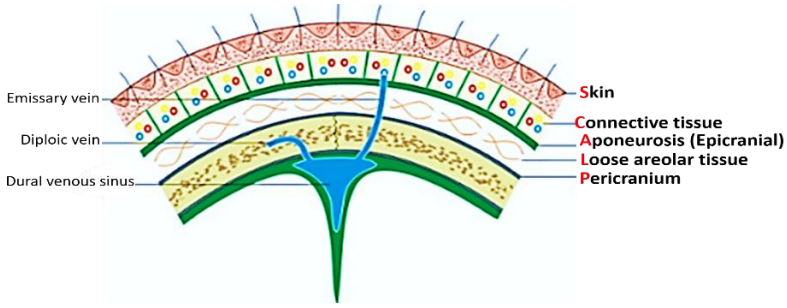
PNS (1)

Anatomy L1 (**Scalp**)

-Layers of the scalp : 5 layers (S.C.A.L.P.): (الترتيب مهم)



-The first 3 layers **attached together** and move on the underlying layer.

-**Loose areolar tissue** (dangerous zone): allows mobility of the scalp on the skull, site of collection of pus and blood

- **Pericranium**: adherent at the sutures of the skull by sutural ligaments

-**Occipitofrontalis Muscle: (2 frontal bellies and 2 occipital bellies)**

* You must know : there are **NO bony attachment** for frontal bellies

*Their Action: **Frontal belly** → Elevate the eye brows "expression of surprise"

Occipital belly → Pull the scalp backward.

-**Diffuse hematoma**: Bleeding under the first 3 layers , reach the upper eye lids (Black eye).

- **Localized hematoma :** Fracture of the skull bone ,because the periosteum is firmly attached to the sutures.

- **Horizontal Cut wound** of The front of scalp leading to Wide Gap due to retraction of occipitofrontalis muscle.

- **Scalp infection** localized in the **loose areolar layer** spreads to the intracranial dural venous sinuses through emissary veins (valveless), causing **meningitis** or **septicemia**.

Anatomy L2 (**Face**)

-**Structure of face** (3 layers): Skin/superficial fascial/muscles of face

*superficial:

-contains fat ⟶well developed in cheeks (buccal pad of fat) absent in eyelids.

-contain muscles of face (**facial expression**)

*deep fascia: -absent.

*skin:

-contain numerous sweat & sebaceous glands.

-elastic and receive insertion of face muscles & so wounds of face tend to gap.

-senile facial wrinkles occur due to destruction of skin elastic fibers and are aggravated by habitual expressions.

- These wrinkles lie at right angles to the line of pull of underlying muscles .

*muscle:

characters of muscles of face:

-present in superficial fascia /origin from bone/insertion in skin/main muscles of facial expression(But NOT the only) there are: (-muscle of scalp /muscles of auricle/platysma)

-all muscles of facial expression are supplied by facial n.

1) ***Buccinator: muscle of cheek*** **:**

-**its Actions** : compress the cheek against teeth to prevent accumulation of food in vestibule /blowing & whistling

-YOU MUST KNOW : IN its insertion **middle fibers**: decussate at modulus (at angle of mouth) and the upper part of these fibers pass to the lower lip and lower part pass to upper lip.

2)***Orbicularis Oculi: sphincter of eye : parts & action*****:**

-Orbital part-Action : tight closure of eye in exposure to injury.

-Palpebral part-Action : light closure of eye in sleep & blinking.

- **Lacrimal part-Action** : drainage of tears by dilating the lacrimal sac.

3***) Orbicularis oris: sphincter of mouth***

-Action:-approximating the 2 lips together as in blowing whistling / production of speech

-Arterial supply of face : (External carotid art and **internal carotid art)**

- Venous drainage of the face : Ant. facial v.

-Connections: **cavernous sinus** by 2 valveless veins:1-superior ophthalmic v. 2-deep facial v

-(مهم)dangerous area of face is the triangular area around nose & supper lip as infection pass from ant. facial v. to cavernous sinus

Anatomy L3 (***Trigeminal Nerve***)

- The largest cranial nerve/ It is a small motor root and a large sensory root(which is expands to form the trigeminal ganglion)

- The trigeminal ganglion lies within a pouch of dura mater called the trigeminal cave. (Meckel cave) . **HAVE 3 DIVISIONS:**

1) Ophthalmic Nerve (V1)

- purely sensory/enter the lateral wall of the cavernous sinus in the middle cranial fossa/- which enter the orbital cavity through **the superior orbital fissure**

-its branches:

A) The Lacrimal nerve

- enters the lacrimal gland and gives branches to the conjunctiva and the skin of the upper eyelid.

B) The frontal nerve

- divides : supraorbital and supratrochlear nerves

- supply the frontal air sinus and the skin of the forehead and the scalp

C) The nasociliary nerve

- Continues as the anterior ethmoid nerve

- It gives off two internal nasal branches and it then supplies the skin of the tip of the nose with the external nasal nerve.

- Its branches: - Sensory fibers to the ciliary ganglion/-Long ciliary nerves/ Infratrochlear nerve that supplies the skin of the eyelids /-Posterior ethmoidal nerve that is sensory to the ethmoid and sphenoid sinuses

2) *Maxillary Nerve (V2)* -purely sensory

-enter the lateral wall of the cavernous sinus and leaves the skull through the **foramen rotundum**

- It crosses the pterygopalatine fossa to enter the orbit **through the inferior orbital fissure**

- continues as the infraorbital nerve, and it emerges on the face through **the infraorbital foramen.**

-**its branches**: 1)Meningeal branches/2) Zygomatic branch which divides into the zygomaticotemporal (which gives parasympathetic secretomotor fibers to the lacrimal gland via the lacrimal nerve) and the zygomaticofacial /3) Ganglionic branches, which are two short nerves that suspend the pterygopalatine ganglion /4) (Posterior/middle/anterior) superior alveolar which supply the maxillary sinus

3) *Mandibular Nerve (V3)*-Is both motor and sensory

- leave the skull through **the foramen ovale**

=Branches from the Main Trunk of the Mandibular Nerve: it leaves skull by **foramen spinosm**

1-Meningeal branch

2-Nerve to the medial pterygoid muscle, which supplies also the tensor veli palatini muscle and tensor tympani

=Branches from the Anterior Division of the Mandibular Nerve

1-Masseteric nerve to the masseter muscle

2-Deep temporal nerves to the temporalis muscle 3-Nerve to the lateral pterygoid muscle 4-Buccal nerve (ONLY SENSORY)

=Branches from the Posterior Division of the Mandibular Nerve

1-Auriculotemporal nerve 2-Lingual nerve (ONLY MOTOR) 3-Inferior alveolar n.

-Pterygopalatine Ganglion-

-suspended from the maxillary nerve in the pterygopalatine fossa.

-Preganglionic parasympathetic fibers reach the ganglion from the facial nerve via the Greater palatine nerves

- Postganglionic secretomotor fibers pass to the lacrimal and nasal glands..

-The otic ganglion-

-The preganglionic fibers originate in the glossopharyngeal nerve, via the lesser petrosal nerve

-The postganglionic secretomotor fibers reach the parotid salivary gland via the auriculotemporal nerve.

-Submandibular Ganglion-

-Preganglionic parasympathetic fibers reach from the facial nerve via the chorda tympani and the lingual nerves.

- Postganglionic secretomotor fibers pass to the submandibular and the sublingual salivary glands.

