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GENERAL & CELLULAR PHYSIOLOGY

----- Active space -----

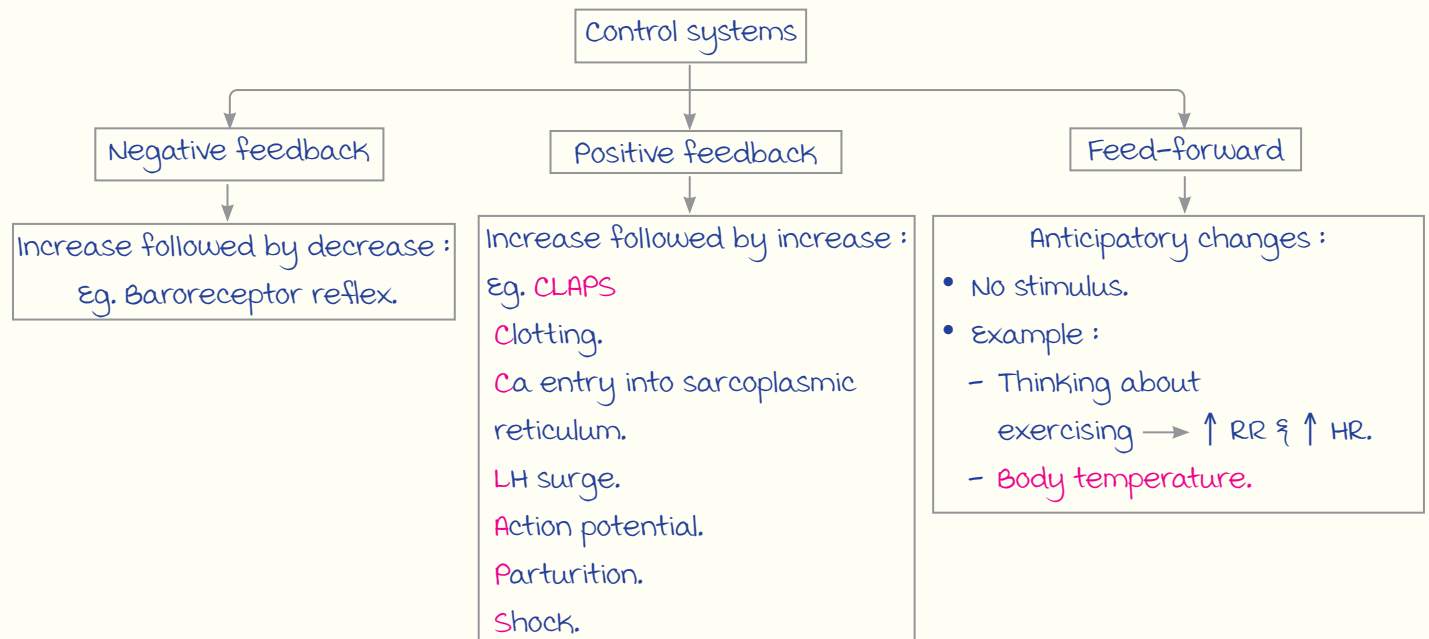
Homeostasis

00:00:10

Claude Bernard : Coined the term milieu interieur (Internal environment).

Walter Cannon : Coined the term homeostasis.

Maintenance of homeostasis :



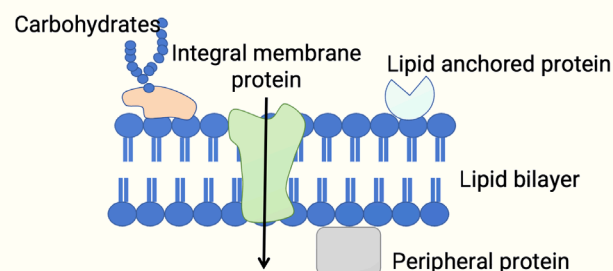
Assessment of effectiveness of negative feedback :

$$\text{Gain} = \frac{\text{Correction}}{\text{Error left after feedback}}$$

- Error left \oplus \rightarrow Not a good control system.
- 0 error left \rightarrow Gain is infinity (Role of kidneys in regulating BP).

Cell Membrane

00:09:00



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Membrane Lipids :

Phospholipids :

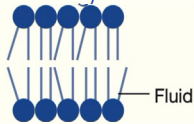
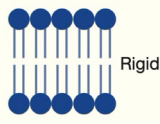
- Phosphatidylcholine/Lecithin/Dipalmitoyl phosphatidylcholine (DPPC) : Present in **surfactant**.
- Sphingomyelin : Present in nerve & surfactant.
 - Lecithin - sphingomyelin ratio : $\frac{L}{S} \geq 2 \rightarrow$ Adequate **fetal lung maturity**.
- Phosphatidylserine (PS) :
 - **Inner surface** of cell membrane.
 - If expressed outside : Eat-me signal \rightarrow Cell undergoes **apoptosis**.
- Phosphatidylinositol : Second messenger.
- Cardiolipin : **mitochondria of heart**.

Glycolipids :

Types	Site	Significance
Cerebrosides	CNS	-
Gangliosides	GIT	Gm-1 gangliosides : Receptors for cholera toxin \rightarrow Fragment B .

Sterols : Cholesterol (Fluidity buffer) \rightarrow maintains membrane fluidity.

Characteristics of fluidity :

	Increased fluidity	Decreased fluidity
effect on health	Good	Bad
Type of fatty acids	unsaturated (Essential)	Saturated (Trans)
Examples	<ul style="list-style-type: none"> • Linoleic acid. • Linolenic acid. • Arachidonic acid. • Omega-3 fatty acids : Abundant in fish. 	<ul style="list-style-type: none"> • Stearic acid. • Palmitic acid. (Abundant in junk food). 

Membrane Proteins :

Transmembrane proteins :

Cystic fibrosis transmembrane conductance regulator (CFTR) :

- Chloride channel.
- mutation : **Cystic fibrosis**.

Peripheral proteins :

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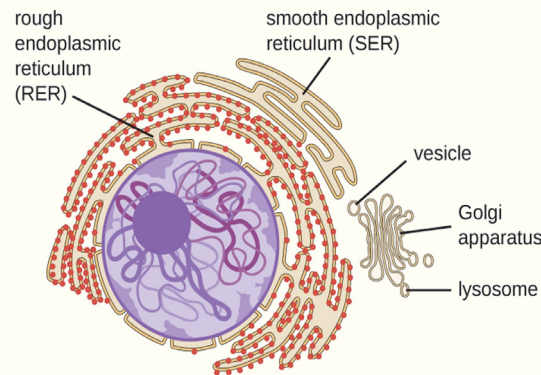
Cell	Protein	Diseases due to mutations
RBC (Biconcave disc)	Spectrin	Elliptocytosis
	Ankyrin	Spherocytosis
Skeletal muscle	Dystrophin	Duchenne muscular Dystrophy (DMD)

Lipid anchored proteins/GPI anchored protein :

- Present in RBC only.
- Examples : CD55 & CD 59
- mutation : Paroxysmal Nocturnal Hemoglobinuria (PNH).

Cell Organelles

00:20:10



Endoplasmic reticulum :

	Rough ER	Smooth ER
Granulations	⊕ due to ribosomes	⊖
Functions	<ul style="list-style-type: none"> • Biosynthesis of proteins. • Along with chaperones, aid in protein folding. • ER-associated degradation : Destruction of misfolded proteins. 	<ul style="list-style-type: none"> • Drug detoxification (By CYP450 in liver). • Calcium storage. • Steroid biosynthesis. (Adrenal gland, liver, testis, ovary)

Golgi apparatus :

Two ends :

- Cis end/receiving end : Receives protein Post translational modification → vesicles.
- Trans end/releasing end : Releases vesicles.

Lysosomes : Aka suicidal bags/residual bodies.

- Involved in acid mediated destruction.
- Enzymes : Acid phosphatase, acid hydrolase.
- Autophagy : During starvation.

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Peroxisomes :

- AKA microbodies.
- Functions :
 - Oxidation of long chain & very long chain fatty acids.
 - Generation & degradation of H_2O_2 by **catalase**.
 - Synthesis of **plasmalogens**.
- Peroxisomal disorders : Zellweger syndrome, Refsum disease.

mitochondria :

- Derived from ovum (**maternal inheritance**).
- Human mitochondrial DNA : **Circular dsDNA** (16,500 base pairs).
- mitochondrial DNA mutations :
 - > 10 times the rate for nuclear DNA.
 - Affects **organs** with **high metabolic** requirements :
Skeletal muscle, CNS, liver.

Nucleus :

- Contain blue prints for DNA : Chromosomes.
- DNA + histones = Chromatin : Repeating structural unit called nucleosomes.
- Nuclear pore complex : Regulates movement of substances in (Importins) & out (Exportins).

MARKER ENZYMES

Cell organelle	marker enzyme
Cell membrane	$Na^+ - K^+$ ATPase
Endoplasmic reticulum	Glucose-6-phosphatase
Golgi apparatus	Galactosyl transferase
Lysosomes	Acid phosphatase
Peroxisomes	Catalase
mitochondria	ATP synthase
Nucleus	RNA polymerase

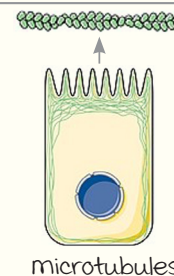
Cytoskeletal Filaments

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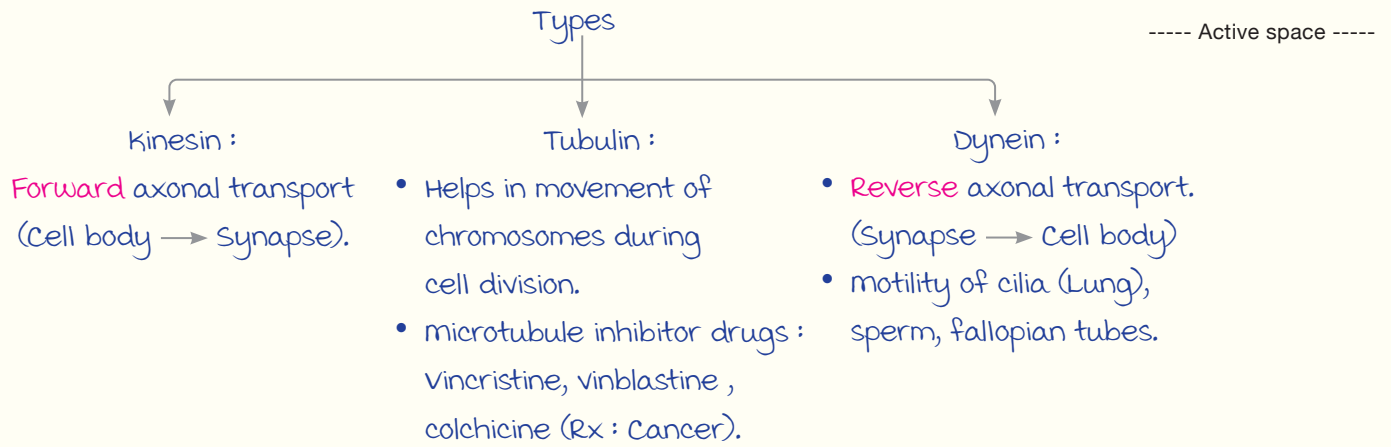
Types :

microtubules :

Size : Largest.



microtubules

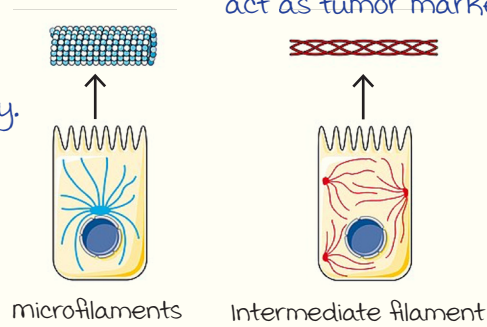


microfilaments :

- Size : Small
- Types : Actin & myosin.
- Function :
 - muscle contraction : Sliding filament theory.
 - Cell motility : By actin polymerisation.
Eg : Tumbling motility in *listeria*.

Intermediate filaments :

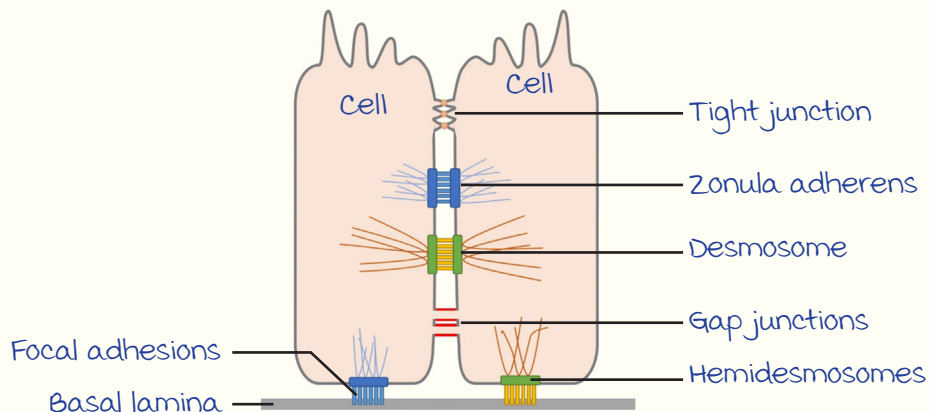
- most abundant & act as tumor markers.



Filament	Tissue	marker for
Keratin	Epithelial tissue	Epithelial carcinoma
	Liver (Mallory-Denk bodies)	Alcoholic liver disease
Desmin	Muscle	Rhabdomyosarcoma
Vimentin	Connective tissue (Fibroblasts)	Mesenchymal tumors
Glial fibrillary acidic protein (GFAP)	Astrocytes	Astrocytoma
Lamin	Nucleus	Progeria (Premature aging)

Cellular Junctions

00:40:37



----- Active space -----

Cell Junctions	Protein	Characteristics & Clinical importance
Cell - Cell junctions		
Zonula adherens	Cadherins	<ul style="list-style-type: none"> Calcium dependent linkages. Linked to actin.
Desmosomes	<ul style="list-style-type: none"> Desmoglein. Desmocollins. 	<ul style="list-style-type: none"> Linked to intermediate filaments. Seen in areas of mechanical stress : Skin, uterine cervix. Antibodies against desmoglein <p style="text-align: center;">↓</p> <p style="text-align: center;">Pemphigus Vulgaris</p>
Zonula occludens	Occludin	-
	Claudin	mutation in claudin ↓ Familial hypomagnesemia with hypercalciuria & nephrocalcinosis
Gap junctions	Connexon (1 Connexon = 6 connexins)	<ul style="list-style-type: none"> Abundant in heart. mutations in connexin → Cardiac arrhythmia. Charcot-Marie-Tooth disease.
Cell basal lamina junctions		
Hemidesmosomes	-	Linked with intermediate filaments
Focal adhesions	-	Linked with actin

Cellular Messenger & Receptors

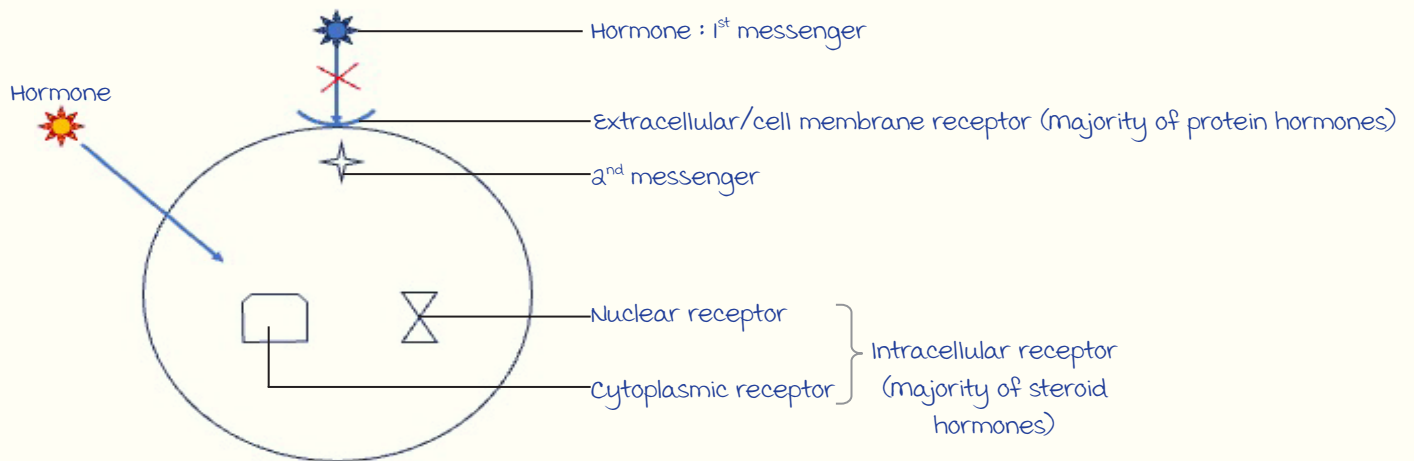
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Cellular messengers/Hormones :

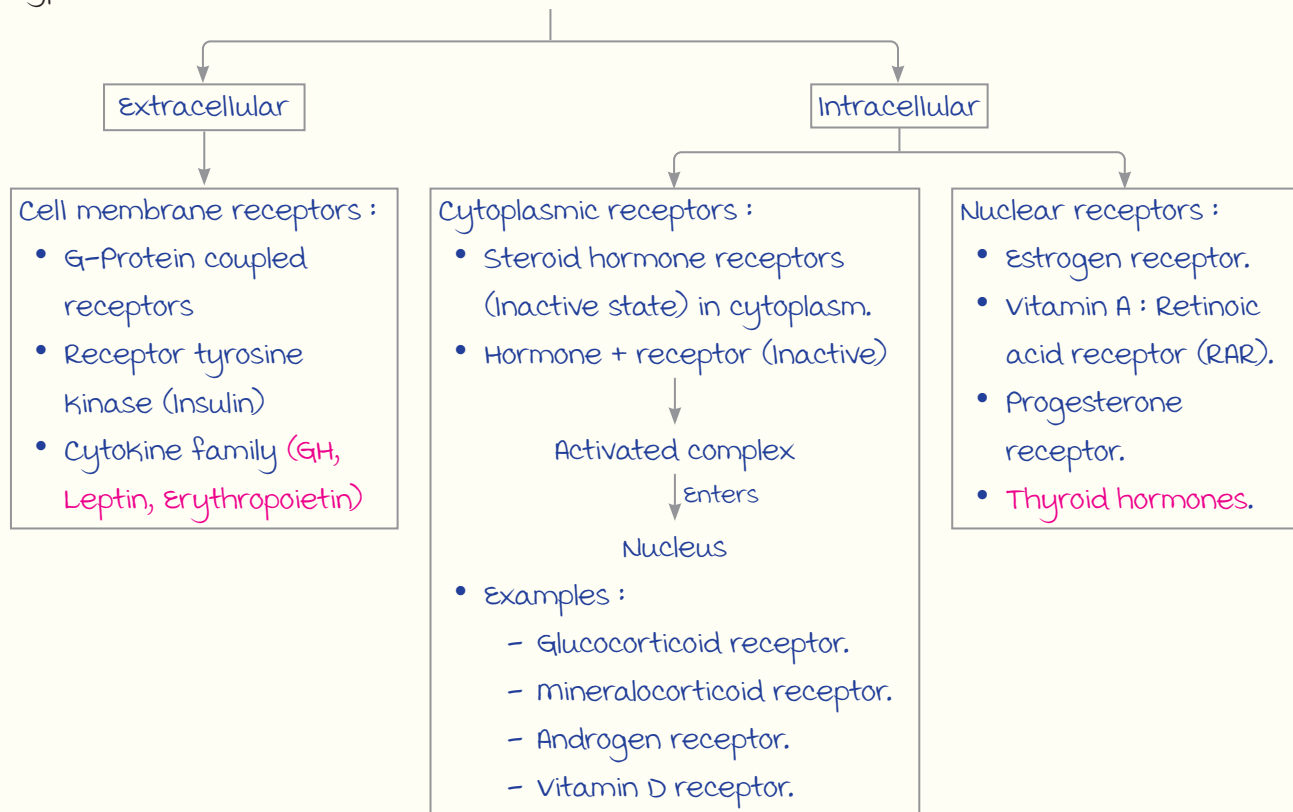
Class	Examples
Amino acid derivatives	Tyrosine → Catecholamines : <ul style="list-style-type: none"> - Epinephrine. - Norepinephrine. - Dopamine.
Protein hormones	Large protein hormones : <ul style="list-style-type: none"> • 51 AA : Insulin. • 84 AA : Parathormone.
Cholesterol derivatives	Steroid hormones : <ul style="list-style-type: none"> • Aldosterone, cortisol. • Estrogen, progesterone. • Testosterone.
Vitamin derivatives	Vitamin A & D

Hormone Receptors :

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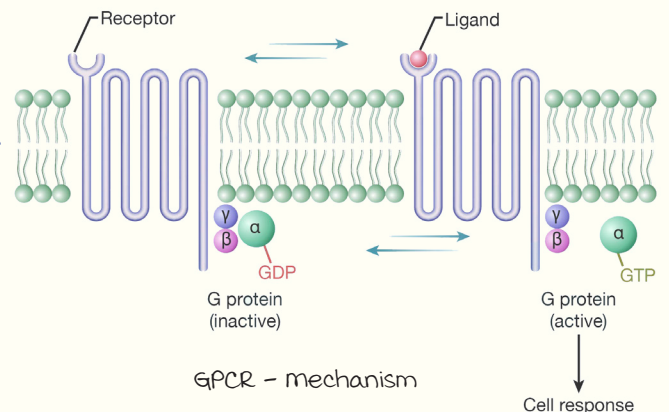
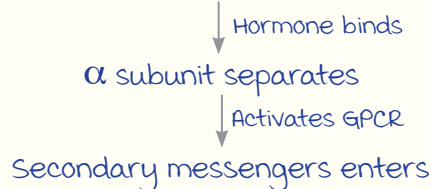


Types :



G protein - coupled receptors (GPCRs) :

- AKA 7 transmembrane/serpentine receptors.
- Heterotrimeric : 3 subunits (Alpha, beta, gamma).
- mechanism of action : Inactive GPCR



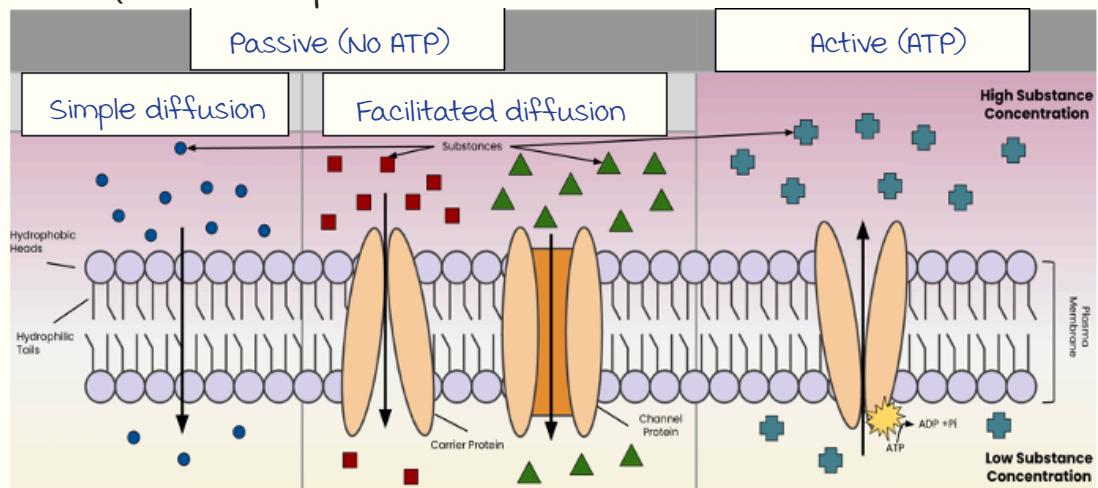
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Second messengers :

2 nd messenger	Hormone	Function
cAMP	vasopressin (va)	Water reabsorption
	Glucagon	metabolism
	Secretin	Electrolyte (HCO_3^-) secretion
Calcium (IP_3 - DAG)	Vasopressin (vi), Endothelin	vasoconstriction
	Oxytocin	uterine contraction
	-	Exocytosis
cGMP	Nitric oxide	vasodilatation
	Natriuretic peptides	Relaxation

Membrane Transport Processes

00:58:55

Passive & Active Transport :

	Types	Characteristics
Passive transport	Simple diffusion	<ul style="list-style-type: none"> Fick's law : Diffusion <ul style="list-style-type: none"> - Directly proportional : membrane surface area, concentration gradient. - Inversely proportional : membrane thickness. Example : Diffusion of gases in lungs.
	Facilitated diffusion	Carrier proteins : GLUT, aquaporins.
Active transport	Primary active transport	Pumps : ATPases
	Secondary active transport	<ul style="list-style-type: none"> Cotransporter (Same direction) : SGLT, Na^+ I^- symporter. Exchangers (Opposite direction) : Cl^- HCO_3^- exchanger. Vesicular transport : Require calcium <ul style="list-style-type: none"> - exocytosis (SNARE proteins). - endocytosis (Clathrin, cubilin)

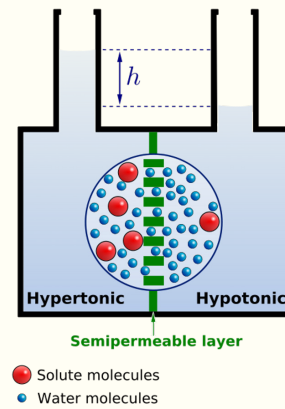
Osmosis :

- Diffusion of water.
- movement :
 \uparrow water concentration / \downarrow solute content \rightarrow \downarrow water concentration / \uparrow solute content

Osmolarity (mOsm/L) :

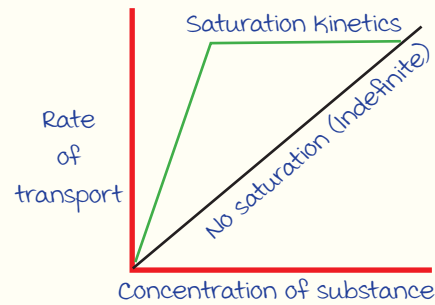
$$2 \times \text{Na}^+ + 0.055 \times \text{Glucose} + 0.36 \times \text{Blood urea nitrogen}$$

(meq/L) (mg/dL) (mg/dL)



Concept Of Saturation Kinetics :

- Followed by :
 - Active transport.
 - Facilitated diffusion.
- Not followed by : Simple diffusion.



Membrane Potentials

01:09:40

Resting membrane Potential (RMP) :

mechanism : Intracellular \uparrow K^+ concentration + Extracellular \downarrow K^+ concentration

\downarrow

Passive diffusion of K^+ out the cell

\downarrow

\uparrow Intracellular negative charge (RMP)

Hyperkalemia :

\uparrow Extracellular K^+ (\downarrow diffusion) \rightarrow Depolarized cell (\uparrow +ve) \rightarrow \uparrow Excitable.

Hypokalemia :

\downarrow Extracellular K^+ (\uparrow diffusion) \rightarrow Hyperpolarized cell (\downarrow +ve) \rightarrow \downarrow Excitable.

Values :

Cell	RMP
Neuron	-70 mV
Skeletal muscle	-90 mV
Cardiac ventricle	
Sinoatrial node	-60 to -40 mV (Restless MP : Oscillatory RMP as they are pacemakers).
Cajal cell (GIT)	
Pre-Botzinger complex	

----- Active space -----

Equilibrium Potential :

No ion movement.

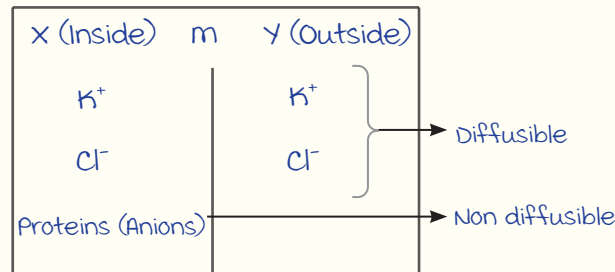
$$\text{Nernst equation : } E_x = \pm 61 \log \frac{C_o}{C_i}$$

Values :

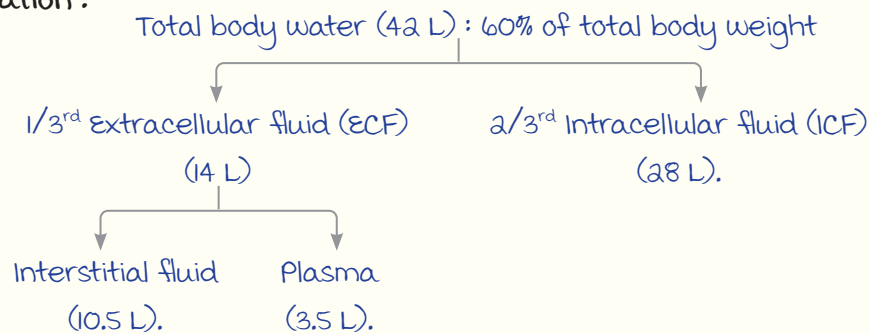
Ion	Equilibrium potential
Na ⁺	+ 60 mV
K ⁺	-90 mV
Cl ⁻	-70 mV (RMP of neuron)
Ca ²⁺	+ 130 mV

Key :

- E : Equilibrium
- x : Ion
- C_o : Extracellular concentration
- C_i : Intracellular concentration

Gibbs Donnan Effect :Presence of **non-diffusible protein** (Anions) affect the distribution of diffusible ions.**Cellular Fluids**

01:18:27

Classification :**Fluid Indicators :**

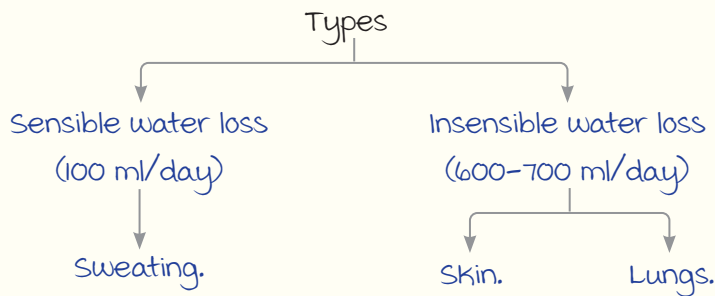
Volume	Indicators
Total body water	Deuterium, Tritium
Extracellular fluid (ECF)	Inulin, sucrose, mannitol
Plasma volume (PV)	Albumin, Evan's Blue dye
Blood volume (BV) = PV / (1 - Hematocrit)	Chromium tagged RBCs
Interstitial fluid = ECF - PV	Nil
Intracellular fluid = TBW - ECF	Nil

Dominant Solutes/Ions :

----- Active space -----

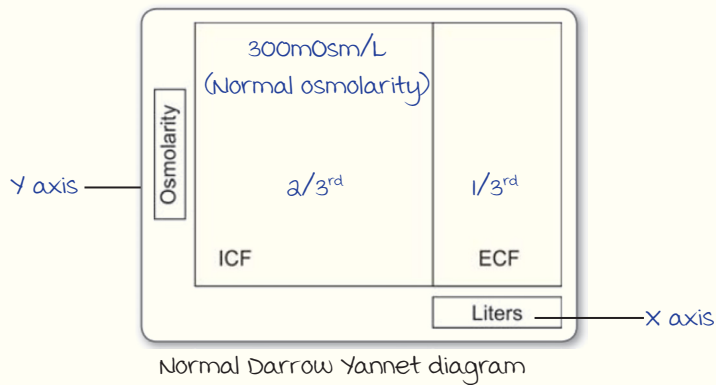
	ECF	ICF
Dominant cations	Na ⁺	K ⁺ > mg ²⁺
Dominant anions	Cl ⁻	Phosphates, protein anions

Water Loss :



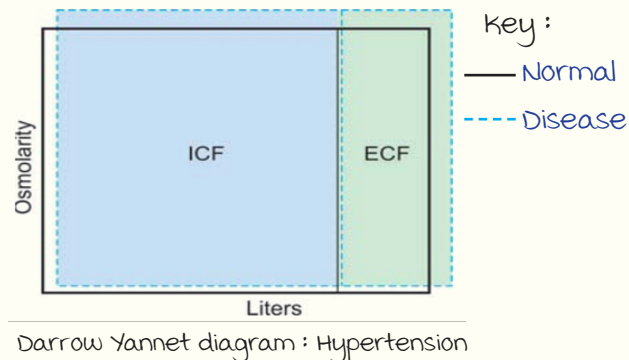
Darrow Yannet Diagram :

- Normal Darrow Yannet diagram.



- Excessive NaCl intake → Hypertension.

	Volume	Osmolarity
ECF	↑	↑
ICF	↓	↑



NERVE MUSCLE PHYSIOLOGY

----- Active space -----

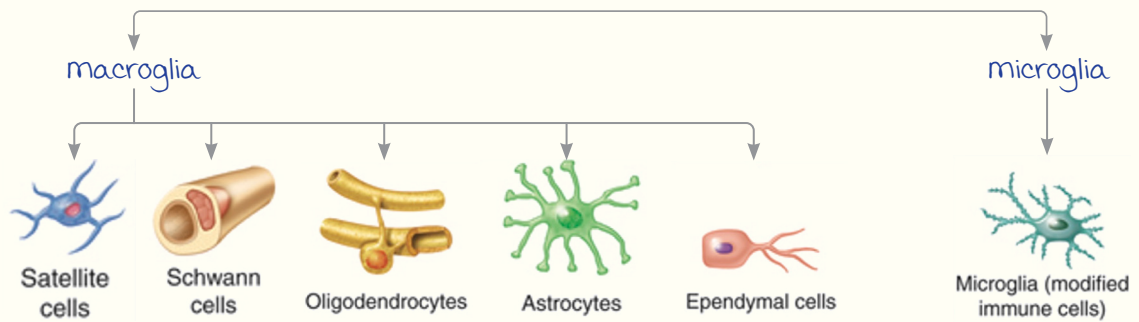
Nerve

00:00:11

Cells in central nervous system :

- Neurons : Functional unit.
- Glial cells : Supporting cells.
1 neuron : 10 glial cells.

Glial Cells Classification :

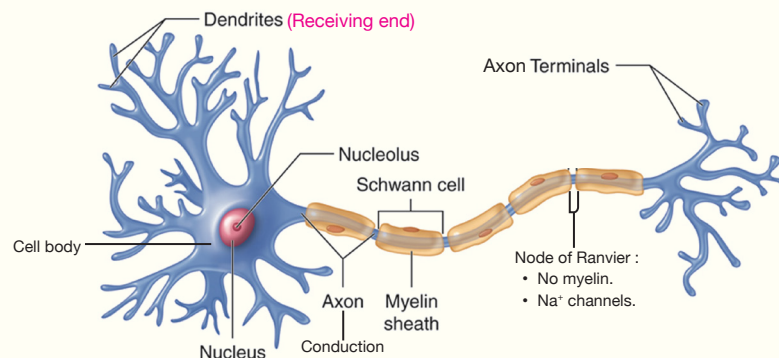


macroglia :

- Astrocytes :
 - Blood-brain barrier.
 - Produce neurotrophins : Nourishment for neurons.
 - **Synaptic clearing** : Takes up excess K^+ & neurotransmitters.
- Oligodendrocytes : CNS → myelination.
- Schwann cells : PNS → myelination.

microglia : Phagocytosis.

