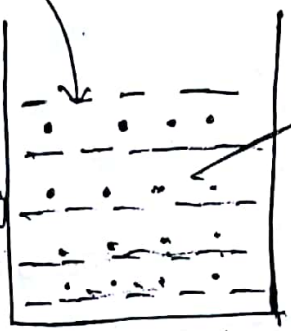
"Q"
⇓
Known quantity of suitable dye (Indicator) Tracer



Unknown * volume

Withdrawl sample (After Mixing)
⇓
Concn of dye "c" **

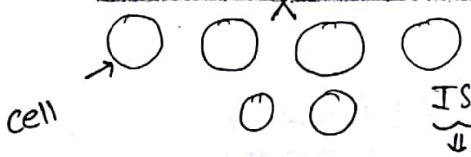
$$V = \frac{Q - e}{c}$$

Amount of dye Metabolized or excreted during Procedure

Volume of body compartment to be Measured

Concn of dye after Mixing.

* Q → ⇒ only Measure Plasma

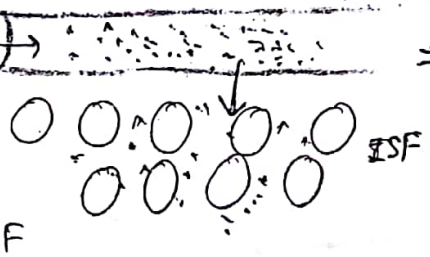


cell, ISF ⇓ Interstitial fluid

Dye will Not cross Capillary Membrane

Dye ⇒ Evan's blue; (T1824)
Radioactive Labelled Iodine;
Albumin.

* Q → ⇒ crossed the capillary Membrane but Not the cell Memb.



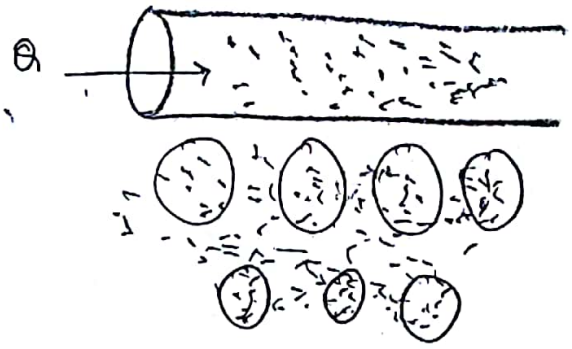
ISF

⇓
Dye ⇒ Inulin
Mannitol
Sucrose;
Radioactive Sodium (Na²⁴)

- It will Measure ECF (Plasma + ISF)

Most accurate

① ⓐ



Cross Capillary Memb & Cell Memb..

⇓

Measures TBW.*

⇓

dye ⇒ D_2O

Most frequently used.

Tritium oxide ;
Amino Pyrine ;
Anti-pyrine .aa

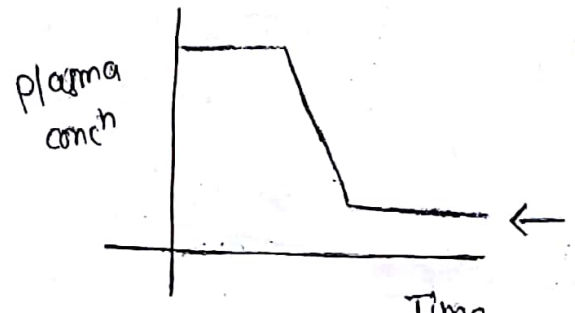
* ♀ GCF Measurement ⇒ TWB − ECF (D_2O − Inulin)

♀ GSF Measurement ⇒ ECF − plasma (Inulin Evan's blue)

→ Indirect estimation

Q. AIIMS'15

We want to determine ECF volume. We take 10gms of Inulin ; After equilibrium ; pl. Insulin 50mg/100ml ; during the procedure 10% excreted ; ECF volume=?



10gm = 10,000mg

$$V = \frac{10,000 - 1000}{500} \simeq 18 \text{ Litre}$$

Qq "XYZ" dye → Plasma volume Measure

⇓

"ABC" dye ⇒ Diffuses out of tissue capillary

Pl. volume Measurement ∵ dye "ABC".

a) Same as ∵ "XYZ"

~~b)~~ Falsely high

c) Falsely Low

$V = \frac{Q - e}{C}$

$\uparrow_{es} V = \frac{Q}{C \downarrow_{es}}$

* Measurement of solute Conc^n

MOLE ⇒ Gram Molecular wt.

32 gm of O_2 = 1 mole of O_2.

58.5 gm of NaCl = 1 mole of NaCl.

67,000 gm of Albumin = 1 mole of albumin.

1 mole = 6.023×10^{23} Molecules

↳ Avogadro No.

Millimole = $\frac{1}{1000}$ th of Mole

OSMOLE ⇒ 1 Osmol = $\frac{1 \text{ Mole}}{\text{No of Freely moving particles Liberated in solution}}$

* 1 Osmol of NaCl = $\frac{1 \text{ mole of NaCl}}{2}$

1 mole of NaCl	=	2 osm
1 mole of KCl	=	3 osm
1 mole of $CaCl_2$	=	3 osm
1 mole of Na_2SO_4	=	3 osm
1 mole of $C_6H_{12}O_6$	=	1 osm.
1 mole of Urea	=	1 osm
1 mole of Albumin	=	1 osm

* Milliosmol ⇒ $\frac{1}{1000}$ th of osmol

OSMOLARITY	OSMOLALITY
• No. of osmols of solute per Liter of solution.	• No. of osmols of solute per kg of Solvent.
• affected by – Temp.	– Not affected by temp; so, better to use

Q. (N) Plasma osmolality ⇒ 280-290 mosm/Litre

* if there is ↑ Plasma osmolality ⇒ eg ⇒ Sweating (Hypo-tonic)

ADH - Thirst Mech^m for Regulation of Plasma osmolality & the Na+ Levels

↳ Stimulates osmoReceptors (Located @ Ant. hypothalamus)

1st ↑ in ADH & b/c Na+ contribution

Thirst comes Later

↳ Supraoptic (↑ Plasmolality by 5 mosm/l) (↑ ADH)

↳ Lateral hypothalamus (↑ Plasmolality 1 mosm/l)

Q. Maxm contribution to plasma osmolality ⇒

a) Sodium & its associated anions ⇒ 270 mosmol

b) Glucose ⇒ 5 mosmol

c) Urea ⇒ 5 mosmol

d) Pl. proteins ⇒ 2 mosmol *

↳ Least contribution

e) Remaining ions ⇒ 8 mosmol

290 mosmols

* (N) Plasma proteins ⇒ 6-8 gm/dl } Fairly high conc^n.

(N) Albumin proteins ⇒ 3.5-5.0 gm/dl

(35-50 gm/L)

67,000 gm of Albumin = 1 mole of Albumin = 1 mosm of Albumin

50 gm of Albumin = $\frac{1}{67,000}$ × 50 mole of Albumin = 0.00075 moles

= 0.00075 osmoles

*** * No. of Moles or osmoles of protein = $\frac{\text{Conc}^n \text{ in gm/Litre}}{\text{Mw}}$

QQ Plasma proteins contributes only 2 mosm to plasma osmolality bcz ⇒

a) high Molal conc^n; high Mw

b) Low Molal conc^n; Low Mw

c) High Molal conc^n, Low Mw

d) Low Molal conc^n; high Mw.

Q. Plasma proteins contributes only 2 mosm/l to plasma osmolality ; b/c of →

a) high conc^n ; high Mw.

b) Low conc^n ; Low Mw.

c) High conc^n ; Low Mw

d) Low conc^n ; high Mw

Proteins — High conc^n ($\overset{\text{gram/litre}}{g/L}$)

but b/c of high Mw

↓

↓ Molal conc^n

∴ Contribution to Plasma osmolality also ↓es.

* How to Measure Plasma osmolality

$$\text{Sm mosm/L} \Rightarrow 2[Na^+ + K^+] + \underset{(\text{mmol/L})}{0.055}\ \underset{\text{mg/dl}}{[\text{Glucose}]} + \underset{(\text{mmol/L})}{0.36}\ \underset{\text{mg/dl.}}{[\text{BUN}]}$$

($\nearrow \frac{1}{18}$ Multiply ∈ mg/dl of Glucose)

↓ mmol/L or meq/L

$$2[Na^+]$$

Q. $Na^+ = 140$ meq/L

$K^+ = 5$ meq/L

Glu = 5 mosmol/L

BUN = 5 mosmol/L

Pl. osmolality = ?

$2[140+5] + 5 + 5$

$= 300$ mosmol/Litre

* Measurement of Plasma osmolality by freezing point depression

⇒ 1 osmol of solute depress freezing point by 1.86°C

QQ. freezing point of soln ∈ 1 mosmol of solute

a) 0°C ; b) +1.86°C ; c) -1.86°C

* 1 mosmol of solute depresses freezing point by 0.00186°C

QQ freezing point of Plasma ⇒

a) 0°C

b) −1.86°C

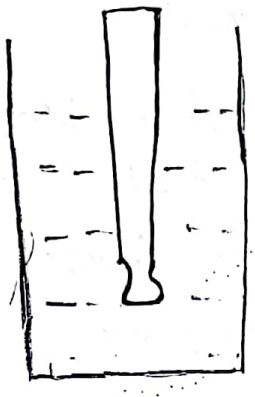
c) −0.54°C

d) +0.54°C

1 mosmol ↔ −0.00186°C

290 → 290 × −0.00186°C

= −0.54°C.



***

$$\text{Pl. Osmol (mosml/L)} = \frac{(\text{F.pt.})^{\circ}\text{C}}{0.00186^{\circ}\text{C}}$$

⇒ More accurate to Measure the plasma osmolality.,

↳ b/c we consider all things ⊕ in plasma @ here

* (N) Pl. osm. by freezing point depression is higher than Pl. osmolality by using formula,

* (N) difference b/w two Method is ≤ 10 mosm/L
* if difference b/w two Methods > 10 mosm/L

↓↓

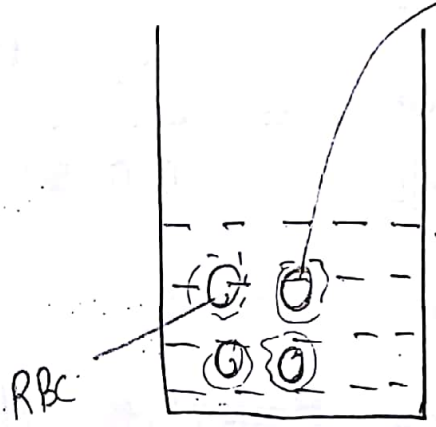
K/as "OSMOLAL GAP"

QQ: Osmolal gap prt. in all of the following except ⇒

a) Mannitol in plasma
b) Methanol in plasma
c) Ethylene glycol in plasma
~~d) Hyperglycemia~~

→ Osmolal gap is seen in the presense of "extraneous Substance" in plasma.

QQ



Into which solution have RBC been placed

~~a) 140 mmol Glucose = 140 mosm Hypotonic~~
b) 280 mmol Glucose = 280 mosm Isotonic
c) 140 mmol NaCl = 280 mosm Isotonic
d) 280 mmol NaCl = 560 mosmol Hypertonic

*	ECF	ICF
Osmolality	290 mosm/L	290 mosm/L
Major cation	Na^+	K^+
Major Anion	Cl^-	Misc phosphates > HCO_3^-
Most osmotically active	Na^+	K^+
Major buffer	HCO_3^-	Proteins (∵ pK of proteins is close to intracellular pH)
pH	7.35 – 7.45	7.1
H^+		Yes (as compare to ECF b/c of Metabolism in ICF)

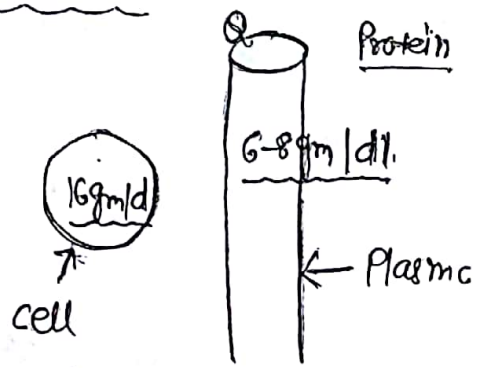
Qq. Which of the following is higher in ECF **

a) Osmolality;

b) proteins

c) Phosphates

~~d) pH~~



OSMOTIC ADAPTATION

In chronic hyperNatremia :⇒ (> 24-48hrs)

ECF 290 mosm/L

Brain cells show osmotic Adaptation.

i> ↑es intracellular Synthesis of osmolytes
- Betaine (BIG)
- Inositol
- Glutamine

ii> Import of sodium

In chronic hypoNatremia :⇒ (> 24-48hrs) brain cells show osmotic adaptation.

i> ↓ intracellular synthesis of osmolytes

ii> Export of K+,

* **Rapid correct of chronic hypoNatremia**

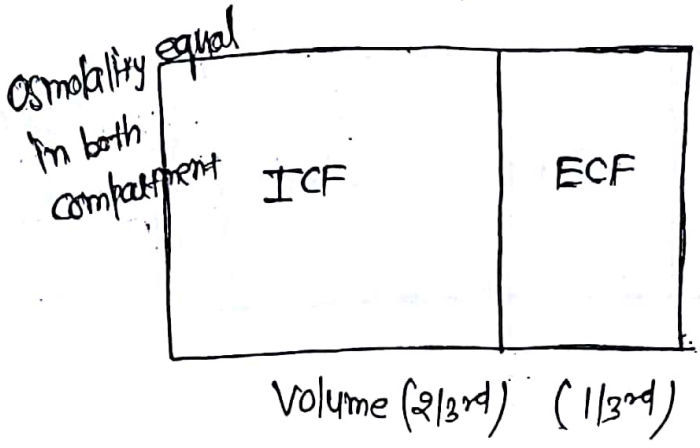
⇓

Result in **central Pontine Myelinosis**

↳ **Result in death.**

So; should Not correct Nat Rapidly; do; correction gradually & Not More than 6 mmol/Lit./day. (on 1st day ⇒ 6-8 mmol/Lit. correction done only & Later ↑es Nat gradually)

* DARROW - YANNET DIAGRAM (D-Y Diagram)

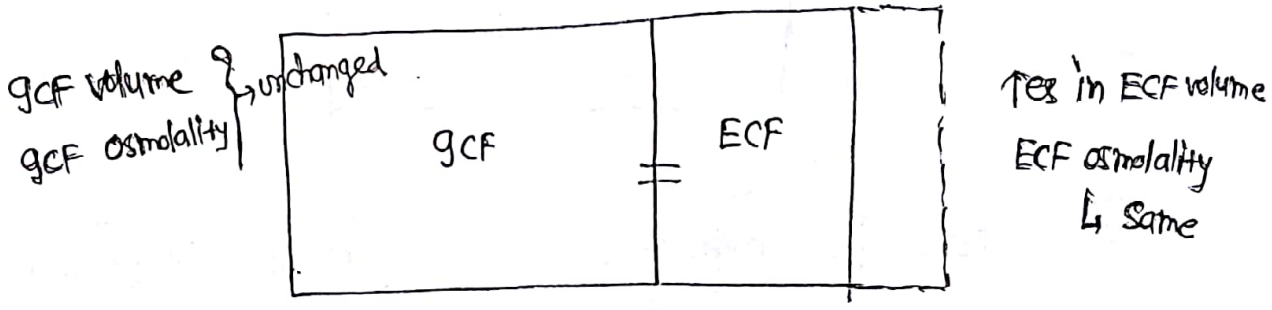


① Addition (Loss of Fluid is from ECF)

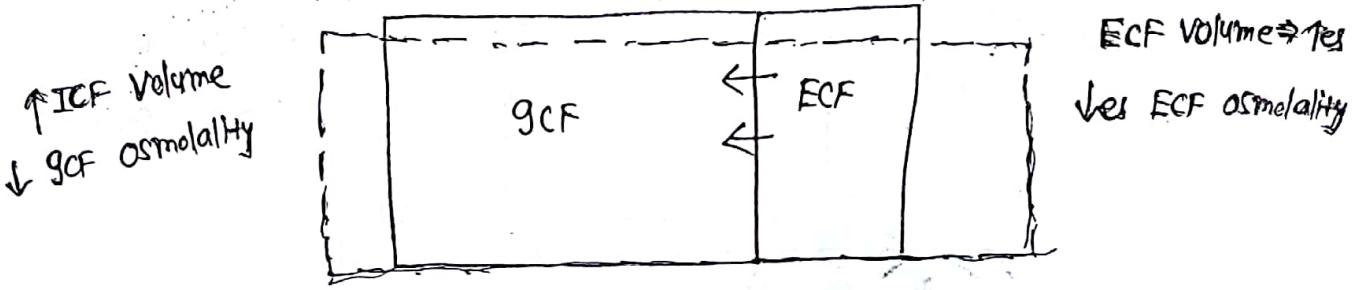
② ECF Osmolality determines shift of fluid;

③ Shift of Fluid will occur till ECF & ICF Osmolality is same

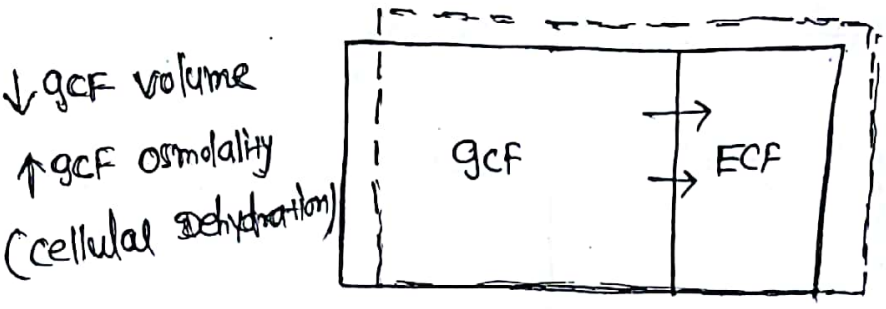
* Addition of Isotonic saline :→



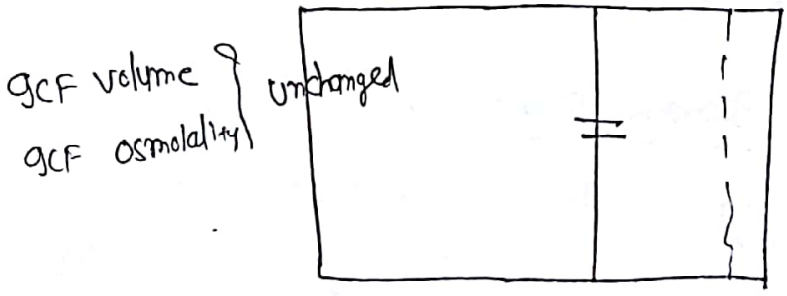
* Addition of Hypotonic saline :→



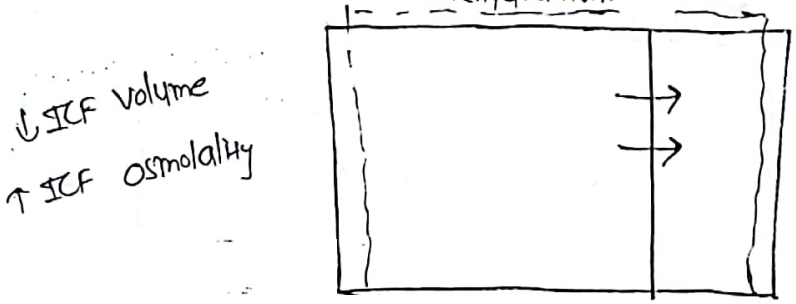
* Addition of Hypertonic saline :⇒



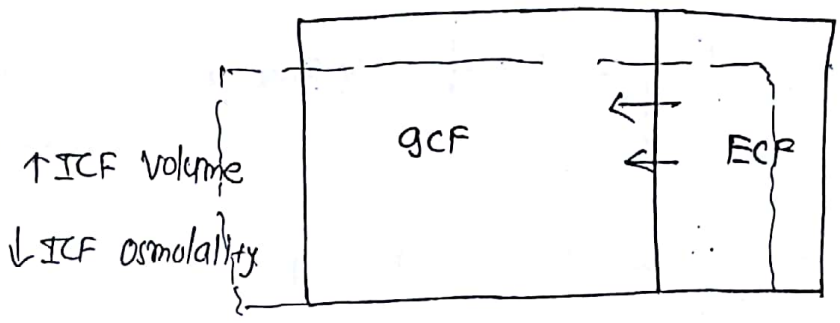
* Loss of gso-tonic fluids :⇒ eg ⇒ Hemorrhage ;
Burns ;
Initial stage of diarrhea & vomiting.
↳ gso osmotic dehydration



* Loss of hypotonic fluids ⇒ eg ⇒ Excessive sweating
Diabetes insipidus
↳ hyperosmotic dehydration.

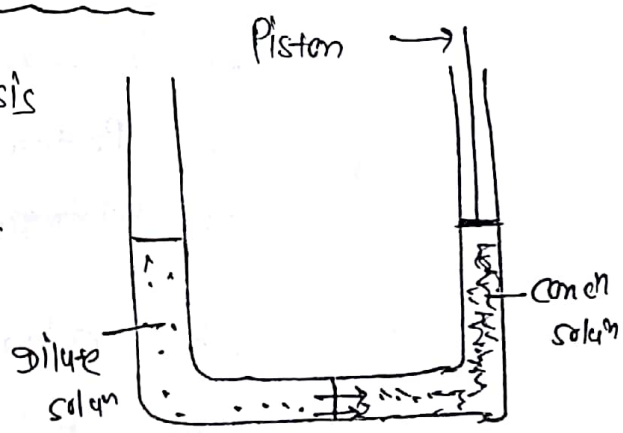


* Loss of hypertonic fluids eg ⇒ Mineralocorticoid deficiency
  ↳ Hypoosmotic dehydration ⇓
  Addison's ds



* OSMOTIC PRESSURE

- Pressure applied to stop osmosis
  ⇓
  Also " osmotic-pressure"



* 1 mosml of solute
  ↳ exert Osmotic pressure of 19.3 mm Hg

QQ Osmotic pressure of plasma
  ⇓
  5500 mm of Hg (290 X 19.3 = 5597)
  ↳ slightly Lower than calculated b/c all solutes Not contributed in osmotic pressure

* Colloid osmotic pressure (oncotic pressure)

→ osmotic pressure exerted by colloids (proteins)

→ 25 – 28 mm of Hg

Osmotic Pressure = No. of mosm of solute × 19.3 × Osmotic coefficient (Reflection coefficient)

= 2 × 19.3 × 0.7

⇒

QQ Which proteins contributes Maxm to colloid os. pressure

a) Albumin

b) Globulin

c) Prothrombin

d) Fibrinogen

QQ Why albumin contribute to colloid osmotic pressure??

a) High conc^n; high Mw

b) Low conc^n; Low Mw

c) High conc^n; Low Mw (compare to other proteins it has less Mw; while its conc^n is high).

d) Low conc^n; High Mw

* Reflection coefficient :⇒ Freely permeable solute : Reflection coefficient (σ) = 0.

Impermeable solute

Reflection coefficient (σ)

↳ 1.0

↳ cell Membrane

* Solute & Reflection coefficient is zero

⇓

don't contribute to osmotic pressure

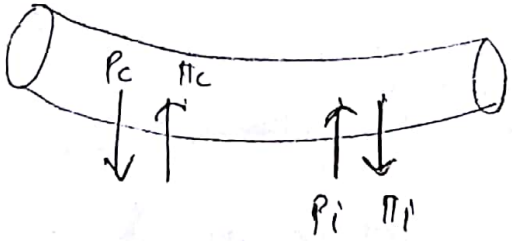
⇓

Also " Ineffective osmoles ".

eg ⇒ Alcohol
Glycerol
Urea ⇒ via facilitated diffusion.
Glucose

* STARLING'S FORCES IN TISSUE CAPILLARY

PUSH = Hydrostatic Pressure
PULL = colloid osmotic Pressure



P_c ⇒ capillary hydrostatic Pressure.

π_c ⇒ capillary colloid osmotic Pressure

P_i = Interstitial fluid hydrostatic pressure

π_i = Interstitial colloid osmotic Pressure

***

Net force ⇒ $P_c - \pi_c - P_i + \pi_i$

P_c = 35 mm of Hg
π_c = 25 mm of Hg
P_i = −1 mm of Hg (bcz of continuous drainage into Lymphatics)
π_i = 0 mm of Hg

⇒ 35 − 25 − (−1) + 0

⇒ +11 mm of Hg.

QQ
AIIMS'15

Net pressure = 3 mm of Hg ;

P_C = 25 mm of Hg

Π_C = ??

P_i = 2 mm of Hg

Π_i = 7 mm of Hg

Net pressure $= P_C - \Pi_C - P_i + \Pi_i$

$3 = 25 - \Pi_C - 2 + 7$

$\boxed{\Pi_C = 27 \text{ mm of Hg}}$ ***

* Rate of tissue Fluid formation $\propto$ Net pressure

$(P_C - \Pi_C - P_i + \Pi_i)$

$= K_f (P_C - \Pi_C - P_i + \Pi_i)$

③ ④ ⑤ ⑥

$K_f \Rightarrow$ Ultrafiltration constant

= Permeability ✕ Surface area

① ②

all six (in No.) affected tissue fluid formation.

* Gn cirrhosis / Nephrotic syndrome } Hypoalbuminemia ↓ ↓ Π_C ⇓ ↑ Rate of tissue fluid formation ⇓ Result in edema

QQ organ ∈ Maxm P_C
↳ Kidney

QQ. organ ∈ Maxm K_b
↳ Kidney

QQ organ ∈ Maxm capillary permeability
(Most permissible capillary)
↳ Liver

Hepatic capillary — Sinusoidal
Glomerulus capillary — Fenestrated

BLOOD VOLUME

B. volume = 8% of body wt.
Plasma = 5% of body wt.
cells = 3% of body wt.

$$\text{Blood volume} = \frac{100}{100 - \text{Hematocrit value}} \times \text{Pl. volume}$$

Q ⇒ Pl. volume = 3L
Hematocrit = 40
Blood volume = $\frac{100}{100-40} \times 3 = 5$ Lit

CELL MEMBRANE

- Thickness = 7.5 nm
  OR
  75 Å

- Lipid Bilayer (Symmetrical Arrangement)
  +
  Protein — function as → Receptors, Antigens, Transport proteins, Channel proteins, Structural proteins, Enzymes.

→ "Fluid Mosaic Model"

Protein
divided into
- Integral
- Peripheral ⇓ Enzymes

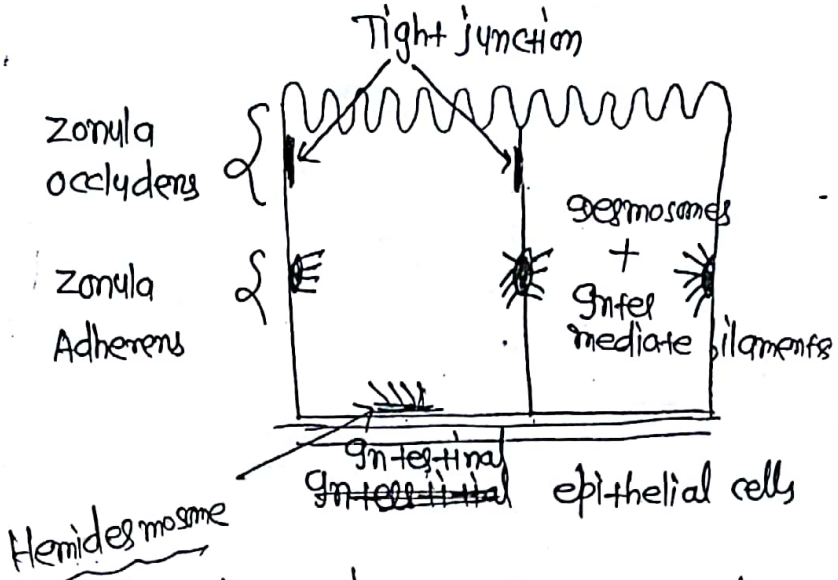
QQ In terms of dry wt. of cell Membrane ; Maxm amount :→
(a) Lipids
(b) Protein ⇒ 52% of dry wt. of cell Membrane

Ration (1:1)

* Cell adhesion Molecules (CAMs) :⇒
  - Cadherins
  - Integrins
  - Selectins
  - Protein belonging to IgG Superfamily.

* TIGHT JUNCTIONS :→ formed by proteins
  ⇓
  - Occluding
  - Claudins
  - JAMs (Junctional Adhesion Molecule).

– Tight junctions are seen in ⇒ b/w endothelial cells of cerebral capillaries
  ↳ BBB ∞
  ⇓
  Astrocyte induce formation of Tight Junction.
  - b/w ~~Interstitial~~ Intestinal epithelial cells (Towards Luminal side)
  - PCT
  - CD

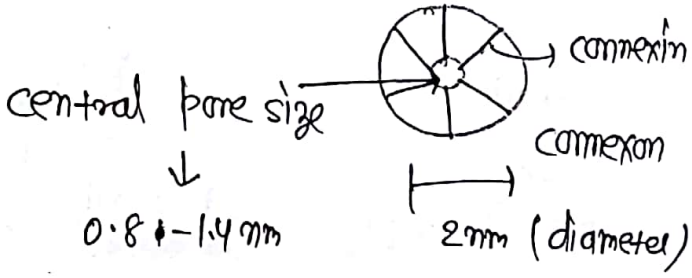


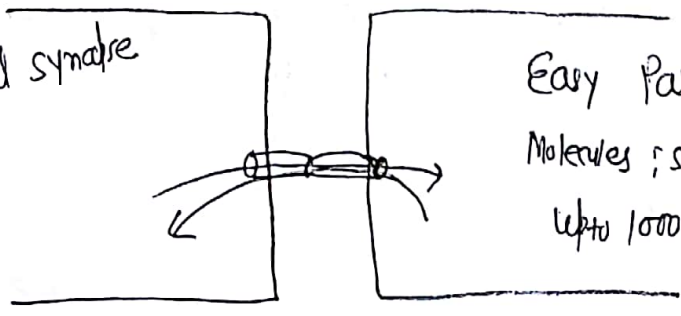
↳ helps in attachment to basement Membrane

GAP JUNCTIONS ⇒ Made of Protein Connexins.

⇓

Each Connexin has 6 subunits Klas "connexins"; which surround central pore





- Gap junction ⟶ Ves Inter cellular junction

(N) Gap b/w Inter cellular ⇒ 20nm
by Gap junction Reduce
by 3nm

eg ⇒ Retina
Cardiac Muscle (Heart – Functional Syncytium)
Single unit type of Smooth Muscle
(In wall of hollow viscera
eg ⇒ GI Muscle)

* If connexon Mutation
↳ Charcot Marie tooth disease
(X-Linked disease).

- TRANSPORT ACROSS CELL MEMBRANE

Passive	Active
– "Downhill transport"	– "Uphill" transport
– Along Electrochemical gradient	– Against electrochemical gradient
– No energy Required	– energy Required
eg ⇒ Simple diffusion	– 10 · Active
Facilated diffusion	– 90 Active
Non-ionic "	
Osmosis	

Simple diffusion

- all Lipid soluble substance;
- Alcohols; steroids
- Respiratory gases

Fick's Law of diffusion :⇒

$$J = -D \frac{A \Delta c}{\Delta x} \quad **$$

J = Net transport; · D = Diffusion coefficient

A = Surface Area

Δc = conc^n gradient.

Δx = thickness of Membrane

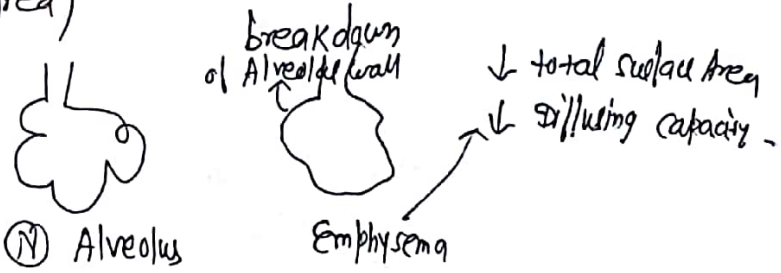
depends on → Lipid solubility. (Most imp.)
→ Molecular size / diameter
→ Mw

Diffusion coefficient ∝ $\frac{\text{Lipid Solubility}}{\text{Molecular diameter} \sqrt{Mw}}$

- if 2 Equal Lipid soluble substance; then Next imp. to determine diffusion coefficient ⇒ Molecular diameter

- $J \propto A$ (surface Area)

In emphysema ⇒

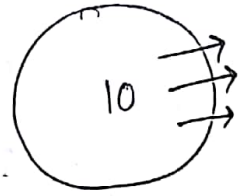


* gn Pulmonary fibrosis ⇒ ↓ Diffusing capacity.
b/c of ↑ Thickness.

$$J = \frac{D A \Delta C}{\Delta X}$$

Shows direction of transport from higher Conc^n to Lower conc^n.

QQ. Membrane permeant Substance



Intracellular conc^n
Surface area
thickness of Membrane
} X 2

the extracellular conc^n ⇒ Same

Rate of transport ⇒

a) 2X ; ~~b) 3X~~ ; c) $\frac{1}{2}$; d) $\frac{1}{3}$

$$J = - \frac{D A \Delta C}{\Delta X}$$

Initially ⇒ 10-5 ⇒5
after double ⇒ 20-5 ⇒15
} Conc^n gradient

3 times Tes

FACILLIATED DIFFUSION

Carrier Mediated

i) Stereospecificity

↳ Carrier protein is specific for a substance or structurally similar substance

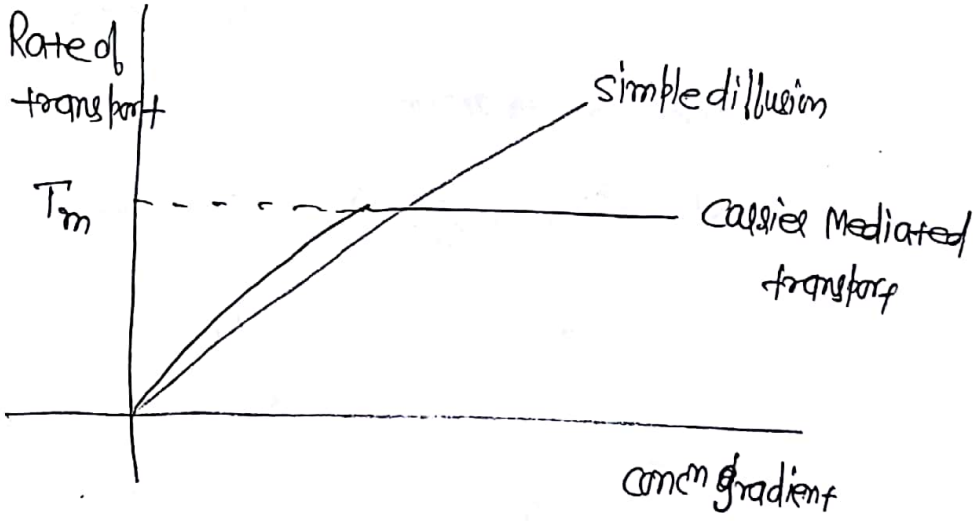
Glucose → GLUT ← Galactose

So; Galactose ⊕ ves Absorption of Glucose

ii) Saturation Kinetics

Carrier protein – tend to get saturated

– T_m (transport Maxima)



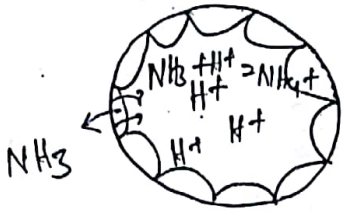
eg :- GLUT ⇒ for Glucose;

AA transporters

Urea transporters :- In Kidney ⇒ UTA1, UTA2, UTA3; UTA4

RBC, Vasa Recta ⇒ UTB

NON IONIC DIFFUSION



Collecting duct

Glutamine $\xrightarrow{\text{Glutaminase}}$ NH_3

* NH_3 Moves from cell to Lumen & form NH_4^+ inside the Lumen.

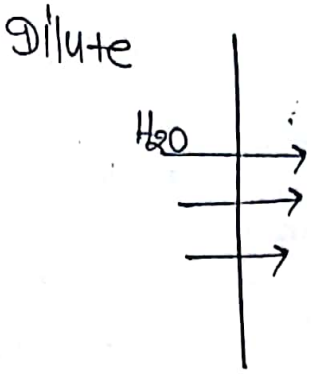
- Secretion of NH_3 → PCT (No H^+ in lumen to bind NH_3)
  → Collecting duct.

- Non-ionic diffusion of NH_3 seen in → Collecting duct.

eg :→ Secretion of NH_3 by collecting duct cells;
Excretion of weak acids & weak bases by the kidney;
Absorption of weak acids (Salicylates) in Stomach;
Absorption of bile acids in distal ileum.

OSMOSIS

- Movement of water from dilute to conc^{n} solution;



Q. Movement of H_2O is by →

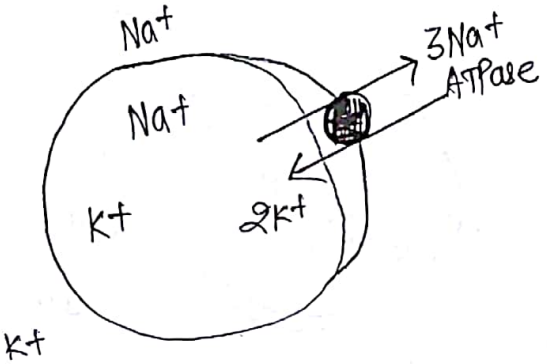
~~a~~ Passive transport

~~b~~ Osmosis

ACTIVE TRANSPORT

- Primary
  - $Na^+ - K^+$ ATPase
  - $H^+ - K^+$ ATPase
  - SERCA (Sarcoplasmic E.R. Ca^{++} Pump)
    - ↳ Seen in Muscle
- Secondary
  - Co-transport (symport)
  - Counter-transport (Antiport)

$Na^+ - K^+$ ATPase Pump



Coupling Ratio

3 : 2

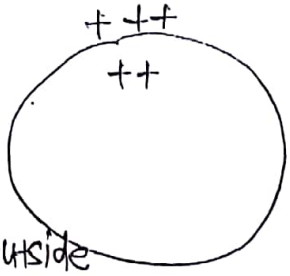
↳ b/c of two-stage process (1st ly sodium goes & then Potassium go

- Electrogenic Pump

Net loss of one ⊕ve charge

↓

Inside become ⊖ve w.r.t. outside



RMP = −90mv;

Contribution of Na+ − K+ ATPase = −4mv;

⇓

No+ sullicient to Make RMP.

Na+- K+ ATPase Pump Utilize 25% of total energy of cell. (In Neurons ⇒ 75% of total energy of cell).

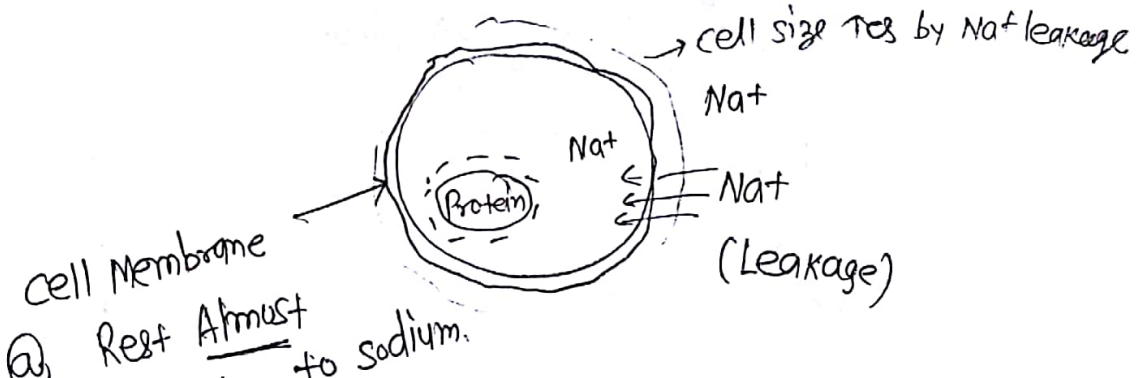
⇓

So; it contribute significantly to BMR

QQ. Most imp. Function of Na+-K+ ATPase Pump

⇓

Cell volume Regulation



Res cell size Result in burst.

⇓

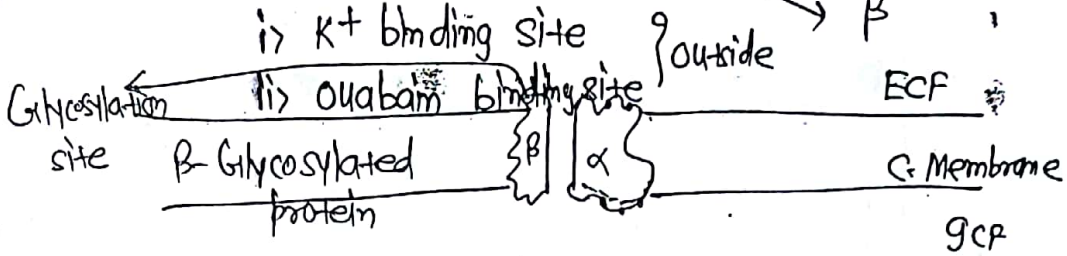
Na+ K+ Pump do net loss of one osmotically active particle

⇓

Maintains cell volume

* Structure of $Na^+ - K^+$ ATPase Pump ⇒

Heterodimer → α ⇒ Larger one (almost double of β = 100 units ↳ 55 units)
→ β



i) Na+ binding site
ii) ATP binding site
iii) Phosphorylation site.
} Inside

Aspartate 376 ⇐ iii) Phosphorylation site.

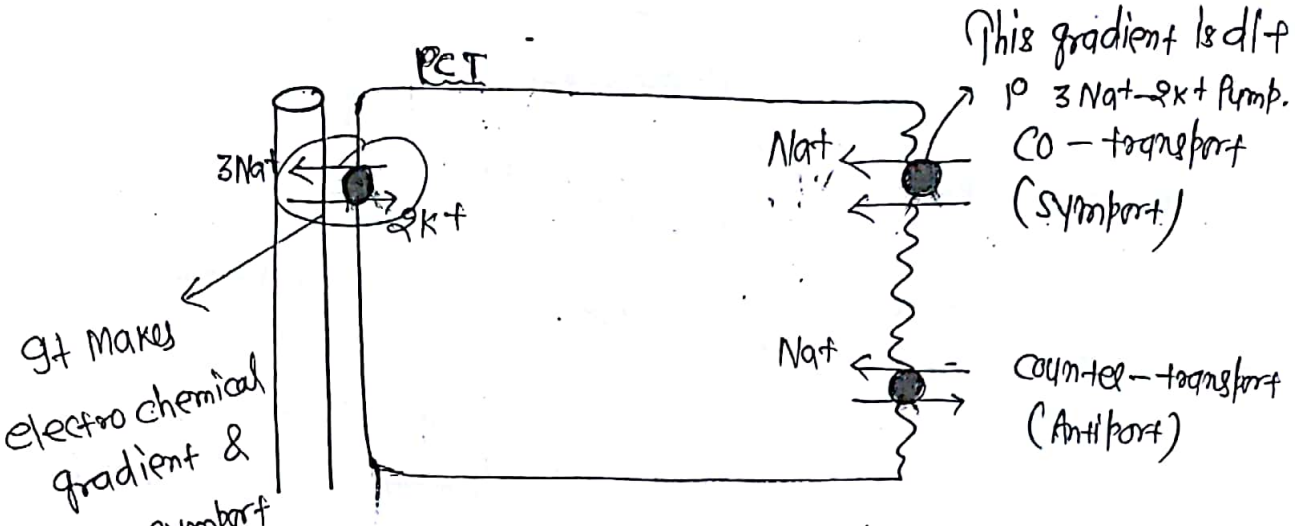
ATP —ATPase→ ADP + (P) + Energy
(goes here)

* All the binding site is prt. @ α-Unit.

• β-Unit has 3 extracellular Glycosylation sites.