Anatomy L4 (***Facial Nerve***)

-its nucleus:

1) **Main Motor** : - supplies the muscles of the upper part of the face (from both cerebral hemispheres) \ - muscles of the lower part of the face receives only (from the opposite cerebral hemisphere)

2) **Parasympathetic** : They are the: A. *superior salivatory* (receive: 1) afferent fiber from hypothalamus / 2) information of taste)

B. *lacrimal nuclei* (receives : 1)afferent from hypothalamus (for emotional responses) 2) from sensory nuclei of the trigeminal n(for reflex lacrimation secondary to irritation of the cornea or conjunctiva))

3) **Sensory Nucleus** (Sensations of taste)

-its course:

=traverses the **posterior cranial fossa** by pontomedullary junction, leaves the cranial cavity by the **internal auditory meatus** ,runs through **facial canal** (above the vestibule of the inner ear+ bends sharply(called geniculum and carries the geniculate ganglion) backwards above the promontory in the medial wall of middle ear cavity) , exits from the **stylomastoid foramen**, enters the posteromedial surface of **parotid gland** (here,give 5 terminal branches)

-geniculate ganglion: sensory ganglion of CN VII

-its branches : 10 branches

-Within the facial canal gives (-Greater petrosal n -Nerve to the stapedius

-Chorda tympani n.)

-At stylomastoid foramen; Gives off the posterior auricular

-Within parotid gland (Temporal,Zygomatic, Buccal, Marginal mandibular, Cervical.)

- Nerves to stylohyoid & posterior bellies of digastric

-its supplies :

=Somatic motor : facial expression /auricular muscles/ posterior bellies of the digastric/ stylohyoid& stapedius muscles.

=Visceral motor : pterygopalatine ganglion (innervation of lacrimal glands) & submandibular ganglion (innervation of sublingual & submandibular salivary glands.)

=Somatic sensory : geniculate ganglion supply a small area of the skin of the concha of the auricle

=Special sensory (taste) : chorda tympani join lingual nerve to convey taste sensation from anterior 2/3 of tongue & soft palate

Anatomy L5 (**The Orbits, Extraocular Muscles**)

=The orbit is quadrangular pyramidal

-base(bones which circulate it) / -apex (optic canal)

-its openings

1) Orbital opening: expose 1/6 of eye 2) Supraorbital Foramen: transmits supraorbital n. 3) Infraorbital groove and canal: transmit the infraorbital n

4) Nasolacrimal canal: transmits the nasolacrimal duct

5) Inferior orbital fissure: transmits maxillary n and its zygomatic branch, inferior ophthalmic vein &sympathetic n

6) Superior orbital fissure: transmits the (lacrimal ,frontal ,trochlear, oculomotor abducent nasociliary) nerves & superior ophthalmic vein.

7) Optic canal: transmits the optic n &ophthalmic artery.

Ciliary Ganglion

- It receives preganglionic fibers from oculomotor n via nerve to inferior oblique.

- postganglionic fibers leave the ganglion in the short ciliary n (supply the sphincter pupillae & the ciliary muscle.)

Eyelids

- superficial surface : skin & deep surface : conjunctiva.

-its glands :

1) glands of Zeis: open directly into the eyelash follicles.

2) The ciliary glands (glands of Moll) : open separately between adjacent lashes

3) The tarsal glands(meibomian gland) :open behind the eyelashes

Lacrimal Gland

- consist of :Large orbital part /Small palpebral part/- open by 12 ducts

Lacrimal Ducts

- The tears circulate across cornea & accumulate in the lacus lacrimalis ,enter canaliculi lacrimales through puncta lacrimalis , canaliculi lacrimales open into lacrimal sac Then to the nasolacrimal duct .

Extraocular Muscles

1) Superior rectus

I: Superior surface of eyeball just posterior to corneoscleral junction

N. S: Oculomotor nerve /A: Raises cornea upward and medially

2) Inferior rectus

I: Inferior surface of eyeball just posterior to corneoscleral junction

N S: Oculomotor nerve A: Depresses cornea downward and medially

3) Medial rectus

I: Medial surface of eyeball just posterior to corneoscleral junction

N. Supply: Oculomotor nerve A: Rotates eyeball so that cornea looks medially

4) Lateral rectus

I: Lateral surface of eyeball just posterior to corneoscleral junction

N. S: Abducent nerve A: Rotates eyeball so that cornea looks laterally

5) Superior oblique

O: Posterior wall of orbital cavity

I: Passes through pulley and is attached to superior surface of eyeball beneath superior rectus

N. S: Trochlear nerve A: Rotates eyeball so that cornea looks downward and laterally

6) Inferior oblique

O: Floor of orbital cavity

I: Lateral surface of eyeball deep to lateral rectus

N. S: Oculomotor nerve A: Rotates eyeball so that cornea looks upward and laterally

7) Levator palpebrae superioris

O: Back of orbital cavity I: Anterior surface and upper margin of superior tarsal plate

N. S: Striated muscle oculomotor nerve, smooth muscle sympathetic A: Raises upper lid

Anatomy L6 (The Eyeball)

-its basic structures:

1.Fibrous layer

= Sclera : -tough opaque part - anterior part it is visible through transparent bulbar conjunctiva as "the white of the eye" - relatively avascular -

= Cornea : -transparent part - completely avascular - its nourishment :1) capillary beds 2) lacrimal fluid and aqueous humor

2. Vascular layer

= Choroid: between sclera & retina - lines most of the sclera – its larger vessels are located externally (near sclera) - finest vessels are innermost, near retina

= ciliary body :- posterior to corneoscleral junction that is muscular & vascular

- contraction and relaxation of ciliary muscle controls thickness, & focus, of lens

- ciliary processes: Folds on internal surface of ciliary body, secrete aqueous humor.

= Iris: thin contractile diaphragm has central aperture, pupil, for transmitting light

- Two involuntary muscles control the size of the pupil:

1)parasympathetically (sphincter pupillae) (constrict pupil, pupillary miosis)

2) sympathetically (dilator pupillae) (dilates the pupil)

3. Inner layer

= Retina consists of : A) The optic part (a neural layer & pigmented layer) -sensitive to light - terminates anteriorly along the ora serrata B) The nonvisual (anterior continuation of pigmented layer and a layer of supporting cells)

- optic disk contains no photoreceptors insensitive to light (called the blind spot)

- macula lutea :lateral to optic disk , specialized for acuity of vision.

- fovea centralis : at central of macula lutea, the area of most acute vision.

Embryology L1 (Development of the Face & Palate)

-Stomodeum, Primitive oral cavity that closed by oral membrane is ectodermal recess

-- face develops from 5 mesodermal swellings which appear around stomodeum

I. Frontonasal process II. 2 maxillary swellings III. 2 mandibular swellings

-Two medial nasal processes unit with each other forming median nasal process

-Median nasal process gives rise to:

1- Part of the nasal septum.

2- Philtrum (middle) of the upper lib.

3- Premaxilla (upper jaw that carries 4 incisor teeth).

4- Primary palate.

-Microstomia (narrow mouth opening): due to excessive fusion of the maxillary and mandibular processes on each side.

-Unilateral cleft palate: due to failure of fusion of the two palatine processes of the maxilla with each other in the midline and with the primary palate on one side, associate with cleft upper lib.

Embryology L2 (Development of the Pharyngeal Arch)

Mesoderm: pharyngeal arches

ectoderm: pharyngeal clefts.

endoderm: pharyngeal pouches.

First pharyngeal arch

- Mandibular nerve of trigeminal nerve (V)
  - Skeletal structures:
- 1- Maxillary process : (MZIP) Maxilla, Zygomatic, Palatine bones and Incus
- 2- Mandibular process (Mackle's cartilage) : (3M) Mandible, Mastoid process and Malleus.
- - Muscles: - Mylohyoid and anterior belly of the digastric(مهم)

Second pharyngeal arch

- Facial nerve (VII)

- Skeletal: 3S 1- Stapes 2- Styloid proces 3-Lesser horn and upper 1/2 of hyoid bone. مهم

- Muscles: - Posterior belly of digastric and stylohyoid.مهم

Third pharyngeal arch:

-Glossopharyngeal nerve (IX).

