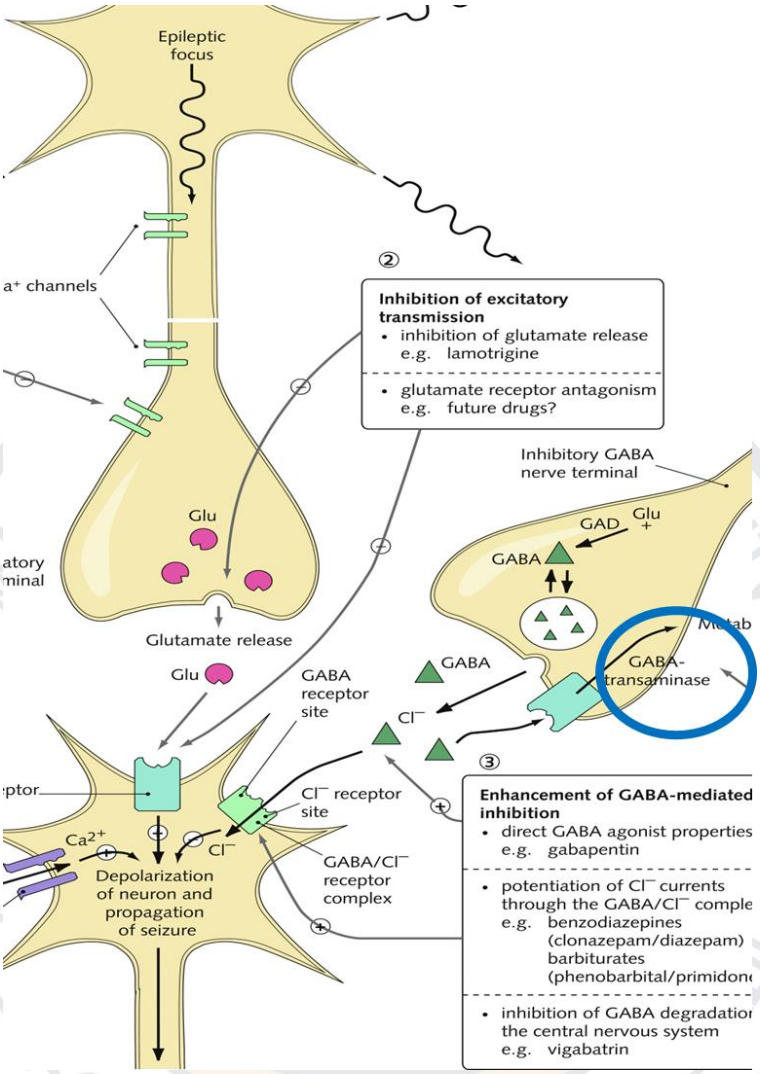
Contraindications

- Should not be used in people with respiratory depression.

II. Potentiate GABA activity:

Mech. of action

- Tiagabine blocks GABA reuptake into presynaptic neurons by inhibiting the GABA transporter (GAT-1)
- Vigabatrin → an irreversible inhibitor of GABA transaminase, the enzyme that inactivates GABA.
- GABA-mimetics, e.g., gabapentin and pregabalin
  They are structurally like GABA but do not affect GABA receptors. Rather, they exert their antiseizure activity by inhibiting the voltage-gated Ca^{++} channels.



Gabapentin & pregabalin

Indications

- Partial seizures
- Neuropathic pain
- Post-herpetic neuralgia

Adverse effects

- Dizziness, ataxia, fatigue
- Weight gain

Contraindications

- Avoid sudden withdrawal
- Avoid use in elderly patients and in those with renal impairment.

Vigabatrin vs Tiagabine

	Vigabatrin	Tiagabine
Indications	Partial seizures	
Adverse effects	Drowsiness, dizziness, visual hallucinations, and visual field defects.	Dizziness, tremor, and difficulty concentrating
Contraindications	Should not be used in people with a history of hallucinations.	

When to start/stop anti-convulsant treatment

It is recommended to start treatment when the patient has suffered two or more seizures within a 2-year period.

Choice of anticonvulsant drug depends on the type of epileptic seizure.

One drug should be used, whenever possible → monotherapy carries the lowest risk of adverse effects.

For most anticonvulsant drugs, the correct dose is the lowest effective dose that does not cause side effects.

Only for refractory cases, more than one drug may be required.

The anticonvulsant drug can be withdrawn after 2 years of being seizure-free.

Is there is a risk of recurrence?

Yes, around 25–40% risk of recurrence. No one can tell exactly, and seizure recurrence is always less if patients continue with treatment indefinitely → the decision to stop treatment is largely a personal one.

Status epileptics

- ☒ Abnormally prolonged (>30 minutes of continuous seizure activity) or repetitive seizures (two or more sequential seizures without full recovery of consciousness between seizures)
- ☒ Status epilepticus is a life-threatening medical emergency that requires immediate treatment because persistent seizure activity causes permanent neuronal injury.
- ☒ Treatment should start when the seizure duration reaches 5 minutes for generalized tonic-clonic seizures and 10 minutes for partial seizures.

1. **Benzodiazepines**
   - Treatment of choice
   - The most used → Lorazepam or diazepam (IV).
   - Recently, midazolam (IM) is tried with equal effectiveness.
2. **IV fosphenytoin or phenytoin**
   - A 2nd therapy if seizures continue.
3. **IV Phenobarbital**

   An acceptable 2nd therapy if seizures continue, but it causes persistent sedation and may induce serious respiratory depression and hypotension.

- ☒ N.B. Refractory status epilepticus → seizures continue following treatment with 1st and 2nd therapy drugs.
- ☒ Refractory status epilepticus is treated with a combination of IV anesthetic drugs.

Antiepileptic drugs during pregnancy

Seizures during pregnancy present risks to the mother and fetus → most women with epilepsy who become pregnant require anticonvulsant drug therapy.

- If possible, valproate, phenobarbital, and topiramate should be avoided, most importantly at the time of conception and early in the pregnancy.
- Lamotrigine and levetiracetam present the lowest level of risk to the fetus → considered for use in pregnancy.
- It is recommended to use the lowest possible doses of anticonvulsant drugs during pregnancy.
- Newborns of mothers who have received enzyme-inducing anticonvulsant drugs during pregnancy may develop a deficiency of vitamin K–dependent clotting factors, resulting in serious hemorrhage during the first 24h of life → prevented by administering IM vitamin K to the newborn shortly after birth.

FACULTY OF MEDICINE
MANSOURA NATIONAL UNIVERSITY

MICROBIOLOGY

Bacterial Meningitis

Meningitis:

Inflammation of the meninges (protective membranes covering the central nervous system).

Clinical types of meningitis:

- **Purulent meningitis:** infections of the meninges associated with a marked, acute inflammatory exudates usually caused by a bacteria.
- **Chronic meningitis:** caused by slow-growing agents (mycobacteria or fungi) that produce granulomatous inflammatory changes.
- **Aseptic meningitis:** commonly caused by virus

Routes of CNS infection

A. Blood-borne spread:

- Most CNS infections result from blood-borne spread; for example, bacteremia or viremia resulting from infection outside the CNS may result in penetration of the blood–brain barrier.
- Examples of infectious agents that commonly infect the CNS by this route are *H. influenzae, N. meningitidis, S. pneumoniae, M. tuberculosis,* and viruses such as enteroviruses.

B. Direct spread:

- Occurs from adjacent infected focus such as middle ear infection (otitis media), mastoiditis, and sinusitis.
- Traumatic, surgical, or congenital lesions may give direct access. For example, fractures of the base of the skull
- The blood–brain barrier is the special defense mechanism of the CNS which serves to minimize passage of infectious agents and toxic metabolites into CSF

Causative organisms of acute purulent meningitis:

- ☒ is usually caused by one of these organisms:
  - *Haemophilus influenzae* type b (Hib).
  - *Neisseria meningitidis (meningococci).*
  - *Streptococcus pneumoniae (pneumococci).*
  - *Listeria monocytogenes*
- ☒ Acute purulent meningitis is caused by encapsulated pathogen.
- ☒ However, many other bacteria can occasionally cause the disease if they gain access to the meninges.
- ☒ N. meningitidis causes epidemic disease.

Bacterial causes according to the age group

- ☒ **Neonates:** *Group B Streptococci, Streptococcus pneumoniae, Listeria monocytogenes, Escherichia coli.*
- ☒ **Infants and young children**: *S. pneumoniae, Neisseria meningitidis, Haemophilus influenzae type B (Hib), Group B Streptococci.*
- ☒ **Teens and young adults**: *N. meningitidis, S. pneumoniae*
- ☒ **Older Adults**: *S. pneumoniae, N. meningitidis. Hib, group B Streptococcus, Listeria monocytogenes*

Mode of transmission (How It Spreads)

- ☒ *Hib, S. pneumoniae and N. meningitidis:* Transmitted by droplet infection during coughing or sneezing
- ☒ Group B *Streptococcus, E. coli and L. monocytogenes:* Mothers can pass these bacteria to their babies during birth.
- ☒ *E. coli and L. monocytogenes* by eating contaminated food.

Neisseria

- Gram-negative diplococci
- All Neisseria are oxidase positive
- The genus contains:
  - ☒ Many commensal species, most of which are harmless inhabitants of the upper respiratory and alimentary tracts.
  - ☒ Two pathogenic species:
    - Neisseria meningitidis (meningococcus), a major cause of meningitis and bacteremia.
    - Neisseria gonorrhoeae (gonococcus), the cause of gonorrhea

Neisseria meningitidis (Meningococci)

- **Morphology**

  Gram negative kidney-shaped diplococci ,non motile ,non-sporulated and have polysaccharide capsule

- **Culture characters**
  - ☒ Aerobic, optimum temperature is 37°C.
  - ☒ 10 %Carbon dioxide enhances growth.
  - ☒ Cannot grow on ordinary media
  - ☒ Grow on chocolate agar or selective media (Thayer-Martin media).
- **Antigenic composition of Neisseria meningitidis**
  - ☒ Polysaccharide capsule: classified into 12 serogroups according to the capsular polysaccharides
  - ☒ The most important disease-producing serogroups are A, B, C, W-135, and Y.

- ☒ Group A strains can cause widespread epidemics.
- ☒ The group B polysaccharide differs from that of the other groups in failing to stimulate the production of bactericidal antibody due to the similarity of its sialic acid polymer to human brain antigens.
- ☒ Recently, in sub-Saharan Africa, (X)

Virulence factors of Neisseria meningitidis

1. Polysaccharide capsule (the most important)
   - antiphagocytic.
   - enables meningococci to resist complement-mediated bactericidal activity and subsequent neutrophil phagocytosis
2. Pili and outer membrane proteins for adhesion.
3. IgA proteases which inactivate IgA.
4. Endotoxin damage the ciliated cells.

Pathogenesis of meningococcal meningitis

- ☒ Source: Case or Carrier
- ☒ Meningococci are found in the nasopharyngeal flora of approximately 10% of healthy individuals
- ☒ Transmission:
  - Transmitted by inhalation of respiratory droplets, then spread from the nasopharynx to blood causing bacteremia, endotoxemia and meningitis.
  - Most common age of infection is between 6 months and 2 years of age, which is the time between loss of trans-placental antibody and the appearance of naturally acquired antibody
  - Complement deficiencies enhance risk

Clinical Manifestations

- Fever
- headache
- Stiff neck or back (rigidity)
- Nausea, and vomiting
- N. meningitidis infections may be accompanied by rash, thrombocytopenia, and other manifestations associated with endotoxemia.