Structure of Neuron :



myelin :

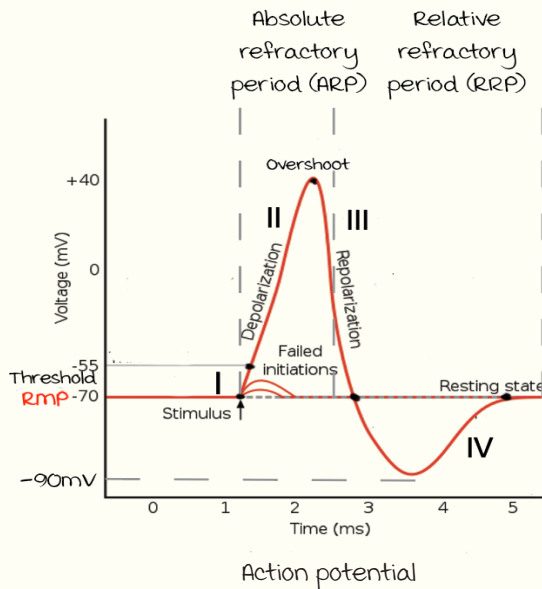
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- Lipid component : Sphingomyelin.
- Protein component : myelin basic protein.
Autoantibody target in multiple sclerosis → Demyelination.
- use : ↑ Nerve conduction velocity.

Factors Affecting Nerve Conduction velocity (NCV) :

- Axon diameter : Directly proportional to NCV.
- myelination : ↑ NCV.
- Temperature : Directly proportional to NCV.
- ↑ Axonal resistance/ ↓ membrane capacitance : ↑ NCV.

Nerve Action Potential :



- Phase I : Local potential (Slow Na influx) (-70 mV → -55 mV).
 - Phase II : Depolarisation (Opening of voltage gated Na channel, fast Na influx).
 - Phase III : Repolarisation (K⁺ efflux).
 - Phase IV : Hyperpolarisation (Cl⁻ influx & slow closure of K⁺ channels).
- ARP : From threshold to initial 1/3rd of repolarization .
- Inactivation of Na⁺ channels.
 - Second stimulus → No response.
- RRP :
- From 1/3rd of repolarization to end of action potential.
 - Second stimulus (maximum strength).
- ↓
Response

Classification of Nerve Fibres :

Erlanger & Gasser Classification					Lloyd Hunt Classification (Only sensory fibres)
Fiber type	myelin	Diameter (µm)	Conduction velocity (m/s)	Functions	
Aα	⊕	maximum	↓	muscle spindle (Proprioception)	Ia
				Golgi tendon organ	Ib
				α motor neurons	⊖
Aβ				Touch, pressure	II
Aγ				motor to muscle spindles (γ motor neuron)	⊖
Aδ			Fast/First pain	III	
B			Pre-ganglionic autonomic	⊖	
C	⊖	minimum	Slowest	Slow/second pain, Postganglionic sympathetic	IV

----- Active space ----- **Nerve Injury :**

Wallerian/Distal degeneration	Retrograde/Proximal degeneration
usually begins within 24 hrs after injury	within 36 hours of injury
Axon degeneration → myelin sheath degeneration → Debris cleared by macrophages & Schwann cells	<ul style="list-style-type: none"> Nucleus pushed to periphery Destruction of Nissl bodies (RER) → Chromatolysis

Nerve Regeneration :

- Slow process : Begins after 96 hours of injury.
- Rate : 1 - 3 mm/day.

Identification test :

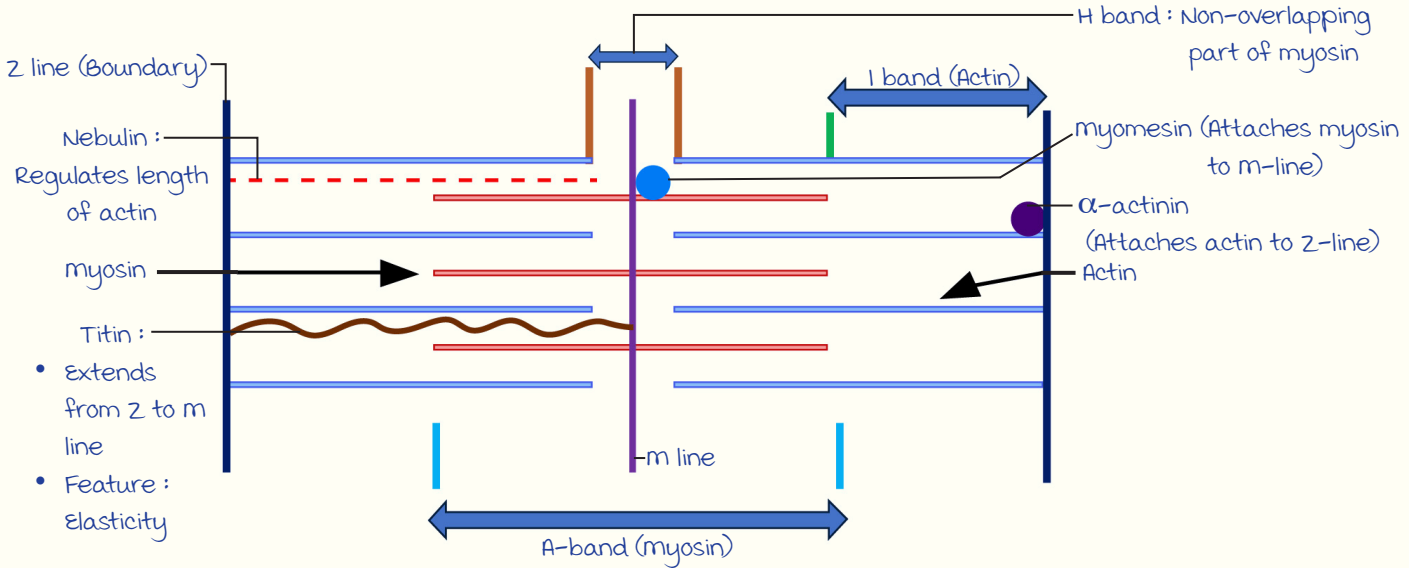
Tinel's sign : On tapping area over injured nerve → Tingling sensation present → Nerve is regenerating.

Skeletal Muscle

00:25:12

Functional unit : Sarcomere (Between 2 Z lines) → Proteins → Actin, myosin.

Structure of a sarcomere :

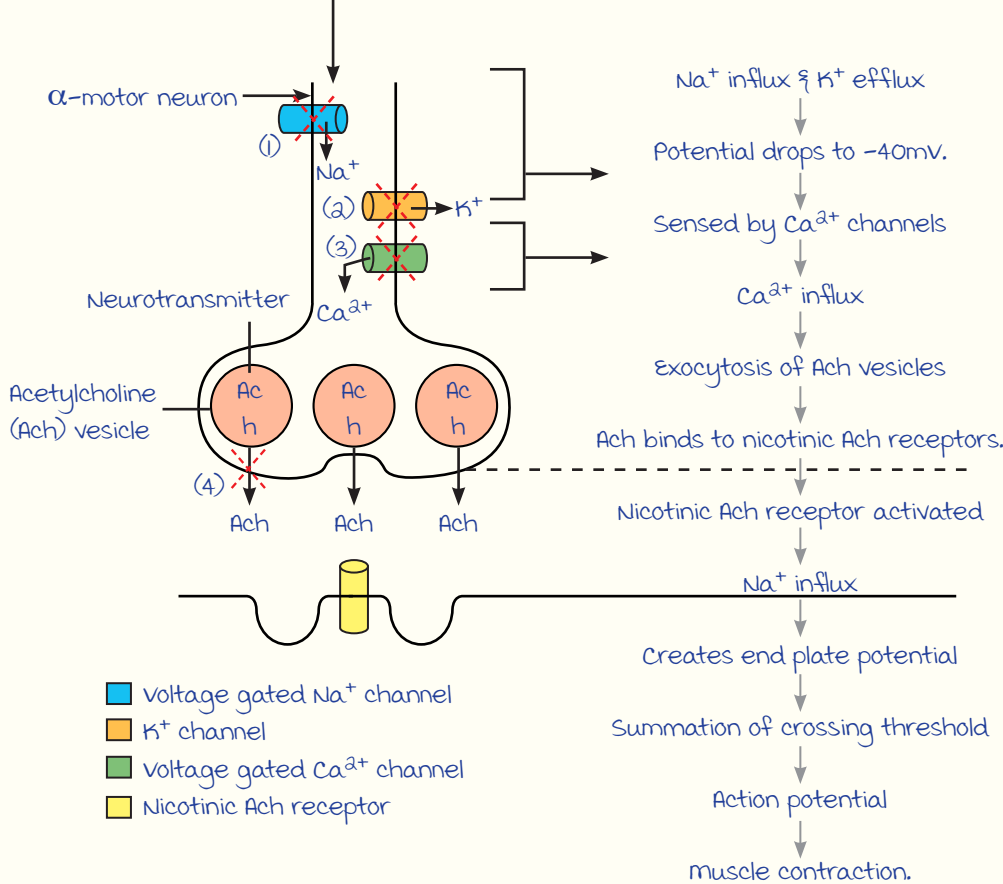


Skeletal muscle proteins :

Contractile proteins	Supportive proteins	Regulatory proteins	Relaxation proteins
<ul style="list-style-type: none"> Actin myosin 	<ul style="list-style-type: none"> Titin Desmin Dystrophin 	<ul style="list-style-type: none"> Troponin Tropomyosin 	<ul style="list-style-type: none"> Ca²⁺ pump : Sarcoplasmic reticulum Calcium ATPase (SERCA)

Neuromuscular Transmission :

Action potential (resting membrane potential = -70mv)



----- Active space -----

Blockers/Toxins :

1. **Tetrodotoxin :**
Present in pufferfish.
2. **Dendrotoxin**
3. **Conotoxin**
4. **Botulinium toxin :**
- Blocks release of ACh.
- Flaccid paralysis.

Diseases :

- Lambert Eaton myasthenia Syndrome (LEMS) :
Autoantibodies against voltage gated Ca²⁺ channels.
- myasthenia gravis : Autoantibodies against Nicotinic ACh receptor.

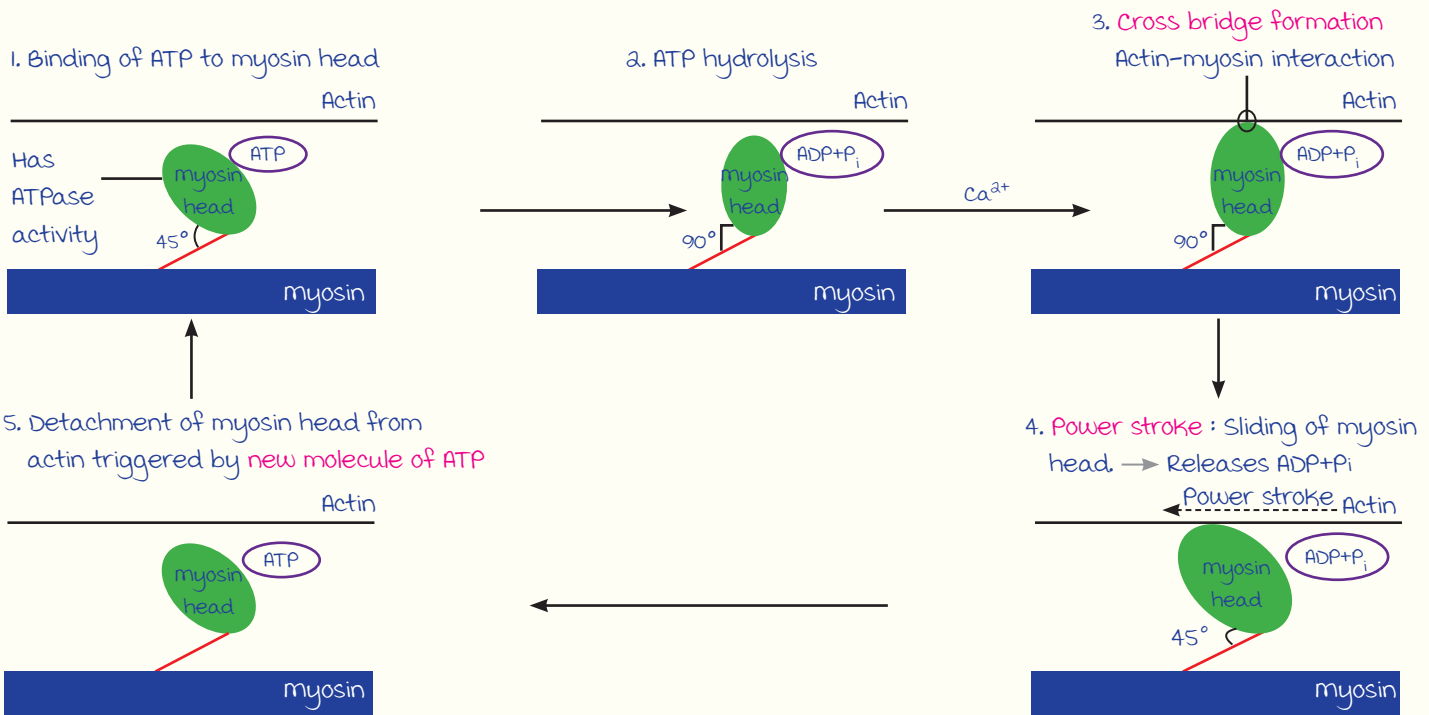
Skeletal muscle Calcium Channels :

Dihydropyridine receptor (DHPR) }
 Ryanodine receptor (RYR) } **mechanical interaction.**

- Release Ca²⁺ → Contraction.
- Overactive RYR → malignant hyperthermia.

SERCA : Ca²⁺ storage → muscle relaxation.

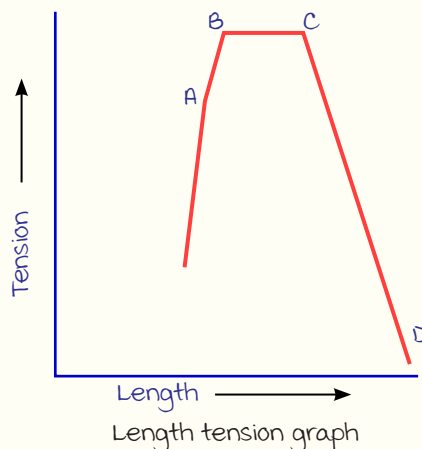
----- Active space ----- **molecular mechanisms of muscle contraction :**



Properties of Skeletal muscles :

Length tension relationship : Tension \propto actin - myosin overlap.

	Actin myosin overlap	Tension generated	Image
Point D	Absent	No tension	
Point B & C	Optimal	Maximum tension (T _{max})	
Point A	Present, but not optimal	Less tension	



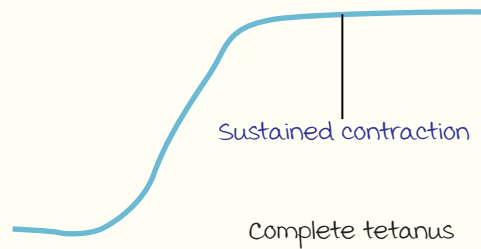
Skeletal muscle fibre types :

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Characteristics	Type I fibres	Type II fibres	
		Type II a	Type II b
Color	Red	Red	White
myoglobin content	⊕ High	⊕ High	⊖ Absent
Diameter	Small	Large	Large
myosin ATPase (Contraction)	Slow	Fast	Fast
O _a storage	⊕	⊕	⊖
Pathway to generate ATP	Aerobic pathway (Oxidation)	Aerobic or anaerobic pathway	Anaerobic pathway (Glycolysis)
Recruitment order	First	Second	Last
Activities best suited	Sitting	Standing	Running

Stimulation of muscle :

- Continuous Stimulation of muscle
↓
State of sustained contraction
(No relaxation)
↓
Tetanic contraction.



- Tetanising Frequency (TF) : $\frac{1}{\text{Contraction period}}$

Cardiac & Smooth Muscle

00:53:28

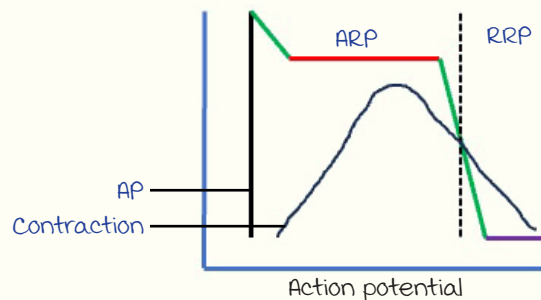
Cardiac muscle :

Features :

- Striated, involuntary.
- Functional syncytium : Synchronized contraction.
- D/t Intercalated disk containing cardiac gap junctions & Connexins (Protein).
- Calcium-induced calcium release (CICR) :
Calcium from extracellular source $\xrightarrow{\text{Induces release}}$ Calcium from intracellular source.
- Phospholamban : Inhibits SERCA \rightarrow Inhibits Ca²⁺ Storage \rightarrow Affects relaxation.

Absence of tetanisation :

major part of contraction in ARP
↓
No summation possible
↓
No tetany (Evolutionary adaptation).



----- Active space -----

Smooth muscle :

Features :

- Involuntary.
- Types :
 - Single unit (well developed gap junction).
 - multi unit.
- Dense bodies \oplus (2 lines \ominus).
- Calcium binding proteins : **Calmodulin** (Troponin \ominus).
- Exclusive properties :
 - Plasticity.
 - **Latch bridge mechanisms** : Sustained contraction using \downarrow ATP in GIT.

Locations :

- Single unit smooth muscle : GIT, uterus, urinary bladder, ureter.
- multi unit smooth muscle : Iris, ciliary body, piloerector muscle.

Control of smooth muscles :

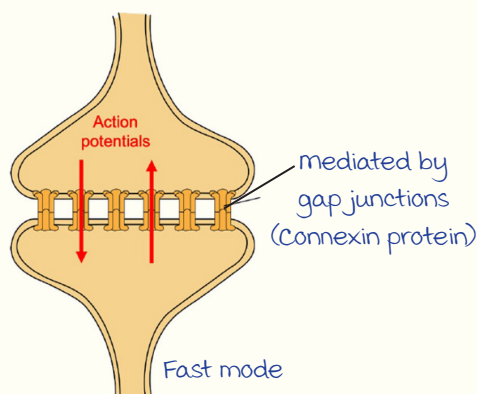
- No well defined neuromuscular junction regulated by ANS.
- Varicosities : Contain neurotransmitters Ach & norepinephrine (High activity of smooth muscles).
- **Synapse en passant** : One neuron innervates multiple smooth muscle cells.

Synaptic Transmission

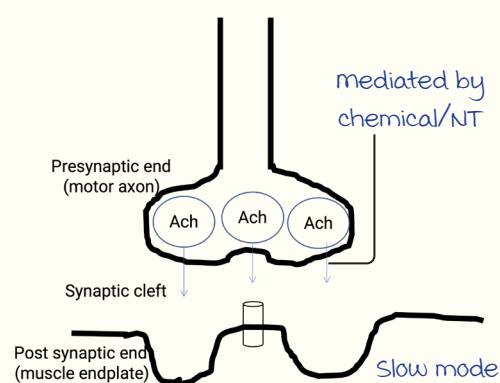
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Types :

- Electrical :



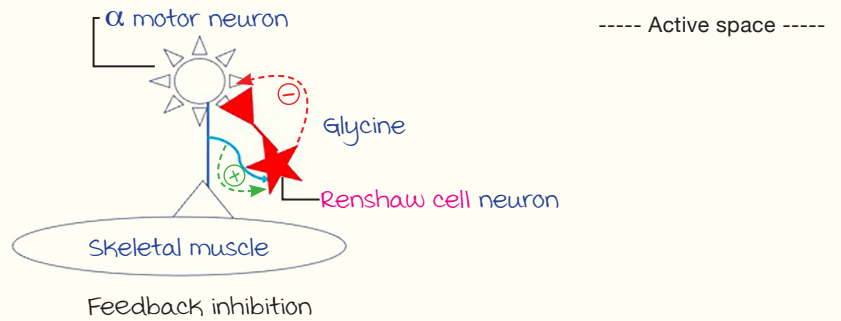
- Chemical :



Post Synaptic potentials (PSP) :

	excitatory PSP	Inhibitory PSP
Post-synaptic neuron membrane potential	more positive	more negative
Fast	$\text{Na}^+/\text{Ca}^{2+}$ influx	Cl^- influx, K^+ efflux
Slow	$\downarrow \text{K}^+$ efflux	$\uparrow \text{K}^+$ efflux

Regulation : Feedback inhibition.
 Function : Controls α motor neuron firing.

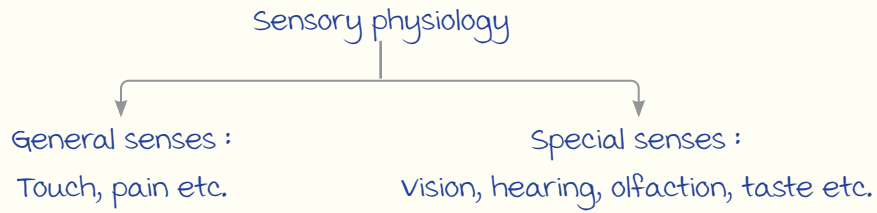


Neurotransmitters

01:08:03

NT	Location	Function	Other points
Acetylcholine	Neuromuscular junction, nucleus basalis of meynert	muscle contraction, REM sleep.	<ul style="list-style-type: none"> Botulinium toxin : Inhibits release of ACh Receptors : Nicotinic (NMJ) & muscarinic (GIT)
Norepinephrine	Locus coeruleus	Activates reticular activating system → State of arousal	-
Dopamine	1. Nigrostriatal pathway : Basal ganglia.	motor control	-
	2. mesolimbic : a. Ventral tegmental area b. Nucleus accumbens	a. Reward centre b. Addiction	
	3. Tuberoinfundibular	Inhibits prolactin	
Serotonin	Raphe nucleus	maintains wakeful state	-
	Platelets	Platelet aggregation	
Histamine	Hypothalamus	Arousal	-
Glutamate	Hippocampus, sub thalamic nucleus.	Learning & memory	major excitatory NT in brain
GABA	-	Hyperpolarisation	<ul style="list-style-type: none"> major inhibitory NT Tetanospasmin (Bacterial toxin) ↓ Inhibits GABA → Spastic paralysis
Glycine	Renshaw cells in spinal cord	Inhibit α motor neuron	<ul style="list-style-type: none"> Both inhibitory and excitatory NT Antagonist : Strychnine
Nitric oxide	Hippocampus	Learning & memory	Gaseous NT
Carbon monoxide	-	Pain processing & olfaction.	<ul style="list-style-type: none"> Produced by enzymatic degradation of heme Gaseous NT

NEUROPHYSIOLOGY : PART 1

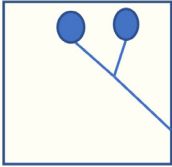
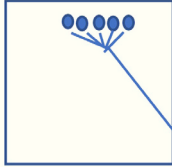

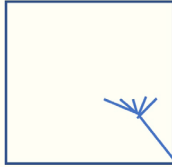


General Senses

00:00:33

Receptors :

Touch receptors :

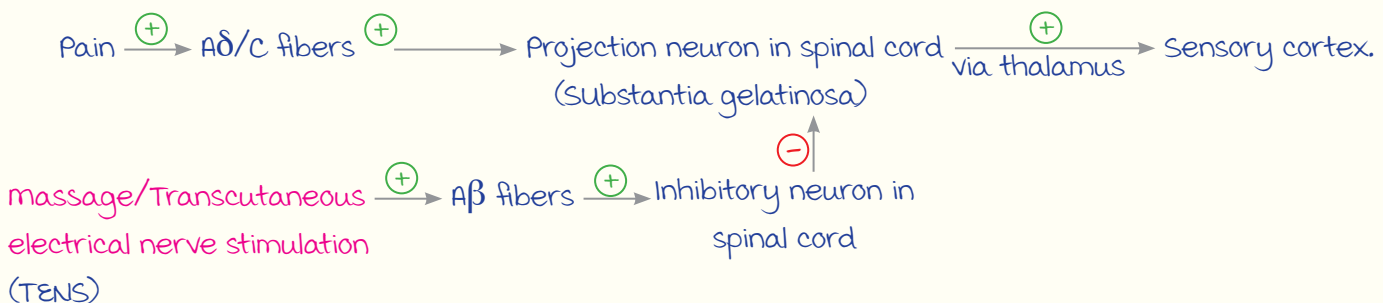
	meissner corpuscle	merkel cells	Pacinian corpuscle	Ruffini endings
Level	Superficial		Deep	
Sensation	Discriminatory touch, stroking	Texture, edges (Braille)	Pressure, vibration	Skin stretch
Adaptation	Rapid	Slow	Rapid	Slow
Appearance				

Pain receptors : Free nerve endings of A delta & C fibers.

	A Delta fibers	C fibers
Type of pain	First pain (Fast)	Second pain (Slow)
myelination	Present	Absent
Tract	Neospinothalamic tract (Newer)	Paleospinothalamic tract (Very old)
Neurotransmitter	Glutamate	Substance P

Gate control theory of pain (melzack & wall) :

- "Non-painful sensations can override & ↓ painful sensations."
- mechanism :



Note :

----- Active space -----

1. Pain relief in acupuncture :

Activation of endogenous opioid analgesic system in **periaqueductal gray matter** } Releases → Endogenous morphine (Endorphins) → Pain relief.

2. Allodynia : Non-painful stimulus causing painful sensation.

Somatosensory Pathways :

	Dorsal column pathway	Anterolateral pathway
Sensation	Proprioception, touch, vibration	Pain, temperature
Distribution in spinal cord	Ipsilateral (I/L)	Contralateral (C/L)
Level of crossing over	At medulla	At spinal cord

Brown-Séquard syndrome : Hemisection of spinal cord.

- **I/L** loss of proprioception, touch, vibration (**Dorsal column** senses).
- **C/L** loss of pain & temperature (**Anterolateral column** senses).

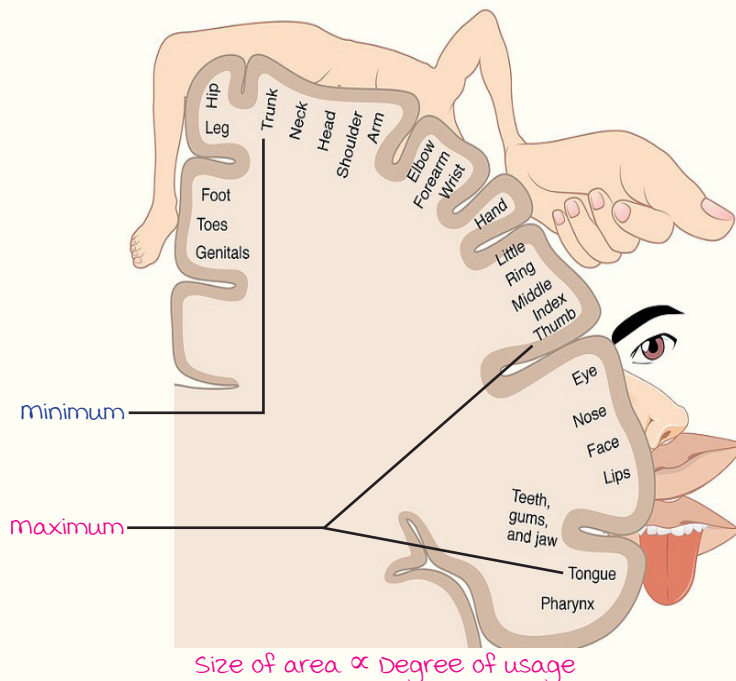
Sensory Homunculus :

Ventral posterolateral (VPL) nucleus → Projected to → Sensory cortex (Represented by sensory homunculus)
(Thalamic nucleus for touch & pain)

Cortical plasticity :

Encroachment of a cortical area by a neighboring cortical area → Basis for **phantom limb**.

Weber-Fechner law : magnitude of sensation felt \propto **Log intensity** of initial stimulus.



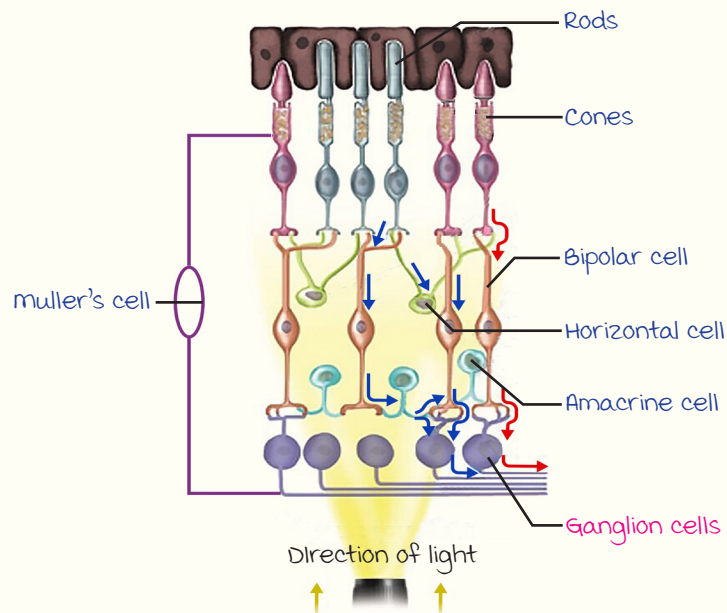
----- Active space -----

Vision

00:17:01

Retina :

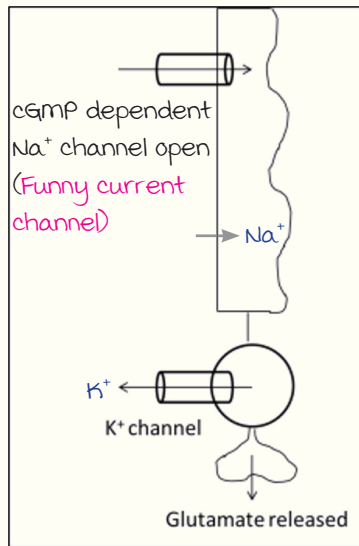
Cell Type	Characteristics
Rods	<ul style="list-style-type: none"> Receptors of night vision. more sensitive to light.
Cones	<ul style="list-style-type: none"> Receptors of day vision/colour vision. ↑ in foveal region.
Bipolar cells	<ul style="list-style-type: none"> Receives signals from rods and cones and makes connection with ganglion cells.
Ganglion cells	<ul style="list-style-type: none"> Only output cell of retina (Their axons are the optic nerve) Only retinal cell capable of producing action potential.
Horizontal cells	<ul style="list-style-type: none"> Connects rods and cones. Sharpens the signal by lateral inhibition.
Amacrine cells	<ul style="list-style-type: none"> Purely depolarising cells of retina. Connects ganglion cells. Sharpens the signal by lateral inhibition.
muller's cells/Retinal glial cells	<ul style="list-style-type: none"> Supporting glial cells. No role in vision.



Physiology of Vision :

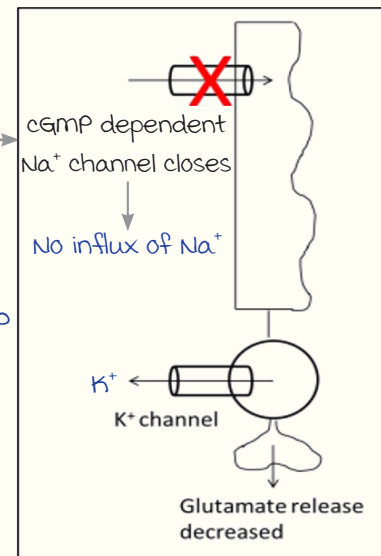
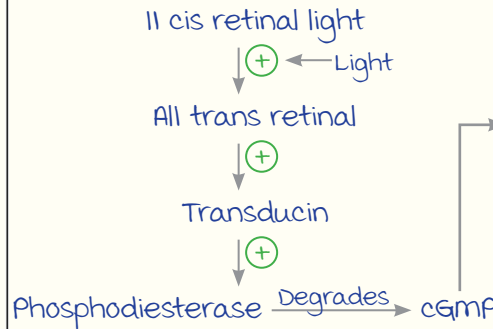
----- Active space -----

a) Dark state :



Rod in dark state : Depolarisation

b) Light reflex :



Rod in light state : Hyperpolarisation

Lateral Geniculate Body :

Retina → Lateral geniculate body (LGB) in thalamus

Contains 6 layers.

- magnocellular layer (Contains large cells)
- Parvocellular layer (Contains small cells)

	magnocellular pathway	Parvocellular pathway
Origin	Layers 1 and 2 of LGB	Layers 3, 4, 5, 6 of LGB
Termination	Layer 4 of visual cortex	Layer 4 of visual cortex
Function	Eye movements	<ul style="list-style-type: none"> • Color vision • Finer details

Koniocellular pathway (minor) :

- Originates from **K** cells.
- Detection of **blue** colour.

Both LGBs receive stimuli from both eyes :

- I/L eye : Layers 2, 3, 5.
- C/L eye : Layers 1, 4, 6.

Visual Cortex :

Thalamus → visual cortex/Striate cortex/Striae of Gennari.

- Area 17, 18, 19.
- In **calcarine sulcus** of occipital lobe.

Colour vision :

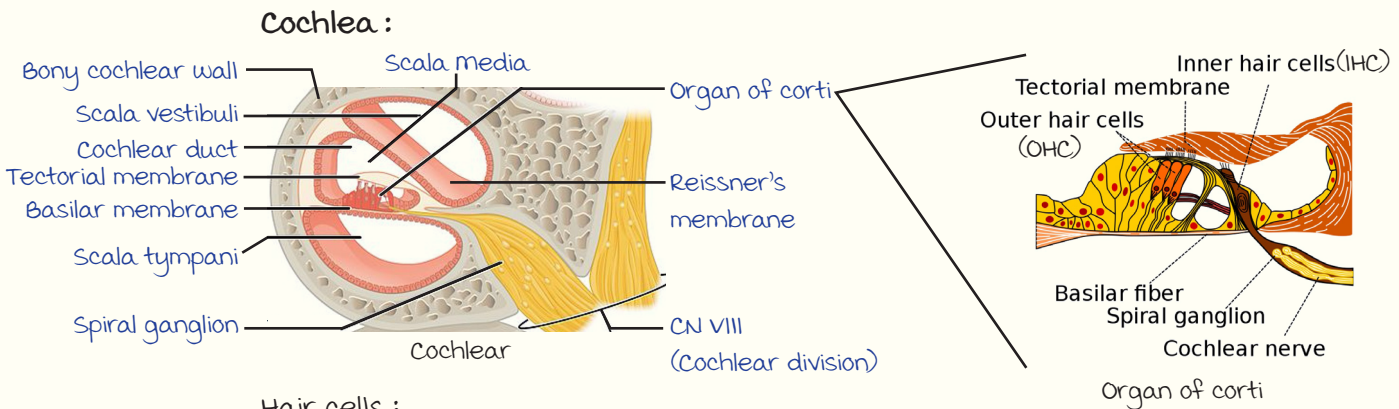
Pathway : Retina (Cones) → Thalamus (Parvocellular pathway) → visual cortex.