- **Skeletal structures:** Lower 1/2 of the hyoid bone and greater horn.
- **Muscles:** Stylopharyngeus muscle.

Forth pharyngeal arch

-Superior laryngeal nerve of vagus (X).

- B.v: 1- Left side, Arch of aorta. 2- Right side, right subclavian artery.

- Skeletal structures: 1- Epiglottis. 2- Upper 2/3 of the thyroid cartilage. 3- Cuneiform cartilage.

- Muscles: Cricothyroid muscle

Sixth pharyngeal arch:

- Recurrent laryngeal nerve of vagus (X).
- B.v: 1- Pulmonary arteries on both sides 2- Ductus arteriosus on left side.
- Skeletal structures: Lower 1 /3 of the thyroid cartilage, Cricoid, arytenoid and corniculate cartilages.
- Muscles: All intrinsic muscles of larynx except cricothyroid.

Histology L1&2 (The Eye)

=The cornea (transparent, non vascular) -composed of 5 layers :

1- Anterior epithelium

- non- keratinized stratified squamous -The basal cells are columnar(**mitotic figures**) -polyhedral cells have free nerve endings (**trigger blinking reflex**)

-squamous cell show **microvilli**

2- Bowman's membrane

-non-cellular membrane /-Formed of (**collagen type V**)

-It acts **as protective barrier** to stroma & protect the epithelial innervation

3- C.T. (stroma)

- (**90%** of the corneal thickness) /-formed of **parallel collagen fibers (types I)**

- there are fibroblast- like cells (**keratocytes**) -**LASIK occurs in stroma**

4- Descemet's membrane

- non-cellular membrane /-Formed by the endothelial

5- Endothelium

- simple squamous cells that are active in:**protein synthesis /pumping sodium ions**

=The sclera (-irregular white collagenous fibers, elastic fibers, fibroblasts/covered by conjunctiva**)**

***The corneo- scleral junction (limbus):(مهم)**

-The corneal epithelium—> bulbar conjunctiva

-Bowman's membrane stops abruptly at limbus

-The regular stroma of the cornea—> the irregular stroma of the sclera

-Descemet's membrane—> the Trabecular meshwork (spaces of Fontana)

=The Iris (colored disc**)**

-pupil in its center /-changes the pupil size /- share in formation of aqueous humor

- Anterior surface: lined by endothelium & **had melanocytes**

-Posterior surface: **2 layers of pigmented cuboidal** epithelium

-Muscles of the iris:

1) The dilator pupillae muscle: is **myoepithelial cells partially pigmented**

2)The sphincter pupillae muscle: **circular band of smooth ms**

=The ciliary body ((composed of Ciliary processes & Ciliary muscles**))**

1- The ciliary epithelium: (two layers of cuboidal epithelium :surface layer **is non-pigmented (A)** +the deep layer **is pigmented (B)** rich in melanin /-secrets the aqueous humor)

2- The ciliary muscle: (smooth muscles) attached to the suspensory ligament of the lens /- for Accommodation

=The choroid (highly vascular, pigmented**)** -has Bruch's membrane

=The lens(avascular ,biconvex disc**)**

-composed of 3 parts : capsule(**type IV collagen**), cortex, nucleus

-Lens epithelium: single layer of cubical cells

=The retina (Photoreception**) :**

1- Pigmented epithelium: Single layer of cuboidal cells /-contains numerous melanin granules/-form blood- retinal barrier

2- Rods (↑ in #) & Cones layer: photoreceptors

-Fovea centralis: area of highest visual acuity (sharp vision)/-Contains Cones only
-blind spot: has no photoreceptors /- Consists of optic nerve fibers

=Accessory structures of the eye

1- the conjunctiva (transparent mucus membrane)

-Covers the anterior part of the eye except the cornea & lines internal surface of the eye lids

2- the eye lids(covered e thin skin that has no subcutaneous fat)

- Zeis glands are sebaceous glands open at eye lashes.

- Moll glands are sweat glands open between the eye lashes

-Meibomian gland modified sebaceous gland- to minimize evaporation tear

3- the lacrimal apparatus (compound tubulo- alveolar)

-Lacrimal canaliculi: Lined with stratified squamous epithelium/ -Lacrimal sac: respiratory epithelium /-Nasolacrimal duct: opens in the nasal cavity below inferior concha

Histology L3 (The Ear)

1)The External ear

1- Auricle :directs sound waves into the ear canal

2- External auditory canal: keratinized stratified squamous epithelium

3- Tympanic membrane(Ear Drum): 4 layers: Stratified squamous epi/collagenous fibers Radially +Circularly arranged /simple cuboidal epithelium.

2) The Middle Ear(tympanic cavity): Air filled ,Lined with simple cuboidal epi- composed of:

3 bony ossicles(malleus ,incus ,stapes) are compact bone without epiphysis

2 muscles : (Tensor tympani & Stapedius) striated involuntary ms

2 windows: Oval window(fenestra vestibule)+Round window(fenestra cochlea)

1 chorda tympani n.

Eustachian tube:

It has 2 parts:

→ Bony part (tympanic): lined with simple columnar ciliated epithelium

→ Cartilaginous part (pharyngeal): lined with respiratory epi

3-The Inner Ear (labyrinth)

- Consists of:

1) **bony labyrinth :**lined with endosteum, & is filled with fluid called **perilymph(Na more K)**

- It Consists of 3 parts:

Cochlea (Hearing**) :** - Makes 2½ turns around a bony axis "modiolus(spongy bone)

- its membranous part "cochlear duct" which divides the bony canal into 3 spaces :

Scala vestibuli (above)+ Scala tympani (below): BOTH contain perilymph(meet at HELICOTREMA)

Scala media (middle) : contains **endolymph, & organ of Corti(Neuroepithelium)**

-Stria vascularis : covered by (e pseudo-stratified columnar cells) its cells secrete endolymph

-vestibular membrane :e simple squamous epi

-basilar membrane :e simple squamous epithelium

3 semicircular canals

Vestibule (Equilibrium)

-Contains → utricle+ saccule(simple squamous epith. Filled with **endolymph**) : Show kinocilium surrounded e several **stereocilia**

Otolithic membrane

gelatinous membrane (protein & crystals of Ca^{+} carbonate (Otoconia))

has Critical role in the brain's interpretation of equilibrium

Movement of head & Linear acceleration (horizontal &vertical)

2) **membranous labyrinth :** filled with fluid called **endolymph(K MORE Na)**

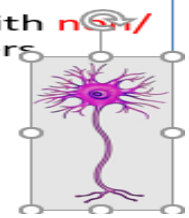
Histology L4 (PNS)

=Axolemma: plasma membrane around nerve cell axon

= Neurilemma : plasma membrane of Schwan cells that present in myelinated axon

- Osmic acid is used to stain the myelin

Sensory ganglia	Autonomic ganglia
Sensory ganglia (31pairs) carry **afferent** impulses to CNS Nerve cell bodies are: Rounded shape(unipolar) Covered with thick capsule Large , few in numbers Central nuclei Arranged in groups between the fibers The groups of cells are separated with myelinated nerve fibers satellite cells are more around each nerve cell	Motor ganglia (21-23 pairs) Carry **efferent** impulses from CNS Nerve cell bodies are: Multipolar Thin capsule Small , numerous Eccentric nuclei Scattered , no groups The cells are separated with non/ little mylinated nerve fibers satellite cells are less