Laboratory diagnosis of meningococcal meningitis

☒ **Samples:**

- CSF is the proper sample for diagnosis (3-10 ml), obtained by lumbar puncture under complete aseptic precaution.
- blood, or skin lesions samples can be also used for diagnosis.
- nasopharynx: carrier or early in the disease.

☒ **CSF is examined for:**

- Physical (pressure , turbidity)
- chemical (protein, and glucose)
- Haematological (cells)
- Bacteriological characters (microscopy and culture)

A. In acute bacterial meningitis, CSF is

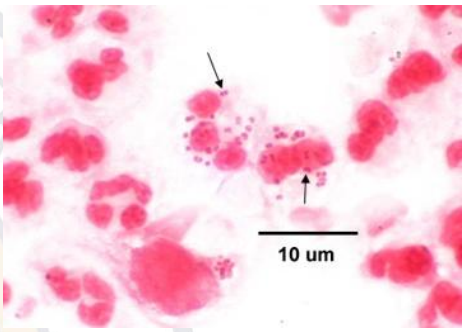
- Turbid, under tension, low glucose value, high protein level, and contains polymorphonuclear cells

NB : Polymorphonuclear cells are not usually seen in normal CSF

B. Direct film

- Direct Gram smears of CSF in meningitis usually demonstrate the typical bean-shaped, Gram-negative diplococci inside and outside the polymorphonuclear cells.
- Detection of intracellular Gram negative diplococci is diagnostic of meningococcal meningitis.

C. Culture



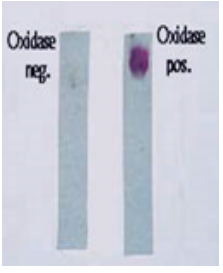
1. Culture characters:

- Aerobic.
- Optimum temperature: 37 °C, with narrow temperature range (30-38°C), no growth at 22°C.
- 10% Co2 and moist atmosphere are required for growth.

2. Media:

- cannot grow on ordinary media
- can grow on chocolate agar.
- Thayer-Martin media is selective media for Pathogenic Neisseria, contains antimicrobials which inhibit the growth of organisms other than pathogenic *Neisseria*.
  - **V**ancomycin kill most gram-positive bacteria
  - **C**olistin kill most gram-negative bacteria including the commensal *Neisseria* spp.,except pathogenic *Neisseria*
  - **N**ystatin kill most fungi.

D. Biochemical reactions:



1. **Oxidase test:** all pathogenic Neisseria are oxidase positive.
2. **Sugar fermentation:** *N. Meningitidis* ferment glucose and maltose with acid production.

E. Serological test

Detection of meningococcal antigen

☒ Rapid diagnosis: may be obtained by detection of meningococcal antigen in CSF.

☒ Help if patient started antibiotics

☒ Latex agglutination available for N. meningitidis groups A,B,C,Y and W135

Prevention of meningococcal meningitis

☒ **Meningococcal Vaccines**

- Meningococcal conjugate vaccines (MenACWY vaccines).
- Serogroup B meningococcal vaccines (MenB vaccines).

☒ **Chemoprophylaxis**

- In case of close contact with meningococcal meningitis case.
- Rifampicin or Ciprofloxacin is the chemoprophylactic agent of choice.
- Ceftrixone, an alternative

Treatment:

☒ Penicillin, Ampicillin and Ceftriaxone are used to treat meningitis

☒ Ceftriaxone is the drug of choice during epidemics because of its antimeningococcal activity and good CSF penetration .

Laboratory diagnosis of other causes of bacterial meningitis

- **Sample:** CSF.
- **Direct film stained by Gram stain:** usually demonstrate inside and outside the polymorphonuclear cells the causative organism:
  - ☒ H. influenzae: Gram-negative cocco bacilli.
  - ☒ Streptcoccus pneumoniae : Gram - positive capsulsated diplococci
  - ☒ Listeria: Gram positive bacilli arranged in short chains.
  - ☒ Mycobacterial meningitis:
    - CSF is less turbid.
    - CSF contains lymphocytes; low glucose and high protein levels.
    - Direct film of CSF is examined by Ziehl-Neelsen stain to demonstrate acid fast bacilli

Listeria monocytogenes

Natural habitat

- Listeria species are widely distributed in nature.
- Found in humans, animals, birds, fish, oysters & ticks.
- It is carried in intestinal tract of 2 to 12% of humans without any symptoms.
- It causes listeriosis in animals and humans.

Morphology:

Small gram positive rods, arranged in short chains, non- sporing, non-capsulated, motile at 22–25°c, but are non-motile at 37°c as peritrichate flagella are produced at room temperature but not at 37°c .

Cultural characters:

- Grows on ordinary medium.
- Produces β- hemolysis on blood agar.
- The optimal growth temperature for is 30-35° C.
- Can grow slowly in the cold even at temperatures as low as 1°C, so can grow in contaminated food stored in the refrigerator .

Virulence factors of L. monocytogenes

☒ **Growth at low temperatures:** L. monocytogenes can grow at low temperature so it can accumulate in contaminated food stored in the refrigerator.

☒ **Motility:** Which may help in attachment and penetration of the intestinal mucosa

- **Adherence and Invasion:** Listeria can attach to and enter mammalian cells using a surface protein called internalin. The bacteria are then taken up by phagocytes.
- **Facultative intracellular bacteria:** After engulfment, the bacterium may escape from the phagosome before phagolysosome fusion occurs by toxin, which also acts as a hemolysin (listeriolysin O).

Listeriosis

Infection is transmitted by:

- Eating contaminated meat, vegetables, and milk products as L. monocytogenes can multiply at low temperatures, so it can contaminate food stored in the refrigerator
- Congenital transmission across the placenta (Intrauterine infection)
- Birth canal transmission can occur during labor by bacteria colonizing the genital tract of the mother.
- The risk of disease is increased at the extremes of life (in infants less than 1 month of age or adults over 60 years of age and immunocompromised individuals as well as women in late pregnancy .

Clinical features

- Range from mild influenza-like symptoms to meningitis
- Congenital listeriosis causes: abortion, stillbirth, delivery of infant with signs of congenital infection
- When infection is acquired during labor by bacteria colonizing the genital tract of the mother, meningitis occurs.
- Immunocompromised hosts are more susceptible to serious generalized infections

Diagnosis of listeriosis

- Sample: CSF, blood, or focal lesions.
- Direct Gram stained smear: In meningitis, Gram-positive rods arranged in short chains in CSF
- Culture:

- Culture on blood agar produces β- hemolytic colonies.
- Blood and CSF culture reveals Gram-positive rods arranged in short chains .

Treatment:

- L. monocytogenes is susceptible to penicillin G, ampicillin, and trimethoprim/sulfamethoxazole, all of which have been used effectively.
- Ampicillin combined with gentamicin is considered the treatment of choice for fulminant cases.
- Erythromycin is also effective.

Control

- No vaccines are currently available
- Hygienic food processing and storage
- Individuals in high-risk groups should avoid uncooked food.
- A safe water supply and proper disposal of feces is important.

Viral meningitis

Also known as aseptic meningitis, is a type of meningitis due to a viral infection. It results in inflammation of the meninges (the membranes covering the brain and spinal cord).

Signs and symptoms:

- **Fever**
- **headaches**
- **Neck stiffness**.

In contrast to bacterial meningitis, symptoms are often less severe and do not progress as quickly.	**Nausea, vomiting, photophobia (light sensitivity), muscle aches and malaise due to meningeal irritation.** **Increased cranial pressure**	**In severe cases, people may experience concomitant encephalitis (meningoencephalitis), which is suggested by symptoms such as altered mental status and seizures.**

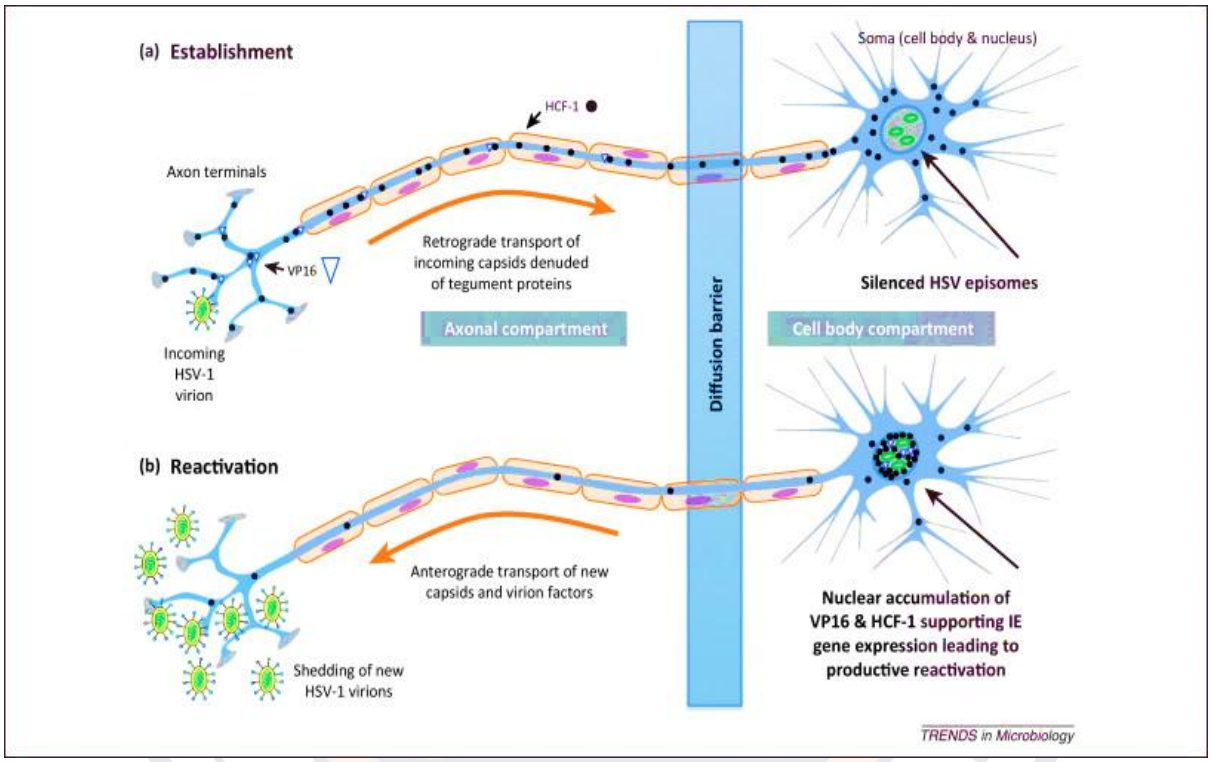
Causative agents of viral meningitis:

- Enteroviruses: Echovirus, Poliovirus, Coxsackie A virus
- Herpes: Herpes simplex virus type 1 (HSV-1 / HHV-1) or type 2 (HSV-2 / HHV-2), Varicella zoster (VZV / HHV-3); also causes chickenpox and shingles (herpes zoster), Epstein–Barr virus (EBV / HHV-4), Cytomegalovirus (CMV / HHV-5).
- Measles, Mumps, influenza.
- Human immunodeficiency virus (HIV).
- Lymphocytic choriomeningitis virus (LCMV).
- St. Louis encephalitis virus, West Nile virus.