*	Hormones		No. of $Na^+ - K^+$ ATPase Pump	Activity $Na^+ K^+$ ATPase Pump
①	Thyroid	→	↑ es	↑
②	Aldosterone	→	↑	↑
③	Insulin	→	⊖	↑
④	Dopamine	→	⊖	↓
⑤	ANP	→	⊖	↓

Secondry Active Transport



Co-transport in PCT ⇒ Na+- Glucose
Na+- Amino acid
Na+- Ip (Inorganic phosphate)

Co- transport in Thick ascending Limb (TAL) ⇒ Na+- K+-2Cl⁻ Co-transport

In DCT ⇒ Na+ - Cl⁻ Co-transport

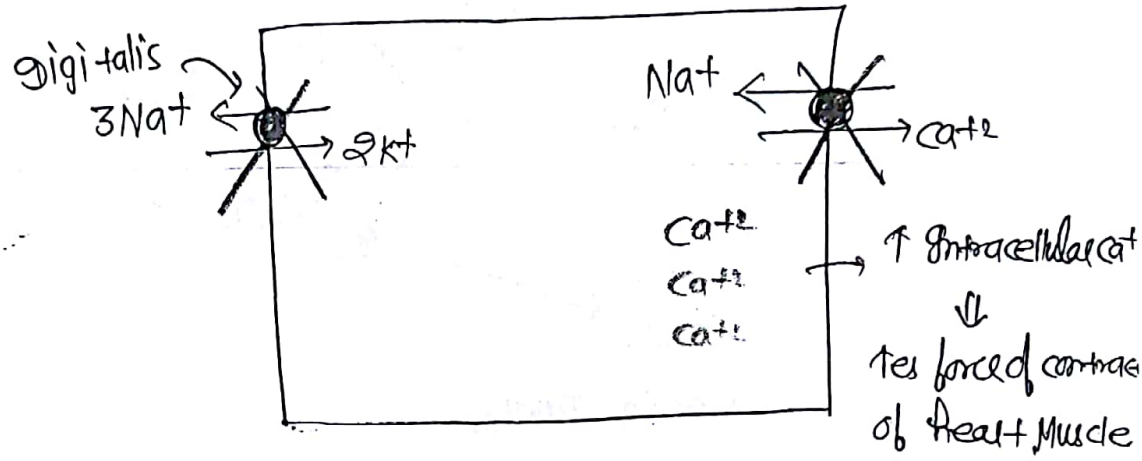
In intestinal epithelium ⇒ Na+- Glucose Co-transport
Na+- Amino Acid Co-transport

In Distal ileum ⇒ Na+- Bile salt Co-transport

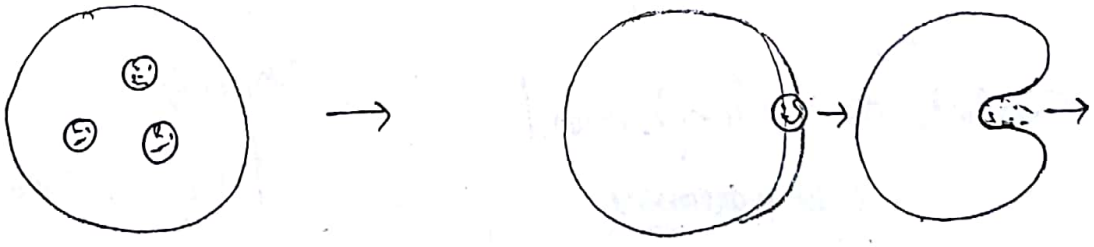
In Thyroid ⇒ NIS (Na+- Iodide Symport)

COUNTER TRANSPORT :→

- In PCT :→ $Na^+ - H^+$
- In Myocardial cell :→ $Na^+ - Ca^{+2}$

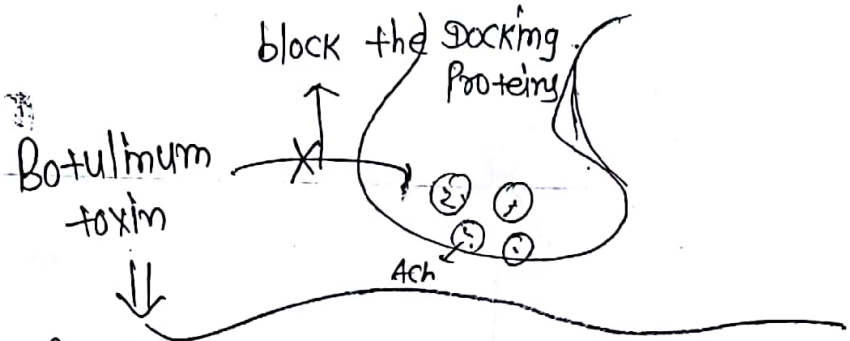


EXOCYTOSIS



- Yes Total Area of cell Membrane
- We Need ⇒ Ca^{+2}
  ATP
  Docking Proteins

- Docking Proteins
  - Syntaxin / T-SNARE Protein
  - Synaptobrevin / V-SNARE Protein
  - SNAP-25



- 2 Pathways of Exocytosis

Non-constitutive OR Regulated Pathway
⇓
Synthesis of Enzyme/hormone/Neurotransmitter
⇓ blb
Processing
⇓ blb
Storage ⇒ blb ⇒ Release
Mast imb. Steb

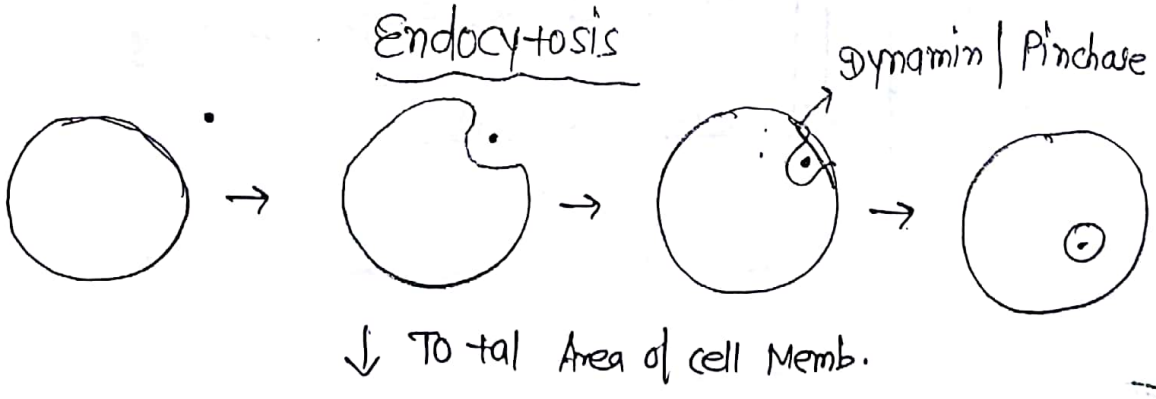
Constitutive Pathway.
↳ also Regulated Pathway
⇓
Synthesis
↓ blb; No storage
Release

eg of Non-constituted Pathway :→

- Secretion of Insulin by β-cells
- Secretion of Glucagon by α-cells
- Secretion of Ach at NMJ;
- Secretion of selotonin by Raphe Magnus Nucleus cells
- Secretion of Enzyme by Pancreatic Acinal cells.

eg of constituted Pathway :→

- Immunoglobuling by plasma cells
- Collagen by fibroblasts

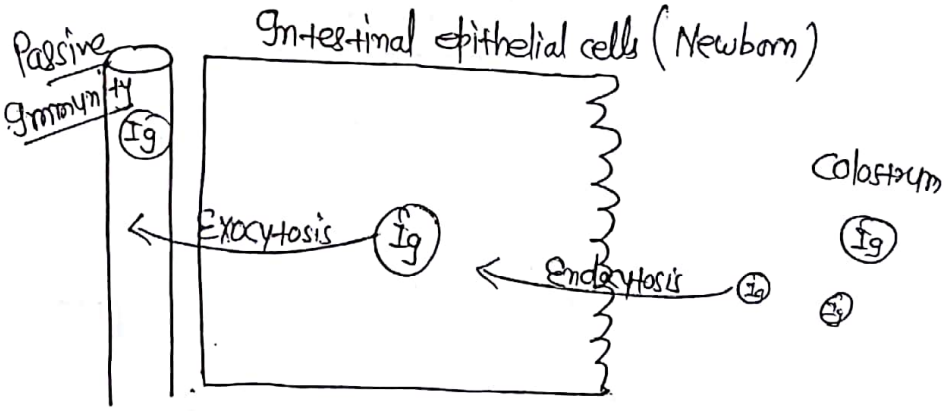


↓ Total Area of cell Memb.

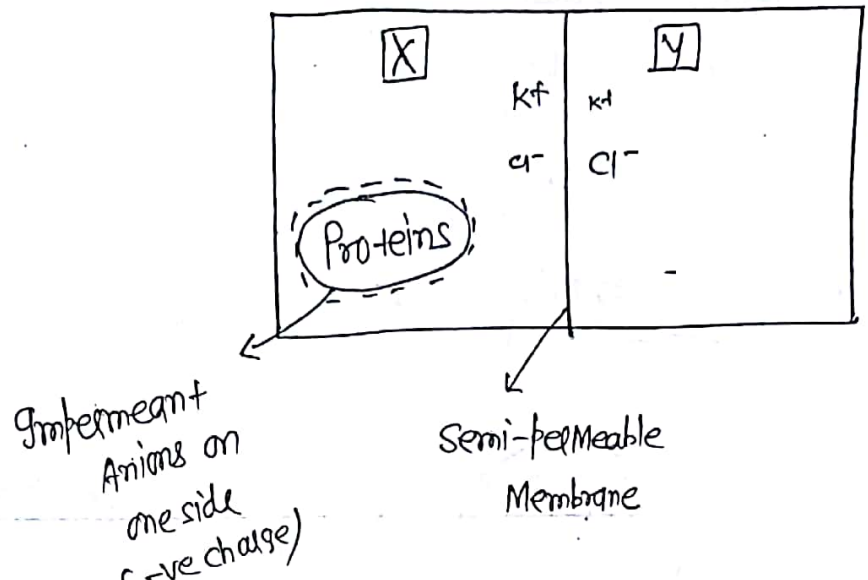
⇒ Endocytosis & Exocytosis occur simultaneously; Never alone so; cell Membrane size = Constant.

- Ca^{+2}
- ATP
- clathrin — Receptor Mediated Endocytosis
- caveolin — ⊕ In Endothelial cells
  - For Absorption of Nutrients
- Dynamin/ Pinchase

TRANSCYTOSIS / CYTOPEMPSIS



DONNAN EFFECT ⇒ Seen on diffusible ion ↓ Cl^- & K^+



At eqm ⇒ [K+] in [X] > [K+] in [Y]

Cl^- in [Y] > [Cl] in X

Result ⇒ i) Unequal distribution of diffusible ion @ eqm;

ii) More No. of osmotically active particles on one side.

Where to see ⇒ b/w Intracellular & Extracellular compartment

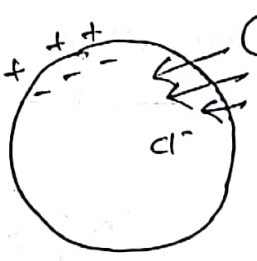
– seen b/w Intravascular & Extravascular compartment

Gibbs – Donnan eqm ⇒ At eqm

$$\frac{[K^+_X]}{[K^+_Y]} = \frac{[Cl^-_Y]}{[Cl^-_X]}$$

$$\Rightarrow \underbrace{[K^+_x]\,[Cl^-_x]}_{\text{Products of diffusible ion on one side}} = \underbrace{[K^+_y]\,[Cl^-_y]}_{\text{Products of diffusible ion on other side}}$$

* **NERNST Equation** :⇒



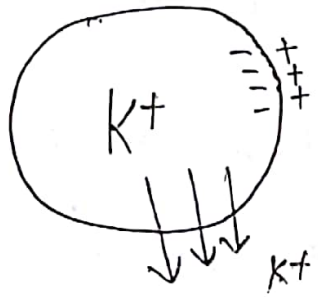
if cell Memb. is free Permeable to chloride

⇓

At a time ⊖ve charges inside the cell Repels Cl⁻ & stop Movement

⇓

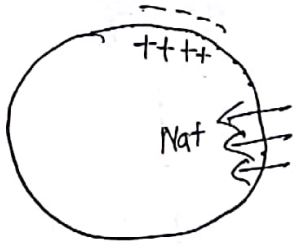
eqm potential. (⊖ve)



At a time ⊖ve charges Inside (Made by K+) cell attracts K+ & stop Movement

⇓

eqm potential (⊖ve)



At a time ⊖ve charges Inside cell Repel Na+ & stop Movement

⇓

eqm potential (⊖ve)

• If the cell Membrane becomes freely permeable to ion

↓

Magnitude of potential difference for that ion at eqm is called "eqm potential / Nernst Potential". It can be calculated by Nernst eqn :-

(There is No change in concⁿ of ion @ eqm).

$$E_{(mV)} = 2.3 \frac{RT}{FZ} \log \frac{C_1}{C_2}$$

R = Gas constant

T = Absolute temp.

F = Faraday constant

Z = valency

At 37°C;

$$2.3 \frac{RT}{F} = 61.5$$

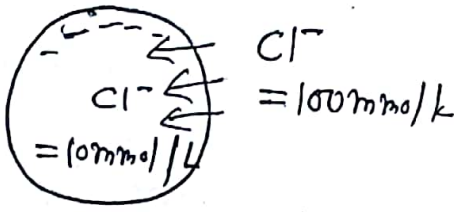
**

$$E_{(mV)} = \frac{61.5}{Z} \log \frac{C_1}{C_2}$$

Q9.

$2.3 \frac{RT}{F} = 60mv$

$E_{Cl^-} = ?$



2 steps Method

i) calculate the potential

ii) Decide sign

$E_{Cl^-} = \frac{2.3RT}{FZ} \log \frac{C_1}{C_2}$

$= \frac{60}{1} \times \log \frac{100}{10} = \frac{60}{1} = 60$

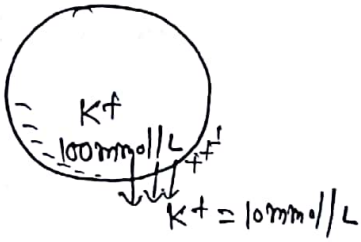
$= -60mv$

Q10

$2.3 \frac{RT}{F} = 60mv$

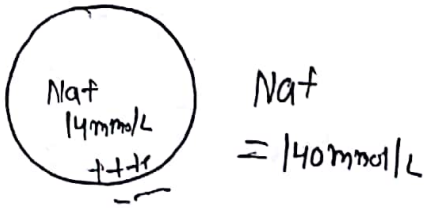
$E_{K+} = ??$

$E_{K+} = -60mv$



Q11

$E_{Na+} = +60mv.$



QQ $\frac{2.3RT}{F} = 60mV$

$E_{Ca^{+2}}$ in X w.r.t Y

X	Y
$CaCl_2$	$CaCl_2$
10mmol/L	100mmol/L
	Ca^{+2} freely permeable @ here

$\frac{2.3RT}{FXZ} \log \frac{C_1}{C_2} \Rightarrow \frac{60}{2} \log 10.$

$= +30mV.$

* (N) Value of Eqm potential ⇒

$E_{K+} = -90mV$

$E_{Cl^-} = -70mV$

$E_{Mg^{+2}} = 0mV$

$E_{Na+} = +61mV$

$E_{Ca^{+2}} = +125mV$

Resting Membrane potential

- GOLDMAN HODGKIN KATZ eqn / OR / Constant field eqn → · Concn gradient of 3 ions (Na^+; K^+; Cl^-) · Cell Membrane permeability.

$$RMP = -61.5 \log \frac{C_{Cl^-_o} \times P_{Cl^-} + C_{K+_i} \times P_{K+} + C_{Na+_i} \times P_{Na+}}{C_{Cl^-_i} \times P_{Cl^-} + C_{K+_o} \times P_{K+} + C_{Na+_o} \times P_{Na+}}$$

At Rest; $P_{K+} >>>> P_{Cl-} > P_{Na+}$

QQ
- Which ion contribute Maxim to RMP
- Most diffusible ion @ Rest
- Cell Membrane is most permeable to which ion @ Rest

} $K+$

QQ
Tes Extracellular $Na+$ effect on RMP ??

a) More ⊖ve

b) Less ⊖ve

c) ~~Same~~

*

		RMP
Most Neurons	⇒	−70mv
Large Motor Neurons	⇒	−90mv
Skeletal Muscles	⇒	−90mv
Cardiac Muscles	⇒	−90mv
PaceMaker Cells	⇒	−50 to −60 mv
Smooth Muscle cells	⇒	−45 to −65mv
Hair cells (cochlea)	⇒	−65 mv
Rods & cones	⇒	−40 mv
RBCs	⇒	−10mv

* RBC Membrane @ Rest
↳ $P_{Cl-} > P_{K+}$

P_{Cl} = Permeability of $Cl-$
P_{K+} = Permeability of $K+$

Q9. Effect of hypokalemia on RMP ⇒

↓ K+

↓

↑ conc^{n} gradient for K+

↓

↑ tendency of K+ to leave cell
(↑ diffusion potential of K+)

↓

Inside becomes More -ve w.r.t outside

↓

K/as "Hyperpolarization"

↖ Yes in potential
↓ es in excitability.

K+
140 mmol/L

K+
(3.5 - 5.0 mmol/L)

140 - 5 = 135
140 - 2 = 138

Symptoms ⇒ ① Muscle weakness (M/c symptom)

Q9 Effect of hyperkalemia on RMP ⇒

↑ K+

↓

↓es conc^{n} gradient of K+

↓

K+
140 mmol/L

K+ 10.0
3.5 - 7.0 mmol/L

conc^{n} gradient = 140 - 5.0 = 135
= 140 - 10.0 = 130

↓

↓es tendency of K+ to leave the cell

↓

↓es Diffusion potential of K+

↓

Inside becomes Less ⊖ve w.r.t. outside

↓

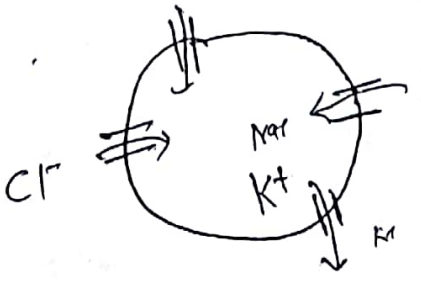
K/a "Depolarization"

↳ ↓es Polarization

↑es excitability

M/c symptom ⇒ Arrythmia

* CHANNELS → Voltage gated channels
→ Ligand Gated channels
→ Mechano Sensitive channels
Ca^{+2} → Phosphorylation



via channels ions comes only according to their Conc^n gradient.

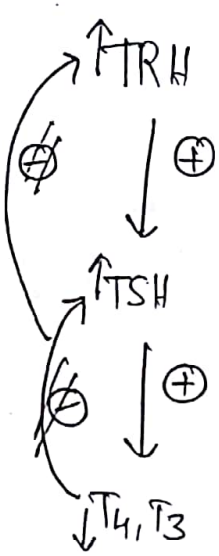
- Dimer → Cl^- channels (In bacteria, Animals)
- Trimer → ENaC
  α, β, γ
  ↙
  transport Na^+.
- Tetramer → K^+ channel 

  Aquaporin 
- Pentamer → Cl^- channel (In humans)
  Ligand gated channel (Ach Receptors)

FEEDBACK MECHANISM

Negative

- Most control system function as Negative feedback Mechⁿ.
- Stabiliging Mechⁿ.



Positive

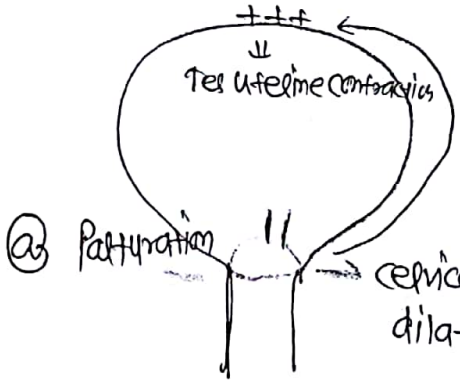
- eg ⇒ C = clotting ;
  Ca^{+2} Release from Sarcoplasmic Reticulum during Muscle contraction.

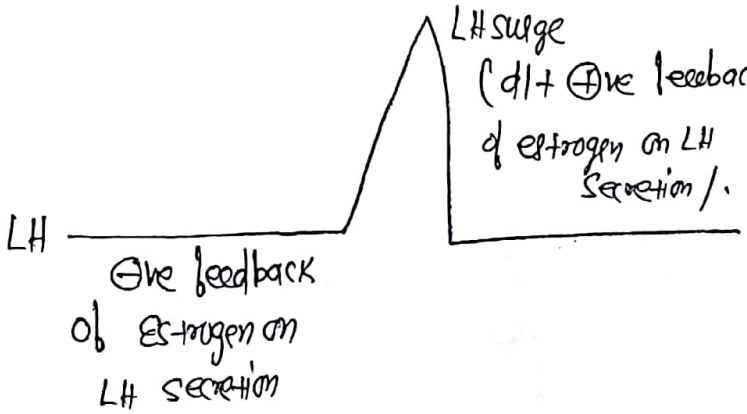
L = LH surge

A = Action Potential

P = Parturation

S = Shock

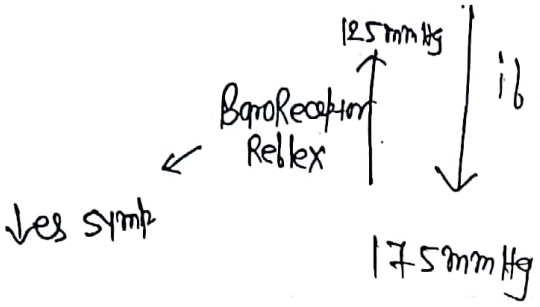




* Gain of the feedback system :⇒

Gain ⇒ correction over Error is gain. = $\frac{\text{correction}}{\text{Error}}$

(Q9) (N) Mean Arterial Pressure ⇒ 100 mm Hg



⇒ Correction = 50 mm of Hg.
Error = 25 mm of Hg

Gain = $\frac{50}{25}$ 2 = 2

(Q8) (N) MAP

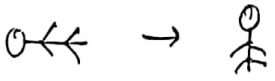
100 mm Hg —— Hemorrhage ——→ 70 mm Hg

90 mm Hg ←—— BR Reflex
Tes symp.

Gain = $\frac{20}{10}$ = 2

* Baroreceptor control Mech^m — Temp. control system

Gain 2 — (33)

Q10  ↓ in his BP by 10 mm of Hg;
Baroreceptor ↑ his B.P by 8 mm Hg

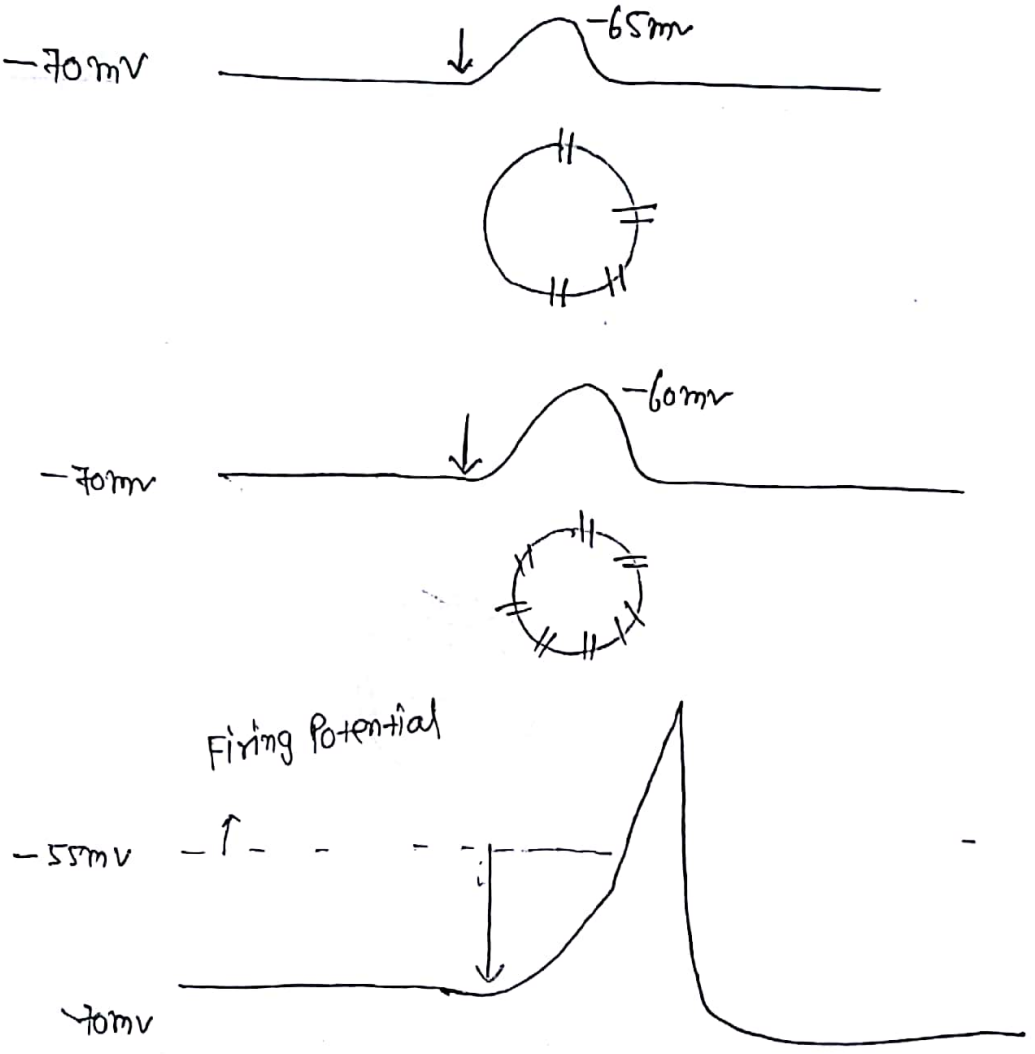
Gain ⇒ 4 = $\frac{8}{2}$ = 4.

FEED FORWARD MECHANISM ⇒ K/a "Adaptative control"

↳ Seen in control of Motor activity

NERVE PHYSIOLOGY

Local Potential & Action Potential :→



Local potential

- Graded Response
- By Sub-threshold Stimuli
- Decremental changage
  - Yes over time & place.
- Not self propagated
- May/Maynt followed by Some action.
- Depolarising / Hyperpolarising
  - ⇓ EPSP
  - ⇓ IPSP (Inhibitory Post-Synaptic Potential).
- Summation ⊕
  - SPATIAL
    - ↓ over space
    - No. of Sub-threshold Stimuli given simultaneously ⇓ Produce Action potential
  - TEMPORAL
    - ↓ over time
    - ↑ frequency of Sub-threshold Stimuli ⇒ Produce Action potential

Action potential

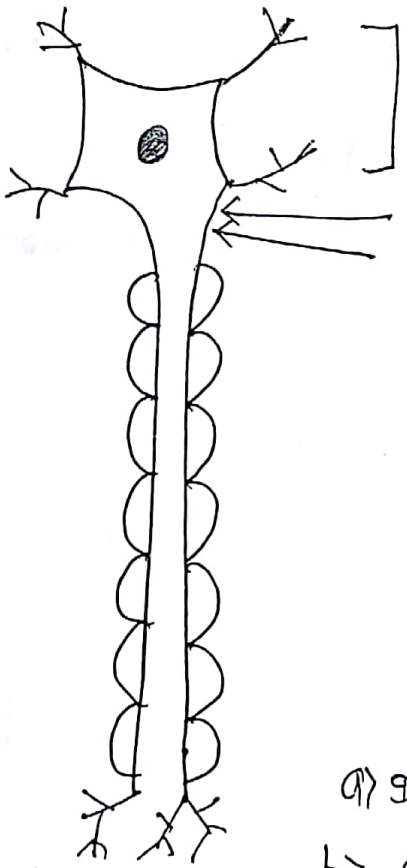
- All-or-None Response
- by threshold or supra-threshold stimuli
- travel ✗ decrement
- Self propagated
- followed by Same action
- Always depolarizing.
- Summation ⊖

LOCAL POTENTIAL

ACTION POTENTIAL

eg ⇒ . EPSP ;
. IPSP ;
. Receptor potential ;
(Generator potential)
. Motor end plate potential
(At NMJ)

* Site of genelation of Action potential :⇒



SOMA Dendritic zone QQ
(Graded electrogenesis)

Axon hillock (Part of cell body) Very high conc^n of Na+ channel/unit Area
Initial segment

QQ. Site of genelation of Action Potential in Spinal Motor Neuron

a) Dendrites
b) Soma
c) Axon hillock
d) Axon

a) Dendrites
b) Soma
c) A-H
d) Initial segment.

* Initial Segment can generate Action potential b/c of
  - ↳ very high conc^n of Nat channel / unit area

QQ Conc^n of Nat channel / unit Area

Nodes of Ranvier ⇒ 2,000 - 12,000 / sq Micrometers

Initial Segment ⇒ 500 / $(\mu m)^2$

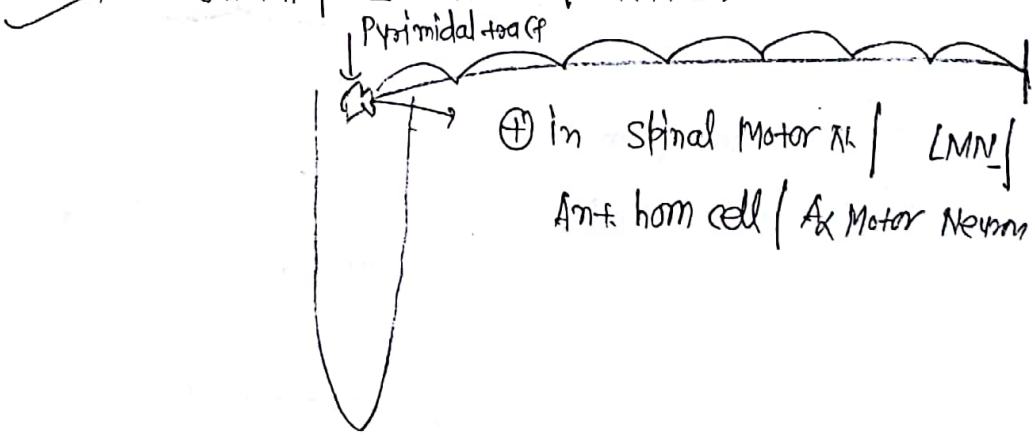
Sulface of Myelin ⇒ 25 / $(\mu m)^2$

↙

Least

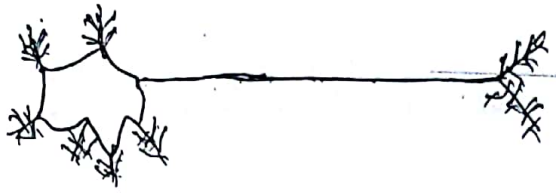
QQ Site of Generation of Action potential in Sensory Neuron :

i) Soma
ii) Dendrites
iii) Initial segments
iv) Initial / 1st Node of Ranvier

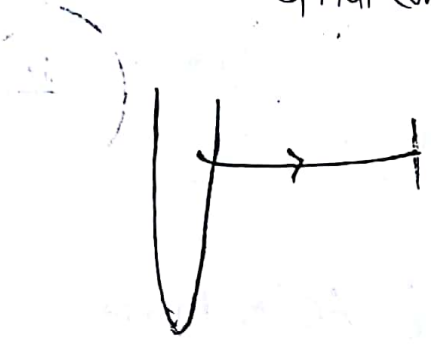


* Spinal Motor Neuron

- Multipolar Neuron



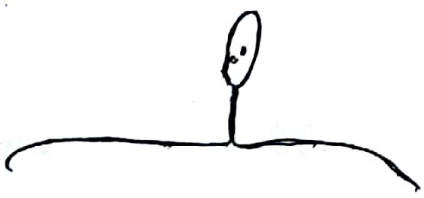
- Cell body – Anti Horn of Spinal cord



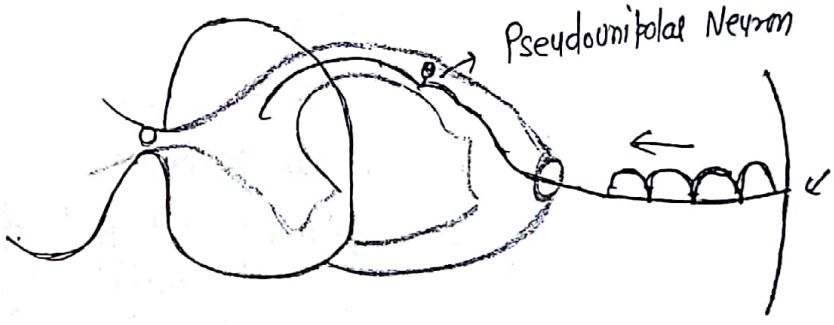
- Carry impulses from Spinal cord to Periphery

1st order sensory Neuron

- Pseudounipolar Neuron

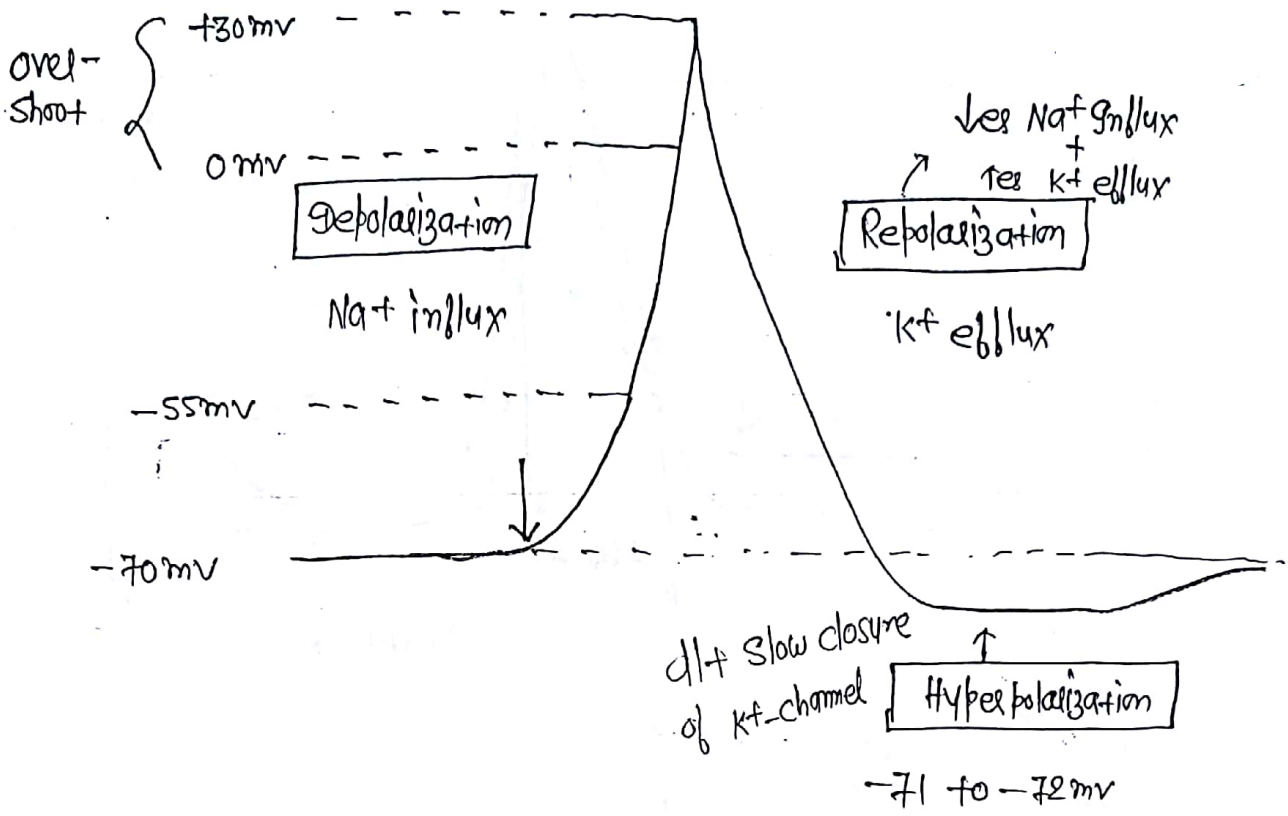


Dorsal Root Ganglion



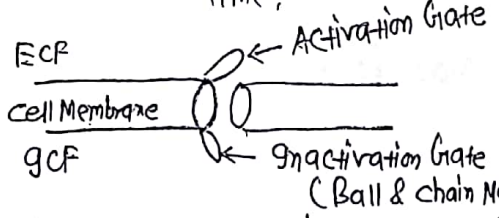
- Carry impulses from Periphery to Spinal cord.

* Phases of Action potential :⇒



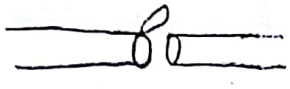
Na+ channels

- Fast channels
- -70 to +30mv
- closure is dependent on time:



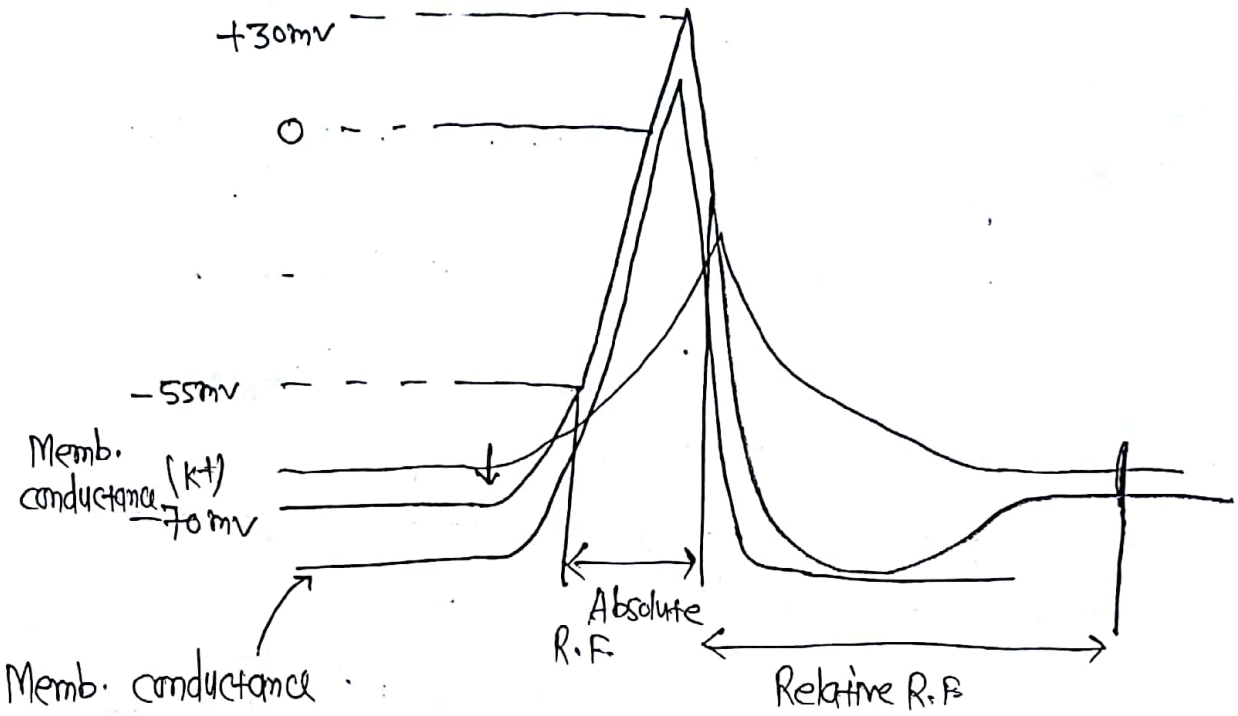
K+ channels

- Slow channels
- -70 to +30mv
- closure is dependent on time



* Membrane conductance for Na+ & K+ during Action potential

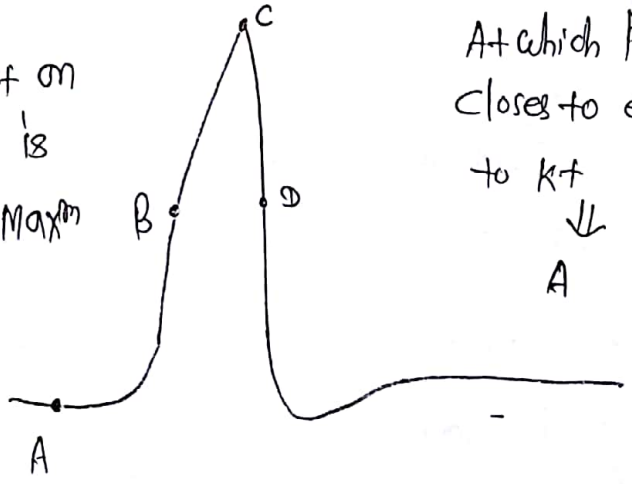
↳



QQ. At which point on Action potential is Memb. conductance Maxm for Sodium

⇓

C



At which point on A.P. closes to equilibrium potential to K+

⇓

A

At which point Memb. conductance Maxm for K+

⇓

D

At which point on A.P. closer to E_{Na^+} (equilibrium potential of Na+)

⇓

C

REFRACTORY PERIOD

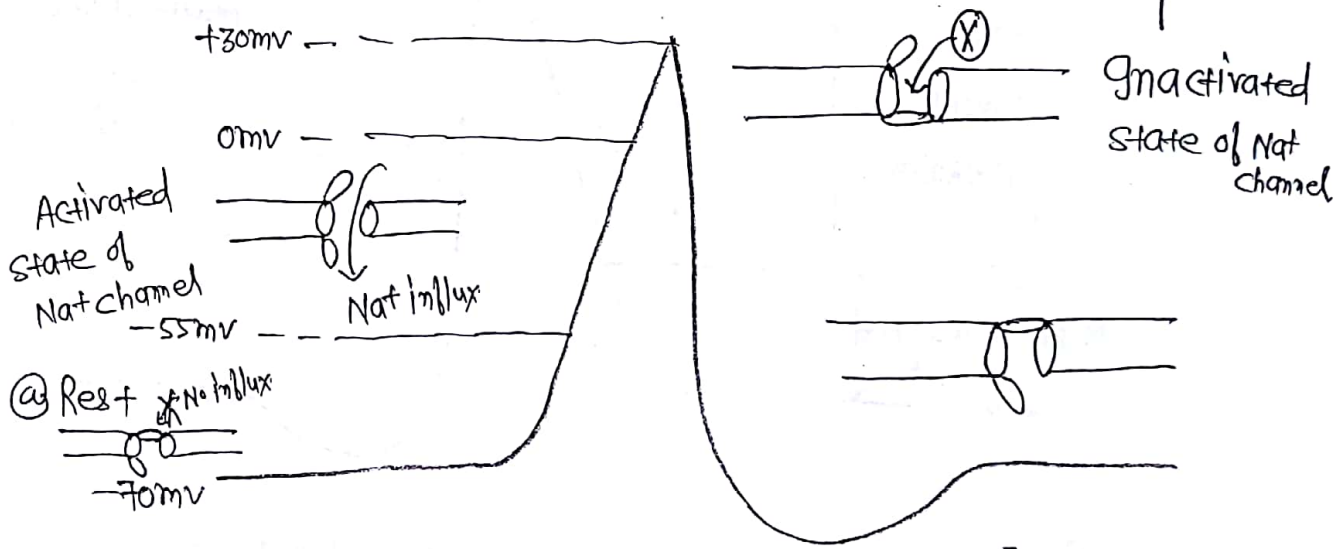
Absolute Refractory Period

From firing level till Repolarization is 1/3rd complete

It is Responsible for Absolute Refractory Period

Relative Refractory Period

From 1/3rd Repolarization till End of hyperpolarization



*

Hyperkalemia

Mild – Moderate hyperkalemia

↓

Depolarization

↓

↑ excitability

↓

Arrythmia

Severe Hyperkalemia

↓

Persistant Depolarization State

↓

↕ excitability (blc of Inactivated Na+ channel)

↓

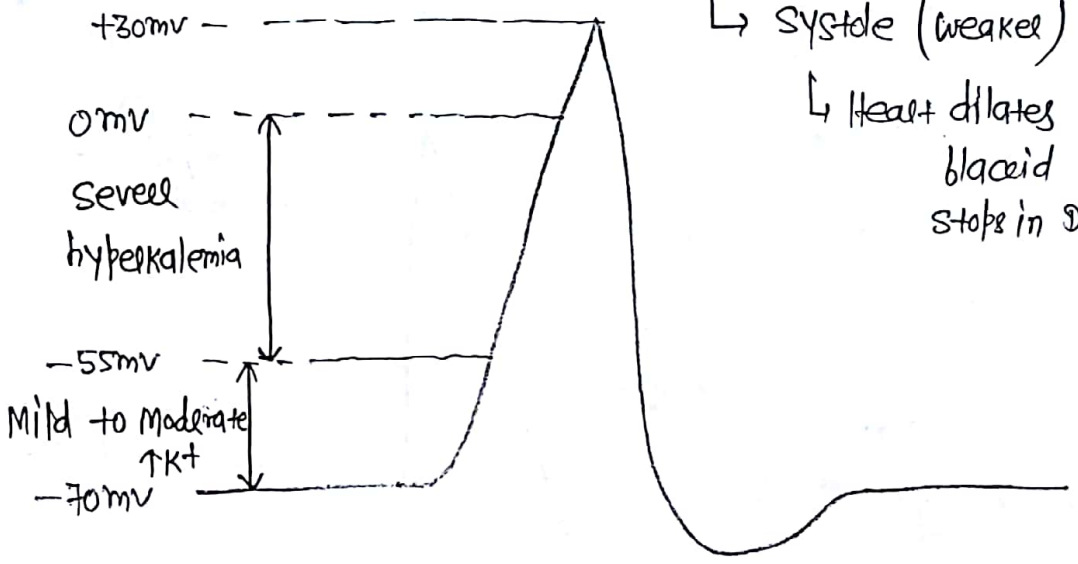
↓ contractility

↳ systole (weaker)

↳ Heart dilates

flaccid

stops in Diastole



QQ. Neuron is least excitable during :-

a) Depolarization

b) Repolarization

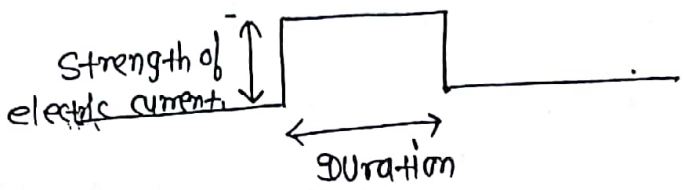
c) Hyperpolarization

In hypercalcemia ⇒ Heart stops in systole (calcium Rigor)

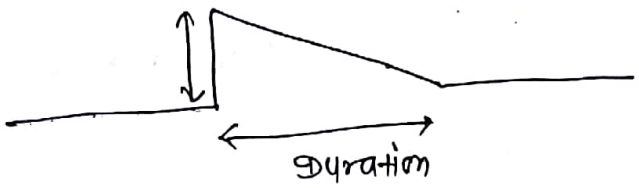
ACCOMODATION

– It is slowly Rising Subthreshold stimulus ; fails to produce a Response.
↳ electric current.

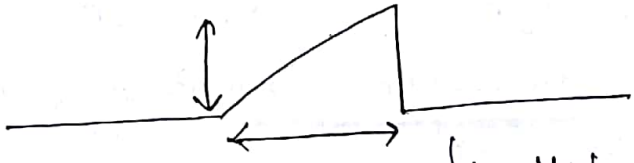
A)



B)



C)

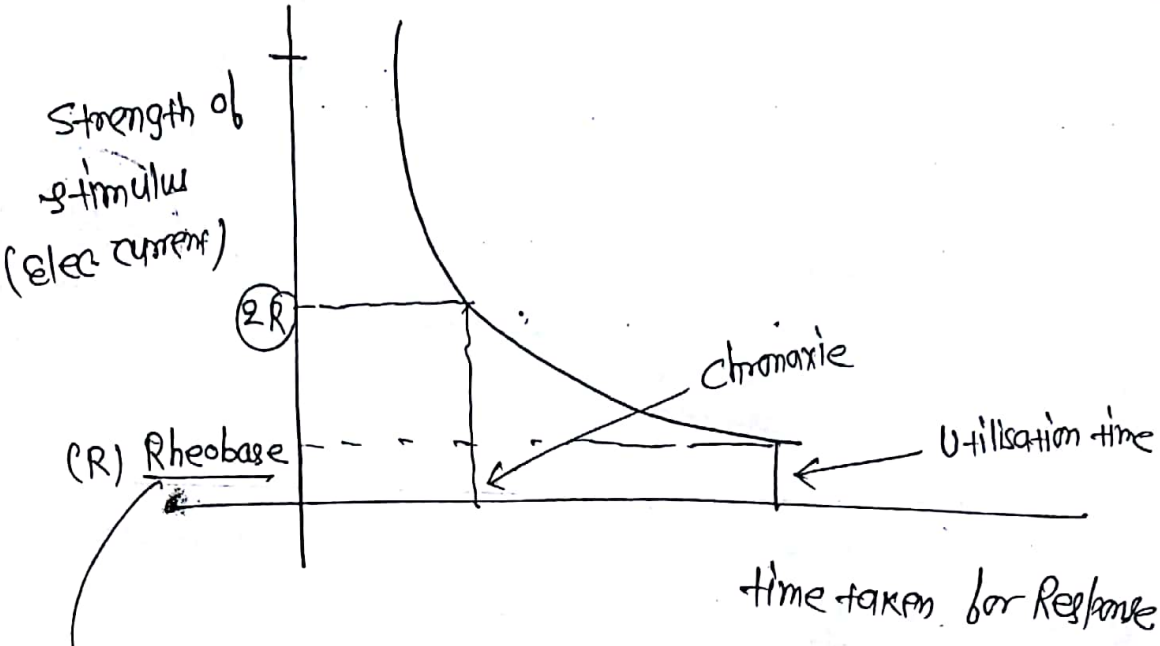


Least Likely to Reproduce Response

Slowly Rising.