Retinal cones :

	L cone	m cone	S cone
Wavelength	Long	medium	Short
Detects	Red	Green	Blue
Defect causes	Protanopia	Deutanopia	Tritanopia

Hearing

00:31:37



Hair cells :

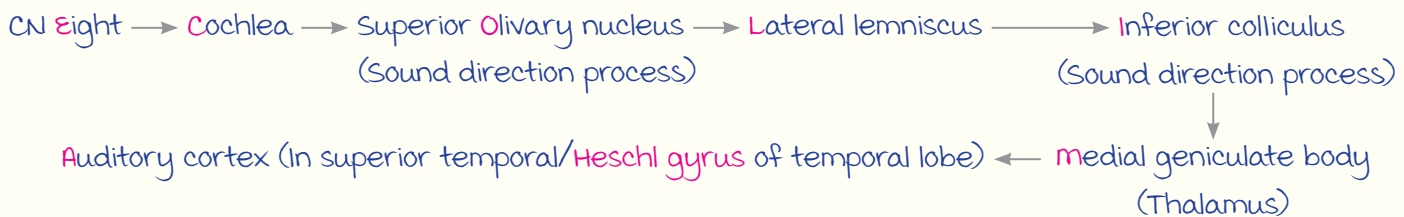
- Receptors for hearing.
- Covered by tectorial membrane.
- All hair cells bend towards kinocilium → Depolarisation (D/t influx of K^+) → measured as otoacoustic emissions.
- Smallest hair cell : Stereocilium.
- Tallest hair cell : Kinocilium.

Basilar membrane :

	Base	Apex
Size	Broad	Narrow
Close to	Oval window	Helicotrema
Sensitive to	↑ Frequency sound waves	↓ Frequency sound waves

Auditory Pathway :

mnemonic : **ECOLI MA.**



Olfaction

00:39:35

Receptors :

- Bipolar neurons (Combine to form CN I).
- Location : Olfactory epithelium in upper part of nose.
- Olfactory epithelium : Contains bipolar neurons, sustentacular cells (Supporting cells), basal stem cells (↑ Regenerative capacity).

Olfactory bulb :

- Receives information from olfactory epithelium.
- Contains :

	Excitatory cells	Inhibitory cells
Types	mitral cells, tufted cells	Periglomerular cells, granule cells
Neurotransmitter	Glutamate	GABA

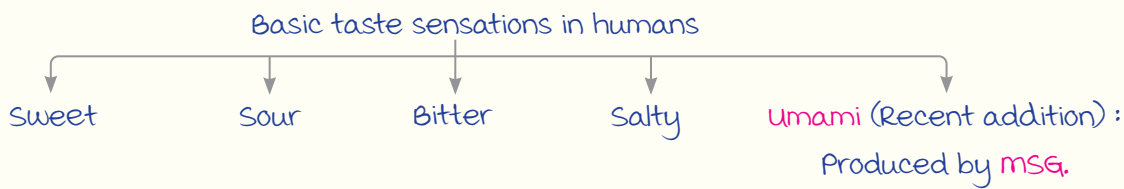
----- Active space -----

Higher centres :

	Function
Olfactory cortex Orbitofrontal cortex	Conscious discrimination of odor.
Amygdala	Processing of emotions evoked by smells.
Entorhinal cortex	Processing of memories evoked by smells.

Taste

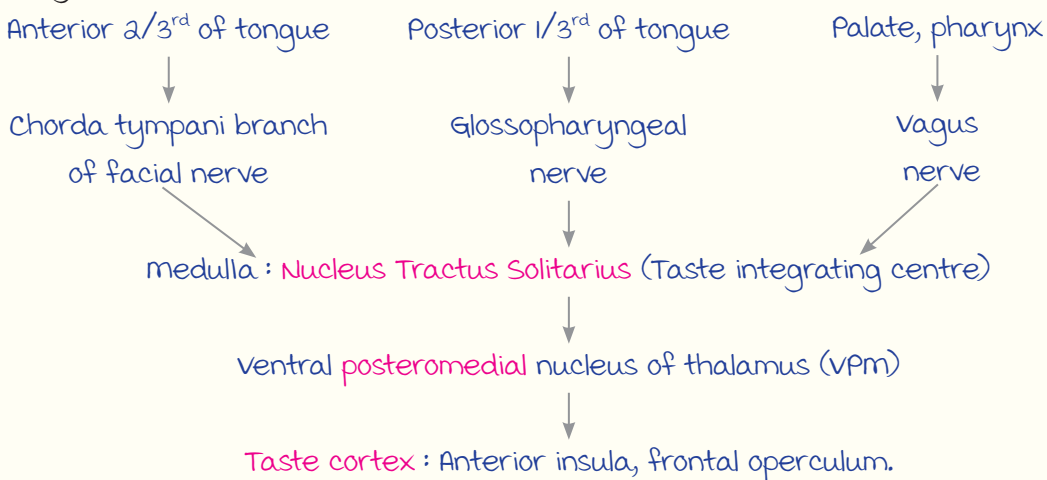
00:42:40



Receptor for taste :

	Receptor type	Receptors
Salty	Ionotropic	Epithelial sodium channel (ENaC)
Sour		ENaC, HCN channels, TRP channels
Sweet	metabotropic (G Protein coupled)	T1R2, T1R3
Bitter		T2R
Umami		mGluR4, T1R1, T1R3

Pathway :



----- Active space -----

Motor Physiology

00:45:55

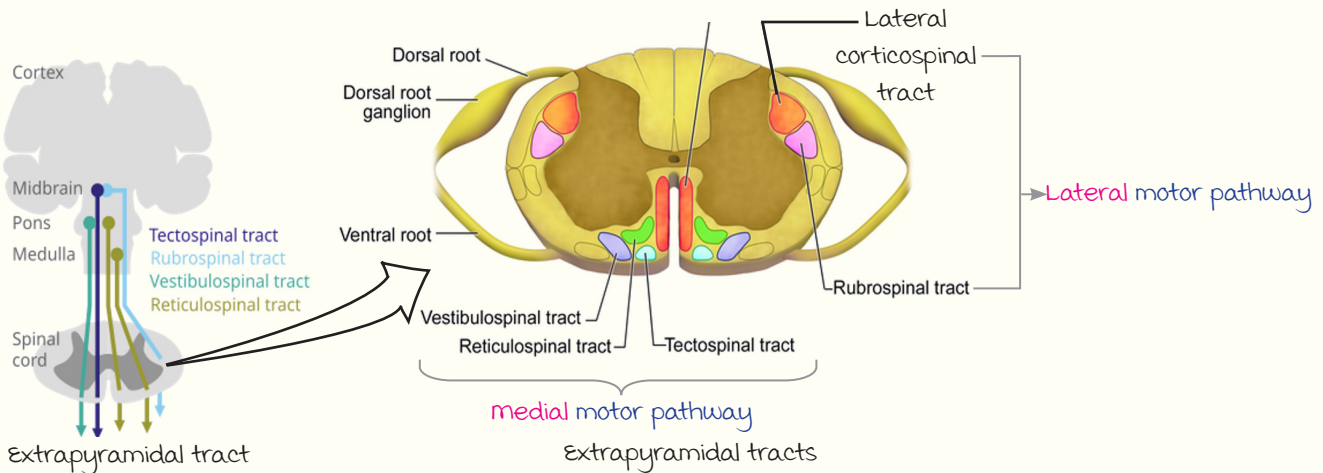
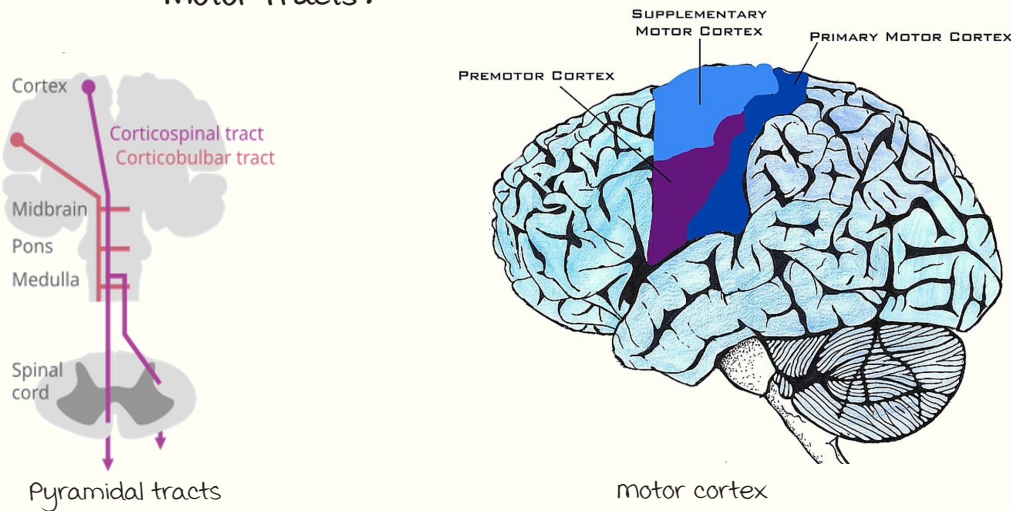
motor pathway (Descending) :

motor cortex → Spinal cord (Alpha & gamma motor neurons) → Skeletal muscle.

motor Cortex :

	Primary motor cortex	Premotor cortex	Supplementary motor cortex
Location	Precentral gyrus : Frontal lobe	Anterior to precentral gyrus	-
Brodmann area	4	6	6
Function	Execution of motor movements	Orient the body for movement	Bimanual coordination for complex tasks

motor Tracts :

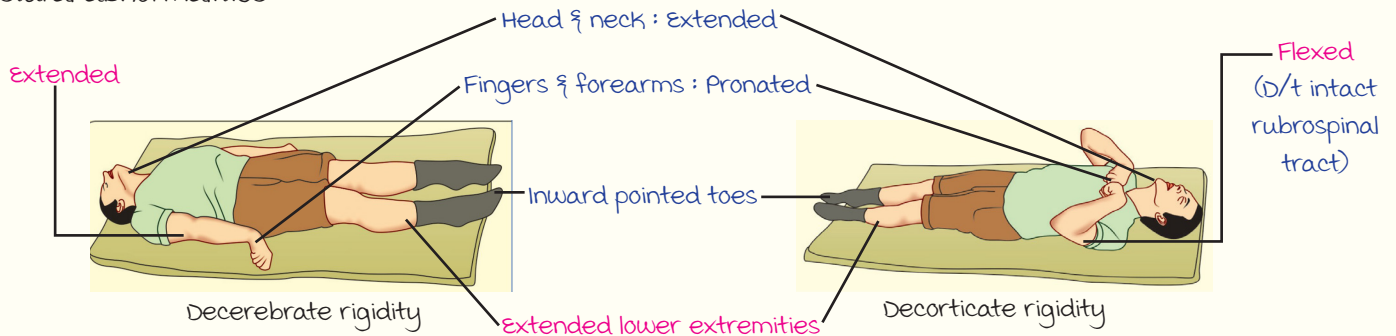


Lateral motor pathway vs. medial motor pathway :

----- Active space -----

	Lateral motor pathway	medial motor pathway
Function	Fine, skilled, voluntary movements (Writing)	Posture
Muscle groups supplied	Flexors	Extensors

Postural abnormalities :

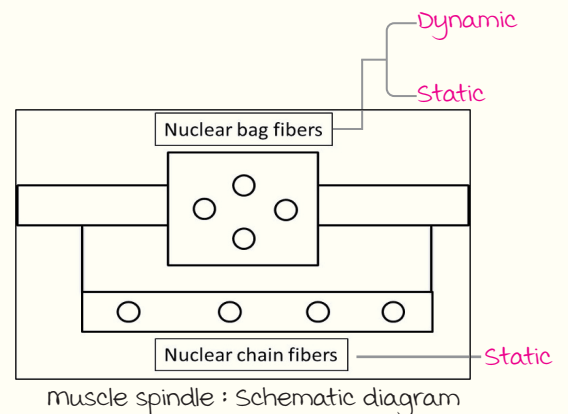
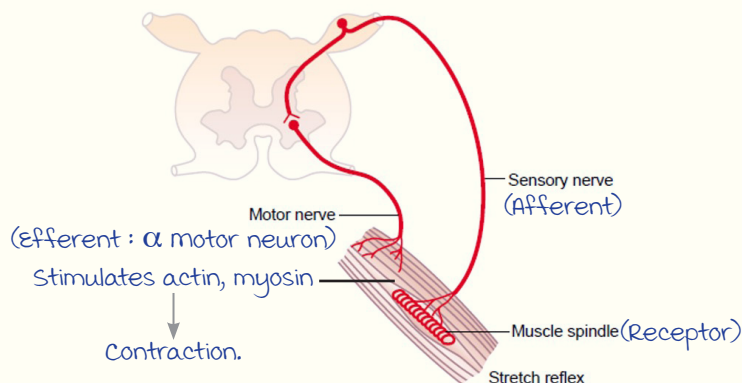


Upper motor neuron (UMN) lesion vs. Lower motor neuron (LMN) lesion :

	UMN lesion	LMN lesion
Atrophy	-	+
Fasciculations	-	+
Tone	↑	↓
Weakness	Regional	Segmental
Reflexes	Exaggerated	Sluggish
Babinski sign	Positive	-

REFLEXES

Stretch Reflex :



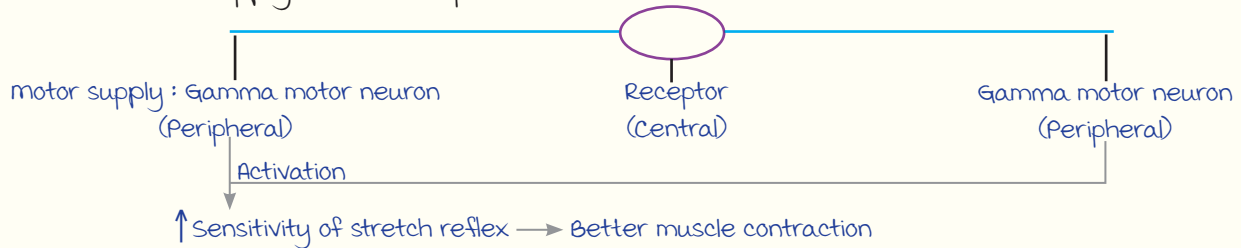
Sensory supply :

	Primary (Group Ia) ending	Secondary (Group II) ending
AKA	Annulospiral ending	Flower spray ending
Innervates	<ul style="list-style-type: none"> Dynamic nuclear bag fibres Static nuclear bag fibres Nuclear chain fibres 	<ul style="list-style-type: none"> Static nuclear bag fibres Nuclear chain fibres

----- Active space ----- Pathway :

- Stimulus : Stretch.
- Receptor : muscle spindle.
- Afferent : Group Ia & II endings.
- Center : Spinal cord.
- Efferent : α motor neuron.
- Effector : Skeletal muscle (Actin & myosin).
- Effect : muscle contraction.

motor supply of muscle spindle :



Alpha-gamma coactivation : Simultaneous activation of alpha & gamma motor neurons leading to muscle spindle contraction.

Inverse Stretch Reflex :

- Overstretched muscle → Relaxation of muscle.
- Receptor : Golgi tendon organs.

Stretch reflex vs. Inverse stretch reflex :

	Stretch Reflex	Inverse Stretch Reflex
Receptor	muscle spindle	Golgi tendon organ
Detects	muscle length	muscle tension
Afferent	Group Ia endings and group II endings	Group Ib endings
Center	Spinal cord	Spinal cord
Efferent	α motor neuron (α MN)	α motor neuron
Effect	Contraction	Relaxation
Reason for the effect	Activation of α MN	Inhibition of α MN
Number of synapses involved	Single : monosynaptic reflex	Two : disynaptic reflex
AKA	myotatic reflex	Lengthening reaction

Withdrawal Reflex :

- AKA Flexor withdrawal reflex.
- **Polysynaptic** reflex.
- Prick to \textcircled{R} foot :
 - Flexion of \textcircled{R} foot → **withdrawal** from painful stimulus.
(Flexor \oplus , Extensor \ominus)
 - Extension of \textcircled{L} foot → **Supporting** the body.
(Flexor \ominus , Extensor \oplus)

NEUROPHYSIOLOGY : PART 2

----- Active space -----

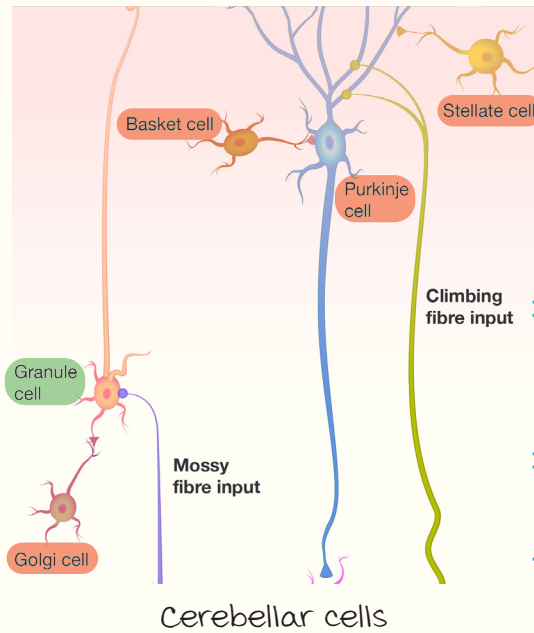
Cerebellum

00:00:24

Function : Coordination through start-stop signaling.

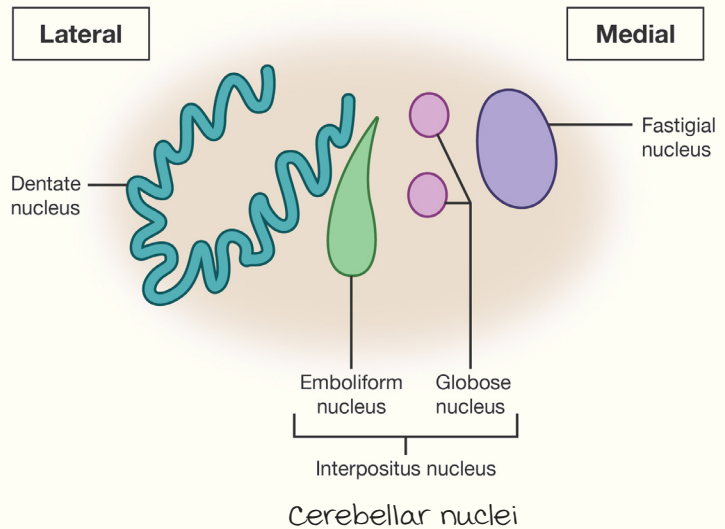
Rule of 5, 4, 3 :

5 cerebellar cells :



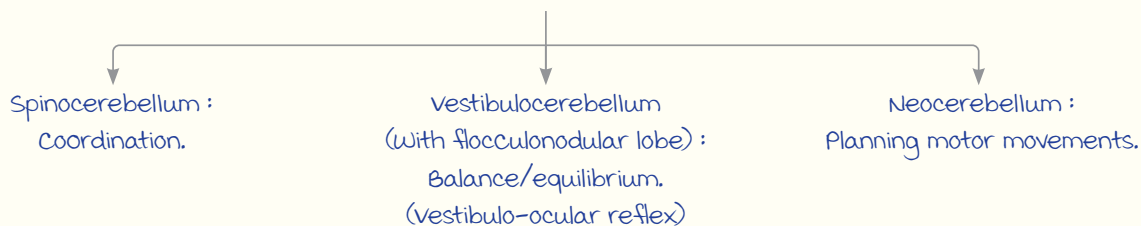
4 cerebellar deep nuclei :

All are excitatory.
Mnemonic : **DEFG**.



- : Inhibitory cells (GABA).
- : Excitatory cell (Glutamate).

3 cerebellar parts :

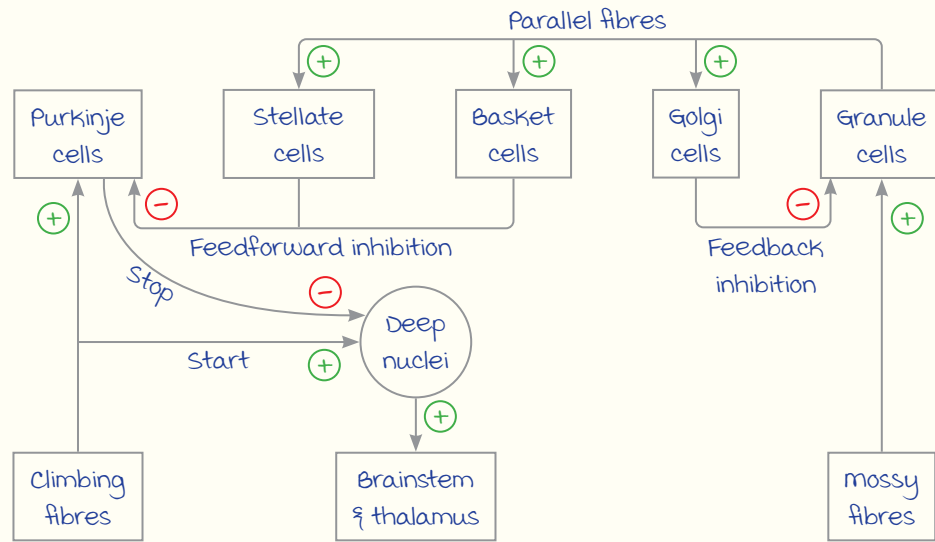


Afferents to Cerebellum :

	Climbing fibers	mossy fibers
Origin	Inferior olivary nucleus	Cell bodies in spinal cord & brainstem
AKA	Olivocerebellar	Spinocerebellar

----- Active space -----

Start-Stop Signaling :



Features of Cerebellar Diseases :

1. Decomposition of movement.
2. Hypotonia.
3. Pendular knee jerk.
4. **Ataxia.**
5. Dysmetria.
6. **Intention tremor** : Absent at rest.
7. Dysdiadochokinesia.
8. Rebound phenomenon.
9. Dysarthria.
10. Nystagmus.

Basal Ganglia

00:10:40

Inhibitory to both voluntary & involuntary movements even at rest.

Nuclei :

Nuclei	Striatum (Input nuclei)		Globus pallidus (GP)		Substantia nigra	Subthalamic nucleus
	Caudate	Putamen	GP interna (Output nuclei)	GP externa		
Neurotransmitter	GABA				Dopamine	Glutamate : excitatory

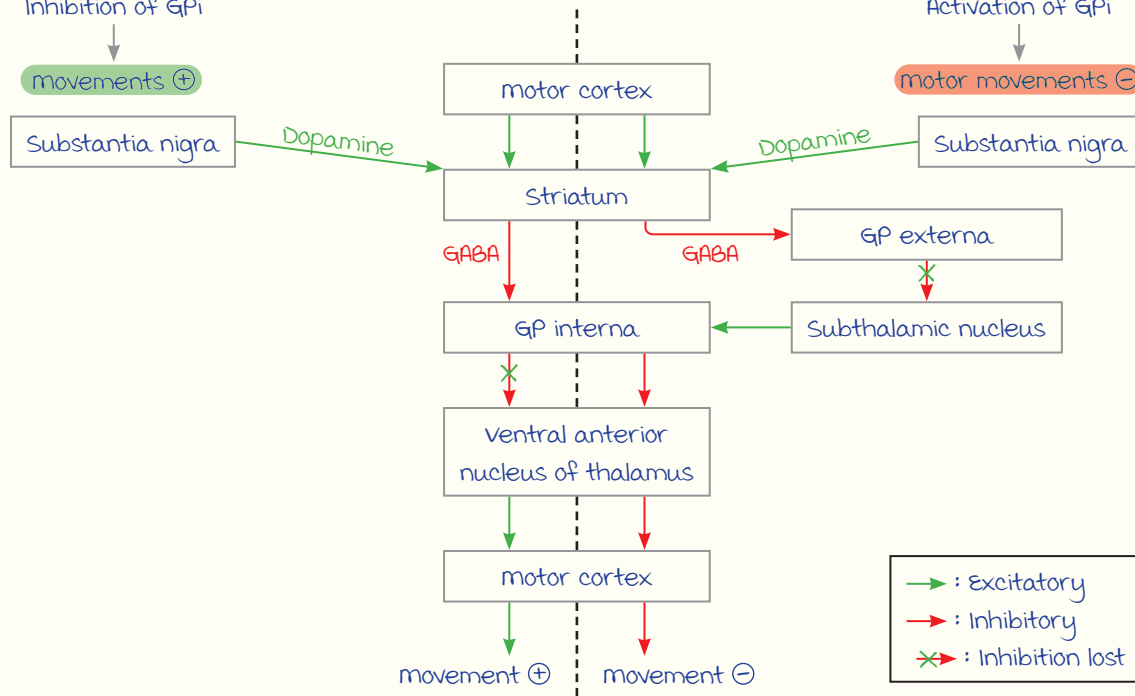
Pathways :

1. Direct pathway :
Inhibition of GPi

movements ⊕

2. Indirect pathway :
Activation of GPi

motor movements ⊖



----- Active space -----

Role of dopamine :

- Facilitation of movements.
- ↓ Dopamine → Bradykinesia (Parkinson's disease).

Effect of Lesions :

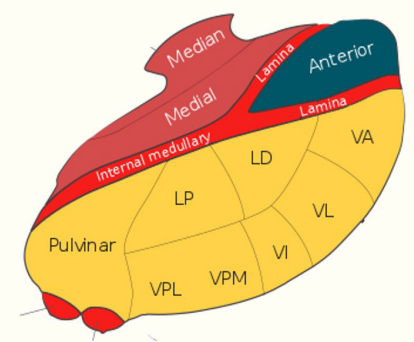
Site of lesion	Involuntary movement
Substantia nigra (Pars compacta)	Resting pill rolling tremor (Parkinsonism)
Caudate nucleus	Chorea
Globus pallidus	Athetosis
Subthalamic nucleus	Hemiballismus (Sudden violent contraction of a large joint)

Thalamus & Limbic System

00:21:11

THALAMUS

Thalamic nuclei	Function
Lateral geniculate bodies	Vision
medial geniculate bodies	Hearing
ventral posterior lateral (VPL) and ventral posteromedial nuclei (VPM)	Transmit somatosensory information to sensory cortex
ventral anterior and ventral lateral nuclei	motor functions
Anterior nuclei	Papez circuit : Learning and memory
Dorsomedial thalamic nucleus	Olfaction (smell)



Thalamic nuclei

----- Active space -----

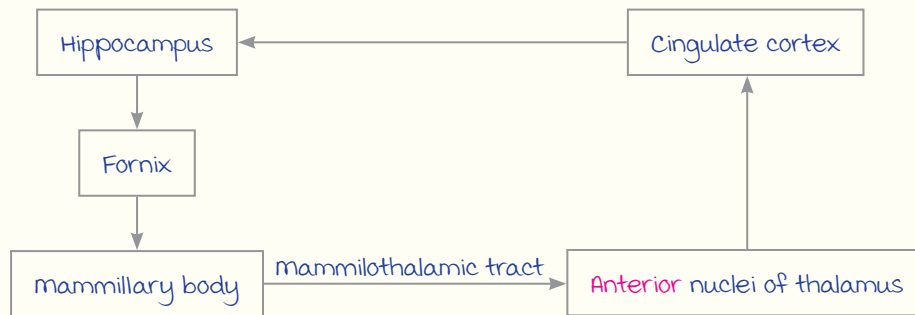
LIMBIC SYSTEM

- Rim of cortical tissue.
- Evolutionarily very old.
- AKA rhinencephalon.

Functions :

- Regulation of emotions (Amygdala).
- Olfaction.
- memory.

Papez circuit : Regulates memory & emotions.



Hypothalamus :

Hypothalamic nuclei	Function
Anterior	Response to heat
Posterior	Response to cold
Lateral	Secretes orexin → ↑ Feeding
Ventromedial	Satiety
Suprachiasmatic (master clock)	Circadian rhythm
Supraoptic	Antidiuretic hormone (ADH)
Paraventricular	Oxytocin
ventro-lateral Preoptic (VLPO)	Sleep
mammillary bodies	memory

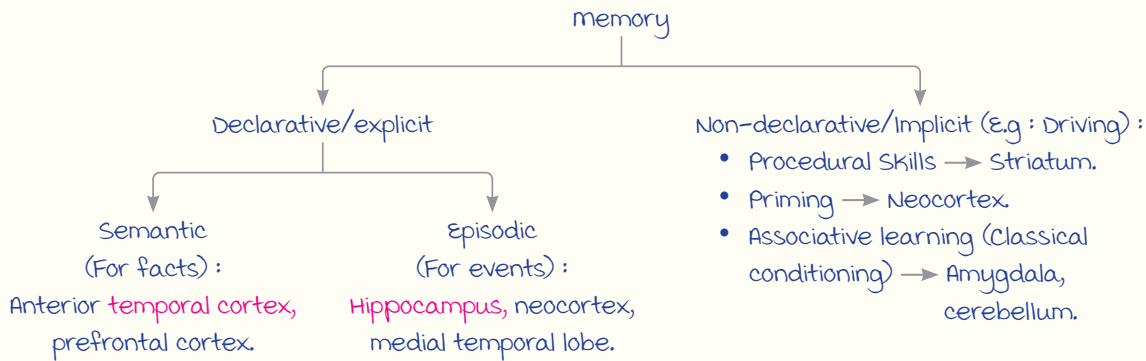
Cerebral Hemispheres & Functions

00:28:10

	Left hemisphere	Right hemisphere
AKA	Categorical hemisphere	Representational hemisphere
Previously called	Dominant hemisphere (Dominant in 96% of R handers & 70% of L handers.)	Non-dominant hemisphere
Functions	Language & speech	<ul style="list-style-type: none"> • Visuospatial relations • Music & creativity
Effect of lesions	Aphasia, dyslexia, acalculia	Hemispatial neglect, agnosia

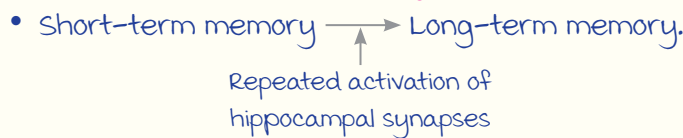
LEARNING & MEMORY

----- Active space -----



Role of Brain Regions :

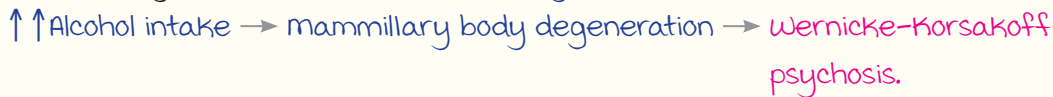
1. Hippocampus : Consolidation/Long-term potentiation.



- Hippocampal lesion -> Anterograde amnesia.

(Inability to form new long-term memories).

2. Mammillary bodies : Recollective memory.



3. Anterior nucleus of thalamus : Recent memory (Lesion -> Loss of recent memory).

4. Basal forebrain (Nucleus basalis of Meynert) :

- Acetylcholine synthesis.
- Lesion -> Alzheimer's disease.

5. Amygdala : Emotions + memory.

6. Entorhinal cortex : Smell + memory.

LANGUAGE & SPEECH

Speech areas :

	Broca's area	Wernicke's area	Arcuate Fasciculus	Angular gyrus
Location	Ⓛ inferior frontal gyrus	Superior temporal gyrus	Connects Broca's & Wernicke's areas	-
Brodmann area	44, 45	22		39
Function	motor area for speech (vocalization)	Sensory area for speech (Comprehension)		Vision-speech correlation
Lesion	Broca's/ non-fluent aphasia	Wernicke's/ fluent aphasia	Conduction aphasia	Anomic aphasia

----- Active space -----

Fluid Systems in the Brain

00:40:42

Cerebrospinal Fluid (CSF) :

- Volume : 150 mL.
- Rate of production : 550 mL/day.
- Turnover : 3.7 times/day.
- Normal pressure :
 - 70-180 mmH_aO.
 - Average pressure (Filtration = absorption) : 112 mmH_aO.
- Regulation : At the level of absorption.

CSF vs Plasma concentrations :

CSF > Plasma	Cl ⁻ , mg ²⁺
CSF = Plasma	HCO ₃ ⁻ , osmolarity
CSF < Plasma	Glucose (2/3 rd of plasma), proteins

CSF marker : β_a transferrin.

- Exclusively found in CSF.
- Significance : CSF rhinorrhea/otorrhea Dx.

Cerebral Blood Flow (CBF) :

- Rate : 750 ml/min (14% of cardiac output).
- O_a consumption : 20% of total body consumption.
- Regulation :
 - Autoregulation : Constant blood flow despite change in pressure (Range : 65-140 mmHg).
 - Hypercarbia (↑pCO_a) → ↑CBF.
 - Hypothermia : 1°C ↓ in body temperature → 7% ↓ in CBF (Therapeutic in Neuro-Sx).

Circumventricular organs : Parts of brain outside blood-brain barrier.

- Subfornical organ (SFO).
- Organum vasculosum of laminae terminalis (OVLT).
- Area postrema (Involved in vomiting).
- Posterior pituitary.

Sleep

00:48:13

EEG waves :

EEG wave	Frequency (Hz)	Seen during
Alpha : α	8-12	Relaxation
Beta : β	13-30	Attention/wakefulness
Theta : θ	4-7	A/w memory
Delta (Slow) : δ	< 4	Deep sleep
Gamma : γ	> 60	Focused attention

Stages of Sleep :

----- Active space -----

Non-rapid eye movement (NREM) sleep :

N_1 → Stage 1 : Theta waves.