Herpes viruses

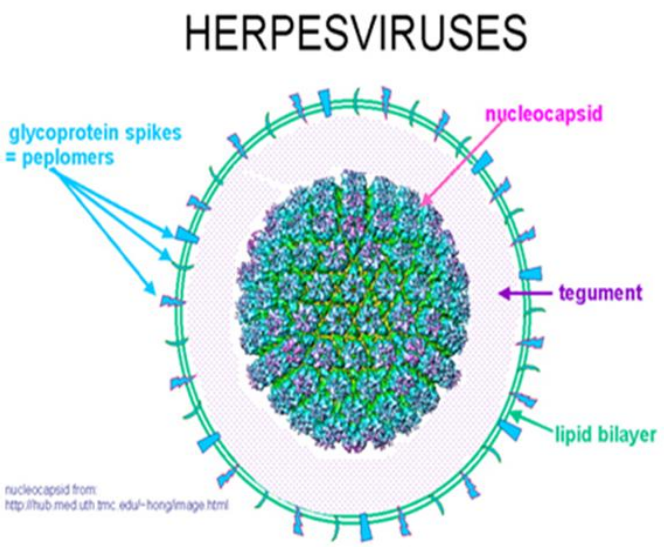
Eight human herpesvirus species are known.

- **All have the ability to enter a latent state following primary infection and to be reactivated at a later time.**



Structure:

- Virion: icosahedral
- Genome: Double stranded DNA, linear
- Envelope: Contains glycoprotein spikes



Classification of Herpesviruses

They have been divided into three subfamilies:

Alpha herpesvirinae	*Gamma herpesvirinae*	*Beta herpesvirinae*
Herpes simplex virus types 1 (HSV-1 or HHV-1)	Epstein-Barr virus (HHV-4).	Cytomegalovirus (HHV-5)
Herpes simplex virus types 2 (HSV-2 or HHV-2)	Kaposi's sarcoma-associated herpes virus (KSHV) or (HHV-8).	Human herpes viruses types 6 (HHV-6)
Varicella – Zoster virus (VZV or HHV-3).		HHV-7.

Herpes simplex viruses

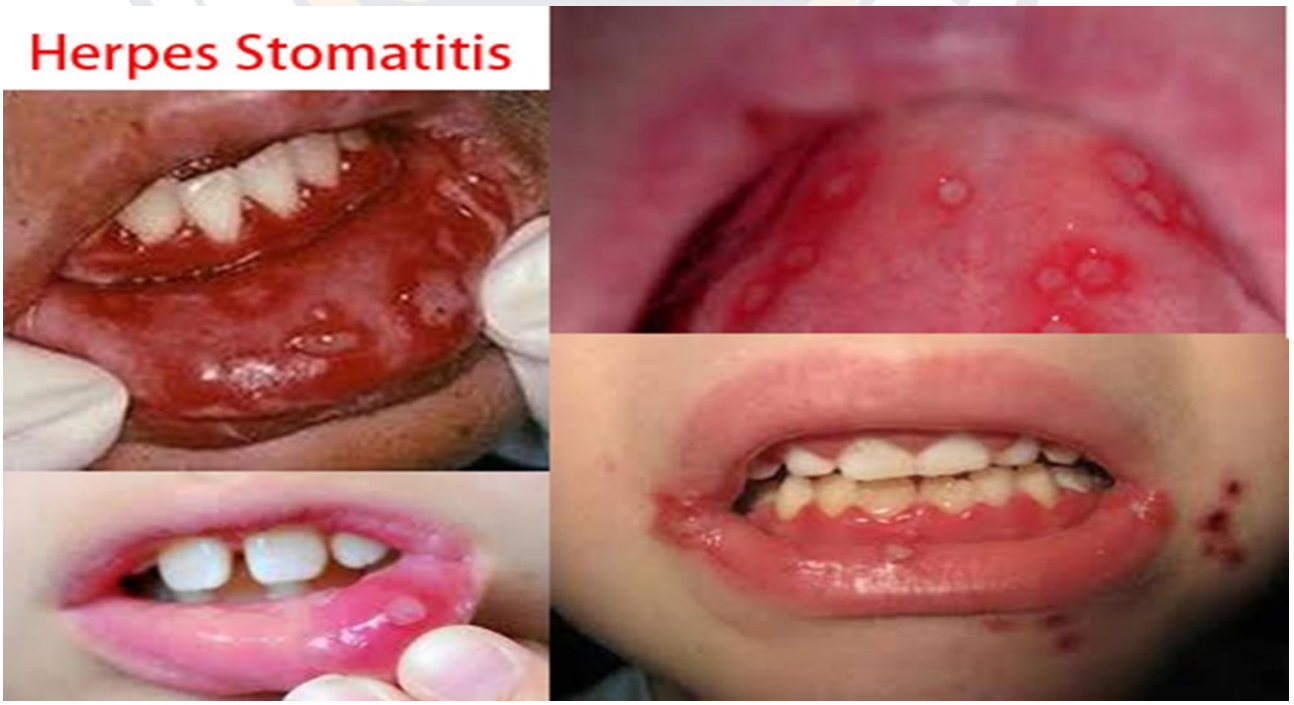
- There are 2 distinct herpes simplex viruses, type 1 and type 2.
- The two viruses cross-react serologically but some unique proteins exist for each type.

Transmission and pathogenesis:

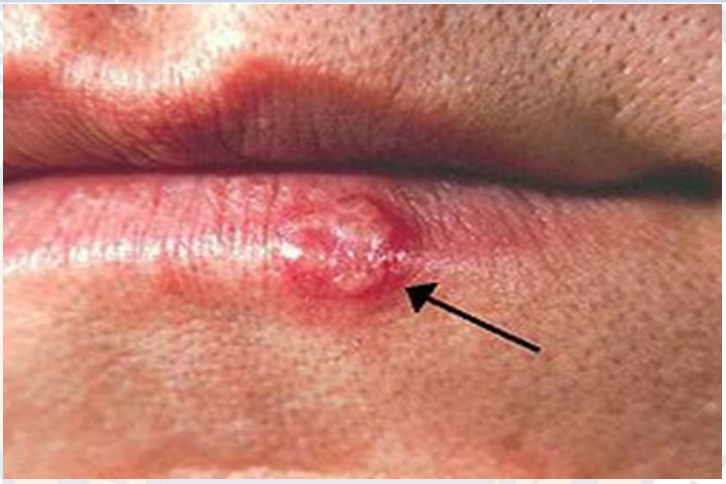
	HSV-1	HSV-2
Mode of transmission	Primarily in saliva (kissing)	by sexual contact
• Multiplies locally in the mucous membrane or a braded skin causing vesicular lesion.		
Site of lesion	Mainly orofacial lesions	Genital lesions
However, both types of HSV can infect oral or genital mucosa depending on regions of contact.		

Clinical syndromes

	HSV-1	HSV-2
Primary infection	- Acute gingivostomatitis. - Herpes libialis (cold sores - Herpetic whitlow: is a pustular lesion of the skin of finger or hand of medical personnel. - Keratoconjunctivitis, encephalitis. - Disseminated infections, such as esophagitis and pneumonia in immuno-compromised.	- Genital herpes: vesiculo-ulcerative lesions on external genitalia as well as the cervix. - Neonatal infection: Originates chiefly from contact with vesicular lesions within the birth canal. Neonatal herpes varies from a severe generalized disease often involving the CNS, through milder local lesion to asymptomatic infection. - Aseptic meningitis.



	HSV-1	HSV-2
Latency	• Trigeminal ganglia.	• Sacral ganglia.
Reactivation:	• In response to stimuli as common colds, hormonal changes and sunlight.	
	• Cold sores. • Keratitis	• Occur more frequently. • Often asymptomatic but still results in viral shedding.



Diagnosis:

- Detection of viral particles.
- Virus isolation from herpetic lesions
- Serologic diagnosis.
- Histological staining (Giemsa stain) of scrapings or swabs from the base of skin lesions.

Treatment:

- Acyclovir, Famciclovir, and Valacyclovir are the treatment of choices.
- It shortens the duration of the lesion and decreases shedding of the virus.
- No drug treatment prevents recurrences.
- No effect on the latent state.

Varicella-Zoster virus

A. Primary infection: Varicella or chicken pox.

I.P: 14-21 days **Transmission and pathogenesis:** by droplets and by direct contact with the lesions	**Clinical findings:** A mild febrile illness with a characteristic vesicular rash which starts on the trunk and spreads to the limbs and face. Vesicles appear in successive waves so that the lesions of different stages are present together. **Complications of Varicella** are rare as meningitis, encephalitis and pneumonia.

Neonatal Varicella

- Early in pregnancy: fetal infection is uncommon, but can result in multiple developmental abnormalities (damage to the lens, retina and brain).
- Near the time of birth: fetal infection is more common and may exhibit typical varicella at birth or shortly thereafter.
- The severity of the disease depends on whether the mother has begun to produce anti-VZV IgG by the time of delivery or not.

B. Latency

- Trigeminal and dorsal root ganglia being most common sites of latency.

C. Reactivation (Zoster or shingles)

- Zoster is a sporadic disease of adults or immunosuppressed patients.
- Painful vesicles along the course of a sensory nerve of the head or the trunk (a belt of roses from hell). The pain can last for weeks and post-zoster neuralgia may exist.
- In immunocompromised, disseminated infection as pneumonia can occur.

Diagnosis:
• Mainly clinically. But, laboratory diagnosis can be done as on the same line used for HSV. • A rise in antibody titer can be used to diagnose varicella, but is less useful in diagnosis of zoster, since antibody is already present.
Treatment:
• No antiviral therapy is necessary for chicken pox in normal • Systemic disease in immunocompromised patients can be treated with acyclovir.
Prevention:
• Varicella-Zoster immunoglobulin (VZIG): Can be used to prevent varicella and disseminated zoster in immunocompromised people exposed to the virus. • VZV vaccine: a live attenuated vaccine, one dose is recommended for children 1 to 12 years of age. It prevents varicella, but zoster still occurs in those previously infected because the vaccine does not eliminate the latent state.

characters	Chicken pox (varicella)	Shingles (Zoster)
Symptoms	Fever itching rash	Painful vesicles along the course of a sensory nerve of the head or the trunk (a belt of roses from hell). The pain can last for weeks and post-zoster neuralgia may exist.
Rash	Itching Non grouped vesicles.	Painful Grouped vesicles
Complications	rare	More often

characters	Chicken pox (varicella)	Shingles (Zoster)
Definition	Contagious disease causes by infection with varicella-zoster virus	Infection of nerve and skin around them, caused by reactivation of Varicella-zoster virus
Age of the patient	All ages are susceptible but, much more common in children	Occur in adults
Transmission	By air droplet pathway.	After chicken pox, the virus remains latent in the nerve ganglia. Under certain conditions, the virus is activated
Type of the infection	Primary infection	Reactivation of old infection

Cytomegalovirus (CMV)

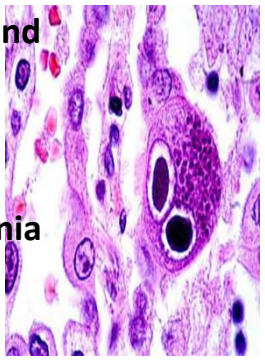
Transmission and pathogenesis:

Early in life:	Later in life:
- Transplacentally - within birth canal - Via breast milk.	- Saliva (most common route), - Sexually, - Blood transfusion - Organs transplant.