↳ Nat channel open & Kt also open
⇓
b/c time taken to open; it has

STRENGTH - DURATION CURVE



→ Minm strength of stimulus (E. current) ≤ when applied for a prolonged | Not defined Period of time; produces a Response

(2) Utilisation time ⇒ Time taken by Rheobase current to produces a Response.

chronaxie ⇒ Time taken by a current ; which is twice the Rheobase

** {Lessel the Chronaxie ⇒ More excitable tissue}

$Chronaxie_{(Nerve)} < Chronaxie_{(SK.\ Muscle)}$

- Nerve libres ⇒ (A) (B) (C)

$chr_A < chr_B < chr_C$

↑ Diameter
↑ Surface Area
↑ No. of Nat channel
↓ time taken for Response

* Chronaxie $_{\text{Skeletal Muscle}}$ < Chronaxie $_{\text{C.M.}}$ < Chronaxie $_{\text{Smooth Muscle}}$

QQ. After N. injury ⇒ Yes Chronaxie

but as Regeneration begins ⇒ Yes Chronaxie

* After N. injury → Strength–duration curve done in Regular intervals

* FACTOR AFFECTING VELOCITY OF CONDUCTION OF N. IMPULSE

① Diameter ⇒ Large diameter

⇓

↑ Surface area

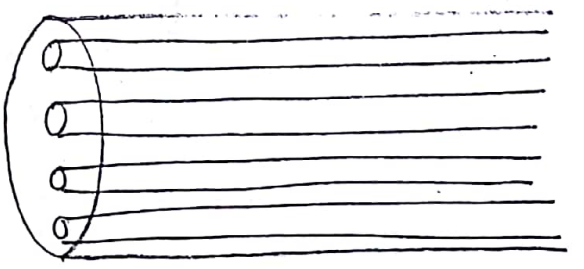
⇓

↑ No. of Na+ channel

⇓

Yes Velocity.

$$\frac{1}{R} = \frac{1}{R_1} + \frac{1}{R_2} + \frac{1}{R_3} + \dots$$



↑ Diameter ⇒ ↓ Axoplasmic Resistance (R_A or Rin)

↓

↑ Velocity of conduction

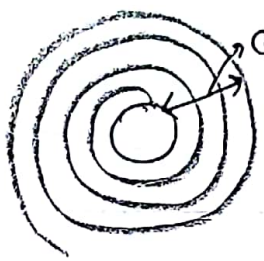
Q. Large diameter N. fiber has

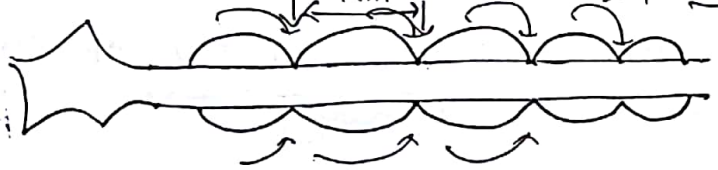
a) ~~Low R_A~~ (→ ∴ Fast velocity)

b) High R_A

② Myelin ⇒ • Lipid Rich ;

• Insulators. like work





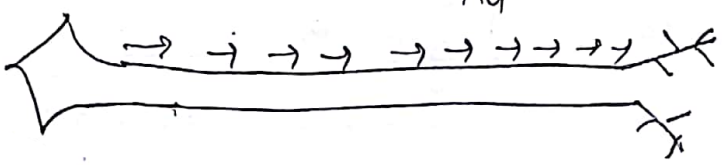
Saltatory conduction

Myelin Nerve → high Memb. Resistance (R_A)

↳ it Fast velocity of conduction.

QQ A Large diameter ; Myelina N. fiber has Low R_a ; high $\frac{R_M}{4}$ Membrane Resistance

QQ Fastest velocity ⊕ in N. fiber has High $\frac{Rm}{Ra}$ Ratio.



Unmyelinated N. fibre

⇓

Less Resistance, but velocity Less as compare to Myelinated N. fibre

* Small diameter always Unmyelinated.

(3) Membrane capacitance ⇒

- Cell Membrane ⟶ High capacitance
  - Lipid bilayer
    - Acts as Parallel plate capacitor
  - + Myelin
    - ↑ Res Memb. Resistance
    - ↓ Ves Memb. capacitance

QQ. Large diameter ; Myelin N. fiber has Low R_A ; High R_M ; Low capacitance

QQ Fastest velocity ⊕ in N. fiber ∵ High Resistance (R_M) Low capacitance

if Nothing in question takes R_M ⇒ Resistance

QQ Nodes
- Low Resistance (R_M) ; High capacitance

CLASSIFICATION OF NERVE FIBERS

ERLANGER & GASSER CLASSIFICATION

- It is for Sensory, Motor; Autonomic kind of Neurons

A
- A — A_α
  - A_β
  - A_γ
  - A_δ

(↓ Diameter, ↓ velocity)

B — B

C — C = Unmyelinated

A, B = Myelinated.

A_α = Somatic Motor ----------> No Number given

Proprioception (Fastest Sensory conduction) ----> I

- I_a ((Sensory fibres from Muscle spindle)
- I_b (Sensory fibres from Golgi tendon organ).

A_β = Purely Sensory fibres

↳ for Fine touch; Vibration
Proprioception (for Muscle spindle)
Deep pressure (PO KINa) } ---- II

A_γ = Motor fibres to Muscle spindle ---------- No Number given

LLYOD & HUNT'S CLASSIFICATION

- It is for Sensory Neurons
- Numerical classification

Aδ = Fast Pain, Temperature (cold) } — III
Somatic Mechanoreceptors

B = Pre ganglionic Auto. — No Number given

C = Post ganglionic Sympathetic — No Number given

↳ Crude touch, Pressure, Slow pain, Temp (cold & warmth); ITCH; Tickle — IV

Total No. of Neurons = 100 Billion Neurons
⇓
Glial cells >>>> Neurons

- % of Human genes code for CNS = 40 %
- Unmyelinated = Type IV
- Most Numerous = C
- Fine touch = Aβ
- Crude touch = C
- Pressure = C
- Deep pressure = Aβ
- Vibration = Aβ
- Slow pain = C
- Fast Pain = Aδ
- cold = Aδ & C
- warm = C

Afferent from Muscle spindle
⇓
Ia, II

Afferent from Golgi tendon organ
⇓
Ib

Motor to Extrafusal Muscle fibers
⇓
Aα

Motor to Intrafusal Muscle fibers
⇓
Aγ

SUSCEPTIBILITY

PRESSURE ⇒ A > B > C

↙

A_α is More Susceptible (Saturday Night Palsy OR Sunday Morning Palsy)

HYPOXIA ⇒ B > A > C

LOCAL ANESTHESIA ⇒ C > B > A X

B > C > A X

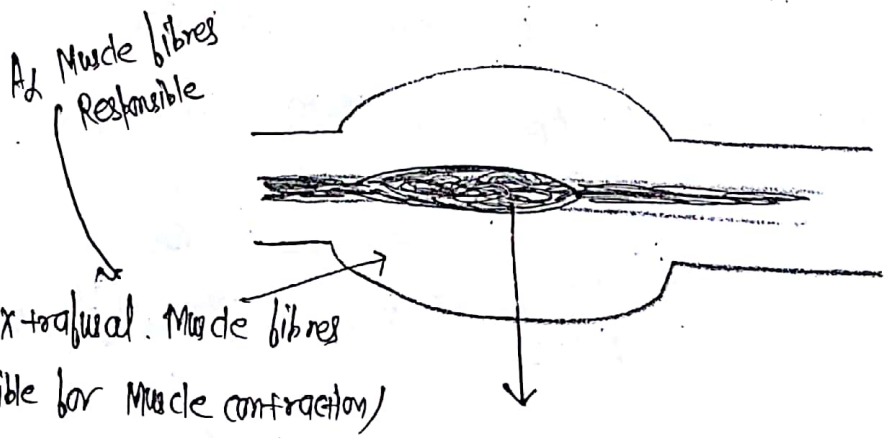
$A_\gamma > A_\delta = A_\beta > A_\alpha > B > C$ (AIIMS Nov 19)

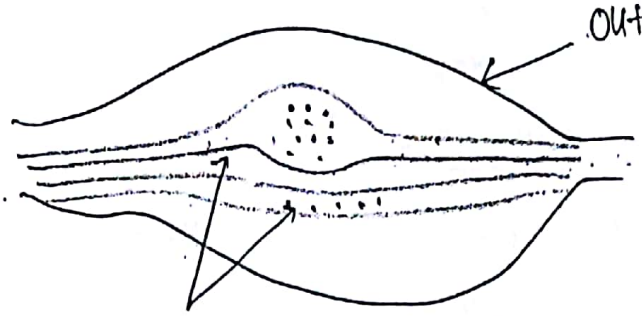
↓ Most Susceptible

↳ Least Susceptible

MUSCLE SPINDLE

- Receptor for Muscle Length (Stretch)





Intrafusal Muscle fibers (5-6 in No.)

Nucleal Bag (1-3)

Nucleal chain (4-5 in No.)

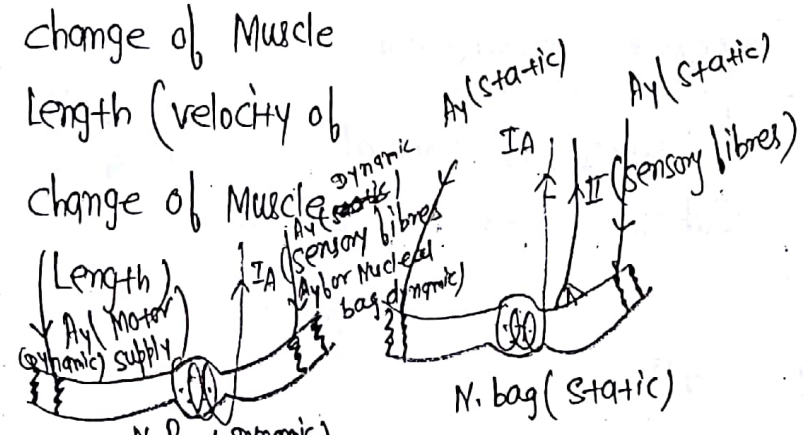
Nucleal Bag (Dynamic)

Nucleal Bag (Static)

Means for N. chain (Static Response)

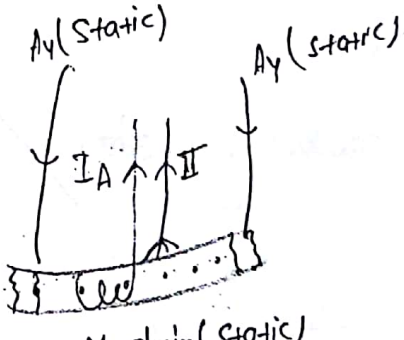
Detects Rate of change of Muscle Length (velocity of change of Muscle Length)

Detect Steady Length.



IA → Klas → Annulospinal Ending

II ⇒ Flower Spray Ending



* Muscle spindle can be stimulated in 2 ways :-

i> ↑ Length of Muscle (Stretch)

⇓

Stimulate Muscle spindle

ii> ↑ Ay Motor Neuron discharge

⇓

causes Contraction of Ends of Intrafusal Muscle fibers

⇓

Stretches Receptor portion of Intrafusal Muscle fibers.

⇓

↑ Firing Rate

(Stimulate Muscle spindle).

AXOPLASMIC TRANSPORT

↳ Refers to Physical transport of Substance through Axoplasm

conduction of Action Potential

⇓

Ele.

↳ We Need. Ca^{+2}

ATP

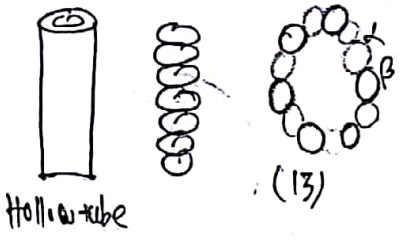
Microtubules

↳ Hollow tube

↳ Made of tubulins — α — β

Anterograde transport. ↓

↑ Retrograde transport



Microtubules ⇒ 2 Ends

"+" ⇓ Assembly end

"−" ⇓ Disassembly End.

↳ ↑. Serve as "Tracks".

Microfilaments ⇒ Solid tubes
(Sometimes serve as "Tracks")

Molecular Motors ⇒ Kinesin
Dyenin
Myosin V

Types of Axoplasmic transport

Fast

- Antelograde
  - ↳ 400 mm/day
  - towards "+" end
  - Requires Kinesin ; Myosin V
  - Transport ⇒ Neuropeptide; Vesicles; Mitochondria; Reticulum ; Lysosomes
- Retrograde
  - ↳ 200 mm/day
  - towards "−" end
  - Dyenin
  - Transport ⇒ Neurotropic virus (Rabies virus), Tetanus toxins, Nerve growth factors

Slow always Antelograde
0.5 to 10 mm/day

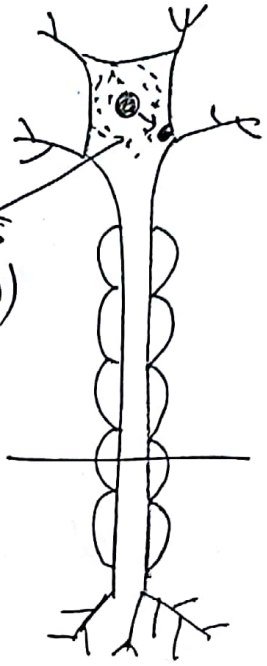
Q9 Neurofilaments doesn't Require for Axoplasmic transport.

WALLERIAN DEGENERATION

- Seddon's classification of Nerve Injuries :-

		Degeneration	Regeneration
NEUROPRAXIA	⇒ Temporary loss of Function	−	−
AXONTEMESIS	⇒ Neurilemma is Intact	+	+
NEURONTEMESIS	⇒ Neurilemma is destroyed	+	−

WALLERIAN DEGENERATION



Change in cell body

⇒ early 24–48 hrs

↳ Chromatolysis

Nucleus Moves to Periphery

Change in Distal segment

Within few hours of injury

↳ Swelling of Axis cylinder

on 3–5 days

↳ Axonal degeneration

8th day

↳ Myelin Degeneration starts

32nd day

↳ Myelin Degeneration complete

* Similar changes in Proximal segment but upto Nearest Node of Ranvier

QQ 1st change after N. injury ⇒

~~a)~~ Chromatolysis
b) Axonal deg.

a) Chromatolysis
~~b)~~ Axonal degeneration starts (Swelling)

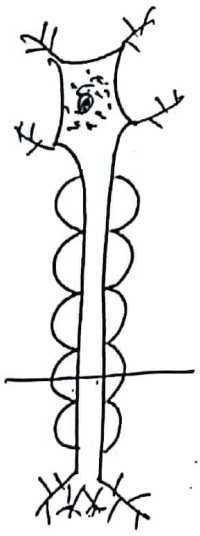
#

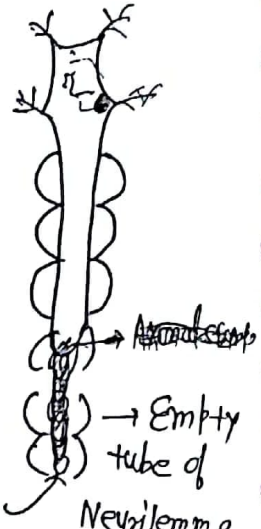
Sequence of events after Axonal injury :-

Chromatolysis → Axonal degeneration

↓

Ghost tube ← Myelin degeneration

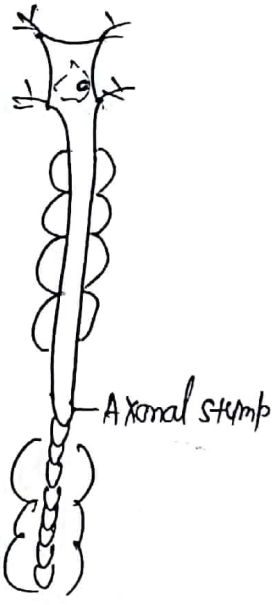




Macrophage

↓

Ghost tube



Regeneration :⇒

Sprouting of Axonal stump

↓

Enters into Ghost tube

↓

Myelin is Laid Down

In Sheets

- Rate of Regeneration

↓

1mm/day or 1inch/Month.

⇒ Regeneration usually complete by 1 year

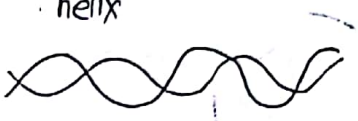
SKELETAL MUSCLE PHYSIOLOGY

- Skeletal Muscle
  - Voluntary
  - Striated

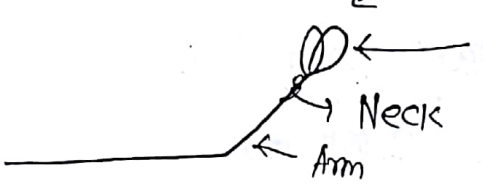
They have :-

① CONTRACTILE PROTEINS :-

- ACTIN — 2 Strands of Actin in double helix

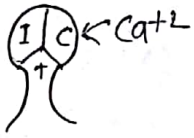


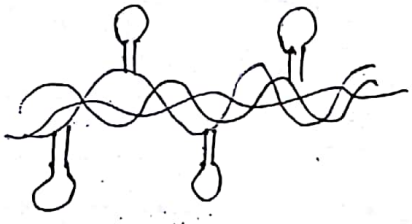
- MYOSIN



② Regulating proteins :-

- Tropomyosin → 1 Molecules of Tropomyosin covers 7 Active Site of Actin
- Troponin
  - Globular protein ⇒





↓ after Ca^{+2} attaches to Tropomyosin-C

Conformational change in Troponin

↓

causes Tropomyosin to slide

↓

Result in Active Sites on Actin

↓

Actin–Myosin cross bridge formation & cross bridge cycling

③ Structural Protein ⇒

↳ Actinin ⇒ binds actin to Z-Line

Titin ⇒ binds Z-Line to M-Line

↳ Responsible for Elasticity

↳ Forms "Scaffolding" (Structural Support)

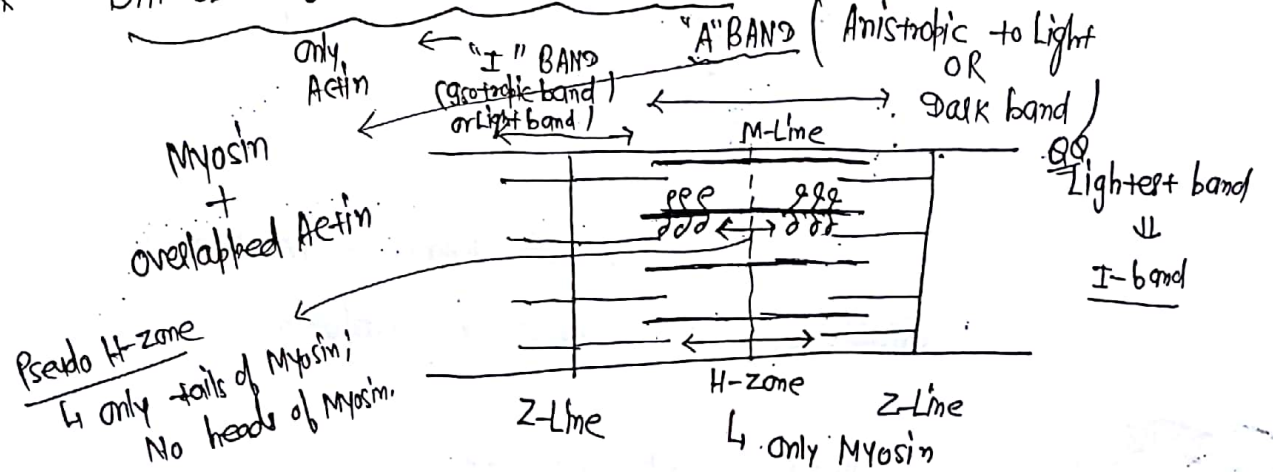
↳ Largest known Protein

$M_w \approx 3,000,000$

Mutation in Titin ⇒ Tibialis Muscular dystrophy

Desmin ⇒ Binds Z-Line to Plasma Membrane

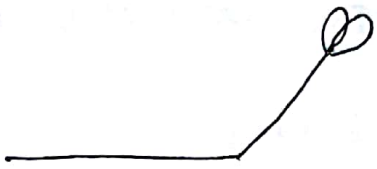
* BANDS ON SKELETAL MUSCLE :→

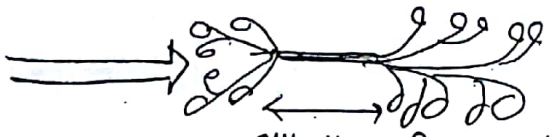


SARCOMERE ⇒ $\frac{1}{2}$ I-Band + A-band + $\frac{1}{2}$ A-band

M-Line ⇒ Connect Myosin Molecules to each other

*





ONLY MYOSIN (A BIS); No head

Thick filament ⊖

⇓

"Bunch of Golf Sticks"

B/w two Z-Line = Sarcomere.

* Pseudo H-Zone ⇒ Formed by Reversal of Polarity of Myosin heads.

* During Muscle contraction ⇒ The I-band ↓es

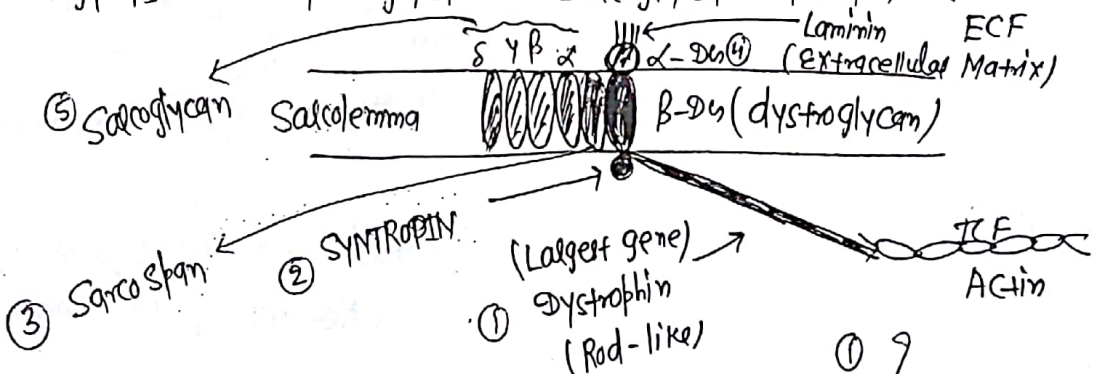
H-Zone = ↓es | disappears

(QQ) A-band = UNCHANGED

SARCOLEMMAL PROTEINS

Muscle fiber = Muscle cell

* It is "Dystroglycan – Sarcoglycan" Complex.



① ② ③ ④ ⑤ ⇒ all are Sarcolemmal protein

⇓

Laminin is Not Sarcolemmal protein

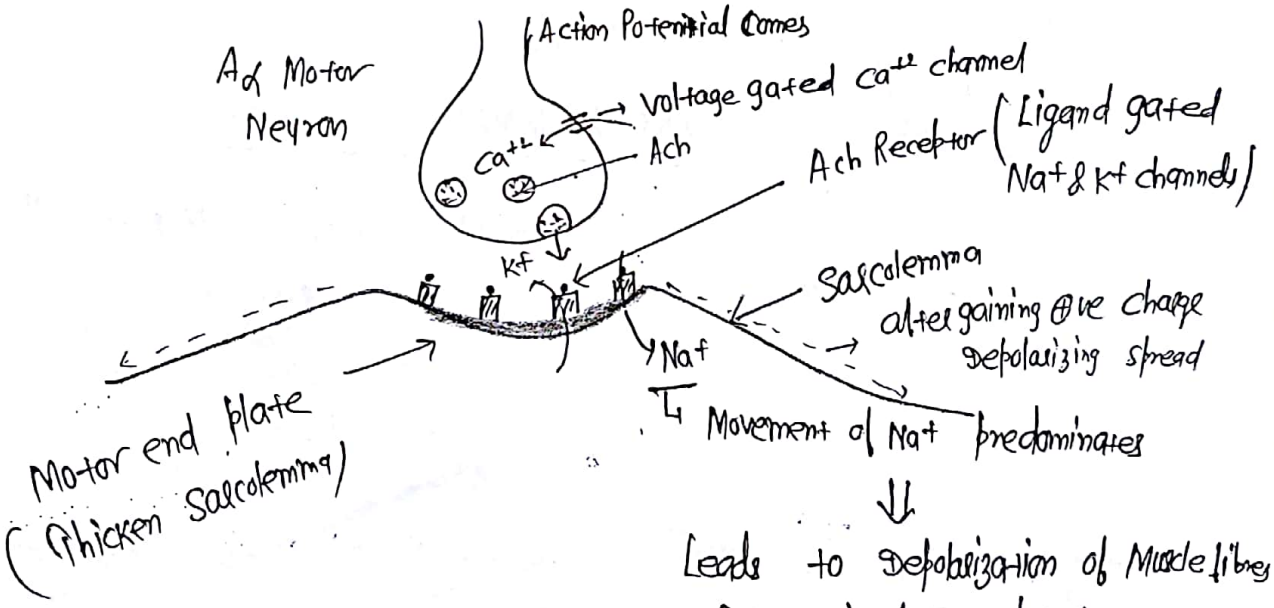
if dystrophin ⊖ ⇒ Duchenne's Muscular dystrophy

if dystrophin ⊕; but Reduced ⇒ Becker's Muscular dystrophy

if Sarcoglycan ~~Mutation~~ ⇒ Limb Girdle dystrophy
(Mutation of sarcoglycan)

* Function of dystrophin ⇒ Probably Amplifies force generated by Actin & Myosin.

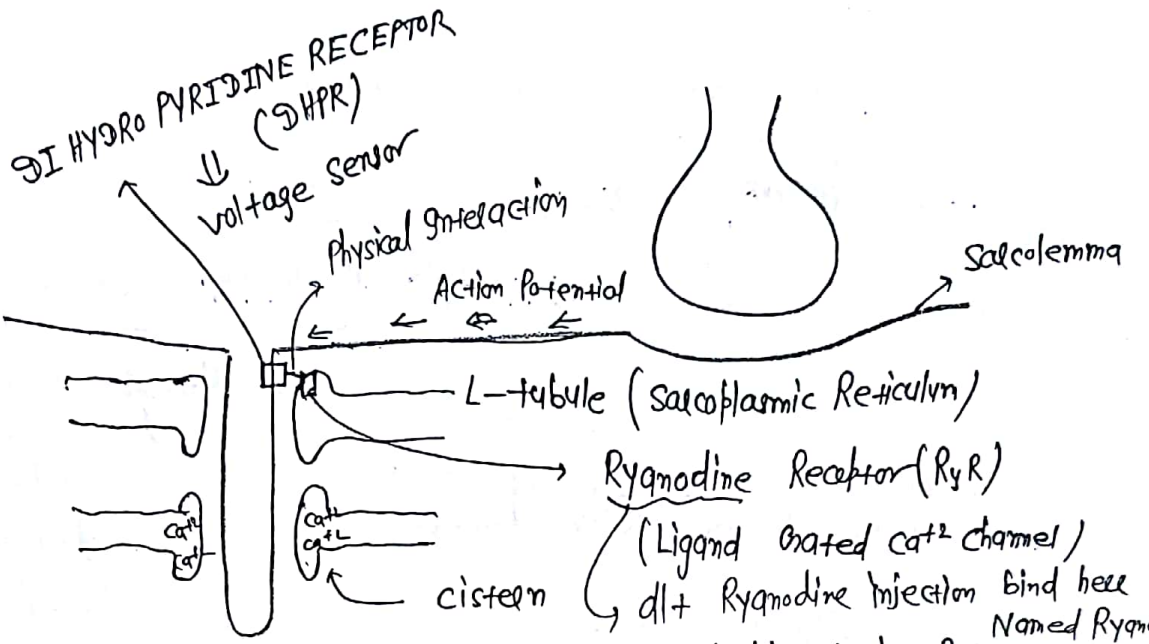
* NEUROMUSCULAR JUNCTION



LAMBERT EATON SYNDROME ⇒ Ab against Pre-synaptic voltage gated Ca^{+2} channel

MYASTHENIA GRAVIS ⇒ Ab against Post-synaptic Ligand gated Na^+ & K^+ channels

SARCOTUBULAR JUNCTION



Triad ⇒ cistern + T- tubule + cistern

* as DHPR get conformational change
⇓
RyR gets interaction ~ DHPR & Release Ca^{+2}
⇓
K/as " Ca^{+2} Induce Ca^{+2} Release"

→ Excitation - contraction coupling
↳ Agent ⇒ Ca^{2+}

* Trigger for Muscle contraction ⇒ Availability of Sarcoplasmic Ca^{+2}

(Q9) Muscle contraction continues till :-

a) ~~Ca^{+2}~~ Ca^{+2} is available;

b) ATP is available;

(Q8) Relaxation of Muscle by :-

Removal of Sarcoplasmic Ca^{+2}

↳ by 1° Active transport

↳ through SERCA

each ATP

↳ by hydrolyze 2 Ca^{+2}

goes into Sarcoplasmic Reticulum.

→ So; it is active process.

ACTIN - MYOSIN CROSS BRIDGE CYCLING

- Responsible for sliding filament theory of Muscle contraction.

* When a Muscle @ Rest ⇒

Myosin head is in a ⇒ High Energy / High affinity state!

Recocking of Myosin head / Hydrolysis of ATP

ATP $\xrightarrow{\text{ATPase}}$ ADP + Pi + E

COCKED STATE

↑ it doesn't mean Relaxation ↳ seen after Ca^{+2} goes

Detachment of Myosine head ← conformational change ← ATP Attaches to Myosin head

Power stroke ← Myosin head utilize the energy & take action along it

Ca^{+2} → energy of Myosin head

Sequence ⇒ Powel Stroke

⇓

ATP attaches to Myosin head

⇓

Detachment of Myosine head

⇓

Hydrolysis of ATP

⇓

Recocking of Myosine-head,

* In Rigor Mortis Case ⇒ Cell Membranes became leaky

↓

Ca^{+2} comes out of Sarcoplasmic Reticulum & comes in Sarcoplasm.

↓

but there is No ATP to goes Inside the Sarcoplasmic Reticulum

Result in contracted state ←

* Only 1 ATP Requires in Actin - Myosin cross-bridge cycling

TYPE - Of Muscle fibres

Type-I	Type-II
S → Slow, Small	Fast; Large
O → oxidative	Glycolytic
R → RED	White

R
Y

- Faster Myosin ATPase Activity ⇒ II
- Longer twitch duration ⇒ I
- Having More Mitochondria ⇒ I
- Higher cap. Density ⇒ I
- More Myoglobin ⇒ I
- Easily fatiguability ⇒ II

I ↓ Slow; Sustained contraction

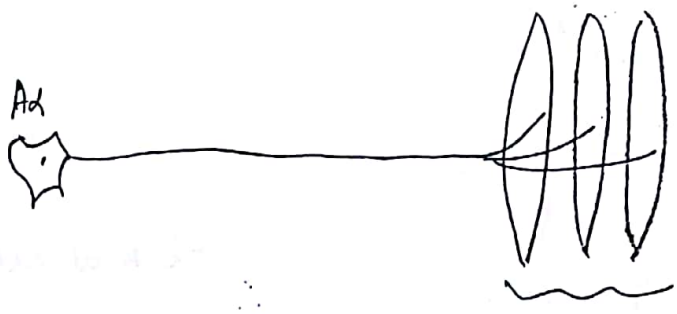
II ↓ Brief Powerful control.

* Size principle ⇒ During Muscle contraction (Graded)

↓↓

1st Type-I Muscle fibres comes → then → Type-II Muscle fibres comes (so: Reserve Muscle fibres)

MOTOR UNIT ⇒ Single A_α Motor Neurons + all Muscle fibres it supplies.



ONLY one type of Muscle fibres in one Motor Unit.

Extraocular Muscle ⇒ Very fine control Needed

⇓

4-5 Muscle fibres / Motor Unit

Muscles of Back ⇒ No need of fine control

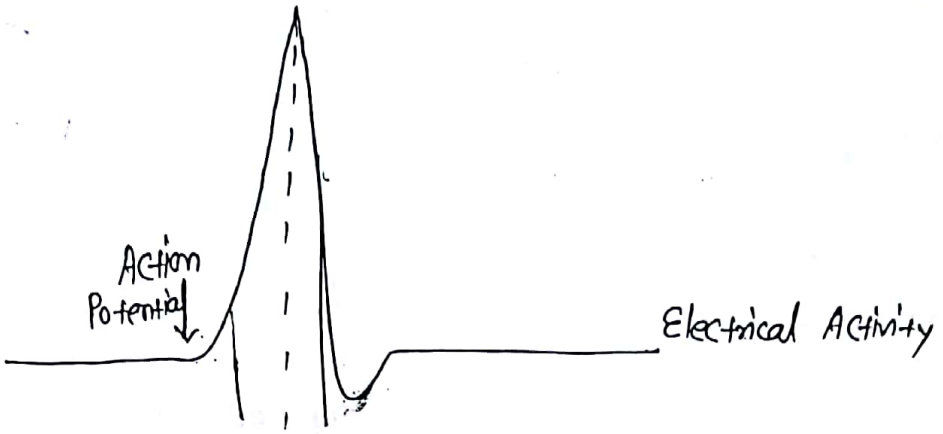
⇓

600 Motor fibres / Motor Unit.

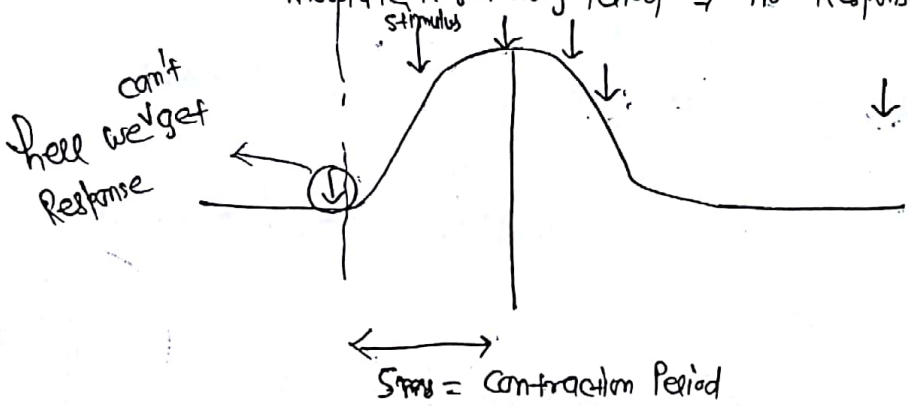
* **Nomenclature of Motor Unit** :→

	I	IIa	IIb
M. fibres	Slow; oxidative (SO)	Fast; oxidative; Glycolytic (FOG)	Fast; Glycolytic (FG)
Motor Unit	(S) SLow	(FR) Fast & Resistance to fatigue	(FF) Fast & fatiguable
eg :-	Standing ⇓ "S" Motor Unit of calf Muscle	Walking ⇓ "S" Motor Unit + "FR" Motor Unit	Running S + FR + FF Motor Unit

* COMPLETE & INCOMPLETE TETANUS



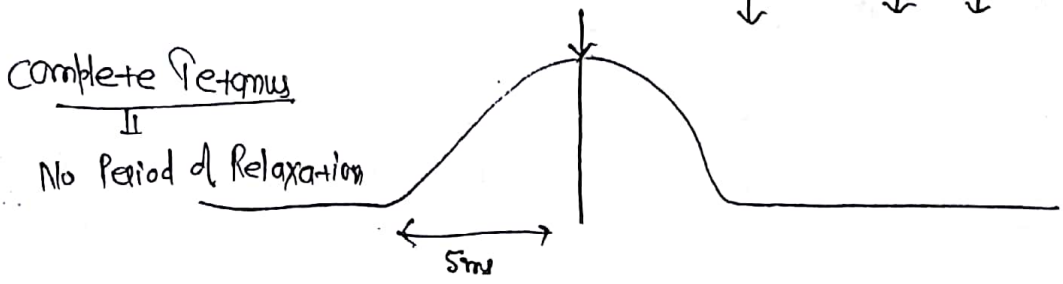
Absolute Refractory Period ⇒ No Response in 2nd stimulus

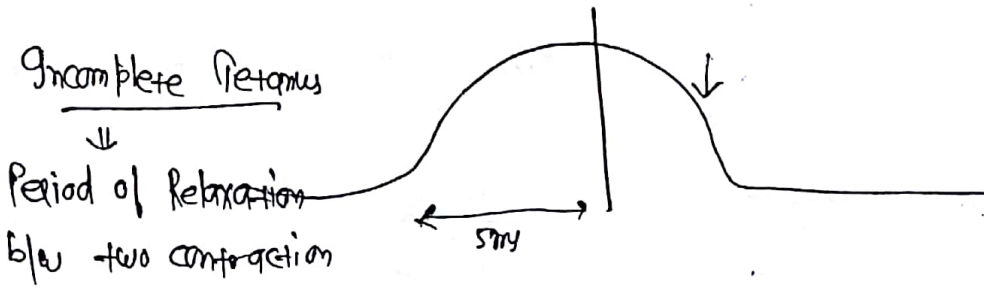


⇓

No Absolute Refractory Period

Tetanus ⇒ State of continous contraction.





⇒ On Successive Stimulation ↑ Height of Successive contraction

⇓

Also " Beneficial effect/ Staircase/ Treppe"

⇓

d/t accumulation of the cal in S

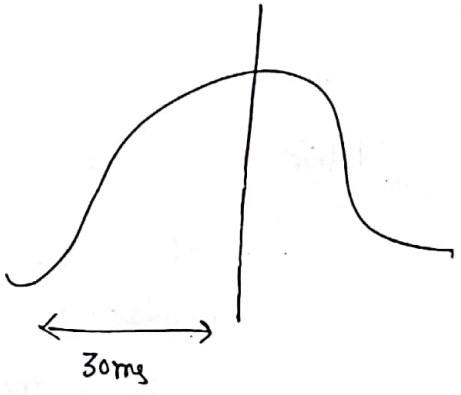
TETANIZING FREQUENCY ⇒ $\frac{1}{\text{Contraction Period (in sec)}}$

$= \frac{1}{5 \text{ ms}} = \frac{1000}{5} = 200$ Stimuli/sec.

$= 200$ Hz.

* If frequency of Stimulation is > 200 Hz ⇒ complete tetanus
* If frequency of Stimulation is < 200 Hz ⇒ Incomplete tetanus

QQ.



Tetanizing frequency

⇓

$\frac{1000}{30} = 33.33$ Hz.

* Day-to-Day activities can't possible without Tetanus.

TYPES OF MUSCLE CONTRACTION

ISOTONIC

Tone | Tension = Same

Length = ↓

External work = done

Heat Release = More

eg ⇒ all day to day activities

ISOMETRIC

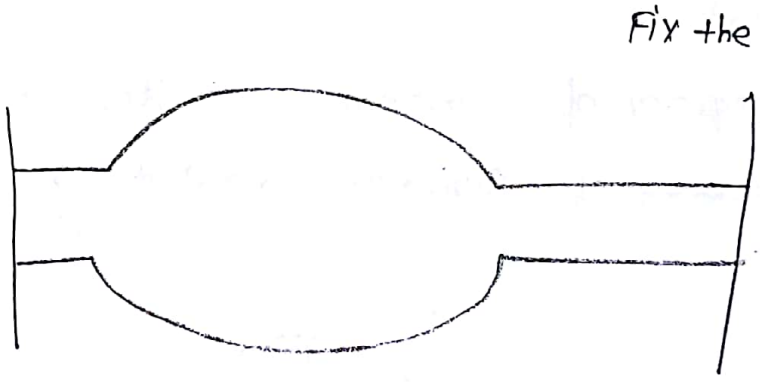
Length = Same

Tension = ↑

No External work

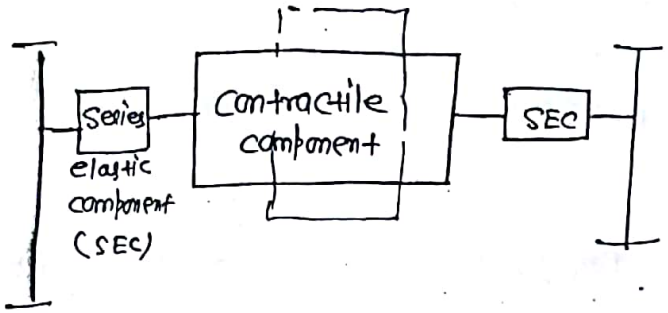
eg ⇒ Place hand on wall & Push against it.

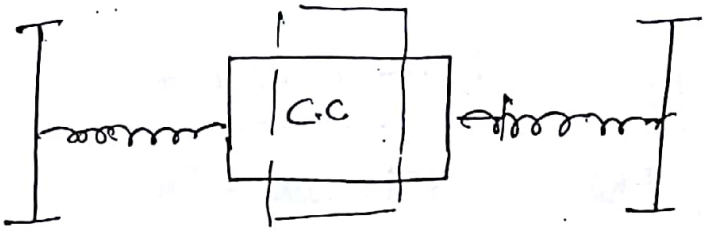
How does isometric contraction takes place ??



Muscle

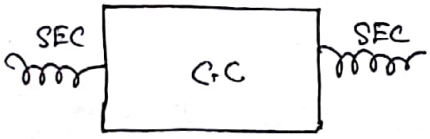
- Contractile components
- Elastic components
  - Elastic fibres in tendons
  - Titin





Isometric
⇓
- ↓ Contractile component
- Stretch of series elastic component
- Total Length = Same

In Isotonic contraction ⇒



Isotonic
↓ Contractile component

Series elastic component
⇓
Folded

HEAT RELEASED DURING MUSCLE CONTRACTION

	ISOTONIC	ISOMETRIC
i) Resting heat	⊕	⊕
ii) Initial heat		
↳ Activation heat	⊕	⊕
↳ Shortening heat	⊕	⊕
iii) Recovery heat (Stop giving stimulus & heat generated by Muscle)	⊕	⊕

iv) Relaxation Heat ⇒ a ⊕ ⊖

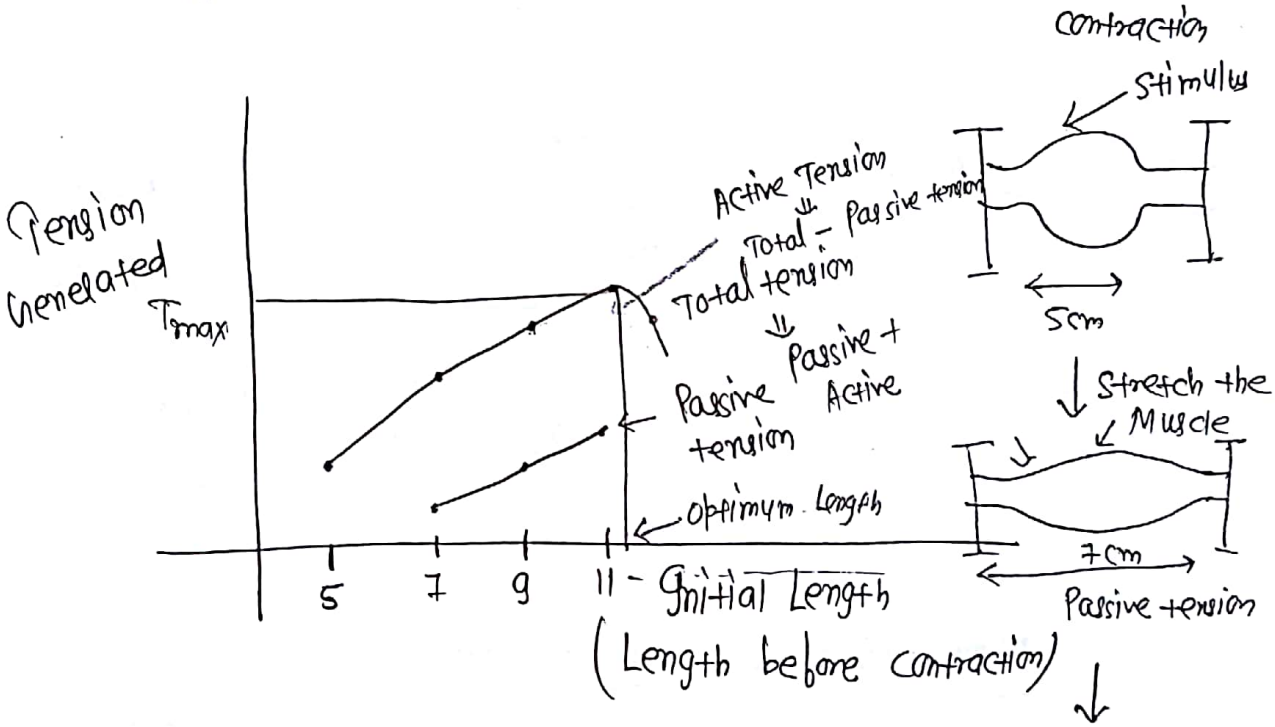
↑ a (Total heat)

* Total heat genelation is More in ⇒ Isotonic contraction

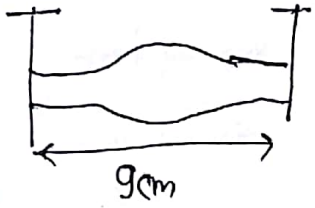
LENGTH- TENSION RELATIONSHIP

FRANK – STARLING's LAW

– Applicable for isometric contraction; Not for Isotonic contraction



During isometric Muscle contraction; More the Initial Length; More is the total & Active tension generated; but upto a Physiological Limit; beyond which further Inc in Initial Length; Dec the total & active tension generated



In case of cardiac Muscle :→

⇒

↑ Venous Return

⇓

↑ Filling (↑ End diastolic volume / ↳ Preload)

⇓

↑ Initial Length

⇓

↑ Tension generated

⇓

↑ Stroke volume

↑ cardiac output ⇐ but up-to physiological limit.

In Dilated cardiomyopathy ⇒ ↑↑↑ Initial Length

↓

↓ Tension generates

⇓

↓ stroke volume ⇒ Failure (common)

Optimum Length ⇒ It is that Initial Length ; at which if Muscle contracts isometrically ; then the total & active tension generated is maximum.