-Classification of receptors (مهم)

1) Receptors in epithelium: "Exteroceptors"

-Free nerve endings : -unmyelinated sensory nerve fibers -for pain & temperature

- Sites: epidermis of skin, corneal ,conjunctiva & oral cavity

-Root hair plexus or plexus of bonnet : - basket – like structure -for touch sensation -around the base of hair follicles

Merkle tactile disc : - detect touch & pressure -in epidermis (superficial) of the skin of soles & palms

Neuroepithelium endings: -Taste buds / tongue -Olfactory epithelium / nose -Organ of Corti / ear -Macula utriculi, macula sacculi & crista ampullaris for equilibrium/ ear -Photoreceptors / retina (مهم)

2) Receptors in CT:

Meissner corpuscle : - Oval shape, encapsulated -detect light touch & Low frequency vibration -in the dermal papillae (deep) of skin

Krause end bulb:- Rounded ,encapsulated-deep in the dermis of the skin -Detect touch/ cold

Pacinian corpuscle : - oval encapsulated -deep in dermis ,periosteum of bone, joint capsule, pancreas -Detect deep touch, high frequency vibration, pressure

Ruffini corpuscle:-Fusiform encapsulated-Detect pressure-deep in the dermis(sole)

Golgi tendon organ (tendon spindle) : - in tendons near the insertion -for tensions

3) Muscle spindles

-within the skeletal muscles (lie parallel to its fibers)

-Responsible for regulation of muscle tone, movement, body posture

-More numerous in muscles involved with fine movements

Pharmacology L1 (Adrenergic Agonists)

-which also called (sympathomimetic)

-Adrenergic neurons release norepinephrine as primary neurotransmitter

→a1-Adrenoceptors(as same as action of sympathatic) :

-Pressor agents: Phenylephrine(nasal decongestant/mydriatic agent/V.C)

-Mucosal decongestants: Pseudoephedrine, Oxymetazoline Should not be used in:

Prolonged use/hypertensive patients /Children below 2y

→Selective B2 agonists : used in treatment of: bronchial asthma /Premature labour

-as Salmeterol & Formoterol(highly efficacious when combine with corticosteroid)

→Selective B1-agonist : as Dobutamine (used in CHF)

→Mixed Alpha & Beta agonists (drug of choice in emergency situations)

Pharmacology L2 (ANS – Cholinergic)

= Direct Acting Cholinergic Agonists

Acetylcholine– N/M Carbachol– N/M Bethanechol– M Pilocarpine – M

Indications – Urinary retention after surgery or postpartum, Glaucoma

Adverse effects –

Muscarinic (M): salivation, flushing, bronchospasm, sweating, nausea, abdominal pain – acid indigestion and GI cramping, diarrhea, and possibly, decreased blood pressure.

Nicotinic (N)- Fasciculations, respiratory arrest

= Nicotine

MOA- Low doses – ganglionic stimulation causing euphoria and arousal. CNS effects cause relaxation and improves attention (Acute)

Adverse effects – Vomiting, convulsions, hypertension, cardiac arrhythmias, Respiratory arrest – (depolarizing blockade), Muscarinic effects - PNS ganglia stimulation.

=Succinylcholine :

MOA - Overstimulation results in depolarizing blockade

Indications – muscle relaxation/paralysis associated with intubation, other procedures

Adverse effects – Fasciculations, respiratory arrest, malignant hyperthermia

= Indirect Acting Cholinergic Agonists (All the following indirect effect except?**)** <- **الدكتورة حكت**

1)Reversible

-Edrophonium -Neostigmine -Pyridostigmine -Physostigmine

MOA - Prolongs duration of Ach by binding with and blocking acetylcholinesterase.

Indications – Myasthenia Gravis, Glaucoma, Atropine Poisoning

-Used in Alzheimer's : Donepezil/ Galantamine/ Rivastigmine
-Irreversible (Echothiophate**)**

Pharmacology L3(Local Anesthetics)

= LA: -applied locally & block nerve conduction of sensory impulses -transient loss of sensation without loss of consciousness

=MOA : Prevent the initiation and propagation of nerve impulse

= Clinical Uses

1)Before endoscopy

2)Surface anaesthesia (for painful m.m lesions)

3)Infiltration anaesthesia e.g : -Subcutaneous inf: suturing

-Submucosal inf: dental procedures

-Intraarticular injections (with corticosteroids)

4)Regional anaesthesia

=ph.k - effective within 5 min, duration of action 1-1.5 h (doubled by adding vasoconstrictors) - Lidocaine t1/2 (1.5 h), Bupivacaine t1/2 (3 hrs) (long acting)

- **Avoid use** of vasoconstrictors for extremity (finger, toe, nose, penis), due to cut off blood supply & organ damage

= Epidural Anaesthesia

- Lumbar epidural is widely used in **obstetrics (**Pain management**)**

- A cannula with catheter inserted into epidural space so drugs can be delivered **as needed** to extend the duration of the block

-Used to : Post operative analgesia /Improves outcome by reducing risk of (DVT, chest infection)

= Spinal Anaesthesia

-drug is injected into (CSF) -A spinal block is a single injection

=**Lidocaine** is the first choice drug for surface and for injection

=**Bupivacaine** is used for peripheral nerve blocks and for epidural and spinal anaesthesia

=**Pethidine** is the drug of choice for analgesia during labour

=Side effects results from large doses, repeated administrations, systemic absorption of LA & high plasma concentration

Biochemistry (L1&2) Biochemistry of Vision I & II

= Rhodopsin:- the only visual pigment in rods

-It consists of the transmembrane protein (GPCR) called opsin (detect the light) and light sensitive moiety called retinal(activated or stimulated by light)

-YOU MUST KNOW! The biological form of Vitamin A in Retina is the aldehyde form

*At present of light retinal loss its color(photobleaching)which has chromophore

- Schiff base linkage: one of the reversible covalent bond between Opsin & Rhodopsin

= Iodopsin: the visual pigment in cones /which give us color vision

= Phototransduction Cascade

-In darkness, rhodopsin is inactive and cGMP level high, Na+ channels open/-The inhibitory neurotransmitter released which make bipolar cell switch off.

- In presence of light, rhodopsin is activate lead to closure of Na+ channels due to decreases cGMP →hyperpolarizes the cell → bipolar cell switch on.

-cGMP is the second messenger in phototransduction cascade

= Photoisomerization of retinal

1)from 11-cis Retinal To All Trans-retinal 2)Activation of Opsin 3)Shift in the absorption spectrum of Opsin from (visible) To (UV)

= Regeneration of Visual Pigment

-11-cis retinal (Reduction)to all trans retinol (Esterification) to all trans retinyl ester by "LRAT" then (Isomerization) to 11-cis retinol by "RPE65" which is the rate limiting step here, Finally (Oxidation) to 11-cis retinal

ROD	***CONE***
Function in dim light(scotopic)/more in #n	Function in day light(photopic)
Not perceive color(monochromatic)	For color vision(trichromatic)
high sensitivity and low resolution Loss causes night blindness	low sensitivity and high resolution Loss causes legal blindness

=Light and Dark Adaptation

Dark adaptation: is the slow recovery of visual sensitivity (20-30 min regeneration of rods is slow) after exposure to a bright/strong light

Light adaptation: is the adaptation to increased level of illumination 5 min

-Mechanisms :

1)Pupil size to adjust amount of light reaching the retina

2)Switch-over between rods and cones

3)Bleaching / regeneration of photopigments

=The 4 main forms of vitamin A:

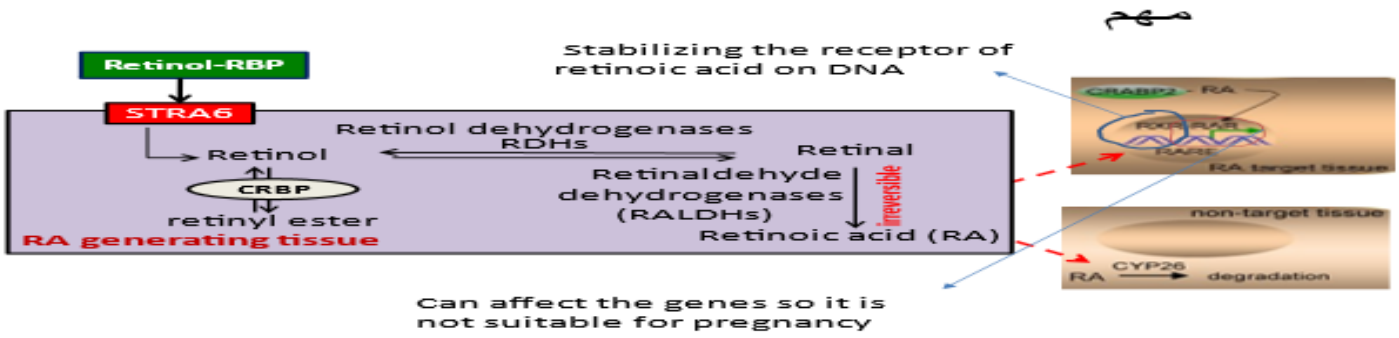
1) **Retinol** (MOVEMENT FORM)
2) **retinal**(retinaldehyde) The biological active form only in Retina
3) **Retinoic acid (**the biologically active metabolite of vitamin A**)**
4) **retinyl ester(**storage form**)**

=Vitamin A Absorption & Metabolism

→ retinyl esters stored in stellate cells in liver

→CRBP I : cellular retinol binding proteins in tissues

→CRBPII : in small intestine



Biochemistry (L3) Biochemistry of Taste & Smell

- There are 5 primary taste sensations:

=Sweet taste: - indicates energy rich nutrients (e.g. glucose)

-its receptor: heteromeric GPCR (T1R2 and T1R3 proteins)

-second messenger: cAMP (that activates a protein kinase (PKA) that depolarizes the receptor cells by closing K+ channels at the basolateral membrane)

- Artificial sweeteners : through second messenger IP3 which induces the release of Ca2+ from intracellular stores

=Salty taste: -modulating diet for electrolyte balance (e.g. NaCL)

-its receptor: amiloride -sensitive Na+ channels

=Sour taste: typically the taste of acids (e.g. lemon)

-its receptor: H+ ions through amiloride -sensitive Na+ channels or from the blockade of K+ channels

=Bitter taste: allows sensing of diverse natural toxins/ include alkaloids like quinine and caffeine

- its receptor :least one depolarize by blocking apical K+ channels, most bind to G protein-coupled receptors (GPCRs) of the T2R receptors.

- the membrane-bound G-protein: "gustducin

- second messenger : IP3 (causes the release of Ca2+ from intracellular stores)

=Umami taste: the taste of amino acid glutamate found in breast milk (10X) & many foods (e.g. meat, tomatoes, mushrooms, onions)

-its receptors :1) Metabotrophic glutamate receptor 4 " mGluR4"

(causes Ca 2+ to be released from intracellular stores such as the endoplasmic reticulum (ER).)

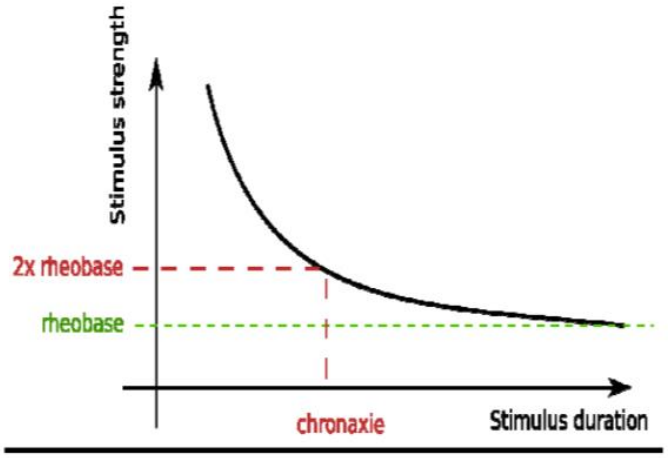
2)Heteromeric GPCR consists of T1R1 and T1R3 proteins. (increases the intracellular level of Ca 2+)

Physiology L1 (Physiology of peripheral nerves)

-current sink : conduction of impulse in the unmyelinated nerve fiber

-Saltatory (jumping or node to node conduction): conduction of impulse in the myelinated nerve fiber

** Strength-duration curve



Rheobase: It is the minimal strength of current that can excite the nerve (threshold).

Utilization time : It is the time needed for excitation by Rheobase

Chronaxie : It is the time needed by a current double the rheobase to excite the nerve.

- **measure the excitability**

Minimal time : It is the minimal time below which no excitation occurs whatever the strength of the stimulus

N.B.: Stimulation at the cathodal end resulted in three types of depolarization:

	catelectrotonus	*local response*	*firing level*
-Stimulus	Subthreshold	Subthreshold	Threshold or more
-Depolarization	Less than 7mv.	From 7 to 25	25 or more
-Mechanism	Passive	Passive and partial active)	active
-Forces affect the membrane	Repolarization mask this effect	Repolarization mask this effect	Depolarization force is more& action potential resulted

Physiology L2 (ANS)

Types of Autonomic Ganglia		
Lateral ganglia = Sympathetic chain	**Collateral ganglia**	**Terminal ganglia**

Paravertebral = Lateral -3cervicle ganglia **(superior/ middle / inferior) -12 thoracic** **-4 lumbar -4 sacral**	**Near the origin of big arteries (plexuses)**	**Near or in the wall of organs**
Always sympathetic	**Sympathetic (celiac / renal / sup. & Inferior mesenteric ganglia)** **Parasympathetic (otic / ciliary / sphenopalatine & submandibular ganglia)**	**Always parasympathetic**

		Origin	Supply?
Cervical division		Upper 2 thoracic segments & relay in the sup. Cervical sympathetic ganglia	It follows the course of carotid arteries: -eye -glands -skin -cerebral arteries
Thoracic division		Upper 4 thoracic segments & relay in the cervical and upper 4 thoracic ganglia	Form the superficial & deep cardiopulmonary plexuses -Heart -Lung
Splanchnic division	Abdominal division	Lower 8 thoracic segments & relay in celiac, renal & mesenteric ganglia	-GIT -GI secretions - spleen - liver - splanchnic vessels - endocrine pancreas - kidney
	Pelvic division	Upper 2 lumbar segments	-urinary bladder - rectum - sex organs
Somatic division	Upper limb	4^{th} to 8^{th} thoracic segments & relay in the lower cervical and upper 4 thoracic	-Skin: 1- sweat glands 2- cutaneous B.Vs 3- erector pilea muscles -Skeletal muscles: 1-Blood vessels
	Lower limb	10^{th} thoracic to 2^{nd} lumbar segments & relay in the lumbar and sacral ganglia	

-**Mild vasoconstriction** effect on the cerebral arteries during the sympathetic excitement (cerebral blood flow **increase** due to ↑ in BP).

- the direct sympathetic effect on the coronary B.V is vasoconstriction, but they **dilate** because accumulation of metabolites.