Clinical Significance:

A. Primary infection:

In healthy individuals may cause:



- **Asymptomatic infection with intermittent shedding in saliva and urine.**
- **Infectious mononucleosis –like syndrome: similar to EBV infection but heterophil antibodies negative.**
- **Infection of immunodeficient patiants. Hepatitis and pneumonia are common,**
- **Congenital infections: the most common intrauterine viral infection:**
- In-utero it causes abortion, still birth or cytomegalic inclusion disease. Mental retardation, microcephaly blindness and deafness.
- Perinatal infection from the birth canal or from the milk usually subclinical infection.

B- Latency and reactivation:

- Latency is established in monocytes, macrophages and kidney.
- Repeated episodes of asymptomatic virus shedding over prolonged periods of times.

Diagnosis:

- Virus isolation in cell culture, CPE is 2-3 weeks (typical swollen and translucent cells with intranuclear inclusion bodies.
- Fluorescent antibody & histological staining of inclusions in giant cells in urine and in tissue. The inclusion bodies are intranuclear oval (owls eye) shape
- PCR for detection of CMV nucleic acid in tissues or body fluid as CSF.
- Serological test to detect rising IgG titer or IgM.

Treatment: Gancyclovir

Preventive measures:

- For pregnant women, the saliva and urine of infected children are the main sources of CMV infection.
- Secondary source is sexual contact.

Prevention behaviors:

Hygiene and behavioral measures that may be taken in order to reduce the viral spread:

- Hand washing whenever there is contact with a child saliva or urine,
- Do not sharing drinking glasses or eating utensils with young children,
- Do not kissing young children on the mouth or cheek.
- All women who are CMV seronegative and are planning to become pregnant or are pregnant should be informed about the risks of fetus infection and transmission.

Epstein Barr virus (EBV)

- EBV is structurally and morphologically identical to other herpesviruses but is genetically different
- **Transmission** of EBV occurs by intimate contact with infected saliva.
- Viral replication occurs in oropharyngeal epithelium.
- Then some of progeny virus infect B lymphocytes → polyclonal B cells proliferation & non-specific increase of IgM, IgG and IgA.

- **Infected B cells are rejected by cytotoxic T cells which change in shape and appear as atypical T lymphocytes in peripheral blood**

Clinical Significance:

1. **Infectious mononucleosis:**
   - Disease is manifested by fever, headache, malaise,
   - Lymphadenopathy and increased level of liver enzymes
   - EBV and malignancies:
   - Burkitt's lymphoma (jaw malignancy in African children)
   - Nasopharyngeal carcinoma.

3- Latency and reactivation: in B lymphocytes,

- reactivation, results in lytic cycle

Laboratory diagnosis:

- Blood smear to detect lymphocytosis.

Detection of EBV in patieint's peripheral lymphocytes by DNA hybridization.

- Detection of heterophile antibodies.
- Detection of EBV specific antibodies.
- Virus isolation from saliva.

No drug available to treat EBV. Vaccine is being developed.

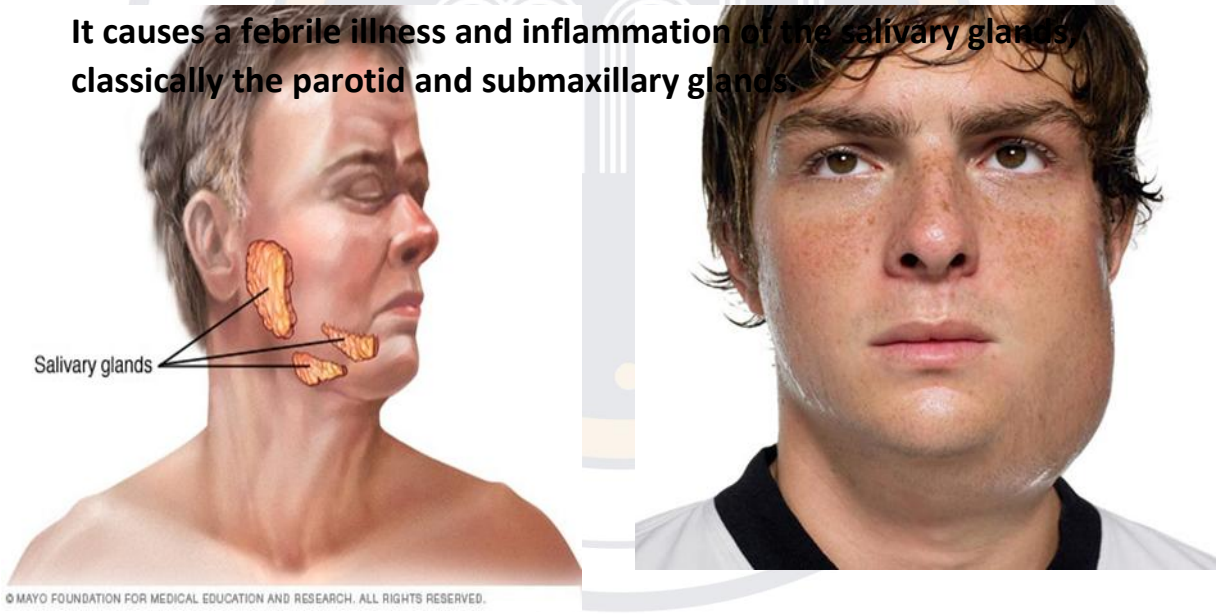
Mumps Virus

Mode of transmission:

Spread by the respiratory route, and has a relatively long incubation of (21 days).

Clinical picture:

It causes a febrile illness and inflammation of the salivary glands, classically the parotid and submaxillary glands.



Complications:

- **Aseptic meningitis:** fairly common complication. In about half of the mumps meningitis cases, parotitis will not be apparent.

Mumps meningoencephalitis: is rare but a more serious development.

- **Orchitis:** can occur, more often after puberty, but is rarely followed by infertility. Other glandular tissue is very occasionally involved e.g.. pancreatitis, oophoritis or thyroiditis.

Diagnosis:

- Isolation of the virus from saliva, CSF or urine by culture on monkey kidney cells.
- Serologically: Confirmed Diagnosis by positive IgM antibodies by using CF, HI and ELISA.

Prevention:

- Live attenuated virus vaccine given in MMR vaccine.

Measles Virus

Mode of transmission:

- Measles is **one of the most infectious diseases** known.
- **Transmission is by respiratory droplets.** After infecting the cells lining the upper respiratory tract, the virus enters the blood and spreads to the skin. The virus can also infect via the eye and multiply in the conjunctivae.
- **Incubation period:** 10-12 day.

Clinical manifestations:

- Prodromal phase is characterized by fever, dry cough, sore throat, conjunctivitis, and Koplik's spots (raised red spots with white centers in the mouth).
- After few days, the characteristic red, maculopapular rash starts on the head and then spreads to body.

Complications:

- Bronchopneumonia and otitis media (with or without secondary bacterial infections).
- Encephalitis occurs in ~1:2000 cases.
- Subacute sclerosing pan-encephalitis: It is a chronic infection in which the virus multiplies in the brain resulting in neurodegenerative disease.

Diagnosis

- Measles is easy to diagnose clinically. Laboratory diagnosis is rarely needed.

Prevention

Trivalent live attenuated vaccine (MMR) is usually given by subcutaneus injection. It is given at 12 – 15 months age. A single dose of the MMR vaccine gives around 90% protection against measles and mumps and 95-99% against rubella.

Treatment

- No specific drugs.
- Symptomatic treatment only.

Case scenario, Clinical Correlate, Practice points:

- A 16 year-old boy presented with a one week history of sore throat, fever and profound fatigue. Physical examination revealed a fever of 39.5°C, cervical lymphadenopathy, exudative pharyngitis and mild hepatosplenomegaly. His WBCs was 12.500/µl with 20% neutrophils, 24% monocytes, 42% lymphocytes, 12% atypical lymphocytes. A rapid serologic test performed at physician office revealed the presence of heterophil antibodies.
- What is the cause of this body illness?
- Define the most likely case diagnosis?
- What is the most likely causative organism?
- Identify the pathogenesis of the causative organism?

Viral and Fungal encephalitis

ILO1: - List the causative organisms of encephalitis (viral, fungal, bacterial).

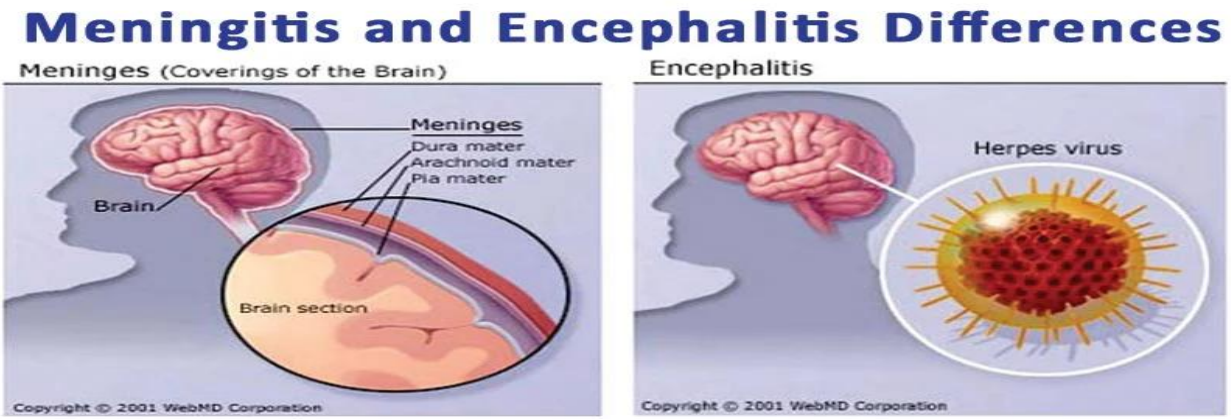
Definitions

Encephalitis

Inflammation of the brain parenchyma associated with clinical evidence of brain dysfunction usually a result of viral infection.

Meningitis: Inflammation of the meninges.

Meningoencephalitis: Inflammation of the meninges and brain parenchyma.



Causes of Encephalitis:

Viral:

1. **Common Viruses**

- Herpes Simplex Virus (HSV-1 & HSV-2): Most common cause, especially HSV-1. Can be severe and life-threatening.
- Varicella-Zoster Virus (VZV):
- Epstein-Barr Virus (EBV):
- Cytomegalovirus (CMV):

2. Arboviruses (Mosquito- or Tick-Borne Viruses)

- West Nile Virus: Leading
- Japanese Encephalitis Virus:
- Zika Virus: Can cause encephalitis, especially in newborns.
- St. Louis Encephalitis Virus:
- Tick-borne Encephalitis Virus:

3. Enteroviruses

- Coxsackievirus & Echovirus.:
- Poliovirus: Rare due to vaccination but can cause encephalitis.

4. Rabies Virus

5. Measles, Mumps, and Rubella Viruses

- Rare due to vaccination but can cause post-infectious encephalitis.
- Subacute Sclerosing Panencephalitis (SSPE): A late complication of measles.

6. Human Immunodeficiency Virus (HIV)

Fungal: Candida, Mucor, Aspergillus, Cryptococcus.

Bacterial: N. Meningitidis, Mycoplasma, Pneumococcus, Treponema pallidum.

ILO2: - Differentiate between primary and secondary viral encephalitis.

Viral Encephalitis

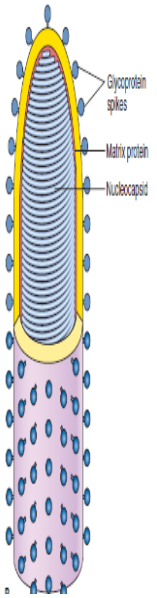
Primary Encephalitis:

- Direct infection of the brain & spinal cord.
- Eastern equine encephalitis virus, Western equine encephalitis virus (rare in Egypt due to cross immunity with West Nile Fever Virus) and Rabies virus and La Crosse encephalitis virus

Secondary encephalitis:

- An infection first occurs elsewhere in the body then travels to the brain. May results from a faulty immune system reaction to an infection elsewhere in the body (post-infection encephalitis).
- Measles, rubella and Varicella zoster Virus.