QQ At optimum Length ; All are Max^m except ⇒

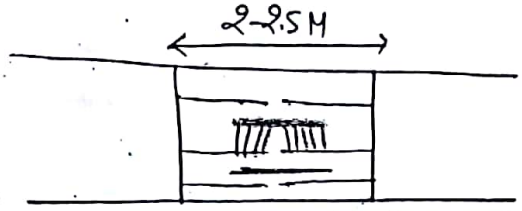
(A) Total tension;

(B) Active tension;

(C) Passive tension

Optimum Length ⇒ Corresponds to Sarcomere Length of 2-2.5 M

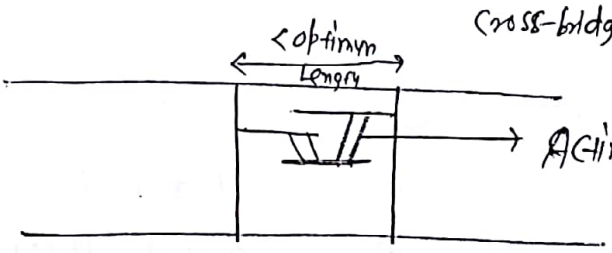
↳ Maximum overlap b/w Actin & Myosin
↳ Maximum Number of Actin - Myosin cross bridges
↳ also K/as "Resting Length".



Optimum Length

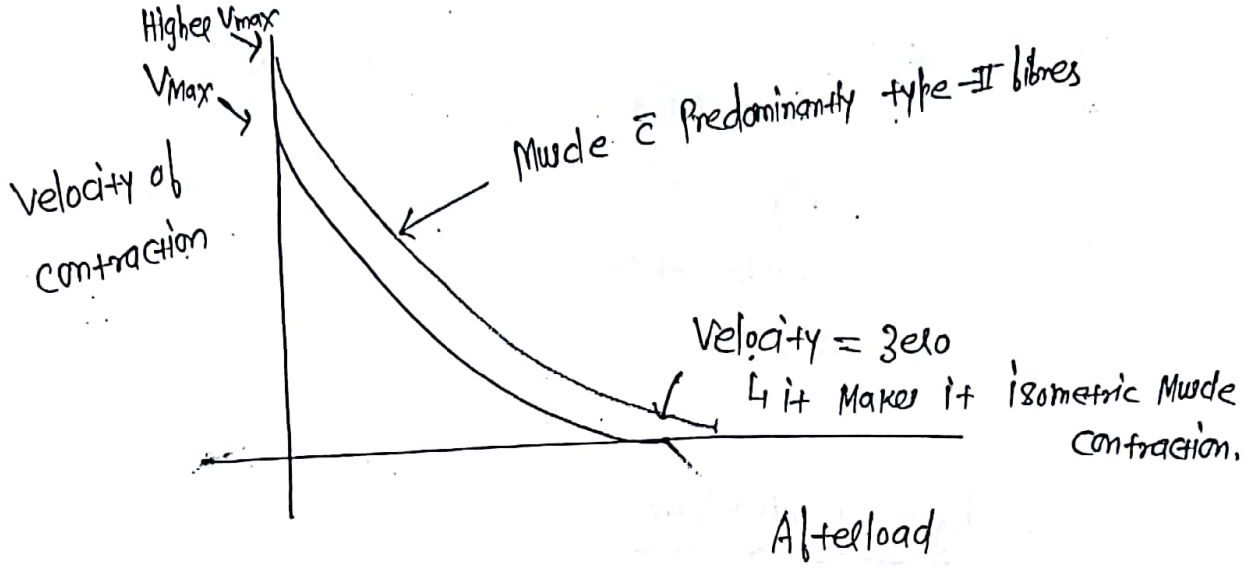
If Initial Length is More than optimal Length ⇒ Less Actin-Myosin cross-bridge (+)

If Initial Length is Less than optimal Length ⇒ Less Actin-Myosin cross-bridge (-)



LOAD-VELOCITY RELATIONSHIP

- Valid for Isotonic Muscle



Afterload for the heart ⇒ Total Peripheral Resistance

* SOURCES OF Energy during exercise :-

1. ATP Stores ⇒ Sustain the exercise for 1-2 sec only
   ⇓ In Trained Athelefes → 3sec
   1st source of energy

2. ATP from Creatine phosphate ⇒ Sustain the exercise for 7-8 sec

   Also "Phosphagen System"
   ↳ Sustain 8-10 sec

3. ATP from Glycolytic Metabolism ⇒ Sustain the exercise for 1-1.5 min

4. ATP from oxidative Metabolism ⇒ Sustain for Long time

Energy Substrate ⇒ 1st Stored then Glucose then Fatty acid
Glycogen
↳ After 1 or 2 hours of Exercise

* Phosphagen system (Major source) :→

For 100 metre sprint
Diving
Long jump
High jump
Javelin throw
Discus

* Phosphagen + Glycolytic :→

200 metre Run ;
100 m Swim ;

* Glycolytic :→ (Major source)
400 m Run
200 m Swim

* oxidative :→ For Any Prolonged duration of exercise →
- Marathon
- Boxing
- Rowing

TRAINING OF ATHELETE

ENDURANCE TRAINING

⇉ ↑ Stamina
⇉ ↑ Efficiency of CVS & Respiratory System to tolerate exercise

STRENGTH TRAINING

⇉ ↑ Strength/Power
⇉ ↑ Bulk of Muscle (Hypertrophy)

⇒ Load ⇒ Submaximal

Duration ⇒ Prolonged

⇒ Tes oxidative capacity

⇒ Achieved by ⇒ Walking
Jogging
Swimming

⇒ Load ⇒ Maximal OR
Near Maximal

Duration ⇒ Brief

⇒ Tes 'Glycolytic capacity

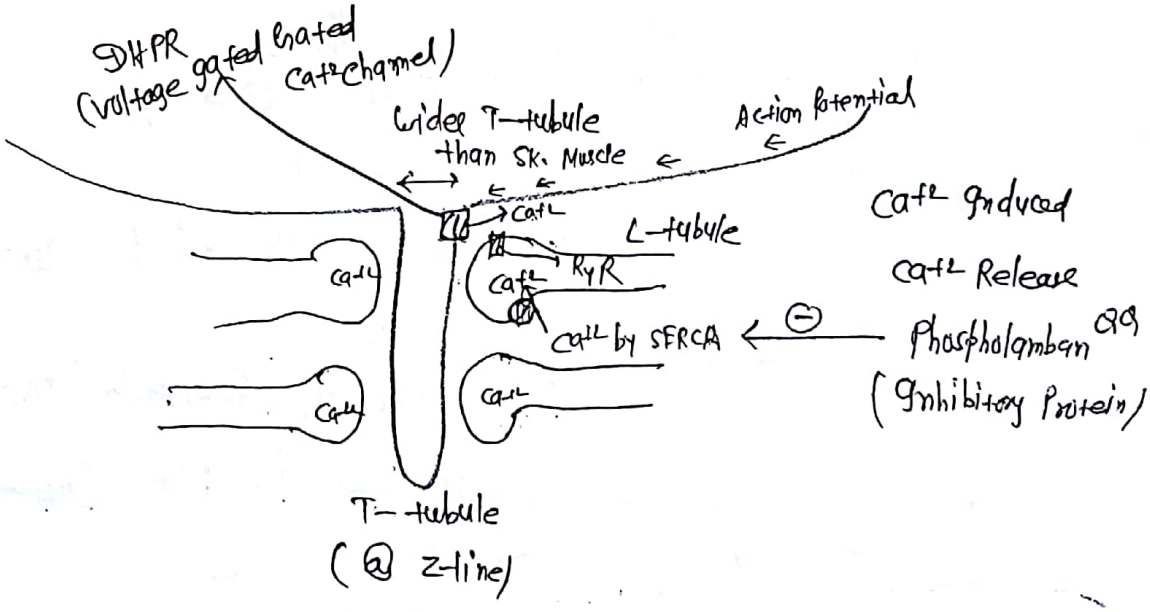
⇒ Achieved by ⇒ Training;
Gymming.

qq CARDIOVASCULAR SYSTEM

Cardiac Muscle ⇒

- Striated
- Involuntary Muscle
- Extensive branching
- Intercalated Discs
  - At Z-line
  - ↑ Cell - to - Cell Cohesion
  - dlt it heart is "Mechanical syncytium"
- Gap Junctions ⊕
  - At Z-line
  - dlt it heart is "Functional Syncytium"

*



	Skeletal Muscle	Cardiac Muscle
T-tubule ⇒	At A-I junction	At Z-line
Sarcoplasmic Reticulum ⇒	Better developed	
Source of Ca^{+2} ⇒	S.R	ECF + S.R
DHPR ⇒	Voltage Sensor	Voltage gated Ca^{+2} channel
Relaxation ⇒	SERCA	SERCA + Na^{+}-Ca^{+2} Antiport

* if we Remove Phospholamban protein

⇓

↑ SERCA activity

⇓

↑ Rate of Removal of Sarcoplasmic Ca^{2+}

⇓

↑ Rate of Relaxation (Muscle)

↳ Klas " Lusitrophy "

by ↑ Sympathetic Activity

↓ β-sympathetic
↑ cAMP

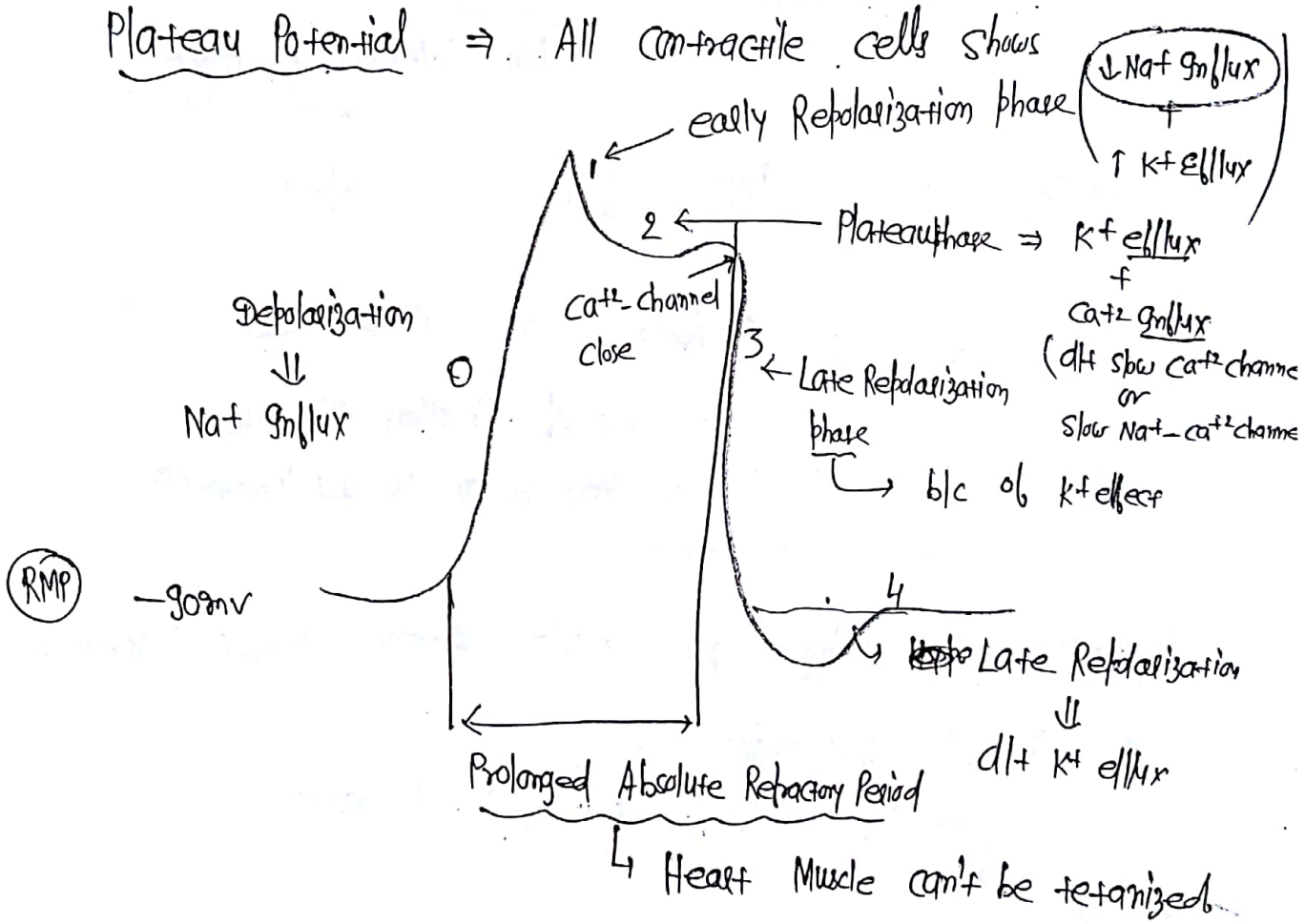
Phosphorylation of Phospholamban

* ↑ Symphathetic ⇒

⊕ve chrono-tropic (↑ Heart Rate)
⊕ve Ino-tropic (↑ Force)
⊕ve Bathmo-tropic (↑ Excitement)
⊕ve Dromo-tropic (↑ conductivity)
⊕ve Lusi-tropic (↑ Muscle Relaxation)

* Electrical Activity of Heart ⇒

Plateau Potential ⇒ All contractile cells shows



↳ Heart Muscle can't be tetanized.

* Conducting System of Heart ⇒

Modified contractile cells.

i) SA Node

ii) Inter Nodal tracts — Anterior, Middle, Posterior

iii) AV Node ⇒ Nodal delay. (as it passes through AV Node it slow)
92 ms = 0.92 sec

iv) Bundle of His

v) Bundle Branches — (RT), (LT)

vi) Purkinje fibres

No NMJ ⊕ in Heart.

Fastest. ⇒ Purkinje fibres ⇒ 4m/sec

Slowest conducting ⇒ AV Node ⇒ 0.05 m/sec
↳ b/c of Smallest Diameter & very few or No gap junction ⊕.

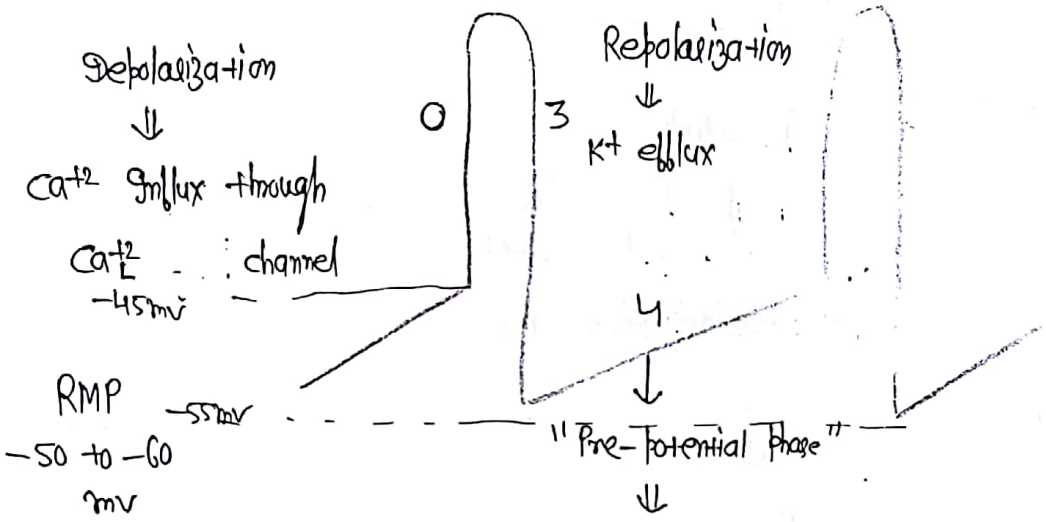
Advantage of Nodal delay ⇒ Atria contract Ahead of ventricles

* Atrial contraction
Responsible for ↳ and Rapid filling of ventricle

Pacemaker Potential ⇒ @ SA Node & AV Node

All of Rest have "Plateau potential"
↓ also in contractile cells.
eg = Bundle of his; Purkinje cells

PACEMAKER POTENTIAL



↓

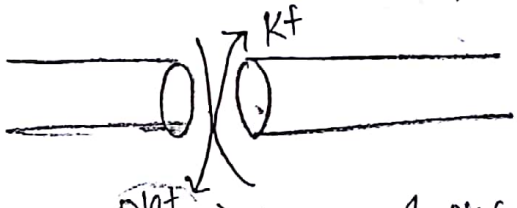
"Spontaneous depolarizing till firing Level"

↳ by gain of ⊕ve charge

↓

① by ↓ K+ efflux

② by opening of "F" channel (it permits Movement of both Na+ & K+)
↳ Funny



b/c both electrical & chemical gradient ↑

⇒ Movement of Na+ predominates & cause Net gain of ⊕ve charge

(3) Ca^{+2} influx through Ca_T channels

(QQ) Pre-potential starts ∵

↳ ↓ in K^+ efflux

Main Reason for Pre-potential

↳ Ca^{+2} influx through Ca_T channels.

* Effect of Sympathetic discharge on Pacemaker Potential

↑ Symp.

↓ β Receptor (↑CAMP)

↓ Depolarization Time

↓

↑ HR

* Effect of Parasympathetic discharge on Pacemaker Potential

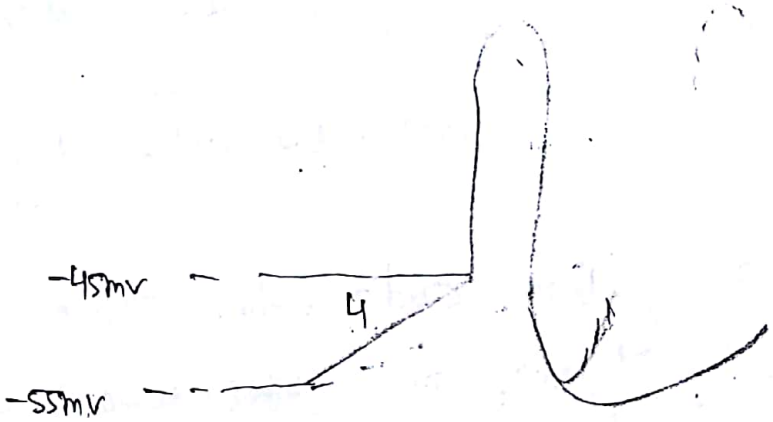
↑ P.S. → via G-protein → opens K_{Ach} channels in phase 4

↓ CAMP → ↓ Phosphorylation channel → Less open & Result in ↑ Depolarization time

↓ Slope of Phase 4 (QQ)

↑ Depolarization time → ↓ H.R.

↓ Slope of Phase 4 (QQ) → ↓ H.R.



QQ Parasympathetic affects Phase 4 & 0 both.

* Intrinsic Rate of discharge of SA Node] → 100/min

↓ bic of Resting vagal tone

Resting heart Rate → 70-80/min [i.e vagus is effective @ Rest

QQ Heart Rate of Transplanted Heart

↳ 100/min (No connection ε Symphathetic & Palasymphathetic)

↳ In exercise; epinephrine from Adrenal Medulla works here

Atheletes ⇒ has very high Resting vagal tone

⇓

Bradycardia @ Rest

↳ Advantage ⇒ high cardiac Reserve

⇓

Maxm cardiac output − Basal cardiac output.

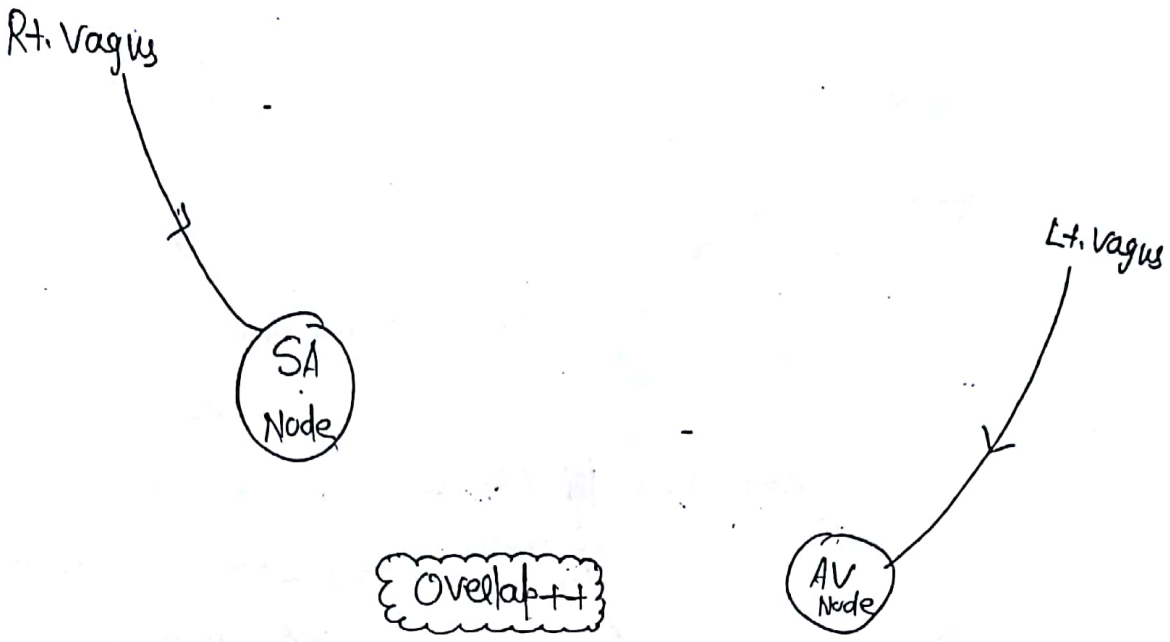
In (N) Individual ⇒ Basal cardiac output = 5L/min

4-5 times Tes ← Maxm cardiac output = 20-25 L/min

In Atheletes ⇒ Basal cardiac output = 4.0 L/min

↓ 6-7 times Tes

Maxm cardiac output = 25-28 L/min



*

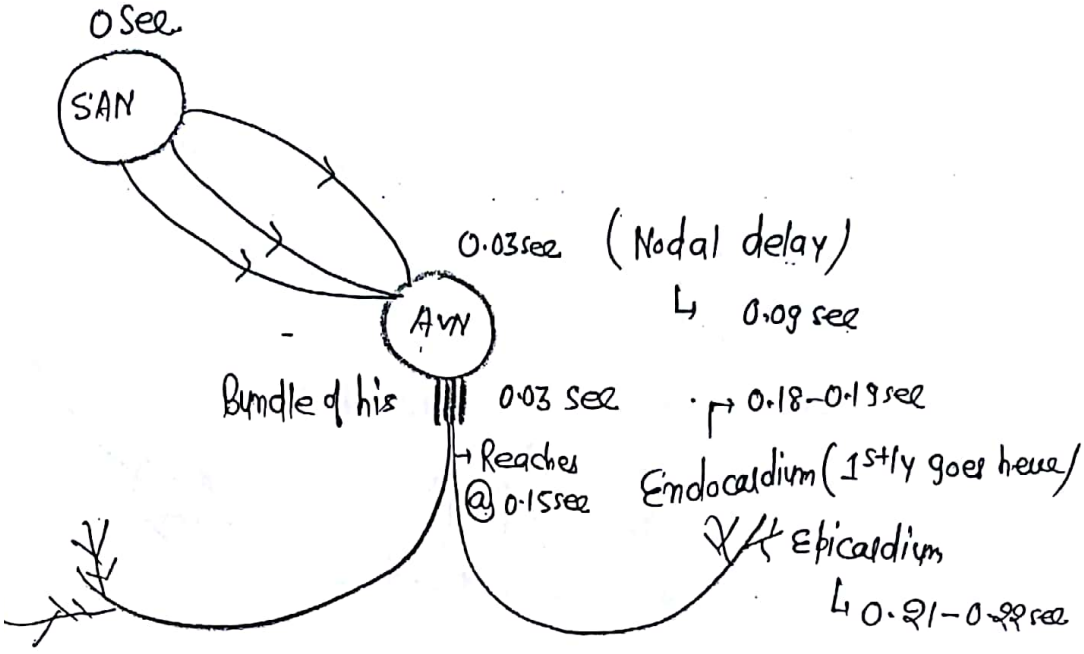
	Heart Rate	Force of contraction
Sympathetic	↑	↑
Parasympathetic	↓	⊖

(No vagus to ventricles)

QQ Parasympathetic is prt. in all except =>

a) SAN;
b) AVN;
c) Atrial Myocardium
d) Ventricle Myocardium

CONDUCTION OF CARDIAC IMPULSE



VENTRICLE DEPLORIZATION

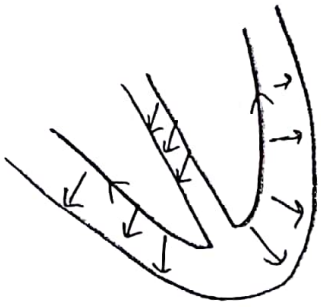
1St to depolarize ⇒ Left upper part of Interventricular septum

↓

Septal depolarization (Left → Right)

↓

Endocardium then Epicardium QQ 2016 NEET



↓

Last to depolarize ⇒ Base of heart (Epicardium)

- Pulmonary conus
- Small superior most portion of Interventricular septum Near Base of heart

* VENTRICULAR REPOLARIZATION ⇒

1st part to Repolarize ⇒ Apex; Epicardium

Last part of Repolarize ⇒ Base; Endocardium

* During Repolarization Heart is already in contracted state

⇓

there is very high pressure in Endocardium (b/c of circular Nature)

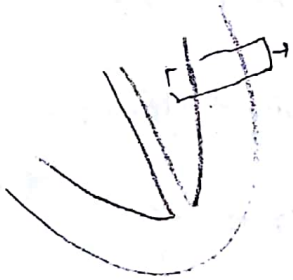
⇓

This high pressure doesn't permit ionic change

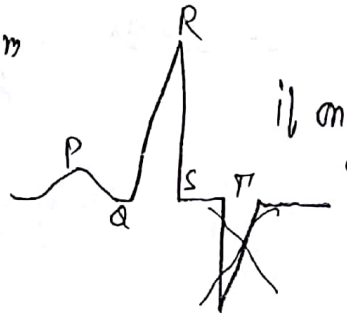
⇓

Repolarization is from Epicardium → Endocardium

Q: Isolated piece of vent. Myocardium



→ Shows both electrical activity & conductional activity

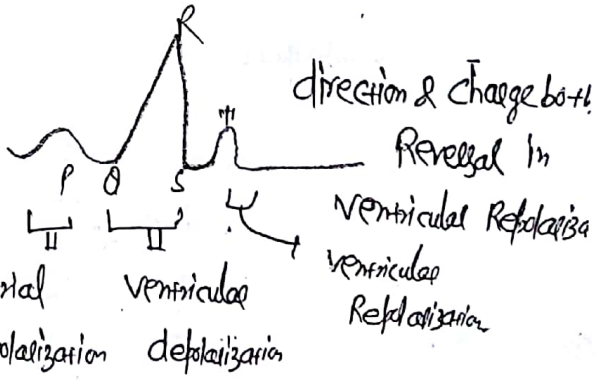


if only Reversal of Charge was taking in ventricular Repolarization

Repolarization is from ⇒ both surface has equal pressure

a) Endo → Epi

b) Epi → Endo



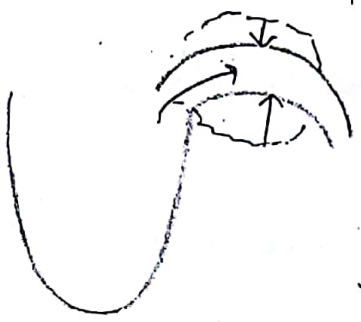
direction & Charge both Reversal in

VESSELS

1. WINDKESSEL VESSELS

↳ Aorta & Large Arteries

Elastic tissue ++



during diastolic

↳ Diastolic Blood Pressure

↓

Elastic Recoil of Aorta & Large Arteries;

depend on Total Peripheral Resistance

2. Resistance vessels

↳ Arterioles (only 1/4 of TBV present here). ← Least % of blood volume

Smooth Muscle ++

Sympathetic ++

↑ Sympathetic innervation of more Smooth Muscle

↓

Vasomotor contraction

↓

↓ Radius

↓

↑↑↑↑ Resistance

$$R \propto \frac{1}{r^4}$$

↳ Small changage in Radius

↳ Large changage in Resistance

③ Exchange vessels ⇒ Capillaries

4 ~ 5% of Total blood volume

⇓

No Smooth Muscle

No Symphathetic Innervation

* Pre-capillary Sphincters & Terminal Arterioles } Respond to Local Metabolite.

⇓

↓PO_2, ↑PCO_2, ↑H+, ↓PH, ↑Lactic acid, ↑Adenosine, ↑temp., ↑K+ } Local hypoxia

⇒ Causes Relaxation of pre-capillary sphincters & terminal arteriole.

⇓

↑ Capillary flow.

$\theta\theta$ // O_2 Sensitive K+ channel ↓PO_2 ← Pulmonary vasoconstriction ↓

↓PO_2

↓

Closure of O_2-Sensitive K+ channel

↓

↓ K+ Efflux

↓

Depolarization

↳ vasoconstriction

ATP dependent K+ Channels → Vasodilation (Rest all area)

↓PO_2

↓

↓ATP

↓

Opening of ATP dependent K+ channels

↓

↑K+ efflux

⇓

Hyperpolarization ⇒ Vasodilation

Resting Skeletal Muscle blood flow :→

3-4 ml/min/100 gm of tissue

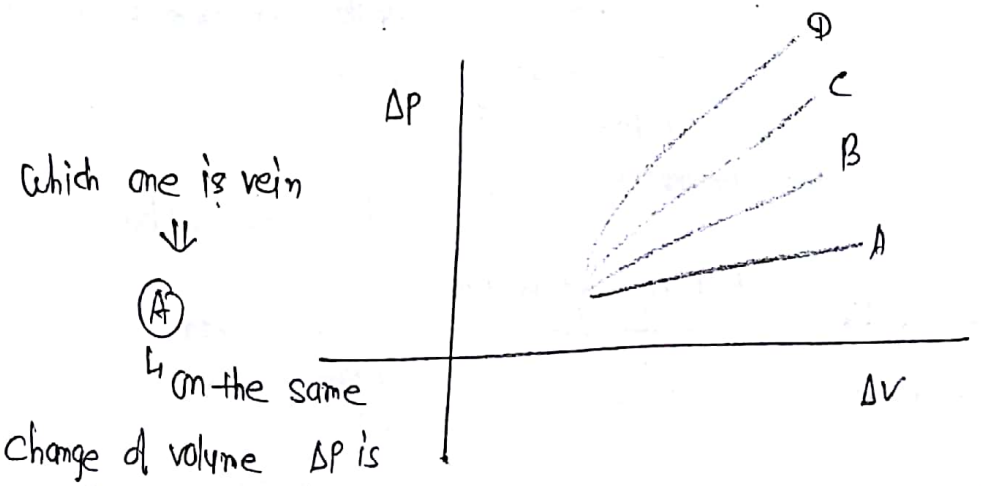
On exercise ↓ Local Metabolites (20-25 times)

80-90 ml/min/100 gm of tissue

④ CAPACITANCE VESSELS ⇒ Venules; Veins & Vena cava

↳ ~ 2/3rd of blood volume prt. on venous side (60%)

↳ have capacity to expand



Which one is vein

⇓

(A)

↳ on the same change of volume ΔP is least b/c of expansion

Compliance

⇓

distensibility of vein

Small veins = 46% of blood volume

Large veins = 14-18% of blood volume

→ Sympathetic (+) ⇒ Arteriole ↑ sympathetic Vein

Arteriolar constriction

↑ MAP ← ↑DBP ← ↑ TPR

Venoconstriction

↓ venous compliance ⇒ ↑ venous Return

⑤ Shunt Vessels ⇒ Arterio-Venous Anastomosis

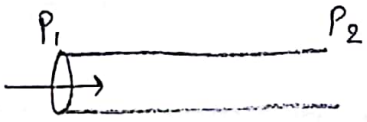
- Prt. in: Finger tips ⊕, Ear lobes ⊕⊕
- Function ⇒ Temperature Regulation.
- Sympathetic-Supply ⊕

Imp.

HEMODYNAMICS

① Based on ohm's Law :-

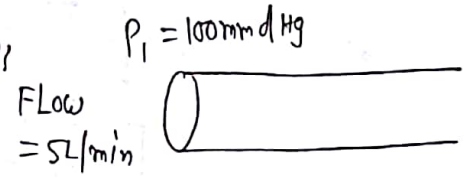
$$\text{Flow} = \frac{P_1 - P_2}{\text{Resistance}}$$



Flow $\propto \Delta P$

Flow $\propto \frac{1}{\text{Resistance}}$

Q: Resistance in Wood Units ??

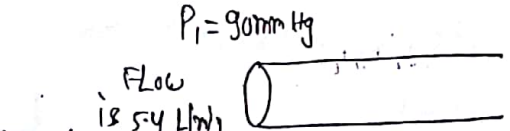


$$\text{Resistance (Wood Units)} = \frac{\Delta P \text{ mm Hg}}{\text{Flow L/min}} = \frac{100-0}{5} = 20 \text{ mm Hg min/L}$$

20 Wood Units

Q. Resistance in R Units ??

(PRU) ↳ Peripheral Resistance Unit



$$\text{Resistance (PRU)} = \frac{\Delta P \text{ (mm of Hg)}}{\text{Flow (ml/sec)}} = \frac{90-0}{90} = 1 \text{ PRU}$$

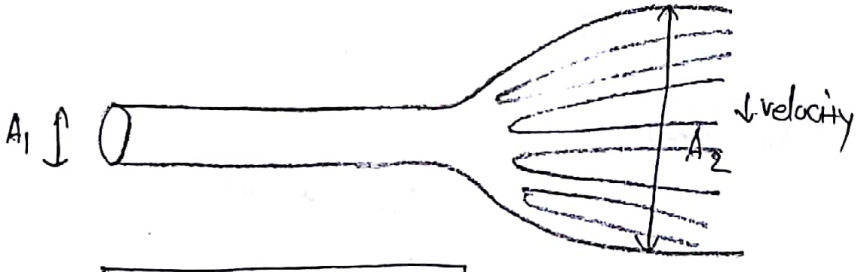
$$\frac{\text{g} \Downarrow}{\text{ml} \times 1000} = 90$$

② Velocity of Flow :→ It is Inverse of total cross sectional Area

Aorta ⇒ $4.5\ cm^2$ (Total cross-sectional Area)

Capillaries ⇒ $4500\ cm^2$ (Total cross-sectional Area)

(QQ) Maxm velocity ⇒ @ Aorta



$$V_1 \times A_1 = V_2 A_2$$

$$V_1 A_1 = V_2 A_2$$

③ HAGEN – POISEUILLE'S LAW :→

$$R = \frac{8\eta L}{\pi r^4}$$

η = Viscosity (depend on RBC count)

L = Length

r = Radius

We know;

$$\text{Flow} = \frac{\Delta P}{R} = \frac{\Delta P \times \pi r^4}{8\eta L}$$

$$\text{Flow} = \frac{\pi}{8} \times \frac{\Delta P r^4}{\eta L}$$

Flow $\propto \Delta P$; Flow $\propto \frac{1}{\eta}$;

Flow $\propto r^4$; Flow $\propto \frac{1}{L}$

In Anemia ⇒ blood viscocity ↓

↳ Result in hyperdynamic circulation

(QQ) Radius is ↑es by 50% ; blow ↑es by

a) 5X; b) 8X; c) 10X; d) 16X

$$X + \frac{50}{100}X = \frac{3}{2}X \qquad \frac{8t}{16} = 5 \text{ times}$$

(QQ) Radius & Length of a vessels are both double ; Flow ↑es by how many times

a) 5X; b) 8X; c) 10X; d) 16X

(4) Laminal blow & Turbulant blow ⇒

Laminal blow ⇒ ⇒ Max^m velocity @ centre

Turbulant blow ⇒

Tendency for turbulance → Given by Reynold's No.**

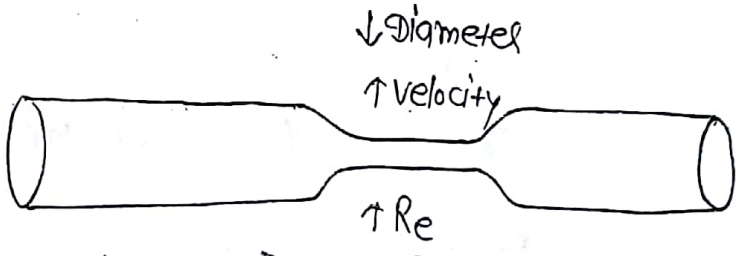
$$\Rightarrow \boxed{Re = \frac{\rho V D}{\eta}}$$

Most imp. factor
↳ velocity of flow

ρ = Density
D = Diameter (cm)
V = velocity of flow (cm/sec)
η = viscosity (Poise)

$Re > 3000 \Rightarrow$ Turbulent flow

$Re < 2000 \Rightarrow$ Laminar flow

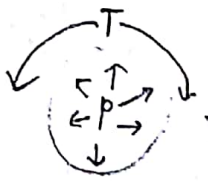


Korotkoff Sounds → Seen turbulant flow
↳ heard dft turbulent flow.

↳ bic velocity of Flow is Most imkortant Factor in Reynold's Number

⑤ Laplace's Law ⇒

For thin walled visus

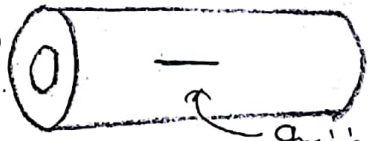


P = Distending Pressure
T = wall tension

$P = \frac{T}{r}$ (cylinder eg Bloodvessels)

$P = \frac{2T}{r}$ (sphere eg Alveolus) → $T = \frac{Pr}{2}$

$\boxed{T = Pr}$; capillary ⇒ ↓ wall tension



Incision & check wall tension

- capillaries don't Rupture inspite of being thin walled

* If wall thickness (w) is significant :-

$$T = \frac{Pr}{w} \quad ; \quad T = \frac{Pr}{2w}$$

QQ. Left ventricle wall stress (wall tension) can be ↓ by ↑ in :-

a) Distending Pressure;

b) Radius

$$T = \frac{Pr}{2w}$$

↳ In Dilated cardiomyopathy patient there is less wall tension

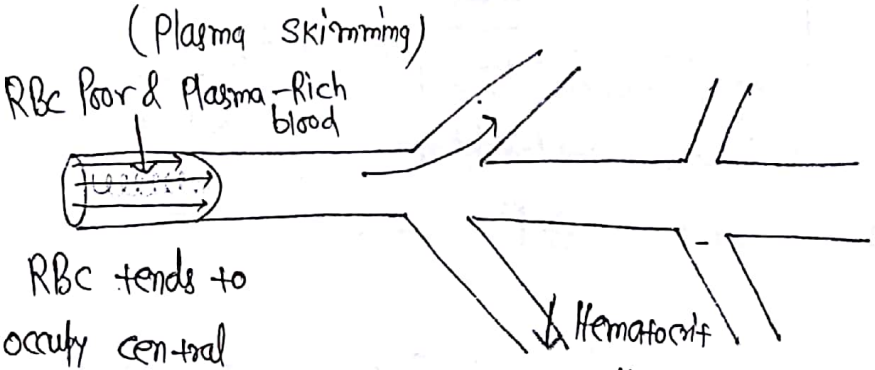
c) Afterload (Total Peripheral Resistance)

↳ In case of Heart.

d) ~~Wall~~ Wall thickness

(6) FAHRAES - LINDQUIST Effect :-

(Plasma skimming)



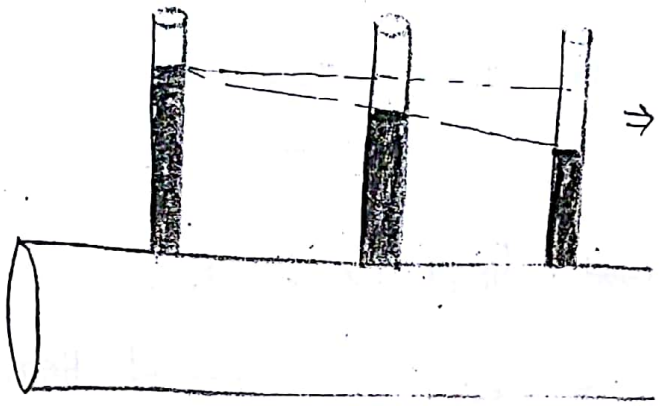
↓ Blood viscosity in vessels < 1mm in diameter

• It helps to Maintain the flow

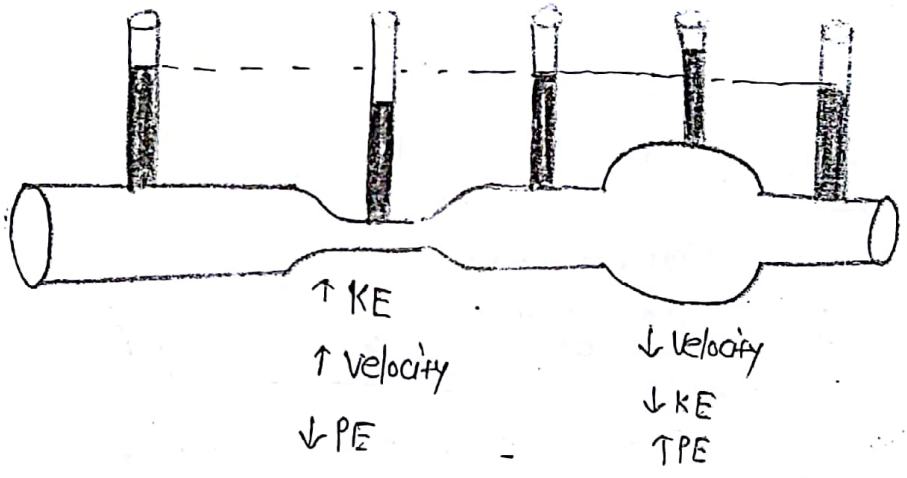
⑦ BERNOULLI'S :⇒

Total energy = Kinetic energy + Potential energy

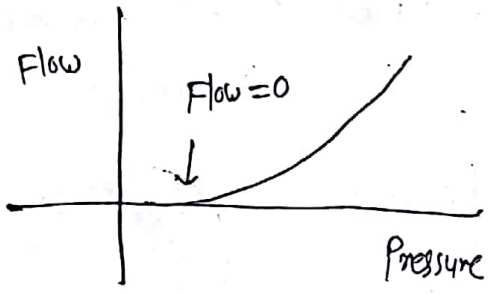
Total energy of Flow = Kinetic energy of Flow + Potential energy (Lateral pressure exerted by flowing bloods).



⇒ ↓ Lateral Pressure along Length of tube (b/c of loss of energy d/t friction)



⑧ Critical closing Pressure :⇒ It is the pressure in small & thin walled vessels ; when there is No Flow



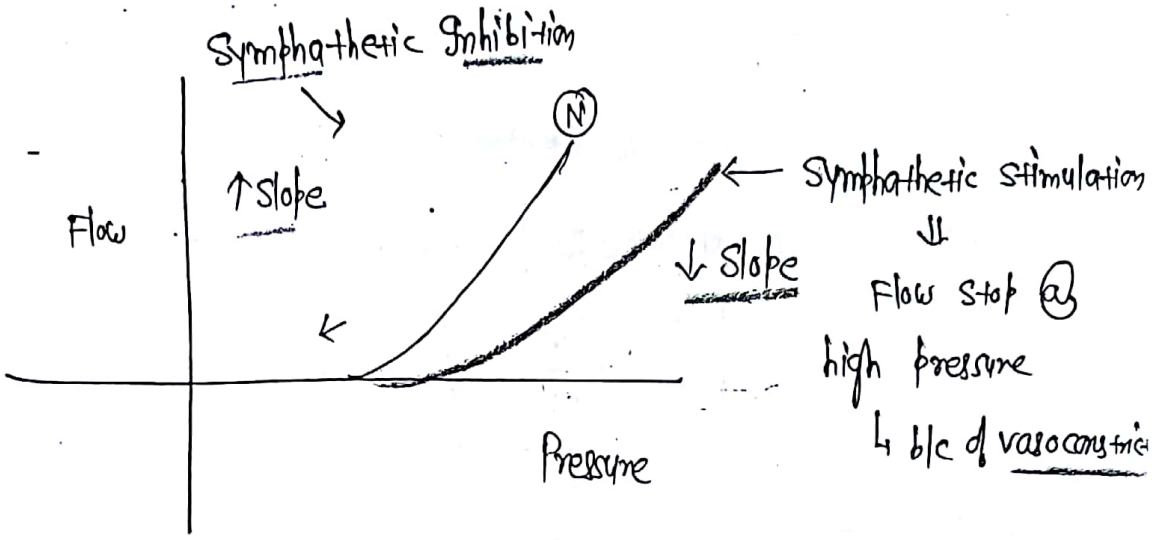
⇓

Reason ⇒ i) Collateral inflow into the Arteriolar Meshwork;
ii) Rouleaux formation

iii) External Tissue Pressure > Distending pressure Inside vessel.

iv) High Vascular Smooth Muscle tone (eg in Arterioles)

QQ.



* Parasymfathetic Not Seen @ blood vessels few exception only.

MYOCARDIAL O_2 demand

- "Hard working organ"
- Oxidative Metabolism (< 1% ⇒ Glycolytic)
- Fuel for heart -- Fatty acids

(QQ) Basal O_2 demand ⇒ Quiescent heart
↳ 2ml/min/100gm of tissue

Demand of Skeletal Muscle @ Rest ⇒ 0-2 ml/min/100gm of tissue

Beating heart @ ⇒ 9ml/min/100gm
Rest

* Factors Yes Myocardial O_2 demand :⇒

① Heart Rate;

② Duration of systole;

③ Intra Myocardial tension

$$T = \frac{Pr}{2w}$$

④ Work done by heart = Stroke volume X Mean Arterial Pressure

↑ SV ↑ MAP

↑ Vol. work ↑ Pressure work

In AR In AS

↑ O_2 demand ∵ Yes in Pressure work is

∨

∴ In volume work

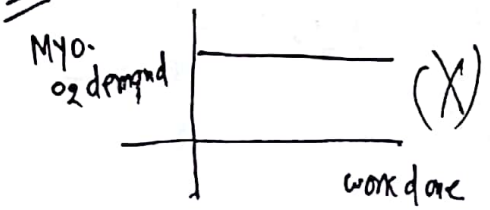
⇒ In patient of AS higher O_2 demand than AR.