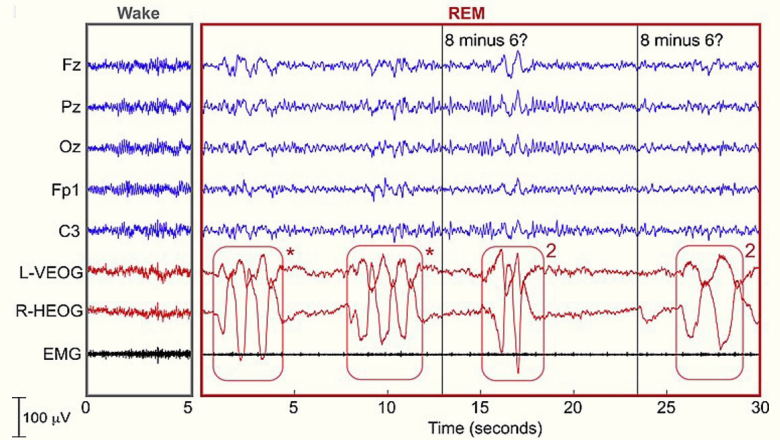
N_2 → Stage 2 : K-complex & sleep spindles (Resemble α waves).

N_3 → Stage 3 : Delta waves.

→ Stage 4 : Delta waves.

Rapid eye movement (REM) sleep :

- EOG (Electrooculography) : Eye movements (+).
- EMG : Flat → muscle atonia (+) (Except diaphragm & extraocular muscles).
- EEG : β waves (+) (AKA Paradoxical sleep).
- Pontogeniculo occipital (PGO) spikes (+) → Regulate eye movements.
- Genital organ enlargement (+).



Regulation of Sleep :

Brain areas	Neurotransmitter (NT)	NT levels		
		NREM	REM	
Cholinergic nuclei of pons-midbrain junction (REM-on neurons)	Acetylcholine	-	↑	} Promotes wakefulness
Locus ceruleus	Norepinephrine	↓	↓	
Raphe nuclei	Serotonin	↓	↓	
Tuberomammillary nuclei	Histamine	↓	↓	
Lateral hypothalamus	Orexin	↓	↓	

metabolic end product : ↑ Adenosine → Promotes sleep.
 Caffeine ⊖

Parasomnias :

During NREM :

- Somnambulism : Sleep walking (N_3).
- Sleep talking.
- Nocturnal enuresis : Bedwetting.
- Sleep bruxism : Teeth grinding (N_2).
- Night terrors/Pavor nocturnus.

During REM : Nightmares, narcolepsy.

RESPIRATORY PHYSIOLOGY : PART 1

Airway Generations

00:00:40

Weibel model (23 airway generations) :

Trachea → Bronchi → Bronchioles → Terminal bronchioles (16th gen)



(23rd gen) Alveolar sacs ← Alveolar ducts ← Respiratory bronchioles

CONDUCTING AIRWAYS

First 16 generations → Conduct air, **no gas exchange** (AKA dead spaces).

Histology :

Pseudostratified columnar ciliated epithelium : Ciliary movement (Using dynein) clears sputum.

Stem cells :

- Basal cells.
- Clara cells (Regeneration).

Airway smooth muscle :

- Contraction → Bronchoconstriction $\xrightarrow{\text{Exaggerated}}$ Bronchial asthma.
- Relaxation → Bronchodilation.

↑ Bronchoconstriction	↑ Bronchodilation
<ul style="list-style-type: none"> • Parasympathetic activation. • Acetylcholine. • Histamine. • Leucotrienes (most potent). 	<ul style="list-style-type: none"> • Sympathetic activation (β_2 receptor). • Nitric oxide. • Prostaglandin.

Note : Absence of dynein



Kartagener syndrome (Under immotile cilia syndrome) :

- **Situs inversus** (Improper rotation of internal organs d/t inadequate ciliary movement).
- **Asthenospermia** (Immotile sperm).

ALVEOLAR AIRWAYS

----- Active space -----

Last 7 generations → Gas exchange ⊕ (AKA exchange/respiratory airways).

Pneumocytes :

Cells of alveolar airways.

	Type I pneumocyte	Type II pneumocyte
Size	Large & flat (↑ surface area)	Small
Number	↓	↑
Function	-	<ul style="list-style-type: none"> Produce surfactant (Stored as lamellar bodies) Stem cell function

Surfactant :

Composition :

Surfactant lipids	Surfactant proteins (SP)
Lecithin/Dipalmitoylphosphatidylcholine (major)	SP-A, SP-B
Sphingomyelin (minor)	SP-C, SP-D

Normal lecithin : sphingomyelin ratio ≥ 2 (use → Assess **fetal lung maturity**).

Functions :

↓ Surface tension → Prevent alveolar collapse.

(Surfactant deficiency → Alveolar collapse → Hyaline membrane disease → Rx : **Lucinactant**)

Regulation of surfactant production :

↑ Production	↓ Production (Pathological)
<ul style="list-style-type: none"> Cortisol Thyroid hormones (T_3, T_4) 	<ul style="list-style-type: none"> ↑ Insulin levels Long term 100% O_2 inhalation main bronchus occlusion Pulmonary artery occlusion

Mechanics Of Breathing

00:15:16

Boyle's law :

$$\text{Pressure (P)} \propto \frac{1}{\text{Volume (V)}}$$

- Inspiration : ↑ V, ↓ P.
- Expiration : ↓ V, ↑ P.

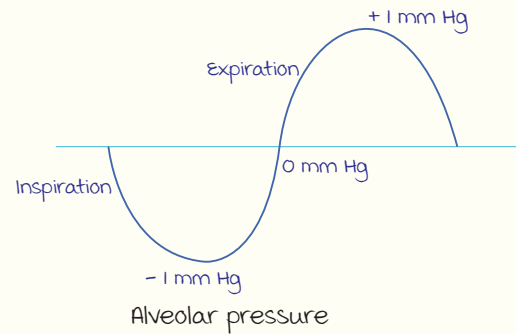
Pressures in the lung :

1. Intrapleural pressure (IPP) :

	At rest	Inspiration	Expiration	Forceful expiration
IPP	-2.5 mmHg	-6 mmHg	-2.5 mmHg	Positive value

----- Active space -----

2. Alveolar pressure (AP).
3. Transpulmonary pressure (TP) :
 $TP = AP - IPP$.



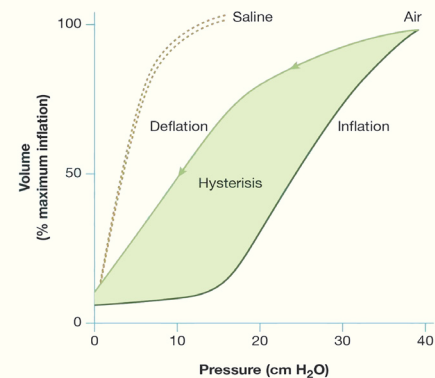
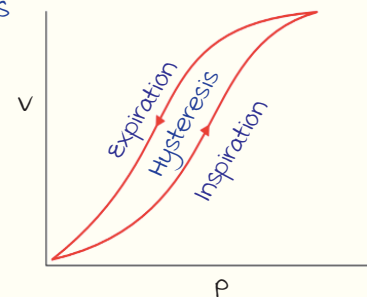
Lung Compliance :

- **Hysteresis** : Difference b/w pressure-volume curves of inspiration & expiration.
- Compliance (C) : maximum during expiration.

$$C = \frac{\Delta V \text{ (Change in volume)}}{\Delta P \text{ (Change in pressure)}}$$

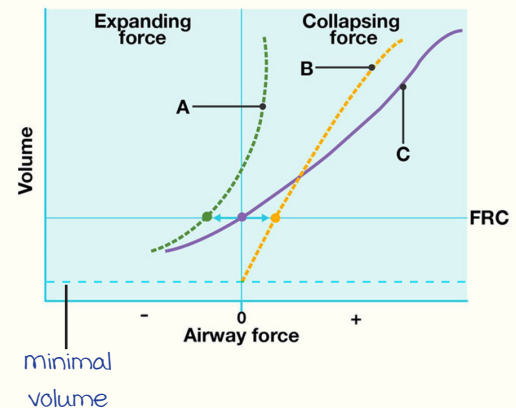
Air-filled lung vs saline-filled lung :

Saline filled lung
 ↓
 No air fluid interface
 ↓
 No surface tension
 ↓
 No hysteresis.



Lung vs chest wall vs lung + chest wall :

1. **Equilibrium volume** :
 - volume at which opposing forces (Expanding & collapsing) reach equilibrium.
 - Occurs at functional residual capacity (FRC).
2. **minimal volume** :
 - volume of air remaining in the lungs after complete lung collapse.
 - Seen in **pneumothorax**.



Index :

- A : Chest wall compliance.
- B : Lung compliance.
- C : Total compliance. (Chest wall + lung)

Effect of diseases on lung compliance :

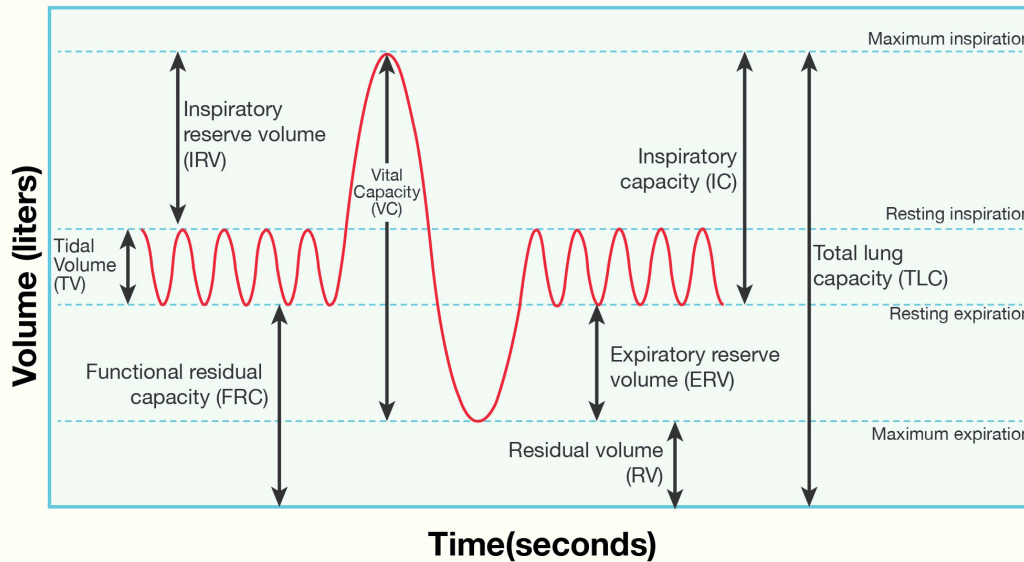
- Emphysema → ↑ Compliance.
- Fibrosis → ↓ Compliance.

Spirometry

00:26:41

----- Active space -----

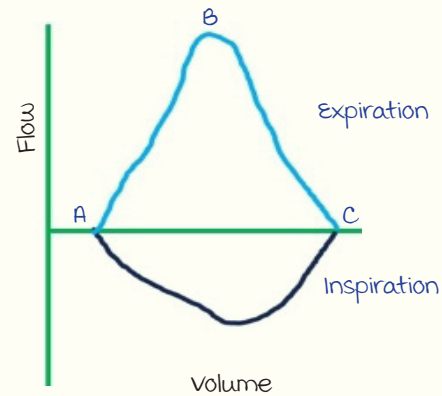
Static Lung volumes & Capacities :



- Normal values :
1. TV = 500mL.
 2. IRV = 2-3 L.
 3. ERV = 1.3 L.
 4. RV = 1.2 L.
 5. FRC = 2.5 L.

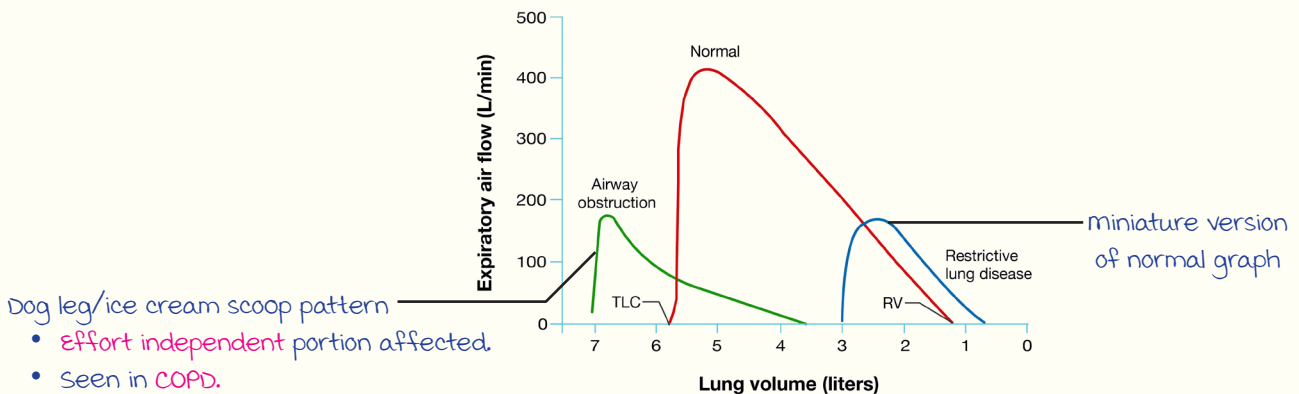
Dynamic Lung Volumes :

- $FEV = TLC - RV$.
- FEV_1 : volume of air expired in first second.
- FEV_1/FVC ratio
 - \downarrow \rightarrow Obstructive lung disease.
 - Normal/ \uparrow \rightarrow Restrictive lung disease.
- AB segment (Effort dependent) :
 - Air expired from large airways (Trachea & bronchi).
- BC segment (Effort independent) :
 - Air expired from medium & small airways.
 - Affected in COPD.



Time dependent flow volume loop :
 A : TLC
 B : Peak expiratory flow rate (PEFR)
 C : RV

Effect of diseases :

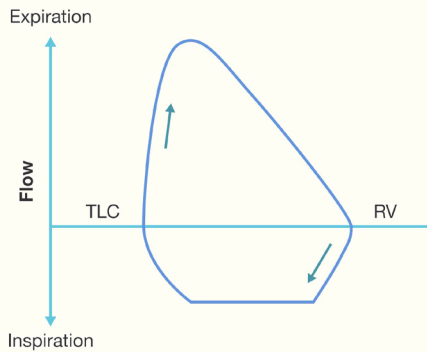


- Dog leg/ice cream scoop pattern
- effort independent portion affected.
- Seen in COPD.

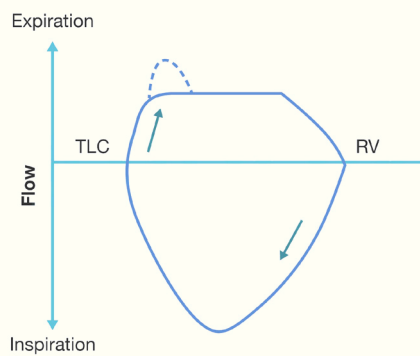
----- Active space -----

Types of obstructive diseases :

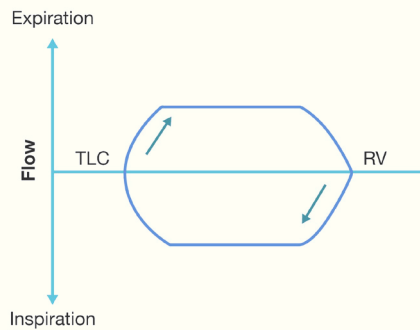
1. Variable extrathoracic :
Inspiration affected.



2. Variable intrathoracic :
Expiration affected.



3. Fixed (Intra or extrathoracic) : Both inspiration & expiration affected.



Limitations of spirometry : Cannot determine RV, FRC, TLC.

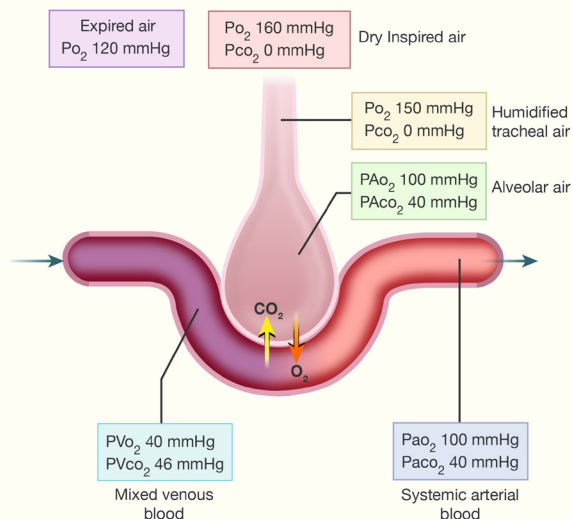
Alternative measuring techniques :

- Helium dilution technique : For FRC.
- Nitrogen washout technique.
- Body plethysmography : m/c used.

Alveolar Ventilation & Pulmonary Circulation

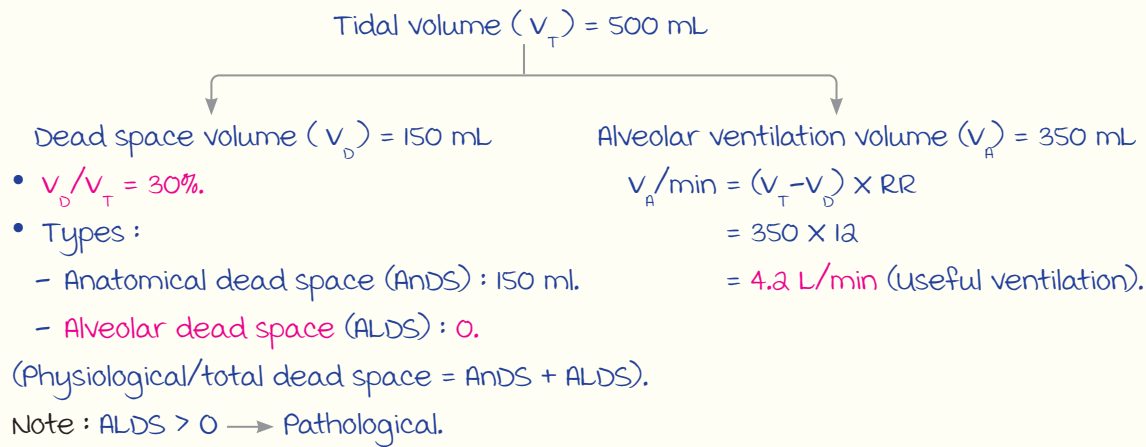
00:39:10

VENTILATION (V)



Partial pressures of gases in the lung

----- Active space -----



measurement of dead space :

1. Anatomical dead space : Single breath nitrogen/Fowler's method.
2. Physiological dead space : Bohr's equation.

$$V_D = V_T \times \frac{PA_{CO_2} - PE_{CO_2}}{PA_{CO_2}}$$

$$PA_{CO_2} : \text{Alveolar } CO_2$$


$$PE_{CO_2} : \text{Expired } CO_2$$

PERFUSION (Q)

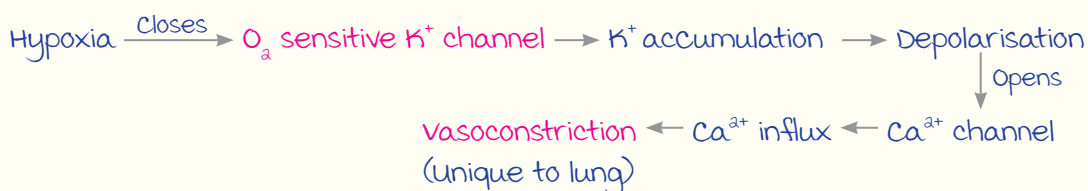
Pulmonary circulation (Deoxygenated blood) : 5.5 L/min.

- Highly distensible.
- Low pressure.

Zonal distribution of blood flow in the lung :

Lung zones	Blood flow
 <p>Zone 1 Apex</p>	minimal (d/t compression of blood vessels)
Zone 2 middle	Intermittent blood flow (waterfall effect)
Zone 3 Base	Highest (Continuous blood flow)

Effect of hypoxia :



----- Active space -----

VENTILATION - PERFUSION (V/Q) RATIO

Lung zone	V/Q ratio
Apex	~ 3.3
middle	0.8
Base	0.6

Ventilation perfusion mismatch :

$v/q = 0 (v=0)$	$v/q = \text{Infinity} (q=0)$
Shunt blood (Physiological)	Anatomical dead space
Foreign body causing airflow obstruction	Pulmonary embolism

RESPIRATORY PHYSIOLOGY : PART 2

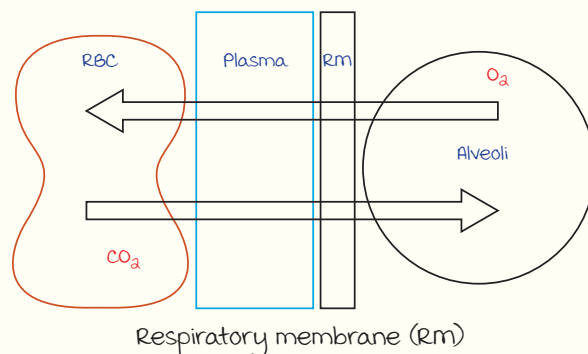
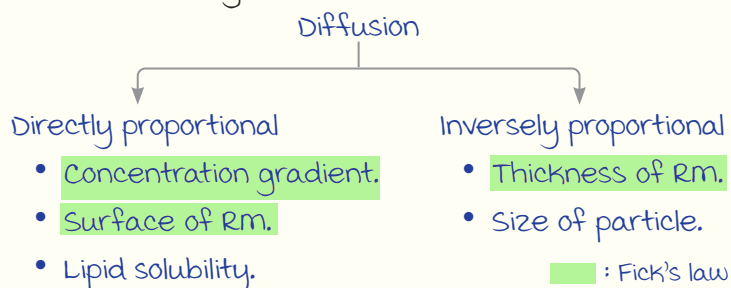
----- Active space -----

Diffusion & Transport Of Gases

00:00:09

Diffusion of Gases :

Factors affecting diffusion :



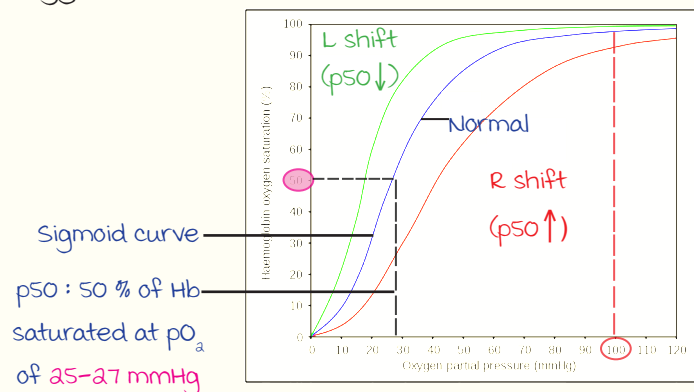
Diffusing capacity of the lungs for carbon monoxide (DLCO) :

- CO : 210 × O₂ affinity to Hb.
- Normal value of DLCO = 25 mL/min/mmHg.

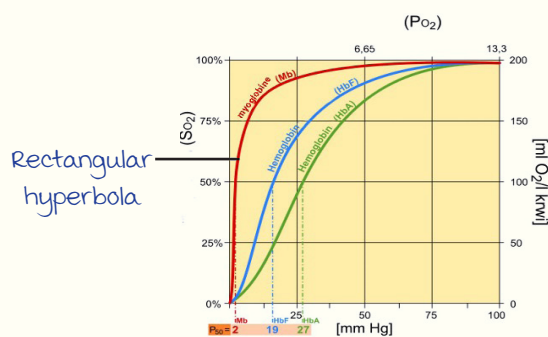
↓ DLCO	↑ DLCO
Anemia	Polycythemia
Emphysema	Exercise

Oxygen Transport :

Oxygen dissociation curve :



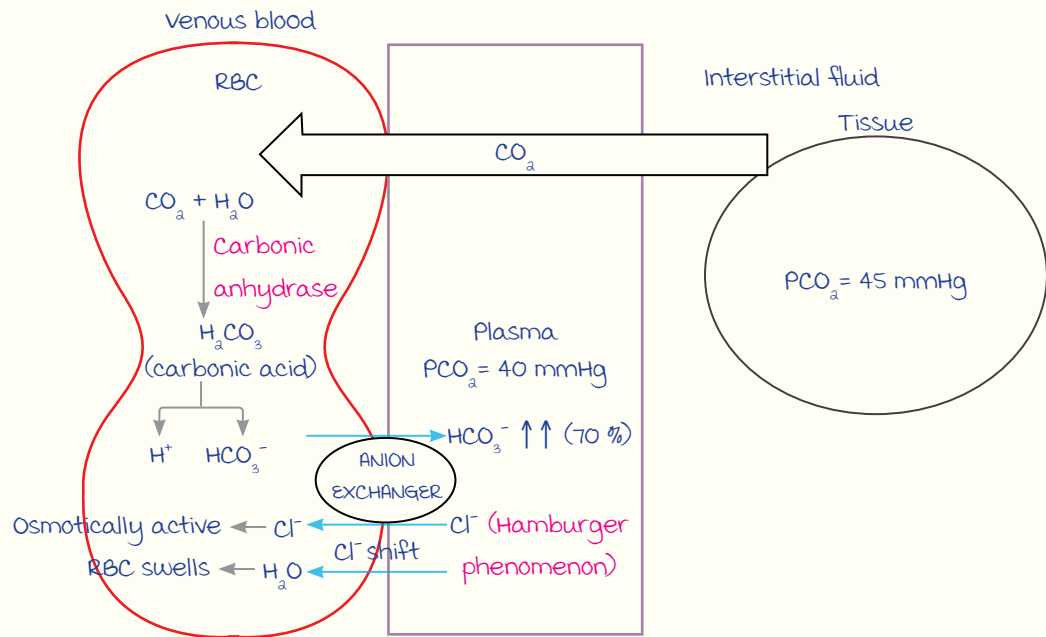
Oxygen-myoglobin dissociation curve :



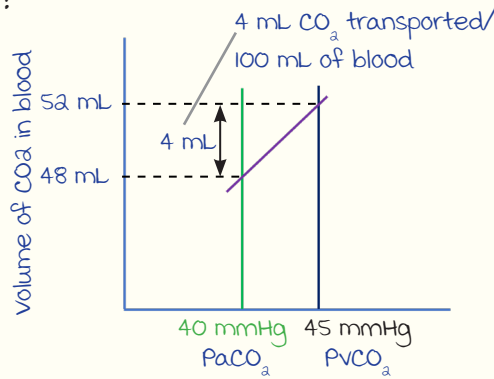
Left shift	Right shift
<ul style="list-style-type: none"> • Hypocarbica • Alkalosis • Fetal hemoglobin (↓ Affinity to 2,3 DPG) • Carbon monoxide • Stored blood (Fall in 2,3 DPG) 	<ul style="list-style-type: none"> • Hypoxia • Hypercarbica • Acidosis • ↑ 2, 3 DPG • High altitude • Thyroid hormones • Exercise

Note : Blood is stored in CPDA (Citrate phosphate dextrose adenine) → ↓ Fall in 2,3-DPG.

----- Active space ----- Carbon Dioxide Transport :



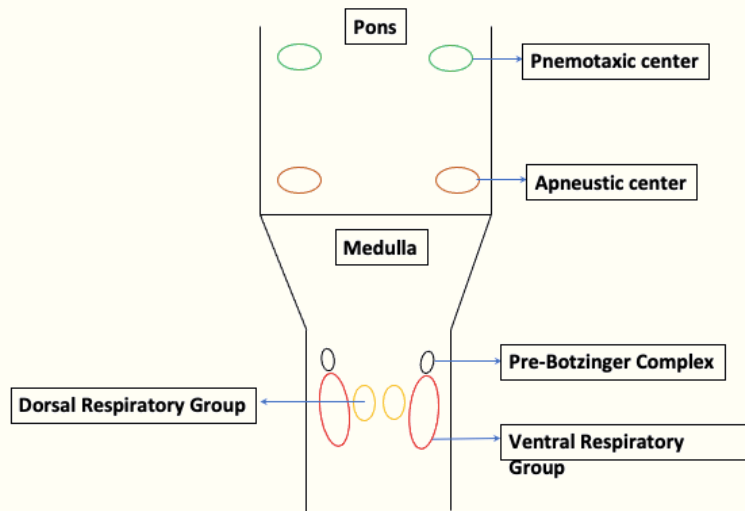
CO_2 Dissociation Curve :



Neural Regulation of Respiration

00:14:50

Neural Control :


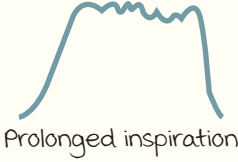

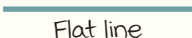


Brain area	Function
Pre Botzinger complex	Pacemaker : Initiates respiration
Pneumotaxic center	<ul style="list-style-type: none"> Limits inspiration (Inhibits apneustic center) Controls respiratory rate
Apneustic center	Prolongs inspiration
Dorsal Respiratory Group (DRG)	Generates RAMP signal for smooth rise in tidal volume during inspiration
Ventral Respiratory Group (VRG)	Controls forceful expiration during exercise

(mnemonic **DIVE** : **D** → Inspiration, **V** → Expiration)

----- Active space -----

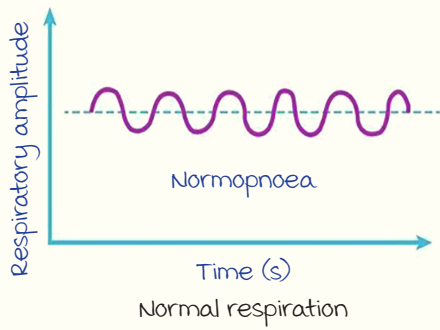
Lesions at Respiratory Centers :

Lesion		Effect	Waveform
Complete transection above pons	A	All respiratory areas intact	 Normal
mid-pontine level section with vagus cut	B	Apneustic center overactivity	 Prolonged inspiration
midway between pons and medulla	C	Regularization absent	 Irregular inspiration
Complete transection below medulla	D	Death inevitable	 Flat line

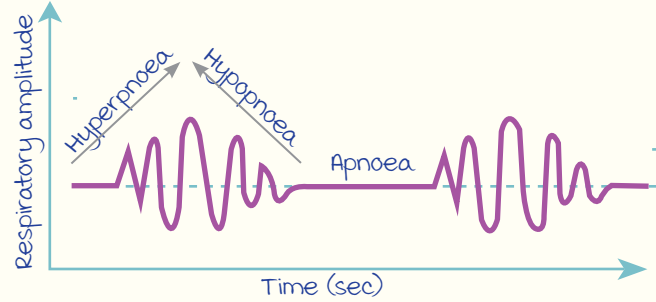
Pulmonary Reflexes :

Reflex	Stimulus	Receptor	Afferent	Effect
Hering-Breuer inflation reflex (Prevent injury)	Overstretch of lung (TV = 1500 mL)	Pulmonary stretch receptors (Slow adapting)	Large myelinated vagal fibres	<ul style="list-style-type: none"> Inhibits inspiration ↑ Duration of expiration
Hering-Breuer deflation reflex (Prevent collapse)	Deflation			<ul style="list-style-type: none"> Inhibits expiration. ↓ Duration of expiration
The paradoxical reflex of Head	Lung inflation	Pulmonary stretch receptors	-	<ul style="list-style-type: none"> Increase in lung inflation Responsible for first breath of newborn
J receptor reflex (A.S. Paintal)	Pulmonary edema, pulmonary congestion	Juxtapulmonary receptors	Unmyelinated vagal C fibres	<ul style="list-style-type: none"> Rapid breathing Bradycardia Hypotension

----- Active space ----- **Altered Breathing (Periodic Breathing) :**

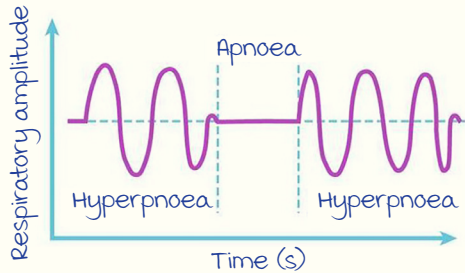


Normal respiration



Cheyne Stokes respiration :

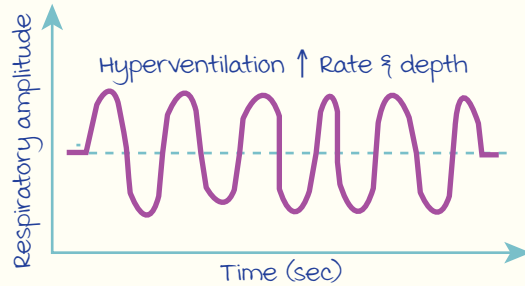
- Waxing & waning.
- Seen in :
 - Physiological : Sleep.
 - Pathological : Congestive cardiac failure, uremia.



Biot's breathing

Seen in :

- Injury to medulla.
- meningitis.



Kussmaul's breathing/acidotic breathing

- ↑Rate & depth (Hyperventilation).
- Seen in : Diabetic ketoacidosis.

Chemical Regulation Of Respiration

00:28:12

Chemicals regulators : O_2 , CO_2 , H^+ .

Types of Chemoreceptors :

	Central chemoreceptors	Peripheral chemoreceptors
Location	Brain	Neck : Carotid & aortic bodies
Sensitive to	pCO_2 (Blood)	$\downarrow pO_2$ (Hypoxia)
MOA	<p>Blood $\uparrow CO_2$ → CSF $CO_2 + H_2O$ → H^+ & HCO_3^- (via Carbonic anhydrase). H^+ directly stimulates central chemoreceptors.</p>	<p>1. Hypoxia ($\downarrow pO_2$) 2. O_2 Sensing K^+ channel closes 3. Depolarization 4. Ca^{2+} channel opens 5. Influx of Ca^{2+} 6. Dopamine release Stimulates afferent nerve endings 7. Brain</p>

In asphyxia :

$\downarrow pO_a$, $\uparrow pCO_a$ & $\uparrow H^+ \rightarrow$ Central & peripheral \rightarrow Chemoreflex \rightarrow Hyperventilation.
Chemoreceptors activated

----- Active space -----

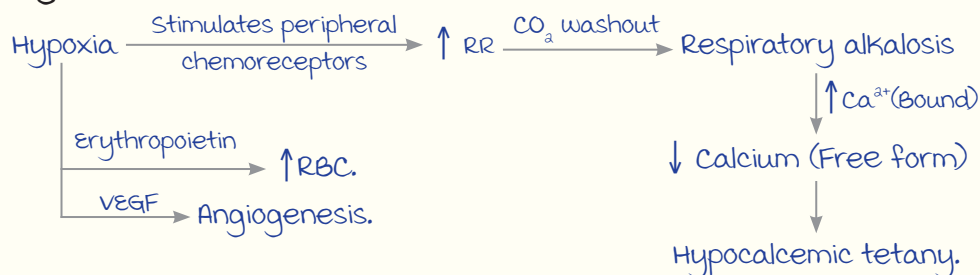
Types of Hypoxia :

	Hypoxic hypoxia	Anemic hypoxia	Stagnant hypoxia	Histotoxic hypoxia
Due to	Low arterial pO_a	Reduced O_a content of blood	Decreased blood flow to tissues	Decreased ability of cells to use oxygen
Arterial pO_a	Decreased	Normal	Normal	Normal
Arterial Hb content	Normal	Decreased	Normal	Normal
Peripheral chemoreceptor stimulation	Stimulated	Not stimulated (D/t normal pO_a)	Stimulated	Stimulated
Examples	<ul style="list-style-type: none"> High altitude COPD 	<ul style="list-style-type: none"> CO poisoning Anemia 	Ischemia	Cyanide poisoning

Environmental Physiology

00:36:55

High Altitude :



Deep Sea Physiology :

High barometric pressure $\xrightarrow{\text{Decompression}}$ Compressed gas released as bubbles.