ILO3: - Identify morphology, pathogenesis, laboratory diagnosis, treatment and vaccination of rabies.



Rhabdoviruses

- Rhabdo in Greek means 'rod-shaped'.
- Virus particles have unique bullet-shaped appearance.
- Nucleocapsid: (-) sense ss RNA associated with nucleoprotein.
- Virus has lipid enveloped with prominent glycoprotein spikes on surface (G protein- hemagglutinates RBCs) & the matrix protein lining the envelope.

Rabies Pathogenesis

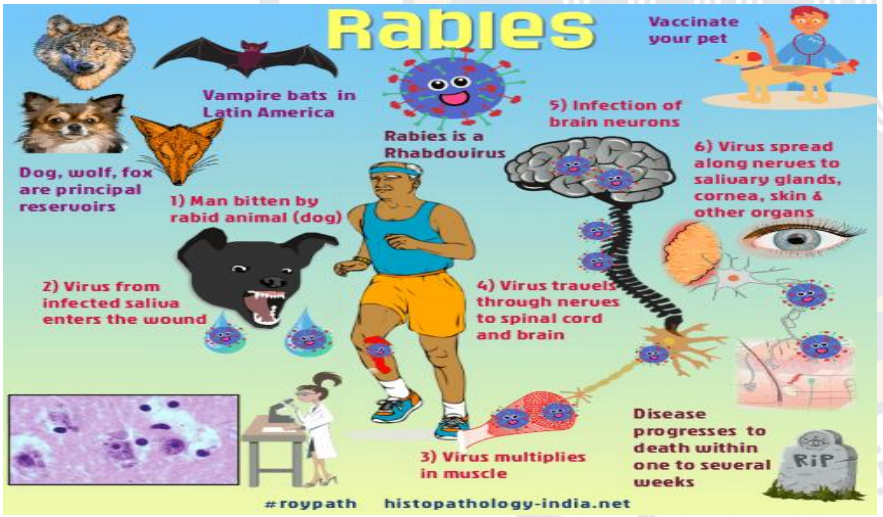
- Rabies **(the word is from the Latin for rage or madness).**

- Transmission **occurs by bite of an infected rabid animal (Rabies virus in dog's saliva, Zoonotic infection).**
- Normal hosts: **foxes, dogs, cats, bats, camels.**
- I.P: **varies from 3-8 weeks to 1 year depending on size & site of inoculation (head/face/neck vs. hands or feet).**
- Viral multiplication and spread

Viral entry occurs from wound or abrasion of skin (site of the bite) directly into blood.

Primary replication of the rabies virus occurs locally in muscle & connective tissue (no symptoms).

Virus then infects peripheral nerves {PNS} then travels along neuronal axons to CNS, to produce photophobia, hydrophobia, severe and fatal encephalitis. Few cases escape these severe consequences.



Rabies Diagnosis

- Specimen: saliva, serum, spinal fluid, and skin biopsies of hair follicles at the nape of the neck and infected brain (postpartum and in animals).
- Detection of viral antigens or nucleic acid: IF & RT-PCR.
- Histopathological diagnosis by detection of Negri bodies in the brain or the spinal cord.

- Isolation of the virus: infected tissue is inoculated into a suckling mice result in encephalitis & death.

Rabies treatment and Vaccination

In veterinary medicine: rabies vaccines are used as a preventive measure.

Vaccination of humans:

- Takes place mainly after exposure to a rabid animal (not to prevent infection but to moderate the severity of the disease).
- In the case of severe exposure: vaccination is often accompanied by injection of rabies immunoglobulin (IG).

Rabies Human Vaccines

- ✓ Nerve Tissue Vaccine: Culture the virus on infected sheep, goat, or mouse brain then inactivated, causes post vaccination encephalitis.
- ✓ Duck embryo Vaccine: culture the virus in embryonated duck eggs then inactivated, 21 injections.
- ✓ Human diploid fibroblast vaccine: culture the virus on human fibroblasts then inactivated, safe, effective but expensive, 6 injections.

ILO4: Fungal Encephalitis

Mucormycosis (Zygomycosis)

Opportunistic mycosis .

Patients: acidosis associated with diabetes mellitus, corticosteroids treatment, sever burn & other debilitating diseases

Etiology: Rhizopus (R. oryzae), Rhizomucor & Mucor.

Clinical Diseases

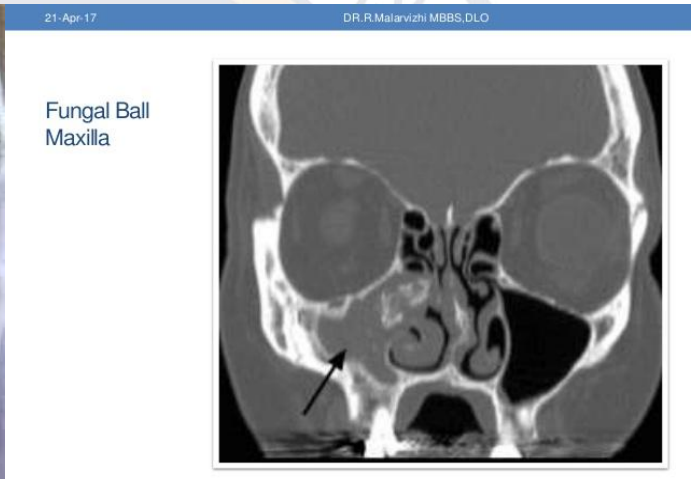
1. Rhinocerebral mucormycosis :

-results from germination of the spores in nose & invasion of the hyphae into blood vessels (angiotrophic), causing thrombosis & infarction .

-The disease progress rapidly with invasion of sinuses, eye, cranial bone & brain. Blood vessels & nerves are damaged.

2 .Thoracic mucormycosis :

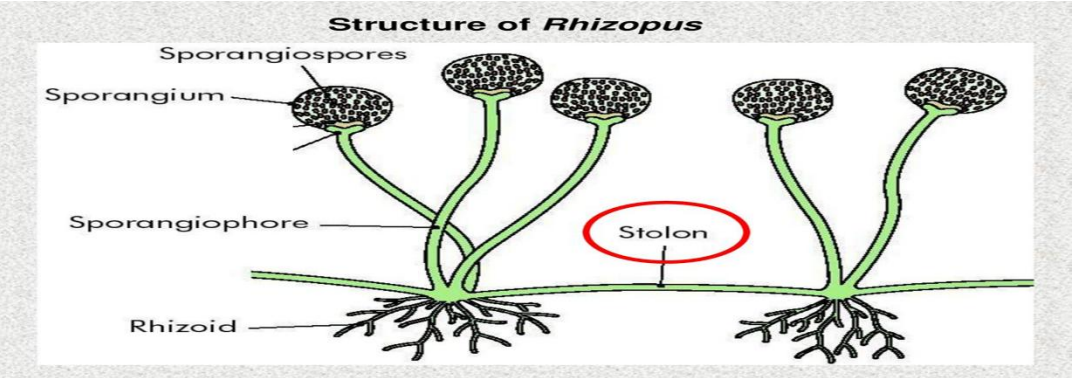
-follows inhalation of the spores with invasion of lung parenchyma & vasculature causing ischemic necrosis & massive tissue destruction .



Laboratory Diagnosis

- Specimen: nasal discharge, tissue or sputum.
- Examination:
  - 10% KOH mount of sample: irregular branching broad hyphae & sparse septations, sporangia containing sporangiospores.
  - Culture on SDA without cycloheximide to show:
    - Rapidly growing cottony colonies
    - Hyphae are hyaline

- Spores are gray to black
- Colony gray to black appearance like dirty snow.



Case Scenario

A 36-year-old man was bitten by his unvaccinated dog and had a deep laceration on the right leg. A week later the man developed fever, headache, and malaise. Three days later, he had agitation, confusion, photophobia, and hydrophobia. On examination, neck rigidity was absent with muscle spasms in all limbs.

Questions

Define the most likely case diagnosis?

What is the most likely causative organism?

What is the morphology of the causative organism?

Identify the pathogenesis of the causative organism?

Describe the laboratory diagnosis of this case.

What is the appropriate treatment of this case?

Western equine encephalitis virus is the causative agent of

a- Pneumonia.
b- Primary encephalitis.
c- Secondary encephalitis.
d- Syphilis.
e- Dermatitis.

Rabies virus belongs to

a. Orthomyxoviruses.

b. Paramyxoviruses.

c. Rhabdoviruses.

d. Togaviruses.

e. Arenaviruses.

FACULTY OF MEDICINE
MANSOURA NATIONAL UNIVERSITY

PARASITOLOGY

Parasitic Infections Affecting Central Nervous System and Special Sense

Parasites affecting CNS:

Parasites:	Diseases:
1. Naegleria fowleri	Primary amoebic meningoencephalitis
2. Acanthamoeba castellani	Granulomatous amoebic meningoencephalitis
3. Trypanosoma bruci	Sleeping sickness
4. Taenia solium	Neurocysticercosis
5. Entamoeba histolytica	Secondary amoebic cerebral abscess

Parasites affecting special sense:

Parasites:	Diseases:
Acanthamoeba castellani	Keratitis & corneal ulcers
Taenia solium	Neurocysticercosis
Onchocerca volvulus	Onchocerciasis

Free-living amoeba

1. Naegleria fowleri
2. Acanthamoeba castellani

Naegleria fowleri

(Brain-eating amoeba)

- **Geographical distribution:** Cosmopolitan.
- **Morphology:**

☒ **Trophozoite:**

a. Amoeboid form:

- Shape: broad anterior, Size: 20 µ. - Nucleus with large central karyosome.
- Actively motile with broad pseudopodia. - It inhabits CNS tissues and CSF.

b. Flagellate form:

- Shape: Pear-shaped, two long flagellae.
- Present in warm water. - It is not present in tissues.

☒ **Cyst:**

- Shape: Rounded with double wall. Size: 10 µ.
- It presents only in soil.

- **Life cycle:**

☒ **Habitat:** Soil and warm fresh water. In man it attacks the CNS.

☒ **Infective stage:** Amoeboid trophozoite.

☒ **Mode of infection:** Through the nasal route.

1. Swimming or sniffing in contaminated water.
2. Inhalation of contaminated air.

- Amoeboid trophozoites in contaminated water enter the nose, migrate through nasal mucosa → olfactory nerve → olfactory pulp → base of the brain → disseminate to the brain tissue.
- The amoeboid trophozoite feeds and divides by simple binary fission.
- In soil trophozoite transforms into cyst stage.
- The amoeboid trophozoite transforms into cyst stage.
- Exystation of the cyst releases trophozoite

Pathogenesis:

Naegleria fowleri causes **primary amoebic meningo-encephalitis (PAM)**.

☒ Amoeboid trophozoite is neurotropic, feeds on nerve tissue resulting in necrosis →acute meningoencephalitis.

☒ It penetrates the cribriform plate and multiplies along the base of the brain, where it feeds on nerve tissue, by means of an amoebostome, resulting in significant necrosis and bleeding; causing acute meningoencephalitis.

☒ In the subarachnoid space, an inflammatory exudate of neutrophils and monocytes is seen.