⇓

So; Pt. of AS commonly presents ∵ Angina

QQ. Work done & Myo. oxygen demand = ~~Constant~~ Relationship

Almost Linear Relationship



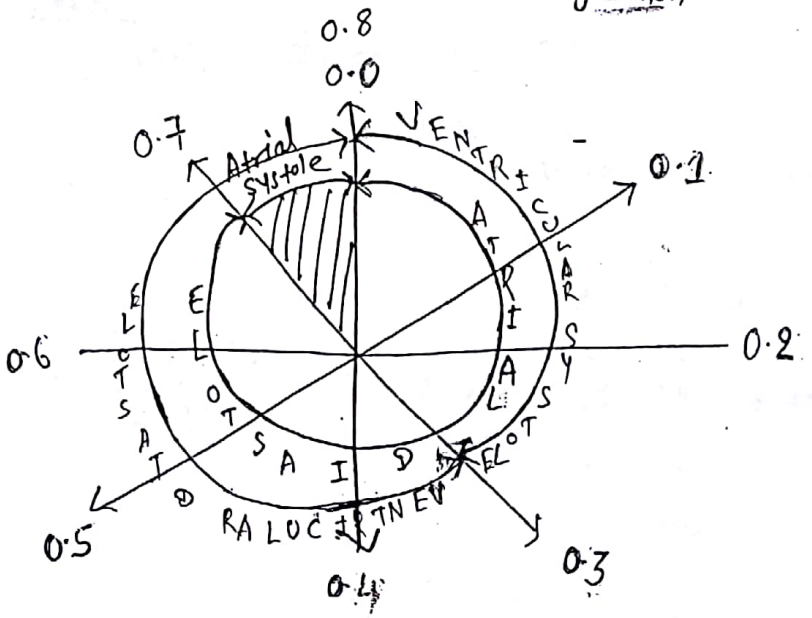
CARDIAC CYCLE **

* Electrical & Mechanical changes which occur in heart from one beat to Next.

* Cardiac cycle time = 0.8 sec

CARDIAC CYCLE S.G

- Atrial event
  - Atrial systole (0.1 sec)
  - Atrial diastole (0.7 sec)
- Ventricular event
  - Ventricular systole
    - Isovolemetric contraction
    - Phase of Rapid ejection
    - Phase of slow ejection
  - Ventricular Diastole
    - Isovolemetric Relaxation
    - 1st Rapid filling phase
    - Diastasis
    - 2nd rapid filling phase (Atrial Systole)



* ATRIAL PRESSURE (Atria ⇒ Low pressure zone)

Diastole ⇒ 0-3 mm Hg

Atria
↳ Primer pump

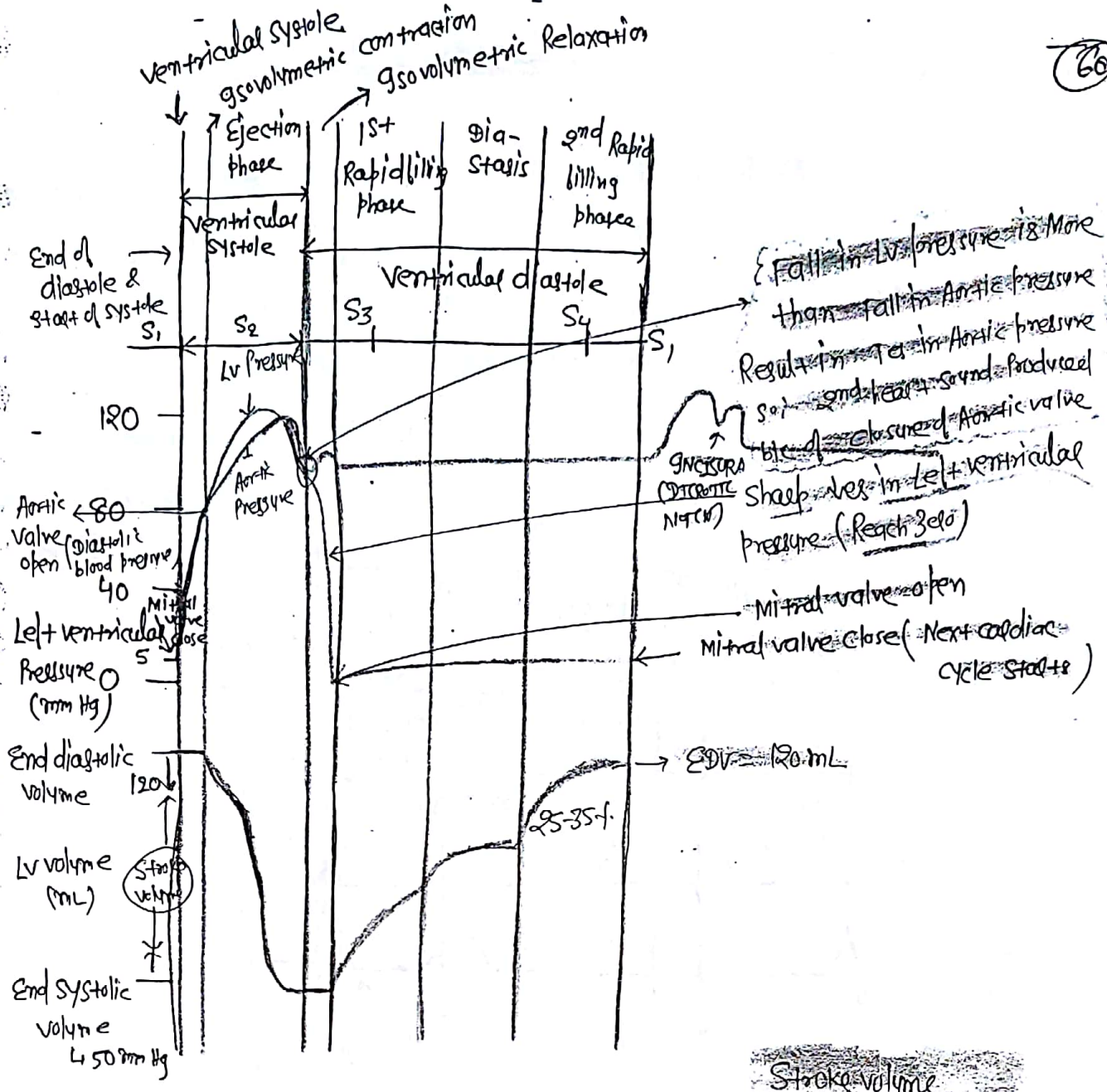
Systole → Right Atrial Pressure ⇒ 4-6 mm Hg
→ Left Atrial Pressure ⇒ 6-8 mm Hg

Pressure of Left Atrial Pressure is More d/t "Physiological shunting"

↳ Part of venous blood from coronary circulation & Bronchial circulation directly into Left Atrium (So, it Receives More blood)

* VENTRICULAR PRESSURE ⇒

	Systolic Pressure	Diastolic Pressure	MAP
Left ventricle	120 mm	0 (0-5 mm)	—
Systemic circulation	120 mm	80 mm	100 mm
Right ventricle	25 mm	0 (0-5 mm)	
Pulmonary circulation	25 mm	9 mm	15 mm



Stroke volume
↳ EDV - ESV

Ejection fraction
↳ $\frac{SV}{EDV}$ = 0.55-0.65
⇓
55-65%

S_1 ⇒ closure of Mitral valve

S_2 ⇒ closure of Aortic valve

S_3 ⇒ 1st Rapid filling Phase
↳ May be ↑ in children & Normal young adults
↳ ⊕ in condition of ↓es ventricular compliance
↳ as in Left ventricular hypertrophy, congestive cardiac failure.

S_4 ⇒ 2nd Rapid filling phase (Always pathological)
↳ coincides ∵ Atrial systole
↳ ↑ in ↓es ventricular compliance

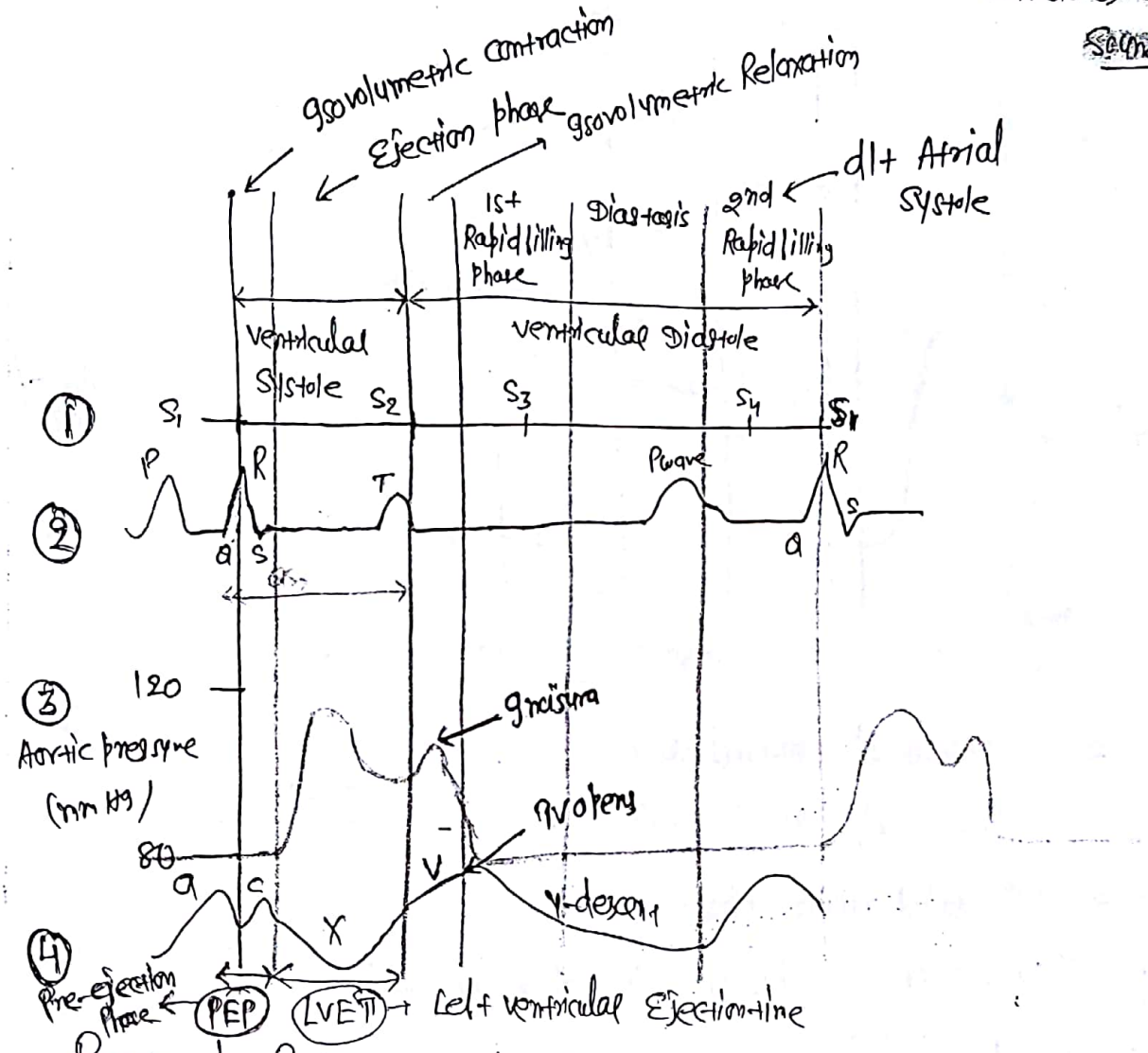
Always pathological

INCISURA ⇒ It is towards the end of ventricular systole;

↳ Left ventricular pressure became lower than Aortic pressure; So; Aortic blood tends to flow back into Left ventricle, but this stream of Aortic blood hits the Now close Aortic valve → INCISURA ON AORTIC PRESSURE CURVE

= Dicrotic Notch"

↳ coincides S2 heart sounds.



Peak of R wave coincides ∴ onset of Isovolumetric Contraction phase (S_1)

S_1 heart Sounds — coincides c → Peak of "R" wave

S_2 heart Sounds — " → End of "T" wave

S_3 heart Sounds — " → b/w "T" & Next "P" wave

S_4 heart Sounds — " → PR Interval.

Jugular Venous Pressure

- ~~Rt side seen~~
- It is better seen; as compare to left.
- JVP has definite upper Level
- Hepatojugular Reflux
- Multiple, positive waves
  - a, c, v
- Multiple Negative waves
  - x-descent; y-descent

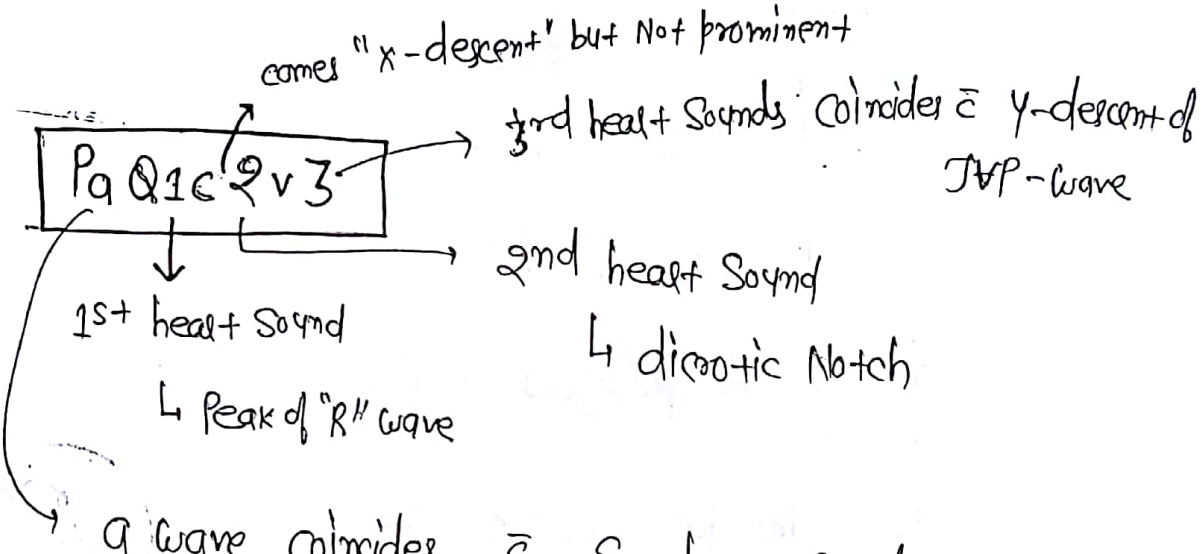
a-wave ⇒ Atrial systole

c-wave ⇒ Bulging of closed ~~Tricuspid valve into Right Atrium~~ during ~~isovolumetric contraction phase~~

X-descent ⇒ Downward pull of closed Tricuspid valve during ejection phase

V-wave ⇒ Venous filling of Right Atrium just before opening of Tricuspid valve

Y-descent ⇒ Flow of blood from Right Atrium into Right Ventricle after opening of Tricuspid valve



* If we Record heart Sounds, ECG & Phonocardiogram Simultaneously ↓

QS2 :- Total Electro-Mechanical Systole

↳ It is from onset of "Q" wave to the onset of "S2" heart sound

↳ It includes Ventricular contraction + Electrical conduction both (QRS complex)

Left ventricular Ejection time (LVET) :-

It is from the onset of carotid pressure Rise to Dicrotic Notch.

Pre-ejection Period (PEP) :- It is

QS_2 = LVET *

QS2 = LVET

(N) PEP / LVET = 0.35 *

(N) PEP / LVET = 0.35

In conduction Abnormality → PEP / LVET → Tes (b/c PEP Prolong & LVET (N))

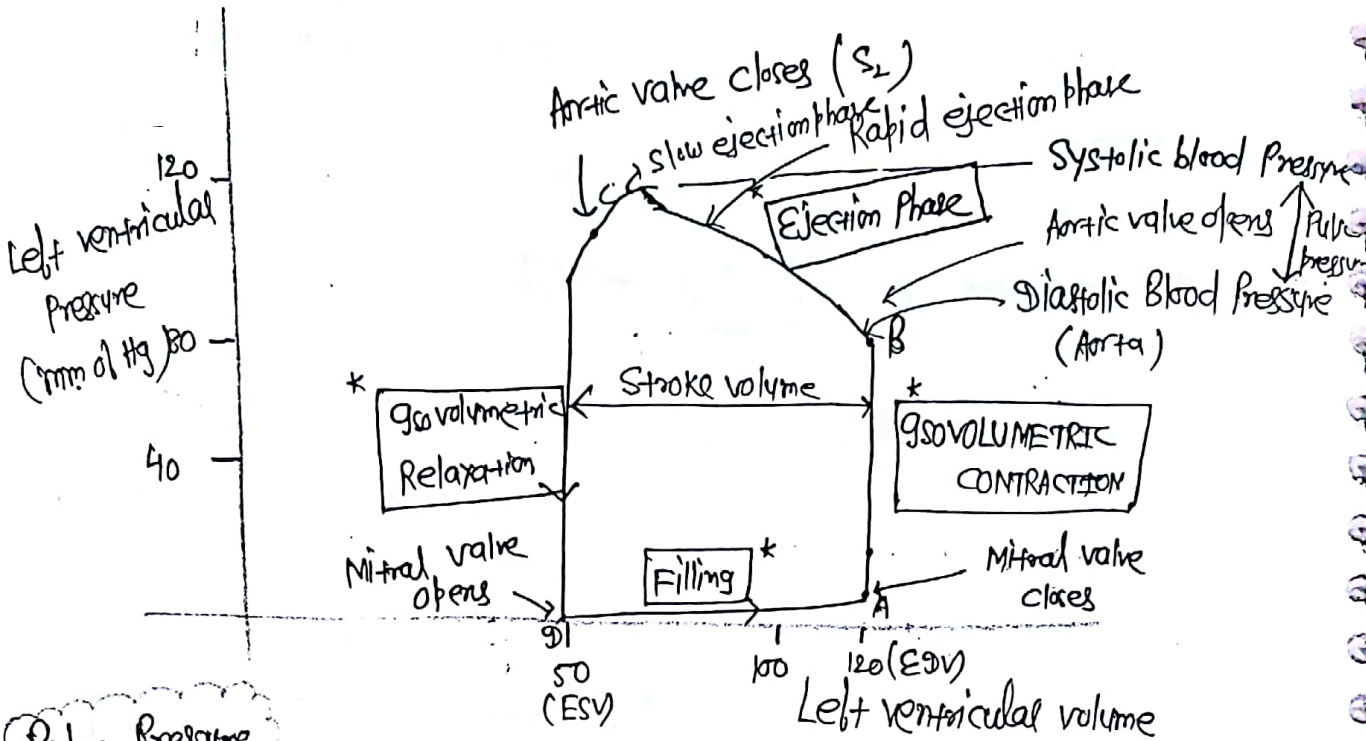
QQ Cardiologist

ECG
Phono cardiogram
Carotid pressure changes
} Recorded Simultaneously

his carotid pressure transducer Not functioning properly ?? Which of the following (N) ??

(A) only QS_2 ; (B) QS_2 & LVET ; (C) LVET & PEP ; (D) All

LEFT-VENTRICULAR PRESSURE VOLUME LOOP

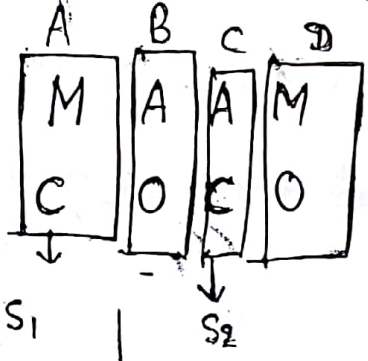


Pulse Pressure

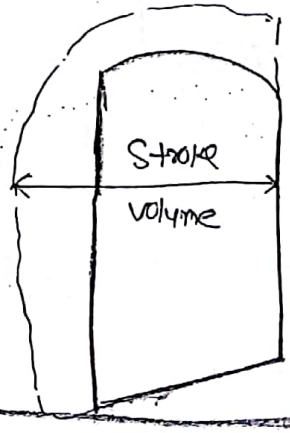
⇓

SBP − DBP

** **Ejection fraction** ⇒ **Stroke Volume** / **End diastolic volume**



Q. Which physiological condn



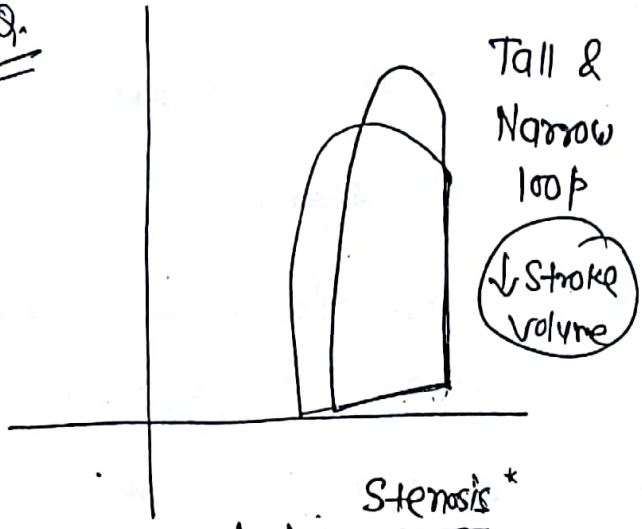
Symphathetic Stimulation of heart:

↑ Myocaldial contractility

↑ Stroke volume

↑ Systemic Peripheral Resistance

QQ.



Aortic Stenosis *

↓ End diastolic volume

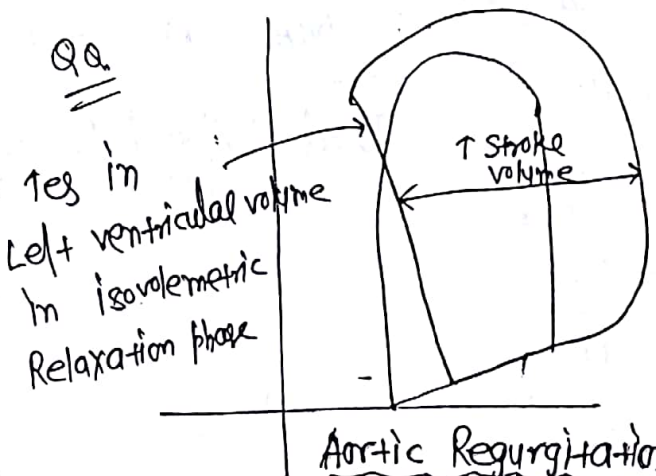
↓ Stroke volume

Mitral stenosis *

⇓

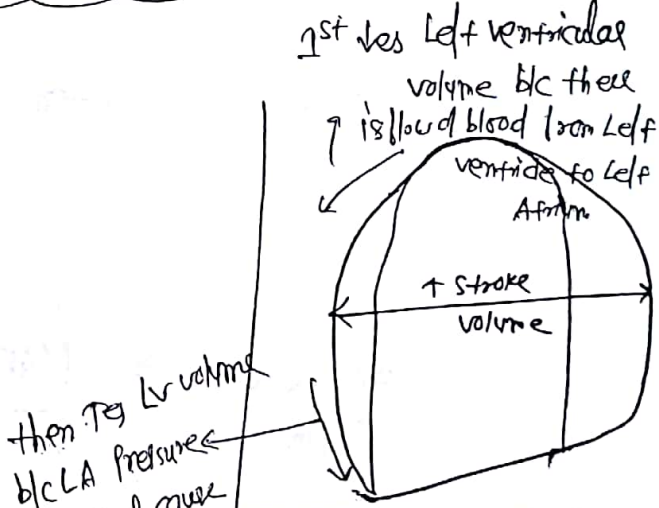
Left side shift of Loop

QQ.



↑es in Left ventricular volume in isovolemetric Relaxation phase

Aortic Regurgitation



then ↑es LV volume b/c LA Pressure ↑es & cause ↑es the LV volume

Mitral Regurgitation

Look @ Isovolumetric Relaxation phase

↓

higher Systolic Pressure *

Lower systolic Pressure *

⇓

Right side shift of loop *

CARDIAC OUTPUT *

- Volume of blood ejected per ventricle/minute
- Cardiac output = 5 Litres/min.
  - ↳ it means Left ventricular output is 5 Litres/min & also Rt. ventricular output is 5 Litres/min
  - Left ventricular output is 1-2 %. More b/c of "Physiological Shunting" *

Cardiac output = Left ventricular output = Systemic blood flow

Cardiac output = Right ventricular output = Pulmonary blood flow

→ C.O. = Systemic blood flow = $\frac{\text{MAP} - \text{Rt. Atrial Pressure (RAP)}}{\text{Total Peripheral Resistance (TPR)}}$ (Mean Atrial Pressure)

$\Rightarrow$ C.O. $\Rightarrow$ $\frac{\text{MAP}^{100} - \text{RAP}^{0-3}}{\text{TPR}}$

5 L/min

$\Rightarrow$ $\text{C.O.} = \frac{\text{M.A.P}}{\text{T.P.R}}$ ** $\Rightarrow$ $\text{M.A.P} = \text{C.O.} \times \text{T.P.R}$

Cardiac output = Pulmonary Blood flow = $\frac{\text{Mean Pulmonary Atrial Pressure (15mm) - LAP (Left Atrial Pressure) (8-12mm PCWP)}}{\text{Pulmonary vascular Resistance}}$

5 L/min 5 L/min

⇒ Cardiac output = Heart Rate X Stroke Volume

↑ Cardiac output ⇒ On Exercise (400-500 % Tes)
Anxiety (200 % Tes)
Excitement
Pregnancy
Standing to Lying Position (Tes venous Return)
Eating (30 % Tes)
Hyperthyroidism
Beri-Beri

↓ Cardiac output ⇒ Lying to Standing Posture (Tes venous Return)
Hemorrhage
Hypothyroidism
Myocardial Infraction

* No change in cardiac output :→ • Sleeping

• Moderate changage in Environment temperature

• Regulation of cardiac output :→

Heart Rate | **Stroke volume**

↑ Heart Rate ⇒ ↑ Cardiac output
(Sympathetic Stimulation)

↑ Sympathetic

↑ Heart Rate

(When the heart Rate ↑es
⇓
Duration of all the phases ↓es
↳ duration of diastole ↓es Much More than duration of systole)

↑ Force of contraction

⇓

Result in better emptying of ventricle

⇓ Stroke volume

↑es

(↓es End Systolic volume) AIIMS May '18 **

Decrease end systolic volume

⇓

↑es cardiac output

Increase cardiac output

* When Heart Rate > 180-200/min

⇓

↓↓ Diastolic Filling time

⇓

↓ Stroke volume

⇓

↓ Cardiac output

CO

Stroke volume Stroke volume

depends on

i) Myocardial contractility
Myocardial contactility

↑ Sympathetic
Inotropes
(Caffeine)

↑ contractility
↑ Stroke volume
↑ Cardiac output

ii) Venous Return
venous rectum

↑ Venous Return
↑ End diastolic Volume (Preload)
↑ tension generated
↑ Stroke volume
↑ Cardiac output

Frank-Starling Law, but Upto a physiological extent.

* Factors which affects venous Return :-

i) Blood volume ; (↑es ⇒ Venous Return ↑es)

ii) Sympathetic Stimulation ;

↑ Sympathetic Stimulation
↓
Venous Constriction
↓
↓ venous compliance
↓
↑es venous Return

iii) POSTURE :-

Lying → Standing (↑es Peripheral Pooling
↓es venous Return)

Standing → Lying (↑es venous Return)

iv) Calf Muscle Contraction
↳ Exercise → ↑contraction ⇒ ↑ venous Return
K/as " Muscle Pump "

v) Deep Inspiration
↳ ↓ Pleural Pressure → ↑es venous Return

* Regulation of C.O.

Homometeric regulation

HOMOMETRIC REGULATION

- Includes factors ; which Tes cardiac output and are Independent of ventricular Muscle fiber Length.
- It includes; all factors which affects :-
  a) Heart Rate *
  b) Myocardial contractility *

HETEROMETRIC REGULATION

- Includes factors which affect Venous Return & ventricular Muscle fibers

* VASCULAR FUNCTION CURVES

I. VENOUS RETURN CURVE :-

Venous Return (5 L/min) ⇒ Mean Systemic filling Pressure (P_{sf}) − Right Atrial Pressure (RAP) / Resistance to venous Return

Mean Systemic filling Pressure (P_{sf}) ⇒ When heart stops beating & circulation comes to stand; still Pressure in all vessels (Arterial & veins) Equilibrates ⇒ This Pressure is called "Mean systemic filling"

Mean systemic filling

- It Represents Distending pressure in circulation @ a particular ~~Blood volume & vascular tone~~

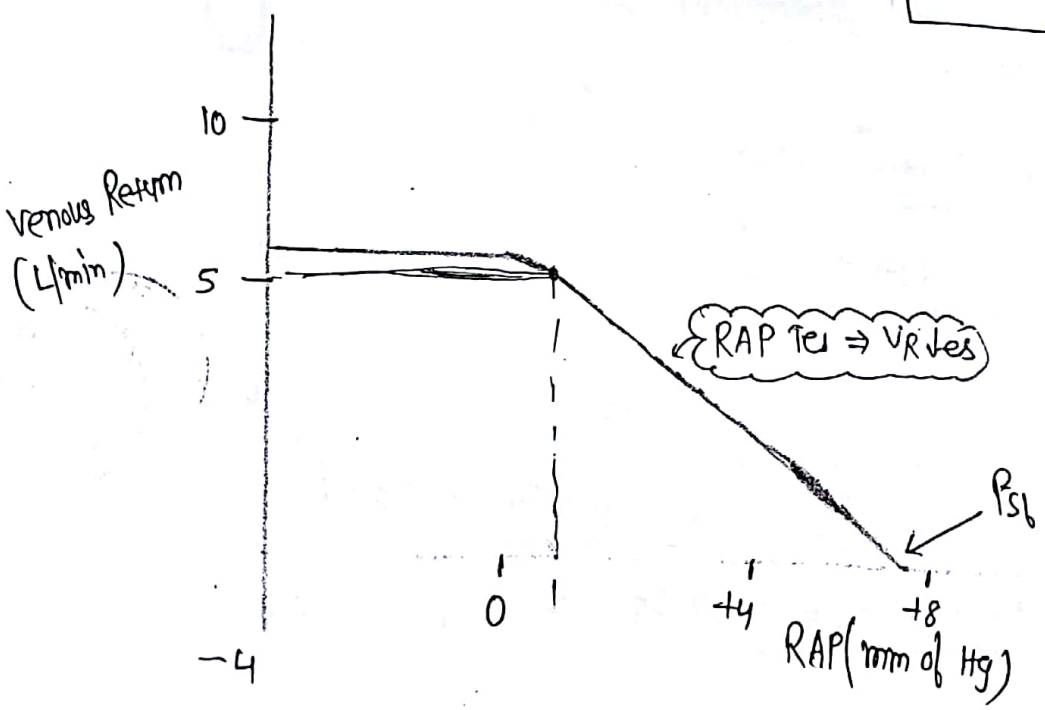
Blood volume and vascular tone

- 2 determinants

↳ Blood volume

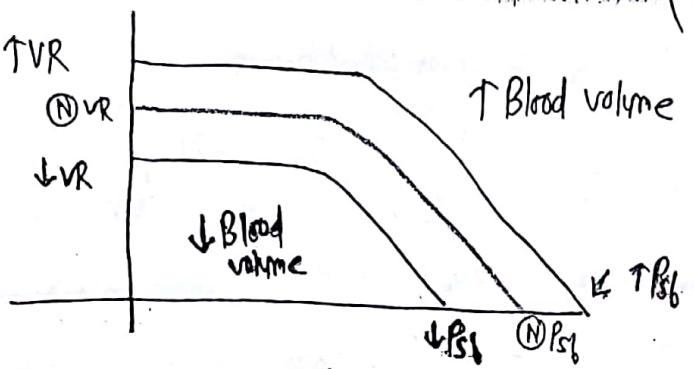
Venous tone.

$$V_R = \frac{P_{sf} - RAP}{Resist.\ VR}$$

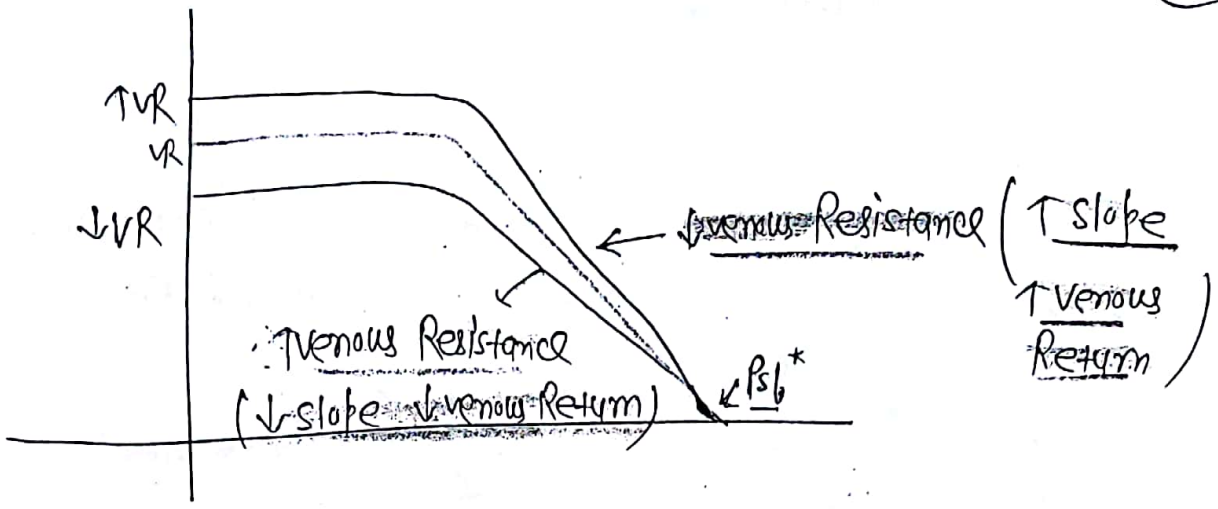


At Right Atrial Pressure (RAP) < 0 mm Hg ⇒ No further ↑es in Venous Return (b/c veins tends to collapse)

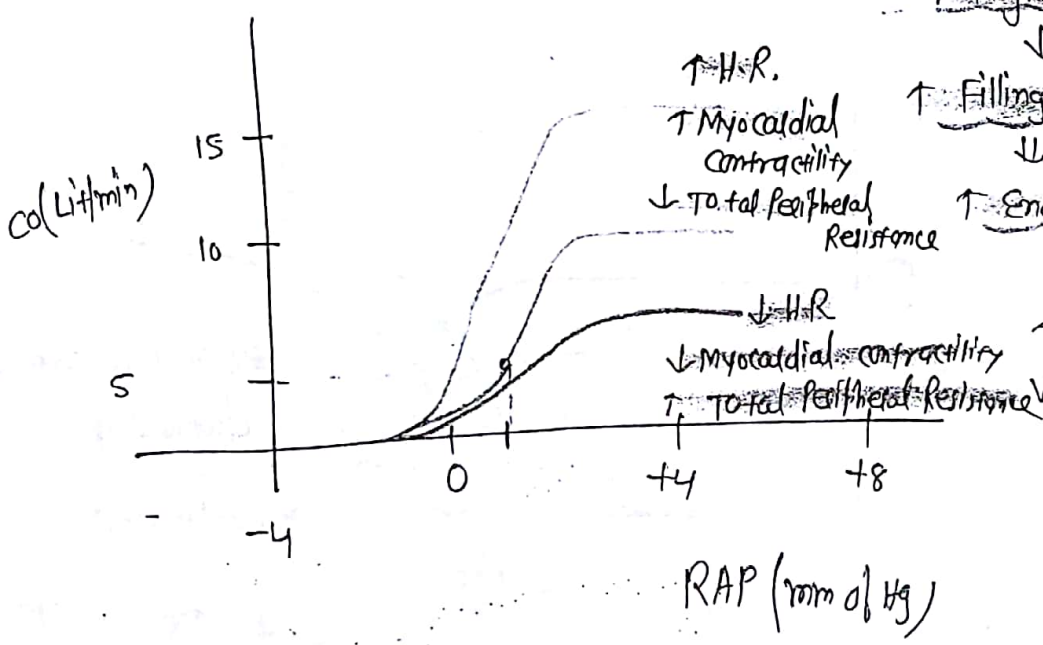
QQ.



QQ

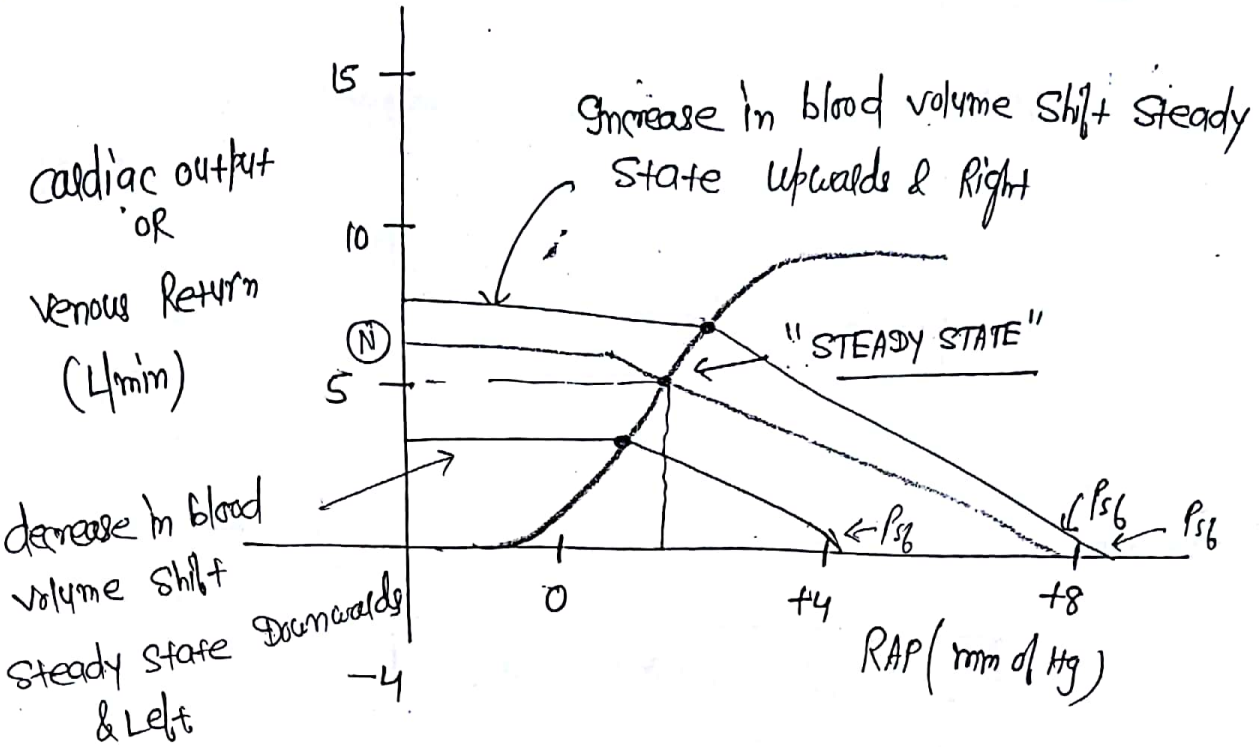


II. CARDIAC OUTPUT CURVES

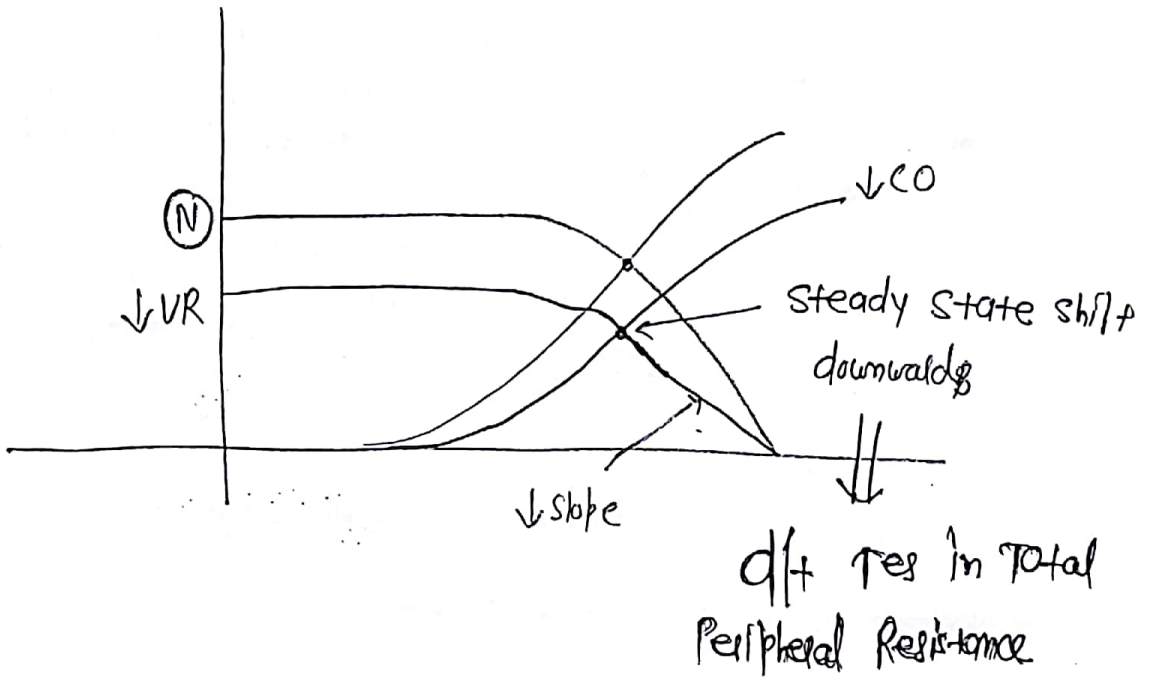


↑ Right Atrial pressure
⇓
↑ Filling of ventricle
⇓
↑ End diastolic volume
⇓
↑ Initial Length of ventricular muscle fiber
⇓
↑ Tension generated
⇓
↑ Stroke volume &
↑ cardiac output

Steady state :-

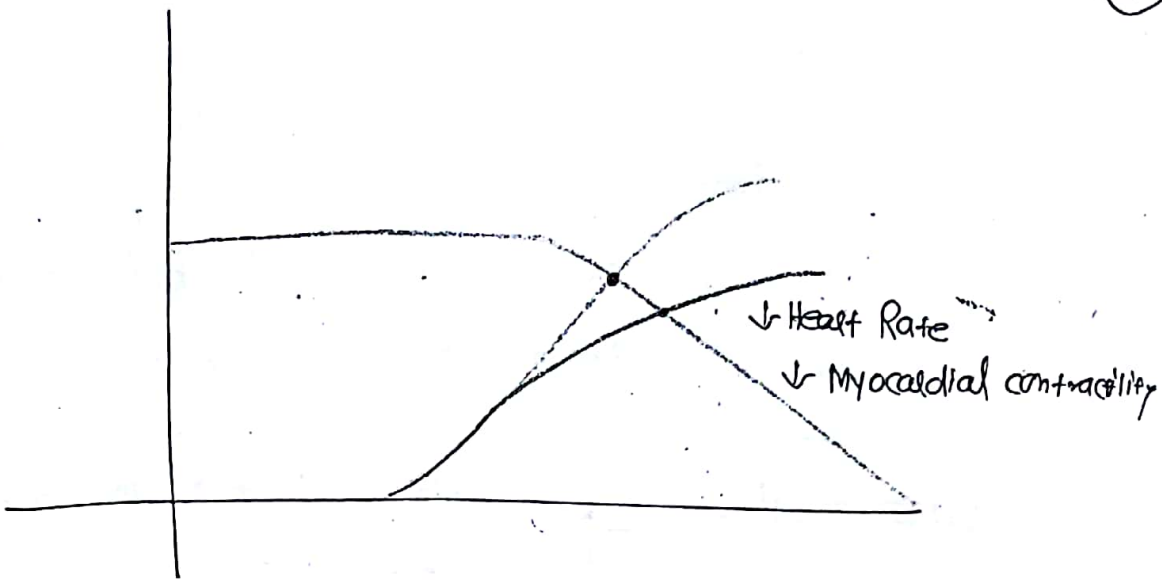


Qq.