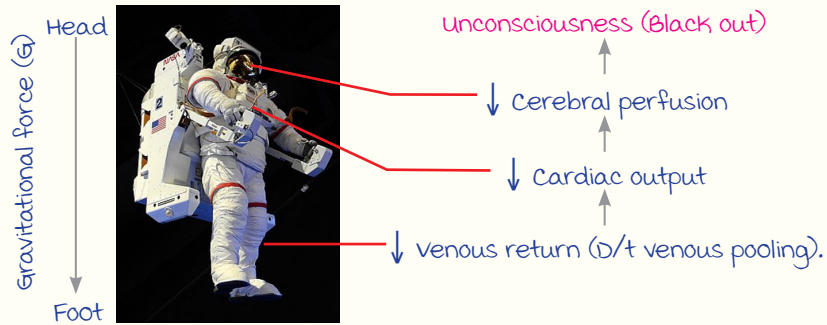
Caisson's disease/decompression sickness :

Accumulation of N_a gas :

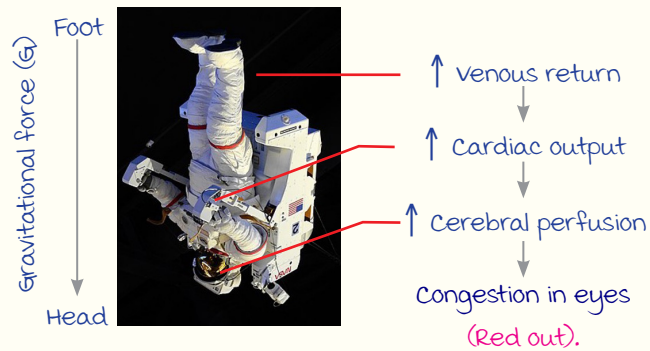
- Crosses blood brain barrier \rightarrow N_a narcosis.
- In joints \rightarrow Bends.
- In lungs \rightarrow Chokes.
- In blood vessels \rightarrow Air embolism \rightarrow Death.

----- Active space ----- **Space Physiology :**

Positive G :



Negative G :



Effects of microgravity :

- Loss of Ca^{2+} & $\text{PO}_4^{2-} \rightarrow \downarrow$ Bone mass
 - \downarrow RBC
- } \downarrow work capacity.

CARDIOVASCULAR PHYSIOLOGY

----- Active space -----

Cardiac Action Potentials

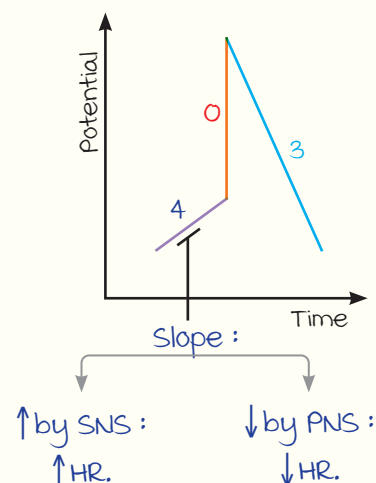
00:00:30

SA Nodal Potential :

Phase	AKA	Ionic activity
Phase 4	Prepotential phase	<ul style="list-style-type: none"> • Ca_T^{2+} influx (Transient) • Na^+ influx (Funny currents/I_f) • $\downarrow K^+$ efflux
Phase 0	Depolarization	Ca_L^{2+} influx (Long lasting)
Phase 3	Repolarization	K^+ efflux

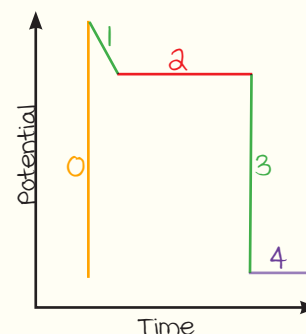
Funny currents (D/t Na^+ influx) :

- AKA Hyperpolarization activated cyclic nucleotide gated (HCN) channels.
- Sensitive to cAMP levels.
- Also seen in rods & cones.
- Inhibited by Ivabradine.



Ventricular Action Potential :

Phase	AKA	Ionic Activity
Phase 0	Early depolarization	Na^+ influx
Phase 1	Early repolarization	K^+ efflux
Phase 2	Plateau	K^+ efflux = Ca_L^{2+} influx
Phase 3	Late repolarization	K^+ efflux
Phase 4	Resting membrane potential (RMP)	K^+ influx, Na^+ efflux through Na^+-K^+ pump

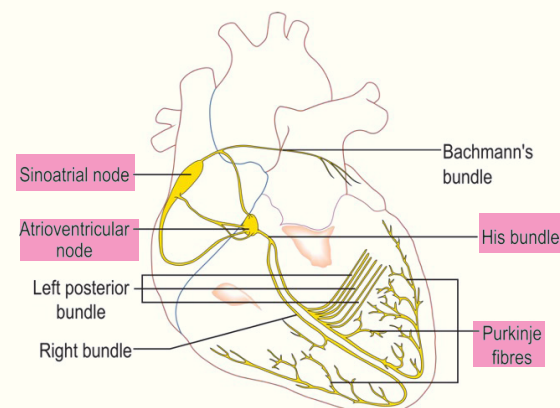


Conduction System, ECG, JVP

00:07:46

Conduction System :

1. SA node : Dominant pacemaker (100 impulses/min).
2. AV node :
Physiological delay for ventricular filling :
Conduction at 0.04 m/s (Slowest).
3. Bundle of His.
4. Purkinje fibres :
↑ Gap junctions : Conduction at 4m/s (Fastest).



----- Active space -----

ECG :

	Cause	Duration (sec)
P wave	Atrial depolarization	0.10
QRS complex	Ventricular depolarization	0.08-0.10
T wave	ventricular repolarization	0.2
u wave	<ul style="list-style-type: none"> Purkinje fiber repolarization Papillary muscle repolarisation 	-

Segments :

PR Segment :

- End of P wave to start of QRS complex.
- AV nodal delay.

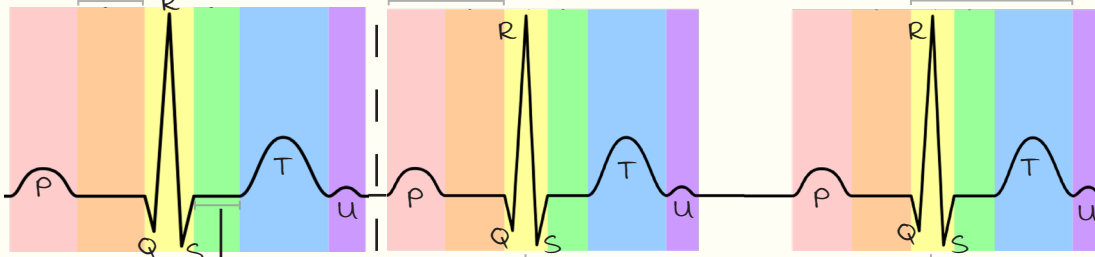
Intervals :

PR interval :

- Start of P wave to start of QRS complex.
- (0.12-0.2s) : AV conduction time.
- If > 0.2s → Heart block.

QT interval (0.35-0.43s) :

- Onset of Q wave to end of T wave.
- Ventricular depol. + repol. (Total ventricular activity).



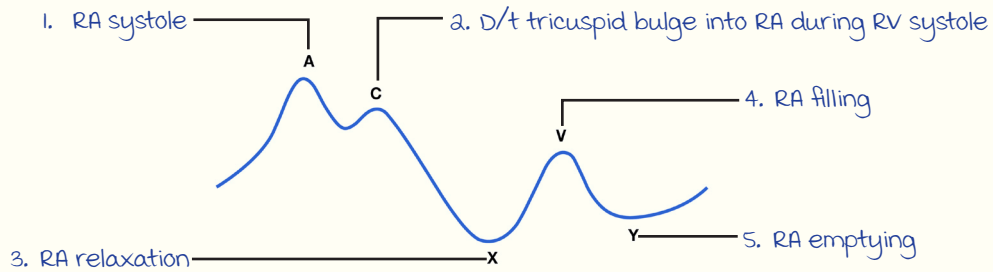
ST segment :

- End of QRS complex to start of T wave.
- Plateau phase of ventricular AP.
- J point : Can Dx MI.

RR interval (0.6-1 s) :

- Interval between 2 successive R waves.
- HR = 1500/No. of small squares.

JVP Waveforms :



Cardiac Cycle

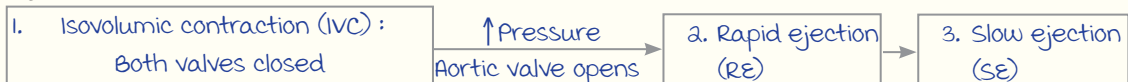
00:18:52

$$\text{Duration of cardiac cycle} = \frac{60}{\text{HR}}$$

Normal duration : 0.8s.

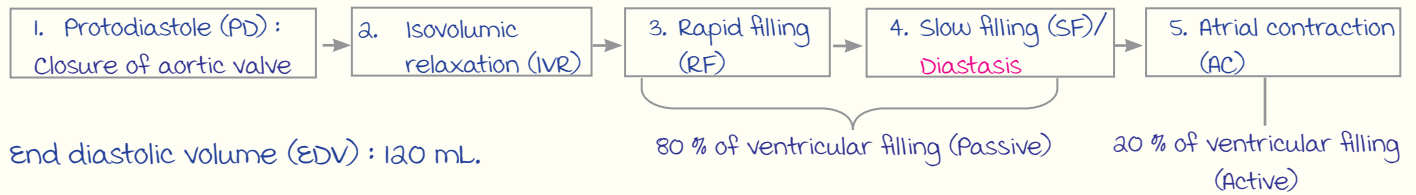
	Atrial	Ventricular
Systole (Short)	0.1 s	0.3 s
Diastole (Long)	0.7 s	0.5 s

Systolic (Ejection) :



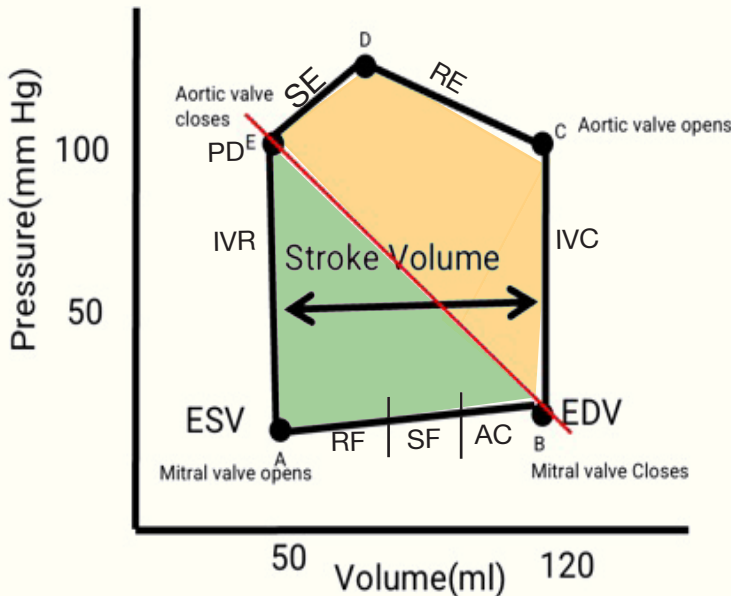
End systolic volume (ESV) : volume of blood left at the end of systole (50 mL).

Diastolic (Filling) :



End diastolic volume (EDV) : 120 mL.

Pressure Volume Graph :



1. Stroke volume (SV) = EDV - ESV
 = 120 - 50
 = 70 mL.

2. Ejection fraction (EF) = $\frac{SV}{EDV} \times 100$
 Normal EF = 55-60%

3. EDV = $\frac{ESV}{1 - EF}$

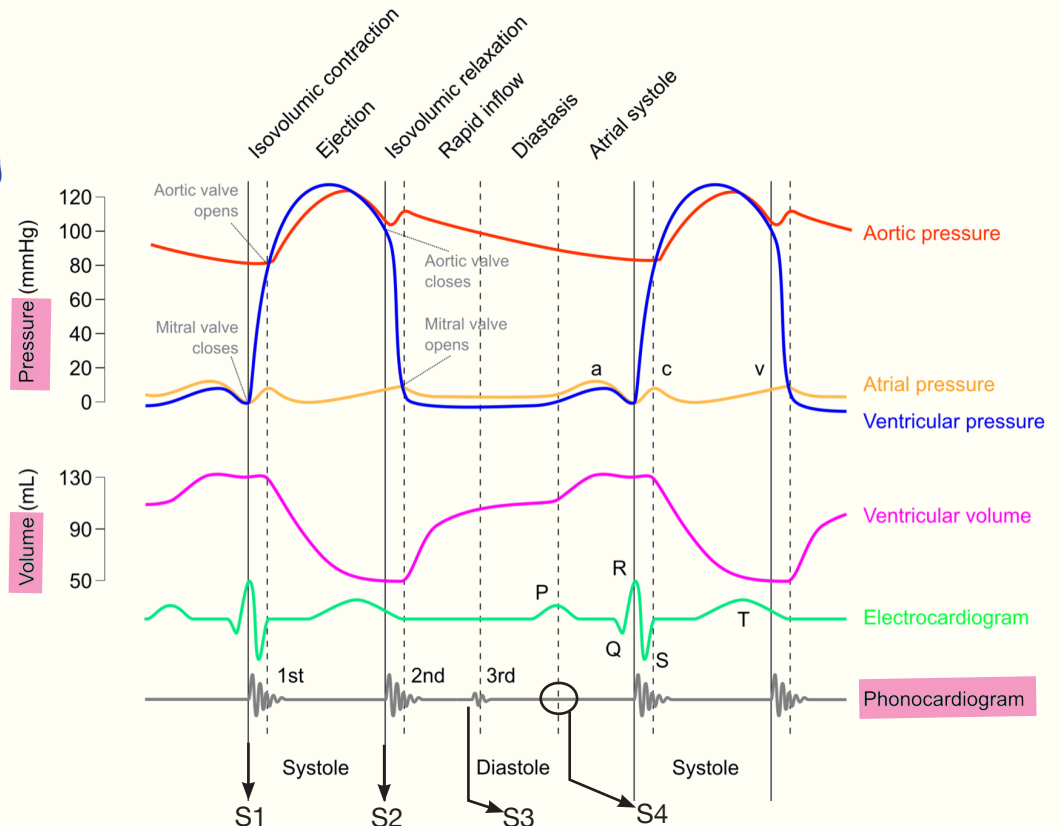
4. ESV = EDV (1 - EF)

Green : Diastole
 Orange : Systole

Wiggers Diagram :

Heart sounds :

- S1 : mitral & Tricuspid valve closure.
- S2 : Aortic & pulmonary valve closure.
- S3 : Rapid filling.
- S4 : Forceful atrial contraction.



----- Active space -----

Cardiac Output (CO)

00:34:43

1. $CO = HR \times SV$

Normal values :

- males : 5.6 L/min.
- Females : 4.9 L/min.

2. Fick's principle :

$$CO = \frac{O_2 \text{ consumed (mL/min)}}{\text{Arteriovenous } O_2 \text{ difference}}$$

3. Cardiac index ratio : CO per m^2 of body surface area/BSA
(Normal : 3.2 L/min/ m^2 of BSA)

Regulation of CO :

mnemonic : **CAP**.

	myocardial contractility	Afterload	Preload
Best marker	EF	Aortic pressure/Total peripheral resistance	EDV
Relation to CO	Directly proportional	Inversely proportional	Directly proportional

Distribution of CO :


Organ	Blood flow
Liver	1500 mL/min (Highest mL/min)
Brain	750 mL/min
Kidney	1250 mL/min OR 420 mL/100g/min (Highest mL/100g/min)
Heart	250 mL/min
Skeletal muscle (Rest)	3 mL/100g/min

Organ	O_2 consumption
Liver	51 mL/min (Highest mL/min)
Heart	10 mL/100g/min (Highest mL/100g/min)
Brain	46 mL/min

Note : Heart has highest AV O_2 difference.
(114 mL/L)**Coronary Circulation**

00:41:20

- Receives blood during diastole (IVR)
- Regulation of coronary circulation : O_2 demand > Adenosine, K^+ , NO.


 Chemical regulation.

Determinants of myocardial O_2 consumption :

1. Intramyocardial tension.
2. HR.
3. Preload & afterload (ventricular wall).

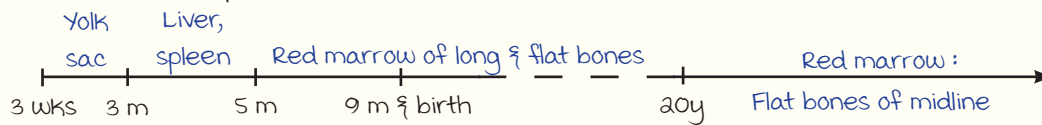
Blood

00:43:16

----- Active space -----

HEMATOPOIESIS

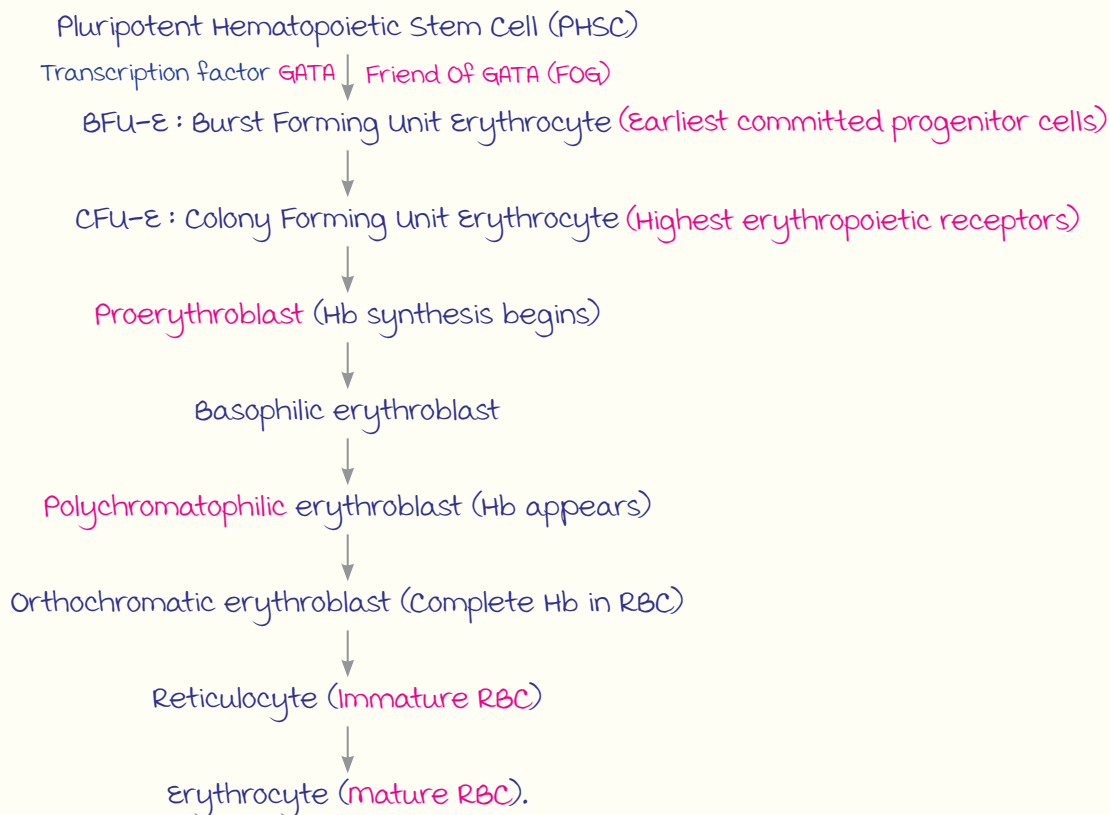
Sites of hematopoiesis :



Note : Hematopoiesis in liver & spleen beyond 5 months age is Pathological.

Erythropoiesis :

Steps :

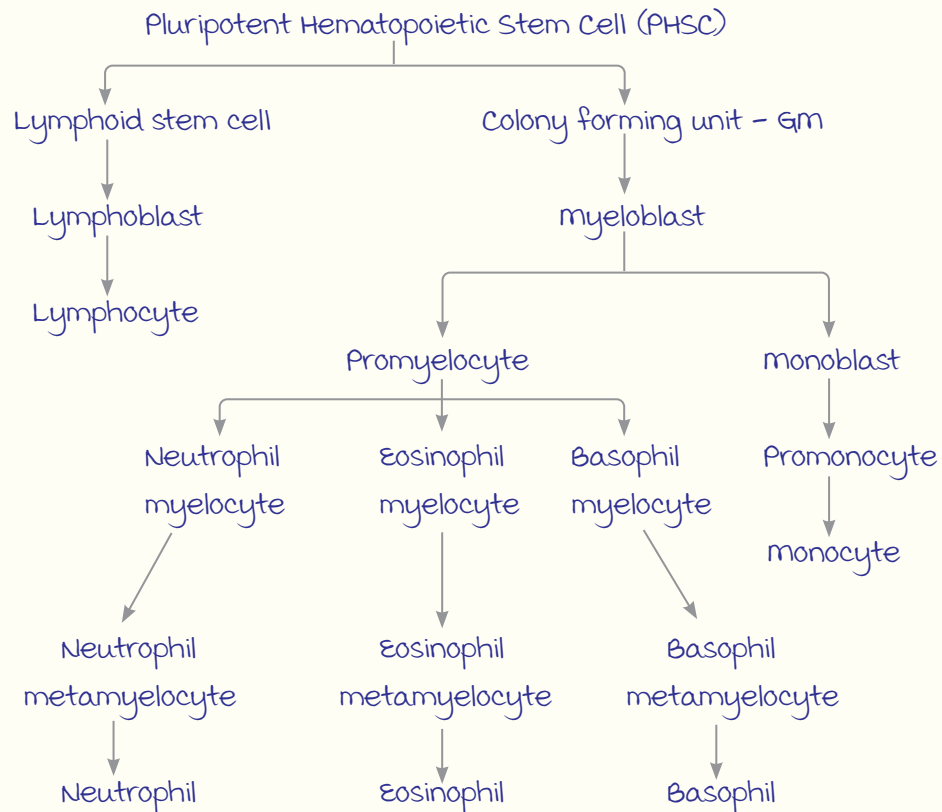


Erythropoietin : Regulation.

- Structure : Glycoprotein
- Sources :
 - Kidney (85%) : Peritubular capillary cells.
 - Liver (15%) : Perivenous hepatocytes.
 - minor : Brain, uterus, oviducts.
- Drug forms : Epoetin alfa, Darbepoetin alfa.
- Stimuli :
 - Hypoxia.
 - Alkalosis (High altitude).
 - Androgens.
 - Catecholamines (β receptor action).
- MOA : Inhibits apoptosis of RBCs.

----- Active space ----- **Leucopoiesis :**

Steps :



Regulation :

- Granulocyte colony stimulating factor (G CSF) → Drug form : **Filgrastim**.
- Granulocyte monocyte colony stimulating factor (Gm CSF) → Drug form : **Sargramostim**.
- IL 5 : **Eosinophil** development.
- IL 3 & 4 : **Basophil** development.

Thrombopoiesis :

Steps :



Regulation :

- Thrombopoietin (Drug form : **Eltrombopag**)
- IL-11 (Drug form : **Oprelvekin**)

BLOOD GROUPING SYSTEMS

----- Active space -----

ABO System :

Blood group	Antigen (RBC)	Antibody (Plasma)
A	A	Anti B
B	B	Anti A
AB	A & B	Nil
O	Nil	Anti A, Anti B

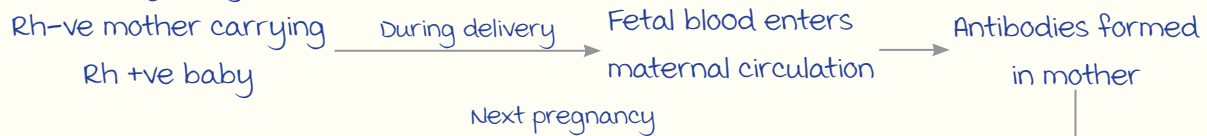
- universal donor : O
- universal recipient: AB

Rh System :

Erythroblastosis fetalis :

- Pathophysiology :

1st pregnancy :



maternal antibodies \rightarrow Hemolysis \rightarrow \uparrow unc. bilirubin \rightarrow Crosses BBB \rightarrow Kernicterus

- Treatment : Anti Rh antibodies.

Other Systems :

	Significance
Kell system	If absent \rightarrow mcleod phenotype \rightarrow RBC with spines (Acanthocytes). \rightarrow Cardiac defects.
P system	• If autoantibodies \oplus \rightarrow Paroxysmal cold hemoglobinuria. • Receptor for Parvovirus B19.
Duffy system	Receptor for Plasmodium vivax.

Blood vessels

00:56:40

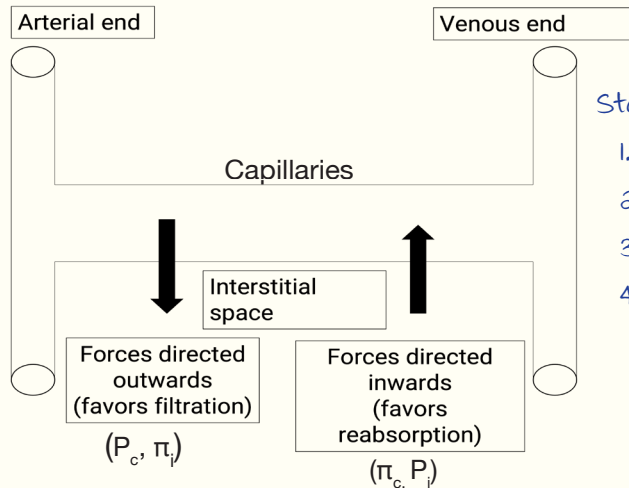
Characteristics :

vessel	Cross-sectional area (m ²)	Blood flow velocity	% of blood contaminated
Aorta	4.5 (min)	40 cm/s (max)	2
Artery	20	-	8
Arteriole	400	-	1
Capillary	4500 (max)	0.05 cm/s (min)	5
venule	4000	-	-
vein	40	20 cm/s	54 (max)
vena cava	18	-	-

----- Active space -----

- max. diameter : Vena cava.
- max. wall thickness : Aorta.
- Shunt vessels : AV anastomosis (Temperature regulation).
- max. BP : Aorta.
- min. BP : vena cava.
- Site of gas exchange : Capillaries.

Starling force :



Starling forces :

1. Capillary hydrostatic pressure (P_c)
2. Capillary oncotic pressure (π_c)
3. Interstitial hydrostatic pressure (P_i)
4. Interstitial oncotic pressure (π_i)

Net filtration pressure = Forces favoring filtration - Forces favoring reabsorption.

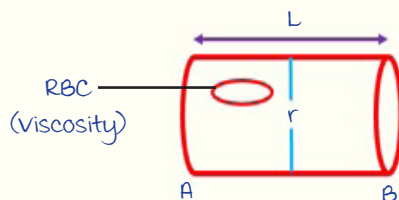
$$NFP = (P_c + \pi_i) - (\pi_c + P_i)$$

Hemodynamics :

Poiseuille-Hagen formula : F (Blood flow) = $(P_A - P_B) \times \pi r^4 / 8 \eta L$.

- Blood flow \propto Pressure difference ($P_A - P_B$).
- Blood flow \propto radius⁴ (r^4).
- Blood flow \propto 1/ Length (L).

Fourth power law : Resistance $\propto \frac{L}{(\text{Radius})^4}$



Blood pressure :

- mean arterial pressure (MAP) :
 - $MAP = DBP + 1/3 PP$.
 - Normal range : 93-100 mmHg.

Reynold's number (Re):

$$Re = \rho Dv / \eta$$

- ρ : Density of fluid
- D : Diameter of tube
- v : velocity of fluid
- η : viscosity of fluid

Significance :

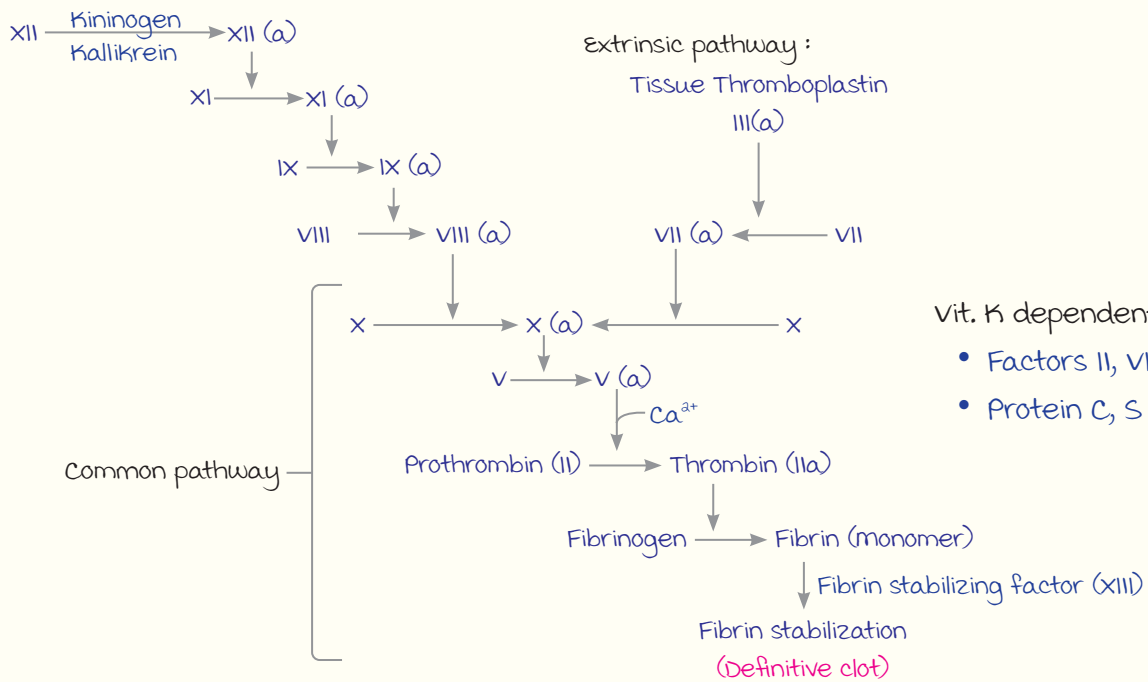
- $\uparrow Re$: Turbulent flow ; $\downarrow Re$: Laminar flow.
- Stenotic valve $\rightarrow \uparrow$ velocity \rightarrow Turbulence \rightarrow Murmur.
- Anemia $\rightarrow \downarrow$ viscosity \rightarrow Turbulence \rightarrow Flow murmur.

----- Active space -----

Coagulation Cascade

01:08:10

Intrinsic pathway :



- Vit. K dependent factors :
- Factors II, VII, IX, X
 - Protein C, S

Test	Normal value	measures
APTT	26-40s	Intrinsic & common coagulation pathways
PT	11-16s	Extrinsic & common coagulation pathways

APTT : Activated Partial Thromboplastin time.
PT : Prothrombin time

Anticoagulation Factors :

1. Thrombin + Thrombomodulin $\xrightarrow{\ominus}$ Factors V, VIII.
(Present everywhere except CNS)
2. Antithrombin III + Heparin $\xrightarrow{\ominus}$ Factors IX, X, XI, XII
3. Tissue Factor Pathway Inhibitor (TFPI).

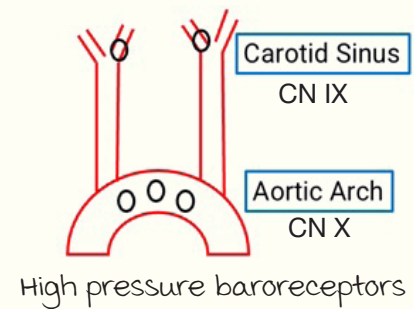
----- Active space -----

Blood Pressure**Regulation of BP :**

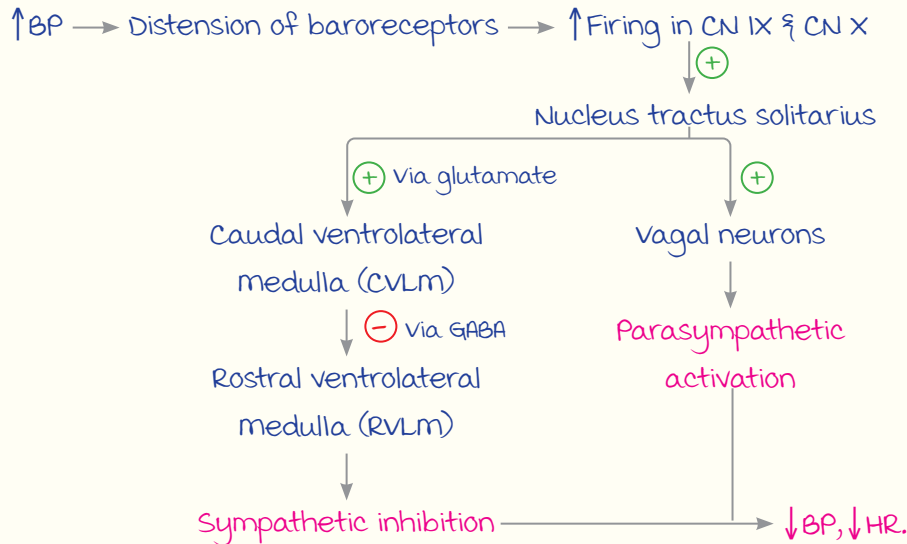
	Short term	Intermediate term	Long term
Time taken	Seconds	Hours	Days
mechanisms	1. Baroreceptor 2. Chemoreflex 3. CNS ischemic reflex	1. Capillary fluid shift 2. Stress relaxation	1. Renin Angiotensin Aldosterone system (RAAS) 2. Blood volume regulation by Kidney

Baroreflex (MAP \rightarrow 70-140 mm Hg) :

- 1st line of BP control.
- Baroreceptors :
 - a. High pressure : Carotid sinus (CN IX), aortic arch (CN X)
 - b. Low pressure/volume sensing : Atrial & pulmonary artery baroreceptors.
 - Type A : (+) By atrial systole.
 - Type B : (+) By atrial diastole.