☒ In the grey matter, there is haemorrhage and extension of the inflammatory exudates, rounded amoebae and necrosis of the tissues are also seen.

☒ In the white matter of the brain and spinal cord, there is demyelination, although amoebae and cellular exudate are absent there. Demyelination may be due to the production of phospholytic enzyme or enzyme-like substance by the growing amoebae in the adjacent grey matter.

Clinical picture:

The clinical course of PAM is dramatic, death usually occurs within a week.

1. Stage I: Nausea, vomiting, severe frontal headache, fever, blocked nose with alteration of smell or taste (acute onset of upper respiratory tract infection).

2. Stage II: Signs of meningeal irritation as stiffness of neck (Kernig's sign), photophobia, seizures, altered mental status, and coma.

Diagnosis:

☒ **Clinical diagnosis**: C/P with History of swimming or diving in lakes or ponds 2-6 days prior to onset.

☒ **Laboratory diagnosis**:

a. Microscopic examination: Wet mounts of CSF revealing trophozoites.
   - CSF is purulent but with no bacteria, raised cell count of neutrophils (leucocytosis), elevated protein (> 1gm / L) and low glucose (< 5gm / L).

b. Culture: non- nutrient agar with *Escherichia coli*. Both trophozoites and cysts can be seen

c. Molecular diagnosis.

d. Mice inoculation.

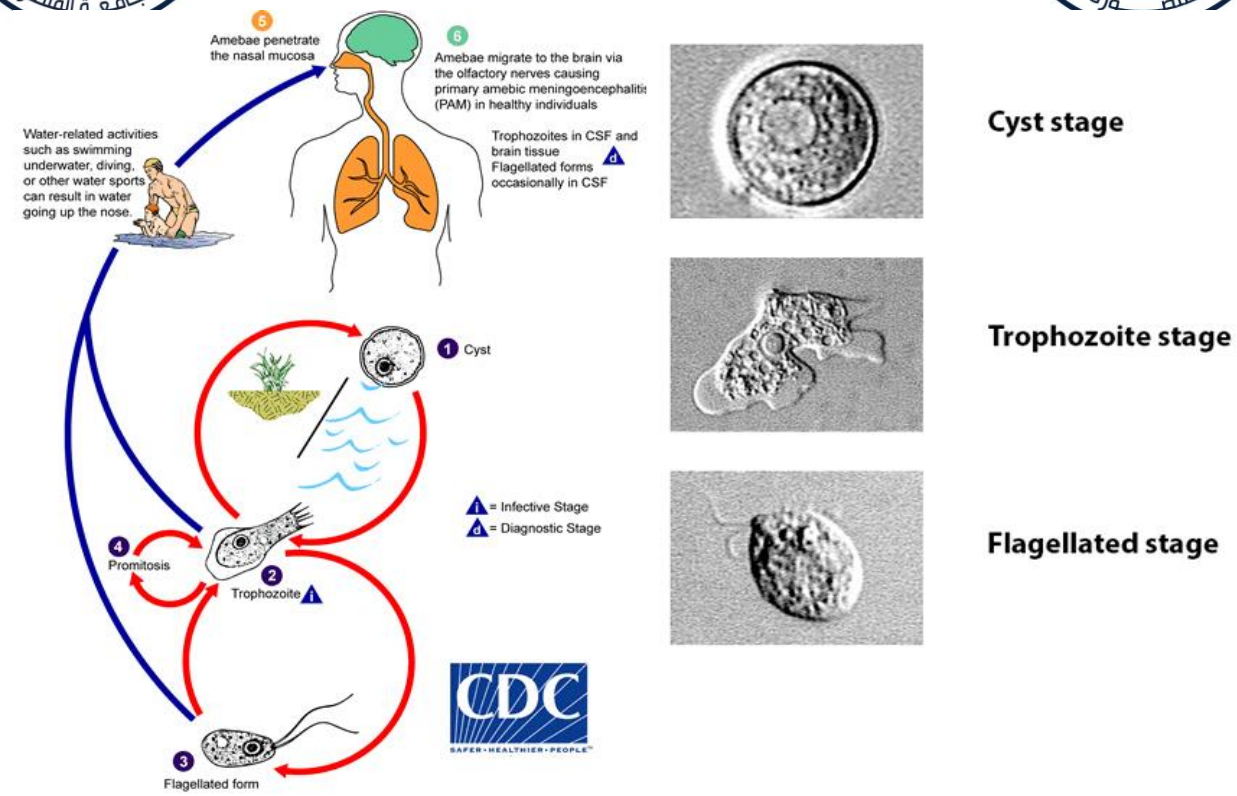
Treatment:

☒ Patient must be hospitalized

☒ I.V. Amphotericin-B, Fluconazole and Rifampicin.

Prevention and control:

1. Adequate chlorination of water of swimming pools and public water supplies.
2. Avoid immersing the head in water during swimming.



Life cycle of *Naeglaria fowleri.*

Acanthamoeba castellani

- **Geographical distribution**: Worldwide.
- **Morphology:**

a. Trophozoite: amoeboid, 20-40 µ in size, characterized by multiple small spiky pseudopodia (**acanthopodia**).

b. Cyst: Rounded, 20 µ in size, double wall. There is no flagellate form.

- **Life cycle:**

☒ **Habitat:**

- In environment: fresh water, soil, and dust.
- In man: CNS, eye, skin and lungs.

☒ **Infective stage:** Trophozoite and cyst.

☒ **Source of infection**: Dust, water and contact lens fluid.

☒ **Mode of infection:**

1. Inhalation of air, aerosol or dust contaminated with trophozoite or cyst.
2. Direct invasion through skin and mucosal ulcers.
3. Through the use of contaminated solutions of contact lenses.

- After inhalation, the trophozoites reach lungs, and then invade the CNS through the blood stream.
- Life cycle is simple between the active trophozoite and the resistant cyst stage, where trophozoites multiply by simple binary fission.

Pathogenesis & Clinical picture:

☒ It is opportunistic parasite causing severe disease in immuno-compromised persons. Both trophozoite and cyst stages may exist in tissues of Man.

☒ **Granulomatous amoebic encephalitis (GAE):**

- The course is chronic, lasting from weeks to years.
- Haematogenous spread from the lungs or skin abrasions focal granulomas as tumours (space occupying lesions).
- Infected tissues contain trophozoites, cysts and multinucleated giant cells. Clinical picture of intracranial space-occupying lesions with headache, seizures, mental deterioration, paresis, nausea and vomiting may also occur.

☒ **Amoebic Keratitis:**

- Infection occurs by direct contact of the cornea with contaminated water or contact lens. The disease is a chronic progressive ulcerative keratitis, characterized by severe unilateral ocular pain, photophobia, annular corneal infiltration, congested conjunctiva and loss of vision or even eye perforation may occur.

☒ **Chronic granulomatous skin lesions.**

Diagnosis:

☒ **Laboratory diagnosis:**

1. GAE of CNS

- Identification of trophozoites and/or cysts in CSF or brain tissue biopsy by wet mount or after staining with Giemsa, or immunofluorescent technique.
- Culture on non-nutrient agar seeded with Escherichia coli.
- CT scan of brain.

2. Amoebic keratitis: Corneal scrapings or histologic sections for detection of the organism by direct microscopy or after staining and culture.

Treatment:

☒ **GAE of CNS:** Sulfamethoxazole/Trimethoprim+ Fluconazole and Rifampicin.

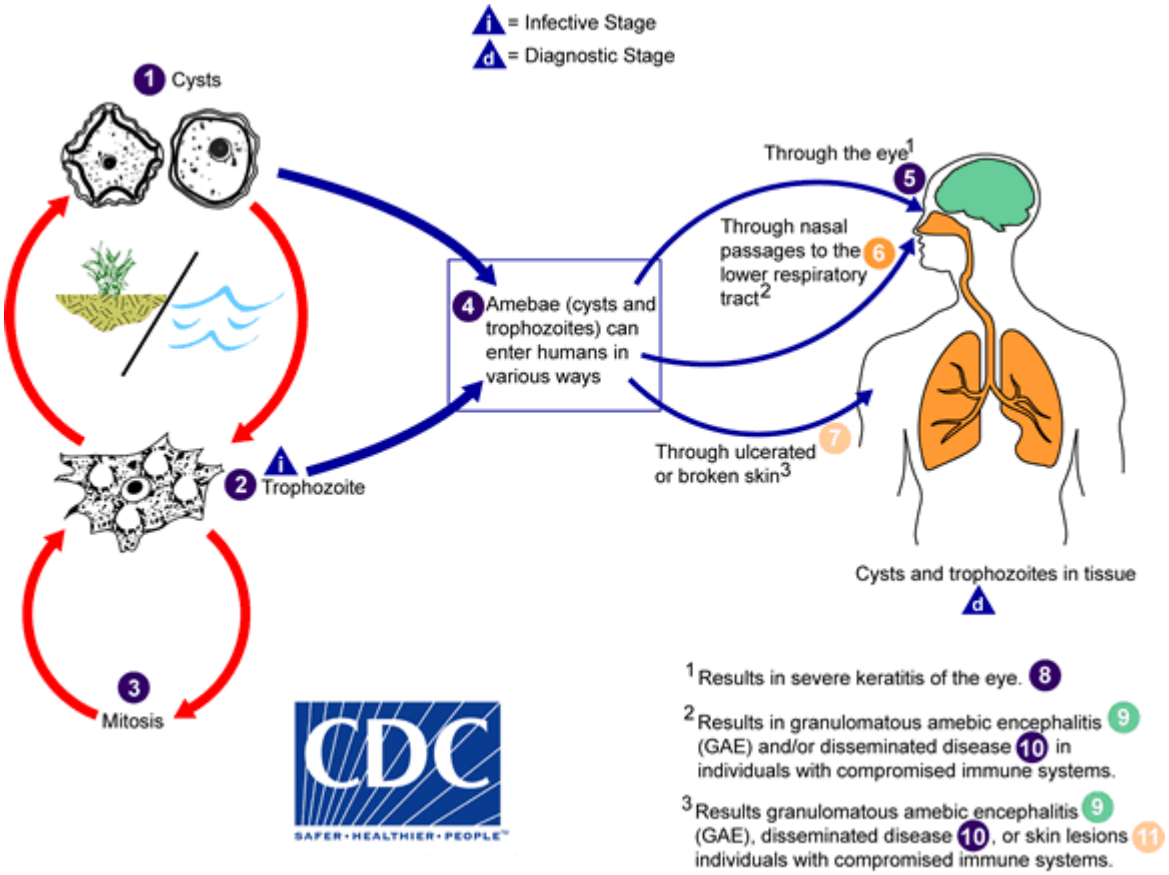
☒ **Keratitis** is treated with antibiotics and topical miconazole ointment. In severe case, keratoplasty can be done.

Prevention and control:

☒ Health education.

☒ Avoid swimming in stagnant water.

☒ The use of proper contact lens fluid.



Life cycle of *Acanthamoeba castellani.*

Trypanosoma bruci

☒ Species: Trypanosoma spp., causing African trypanosomiasis (sleeping sickness) are:

a. *Trypanosoma bruci gambiense*.
b. *Trypanosoma brucirhodesiense*.