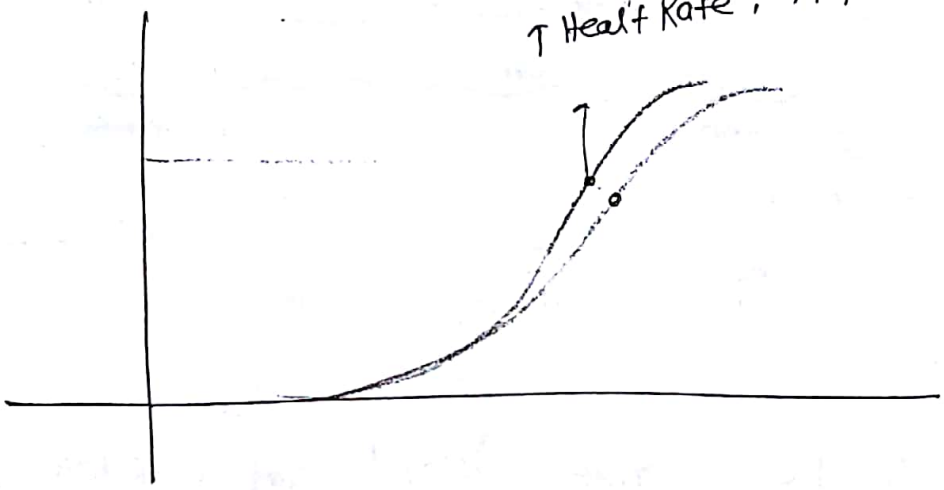
d/t Res in Total Peripheral Resistance

QQ



QQ

↑ Heart Rate ; ↑ Myocardial contractility



KK MEASUREMENT OF CARDIAC OUTPUT

(I) - NON-INVASIVE

↳ Echocardiography & Doppler Studies

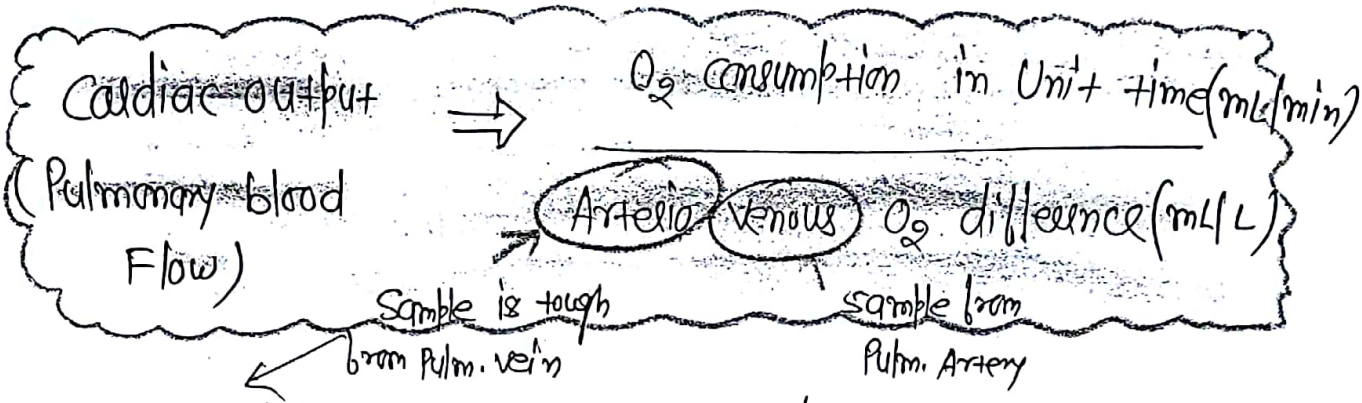
(II) INVASIVE

↳ Fick's principle

Dye dilution technique

Thermodilution technique

FICK'S PRINCIPLE - Amount of a substance taken up by organ / whole body in unit time is equal to the product of Blood flow through organ / whole body in unit time & Arterio-venous difference of that substance



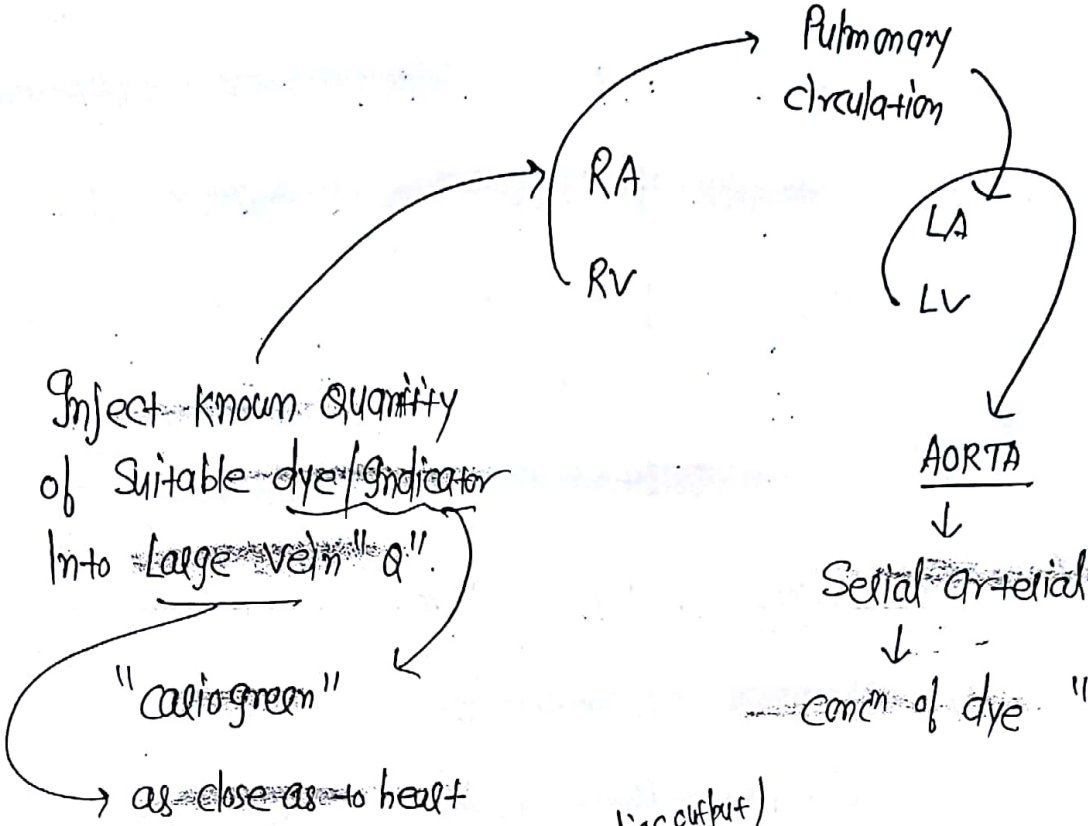
So; taken up by any Systemic Artery $= \frac{250 \text{ mL/min}}{190 \text{ mL/L} - 140 \text{ mL/L}} = \frac{250}{50} = 5 \text{ L/min}$

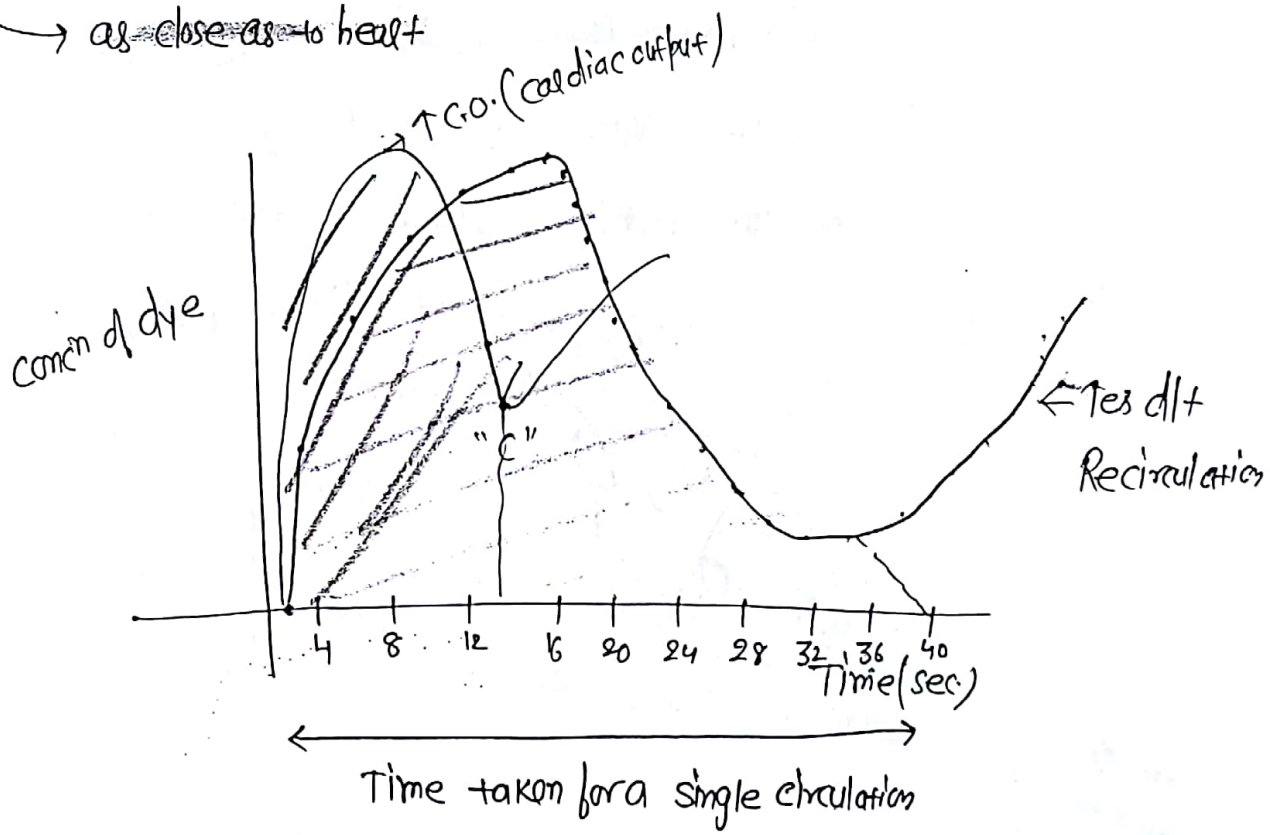
Q) In Fick's principle; Arterial sample is taken from
↳ Any Systemic Artery

QQ) O_2 consumption 600 mL/min
Arterial O_2 .24 mL/mL of blood
Pulm. A O_2 .18 mL/mL of blood

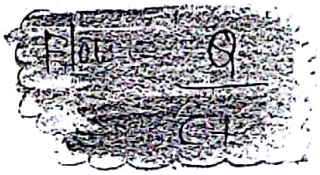
Cardiac output $= \frac{600 \text{ (mL/min)}}{240 \text{ mL/L} - 180 \text{ mL/L}} = \frac{600}{60} = 10 \text{ L/min}$

DYE - DILUTION TECHNIQUE :-





$$\text{Flow} = \frac{Q}{C\,t}$$



C = Conc^n of dye

Q = Volume of Injected dye

if "c" is less = More cardiac output

(N) time = 39 sec

THERMODILUTION TECHNIQUE ⇒ done in CCU settings *

Thermo dilution technique

↳ done by Pulmonary Artery Catheterization → Swan Ganz catheter used

Pulmonary artery catheterization

Instead of dye use warm/cold salime

Instead of conc of dye : use temperature difference

temp. difference

↓ by thermistor

Thermistor

↳ ⊕ at tip of Swan Ganz catheter

K/as " Stewart - Hamilton " principle

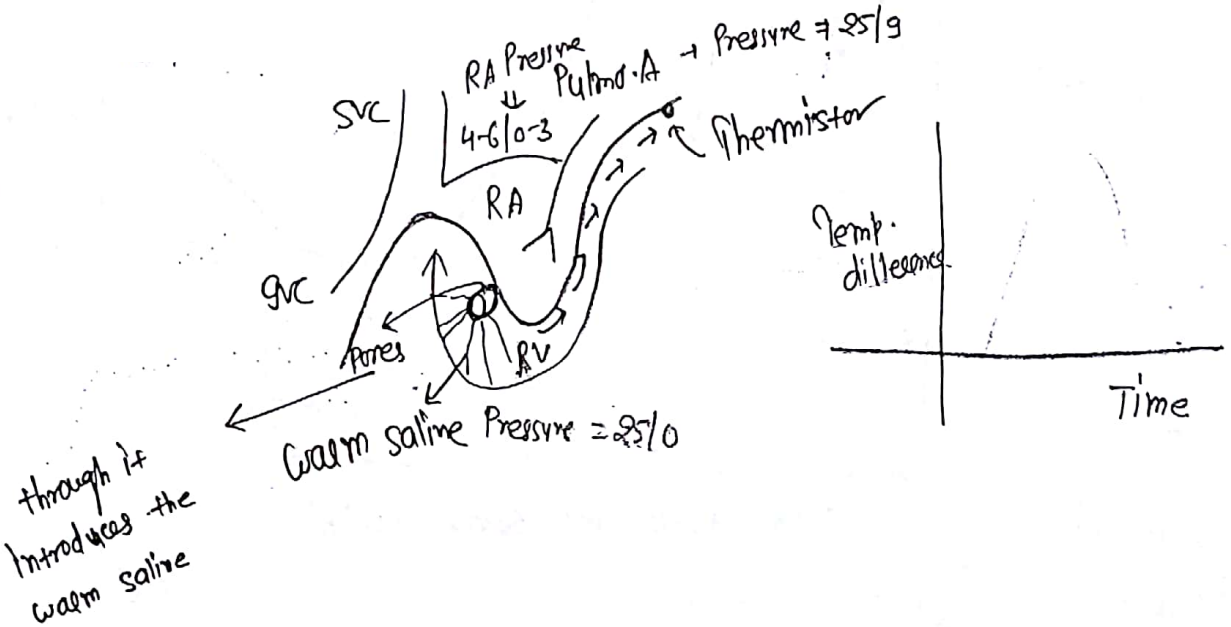
* this technique will be Unreliable in conditions of →

① Tricuspid Regurgitation

② Pulmonary Regurgitation

③ Large ventricular septal defect

④ Very Low cardiac output.



BLOOD PRESSURE

SBP ⇒ Maxm pressure during systole

DBP ⇒ Minm pressure during Diastole

Pulse pressure ⇒ S.B.P − D.B.P.

MAP ⇒ $D.B.P + \frac{1}{3} P.P$ (Pulse pressure)

QQ Best Indicator of TPR ⇒

(1) DBP

(2) ~~MAP~~

2 determinants of Pulse pressure ⇒

a) Stroke volume ⇒ ↑SV ↑P.P. (AR)

↓S.V. ↓P.P. (AS)

b) Arterial compliance (A.C) ⇒ ↑ A.C ↓P.P.

Sclerosis ⟹ ↓ AC TPP.

Sclerosis

QQ Ratio of Strove volume & Arterial compliance approx determine ⇒ SBP

DBP

⟹ PP ∝ $\frac{SV}{ART\ compliance}$

REGULATION OF B.P.

BARORECEPTOR MECH^N

Baroreceptor Mech

"Buffer Nerves"

Stretch Receptor

Stretch receptor

↑ MAP → ↑ Stretch of vessel wall

↓

↑ Firing Rate

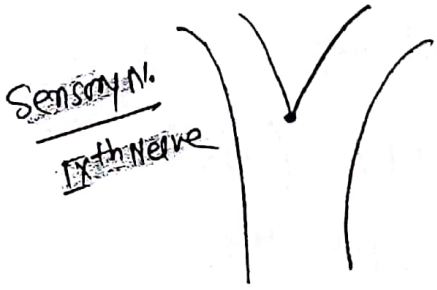
Neural control

→ Response → Immediate

→ Adaptation ⊕

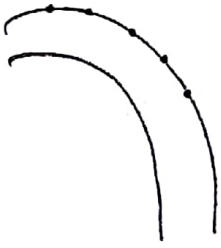
→ Imp. for Short term Regulation

(Min. – to – Min. Regulation)



Sensory N.

IX th Nerve



Sensory N.

X th Nerve

Caloid Sinus

BaloReceptor

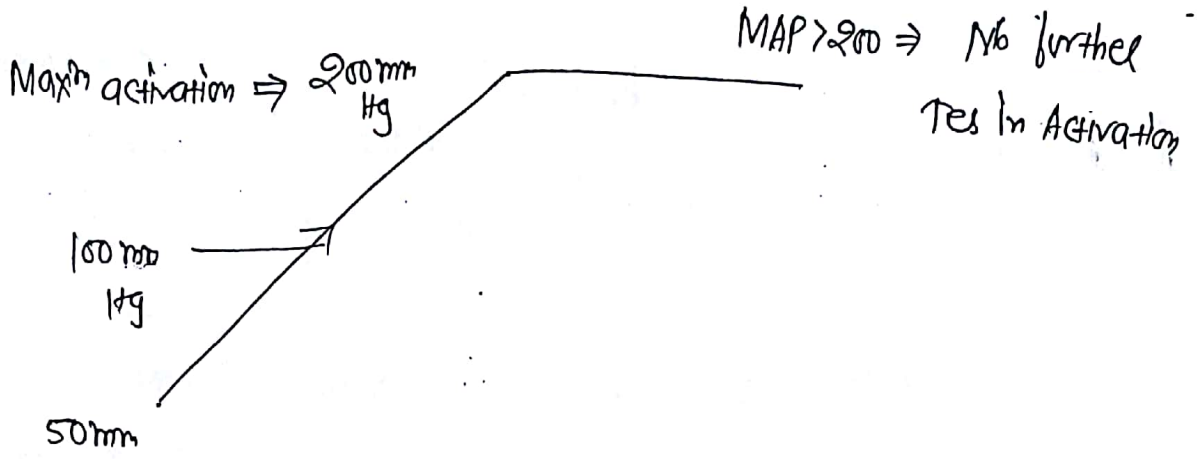
Aortic arch

BaloReceptor

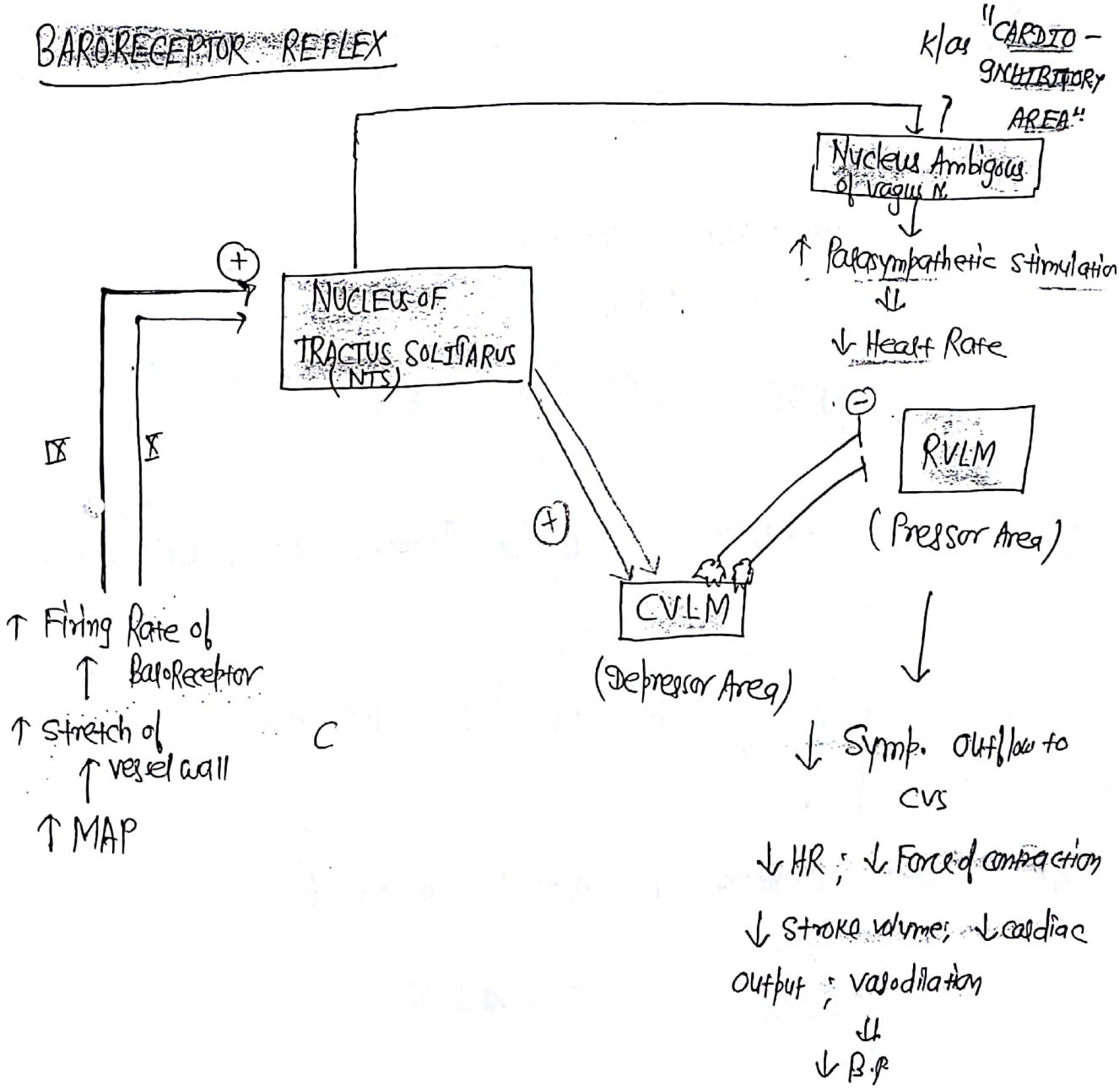
→ 5th time more sensitive than Aortic Arch BaloReceptor

Threshold for Activation of BaloReceptor

↳ MAP of 50 mm Hg



BARORECEPTOR REFLEX



↑ MAP ⟶ ↑ Stretch ⟶ ↑ Firing Rate → ↓ Sympathetic, ↑ Parasympathetic

↓ Heart Rate

dual Role by Sympathetic & Parasympathetic Stimulation → ↓ B.P

↓ ↓MAP → ↓ Stretch → ↓ Firing Rate → ↑ Sympathetic, ↓ Parasympathetic

↑ Heart Rate

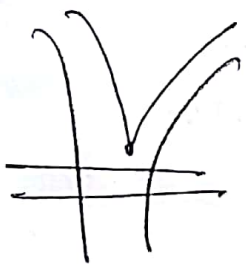
↑ B.P.

QQ. Carotid Sinus Stimulation :-

(A) ↑ B.P. ↑ HR

~~(B)~~ ↓ B.P. ↓ HR (Moderate)

QQ B/L clamping of Carotid Arteries below carotid sinus

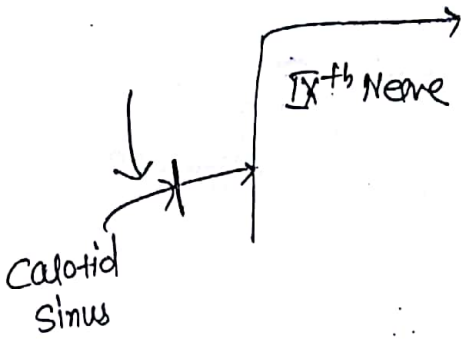


Moderate Rise in B.P. & ↑ HR

QQ B/L clamping of carotid Arteries @ carotid sinus

↓ B.P. & ↓ HR

QQ B/L Section of HERING's Nerve (Carotid Sinus Nerve)

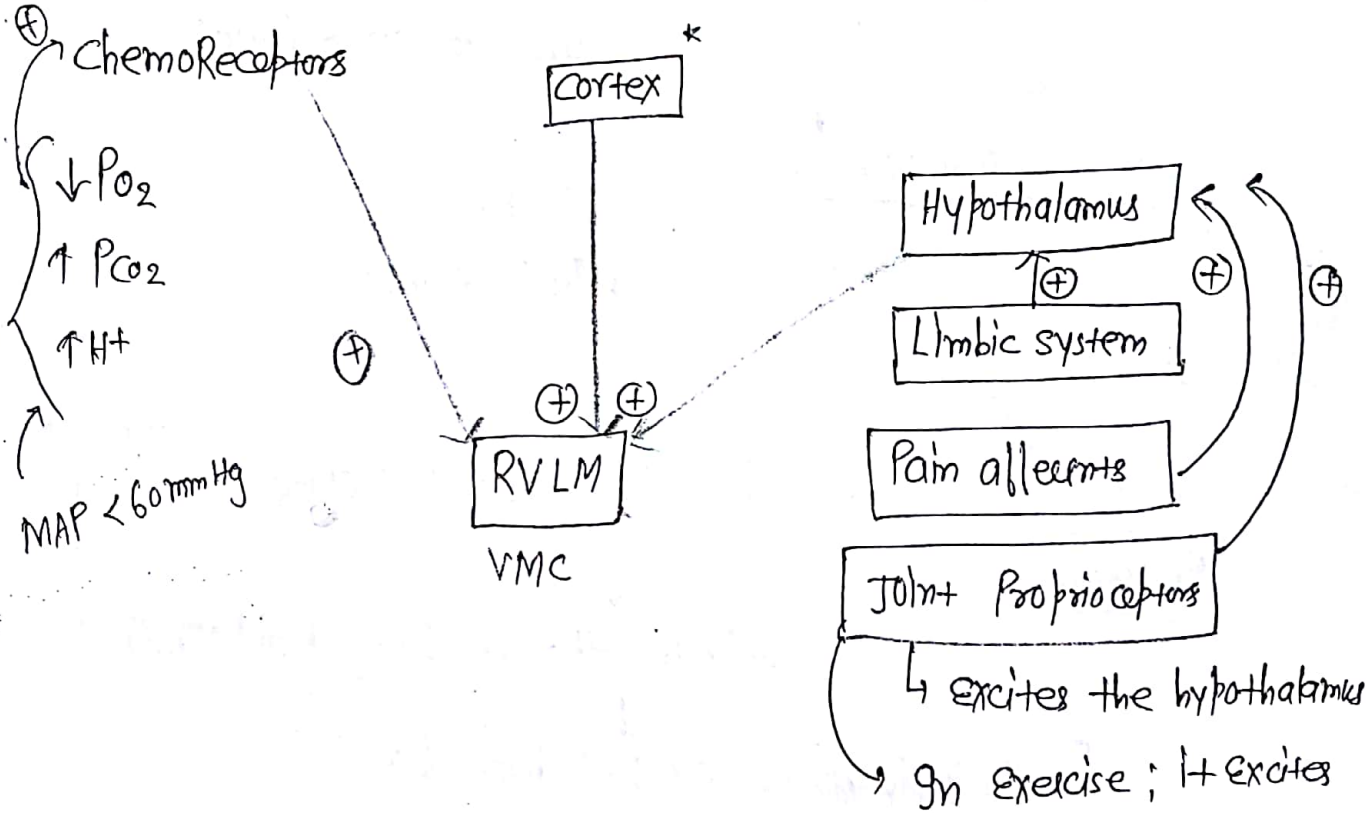


↑ In Sympathetic out flow

⇓

↑ In Blood Pressure & Heart Rate

OTHER INFLUENCES ON VASOMOTOR CENTER [RVLM] :-



CNS ISCHEMIC RESPONSE

- Seen b/w MAP of 65 & 140 mm of Hg
  ↳ cerebral blood flow is constant
  (Ucd Auto Regulation)

⇓

but if MAP < 65 mm of Hg ⇒ ↓es cerebral blood flow

⇓

CNS Ischemia

⇓

direct & very strong stimulation of Vaso Motor centre (VMC)

⇓

↑↑ B.P.
↑↑ HR

* Most powerfully activated @ MAP of 40 mm of Hg

⇓

Klas " LAST DITCH STAND* ".

* CUSHING's RESPONSE ⇒ ↑es Intracranial Pressure

⇓

Compress the cerebral blood vessels

⇓

Reflex Bradycardia ↓ cerebral blood flow

Intact baroreceptor Mechn ↑

⇓

CNS Ischemia

↑↑ B.P.

↳ CNS Ischemic Response

Direct & very ↓ Strong stimulation of VMC

ATRIAL STRETCH RECEPTOR RESPONSE

- Volume Receptors
- ⊕ in Low pressure Zones (Atria & Pulmonary vessels)
- 2 type of Atrial Stretch Receptor

TYPE A

Discharge in Atrial systole

TYPE B

Discharge in Late atrial diastole

↑ Blood volume

↓

Stimulate Atrial stretch Receptor

- ↑ ANP
  - Afferent Arterial dilatation
  - Mesangial cell Relaxation
  - ↓ Na+ Reabsorption
    - Natriuresis

  } ↑GFR

- ↓ ADH
- Vagodilation
- Inhibit Vagal action on SA Node → ↑ HR

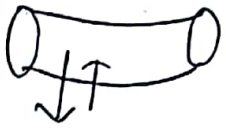
RAAS

Stimuli which ↑es Renin (JG cells) ⇒

- Hypovolemia
- Hemorrhage
- Hypotension
- Dehydration
- Hyponatremia
- Excessive Use of Diuretics
- ↓ Renal afferent arteriole Pressure
- Renal Artery Stenosis
- ↑ Sympathetic
- Prolonged Standing
- Cirrhosis, CCF → Edema ++, ↓ circulating blood volume, ↑ Renin → 2° HYPERALDOSTERONISM.

* CAPILLARY FLUID SHIFT ⇒

↑ MAP
↓
↑ Capillary Pressure
↓
↑ Tissue fluid formation



QQ

MARRY'S LAW

Heart Rate $\propto \frac{1}{\text{Blood Pressure}}$

Physiological basis
⇓
BaroReceptor Response

B.P. $\propto \frac{1}{HR}$

BAINBRIDGE REFLEX

**

Sudden ↑ in blood volume → ↑ Heart Rate
↳ d/t Atrial Stretch ↑Receptor pressure
↳ Direct Stretch of SA Node

BEZOLD-JARISH REFLEX (CORONORY CHEMOREFLEX)

- Injection of -
  - Serotonin
  - Capsaicin
  - Veratridine
  - Phenylguanides

  → Into Carotid Arteries

⇓

Causes Apnea followed by Rapid shallow ventilation

⇓

Hypotension
Bradycardia

RENAL PHYSIOLOGY

Excretion ⇒ Filtration − Reabsorption + Secretion

Glomerular filtration Membrane ⇒

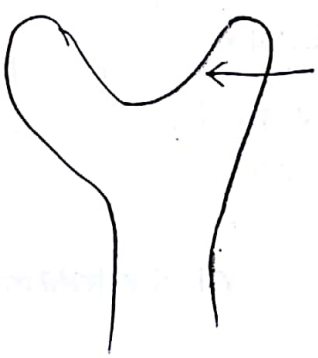
(i) Glomerular capillary Endothelium
- → Fenestrated
- → Large pores ⊕
- → 70–80 nm

(ii) Basement Membrane (Limiting factor for filtration)
- → No Pores
- → Permeability is equivalent to pore size of 8nm
- → Proteoglycans | sialoproteins ⊕

⇓

gives ⊖ve charge to basement Membrane

(iii)



visceral Layer of Bowman's capsule

⇓

Modified to form Podocytes

Filtration slits ⊕
- → 25–30 nm

* Neutral Substance > 8nm ⇒ Not filtered at all.

QQ Least Permeability of size & charge of

7nm ⊖ ⇒ size of Albumin

7nm ⊕

4nm ⊖

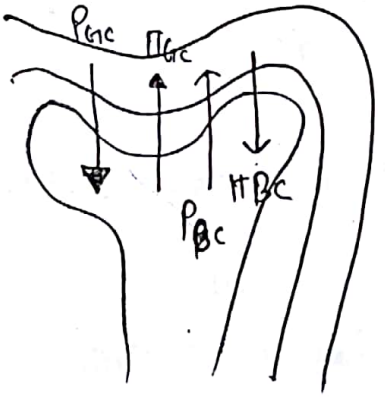
4nm ⊕ve

⇓

1st protein to appear in Urine when basement Memb. loses its ⊖ve charge.

HCO_3^- free filtered b/c of its small size

* Pressure Responsible for FILTERATION :-



Net filtration pressure ⇒

$\Rightarrow P_{GC} - \pi_{GC} - P_{BC} + \pi_{BC}$

$= 45 - 20 - 10 + 0$

$= 15 mmHg$ (=)

$(10 mmHg)$ (=)

* GFR $\propto$ Net filtration pressure

$\propto (P_{GC} - \pi_{GC} - P_{BC} + \pi_{BC})$

$= K_f (P_{GC} - \pi_{GC} - P_{BC} + \pi_{BC})$

③ ④ ⑤ ⑥

K_f = Permeability (①) × Surface Area (②)

all six parameter affects GFR

* ↑ Sympathetic Stimulation

⇓

i) Afferent arteriole Constriction

ii) Mesangial cell contraction

↳ "KINKING" of Glomerular capillary

⇓

↓ Surface area

↓ S.A
↓ GFR

iii) Renin

* ↓n Afferent Arteriole Dilatation

⇓

↑ P_{GC}

⇓

↑ GFR

* ↓n Ureteric Stone OR Benign Hyperplasia of Prostate

⇓

↑ P_{BC}

⇓

↓ GFR

QQ. Blood Flows from afferent to efferent arteriole;

Which Tes ⇒

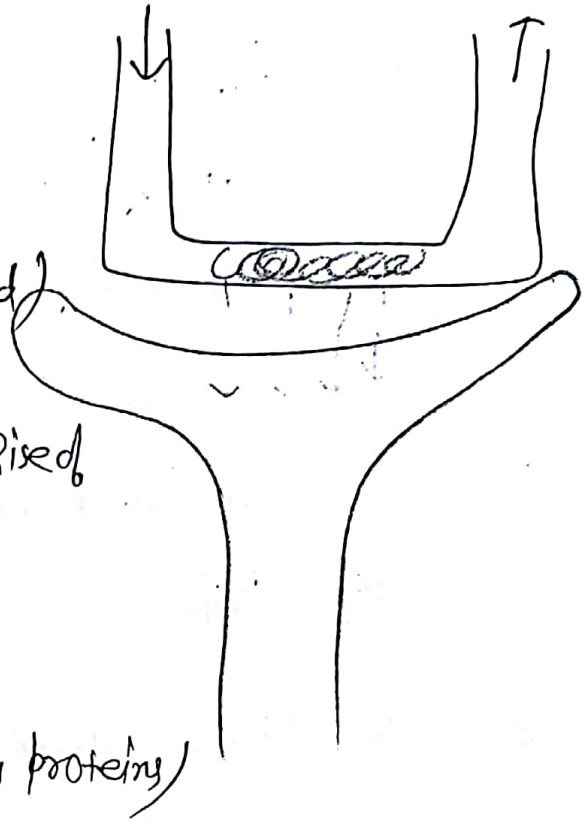
i) P_{GC}

~~ii) π_{GC}~~

iii) P_{BC} (Remain Unchanged)

iv) Net filtration pressure

↳ Yes b/c of Rised π_{GC}



Glomerular filtrate

↳ Ultrafiltrate of plasma

↳ (Plasma - Plasma proteins)

* Sometimes filtration @ the efferent arteriole = O(3ea)

⇒ Renal blood flow ⇒ 1100 - 1200 mL/min (22-23% of cardiac output)

Renal plasma flow ⇒ 625 - 650 mL/min

GFR ⇒ 125 mL/min

Glomerular filtrate ⇒ Ultrafiltrate of Plasma

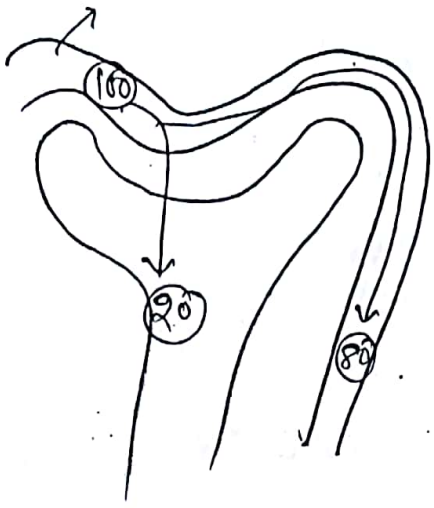
Filtration fraction ⇒ $\frac{GFR}{RPF} = \frac{125 ml/min}{625 ml/min} = 0.16 - 0.20$

$= 16 - 20\%$

freely filtered ⇒ It doesn't Mean 100% filtered

⇓

Maximum 20% filtered in single circulation.



① ↑ GFR

~~a> Afferent Arteriolar dilatation~~

b> Efferent Arteriolar constrication

⇓

dual effect on GFR

Mild to Moderate efferent arteriole constrication ⇒ ↑ P_{GC}, ↑ GFR

↓ also ↑ Filtration fraction → ↑ Π_{GC} (also)

At one point ↑↑ Π_{GC} More than P_{GC} (↑) ; So GFR ↓es

(In Severe efferent arteriolar constriction)

⇓

efferent arteriolar diameter is 1/2 - 1/3 of afferent arteriolar diameter

(↓↓ RPF)

② ↑ Filtration fraction

a> afferent arteriolar dilatation

~~b> Efferent arteriolar constricatk~~

$FF = \frac{GFR\uparrow}{RPF\uparrow} = Same$

$FF = \frac{GFR\uparrow}{RPF\downarrow}$

Q0 Effect of Efferent arteriolar constriction on GFR ↓

a) ~~Initially~~ ↑es then ↓es ;

b) ↑es ;

c) ↓es ;

d) No change.

EFFECT OF ANGIOTENSIN & SYMPATHETIC ON GFR

A	attacks	E
E	attacks	A

Angio-tensin - II ⇒ Efferent arteriole constriction

Sympathetic (epinephrine ⇒ Afferent arteriole constriction (↓GFR)

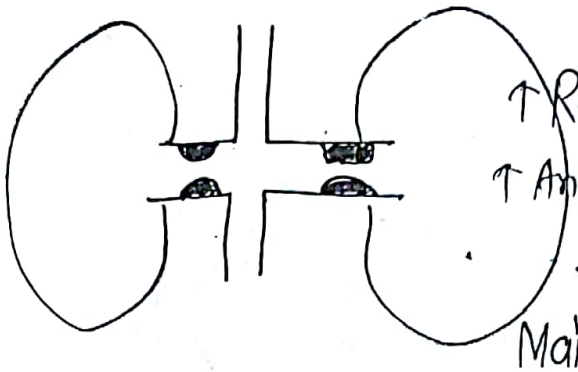
**

Angio II

→ Low conc^n (Physiological cond^n & Renal A. Stenosis) ⇒ Efferent arteriole constriction (↑GFR)

→ High conc^n (Hypovolemia Hemorrhage) ⇒ Both afferent & efferent arteriole constriction (↓GFR)

B/L Renal A Stenosis ⇒



↑ Renin
↑ Angiotensin II (Low conc^n)
⇓
Maintains GFR

Pt. comes ☹ Hypertension

↳ if we give ACE Inhibitor
⇓
it causes to block in Angiotensin II
⇓
Result in "Renal Shutdown"

So; in this patient ACE Inhibitor all Contraindicated.

Renal Handling of different Substances

- Not Filtered / ~~Reabsorbed~~ @ all = Proteins (Albumin)

- Freely filtered; Not Reabsorb; Not secreted ⇒ Inulin

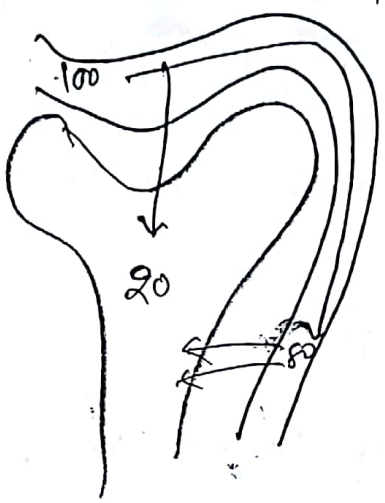
$$Cl_{in} = GFR$$

iii) Freely filtered; completly Reabsorb ⇒

Glucose

Amino acid

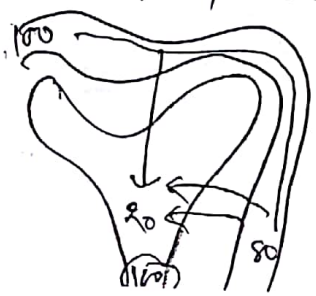
HCO_3^- (if HCO_3^- < 24meq/Litre)



iv) Freely Filtered ; Partly Reabsorb ⇒

- H_2O ⇒ GFR ⇒ 180 Litres/day
  - Urine ⇒ 1–1.5 Litre/day
- Electrolytes
- Urea (52%)

v) Freely filtered; completly secreted ⇒



Para amino hippuric acid

↓↓

Renal plasma flow

C_{PAH} (Excretion)

vi) Freely filtered; Partially secreted :-

- PAH (High conc^n)
- creatinine

* How to calculate the filtration Rate & Excretion Rate :-

Filtration Rate

⇓

GFR × P_x

$\frac{mL}{min} \times \frac{mg}{mL}$

$= \frac{mg}{min}$

Excretion Rate

⇓

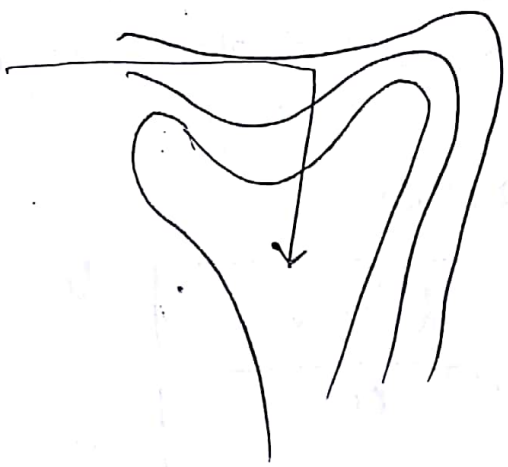
$U_x \times V$ → Rate of urine flow

⇓

Urine conc^n of "x"

$= \frac{mg}{mL} \times \frac{mL}{min}$

$= \frac{mg}{min}$



QQ - Blood glucose = 100 mg/dl = 1 mg/mL

GFR = 100 mL/min

1 mg/min

10 mg/min

~~100 mg/min~~

100,00 mg/min

QQ $Na^+ = 140$ meq/L

GFR = 180 L/Day

filtration Rate / day ??

$= 180 \times 140 = 25,200$ meq/day

CLEARANCE **

- Volume of plasma cleared of that Substance / free of that Substance in Unit time → Clearance of Substance

- Unit ⇒ mL/min.

- $$Cl_X = \frac{U_X \times V}{P_X}$$

U_X = Urinary concn of Substance "X" (mg/mL)

V = Rate of Urine flow (mL/min)

P_X = Plasma concn of "X" (mg/mL)

** $$[Cl_X] = \frac{\frac{mg}{mL} \times \frac{mL}{min}}{\frac{mg}{mL}} = \frac{mL}{min}$$

$Cl_{Inulin} = GFR$

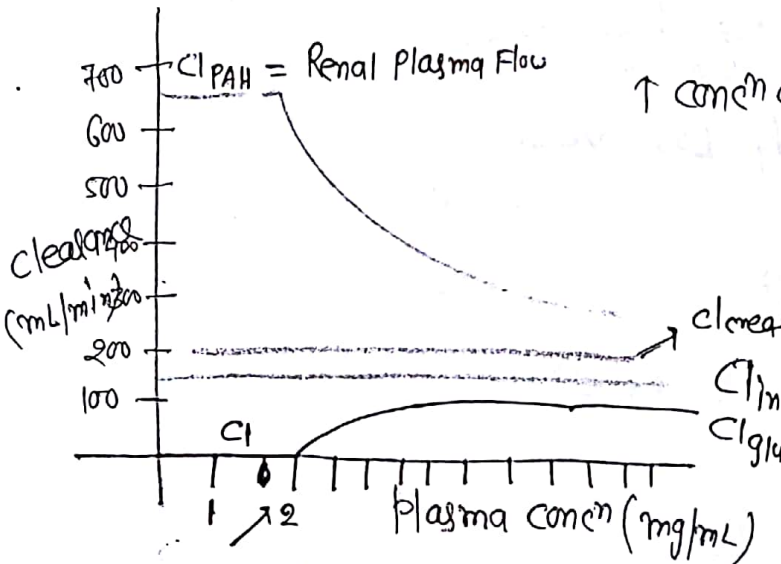
Cl_{PAH} (in Low conc^n) = Renal Plasma flow

For Inulin ⇒ Filtration Rate = Excretion Rate

$\Rightarrow GFR \times P_{in} = U_{in} \times V$

$\Rightarrow GFR = \frac{U_{in} \times V}{P_{in}}$

$\Rightarrow GFR = Cl_{inulin}$ *



↑ conc^n of Plasma PAH
↳ Incomplete secretion
↳ ↓ Cl_{PAH}

Renal threshold
(180-200 mg/dl)
OR
2mg/mL

below 2mg/ml $Cl_{glucose} = 0$; b/c Urinary conc^n of glucose is zero below 2mg/ml.