- mechanism :



Chemoreflex (MAP \rightarrow 40-70 mmHg) :

- Second line of BP control.
- Effect on HR : **variable**.
 - Direct effect : Parasympathetic activation \rightarrow ↓ HR.
 - Indirect effect : Sympathetic activation \rightarrow ↑ HR.

CNS ischemic reflex (MAP < 40 mmHg) : **Last ditch stand phenomenon (Powerful)**.

Waveforms in BP :

----- Active space -----

1. Mayer/Vasomotor waves : Oscillations d/t nervous control (short term) mechanisms of BP.
2. Traube-Hering waves : BP fluctuations synchronized with respiration.
 - Inspiration \rightarrow \downarrow SBP.
 - Expiration (early part) \rightarrow \uparrow BP.

Cardiac Reflexes

01:23:35

Bainbridge reflex :

\uparrow Venous return \rightarrow Atrial reflex \oplus SA node \rightarrow \uparrow HR.

Bezold-Jarisch reflex :

In MI \rightarrow Serotonin accumulation \rightarrow \downarrow HR, \downarrow BP.

Cushing's reflex :

\uparrow Intracranial tension (ICT) \rightarrow \downarrow HR.

Czermak-Hering test :

Carotid sinus massage \rightarrow \downarrow HR.

Marey's law : $BP \propto \frac{1}{HR}$

Chemical Regulation of CVS :

Vasoconstrictors : \uparrow BP

- Urotensin II : most potent.
- Endothelin.
- Vasopressin.
- Angiotensin II.
- Norepinephrine.

Vasodilators : \downarrow BP

- Calcitonin gene-related peptide (CGRP) : most potent.
- NO.
- Prostacyclins (PGI₂).
- Kinins.
- Histamine.

GASTROINTESTINAL PHYSIOLOGY

Layers of intestine :

mucosa → Submucosa → muscularis (Circular & longitudinal) → Serosa.

Enteric nervous system (Little brain) : Two nerve plexuses.

	meissner's/submucosal Plexus	myenteric/Auerbach's Plexus
Location	Submucosa	muscularis
Function	Secretion control	motility control

Daily water turnover in GIT :

Source/location	volume (mL)
Ingested fluid	2000
GI secretions :	
Salivary glands	1500
Stomach	2500 (maximum)
Exocrine pancreas	1500
Bile	500
Intestine	1000
Total (Secretions + Ingested fluid)	9000
Reabsorption :	
Jejunum	5500
Ileum	2000
Colon	1300
Total reabsorbed	8800
Remaining 200 ml : Excreted in stool	

GIT Secretions

00:03:51

Saliva :

3 major salivary glands :

- Parotid : CN IX (Otic ganglion).
 - Sublingual
 - Submandibular
- } CN VII (Submandibular ganglion).

Functions :

Digestion :

- Carbohydrates : Salivary amylase/ptyalin.
- Fats : Lingual lipase.
- Proteins : No enzymes.

Lubrication.

Protection :

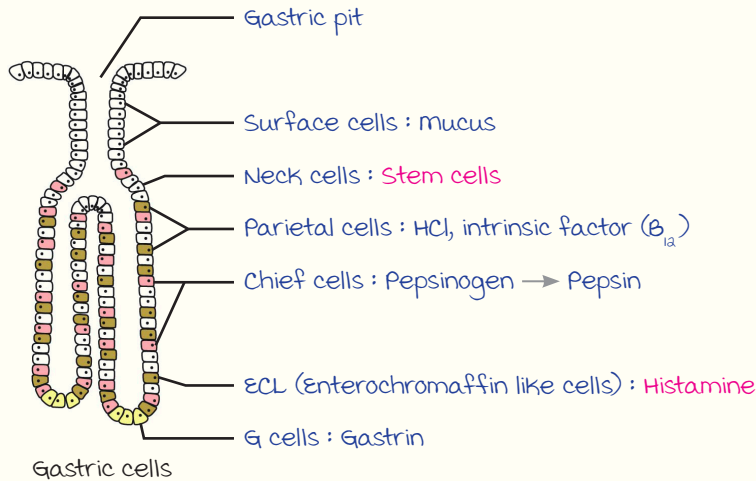
- Secretory IgA.
- Lactoferrin.
- Lysozymes.

----- Active space -----

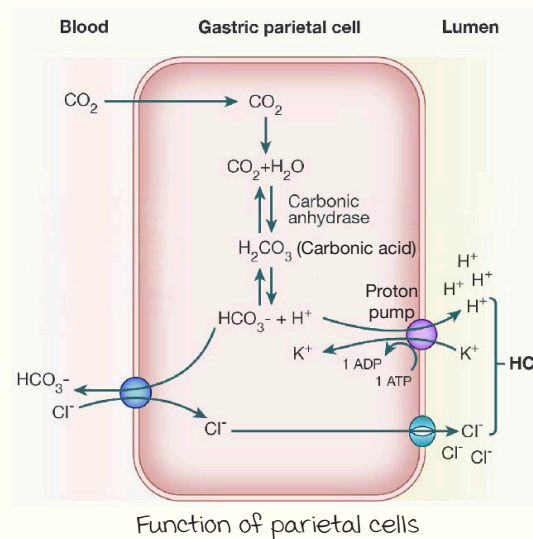
Types of secretions :

	Features	Tonicity (w.r.t plasma)
Acinar cells secretion	<ul style="list-style-type: none"> • Primary secretion. • Rich in NaCl. 	Isotonic
Ductal secretion (Final)	<ul style="list-style-type: none"> • Reabsorbs Na^+ & Cl^-. • Secretes K^+ & HCO_3^-. 	Hypotonic

Gastric Secretion :



Parietal cell :



Postprandial alkaline tide : $\uparrow \text{HCO}_3^-$ levels post food intake.

----- Active space ----- Factors affecting gastric acid secretion :

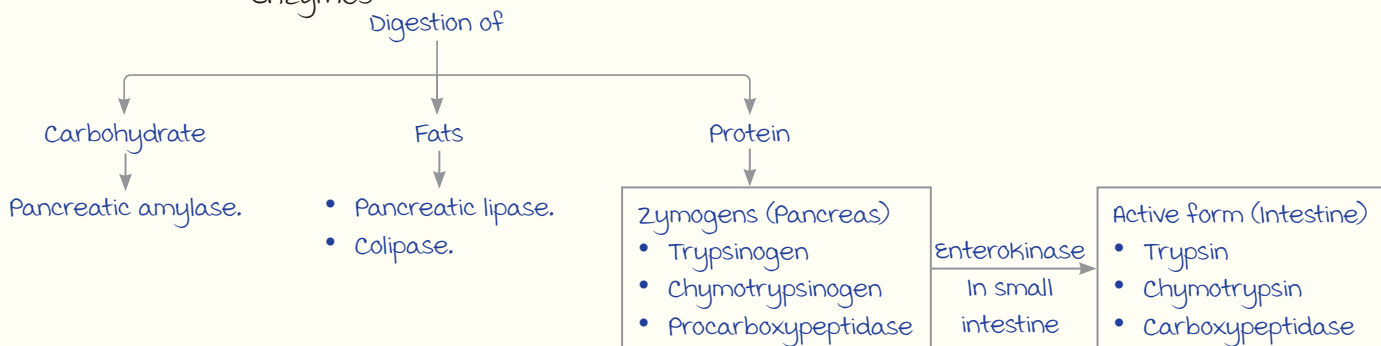
Increase gastric acid secretion	Decrease gastric acid secretion
<ul style="list-style-type: none"> • Histamine • Gastrin • Acetylcholine 	<ul style="list-style-type: none"> • Acid (Negative feedback) • Somatostatins (D cells) • Prostaglandins

Phases of gastric secretion :

	Cephalic phase	Gastric phase	Intestinal phase
Percentage of gastric secretion	30%	60%	10%
Activation factors	Thought, sight, smell, taste of food (Activated in the absence of food)	When food enters stomach	Digested protein products ↓ stimulates Intestinal G cells

Exocrine Pancreatic Secretion :

Enzymes :



Note : Stored as zymogens (inactive form) to prevent autodigestion of pancreas.

Hormones involved in regulation of pancreatic secretion :

- Cholecystokinin : makes pancreatic juice rich in digestive enzymes.
- Secretin : makes pancreatic juice rich in HCO_3^- → Acid neutralisation (Nature's antacid).

Biliary Secretion :

Bile acid → Primary : Cholic acid & chenodeoxycholic acid.
 → Secondary (Intestine) : Deoxycholic acid & lithocholic acid.

Conjugation → In liver : Bile acids + glycine/taurine.

Bile salts :

- Conjugated bile acids + sodium/potassium.
- Cholagogues (Enhances bile salts secretion) : Bile salts.
- Contraction of gall bladder : Cholagogues, eg : CCK.

Enterohepatic circulation :

Recycling of bile salts between liver & small intestine.

- 6 to 8 times/day.
- ↓ energy for bile salts synthesis.

----- Active space -----

Small Intestinal Secretions :

- Goblet cells $\xrightarrow{\text{secretes}}$ mucus
 - Epithelial cells $\xrightarrow{\text{secretes}}$ Water & electrolytes
 - Paneth cells :
 - Base of crypts
 - Store zinc, defensins, lysozymes
- } Present in the crypts of Lieberkuhn.

GI Hormones

00:21:54

Enteroendocrine cell	Secreting hormone
G cells	Gastrin
I cells	Cholecystokinin
S cells	Secretin
K cells	Gastric inhibitory peptide/ glucose dependent insulinotropic peptide (GIP)
mo cells	motilin
D cells	Somatostatin

Gastrin :

- ↑ acid production & pepsin.
- ↑ gastric motility.
- Contraction of lower esophageal sphincter.
- Trophic action : Stimulates mucosal growth.
- Stimuli that increase gastrin secretion : Distension, peptides.
- Stimuli that decrease gastrin secretion : Acid, somatostatin.
- Acts via CCK B receptor.

Cholecystokinin - Pancreozymin :

- Contraction of gall bladder (Cholagogue)
- Relaxation of sphincter of Oddi
- ↑ action of secretin.
- ↓ gastric emptying.
- Stimulates intestinal & colonic motility.
- Release of bile.
- Stimuli : Peptides & fatty acids.
- Acts via CCK A receptor.

Secretin :

- Pancreatic juice rich in HCO_3^- .
- ↑ action of cholecystokinin.
- ↓ gastric acid.
- Contraction of pyloric sphincter : ↓ gastric emptying.
- Stimulus : Acid chyme.

----- Active space -----

Ghrelin :

- Hunger hormone.
- Secreted by :
Stomach → Oxyntic gland.
- Action :
 - Orexigenic → ↑ food intake.
 - ↑ Gastric motility, gastric acid, adipogenesis, growth hormone.
- Ghrelin levels :
 - Peak : Fasting.
 - Low : Obese individuals.
 - High : Anorexia nervosa.

motilin :

- Time keeper hormone.
- Regulates migratory motor complex.

Gastric Inhibitory Polypeptide (GIP) :

↑ insulin levels.

Vasoactive Intestinal Peptide (VIP) :

↑ fluid & electrolyte secretion.

Peptide YY : ↓ ileal motility.

Digestion & Absorption

00:29:48

Carbohydrates, Lipids & Proteins :

Digestion : Enzymes.

	Carbohydrate	Lipid	Protein
Saliva	Salivary amylase	Lingual lipase	No enzyme
Stomach	No enzymes	Gastric lipase	Pepsin
Pancreas	Pancreatic amylase	<ul style="list-style-type: none"> • Pancreatic lipase • Co lipase • Cholesterol esterase Triglycerides ↓ Free fatty acids	Trypsin, chymotrypsin, carboxypeptidase
Small Intestine	Disaccharides : <ul style="list-style-type: none"> • Lactase • Isomaltase • Sucrase 	No enzymes	<ul style="list-style-type: none"> • No enzyme • Dipeptides, tripeptides ↓ Amino acids

Absorption :

	Carbohydrate	Lipid	Protein
Site	Duodenum & Jejunum		
Features	<ul style="list-style-type: none"> • Transport : <ul style="list-style-type: none"> - Glucose : SGLT 1. - Fructose : GLUT 5. • Insulin doesn't regulate intestinal absorption of glucose. 	Fatty acid emulsified by bile salts ↓ via micelles (Transport) Reach brush border cells of intestine ↓ via simple diffusion Absorbed into enterocyte (mucosal cell).	Enterocytes absorb amino acids

Note :

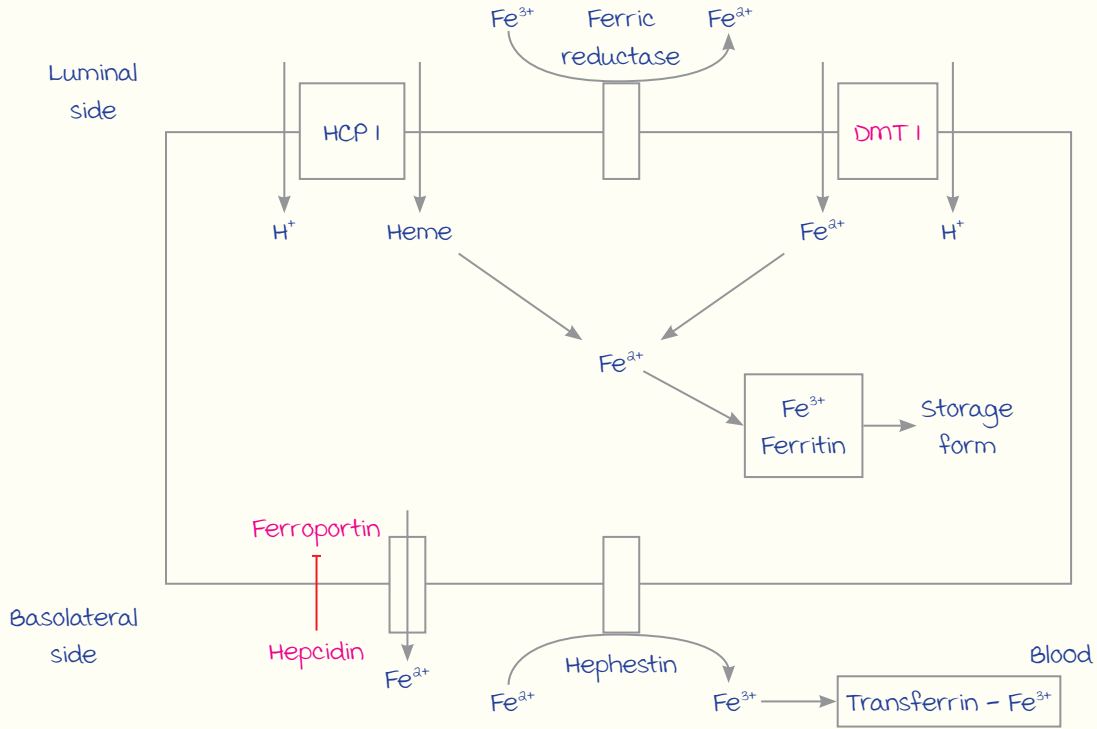
SGLT-1 :

- Basis for Na⁺ absorption along with glucose in ORS.
- mutation → Congenital Glucose Galactose malabsorption (CGGM).

Iron :

Absorption :

----- Active space -----



Regulation of hepcidin :

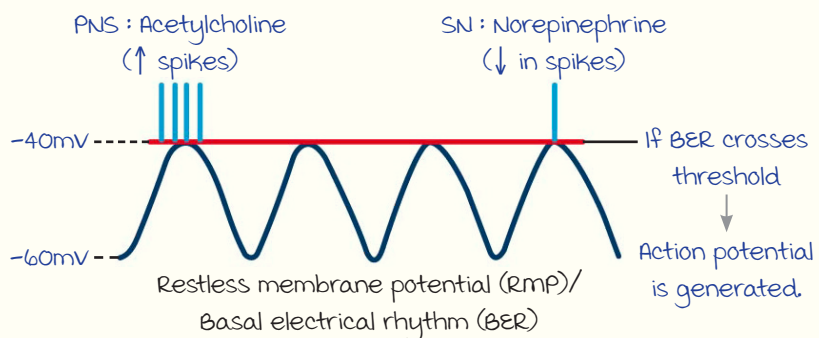
- Source : Liver.
- Levels regulated by **HFE gene**.
 - HFE mutation → Hemochromatosis.
- Function :
 - Negative regulator of iron absorption : Binds to ferroportin & inhibits it.
 - Links body iron stores with iron absorption.
 - Inhibits Fe release from macrophage and other cells by binding to ferroportin.

GI Motility

00:39:29

BER :

Pacemaker : **Interstitial cells of Cajal** → Has RMP.



Frequency of BER (Oscillations/min) :

- Duodenum : 12/min.
- Ileum : 8/min.
- Stomach : 4/min.
- Caecum : 2/min.

----- Active space -----

Motility Patterns :**Deglutition :**

• Phases :

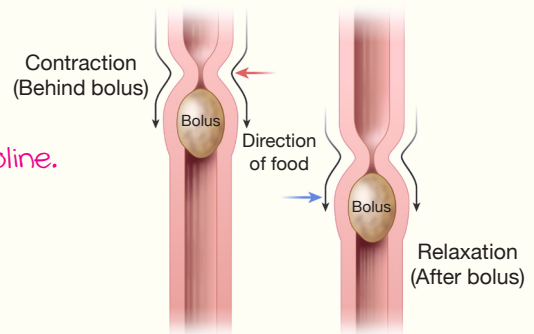
- Oral : Voluntary.
- Pharyngeal } Involuntary.
- Esophageal }

• Deglutition reflex :

- Afferent : Cranial nerves 5, 9, 10.
- Center : **Nucleus tractus solitarius.**
- Efferent : Cranial nerves 5, 7, 12.

Esophageal motility :

- Stretch induced peristalsis.
- Segments :
 - Contracting : **Substance P & acetylcholine.**
 - Relaxing : **Nitric oxide & VIP.**

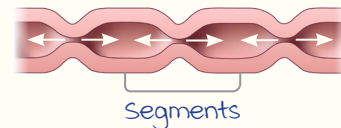
**Gastric motility :**

- Receptive relaxation.
- Retropulsion.
- Gastric emptying
 - Fastest : **Carbohydrates.**
 - Slowest : **Fats.**

↑ gastric emptying	↓ gastric emptying
<ul style="list-style-type: none"> • Gastrin • ↑ gastric volume 	<ul style="list-style-type: none"> • Cholecystokinin & Peptide YY. • Duodenum <ul style="list-style-type: none"> → Fats, carbohydrates & acids → Hyperosmolarity of contents
	} Enterogastric reflex

Small intestinal motility :

- Peristalsis.
- Segmentation :
 - Both ends contract $\xrightarrow{\text{slows food movement}}$ Adequate digestion & absorption.

**Large intestinal motility :**

- Proximal : Haustrations → Combined contraction of circular & longitudinal muscles.
- Distal : mass movements.
 - movement from one segment to another → Rectal distension → Defecation.

migratory motor complex (MMC) :

- Seen during **fasting.**
- migrates from stomach to colon.
- 1 MMC once **every 90 minutes** : Regulated by **motilin.**
- Erythromycin :
 - Rx of **gastroparesis** (m/c : Diabetics).
 - Action : ↑ MMC via motilin (no receptor).

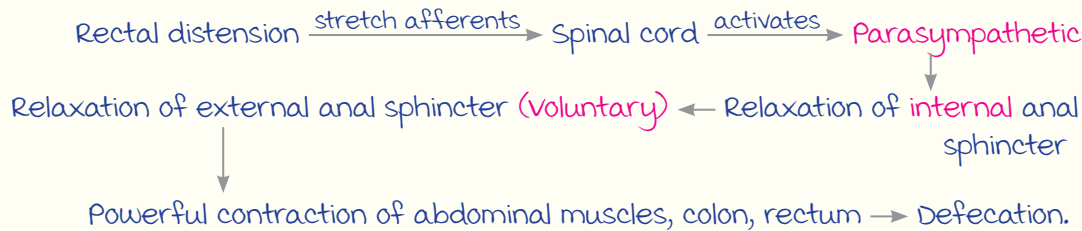
Defecation & Vomiting

00:51:02

----- Active space -----

Defecation Reflex :

Process :



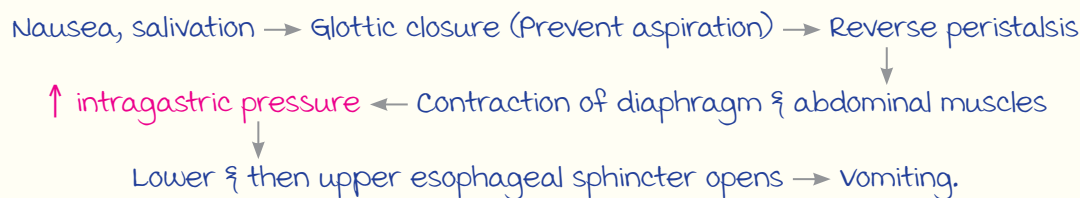
First urge to defecate : Rectal pressure of 18 mmHg.

maximum rectal pressure : 55 mmHg \rightarrow Beyond which involuntary defecation occurs.

Vomiting :

Factors : Neural, humoral, muscular.

Sequence of events :



Dietary Fibers/Roughage :

Examples : Lignin, pectin, cellulose.

Source : Rich in cereals, fruits, vegetables.

Functions :

- Adds bulk in diet.
- ↓ glucose absorption.
- ↓ LDL cholesterol levels.
- makes stools bulky (By holding water).
- Converted to short chain fatty acids by microflora.

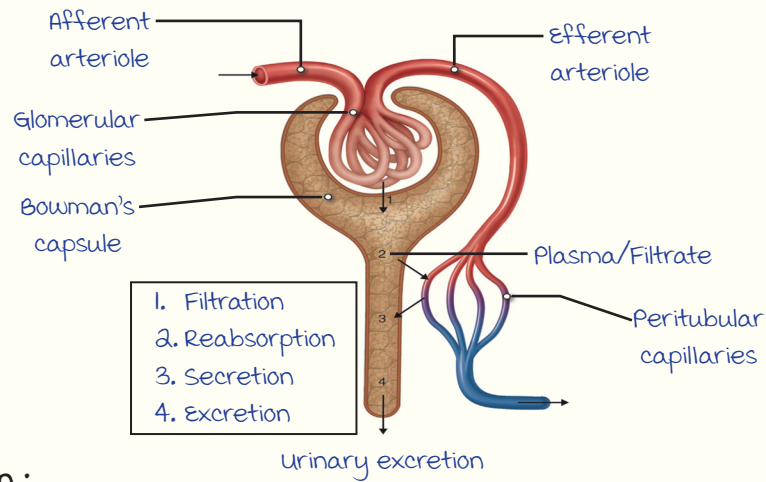
RENAL PHYSIOLOGY

----- Active space -----

Glomerular Filtration & Renal Blood Flow

00:00:20

Nephron : Functional unit of kidney.



Ultrafiltration :

Plasma.

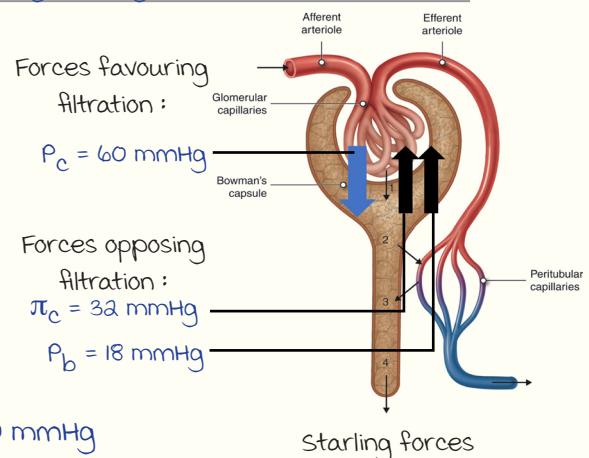
Exception : Proteins, because :

- **Heparan sulfate** : Negatively charged proteins that line glomerular capillaries.
- Fenestrations : Small gap between cells (4-8 nm).
- **Slit diaphragm** :
 - Formed by foot process of podocytes.
 - Integrity maintained by nephrin, podocin, α -actinin.

Protein	mutation (Leads to protein excretion)
1. Nephrin	Congenital Finnish type nephrotic syndrome (NPHS-1 gene)
2. Podocin	Steroid resistant nephrotic syndrome (NPHS-2 gene)
3. α -actinin	Autosomal dominant Focal segmental glomerulosclerosis (FSGS).

Filtration Forces :

- Hydrostatic pressure in glomerular capillaries (P_c).
- Oncotic pressure in glomerular capillary (π_c).
- Hydrostatic pressure in bowman's capsule (P_b).



$$\text{Net filtration pressure} : P_c - (\pi_c + P_b) = 10 \text{ mmHg}$$

Clearance :

$$C_s = \frac{U_s \times V}{P_s}$$

C_s : Clearance rate of a substance.

U_s : Urine concentration.

P_s : Plasma concentration.

V : Urine flow rate.

----- Active space -----

GFR Estimation Markers :

- Inulin : Gold standard.
- Creatinine : m/c.
- Cystatin C : New marker.

Renal Circulation :

Renal blood flow (RBF) : 1250 mL/min (23% of cardiac output).

Renal plasma flow (RPF) : 55% of RBF = 625 mL/min.

Ⓝ Glomerular filtration rate : 125 mL/min.

Filtration fraction :

- $GFR/RPF = 125/625 = 20\%$
- Substances used to measure :
 - GFR : Inulin.
 - RPF : Para-aminohippuric acid.

Regulation of GFR & RBF

00:09:58

Factors :

Factor	RBF	GFR
Constriction of :		
Afferent arteriole (Example : Nor epinephrine)	↓	↓
Efferent arteriole (Example : Angiotensin-II)	↓	Biphasic response : Initially GFR ↑, Later ↓
Dilatation of :		
Afferent arteriole (By Prostaglandins)	↑	↑
Efferent arteriole (Example : ACE inhibitors)	↑	↓

Auto Regulation :

Pressure within 80-180 mmHg → RBF & GFR constant.

Mechanisms :

- myogenic mechanism : ↑ RBF → Stretches vessel wall → Opens Ca^{2+} channels → ↓ RBF ← vasoconstriction

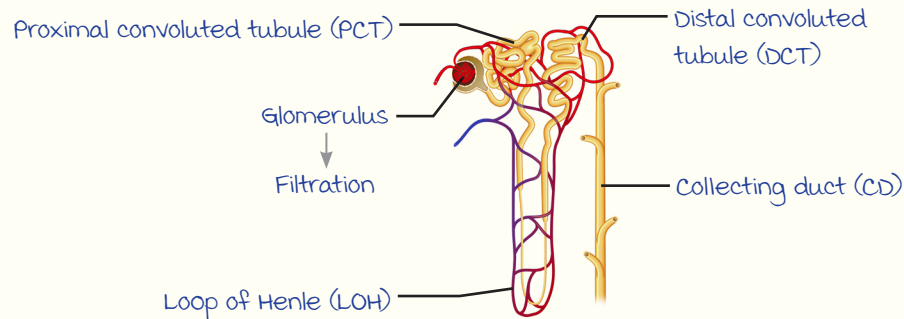
----- Active space -----

- Tubuloglomerular feedback (TGF) :
 $\uparrow \text{GFR} \rightarrow \uparrow \text{Tubular NaCl concentration} \rightarrow \text{Activates macula densa} \xrightarrow{\text{Adenosine constricts Afferent arteriole}} \downarrow \text{GFR.}$
- mesangial cells :
 - $\text{Endothelin, norepinephrine} \rightarrow \text{Contraction} \xrightarrow{\text{Glomerular capillary compression}} \downarrow \text{GFR.}$
 - $\text{Nitric oxide, ANP} \rightarrow \text{Relaxation} \xrightarrow{\text{Glomerular capillary compression}} \uparrow \text{GFR.}$

ANP : Atrial Natriuretic Peptide.

Nephron

00:19:04



Proximal Convoluted Tubules

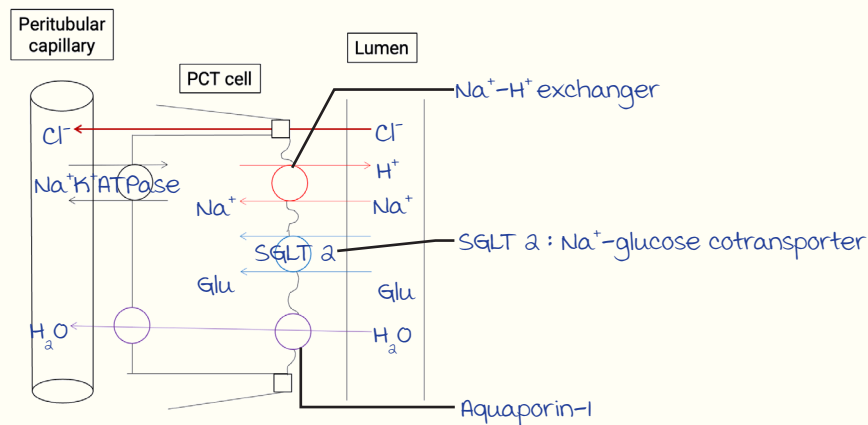
00:19:15

Site of **maximum reabsorption**.

Features : \uparrow mitochondria (ATP) & highly infolded plasma membrane (\uparrow surface area).

PCT Reabsorption :

- 70% of filtered NaCl, water, K^+ , urea, Ca^{2+} .
- 80% of filtered phosphate & bicarbonate.
- 100% of filtered glucose & amino acids.



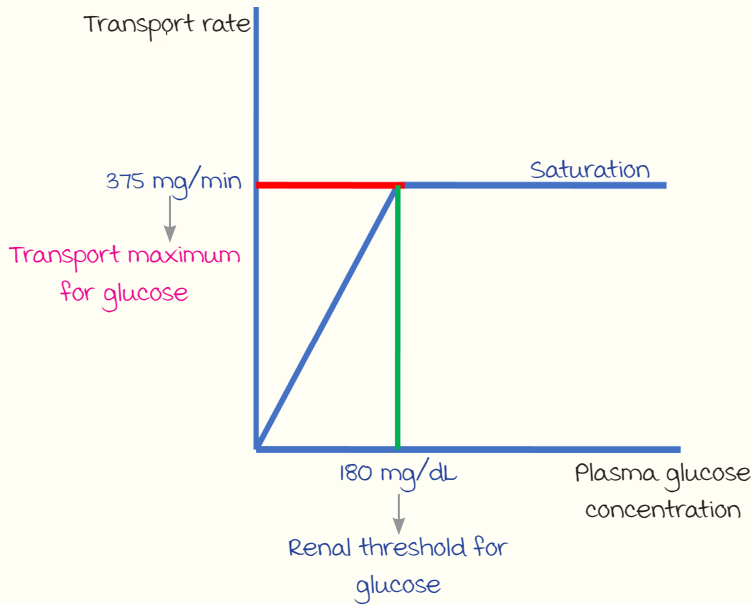
Obligatory water reabsorption : Independent of ADH.

Note : In collecting duct → Facultative water reabsorption (Influence of ADH ⊕).

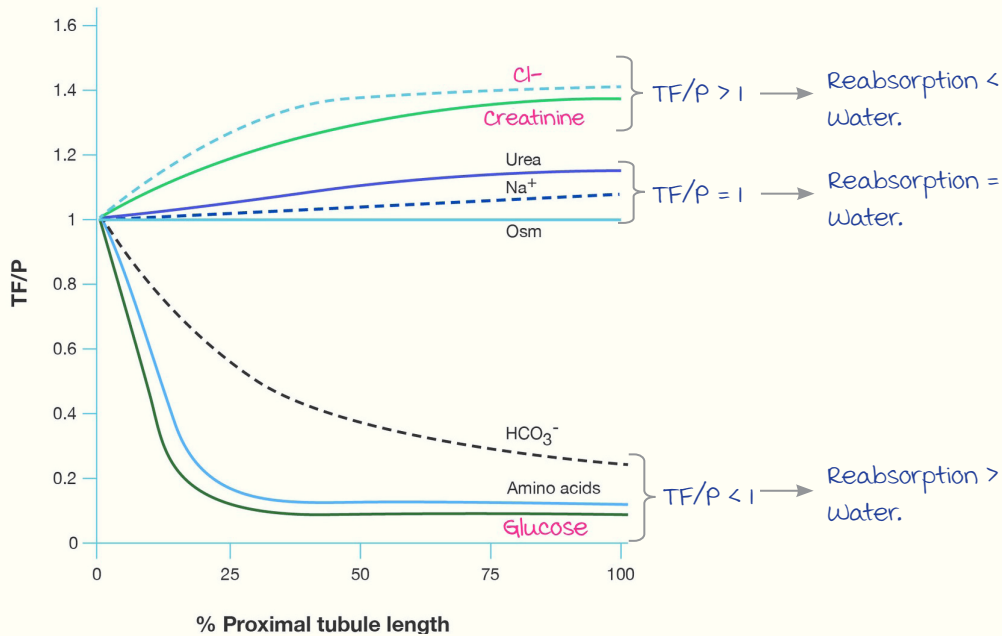
----- Active space -----

Glucose reabsorption :

- Through SGLT-2 : Secondary active transport.
- If plasma glucose > 180 mg/dL → Renal glycosuria.