Physiology L3 (Parasympathetic Nervous System)

Parasympathetic outflow		Origin	Preganglionic fibers relay on?	Supply?	Effects
Cranial outflow	Oculomotor nerve	Edniger-westphal nucleus	Ciliary ganglion	-constrictor pupillae -ciliary muscle	- miosis - increase the power of the lens (near vision
	Glossopharyngeal nerve	Sup.salivatory nucleus in the lower pons	- sphenopalatine ganglion (Fibers to lacrimal & nasal glands) - submandibular ganglion (Fibers to submaxillary gland)	- submaxillary salivary gland -lacrimal & nasal glands	-true secretion (for salivary glands) - vasodilation
	Facial nerve	Inf.salivary nucleus in medulla	Otic ganglion	-parotid salivary gland	-secretomotor (True secretions) -vasodilation
	Vagus	Medulla oblongata	Terminal gang. In the supplied organs	**IN THE TABLE BELOW**	
Sacral outflow		LHC of 2nd, 3rd & 4th sacral segments	Terminal gang. In the supplied organs	-descending colon, rectum & anal canal	-contraction of the rectal wall & relaxation of internal rectal sphincter **(Defecation)**
				-urinary bladder	-contraction of the wall & relaxation of the internal sphincter **(Micturition)**
				-B.Vs of external genitals	Vasodilation **(Erection of penis in male & clitoris in female)**

Vagus nerve supply?	Effect
Heart	-inhibit all cardiac properties -decrease coronary blood flow -decrease O2 consumption of the heart
Bronchi & bronchioles	-bronchoconstriction -increase the bronchial glands secretion
Pulmonary blood vessels	vasodilation
GIT wall	-contraction of the wall (esophagus →proximal part of large intestine) -relaxation of the sphincters
Digestive glands	Secretomotor
Pancreas & liver	Enhance the insulin release
Gall bladder	-motor to the gland (contraction) -relaxation of the sphincter of Oddi

Physiology L4 (Vision)

الخطررر ! ☠⚠

Causes of corneal transparency:

1. The avascularity of the cornea 2.The corneal collagen bundles are regularly arranged.
3. Absence of myelin sheath in the corneal nerve fibers. 4. Relative corneal dehydration 5. The refractive index is **the same in** all the corneal layers =**1.37.**
6. Vitamins as vitamin "A" which prevents keritinization also vitamin B_2 (riboflavin) prevents corneal vascularization.

Function of the aqueous humor: -

1) It supplies avascular cornea and lens with nutrients and removes waste products.2) It maintains intraocular pressure.
3) It plays a role as a refractive medium in the eye.

Intraocular pressure (IOP)

The intraocular pressure in man is **15-20** mmHg. The intraocular pressure remains constant inspite of wide changes in the arterial blood pressure. In man the intra-ocular pressure is measured indirectly by an apparatus called "Tonometers".

Functions of the vitreous:-

1- Shock absorber to protect delicate retina from injury. 2- Support lens in its position 3- Maintain normal globular shape of the eye.4- It plays a role as a refractive medium in the eye.

Functions of the lens:-

1 - It is a transparent media which allow light to reach the retina. 2- Acts as a refractive media having a diopteric power of **15-32** diopter. 3- Accommodation to near and far vision for accurate focusing. 4- Protect retina from harmful ultraviolet rays (by absorb them).

Functions of the iris:

1. **control the amount of light**.
2. It prevents light rays from falling on the periphery of the eye lens to **decrease the spherical and chromatic aberrations.**
3. Constriction of the pupil **increases** the **depth of focus** of the lens system of the eye , this mechanism makes the distance of the object can be changed but it's image still focused on the retina without another new change in accommodation.
4. Recognition of iris patterns by a video camera that captures iris images and translates the landmarks into a computerized code is more **foolproof** than fingerprinting or even DNA testing (basis of the latest identification technology).

**the center of papillary light reflex is →pretectal nucleus in the midbrain

Changes in the pupils during anesthesia:

I- During the **first** stage, the pupils may be of **normal size or slightly dilated** react to light. Moreover, corneal reflex is intact.

II- During the **second** stage, the pupils are **dilated more**, with intact light and corneal reflexes. It is accompanied with sympathetic stimulation.

III- During **the third** stage, the pupils are **constricted** due to release of the Edinger-Westphal nucleus from the normal cortical inhibition, with absence of light and corneal reflexes (Stage of surgical anesthesia).

IV- Stage of deep anesthesia or stage of medullary inhibition, during which the pupils are fully dilated with absence of light and corneal reflexes

Miosis	Mydriasis
I - Pupillary light reflex (light adaptation). 2-Accommodation reflex (near vision). 3- Sleep due to increase of the parasympathetic tone. 4- Surgical anesthesia (stage III). 5- Horner's syndrome (paralysis of cervical sympathetic division). 6- Stimulation of semicircular canals (during rotation). 7-Pontine hemorrhage affects pupillodilator centre. 8-Drugs: a-Parasympathomimetics e.g. • **Acetylcholine & pilocarpine**: acting directly on cholinergic receptors. • **Eserine & prostigmine:** (Anticholine esterase →↑ A.Ch. concentration). b-**Morphine** increases excitability of third cranial nerve nucleus by releasing it from inhibitory cortical effect (in morphine poisoning pupil reaches 1mm i.e pin point pupil very diagnostic sign).	1-Dark adaptation 2-Distant vision 3-Hypersecretion of adrenaline & noradretialine as in pheochromocytoma. 4- Injury of oculomotor nerve. 5-After stoppage of rotation 6- Stage I, II & VI of anesthesia. 7- Pain, emotions fear and asphyxia 8- Drugs: a.Sympathomimetics: as **adrenaline** injection stimulating the peripheral-adrenergic receptors. B.**Cocaine** increases the sensitivity of the dilator pupillae muscle to action of adrenaline or sympathetic stimulation. c.**Atropine** causes marked dilation and cycloplegia (paralysis of constrictor pupillae muscle) for long time.

Microbiology L1

=Clostridium botulinum

- Gram positive spore forming(Oval and subterminal) anaerobic/-Motile by flagella

- Pathogenesis : flaccid motor paralysis

- The toxin (heat labile):

Preformed in food (canned) /Spores ingestion e.g Honey /Spores contaminating wounds /Iatrogenic

- IP: 12-48hrs in food borne, longer in wound botulism (days – 2 w)

=Clostridium tetani

- Gram positive, motile anaerobic rods /-β-Haemolysis when grown on blood agar

-Spore forming: round terminal

- Produce two plasmid coded exotoxins:

1. Tetnospasmin(Neurotoxin)

2. Tetanolysin (haemolysin)

- Pathogenesis: Spastic paralysis (tetanus)

- IP: 3days – 3 weeks

- Source:-Dirty or Infected wound and abscesses /-Chronic skin ulcers/-Cryptogenic

- A highly effective vaccine is available.

- Tetanus immunity is achieved using:

  - A formalized tetanus toxoid.