QQ Which of the following has highest clearance?

a) Inulin;

b) Glucose;

c) Urea;

d) Creatinine

QQ. Cl_{PAH} is used for Measurement of Renal Plasma flow

Technician by Mistake; gives 3 times Recommended dose of PAH

(a) (N) value

(b) Falsely high value

(c) Falsely Low value

FREE H_2O CLEARANCE

Cl_{H_2O} = Rate of Urine flow ($\dot{V}$) − clearance of osmoles

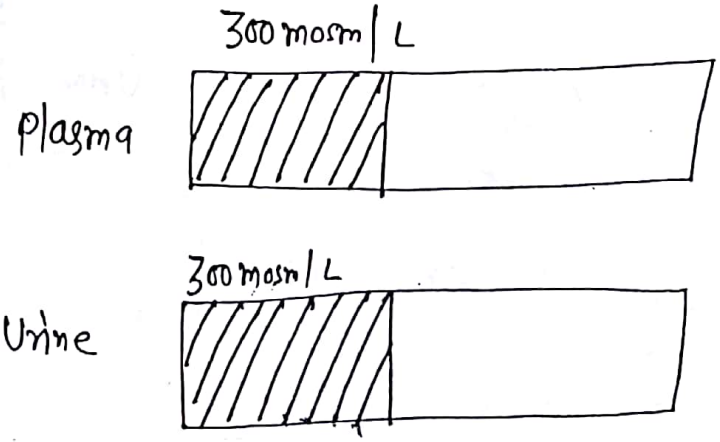
$$Cl_{H_2O} = V - \left[\frac{U_{osm} \times \dot{V}}{P_{osm}}\right]$$

* if Urine is isotonic w.r.t plasma ⇒

$$Cl_{H_2O} = \dot{V} - \left[\frac{U_{osm} \times \dot{V}}{P_{osm}}\right]$$

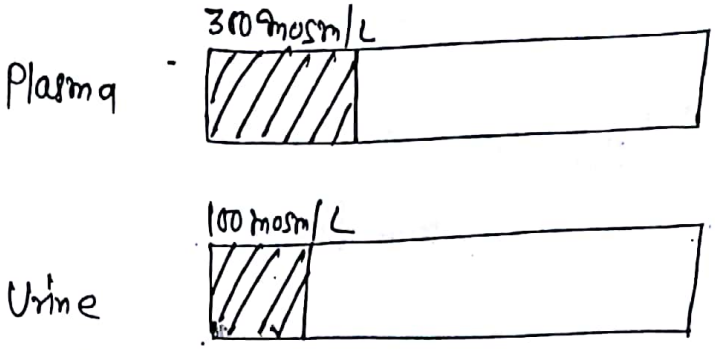
$= \dot{V} - \dot{V}$

$=$ Zero



C_{H_2O} = Zero

* if Urine is Hypotonic :⇒



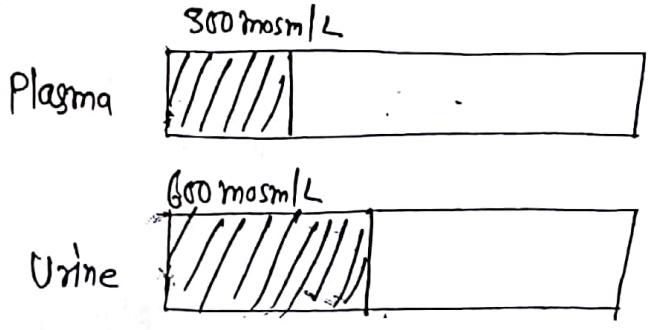
$C_{H_2O} = \dot{V} - \frac{100 \times \dot{V}}{300}$

$= \dot{V} - \frac{1}{3}\dot{V}$

$= \frac{2}{3}\dot{V}$

$C_{H_2O} = \oplus ve$

* if Urine is hypertonic | concentrated :⇒



$C_{H_2O} =$

$\dot{V} - \left(\frac{600^{2} \times \dot{V}}{300}\right)$

$= \dot{V} - 2\dot{V} = \ominus\dot{V}$

$C_{H_2O} = \ominus ve$

Q. $C_{H_2O} = -1.2$ ml/min

Urine is

(a) Isotonic

(b) Hypotonic

(c) ~~Hypertonic~~

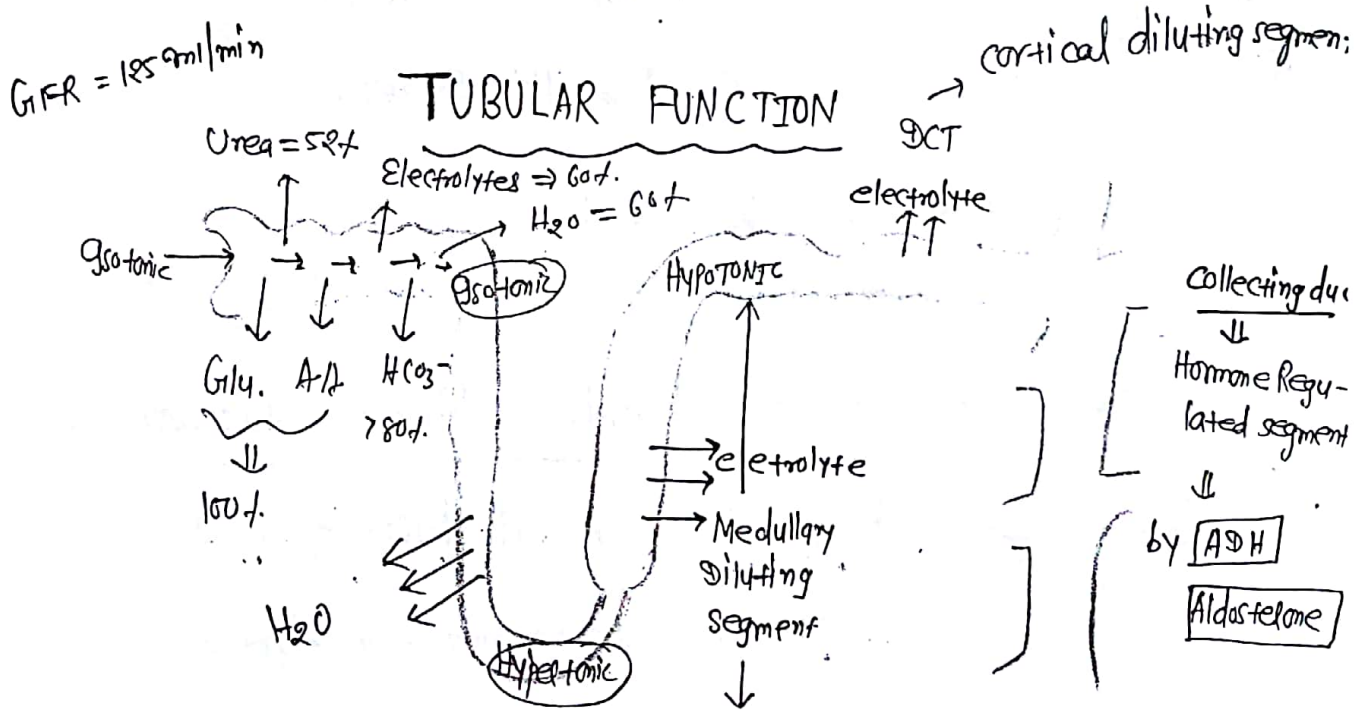
Q In Diabetes Insipidus; $C_{H_2O} = ??$

+ve; Yes

Q. Marathon Runner ; Sweating ++

Maxim Antidiuresis ; $C_{H_2O} = ??$

(a) +ve; (b) ~~-ve~~



PCT ⇒ Angiotensin II ⇒ ↑ Na^+ Reabsorption

PTH ⟶ ↓ Phosphorus Reabsorption
(Phosphaturic Action of PTH)

TAL → Thick ascending Limb ⇒ Angiotensin II ⟶ ↑ Na^+ Reabsorption

DCT ⇒ PTH ⇒ ↑ Ca^{2+} Reabsorption

CD ⇒ ADH ⇒ Yes H_2O Reabsorption

Aldosterone ⇒ Yes Na^+ Reabsorption
Yes K^+ Secretion
Yes H^+ Secretion

ANP ⇒ ↓ Na^+ Reabsorption

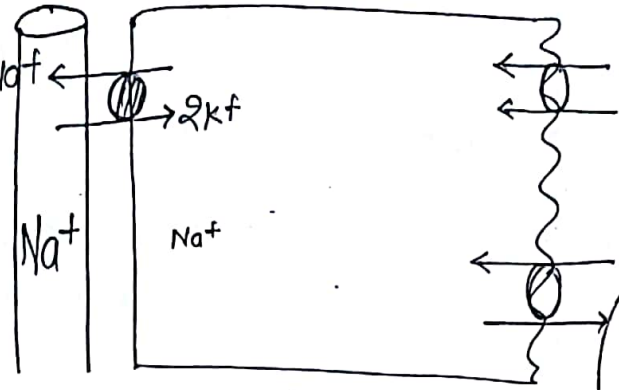
* How does kidney handle different Substances :-

SODIUM ⇒ Reabsorbed in all parts of Nephron
except ⇒ Descending thin segment

PCT :→ Basolateral side of PCT has Na^+-K^+ Pump.

⇓

60 % Na^+ Reabsorb



2° Active co-transport
(Na^+-Glucose
Na^+- Amino acid
Na^+- Pi)

2° Active counter-transport
(Na^+-H^+)

→ Inhibited by Parathormone.

On PCT, (Na^+ - Pi IIa protein)

Na^+ - Pi IIc protein

→ This protein is inhibited by PTH

⇓

↑ Urinary loss of Inorganic Phosphorus

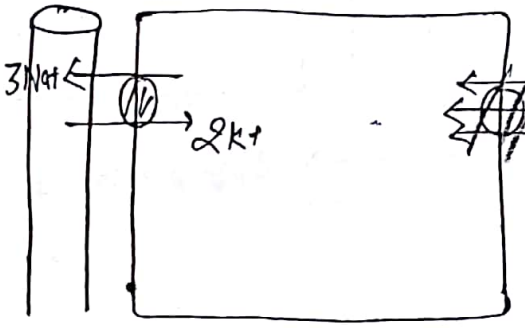
(Phosphaturic action of PTH)

Descending thin segment ⇒ No Reabsorption of Na^+

Thick Ascending Limb ⇒

⇓

30% Na^+ Reabsorb

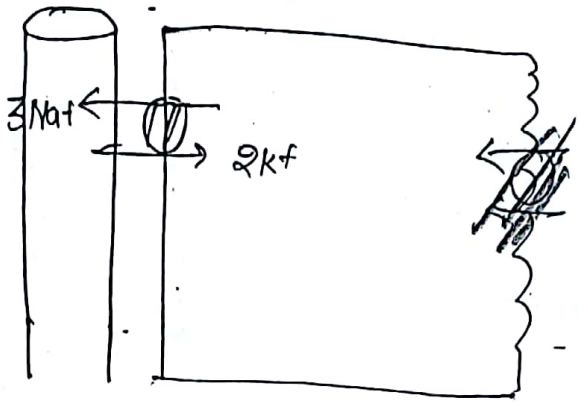


Lasix (Furesomide) works here

$Na^+-K^+-2Cl^-$ Co-transport

(2° active cotransport)

DCT ⇒ 7% Na^+ Reabsorbed

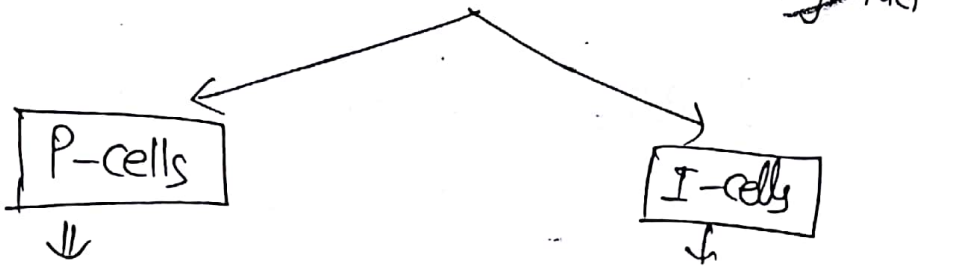


Thiazides acts here

Na^+–Cl^- co-transport

→ Secreted by Zona glomerulosa of Adrenal cortex.

Aldosterone acts on Late DCT & collecting duct

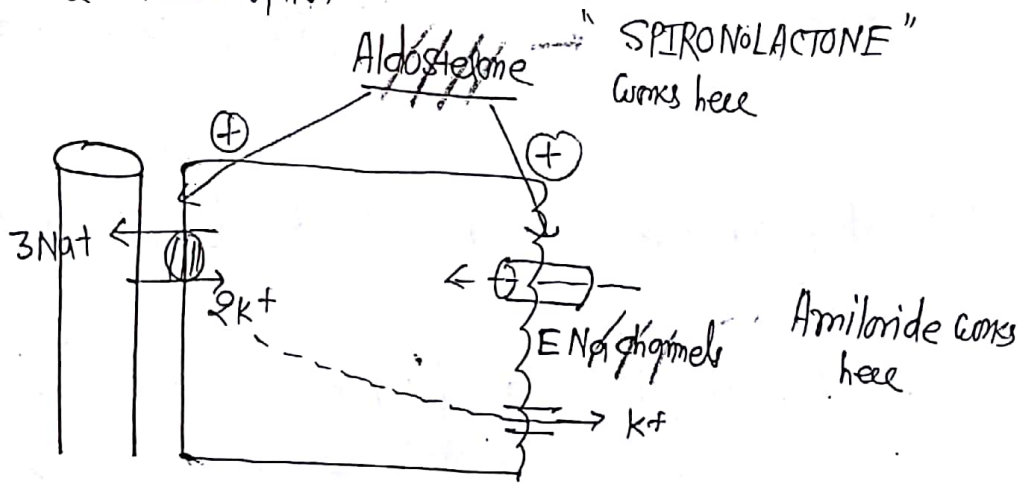


Principal cell

- → Na^+ Reabsorption
- → K^+ secretion
- → H_2O Reabsorption

Intercalated cells

L H^+ secretion



RAAS ⟶ Aldosterone ⇒ ↑ Na^+ Reabsorption

↑ K^+ secretion

↑ H^+ secretion (by "I-cells")

QQ Which gives directly Stimulation to Aldosterone ??

(a) ↑ Na^+ ;-

(b) ↓ Na^+ ; (it works via RAAS)

(c) ~~↑ K^+ ;~~

(d) ↓ K^+

QQ Hyperaldosteronism can Never cause ??

Likely to cause

~~(a) Acidosis ;~~

(b) Alkalosis ;
+
Hypokalemia

QQ

POTASSIUM ⇒ It is both Reabsorbed & Secreted.

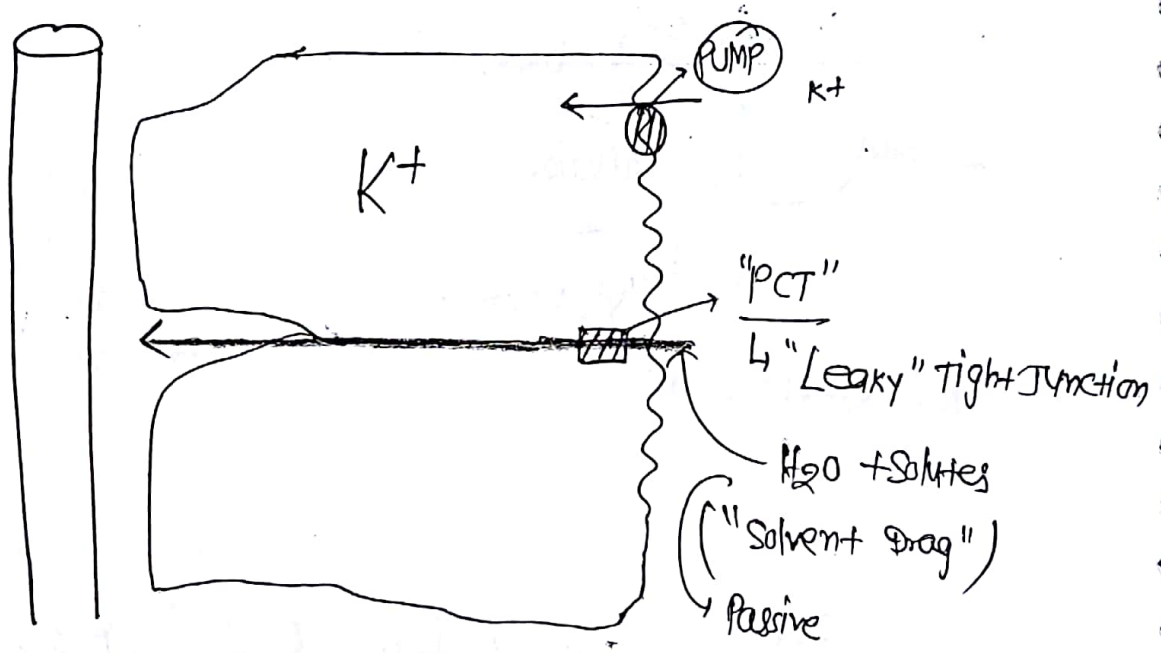
Reabsorption ⇒

- PCT
  - Passive ("Solvent Drag")
  - Active (we don't know about Pump)
- TAL ⇒ Na^+–K^+ – $2Cl^-$ co-transport
  (2° Active co-transport)

Secretion

↳ Collecting duct & Late DCT
(by Aldosterone)

SOLVENT DRAG ⇒



CALCIUM ⇒ Freely filtered & Almost Completly Reabsorbed (99+)

- Mechⁿ of Ca^{+2} Reabsorbtion
  ↳ Similar to Na^+
- Maxᵐ Ca^{+2} Reabsorption ⇒ PCT

* PTH ↑ Ca^{2+} Reabsorption in "DCT"

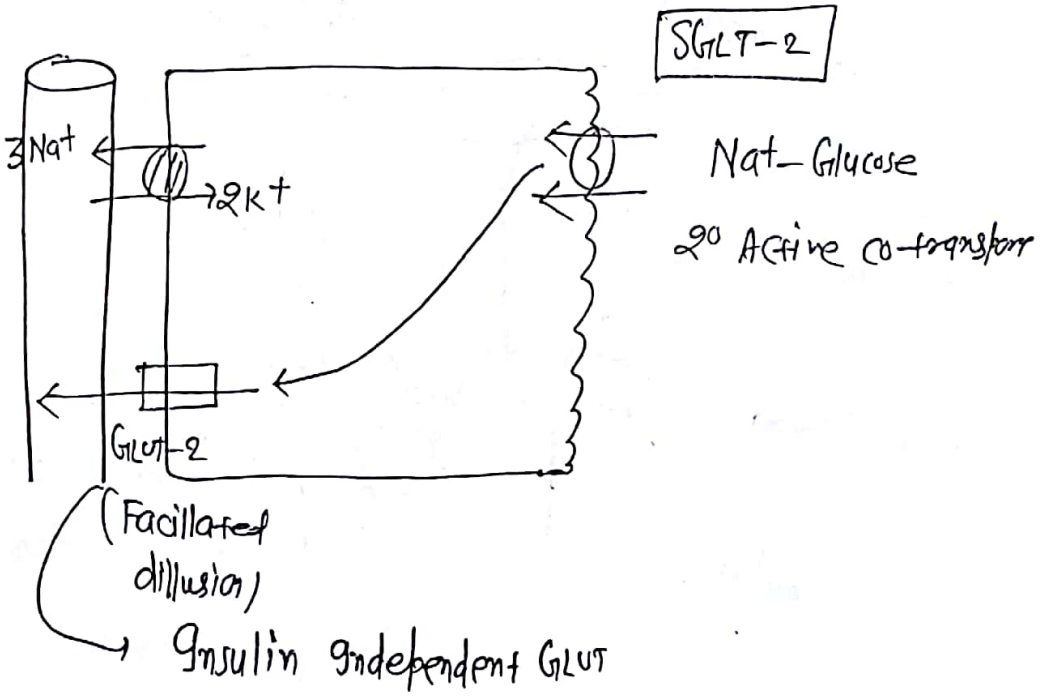
MAGNESIUM ⇒ Max^{im} Mg^{2+} Reabsorption in "Thick Ascending Limb"

- Lasix ⟶ ↑ Urine loss of — Na^+
  Cl^-
  K^+
  Ca^{++}
  Mg^{++}

GLUCOSE

Site = PCT ; 100% Reabsorption

Mechanism :-

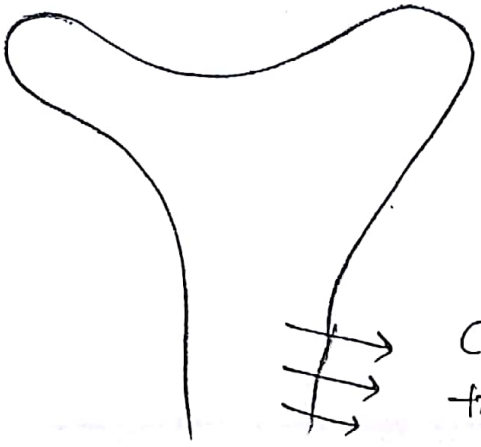


RENAL THRESHOLD ⇒ Plasma conc^{n} beyond which glucose appears in urine

↳ 180 – 200 mg/dl

OR

2 mg/mL



Carrier Mediated transport

⇓

GFR is Rate ← T_mG ⇒ ♂ = 375 mg/min

⇓ ♀ = 300 mg/min

Transport Maxima of Glucose

*

Renal threshold

⇓

2 mg/mL

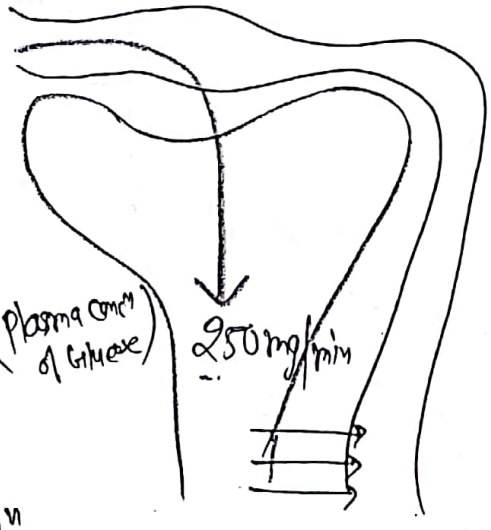
Filtration Rate

⇓

GFR X $P_{Glucose}$ (Plasma conc^{n} of Glucose)

= 125 X 2

= 250 mg/min



250 mg/min

T_mG = 375 mg/min (♂)

= 300 mg/min (♀)

Ideally @ this condⁿ total glucose Reabsorbed & (88)
Not appear in Urine ; but b/c of

"NEPHRON HETEROGENEITY"

↳ All Nephron's Not Works Simultaneously and Not ē Same capacity.

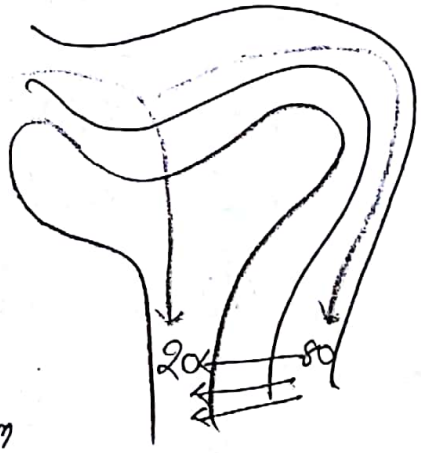
↳ At Plasma glucose of 2mg/mL
↳ Filtration Rate of glucose is 250 mg/min ; which is less-than T_{MG} ; but at P_{GLU} of 2mg/mL → Glucose begins to appear in urine

PAH

- Freely filtered & completely secreted (In Low concⁿ)

PAH (Low concⁿ) ⇒
<20 mg/dl

if ↑ Plasma concⁿ of PAH
↓
Incomplete secretion
↳ clearance PAH ↓

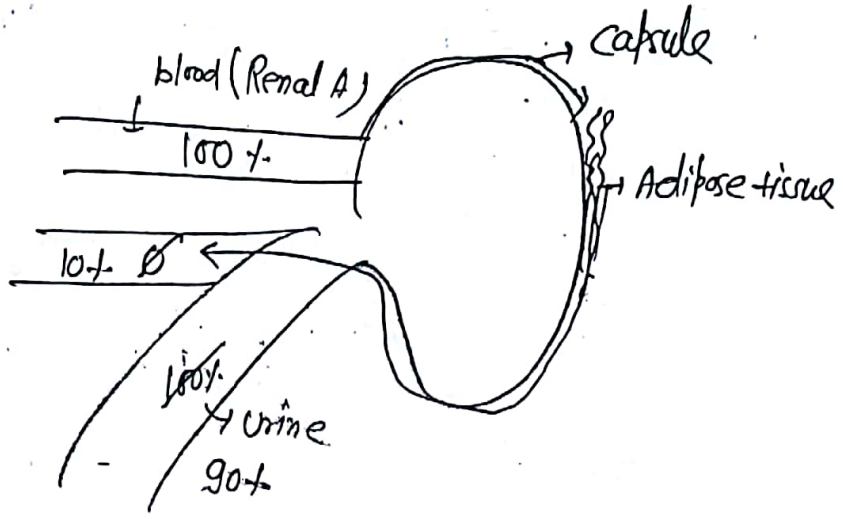


Secretion of PAH
↳ PCT
↳ Carrier Mediated secretion
↳ T_m ⊕
$(T_m)_{PAH}$ = 80 mg/min

QQ PAH (Low conc^n)

⇓

So; PAH has an Extraction Ratio



$$\text{Extraction Ratio} = \frac{\text{Arterial conc}^n - \text{Venous conc}^n}{\text{Arterial conc}^n}$$

$$= \frac{100-10}{100} = \frac{90}{100} = 0.9 \text{ OR } 90\%$$

Why there is an Extraction Ration of PAH??

b/c complete Renal Artery blood doesn't participate in filtration (Small amount goes into Renal capsule & Adipose tissue & directly goes into Renal vein; Not participate in filtration).

QQ. Cl PAH (Low conc^n) ⓐ Actual Renal blood flow

ⓑ Effective Renal blood flow

ⓒ Actual Renal Plasma flow (ARPF)

ⓓ Effective Renal Plasma flow (ERPF)

$$ARPF = \frac{ERPF}{0.9}$$

QQ ERPE = 630 ml/min

ARPF = 91

ARPF = 700 ml/min

** Renal blood flow = $\frac{100}{100 - \text{Hematocrit}} \times$ Renal Plasma flow

GFR = 180 L/day

WATER

2/3 or 66%

Isotonic

AQUAPORIN-I

Obligatory Reabsorption

15-20%

Aquaporin-I

ADH

13-15%

Facultative Reabsorption

Aquaporin-2 on Luminal side & Aquaporin-3 & 4 on Basolateral Membrane

Less No. of Aquaporin

* ADH

P-cell

V_2

G_s

Adenyl Cyclase

ATP

cAMP

Less activity of Protein kinase

Aquaporin-2

P

⇒ ↑ Insertion of Aquaporin-2 on Luminal Membrane

↓

↑ H_2O Reabsorption

↳ concentrated urine

Aquaporin 3 & 4

No. fixed; Not changed (Constitutionally present)

by ADH

$H^{\oplus}$

Filtration ⟶ Not possible
↳ b/c No free form ⊕.

↳ but urine is acidic ; b/c of secretion of H+

Q. Maxm H+ is secreted by -

~~(a) PCT~~ (4200 mmol/day)

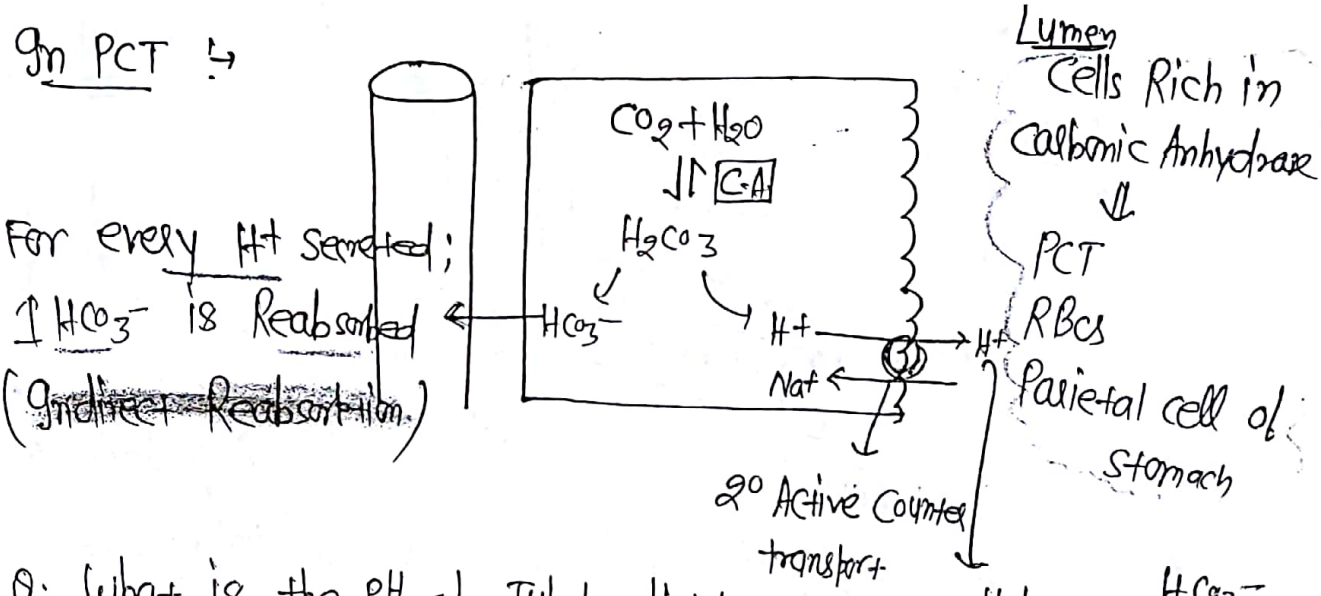
(b) CD (<80 mmol/day)

Q. Urinary Acidification occurs by -

(a) PCT

~~(b) CD~~

On PCT :-

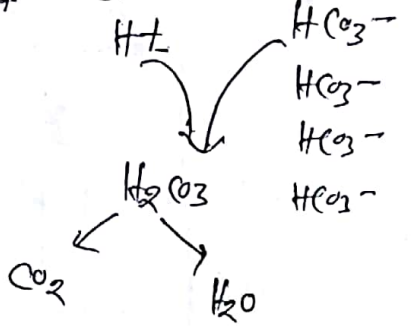


For every H+ secreted;
1 HCO_3^- is Reabsorbed
(~~Indirect Reabsorption~~)

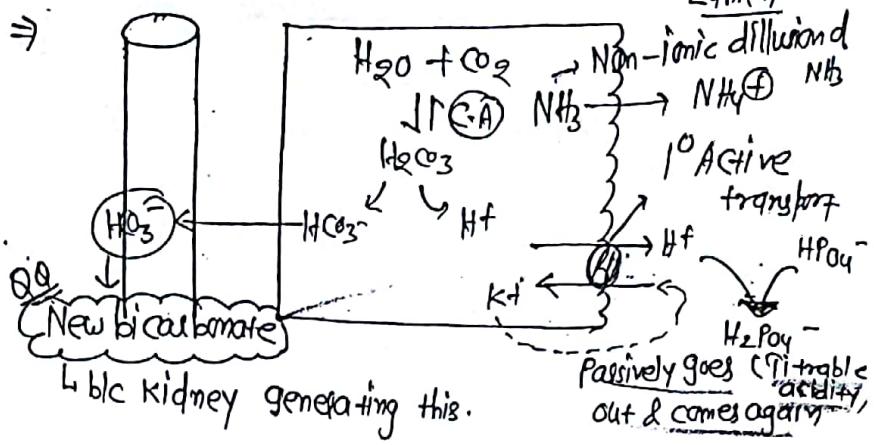
Q: What is the pH of Tubular fluid
(a) the end of PCT;

~~(a)~~ 7.3 (No change in pH)
⇓
b/c whatever H+ secreted is buffered by HCO_3^-

(b) 6.3
(c) 5.3
(d) 4.3



In collecting duct ⇒ (I-cells)



↳ b/c kidney generating this.

HCO_3^-

- → 80% Reabsorb in PCT
- → TAL, DCT] 20% Reabsorb

Mech^n ⇒ Same as in PCT

So; as we enter collecti. duct; No HCO_3^- is there So; New H^+ buffered by HPO_4^-

Urinary buffers ⇒ ① HCO_3^- (bicarbonate)

② HPO_4^{-2} (Phosphate)

③ NH_3 (Inducible Urinary buffer) QQ

⇓

b/c in Acidosis ⇒ ↑ NH_3 production.

Limiting pH of Urine ⇒ pH = 4.5

Factors which affect H^+ secretion ⇒ ① P_{CO_2}

② Aldosterone → ↑ H^+ secretion in collecting duct

③ Carbonate Anhydrase Inhibitor

↳ ↓ H^+ secretion

↳ ↑ Urinary loss of

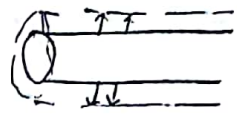
- ↳ Na^+
- HCO_3^-
- H_2O (Osmotic diuretics)

↙ Causes Acidosis ⇓ eg: Acetazolamide

REGULATION OF SODIUM EXCRETION & GFR

① Myogenic Mechⁿ of Autoregulation of GFR :→

B/w MAP of 90 & 200 mm Hg ⇒ GFR is constant.

* ↑ Renal blood flow ⟶ 

↑ Stretch

↓

QQ opening of Mechano-Sensitive Ca^{2+} channel

↓

Ca^{2+} influx

↓

Vascular Smooth Muscle contraction

⊖

** So, GFR constant

So, GFR constant

② Tubuloglomerular feedback (TGF) :⇒

eg of Negative Feedback

↑ GFR ⊖

↓

↑ Na^+, Cl^- Load in Tubular Fluid

↓

Macula Densa

Macula densa acts as sensor QQ

⟶

↑ Na^+, Cl^- Reabsorption by Macula densa cells QQ

Increase Na^+, Cl^- reabsorption by Macula densa cells

→

↑ Activity of Na^+ K^+ ATPase Pump

Increase activity of N^+ K^+ ATPase pump

↑

↑ ATP hydrolysis

↑

↑ Adenosine QQ

Increase adenosine

Ca^{2+} influx

A_1 Receptor ↑ in vascular Smooth Muscle

Vasoconstriction of Afferent Arteriole

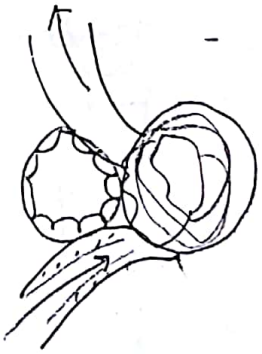
site of action

Juxta Glomerular Apparatus ⇒

① JG cells
- Renin Secreting cells
- In tunica media of afferent arteriole >> efferent arteriole

② Macula densa cells ⇒ prt. @ beginning of DCT
prt @ the end of Loop of henle
- Modified Tubular Epithelial cells
- It is "SENSOR"
- Detect Nat & Cl⁻ Load in Tubular fluid

③ Laci's cells
- Extraglomerular Mesangial cells
- We don't know about exact Role
- It take up immune complexes in certain type of Glomerular Nephritis



* ↓ GFR
↓
Nitric oxide Release
↓
Afferent arteriole dilatation
⊕

③ Glomerulo-tubular Balance (GTB)

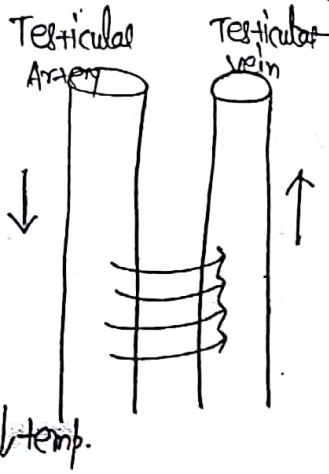
↳ It is Kas "3rd Factor"

↳ Act when 1st two Mechanism fail

↳ More GFR ⇒ More Reabsorption

↳ Site of Action ⇒ PCT

COUNTER-CURRENT MECHANISM



(Heat is translocated from Artery to vein)

2 vessels

↳ close to each other

Parallel to each other

with flow in opposite direction,

Kas "counter-current"

prt. in

- Kidney
- Testicular vessels
- Intestinal villis
- Venae comitantes
  - Pair of veins a/q certain arteries
  - help to conserve heat

Kidney

Testicular vessels

Intestinal villis

Venae comitantes

Pair of veins a/q certain arteries

Help to conserve heat

Counter current → countercurrent

Counter current multiplier → Countercurrent multiplies

↓

Loop of Henle → Loop of henle

↓

Creates Medullary → creates medullary

Intestitium Hyperosmolality → intestitium hyoerosmolality

Counter current exchanger → countercurrent exchange

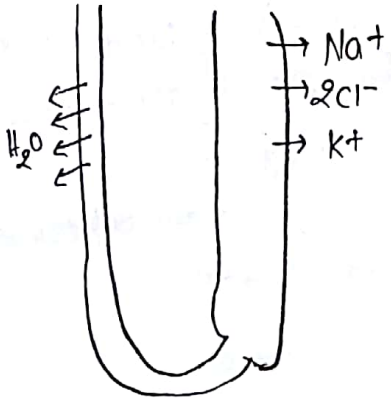
↓

Vasa Recta → vasa recta

↓

Maintains Medullary → maintains medullary

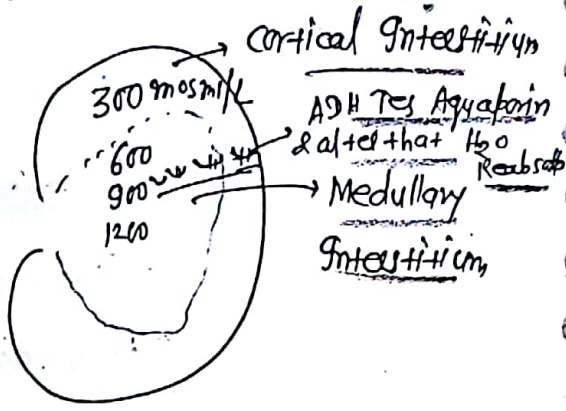
Intestitium Hyperosmolality → Intestitium hyperormolality



2 Limbs of Loop of Henle

↳ differential permeability → Differential permeability

.to produce a conc^{n} Urine; we Need



⇓

① ADH

② Medullary Interstitial hyperosmolality

both are Must for Conc^{n} Urine;

if Any one absent; No Conc^{n} Urine formed

(QQ) Max^{m} Urine Osmolality ⇒ 1200 mosm/L

(QQ) Possible Range of Urinary osmolality ⇒

50 — 1200 mosm/L

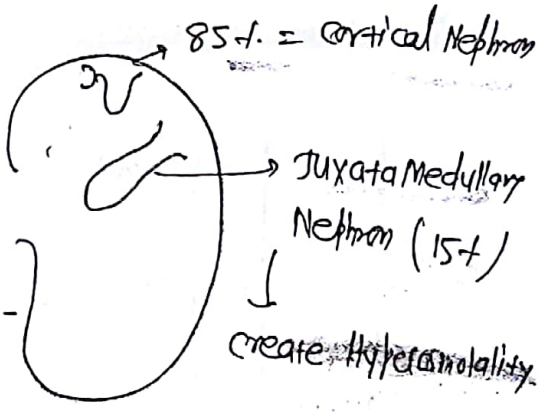
ADH — Max^{m} ADH

(QQ) Usual Range of Urinary osmolality ⇒

300 — 1200 mOsm/L

Isotonic — Hypertonic

* Solutes Responsible for Medullary Interstitium Hyperosmolality :-



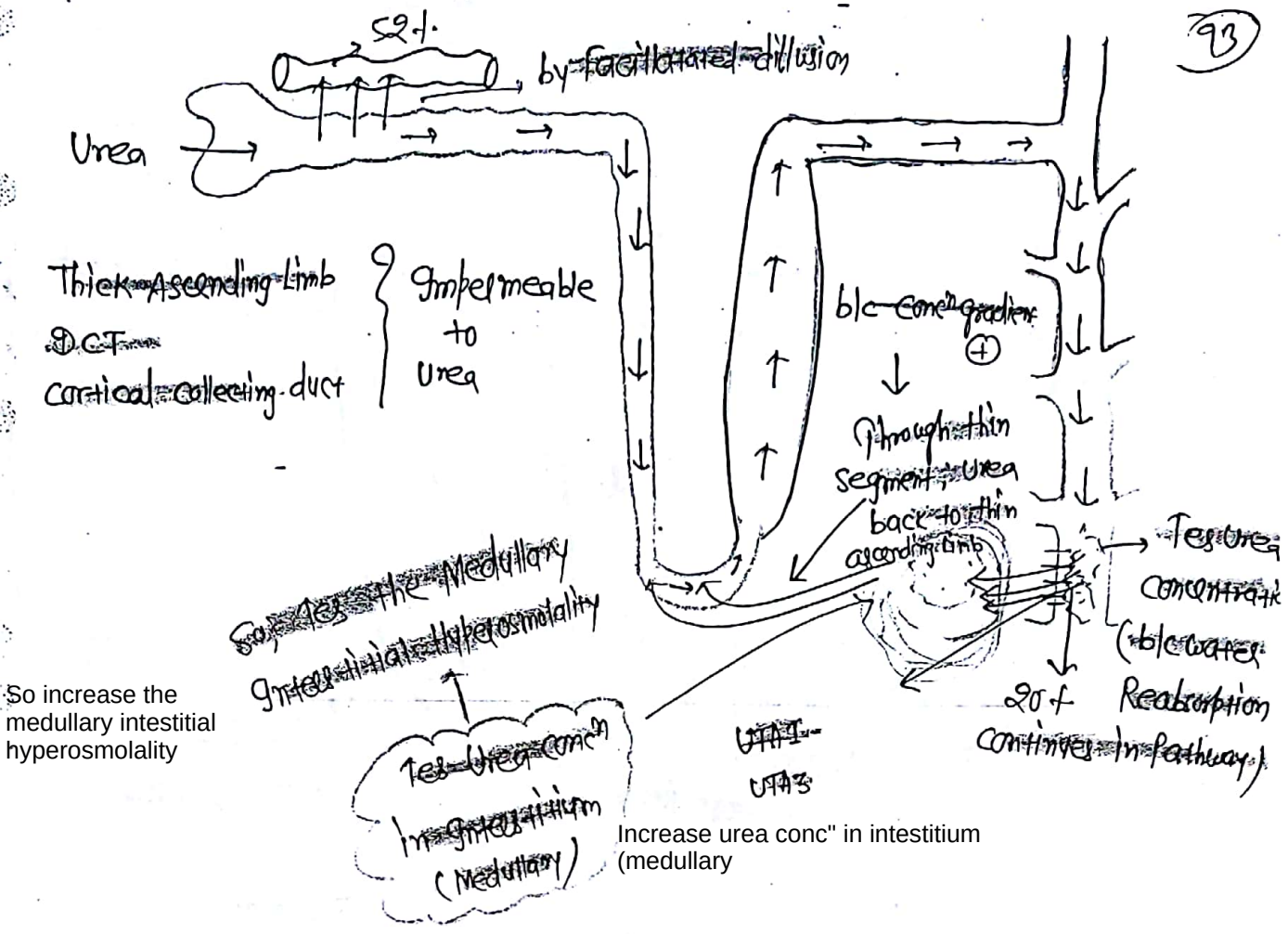
Major ← { Na+, K+, Cl− } TAL

Minor ← Urea from Medullary collecting duct

* Urea is Reabsorb (a) ⇒ PCT, but comes to Medullary Interstitium & Some time Contribute 50% of Medullary Interstitium Hyperosmolality

Urea us reabsorb

PCT but comes to medullary intestitium and sometime contribute 50% of medullary intestitium hyperosmolality



So increase the medullary intestitial hyperosmolality

Increase urea conc" in intestitium (medullary

Urea cycling

Urea cycling

VASA RECTA

- 2 limbs of Vasa Recta all Counter current to each other and with Loop of Henle

2 limbs of vasa recta all counter current with each others and with loop of henle

- Both limbs of Vasa Recta all freely permeable to Salutes & water.

both limbs of vasa recta all freely permeable to salutes and water

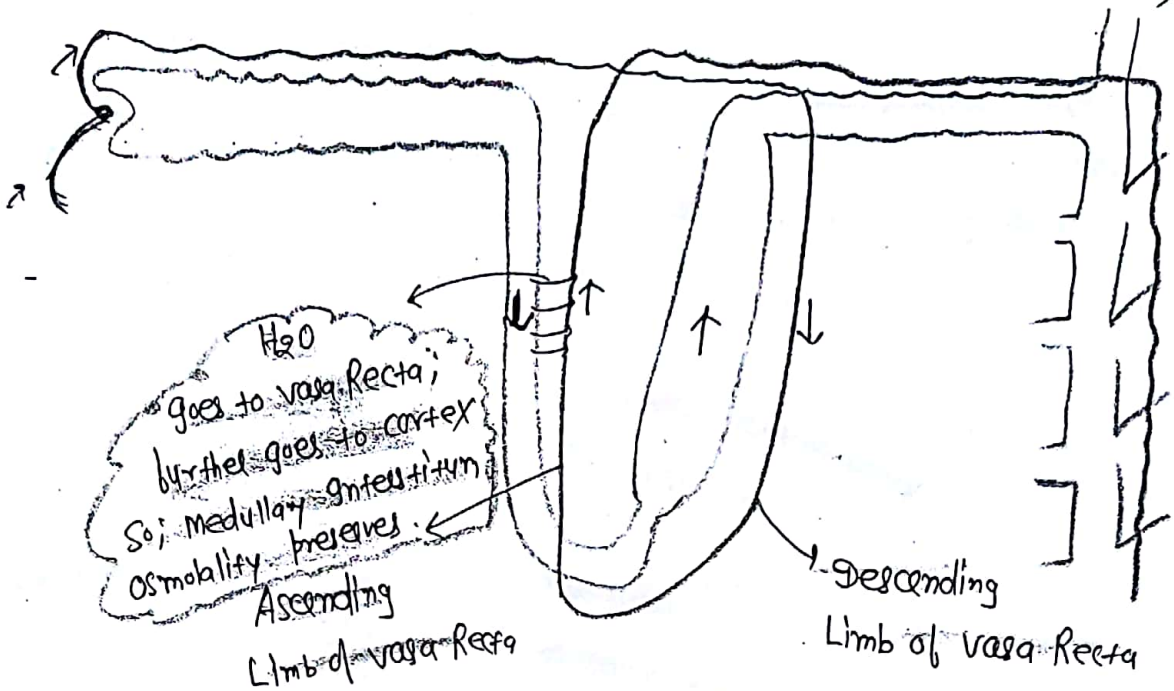
- It has very very very slow Rate of blood flow

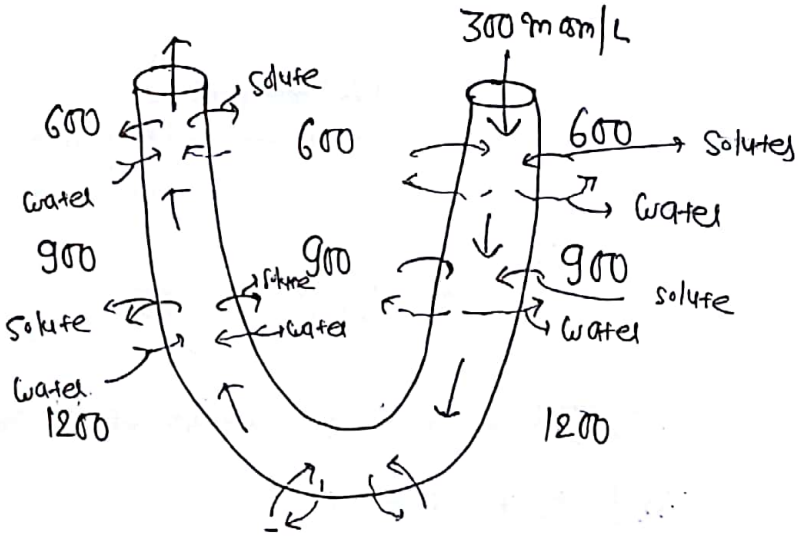
It has very very very slow rate of blood flow

- Vasa Recta => 5% of Renal blood flow.

vasa recta => 5 + of renal blood flow

* 1st part of kidney affected by Anoxia ⇒ Medulla
(b/c of preserved Loop of Henle)





RESPIRATORY SYSTEM

BRONCHODILATION

* ~~Sympathetic stimulation~~ sympathetic stimuation
* ~~Adrenergic agents~~ Adrenergic agents
* Adrenaline
* VIP (By NANC ↳ Nerves)
  * ↓ Bronchial Smooth Muscle Relaxant
  * → Non-Adrenergic Non-Cholinergic

BRCHOCONSTRICTION

* ~~Parasympathetic circulation~~ Parasympt. stimulation
* Ach
* ~~cholinergic Agents~~
* ~~Leuko-trienes~~
* Substance P
* Adenosine
* Cool Air

* Total Pulmonary ventilation ⇒ R.R. (Respiratory Rate) × T.V (Tidal volume)

Alveolar ventilation ⇒ R.R × (T.V − D.S.)

DEAD SPACE (D.S)

Volume of Air which doesn't participate in Respiratory Exchange

* In Infants ⇒ 3.3 ml/kg body weight = 15-30 ml
  In Adults = 2 ml/kg body weight = 140-150 ml

Physiological OR Total Dead Space = Anatomical dead space + Wasted Ventillation

* Wasted ventilation ⇒ $\frac{V}{Q} > 1$

↳ i.e ventilation is in excess of Perfusion; & this ventilation is going to be wasted.

→ Over-ventilated alveoli

→ Under-perfused alveoli

* V/Q > 1:0

⇓ ventilation wasted

⇓

Yes Physiological Dead space

eg ⇒ Thrombus in vessels

V/Q < 1:0

⇓

Wasted Perfusion

⇓

Incomplete oxygenation of blood

⇓

Also "Shunting of blood".

eg ⇒ Foreign body

* In (N) Individual ; Wasted ventilation ⇒ 0

⇓

So; in (N) Individual ; Physiological D.S = Anatomical D.S

Measure by "BOHR's Equation" &

⇓ of CO_2

Partial Pressure in Expired Air (P_ECO_2)

Partial Pressure of CO_2 in Arterial blood ($PaCO_2$)

Tidal volume (V_T)

Measure by FOWLER'S TECHNIQUE &

⇓

Measured N_2 analysis in expired Air after single deep breath of 100% O_2

Bohr's Eqn ⇒ $P_E CO_2 \times V_T = P_a CO_2 \times (V_T - V_D)$

V_D = dead space volume.