Tubular fluid plasma ratio :

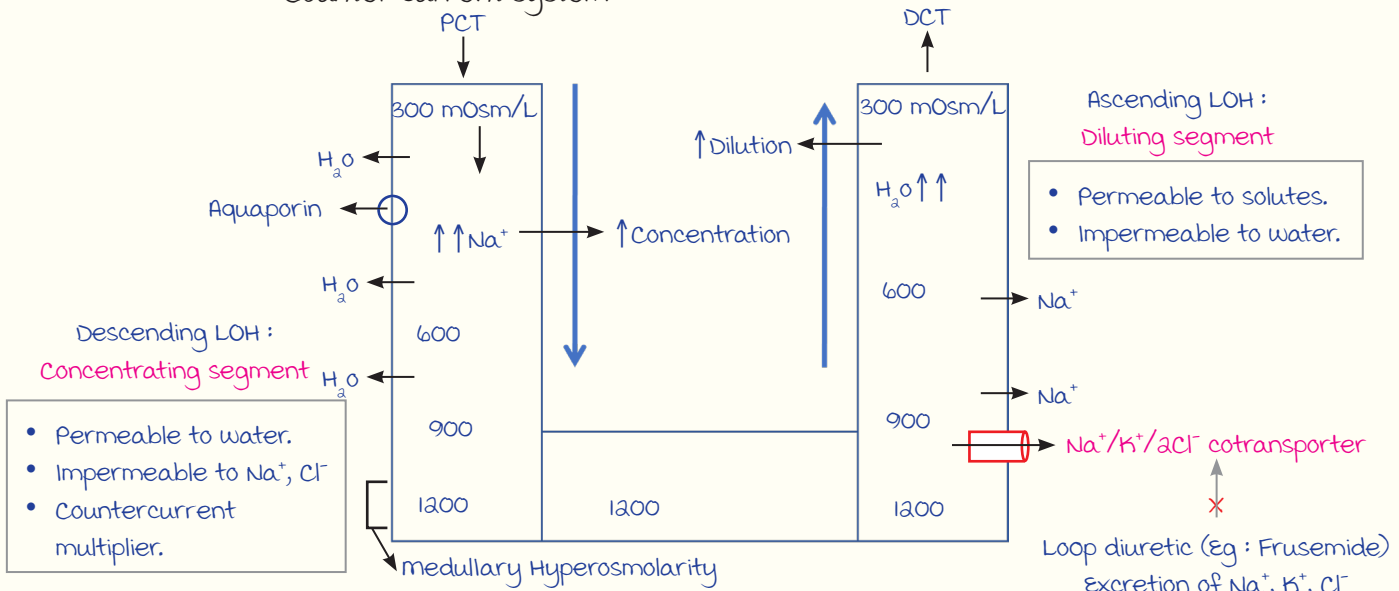


----- Active space -----

Loop Of Henle (LOH)

00:28:48

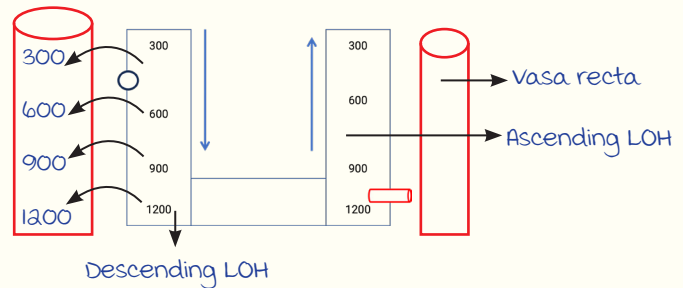
Counter current system :



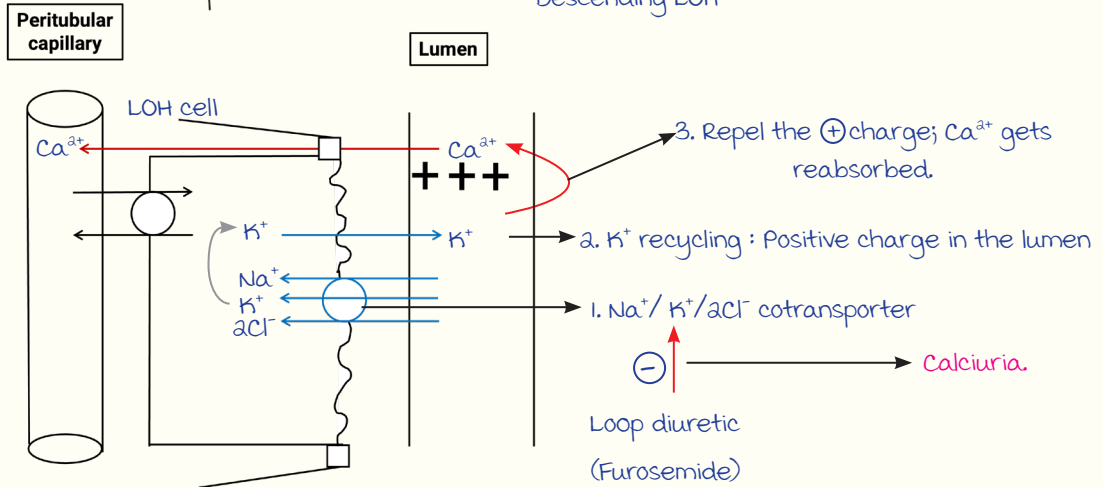
Note : Counter current system is also seen in kidney, limbs, testis, intestine.

Vasa recta :

- AKA Counter current exchanger.
- Blood vessels along LOH with similar osmolarities.
- maintain medullary hyperosmolarity.



Calcium reabsorption :



Distal Convoluted Tubule (DCT)

00:35:53

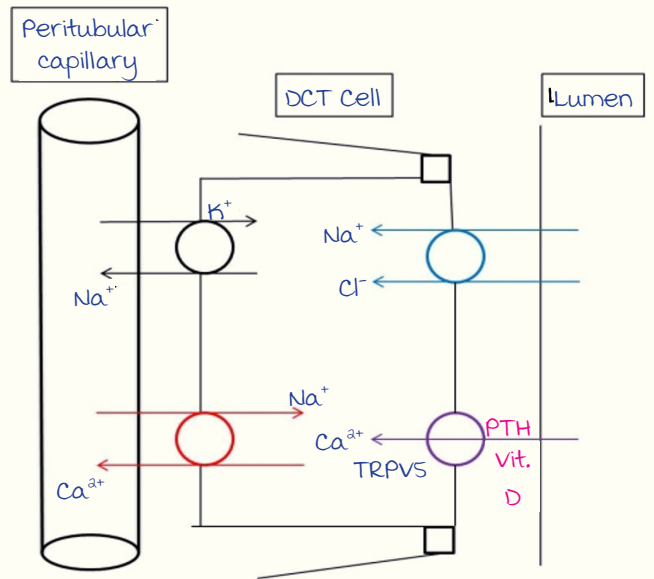
Sodium re-absorption :

$\text{Na}^+ / \text{Cl}^-$ cotransporter mutation $\xrightarrow{\text{mutation}}$ Gitelman's Syndrome.

\ominus

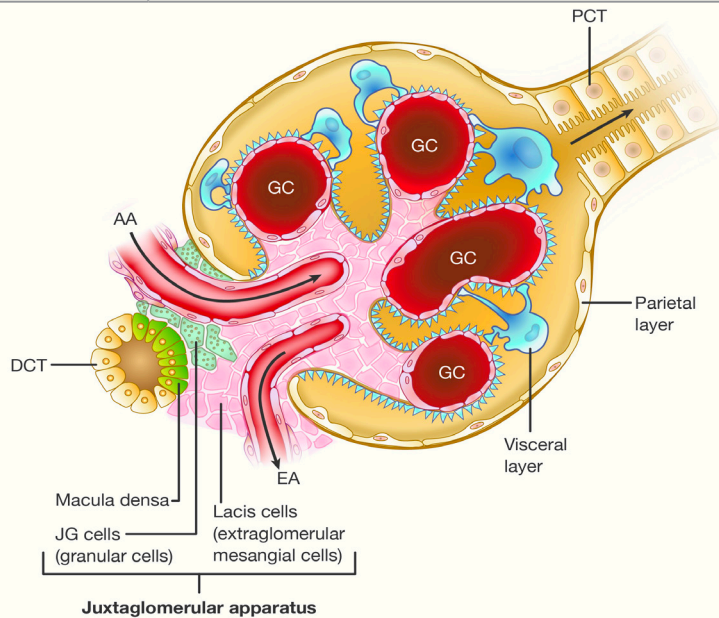
Thiazide diuretics

Calcium re-absorption :
 Ca^{2+} re-absorbed by
 TRPV5 channel.
 (Regulated by PTH & vitamin D)



Juxtaglomerular Apparatus :

Cells	Function
1. Juxta glomerular cells (In afferent arteriole)	AKA Granular cells : Produce renin.
2. macula densa (In thick LOH)	GFR sensors sense \uparrow in GFR \rightarrow Release adenosine Constrict AA & \downarrow GFR. (Tubuloglomerular feedback)
3. Extra glomerular mesangial cells	Supportive cells AKA Lacis cells.



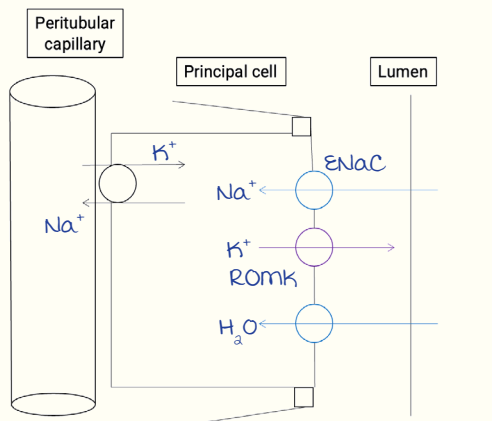
Collecting Duct

00:40:40

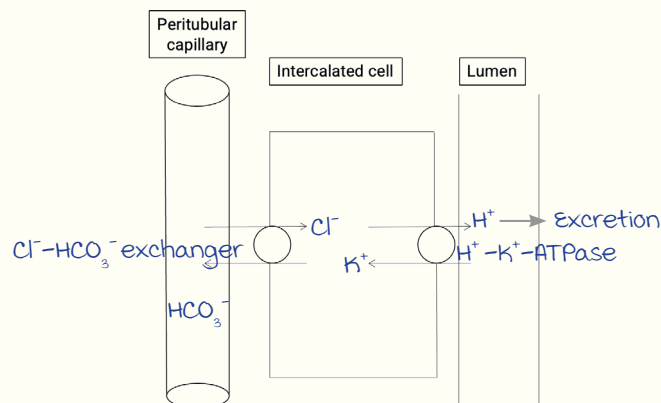
- Two parts : Cortical & medullary collecting duct.
- Two cells : Principal cells & Intercalated cells.
- Two hormones : Aldosterone & anti-diuretic hormone (vasopressin).

----- Active space ----- **Action of Aldosterone :**

In principal cells :



In intercalated cells :



ENaC : Epithelial Na⁺ channels.

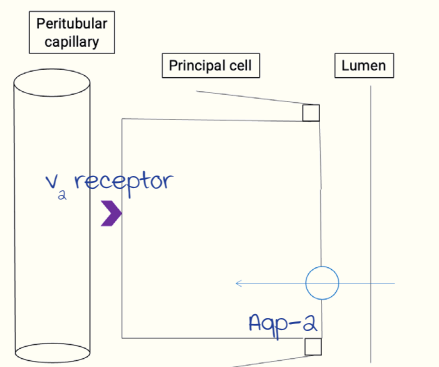
ROMK : Renal outer medullary channels.

Actions of Anti-Diuretic Hormone :

- Facultative water reabsorption.
- **Aquaporin-2** : Facilitated diffusion.

Vasopressin receptors :

- V₁ receptor : vasoconstriction.
- V_a receptor :
 - Water reabsorption using aquaporin-2.
 - V_a blocker : **Conivaptan** (Rx : SIADH).
- V₃ receptor : Releases ACTH from anterior pituitary.



Free water clearance :

Free water clearance	Concentration of urine	Level of ADH	Seen in
Negative	High	High	Syndrome of inappropriate ADH secretion (SIADH)
Positive	Low	Low/Absent	Diabetes Insipidus

Free water clearance = 0 → Renal ability to concentrate & dilute urine lost.

Natriuretic Peptides:

Types :

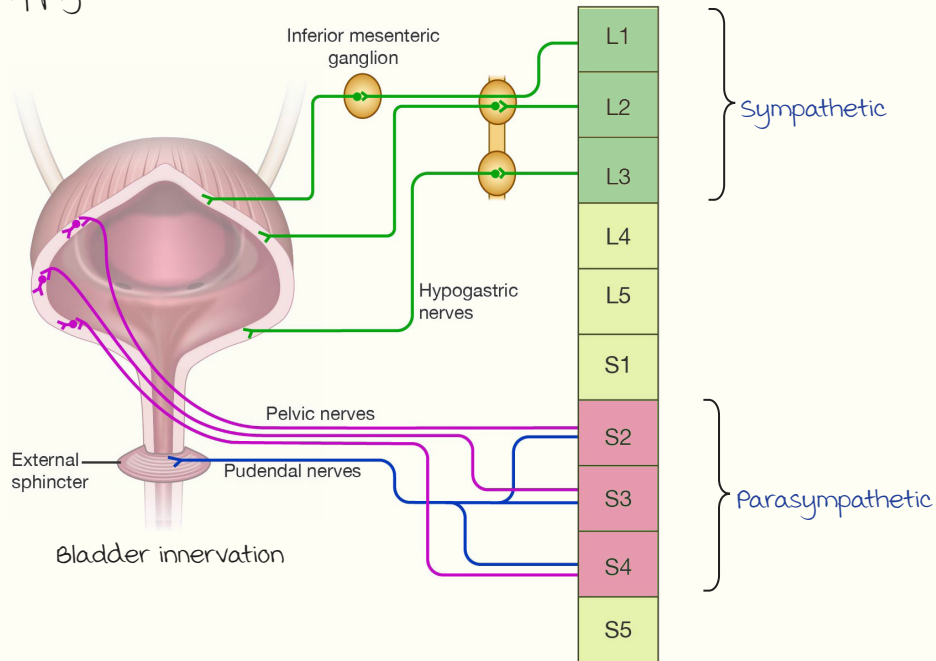
- Type A : ANP
 - Type B : BNP
 - Type C : CNP
- cGMP → Act in late DCT & CD → Natriuresis (Na⁺ excretion).

Micturition

00:47:42

----- Active space -----

Nerve supply :



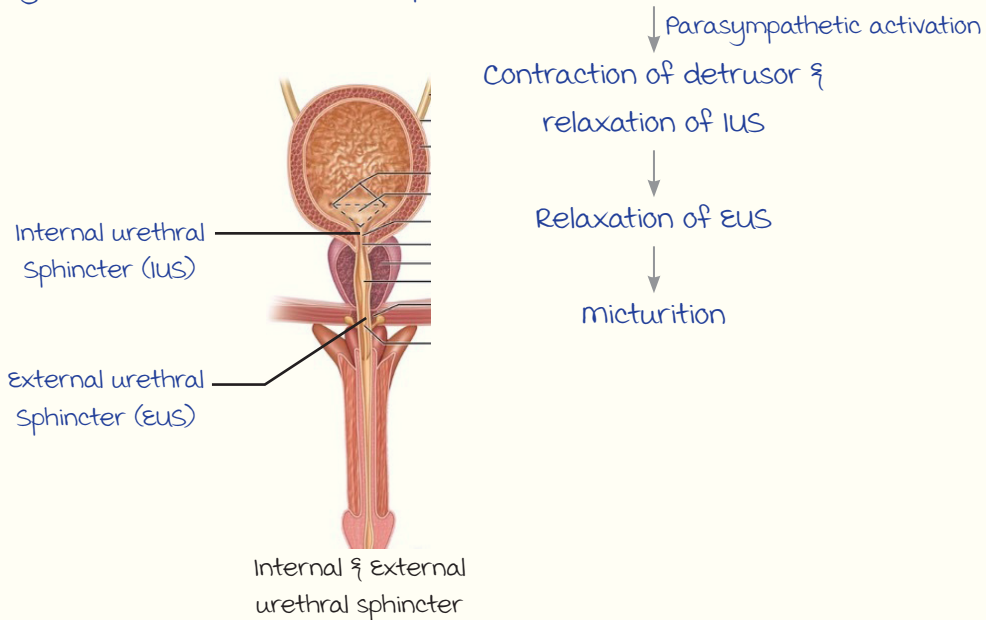
Somatic supply : Pudendal nerves (Voluntary contracts)

Higher centres :

- Facilitatory Centre : Pons → Barrington centre.
- Inhibitory Centre : midbrain.
- Highest Centre : Paracentral lobule (Cortex).

micturition reflex :

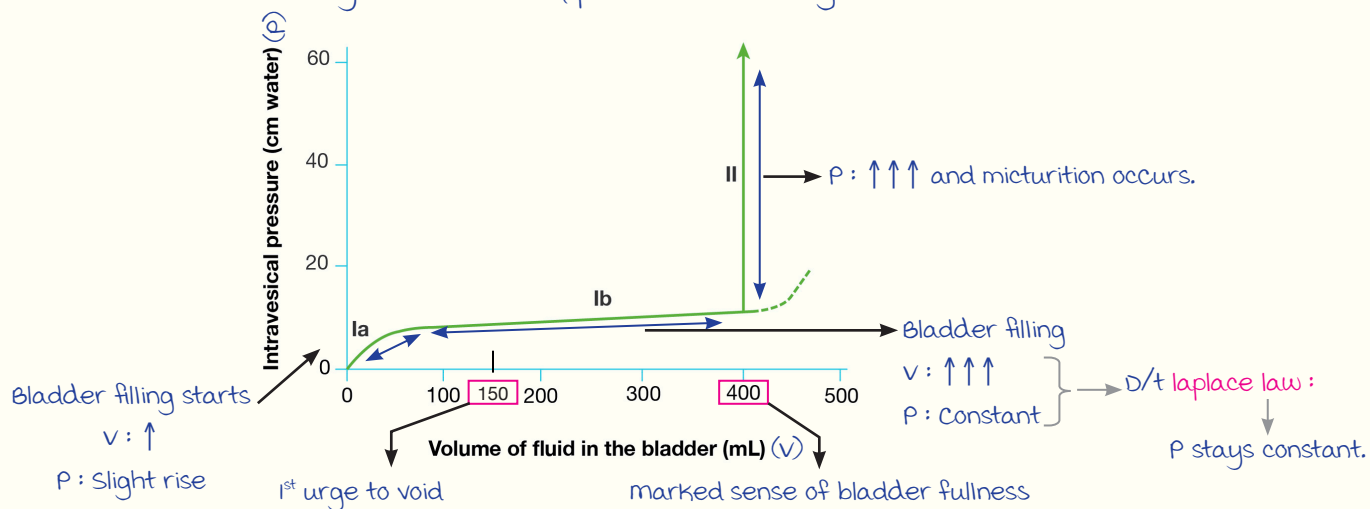
Bladder filling (Stretch) → Afferent to spinal cord (Pelvic nerve)



----- Active space -----

Cystometrogram :

Study of volume (V) & pressure (P) changes in the bladder.



Acid Base Balance

00:52:10

- Normal pH : 7.35 to 7.45 (<6.9/>7.8 → Fatal).
- Deranged pH :
 - Denaturation of proteins.
 - CNS :
 - Acidosis → ↓ Excitability.
 - Alkalosis → ↑ CNS excitability (muscle twitches).

Acid base balance equation :

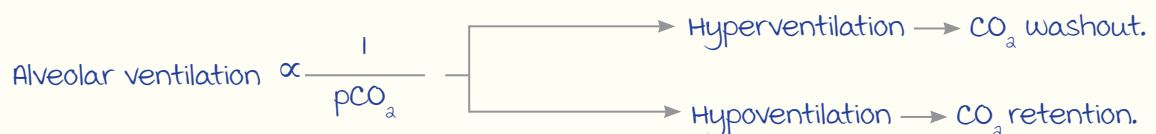


First line defense:

Buffer system :

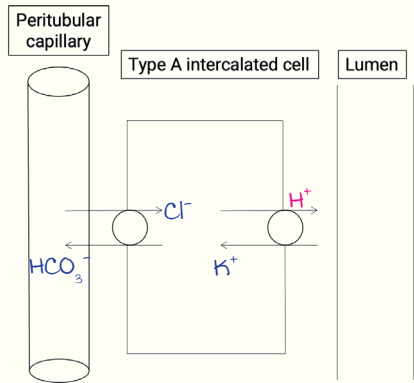
- HCO_3^- : most important extracellular buffer.
- Phosphate : Important intracellular buffer in tubular kidney.
- Protein : most plentiful intracellular buffer.

Second line defense : Lungs (75% correction)



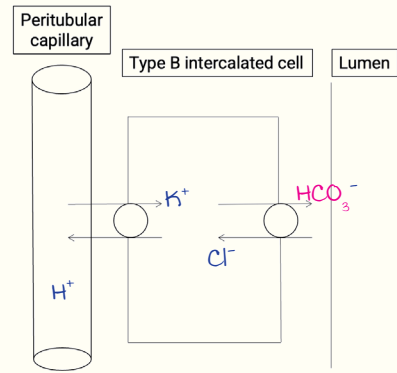
Third line defense : Kidneys (100% correction)

- Excretion of H^+ & HCO_3^-
- Reabsorption of HCO_3^-
- Generation of new HCO_3^- : uses phosphate & ammonia buffer in place of bicarbonate to neutralize acid.



Type A intercalated cell : Acidosis

- Acid excreting
- Acts during acidosis



Type B intercalated cell : Alkalosis

- Base excreting
- Acts during alkalosis

----- Active space -----

Acid Base Disorders :

Normal pCO_2 : 35-45 mmHg.

Normal HCO_3^- : 22-26 mEq/L.

	Causes	
metabolic acidosis (\downarrow pH)	$\uparrow H^+$: <ul style="list-style-type: none"> • Lactic acidosis • Diabetic ketoacidosis • Salicylic acid poisoning 	$\downarrow HCO_3^-$: Diarrhea
metabolic alkalosis (\uparrow pH)	$\downarrow H^+$: <ul style="list-style-type: none"> • Vomiting • Hyperaldosteronism ($\uparrow H^+$ excretion) • Diuretics $\xrightarrow{+ RAAS}$ \uparrow Aldosterone volume contraction alkalosis	$\uparrow HCO_3^-$: Sodium bicarbonate ingestion
Respiratory acidosis ($\uparrow pCO_2$)	<ul style="list-style-type: none"> • Respiratory depression : Opioids • Respiratory muscle paralysis : Polio, Guillain-Barré Syndrome • Airway obstruction : COPD 	
Respiratory alkalosis ($\downarrow pCO_2$)	<ul style="list-style-type: none"> • Hyperventilation • Hypoxia (Eg : High altitude) 	

Note : Respiratory alkalosis \rightarrow Hypocalcemic tetany. (\uparrow Excitability)

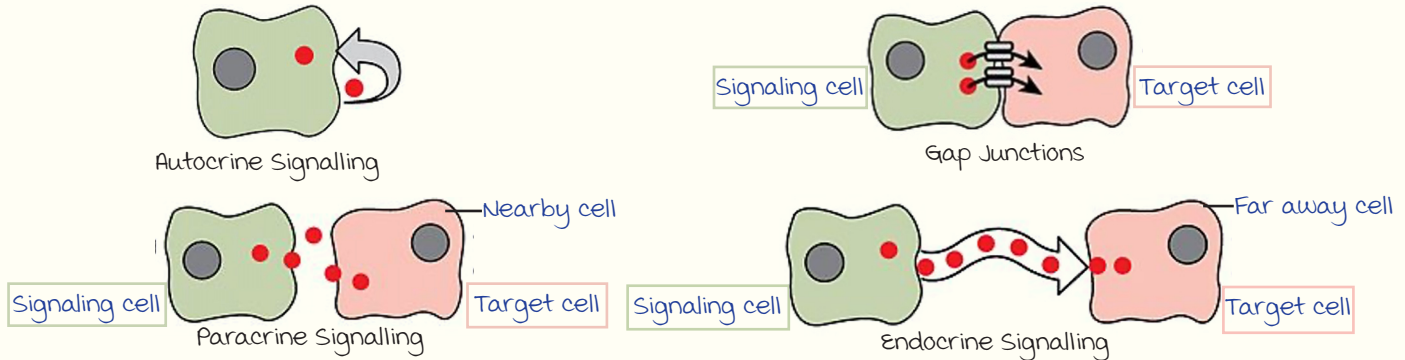
Anion Gap (AG) :

- D/t unmeasured anions (Protein, sulfate, phosphate).
- $AG = Na^+ - (HCO_3^- + Cl^-) = (140 \text{ mEq/L}) - (25 \text{ mEq/L} + 105 \text{ mEq/L}) = 10 \text{ mEq/L}$.

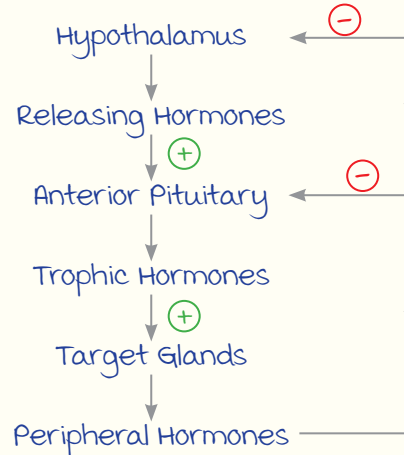
----- Active space -----

ENDOCRINE PHYSIOLOGY

Forms of cell signalling :



Typical negative feedback control of endocrine hormone release :



Hypothalamic & Pituitary Hormones

00:02:54

Pituitary :

Anterior pituitary hormones :

	Cell Type	Hormone
Acidophilic Cells	Somatotrope	Growth Hormone
	Lactotrope	Prolactin
Basophilic Cells	Gonadotrope	FSH, LH
	Thyrotrope	TSH
	Corticotrope	ACTH

Posterior Pituitary Hormones :

Stores & releases oxytocin & vasopressin.

Note :

- Twin hormones : Growth Hormone & Prolactin.
- Common precursor : Proopiomelanocortin (POMC)
 - Endorphin
 - MSH
 - ACTH
- Addison's : \uparrow ACTH (mimics MSH) \rightarrow Hyperpigmentation.

Hypothalamic :

----- Active space -----

Stimulatory hormones with effect on anterior pituitary :

Hypothalamic Hormones	Anterior pituitary hormones
Thyrotropin Releasing hormone (TRH)	Thyroid Stimulating Hormone (TSH)
Corticotropin Releasing hormone (CRH)	Adreno corticotrophin releasing hormone (ACTH)
Gonadotropin Releasing hormone (GnRH)	Follicle stimulating hormone (FSH), Luteinizing Hormone (LH)
Growth Hormone Releasing hormone (GHRH)	Growth Hormone (GH)

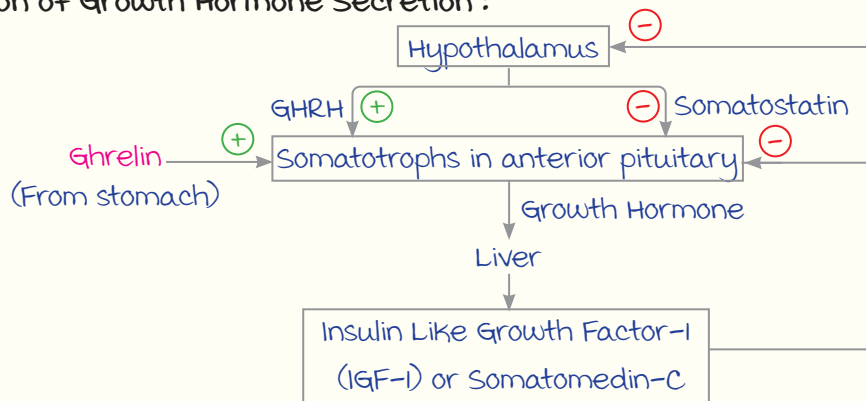
Inhibiting Hormones :

- Prolactin release inhibiting hormone/Dopamine → ⊖ Prolactin.
- Growth hormone inhibiting hormone/Somatostatin → ⊖ GH.

Growth Hormone

00:07:30

Regulation of Growth Hormone Secretion :



Note : Drug forms
 → GHRH : Sermorelin.
 → Somatostatin : Octreotide.

Factors affecting Growth Hormone :

Factors that increase growth hormone secretion	Factors that inhibit growth hormone secretion
<ul style="list-style-type: none"> • Hypoglycemia <ul style="list-style-type: none"> - Exercise - Fasting - Stress - Starvation • Deep sleep (NREM stage 3 & 4) 	<ul style="list-style-type: none"> • Somatostatin • Increase in blood glucose levels (Eg : Glucose infusion) • REM sleep

Actions of Growth Hormone :

Direct actions (Anti-insulin like) :

- Decreased insulin sensitivity.
- Protein synthesis.
- Sodium retention.
- Lipolysis.

----- Active space -----

Indirect actions : mediated by IGF-1 (Insulin like activity).

- Anti lipolytic.
- Protein synthesis.
- Epiphyseal growth.

Growth Hormone Disorders :

Dwarfism : ↓ GH.

Gigantism : ↑ GH.

Acromegaly : ↑ GH.

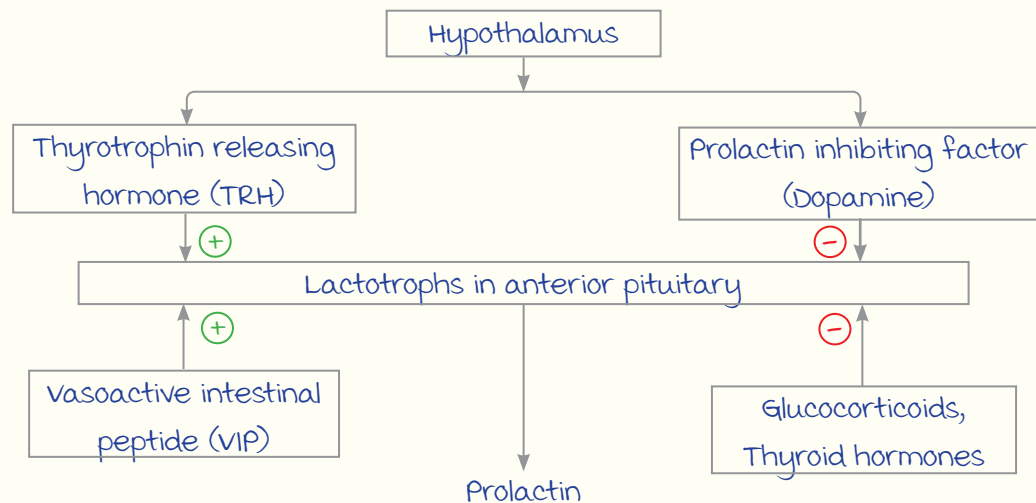
Laron Dwarfism :

- Resistance to growth hormone action.
- Normal/↑ GH + low levels of IGF-1.

Prolactin

00:13:28

Regulation of prolactin secretion :



Factors affecting prolactin secretion :

Factors increasing prolactin secretion	Factors inhibiting prolactin secretion
<ul style="list-style-type: none"> • marked increase during pregnancy and lactation • Sexual intercourse • Dopamine blockers • Exercise 	<ul style="list-style-type: none"> • Somatostatin • Dopamine agonists (Like Bromocriptine)

Note : Prolactin → GnRH inhibitor.

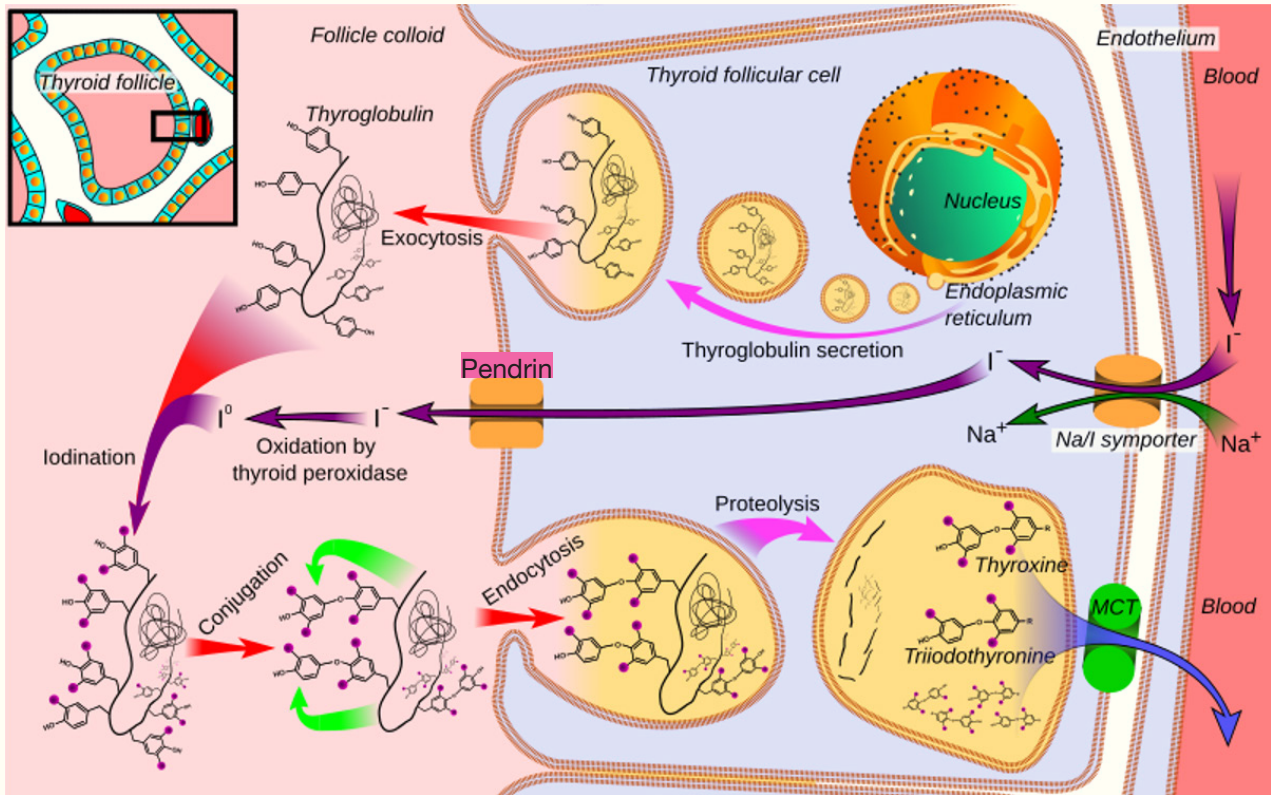
Thyroid Hormone

00:15:58

----- Active space -----

Thyroid Hormone Synthesis :

Thyroid hormones stored for 2 - 3 months in colloid.



Sodium Iodide Symporter (NIS) :

- Secondary active transport.
- Extrathyroidal locations : Salivary glands, lactating breast, placenta.

Note : **Wolff-Chaikoff effect** \rightarrow \uparrow Iodide \rightarrow \downarrow Thyroid iodide organification

\downarrow
 $\downarrow T_3, T_4$

Iodide Chloride Antiport/Pendrin :

- Locations : Thyroid gland & Inner ear.
- mutation : **Pendred syndrome** $\xrightarrow{\text{manifestations}}$
 - \rightarrow Goitre.
 - \rightarrow Sensory neural hearing loss.

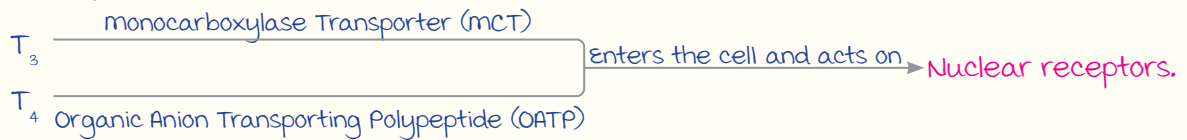
Thyroid hormone binding proteins :

- Albumin.
- **Thyroid Binding Globulin** : Highest affinity to thyroid hormone.
- Prealbumin/Transthyretin : Binds to thyroid hormone & vit A.