Trypanosoma bruci gambiense

(Polymorphic trypanosomes)

- **Geographical distribution**: Central and West Africa.
- **Morphology:**
  - ☒ **In vertebrate hosts:** T. gambiense exists as polymorphic trypomastigotes, which appearing in 3 forms:
    a. Long slender form: 30µ, with a long free flagellum.
    b. Intermediate form
    c. Short stumpy form
  - ☒ **In vector:** they convert to→ Metacyclic trypomastigotes.
- **Life cycle: It passes in 2 hosts.**
  - ☒ **Vertebrate hosts:** Mainly man (D.H.) and domestic animals as pigs, goats and dogs (Reservoir hosts).
  - ☒ **Invertebrate hosts: Both sexes of Glossina palpalis, tsetse fly (I.H.).**
    - **Habitat** (in Man): Blood, lymph nodes, CNS
    - **Infective stage:** Metacyclic trypomastigotes.
    - **Mode of infection:**
      1. Biological transmission by the bite of infected *Glossina*.
      2. Blood transfusion.
      3. Congenital.

- ☒ Man acquires infection by the bite of Glossina, where the infective metacyclic trypomastigotes (in vector saliva) are inoculated in the skin during a blood meal.
- ☒ The metacyclic trypanosomes multiply by binary fission at site of inoculation, causing local swelling, called trypanosomal chancre.
- ☒ The metacyclic forms are transformed into trypomastigotes which spread, via the blood stream and lymphatics, throughout the body, and continue replication by binary fission as extracellular stages.
- ☒ The tsetse fly becomes infected with trypomastigotes when taking a blood meal from an infected vertebrate host.
- ☒ In the midgut, the short stumpy trypomastigotes are transformed into long ribbon forms (procyclic trypomastigotes), multiply by binary fission, leave the midgut, and transform into epimastigotes, which reach the salivary glands, and continue multiplication by binary fission, then transform to the non-dividing metacyclic trypomastigotes (infective form) in vector saliva.
- ☒ The life cycle in vector is a cyclo-propagative development of about 3 weeks.
- ☒ Tsetse fly harbouring the infective metacyclic forms is infective to man and the cycle is repeated.

Pathogenicity and Clinical picture:

T. brucei gambiense **causes West African trypanosomiasis (West African sleeping sickness). This Gambian form is characterized by:**

1. **Trypanosomal chancre**

at the site of bite, an indurated painful swelling, which lasts for 1-2 weeks. It is a local inflammatory response at the site of tsetse bite, with intense cellular infiltration, oedema and divided trypomastigotes.

2. **Stage I disease:**
   - Systemic spread of trypomastigotes
   - Irregular fever, headache, joint and muscle pain.
   - Enlargement of posterior cervical lymph nodes (Winterbottom's sign), or generalized lymphadenopathy and hepatosplenomegaly.
3. **Stage II disease:**
   - invasion of CNS, after several months →
   - Chronic meningoencephalitis. Increases in glial cells occur throughout CNS, and perivascular infiltration with mononuclear cells, leading to ischemic softening of tissues and petechial haemorrhage. There is also neuronal degeneration, and heavy infiltration of meninges with lymphocytes, plasma cells, and morula cells of Mott.
   - It manifested by behavioral changes, such as a mental apathy, slow speech and involuntary movements. coma followed by death from the disease, or concurrent infections.

Diagnosis:

☒ **Clinical diagnosis:** C/P with history of traveling or residence in endemic areas of Africa.

☒ **Laboratory diagnosis:**

- Direct demonstration of polymorphic trypomastigotes by Microscopy of wet mount smears or Giemsa-stained smears in: chancre aspirate, blood, lymph node aspirate, bone marrow, and CSF.
- **CSF examination:**
  - There is raised pressure, cell count (mainly lymphocytes) and proteins in CSF.

- Morula cells of Mott, which are atypical plasma cells with unilateral nucleus and many cytoplasm vacuoles, representing stored immunoglobulins. They are pathognomonic of sleeping sickness.

- **Culture:** on NNN medium.
- **Animal inoculation:** Intraperitoneal inoculation of specimens into guinea pigs, rats or mice. The animal is killed after one week and examined for the trypomastigotes and characteristic pathological lesions.
- Antibody or Antigen detection by ELISA.
- **Molecular diagnosis.**
- **Blood examination:** Anaemia, thrombocytopenia.
- **Imaging:** CT scan and MRI of the brain show cerebral oedema.

Treatment:

1. In stage I: Pentamedine and Suramin.
2. In stage II: Melarsoprol as it can pass blood brain barrier.
3. Treatment of associated medical conditions as anaemia, infections.

Prevention and control:

1-Protection against vector bite by skin repellents.

2- Treatment of patients.

3- Control of *Glossina* (vector).

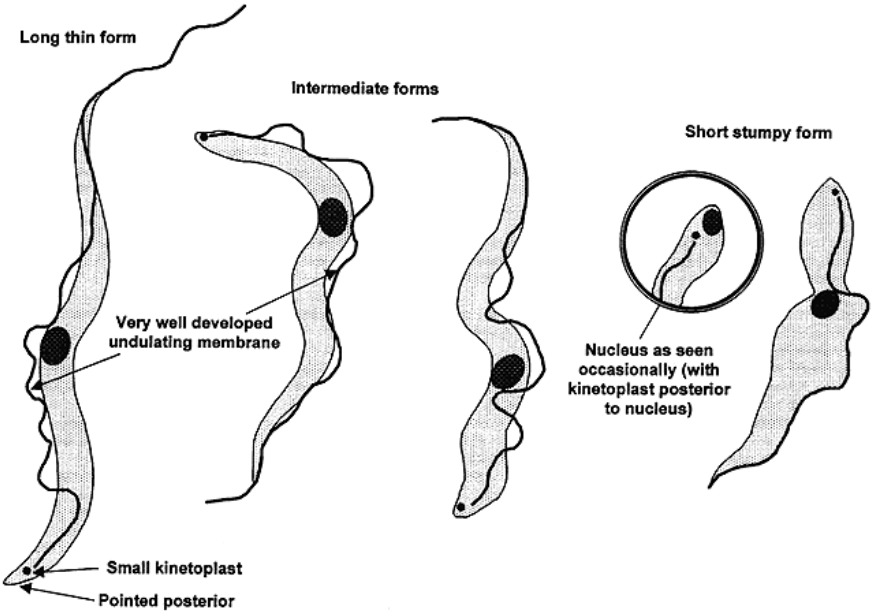
Trypanosoma rhodesiense:

☒ **causes East African trypanosomiasis (East African sleeping sickness).**

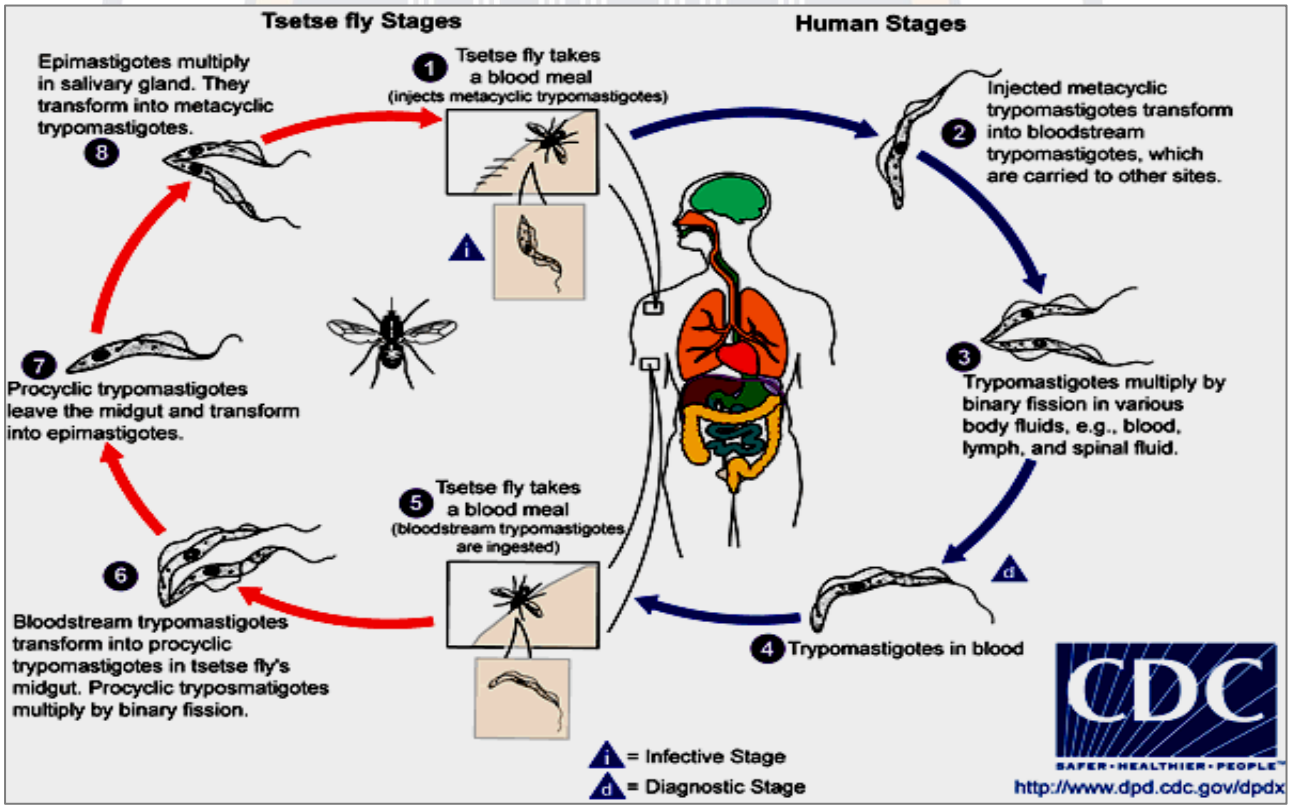
☒ **Geographical distribution:** East and Central Africa.

☒ **Morphology, habitat and life cycle:** They are similar to *T. brucei gambiense*, but the reservoir hosts are wild animals as antelope, and domestic animals as cattle, and the vector is *Glossina morsitans*.

☒ **Clinical features** of Rhodesian disease are similar to Gambian but they cause severe fatal disease in short duration. Acute course; CNS is involved early and patients usually die rapidly.



Morphology of *Trypanosoma brucei*



Life cycle of *Trypanosoma brucei*

Secondary Amoebic Cerebral Abscess

Definition:

- Invasion of brain tissue by Entamoeba histolytica trophozoite (Cyst never detected in tissue).
- E. histolytica trophozoite inhabit large intestine then invasion of submucosal blood vessels may lead to spread of amoebae causing extra intestinal amoebiasis e.g. liver, lung, brain.

Trophozoite:

- Size: 10-60 µ (average 20 µ).
- Shape: Irregular outline with pseudopodia
- Cytoplasm: outer clear refractile ectoplasm and inner granular endoplasm
- Nucleus: It has centrally located fine karyosome and peripheral chromatin dots.

Mode of infection:

1. Ingestion of mature quadrinucleated *E. histolytica* cysts in contaminated food or drink, or through infected food handlers.
2. Mechanical transmission by flies and cockroaches.
3. Autoinfection: feco-oral route (hand to mouth contact).

Pathogenicity and Clinical Picture:

- Haematogenous spread from amoebic liver abscess or pulmonary amoebiasis usually causes single brain abscess. It results in secondary amoebic meningoencephalitis, with severe destruction of brain tissue.
- It manifests as a brain tumor (Space-occupying lesion).