  - Toxoid is administered as part of DTP vaccine -Boosters every 10 yrs

Microbiology L2 (Prions and Rabies)

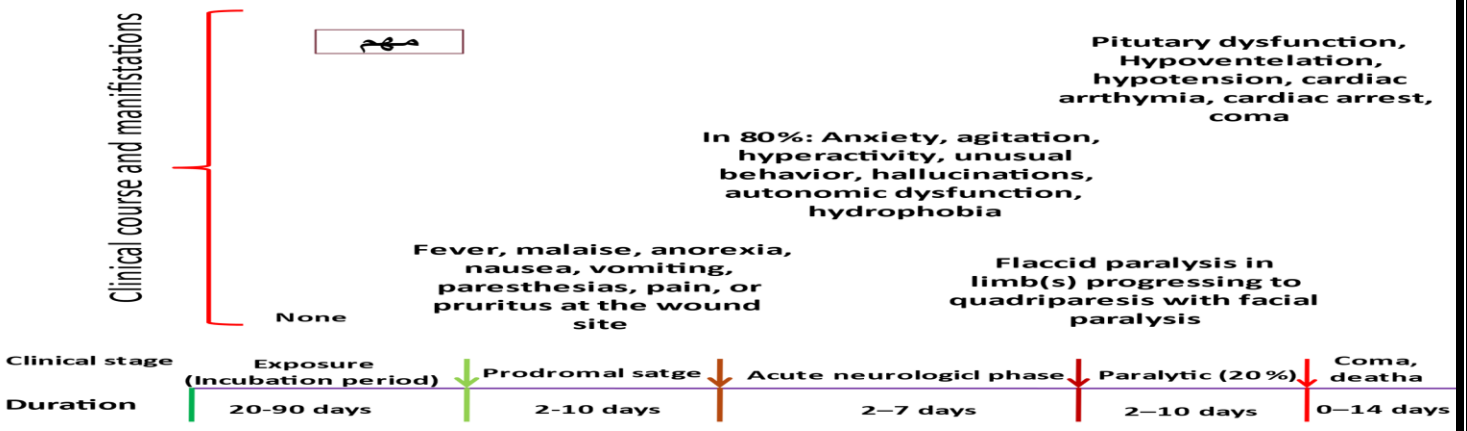
= Prions :- Proteinaceous infectious particle that lacks nucleic acid(CD230)-its Functions: 1)myelin repair in Schwann Cells 2)Cell-cell adhesion 3)Maintenance of long-term memory 4) necessary for self-renewal of bone marrow 5) antioxidative(Prevent neuronal dysfunction)

- it is the caustive agents of bovine spongiform encephalopathy ("mad cow disease") and its human equivalent, Creutzfeldt–Jakob disease (caused by misfolded proteins)

- The most widely diagnostic method of PrP by immunoassay after denaturation

= Rabies- preventable viral disease /- -ssRNA /- Single antigenic type/-IP: 20–90 d

- Pathogenesis : The most characteristic pathologic finding in rabies is the Negri body



مهم

Vaccination Status	Treatmen	Regimen
Not previously vaccinated	Wound cleansing	The wound needs to be thoroughly scrubbed with soap and water, or, if available, iodine solution, 40-70% alcohol, cetrimide 0.1% or a similar compound, or the virucidal agent povidone, all under local anaesthesia if possible. The rabies virus is killed by sunlight, drying, soap, and the other agents mentioned.
	RIG*	Administer 20 IU/kg body weight. If anatomically feasible, the full dose should be infiltrated around the wound(s) and any remaining volume should be administered IM at an anatomical site distant from the vaccination site. Also, RIG should not be administered in the same syringe as the vaccine. Because RIG may partially suppress the active production of antibodies, no more than the recommended dose should be given
	Rabies vaccine	Administer 1 ml IM or 0.1 ml ID in the deltoid area on days 0, 3, 7, 14 and 30. A booster dose on day 90 is optional.
Previously vaccinated	Wound cleansing	The same
	RIG	RIG should not be administered
	Rabies vaccine	If vaccinated within one year: 1 ml IM or 0.1 ml ID on day 0. If vaccinated more than one year prior: 1 ml IM or 0.1 ml ID on days 0, 3, and

Microbiology L3 (Enteroviruses)

= Polioviruses

- Enterovirus (RNA) -Three serotypes -Minimal heterotypic immunity between serotypes

-Rapidly inactivated by : heat, formaldehyde, chlorine, ultraviolet light

-tolerates in stomach acidity

- Reservoir : Human -MOT: Fecal-oral / Oral-oral possible
-Communicability :7-10 days before onset Virus present in stool 3-6 weeks

-Pathogenesis: Destruction of motor neurons commonly in the grey matter of anterior horn of spinal cord

-Diagnosis: -Culture: CPE and neutralization assays -RT-PCR

-Incubation period: 10 -14 days

-4 possible outcomes: 1)Asymptomatic (mostly) 2)Abortive inf (minor disease) 3)Non-paralytic poliomyelitis / CNS 4)Paralytic poliomyelitis (major disease)

-Poliovirus vaccine :

1- Oral Poliovirus Vaccine (OPV) Sabin : -Consists of live attenuated virus of all 3 serotypes - 3 doses -Post vaccine poliomyelitis 1: 2.5 million vaccines
2- Intramuscular Poliovirus Vaccine (IPV) Salk : - Consists of formalin inactivated virus of all 3 poliovirus serotypes -3 doses -Produces serum antibodies only: IgG

= Paralytic poliomyelitis:

-Secondary to permanent damage of Lower motor neurons / No sensory involvement -Flaccid paralysis (weakness, deformity…) -Asymmetrical

-affects proximal muscles (commonly legs) -Recovery may be complete, partial, or absent.

=Paralysis develops more frequently in:

-Adults -muscle trauma -Tonsillectomy -Pregnancy

Microbiology L4

= Group B streptococcus (Streptococcus Agalactiae)

- Facultative anaerobic encapsulated gram + coccus

-B-hemolysis on blood agar -Most strains are bacitracin resistant / hydrolyze hippurate

-9 Serotypes -Normal flora of throat, colon, urethra and, and in 10-40% of women vagina.

-Major virulence factors:

Haemolysin /Polysaccharide capsule /Peptidase and hyaluronidase enzymes

Clinical pic : 1)Early sepsis:

=Risk factors

-Group B streptococcus genitally colonized mother

-prematurity

-Prolonged rupture of membrane (PROM)

-Prolonged labour

-Maternal Chorioamnionitis, leukocytosis and fever

-Previous delivery with GBS disease

=Source of bacteria: Ascending or during delivery

Occurs in the first week of life, though most present within the first 48 hrs.

=Meningitis, pneumonia and septic shock are common.

2) Late sepsis:

-Absent history of complicated delivery

-Usually hospital acquired (medical staff, visitors and mother) -1 week – 3months

Treatment:

-If the mother had a risky delivery then give IV intrapartum antibiotics

-Continue antibiotics for 12-24 hrs with the baby and stop if asymptomatic and cultures negative

-If the baby is symptomatic / cultures positive, then 2-3 weeks of IV antibiotics and stop pending improvement

=M. leprae

-Causative agent : - M. leprae/Acid fast, rod shaped bacillus/Stain Ziehl Neelsen carbol fuchsin.

-Transmission : Airborn

Epidemiology : All ages, from early infancy to very old age/ M:F 2:1/ leprosy is endemic in (parts of India, China, Japan, Nepal, Egypt, and other areas)

Pathogenesis : proliferate within macrophages - distinguished by its chronic slow process and by its damaging lesions.

-The organism has a preference for skin and nerves.

Reservoir : Human

incubation period : 2 - 40 years AV: 5-7y

= Tuberculoid leprosy

- Skin lesions in areas of nerve damage.
-The **skin ulcers** occur by
=direct action of M. leprae on the peripheral nerves
=direct invasion of bacilli in the vascular endothelium
= raised and erythematous border lesion & a dry scaly in center & complete anesthesia.
= large flattened patches with raised and elevated red edges on their skin
= Damage of the nerve can result in wrist drop or foot drop
=loss of sensation
= strong cell-mediated immune response and develops delayed hypersensitivity, which can be shown by a skin test with lepromin

= Lepromatous form

= proliferates within the macrophages.