----- Active space -----

Triiodothyronine (T₃) vs. Thyroxine (T₄):

	T ₃ (Physiological form)	T ₄ (Pharmacological/drug form)
Potency	most	Least
Half Life	1 day	7 days
Plasma protein binding	Less	more
Action	Rapid	Long lasting
In colloid	Less (7%)	more (35%)

Thyroid Hormone Receptors :**effects of thyroid hormones :**

Target tissue	effect	mechanism
Throughout the body	Calorigenic	<ul style="list-style-type: none"> Stimulates metabolism → ↑ O₂ consumption. ↑ in basal metabolic rate.
Heart	Chronotropic and inotropic (Indirect effect)	Increased number of β-adrenergic receptor. (Norepinephrine mediated)
Adipose tissue	Catabolic	Stimulates lipolysis.
muscle	Catabolic	↑ Proteolysis.
Bone	Developmental	Promote normal growth and skeletal development.
CNS	Developmental	↑ myelination → ↑ Nerve conduction velocity.
Cholesterol	Catabolic	↓ Cholesterol levels.

Endocrine Pancreas

00:28:30

Type of cells :

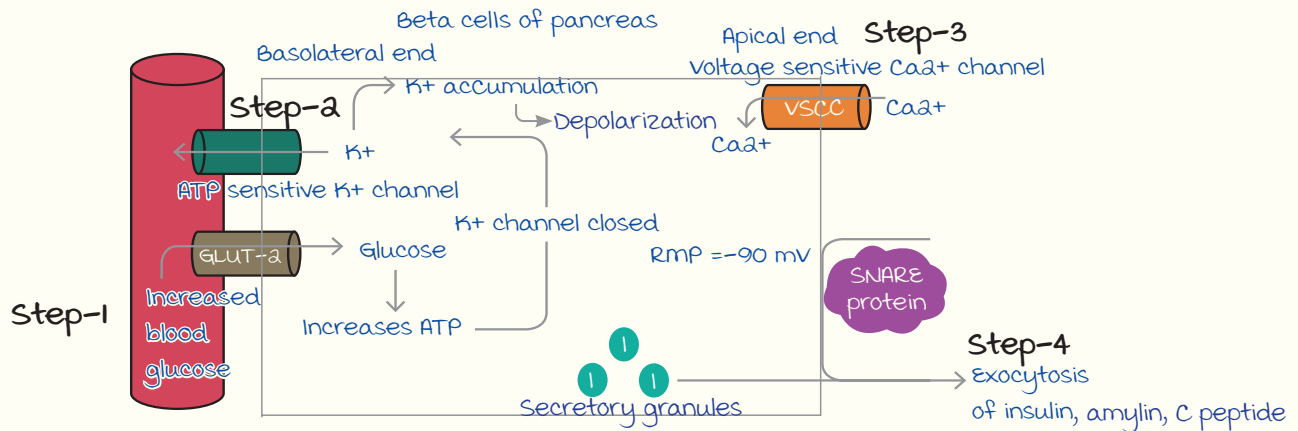
Cell type	Secretion
A cells (or) Alpha cells	Glucagon
B cells (or) Beta cells (60-75%), maximum lie in center of islets	Insulin, Amylin, C peptide
D cells (or) Delta cells	Somatostatin
F cells	Pancreatic polypeptide

Insulin :

major anabolic hormone.

Steps involved in release of insulin :

----- Active space -----



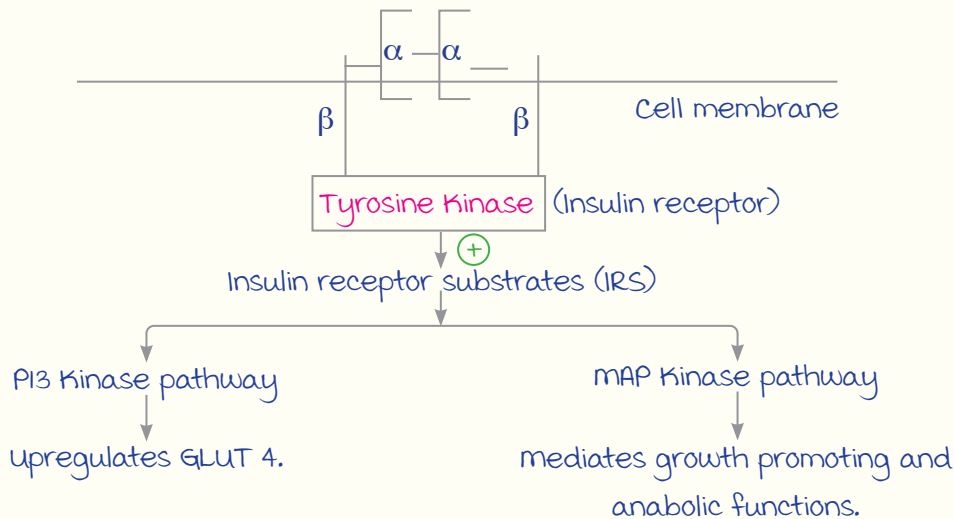
Sites of Insulin dependent glucose uptake :

- Heart
 - Skeletal muscle
 - Adipose tissue
- upregulates GLUT 4 → ↓ Serum glucose.

Note : Exercise (+) AMP activated kinase pathway → ↑ GLUT-4.

Independent of insulin (Hence benefits diabetics).

mechanism of action of insulin :



PI3K : Phosphatidylinositol-3'-Kinase.

MAPK : mitogen Activated Protein Kinase.

----- Active space ----- Factors affecting insulin secretion :

Factors ↑ insulin secretion	Factors ↓ insulin secretion
High blood glucose	Somatostatin
<ul style="list-style-type: none"> • Glucagon • Amino acids like arginine, leucine 	<ul style="list-style-type: none"> • Toxins : Streptozocin, Alloxan • Sympathetic : α adrenergic receptor mediated
ANS { Parasympathetic : Acetylcholine Sympathetic : β receptor mediated	
Gastrin, cholecystokinin, secretin	
Incretin hormones : <ul style="list-style-type: none"> • Glucagon-like peptide - 1 (GLP - 1) • Glucose-dependent insulinotropic peptide (GIP) • Incretin effect : _____ Oral glucose stimulates insulin much more than IV glucose.	

Action on metabolic pathways :

Pathways stimulated by Insulin	Pathways inhibited by Insulin
↑ Glycolysis	↓ Glycogenolysis
↑ Glycogenesis	↓ Gluconeogenesis
↑ Lipogenesis	↓ Lipolysis

Homeostasis of Insulin :

mediated by **hyperglycemic**/Counter-regulatory hormones :

- Cortisol.
- Growth hormone.
- Glucagon.
- Epinephrine.
- Thyroid hormones.

Adrenal Gland

00:40:00

Adrenal gland : Parts & secretions

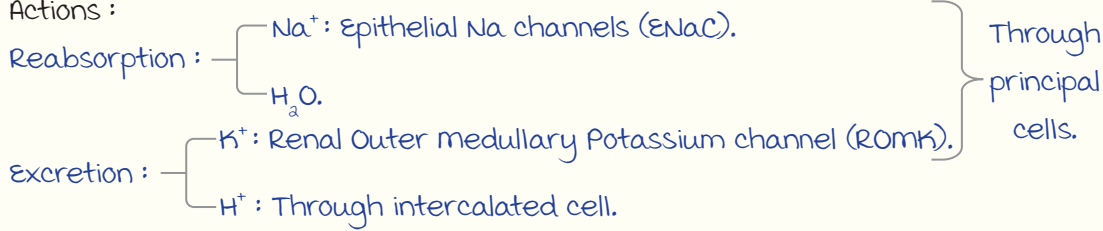
- Connective tissue capsule
- Zona glomerulosa : mineralocorticoids (15%)
 - Secrete **aldosterone**
 - Formation of **new cortical cells**
- Zona fasciculata : Glucocorticoids (50%)
 - Secrete **cortisol**
- Zona reticularis :
 - Secrete **sex steroids** (7%)
- Adrenal medulla :
 - Secrete catecholamines { 90% Epinephrine, 10% Norepinephrine

Aldosterone :

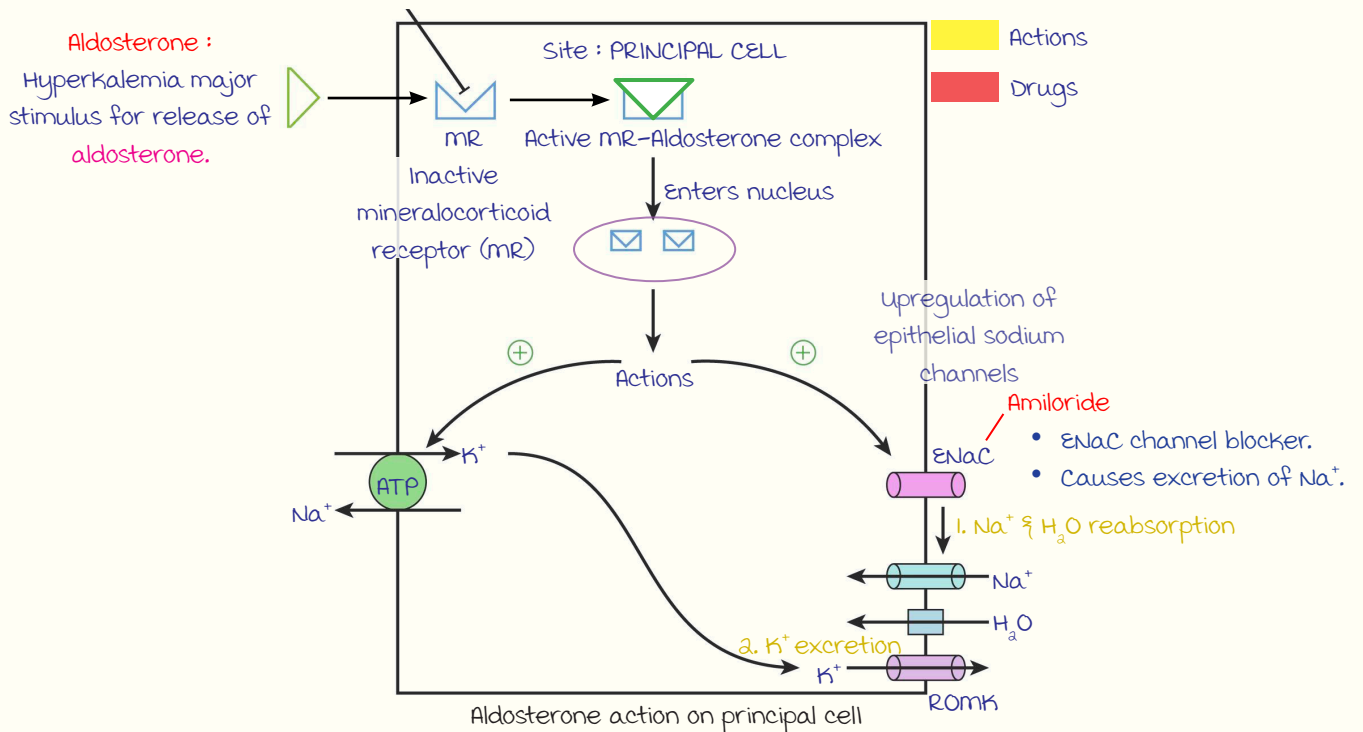
Steroid hormone.

----- Active space -----

Actions :



Mechanism :



Liddle's syndrome :

- Gain of function mutation of ENaC.
- Hypertension (key manifestation).

Aldosterone escape :

- \uparrow in ECF does not lead to edema.
 - Hyperaldosteronism $\rightarrow \uparrow \text{Na}^+$
 - ↳ Pressure diuresis
 - ↳ Natriuresis (via Atrial Natriuretic peptide)
- No edema.

----- Active space -----

Cortisol :

Effect on	mechanism
Carbohydrate metabolism	"Hyperglycemic hormone" → ↑ Gluconeogenesis
Protein metabolism	<ul style="list-style-type: none"> • Catabolic in muscle : Proteolysis • Anabolic in liver : ↑ Synthesis of plasma proteins from liver.
Fat metabolism	Lipolytic
Immune system	Anti-inflammatory agent
Blood cells	<ul style="list-style-type: none"> • Cortisol ↓ the blood levels of : Eosinophils, lymphocytes • Cortisol ↑ the blood levels of : Neutrophils, platelets, RBCs
Nervous system	<ul style="list-style-type: none"> • Alters mood and behaviour • ↑ Appetite
Kidney	↑ Glomerular filtration rate and calcium excretion.
Bone	↑ Bone resorption by ↑ activity of osteoclasts.
Connective tissues	Inhibits fibroblast proliferation and collagen formation. (Delay wound healing & purple striae on skin)
GIT	↑ Gastric acid → Peptic ulcers.
Reproduction	Inhibits GnRH → Amenorrhea, loss of libido, infertility.

Adrenal Sex Steroids :

- Found both in males & females.
- Include :
 - Dehydroepiandrosterone (DHEA) : major.
 - Dehydroepiandrosterone sulfate (DHEAS).
 - Androstenedione.
 - Testosterone (Only small amounts).

Calcium Homeostasis

00:51:00

Normal serum calcium levels : 9 - 11 mg/dL.

Ionized calcium	Protein bound calcium
50% of total calcium	50% of total calcium
Free calcium	Storage form
Physiologically active form	Inactive form

pH changes & calcium :

Respiratory alkalosis → ↓ H⁺ ions → Calcium binds to albumin →

- ↑ Ca²⁺ bound form.
- ↓ Ca²⁺ free form → Hypocalcemic tetany.

Calcium absorption :

----- Active space -----

- Site : Duodenum.
- Facilitating factors : Gastric acid, protein rich diet.
- Inhibiting factors : Phytates & oxalates (Form insoluble complexes).

	PTH/Phosphatonin	Vitamin D	Calcitonin
Stimulus	↓s. calcium	↓s. Ca^{2+} & phosphate ↑PTH	↑s. Ca^{2+}
Bone	PTH $\xrightarrow{+}$ PTH receptor on osteoblast ↓ Releases Osteoclasts $\xleftarrow{+}$ RANKL ↓ ↑ Bone resorption.	Bone mineralization & resorption depending on s. Ca^{2+} levels	Inhibits bone resorption by inhibiting osteoclasts
Kidney	↑ Phosphate excretion (By inhibiting Sodium Phosphate cotransporter in PCT)	↑ Ca^{2+} & phosphate reabsorption	↑ Ca^{2+} excretion
Intestine	Indirectly ↑ vitamin D	↑ Ca^{2+} & phosphate absorption	Inhibits calcium absorption.
Overall effect	↑s. Ca^{2+} & ↓s. phosphate	↑s. Ca^{2+} & phosphate	↓s. Ca^{2+}

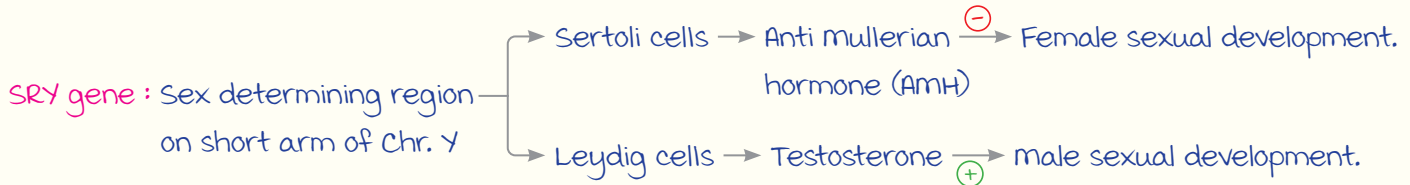
Note : PTH.

- Protein hormone (84 aa) .
- Secreted from chief cells of parathyroid gland.
- Drug form : Teriparatide.

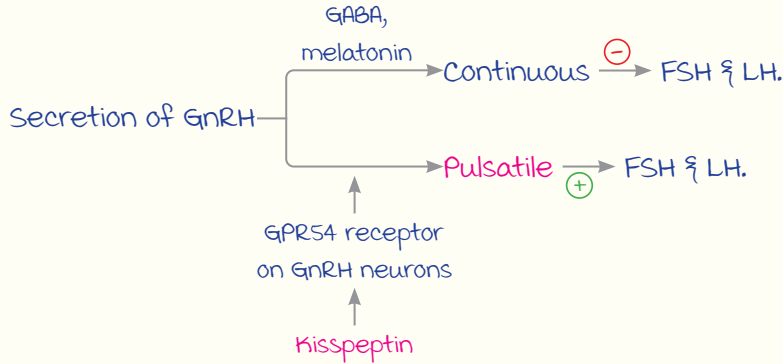
REPRODUCTIVE & EXERCISE PHYSIOLOGY, REGULATION OF BODY TEMPERATURE

Male Reproductive System

00:00:25



Puberty :



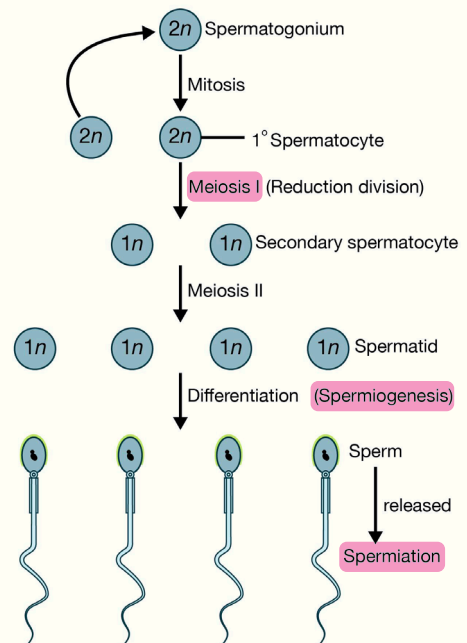
Spermatogenesis :

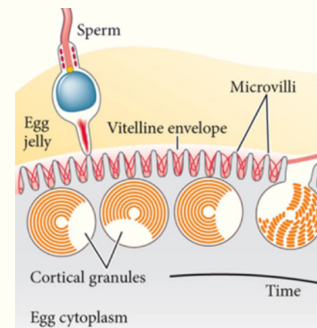
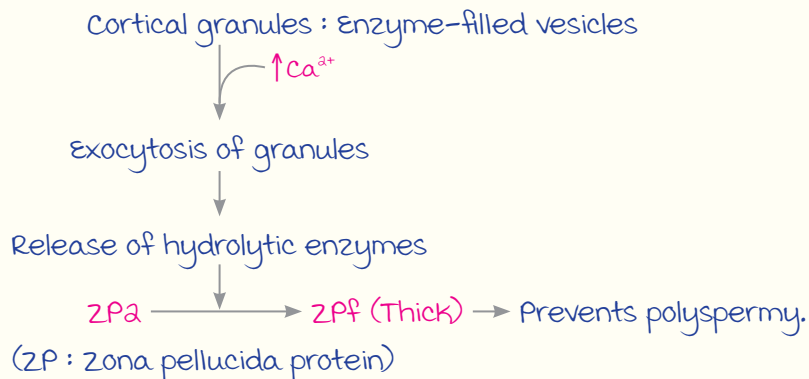
Sperm maturation and motility :

- In epididymis.
 - Activation of **CATSPER** (Ca^{2+} channel)
- ↓
- Forward progressive motility of sperm.

Capacitation of sperm :

- Occurs in **female genital tract**.
- \uparrow Forward motility of sperm.
- Facilitates acrosome reaction.



Cortical Reaction :


----- Active space -----

Functions of Sertoli Cells :

- Secrete AMH.
- Form blood-testis barrier : Protects sperm.
- Nutrition to developing sperm (AKA nurse cells of testis).
- Produce androgen binding protein (ABP).
- Secrete aromatase enzyme.
- Secrete inhibin : Negative feedback regulation of FSH.
- Phagocytosis of dead sperm.

Semen :

Secretions from	% volume	Composition
Seminal vesicle	60%	Fructose, phosphoryl choline (Florence test), ascorbic acid, prostaglandins
Prostate	20 - 30%	Spermine (Barberio's test), fibrinolysin, Zn, acid phosphatase
vas deferens	10%	-

male Sexual Act :
Erection of penis :

- Parasympathetic innervation : S_2, S_3, S_4 (Neurotransmitter : Acetylcholine).
- Non-adrenergic non-cholinergic (NANC) system :
 Nitric oxide $\xrightarrow{\text{via cGMP}}$ Dilation of arteries \rightarrow Compression of veins \rightarrow Penile engorgement.
 - Phosphodiesterase (PDE) : Degrades cGMP.
 - PDE inhibitor (Sildenafil) : Inhibits cGMP degradation \rightarrow \uparrow Erection.

Ejaculation :

- Life span of sperm after ejaculation : 1 - 2 days.
- Sympathetic innervation : $T_{12} - L_2$.
- Steps :
 1. Emission.
 2. Ejaculation proper.

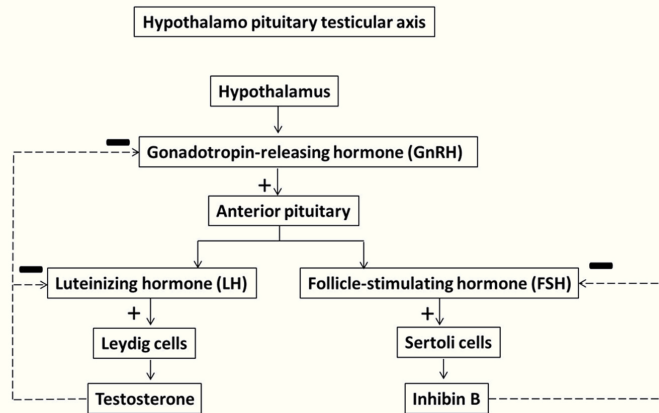
Detumescence/resolution :

Constriction of arterioles by $\left\{ \begin{array}{l} \text{Endothelin.} \\ \text{Norepinephrine.} \end{array} \right.$

----- Active space -----

Regulation of male Reproduction :

Two cell two gonadotropin model :



Functions of testosterone :

- Wolffian system stimulation : Development of **internal** male genital organs.
- Erythropoietin stimulation : \uparrow RBC.
- Anabolic effects : \uparrow muscle mass.
- Bone growth stimulation.
- Testosterone $\xrightarrow{\text{5}\alpha \text{ reductase}}$ Dihydrotestosterone (more potent).
- Initiation & maintenance of spermatogenesis.
- Stimulates Sertoli cells : \uparrow ABP synthesis.
- \uparrow Libido.

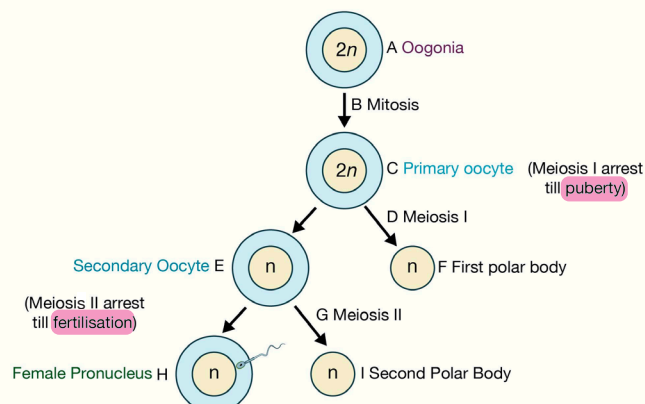
Functions of dihydrotestosterone :

- Pubertal changes.
- masculinization of **external** male genital organs.
- Development of **prostate**. α reductase inhibitor (**Finasteride**) : Therapeutic use in BPH.
- 2^o sexual characteristics : Facial hair, acne, temporal hair recession.

Female Reproductive System

00:20:19

Oogenesis :



menstrual Cycle :

Order of peaking of hormones :

FSH > Estrogen > LH > Progesterone.

LH surge :

- Due to positive feedback effect of ↑estrogen.
- Occurs : 24-36 hrs before ovulation (Peak : 8-10 hrs).

FSH surge (Smaller) :

Lysis of follicular cell → Release of ovum.

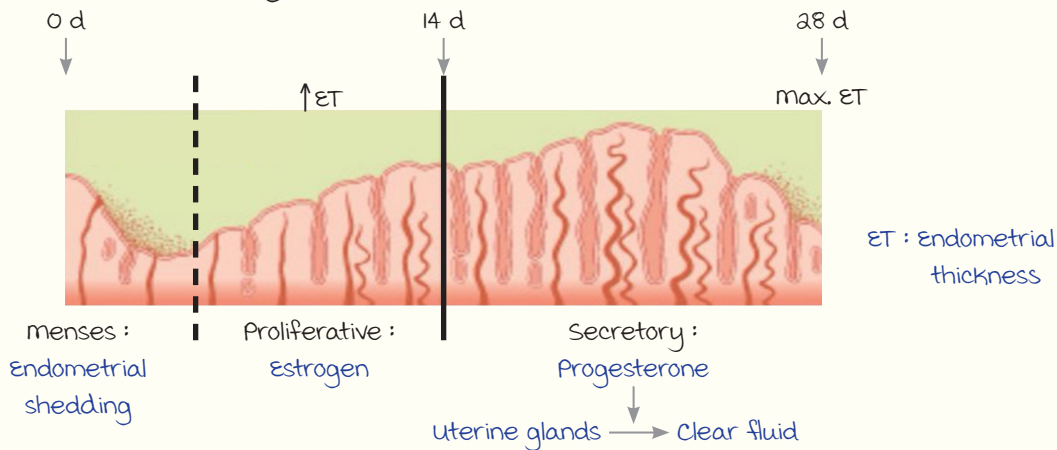
Luteal phase :

Lasts for a duration of 14 days after ovulation,

LH stimulates → Luteinization → Formation of corpus luteum (Secretes progesterone)

If no fertilisation ↓
Regresses 10 days after ovulation.

uterine endometrial changes :

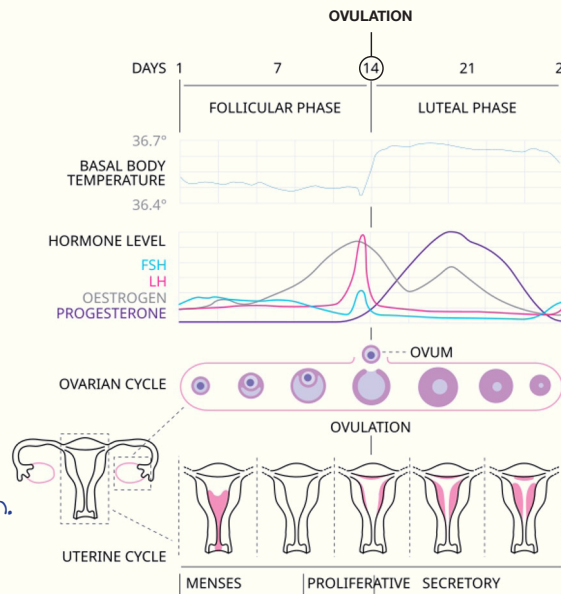


Cervical changes :

- Estrogen → ↓thickness & ↑pH of cervical mucus → Easy penetration of sperm.
- Progesterone → ↑thickness & tenacity of cervical mucus → Hard penetration of sperm.
- **Ovulation** : Cervical mucus is thinnest.

vaginal changes :

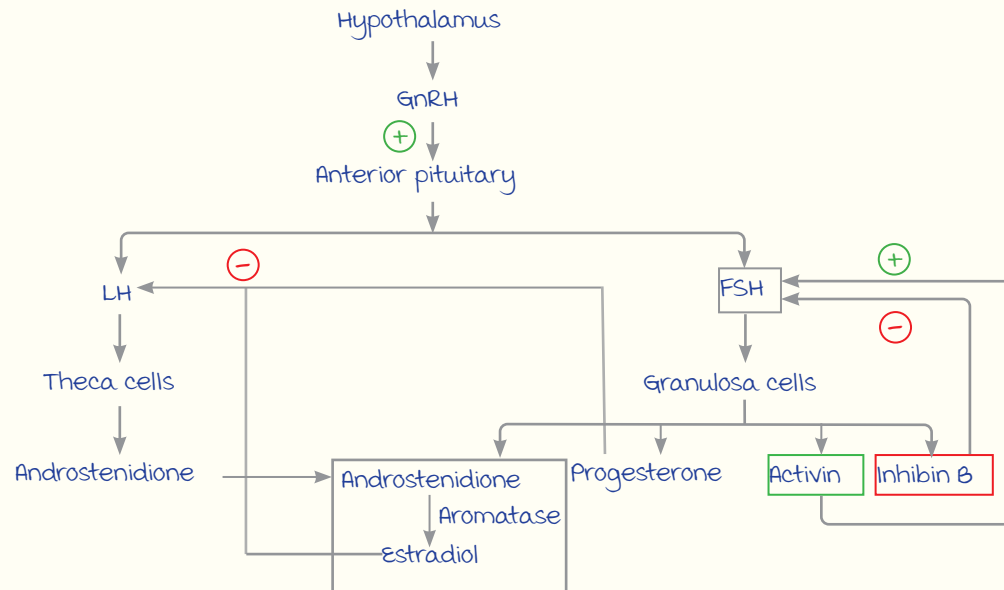
Cell seen	Hormonal influence
Parabasal	Nil
Intermediate	Progesterone
Superficial	Estrogen



----- Active space -----

Regulation of Female Reproduction :

Two cell two gonadotropin model :

**Functions of estrogen and progesterone :**

Organs	Estrogen	Progesterone
uterus	<ul style="list-style-type: none"> • ↑ uterine blood flow. • ↑ content of contractile proteins → ↑ uterine muscle excitability. 	<ul style="list-style-type: none"> • ↓ excitability. • ↓ Sensitivity to oxytocin.
2° sexual characteristics	+++	No effect
Breast	Stimulates ductal growth (GH of breast).	Stimulates Lobular growth.
Bone	<ul style="list-style-type: none"> • Induces apoptosis of osteoclasts → Bone anabolic effect. • ↓ estrogen at menopause → Osteoporosis. 	No effect
Liver	↑ expression of LDL receptor → Plasma cholesterol lowering action	No effect
CVS	<ul style="list-style-type: none"> • ↑ NO levels → Promotes vasodilation. • Inhibits platelet aggregation. 	No effect
CNS	Inhibits neuronal cell death → Neuroprotective action.	<ul style="list-style-type: none"> • ↑ basal body temperature (thermogenic action). • CNS depressant.
Kidney	Na ⁺ & H ₂ O retention.	<ul style="list-style-type: none"> • ↑ dose of progesterone • ↓ Aldosterone • ↑ Na⁺ & H₂O excretion (Diuretic effect)
RS	No effect	<ul style="list-style-type: none"> • Stimulates respiration • ↓ alveolar pCO₂ during luteal phase.

----- Active space -----

Protein hormones :

1. Inhibin (A & B) : Inhibits FSH.
2. Activin : Stimulates FSH.
3. Follistatin : Inhibits FSH.
4. Relaxin :
 - Relaxes pubic symphysis.
 - Dilates cervix.

Human chorionic gonadotropin :

- Glycoprotein.
- 2 subunits :
 - α : Similar to FSH, LH, TSH.
 - β : Similar to LH.
- Functions :
 - maintenance of corpus luteum till 6 weeks of pregnancy.
 - Stimulates Leydig cell \rightarrow Testosterone.
 - Immunosuppressive activity.
 - Secretion of relaxin from corpus luteum.

• AKA super LH :

	LH	hCG
$t_{1/2}$	30 mins	37 hours
Biological activity	x	80x

Lactation :

- Prolactin : milk production.
- Oxytocin : milk ejection.
- Estrogen : Ductal growth.
- Progesterone : Lobular growth.

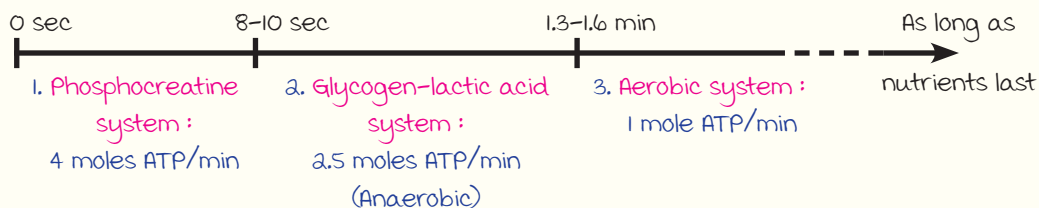
Exercise Physiology

00:38:00

Types of exercise :

	Isotonic (Dynamic)	Isometric (Static)
muscle tension	Constant	Variable
muscle length	Variable	Constant
example	Treadmill running	Pushing against a wall

Energy source :



----- Active space -----

Effects of Exercise :

On blood flow :

Organ	effect
Kidneys	↓
GIT	↓
Heart	↑
Exercising muscle	↑
Brain	No change
Skin	↓ initially, ↑ later (For heat dissipation)

On blood pressure :

Isotonic exercise	Isometric exercise
↑ SBP	↑ SBP
↓ DBP (D/t ↓ TPR)	↑ DBP

On respiratory system :

- $\text{MET} \propto \text{Resting } \text{O}_a \text{ consumption}$.
1 MET = 250 ml/min.
- Peak VO_a :
Highest O_a uptake at the end of test.
- $\text{VO}_a \text{ max}$:
maximum possible O_a consumption (Theoretical value).

Parameter	effect
Respiratory rate	↑ even before exercise ; anticipatory tachypnea
Pulmonary ventilation	↑
pO_a	No change
pCO_a	
pH	
Diffusion of gases	↑
Resting O_a consumption	↑
metabolic equivalents (MET)	↑
Peak VO_a	-
$\text{VO}_a \text{ max}$	-

Regulation of Body Temperature

00:44:48

Role of hypothalamus :

	Anterior hypothalamus	Posterior hypothalamus
Stimulus	Hot temperature	Cold temperature
effects	<ul style="list-style-type: none"> • Cutaneous vasodilation • Sweating • ↑ Thirst • Osmoreceptor stimulation 	<ul style="list-style-type: none"> • vasoconstriction • Shivering • ↑ urinary frequency

Feed-forward control :

↓ skin/shell temperature → Anticipatory corrective response by hypothalamus
↓
Internal/core temperature maintained.

Heat Disorders (mild to Severe) :

----- Active space -----

Heat cramps < Heat syncope < Heat exhaustion < Heat stroke, malignant hyperthermia.
 (mild) (Severe)

Heat stroke :

- Due to loss of thermoregulatory mechanisms.
- **Sweating absent.**
- Forms :
 - Classic : Old age.
 - Exertional : Soldiers.
- **Triad** : Coma + hot & dry skin + rectal temperature $\geq 106^{\circ}\text{F}$.
- Rx : Cool place, cold water, cold clothes, fluid replacement.

malignant hyperthermia :

- Pathophysiology :
 \uparrow activity of ryanodine receptor (RYR) \rightarrow \uparrow **Ca²⁺ release** \rightarrow \uparrow muscle contraction.
 - Precipitating agents :
 - **Succinylcholine.**
 - Halothane.
 - Rx : Dantrolene sodium (Blocks ryanodine receptor).
- ↓
Hyperthermia

Cold Disorders :

Hypothermia :

1. Therapeutic : Every 1°C \downarrow in body temperature \rightarrow 7% \downarrow in cerebral blood flow
 (\downarrow blood loss in neuro Sx).
2. Accidental.