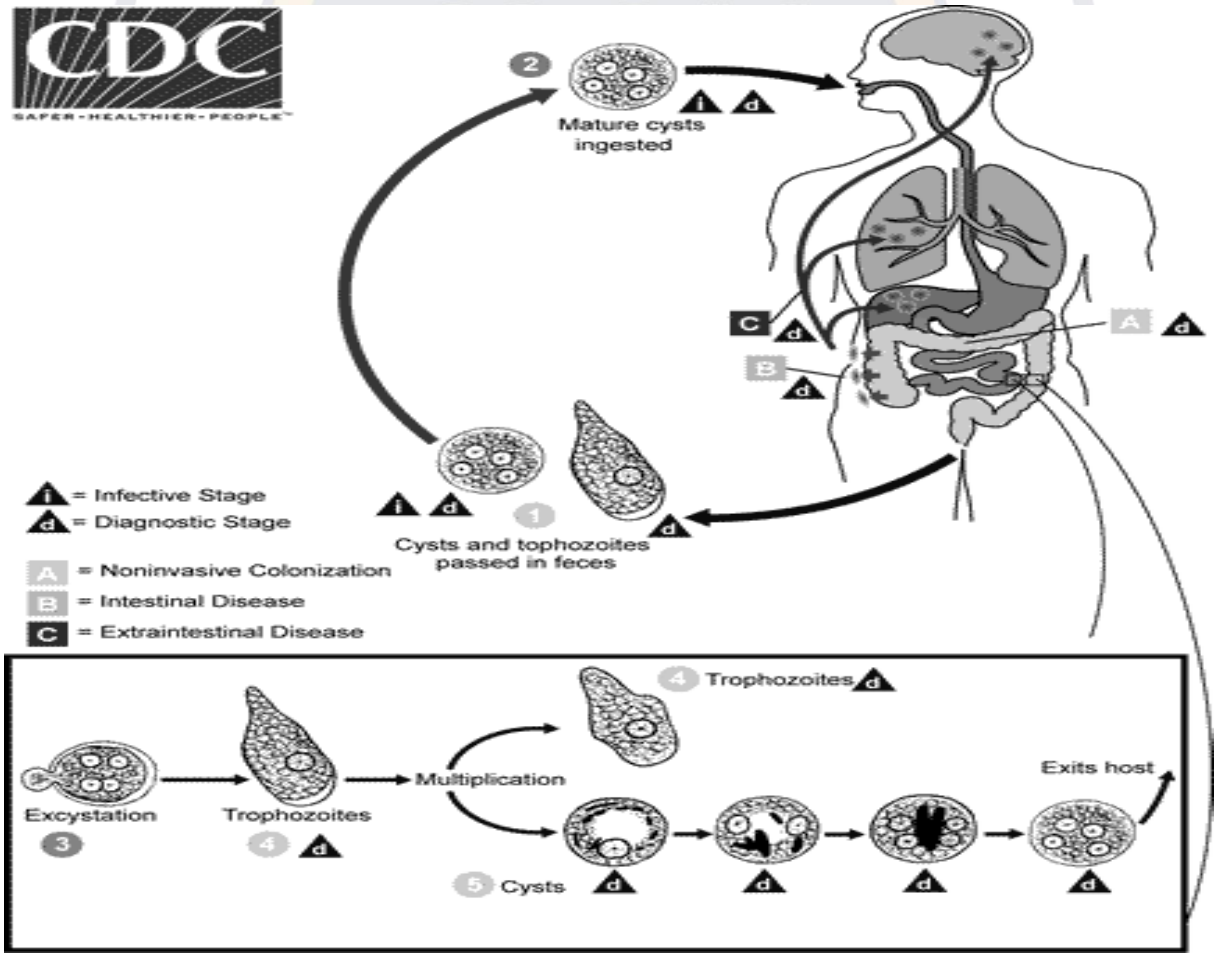
Diagnosis:

- ☒ Microscopic examination for detection of trophozoites in CSF samples.
- ☒ Serodiagnosis: The circulating amoebic antigens or antibodies can be detected by IHA, IFA or ELISA.
- ☒ Radiological examination: by ultra-sonography (US), computed axial tomography (CT) or magnetic resonance imaging (MRI).

Treatment:

Tissue amoebicides: They act against the tissue invasive form (trophozoite).

- Metronidazole. -Tinidazole.



Life cycle of *Entamoeba histolytica*

Neurocysticercosis

Definition:

☒ invasion of the human tissues by the larval stage of Taenia solium (Cysticercus cellulosa).

☒ In this case man acts as an intermediate host.

Mode of infection:

☒ it can develop in different ways:

- Ingestion of food or water contaminated by the eggs of *Taenia solium*.
- Auto- infection either

a. ***External autoinfection*** (Exogenous): the patient harbouring the adult parasite contaminates his fingers with *Taenia solium* eggs, Feco-oral.

b. ***Internal autoinfection*** (Endogenous): antiperistaltic movements of the intestine (in case of vomiting or taking emetic drugs) leads to regurgitation of the gravid segments to the stomach.

Pathogenicity and clinical picture:

☒ The cyst (Cysticercus cellulosa) produces local cellular reaction and infiltration with neutrophils, eosinophils and lymphocytes.

☒ Neurocysticercosis manifests as a brain tumor (Space-occupying lesion).

☒ Cerebral cysticercosis results in severe headache, convulsions and paralysis.

Diagnosis:

1- Serological tests may be helpful in diagnosis as I.H.A.T and ELISA.

2- Imaging: Ultrasound, C.T. and MRI.

3- X-ray for calcified cyst.

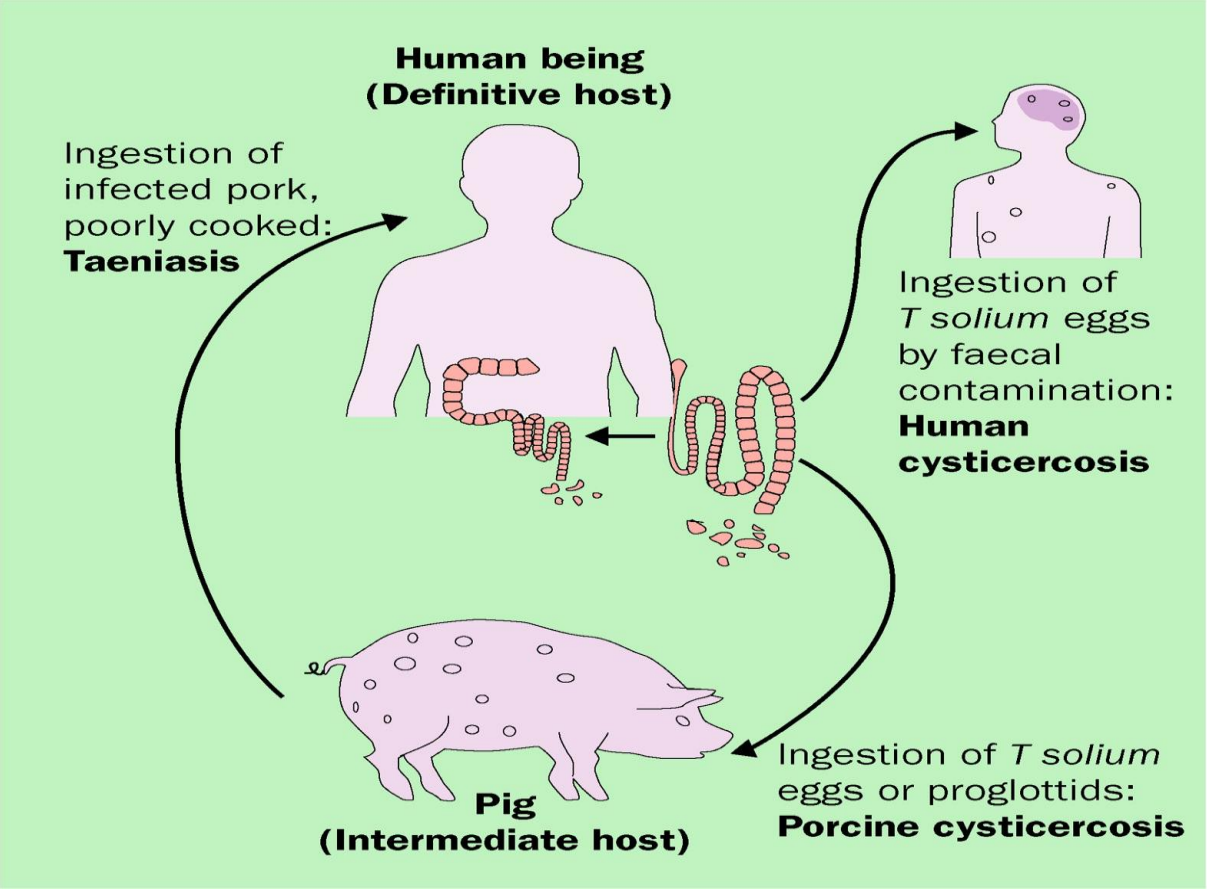
4- Biopsy for histopathological examination.

Treatment:

1. Surgical removal when possible.
2. Praziquantel combined with corticosteroids for cerebral oedema.
3. Albendazole is also effective.

Prevention and control:

1. Early treatment of infected persons to avoid autoinfection
2. In infected patients with the adult parasite, no nauseating drugs is given.
3. Avoid the use of human excreta as fertilizer.
4. Personal cleanliness, fly control and proper washing of raw vegetables.



Life cycle of *Taenia solium*

Parasitic Infections Affecting The Eye

Onchocerciasis

- **Definition:** Infection of human skin and subcutaneous tissue by Onchocerca volvulus adult and microfilaria.
- **Life cycle:**
  - ☒ Habitat: adult worms live in fibrous subcutaneous nodules from the host reaction.
  - ☒ Definitive host: man.
  - ☒ Intermediate host: Simulium (Black fly).
  - ☒ Reservoir host: no.
  - ☒ Infective stage: infective filariform larva in the mouth of Simulium
  - ☒ Mode of infection: through inoculation of the infective filariform larva present in the mouth of intermediate host (Simulium fly) into skin bite.
- **Pathogenicity and clinical picture:**

A. Ocular manifestations (River or Sudan Blindness):

- ☒ This is a serious complication of onchocerciasis resulting in blindness.
- ☒ Common when the nodules are in the scalp, neck and shoulders.
- ☒ The microfilariae have great affinity to the eye tissues.
- ☒ It is characterized by keratitis, iritis, uveitis, choroiditis, retinitis and optical atrophy which end in blindness.
- ☒ **Causes:**
  - Hypersensitivity to toxins from living and dead microfilariae.
  - Mechanical action of the moving microfilariae in the eye tissues.

B. Onchocerca nodule (onchocercoma): Smooth firm, painless fibrous nodule in the subcutaneous tissue surrounding one to several adults.

C. Severe dermatitis:

Oedema and inflammatory cellular infiltration of the dermis against microfilaria forming granuloma with subsequent fibrosis.

D. Disturbed skin pigmentation.

Diagnosis:

A. Clinical diagnosis.

B. Laboratory diagnosis:

☒ Direct detection of microfilaria or adult (Diagnostic stage) in Skin-snip biopsy or aspiration from the nodules or tissue biopsy.

☒ Patch skin test: 10% of Hetrazan in lanolin cream is applied to an area of skin. In positive cases; papular eruption develop after 8-24 hours.

Treatment:

1. Ivermectin against microfilaria.
2. Doxycycline against adult worms.
3. Surgical removal of the nodules.

Prevention and control:

1. Control of Simulium by insecticides application to water running streams and spraying insecticides along riverbanks by airplanes.
2. Mass chemotherapy by ivermectin.
3. Mass nodulectomy.