=Bacilli are numerous in the skin (as many as (10)9/g

=patients present with symmetrically distributed skin nodules ,raised plaques, or diffuse dermal infiltration, which results in lion face appearance.

=Diagnosis : 1) clinical sign 2) Lepromin positive test (Negative In lepromatous leprosy because of humoral immunity not cell mediated.)

Medicine (Peripheral Neuropathy)

= Neuropraxia : Functional deficit

- continuity of n. is intact -perineureum, endoneureum, and epineureum are intact -full recovery -No degeneration

= Axonotmesis : Injury to the axon and endoneureum

- Wallerian degeneration -Recovery can occur by axonal regeneration but it takes longer duration -recovery is possible

= Neurotmesis : - lesion of the axons, endoneureum, perineurem, and epineureum

-Wallerian degeneration -No spontaneous recovery is possible without surgical repair

-Classification of neuropathy

1)Plexopathy: such as brachial plexus lesion

2)Mononeuropathy: such as median neuropathy, Common peroneal n. syndrome.

3)Polyneuropathies: it is a systemic neuropathy that affects almost all nerves in a variable degree. the **longest axons** are affected earlier.

=Acquired polyneuropathies: (مهم) association with

- endocrine disorders: DM - systemic disease CT disease

- deficiency Vitamin deficiency (B12, B6, E), Copper

- Medications & Heavy metals - infections Viral

-Acute inflammatory: Guillain-Barré Syndrome (GBS)

- Chronic Acquired Immune-Mediated Demyelinating Polyneuropathies

Symptoms of polyneuropathy

1) Motor somatic : Weakness/flaccidity/Atrophy \/Hyporeflexia or reflexia Fasciculations
2) Motor autonomic : Orthostatic hypotension/(Tachy/ brady)cardia/Gastroparesis (Urine/Fecal) incontinence /Impotence /Blurred vision /Dryness of skin/Excessive sweating
3) Somatic sensory : Focal sensory loss /Parasthesia/Ataxia
4) Special sense : Loss of: smell /taste -Vertigo

Pathology L1 (Neuroscience Pathology)

=Acute neuronal injury (number of changes occur in neurons**)**
-Within **12** hours of an irreversible hypoxic-ischemic insult, neuronal injury becomes evident on (H&E) staining
=If the changes occur in cell body : shrinkage of cell body, pyknosis of nucleus, disappearance of nucleolus, loss of Nissl substance ("**red neurons**").
=If the changes occur in axon : cell body enlargement, peripheral displacement nucleus, enlargement nucleolus, and peripheral dispersion Nissl substance (**central chromatolysis**)
=Astrocyte Injury and Repair

- **Gliosis** :repair and scar formation in the brain.
-**Gemistocytic astrocyte** : cytoplasm expands & takes on a bright pink hue, &cell extends multiple stout

- **Fibrillary astrocytes** : cytoplasm of astrocytes shrinks &cellular processes become more tightly interwoven (at long standing)
- **Rosenthal fibers**: thick, elongated, brightly eosinophilic protein found in chronic gliosis & low-grade gliomas.
- **Microglial nodules** : aggregates of elongated microglial cells (**rod cell**)at sites of tissue injury
- **Neuronophagia** : collections can be found congregating around and phagocytosing injured neurons

= Demyelinating diseases of the CNS

-Due to : damage to previously normal myelin as MS & multifocal leukoencephalopathy (viral inf) **or** Myelin is not formed properly or has abnormal turnover kinetics

Multiple Sclerosis (MS) : The most common
- caused by an autoimmune response - Episodes of disease activity - M:F 1:2
- rare in childhood & after the age of 50
-S&S : - Unilateral visual impairment, ataxia & nystagmus, motor & sensory impairment - CSF : elevated protein level, moderate pleocytosis, & increased (Ig) with oligoclonal bands.

=NEURODEGENERATIVE DISEASES

- Progressive loss of neurons - Caused by the accumulation of protein aggregates
- Activation of innate immune system is common(TREM2 for Alzheimer disease)

Alzheimer Disease (AD)
- The most common cause of dementia in older adults(Rare before 50)
- Aβ (amyloid β) and tau proteins accumulation is the fundamental abnormality
-S&S : impaired higher intellectual function, memory impairment, & altered mood and behavior
- degree of cortical atrophy, resulting in a widening of the cerebral sulci that is most pronounced in the frontal, temporal, and parietal lobes
- The atrophy produces a compensatory ventricular enlargement (hydrocephalus ex vacuo)

- Amyloid plaques (extracellular - accumulation of Aβ amyloid) and neurofibrillary tangles (intracellular -Tau accumulation).
- Death usually occurs from intercurrent pneumonia

Pathology L1 (Neuroscience Pathology)

= Peripheral neuropathies:

1) Axonal neuropathies:

-Caused by insults that directly injure the axon.

- Wallerian degeneration
- entire distal portion of an affected axon degenerates
- Regeneration of axonal regrowth and remyelination of the distal axon, proximal stump of the axon sprouts and elongate
- Hallmark of A.N : decrease in density of axons/ decrease in signal strength or amplitude of nerve impulses

2) Demyelinating neuropathies

-Damage to Schwann cells or myelin with relative axonal sparing.

-occurs discontinuously : segmental demyelination

- slow nerve conduction velocities but preserved amplitude, normal density of axons
- Regeneration gives thinly myelinated internodes of uneven length (shorter).

= Polyneuropathies

- symmetrical multiple nerves involvement
- length-dependent fashion -more in longest nerves
- "stocking-and-glove" distribution -as DM

= Mononeuritis multiplex: damage randomly affects individual nerves, resulting (right radial nerve palsy & wrist drop, & left foot drop) Often caused by vasculitis.

= simple mononeuropathy: only involves a single nerve & is most commonly result of traumatic injury (carpal tunnel syndrome), or infections as Lyme disease.

=Guillain-Barré Syndrome

- rare **Acute** Inflammatory Demyelinating Polyneuropathy
- A rapidly progressive
- characterized clinically by weakness beginning in the distal limb
- rapidly advances to proximal muscle function "ascending paralysis"

-One of the most common *life-threatening* diseases of PNS

- include Segmental demyelination(perivenular and endoneurial mononuclear cell infiltrates rich in macrophages).

= Chronic Inflammatory Demyelinating Poly(radiculo)neuropathy (CIDP)

- The most common **chronic** acquired inflammatory peripheral neuropathy
- persists for 2 months (at least) or more
- weakness, difficulty in walking, numbness, and pain or tingling sensations

- The time course and the response to steroids distinguish CIDP from GBS
- onion bulbs : multilayered structures due to repeated activation and proliferation of Schwann cells

=Diabetic PN

- the most common cause of peripheral neuropathy
- Distal symmetric sensorimotor polyneuropathy is the most common form of diabetic neuropathy - Sensory axons are more severely affected
-hyperglycemia : accumulation of advanced glycosylation end products(AGEs), increased levels of ROS, microvascular injuries, & changes in axonal metabolism.
- best therapy: Strict glycemic control.

= PERIPHERAL NERVE SHEATH TUMORS:

Schwannomas

- Benign encapsulated tumors - occur in soft tissues, internal organs, or spinal nerve roots.
- most commonly affected CN is vestibular portion of 8th nerve, which includes hearing loss
-Most are sporadic, ~10% are ass with familial (NF2) - Circumscribed masses
- admixture of dense & loose areas referred to as Antoni A(Verocay bodies) and B, respectively

Neurofibromas

- encapsulated benign - localized cutaneous tumors, Diffuse or Plexiform -background stroma contains loose wavy collagen bundles - Malignant Peripheral Nerve Sheath Tumors can arise from them or de novo (50% of MPNST have NF1)