QQ $P_E CO_2$ = given

$P_a CO_2$ = given

$\frac{V_D}{V_T}$ Ratio

$$P_E CO_2 \times V_T = P_a CO_2 \times (V_T - V_D)$$

$$\Rightarrow \frac{P_E CO_2}{P_a CO_2} = \frac{V_T - V_D}{V_T}$$

$$= \frac{P_E CO_2}{P_a CO_2} = 1 - \frac{V_D}{V_T}$$

$$\Rightarrow \frac{V_D}{V_T} = 1 - \frac{P_E CO_2}{P_a CO_2} \Rightarrow \frac{P_a CO_2 - P_E CO_2}{P_a CO_2}$$

(N) Ratio is upto 0.4

SPIROMETRY

LUNG VOLUMES & CAPACITY

TIDAL VOLUME ⇒ Volume of Air Inspired OR expired during a Normal quiet Respiration.

- only volume which is same in Male & females
- 500mL.

INSPIRATORY RESERVE VOLUME ⇒ Volume of Air Inspired Forcefully ; over & above a tidal Inspiration ; with Maxm effort.

3300 ml = ♂
1900 ml = ♀

Expiratory Reserve volume ⇒ Volume of Air expired forcefully ; over & above a tidal expiration ; with Maxm effort.

- ~~1000ml = ♂~~
~~700ml = ♀~~

Residual volume ⇒ Volume of Air ; which Remains in Lung at the end of Maxm expiration

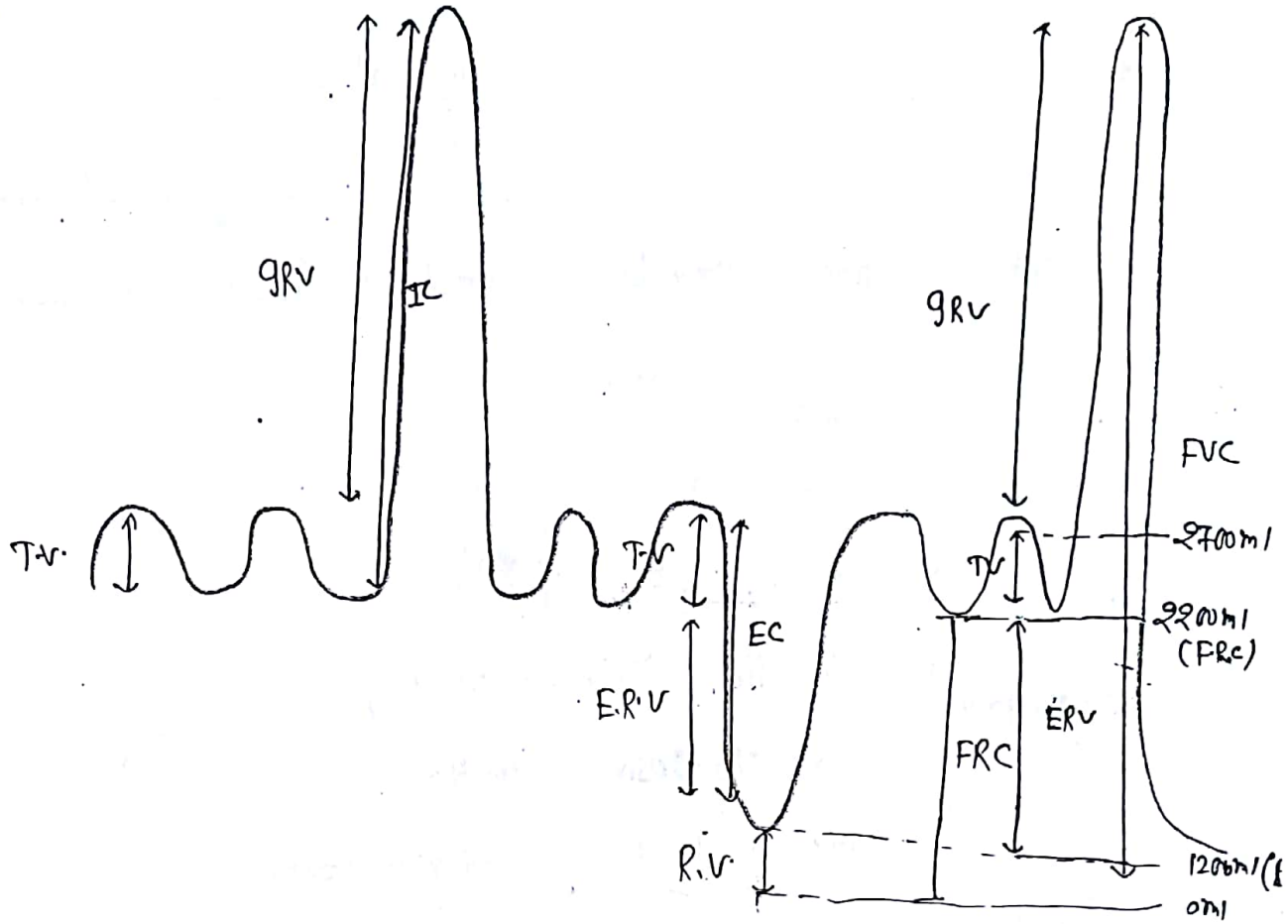
- 1200ml = ♂
- 1100ml = ♀

Inspiratory capacity ⇒ IRV + TV

Expiratory capacity ⇒ ERV + TV

Functional Residual capacity ⇒ Volume of Air ⊕ in Lungs @ the end of (N) expiration

↳ ERV + RV ; (N) Value = 2200ml ♂ ; 1800ml ♀



Forced vital capacity ⇒ Volume of Air expired forcefully after a forcefully inspiration.

↳ $ERV + TV + gRV$

Total Lung capacity = 6000ml or, 4200

↳ $gRV + TV + ERV + RV$

* Lung volume @ the end of Normal expiration ⇒ Functional Residual capacity (FRC)

* Lung volume @ the end of Forceful expiration ⇒ Residual volume (RV)

* Lung volume At the end of Forceful Inspiration
↳ Total Lung capacity.

* volume of Air expired forcefully after a forcefull Inspiration
↳ Forced vital capacity

* which volume can't be Measured by Routine Spirometry

RV
FRC } ⊗
TLC

- For FRC ⇒ ERV + RV.
⇓ Measurement
i) He Dilution technique
ii) N_2 Washout Method
iii) Whole body plethysmography
↳ Most accurate
↳ also Measure volume of air trapped in Bullae

- For R.V. ⇒ RV = FRC − ERV
↳ Measure by Routine Spirometry

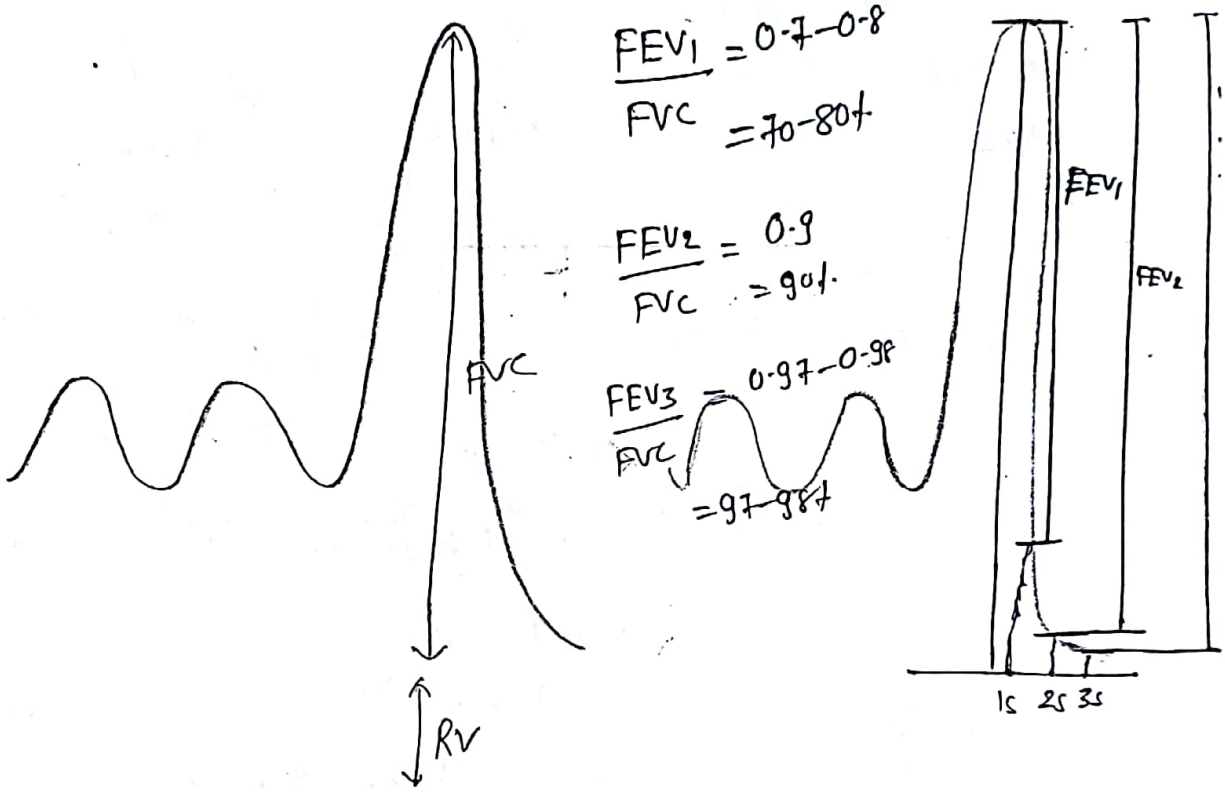
Q N_2 Can be used in Measurement of
a) Anatomical dead space – Single Breath N_2 Analysis
b) FRC – by N_2 washout Method
c) Both

TIMED VITAL CAPACITY

FEV_1 — Forcefully expired volume of Air @ the end of 1 sec

FEV_2 @ 2sec

FEV_3 @ 3sec



$\frac{FEV_1}{FVC} = 0.7-0.8 = 70-80\%$

$\frac{FEV_2}{FVC} = 0.9 = 90\%$

$\frac{FEV_3}{FVC} = 0.97-0.98 = 97-98\%$

Obstructive Lung Disease

$\frac{FEV_1 \downarrow\downarrow}{FVC \downarrow} \downarrow$

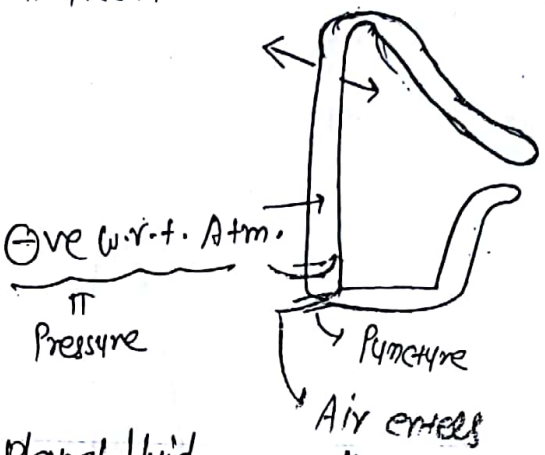
Restrictive Lung Disease

$\frac{\downarrow FEV_1}{\downarrow\downarrow FVC}$ (N) or ↑

VENTILATION

1. INTRAPLEURAL PRESSURE / PLEURAL PRESSURE / INTRATHORACIC PRESSURE / ESOPHAGEAL PRESSURE :-

i) Lung Recoil & chest wall Recoil
⇓
Two opposing forces
↳ 9t creates
⊖ve pressure in pleural space



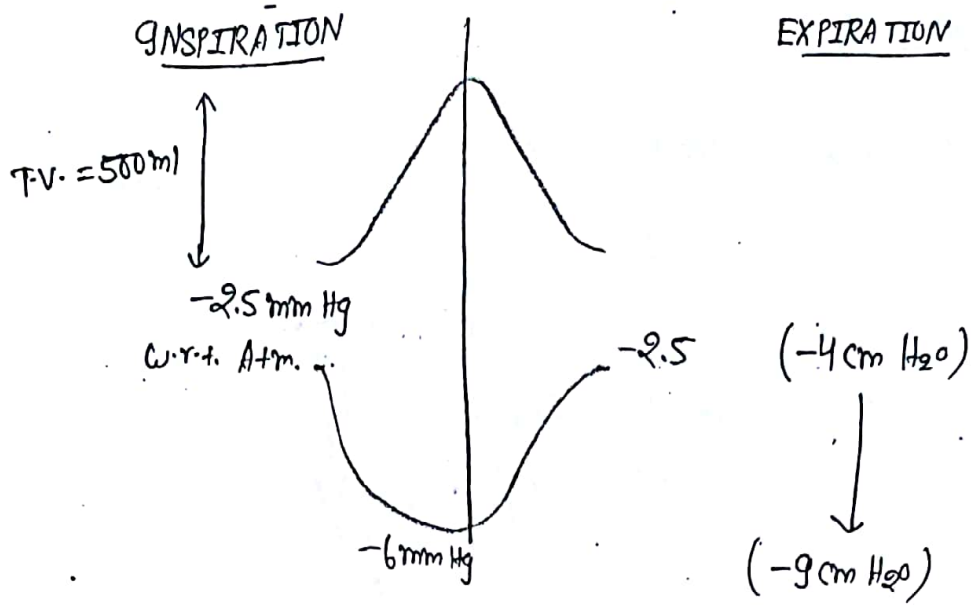
⇓
Zero Pressure w.r.t. Atm.

ii) continuous drainage of pleural fluid into the Lymphatics.

In Emphysema
↳ ↑ chest Recoil force (Lung Recoil force ↓ b/c of destruction of elastic fibres of Lungs)
⇓
Barrel shaped

At FRC
↳ Lung Recoil = Chest wall Recoil
↳ So; it is K/as "Relaxation volume of Lungs"

* What happen to Intrapleural pressure ∈ Respiration :-

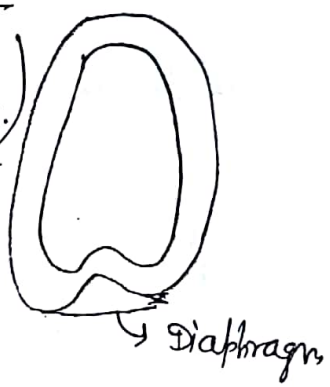


Pleural pressure May ⊕ve during "VALSALVA" → also during Labour

Straining ⇓ Any kind is valsalva (Forcep expiration against Closed Glottis.)

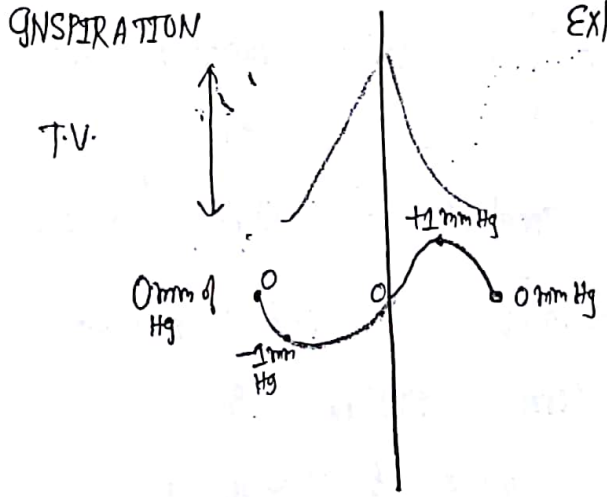
In Forcefully expiration

↳ Pressure goes to -10 mm Hg

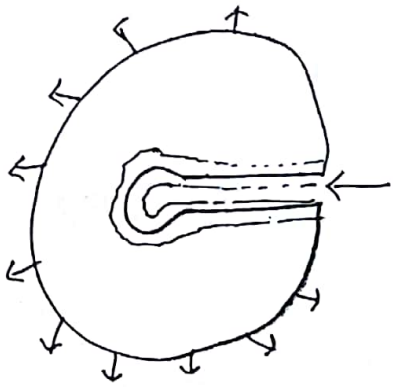


* During valsalva ⇒ ↓ venous Return
↓ Blood Pressure
↓ cardiac output

II. INTRAPULMONARY PRESSURE / AIRWAY PRESSURE / ALVEOLAR PRESSURE



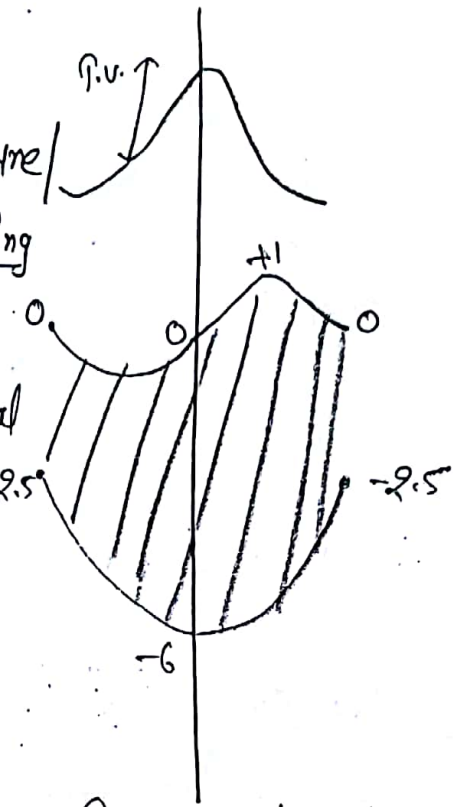
Expiration



NET Pressure :-

Also " Transpulmonary Pressure / Transmural Pressure / Distending Pressure "

⇒ Intrapulmonary - Intrapleural
(P) (P)



QQ Transpulmonary Pressure @ start of Inspiration

↳ 0 − (−2.5) = +2.5 mm of Hg

QQ Transpulmonary Pressure @ end of Inspiration

↳ 0 − (−6) = +6 mm of Hg

LUNG COMPLIANCE

Compliance ⇒ Distensibility

⇒ $$\text{"C"} = \frac{\Delta V}{\Delta P}$$

ΔV = change in volume

ΔP = change in transpulmonary Pressure

(N) value of Lung compliance ⇒ 0.2L / cm H_2O.

Lung + chest wall compliance ⇒ 0.1L / cm H_2O

Q. Change in Lung volume = 600ml ; esophageal Pressure changes from −4 cm of H_2O @ start of Inspiration & −8 cm H_2O @ end of Inspiration ;

Lung compliance = ??

Transpulmonary Pressure ⇒ 0 − (−4) ⇒ +4 ⇒ (+4) = change

↓ ⇒ ↓

0 − (−8) +8

$$C = \frac{\Delta V}{\Delta P} = \frac{600mL}{4 cm H_2O} = 150 mL/cm H_2O.$$

SPECIFIC COMPLIANCE

$$\frac{\text{Compliance}}{\text{FRC}} = \text{Specific compliance}$$

In Emphysema → ↑ compliance (Lung)

↑↑ FRC

↳ So; Specific compliance ↓.

QQ Condⁿ in which compliance ↑ & Specific compliance ↓

↳ Emphysema

* Compliance $\propto \frac{1}{\text{Surface tension}}$; Surface tension $\propto \frac{1}{\text{Surfactant}}$

** Compliance $\propto$ Surfactant

SURFACTANT :→ Secreted by Type-II Pneumocytes

↳ Dipalmitoyl Phosphatidyl Choline

Q. Which is More Numerous :→

Type-I → 40%.

Type-II → 60%.

Q. Which are having More alveolar surface Area :→

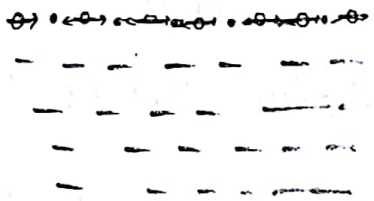
Type-I → 95%.

Type-II

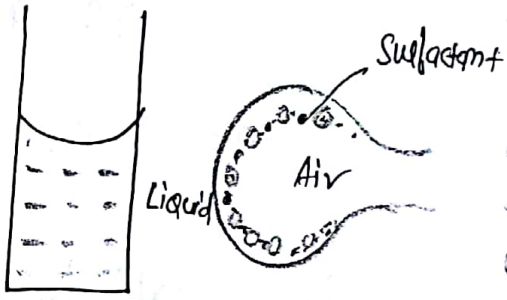
Type-I

* Surface tension → @ Air-Liquid Interface

Air



Liquid



With expiration

↓

Les concn of Surfactant Molecules per Unit Area

⇓

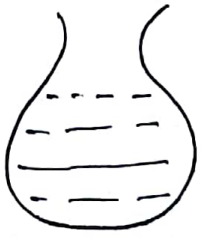
↓↓ Surface tension

⇓

Helps to Maintain alveolar Stability. QQ

(99)

Saline ventilated Lung



No Air-Liquid Interface

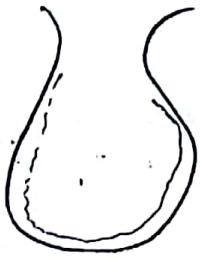
⇓

Surface tension = 0

⇓

↑ compliance (Better compliance)

Air ventilated Lung



Air-Liquid Interface

⇓

Surface tension ⇒ ⊕

⇓

↓ compliance as compare to Saline ventilated Lung.

* Hormones which affect Surfactant ⇒

i) Thyroid ⇒ ↑ type II Pneumocyte activity

So; In Hypothyroidism ⇒ RDS May seen in Newborn

ii) Insulin ⇒ ↓ type II Pneumocyte activity

↳ So; Babies born to Diabetic Mother → More Likely to Suffer from RDS.

iii) Glucocorticoids ⇒ ↑ type II Pneumocyte Maturation

↳ In pre-term babies ⇒ give Steroids

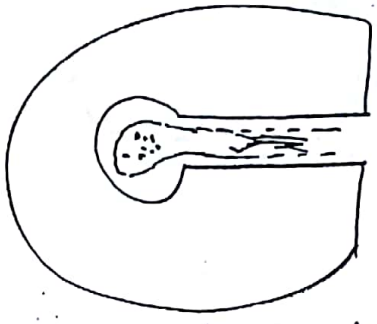
DYNAMIC COMPRESSION OF AIRWAYS

During Forcefully expiration

⇓

Tendency of Airways to collapse

↳ K/as "dynamic compression of Airways".



In Early Bronchial Asthma ⇒ Expiratory wheeze ⊕

At end of Forceful Expiration

⇓

Airway collapse is complete

⇓

Air is trapped in Alveoli

↳ This Air is K/as "Residual volume"

⇓

this is d/t "Dynamic compression of Airways"

WORK DONE IN QUIET BREATHING

⇒ 0.3 – 0.8 kg-m/min

65% (2/3rd) — 35%

against elastic forces — again Resistant forces

43% — 22% — 28% — 7%

against surface tension elasticity — against tissue elasticity — against Airway Resistance — against viscous Resistance

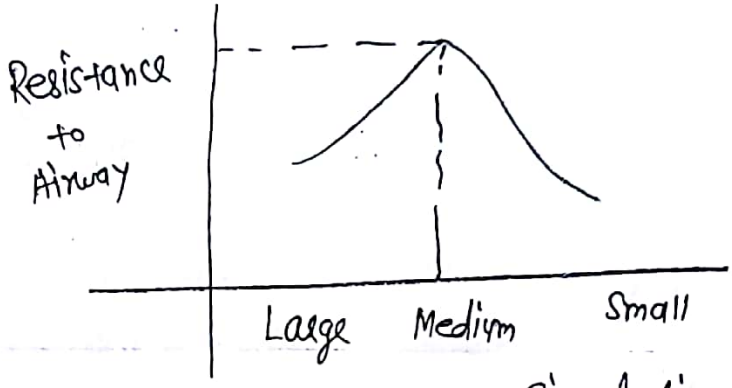
Q: Which Airways have Maxm Resistance to Airflow ?→

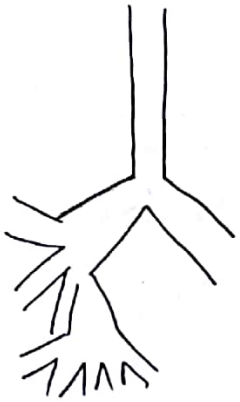
(a) Large sized Airways

(b) ~~Medium~~ Sized Airways

(c) Small " "

$R \propto \frac{1}{r^4}$





WEIBEL'S CLASSIFICATION OF TRACHEOBRONCHIAL TREE :→

* 23 Generation
* Trachea ⇒ Generation zero
* 1-16 ⇒ Conducting zone
* 17-23 ⇒ Respiratory zone

Medium size Airways = 3rd - 5th Generation

	Medium size Airways	Small size Airways
Total cross Sectional Area	↓	↑
velocity of Airflow	↑	↓
Reynold's No. $\left(R_2 \frac{\rho V D}{\eta}\right)$	↑	↓

Turbulant Airflow (+)
↳ dil+ i+ Resistance of Airflow Tes in it.

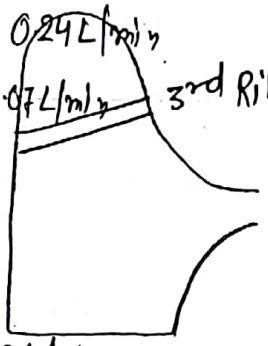
VENTILATION PERFUSION GRADIENT IN ERECT POSTURE

BAD → Base to Apex there is Decrese In
- → Intrapleural pressure
- → Ventilation
- → Perfusion

But $\frac{V}{Q}$ Ratio ⇒ Les from Base to Apex.

$\frac{V}{Q} = 3.3$

Ventilation = 0.24 L/min
Perfusion = 0.07 L/min
3rd Rib ⇒ $\frac{V}{Q} = 1$



$\frac{V}{Q} = 0.63$

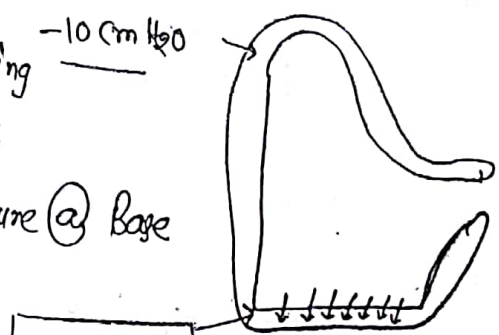
Ventilation = 0.82 L/min
Perfusion = 1.29 L/min

Avg. V/Q Ratio @ Lung ⇒ 0.8

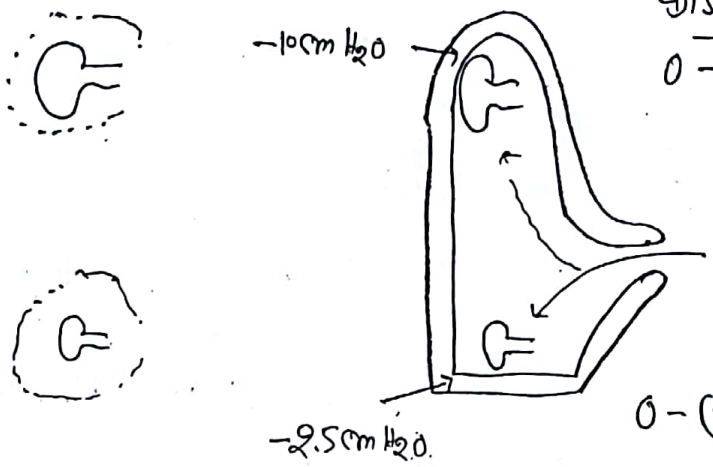
QQ. Pa_{O_2} is Maxim at ⇒ a) Base; ⇒ $\frac{V}{Q} < 1.0$
~~b) Apex.~~
↳ Incomplete oxygenation

* Base to apex Intrapleural Pressure les ⇒

Probable Reason ⇒ During Standing
Weight of Lungs acts as Base
↳ Les Pleural pressure @ Base



* Base to Apex Ves in Ventilation :⇒



Distending Pressure

0 − (−10) = +10 cm H2O

0 − (−2.5) = +2.5 cm H2O

QQ. Ventilation is More in alveoli @ Base ??

a) Alveoli @ Base have More Surfactant;

b) Alveoli @ Base are More compliant

* Base to Apex Ves in Perfusion :⇒

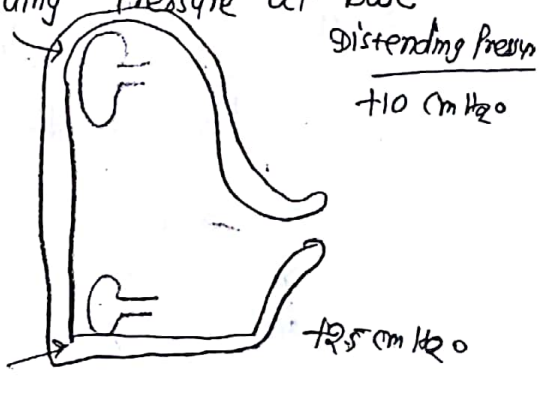
CLOSING VOLUME

- It is the Lung volume at which Airways at base begins to collapse; b/c of Lessed distending Pressure at base

Distending Pressure is less at base

⇓

therefore; Airway & Alveolar diameter is less at base



* Closing volume > Residual volume

↳ b/c it is Not expired volume; it is Lung volume

** FRC > Closing volume > Residual volume

FRC > Closing volume > Residual volume

* Elastic fibers ⇒ Exert Radial traction on Airways

↓

Keep the Airways Patent

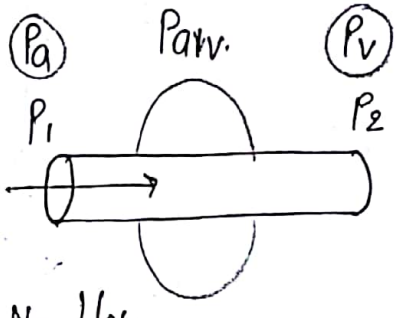
* With Age ⇒ ↓es Lung elastic fibers

Mid 70's ⇒ Huge Reduction(↓) Lung elastic fibers

↳ ↑es tendency of Airways to collapse

↳ closing volume approaches FRC.

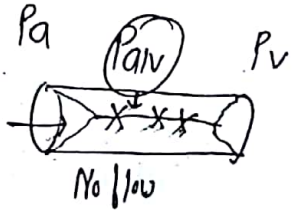
ZONES IN LUNG IN ERECT POSTURE



ZONE 1 ⇒ Zone of No flow

↳ Palveolar > Pa > Pv

↳ No Zone 1 in (N) Lung



Zone 1 prt. at Apex in Hypertension; Hemorrhage; ⊕ve Pressure ventilation

Zone 2 ⇒ Zone of Intermittent Flow / Pulsatile flow. → Klas "Waterfall effect"

During Systole ⇒ $P_a > P_v > P_{AIV}$ ⇒ Flow (+)

During Diastole ⇒ $P_a > P_{AIV} > P_v$ ⇒ Flows stop

↳ Prt. at Apex.

Zone 3 ⇒ Zone of continous flow

$P_a > P_v > P_{AIV}$ Pa> Pv > Paiv

↳ (+) @ Base of Lung

@ Base of lung

PARTIAL PRESSURES

	INSPIRATION	EXPIRATION
% of O_2 ⇒	21%	16%

QQ Mouth – to – Mouth Respiration

At Sea level ; Atm. Pressure = 760 mm of Hg

$$P_{O_2} = \frac{21}{100} \times P_B = \frac{21}{100} \times 760 = 160 \text{ mm of Hg}$$

QQ At High Altitude :- ~~(a) ↓ P_B (Barometric Pressure)~~

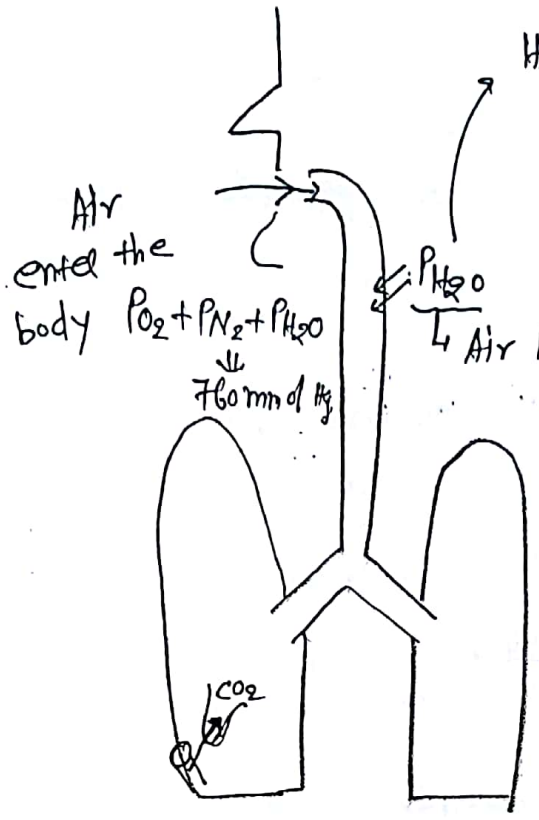
$$P_{O_2} = \frac{21}{100} \times 500 \text{ (if Vesuvius 500 (atm. Pressure))} = 105 \text{ mm of Hg.}$$

(b) ↓ % of O_2

(c) Both

(d) None

$P_{O_2} + P_{N_2} = 760$ mm of Hg



H_2O vapour comes from epithelial cells.

P_{H_2O} = 47 mm of Hg (irrespective to altitude & Environmental temp.)

↳ Air humidifies

Alveolar Partial Pressure of oxygen (P_AO_2)

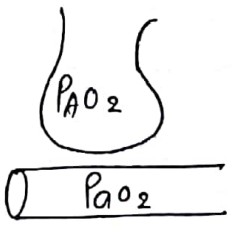
⇒ By Alveolar Gas equation

Alveolar O_2 ⇒

Provided

↳ i) $\frac{V}{Q} \geq 1.0$

ii) Respiratory Memb. ⇒ (N)



HENRY'S LAW

↳ Partial Pressure in the solution is equal to Partial Pressure above the solution.

* Alveolar Gas equation ⇒

$$P_AO_2 = \underbrace{\left[(P_B - P_{H_2O}) \times \text{fraction conc}^n \text{ of } O_2 \right]}_{P_IO_2} - \frac{P_ACO_2}{R}$$

R = Respiratory Quotient

$$R.Q. = \frac{\text{Volume of } CO_2 \text{ Produced}}{\text{Volume of } O_2 \text{ consumed}}$$

for carbohydrate = 1

for Mixed diet = 0.8

$$P_AO_2 = \left[(P_B - P_{H_2O}) \times \text{bractional conc}^n \text{ of } O_2 \right] - \frac{P_ACO_2}{R}$$

At Sea level

$$P_AO_2 = \left[(760 - 47) \times \frac{21}{100} \right] - \frac{40}{0.8}$$

$$\Rightarrow \{P_AO_2 = 105 \text{ mm Hg}\}$$

QQ. How Much is P_AO_2 if he Receives 4 times Atmospheric pressure & 100% O_2.

4 times Atmospheric ⇓ Hyperbaric O_2 chamber ⇓ $4 \times 760 = 3040$

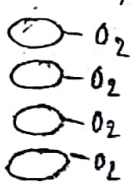
$$P_AO_2 = (3040 - 47) \times \frac{100}{100} - \frac{40}{0.8}$$

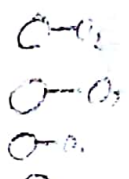
$\simeq$ 3,000 mm Hg.

given in Gram ⊖ve septicemia CO_2 poisoning

RESPIRATORY EXCHANGE

	Arterial Blood	Venous Blood
Total O_2 (ml/dL)	19 ml/dL	14 ml/dL
P_{O_2} (mm of Hg) (Dissolved O_2)	95 mm of Hg	40 mm of Hg
S_{O_2} (%)	97-98%	75%



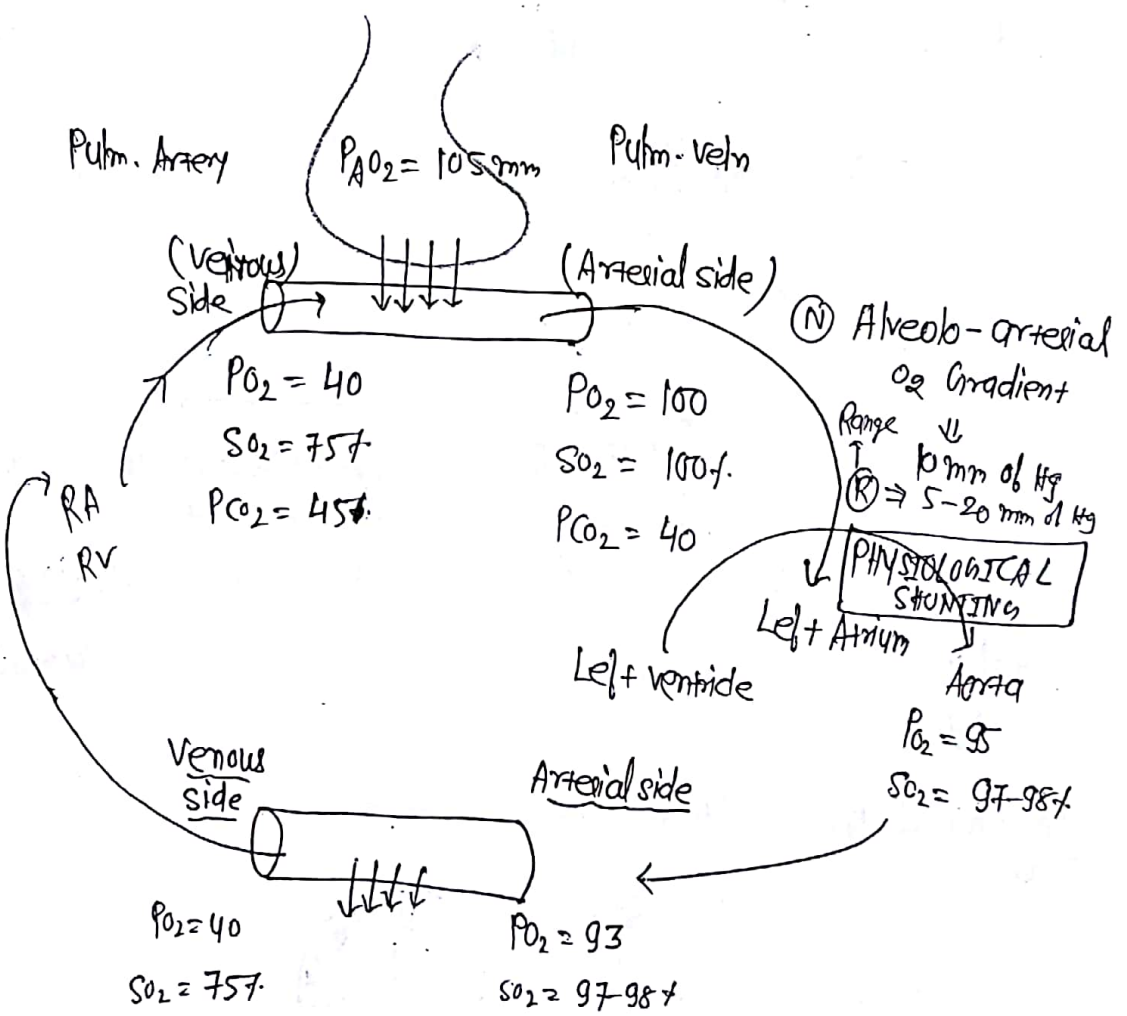


	Arterial Blood	Venous blood
Total CO_2 (mL/dL)	49 mL/dL	53 mL/dL
P_{CO_2} (mm Hg)	40	45

O_2 consumption at Rest ⇒ 250 mL/min

CO_2 production at Rest ⇒ 200 mL/min

$$R.Q = \frac{CO_2 \text{ Produced}}{O_2 \text{ consumed}} = \frac{200 \text{ mL/min}}{250 \text{ mL/min}} = 0.8$$



Q) Alveolo-arterial gradient is Yes in all except ⇒

(a) Rt → Lt. Shunt;

(b) Pulmonary fibrosis

(c) Pulmonary edema;

(d) ~~High~~ altitude ⇒ b/c exchange is Not affected;

↳ as much as Alveolar $P_A O_2$ ↓es ; arterial Pa_{O_2} also ↓es; so; gradient same.

Pulmonary capillary Transient time (Blood stay in Pulmonary capillaries)

↳ 0.75 – 0.85 sec

Tissue capillary Transient time (Blood stay in Tissue capillaries)

↳ 1-2 sec

QQ Large changage in Po_2 ⇒ ~~a) Pulmonary capillaries~~

b) Tissue capillaries

QQ Largest Arterio-venous O_2 difference

↳ Heart

	PaO_2	PvO_2
Normal ⇒	95	~~40~~ ↓
(a) Coronary	95	20

QQ. Min^m Arterio-venous O_2 difference

↳ Kidney

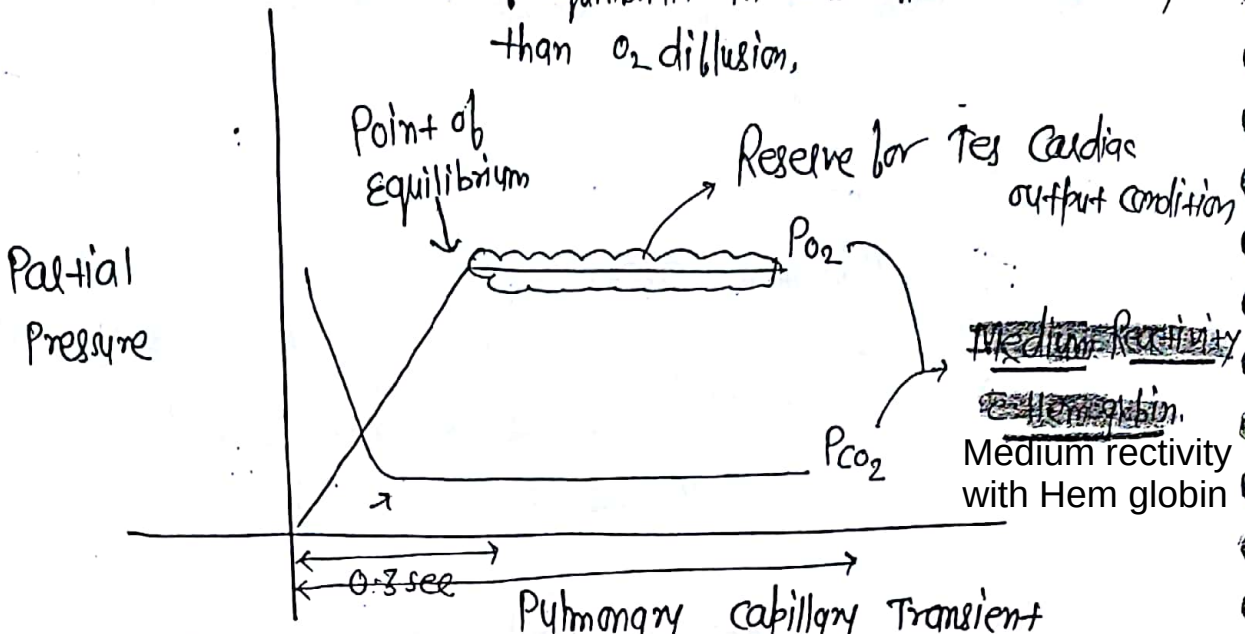
	PaO_2	PvO_2
	95	~~40~~
Kidney	95	70

Renal blood flow = 1100 - 1200 ml/min

↳ 22-23% of C.O.

Blood supply to the kidney is in excess of its Metabolic Need.

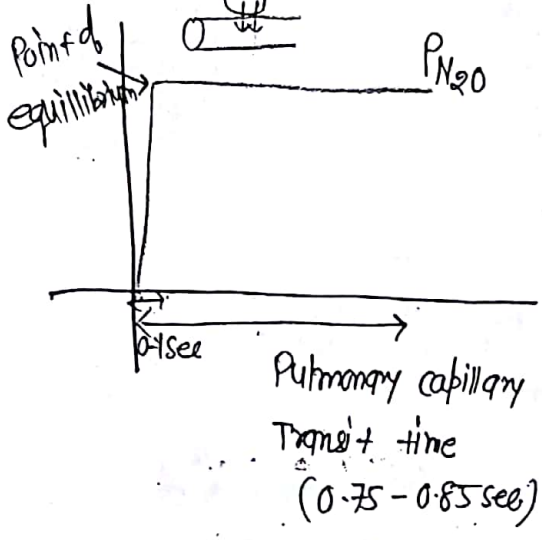
* Point of equilibrium in CO_2 diffusion comes early than O_2 diffusion.



Medium rectivity with Hem globin

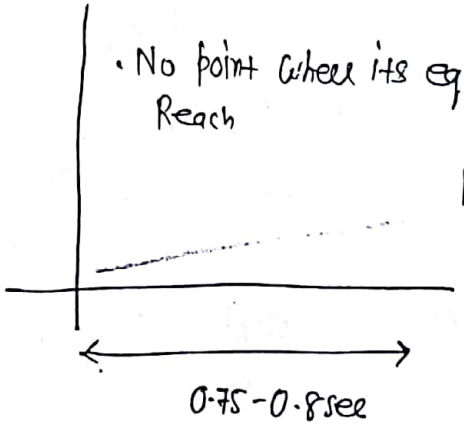
* PERFUSION OF FLOW LIMITED GASES

- N_2O
- Gas which completes Diffusion within Pulmonary capillary transit time
- Nil transit time Reactivity with Hb



PERFUSION OF DIFFUSION LIMITED GASES

- CO
- Gas which doesn't equilibrate with in Pulmonary capillary transit time
- CO has very very high Reactivity with Hb.
- No point where its equillibrium Reach



(99) Which of the following is Diffusion Limited gas ??

(a) N_2O
(b) O_2
(c) CO_2
(d) ~~CO~~

⇒ Perfusion or Flow Limited gas

OXYGEN TRANSPORT

		Arterial blood	Venous blood
(1)	With Hb (As Oxy Hemoglobin)	18.71 mL/dL	13.88 mL/dL
(2)	As dissolved O_2	(95×0.003) 0.29 mL/dL	(40×0.003) 0.12 mL/dL
	Total O_2 =	19 mL/dL	14 mL/dL

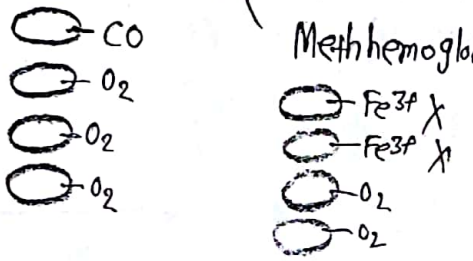
* O_2 content (mL/dL) = (O_2 in combination $\bar{c}$ Hb) + (Dissolved oxygen)

= (Hb(gm/dl) × 1.34 + % saturation) + (Dissolved oxygen $(P_{O_2} \times 0.003)$ mL/dl)

(1 gm of Hb can transport 1.34 ml of O_2)

In Anemia ⇒ a) ↓ Hemoglobin (Fe deficiency Anemia, Hemolytic Anemia)

b) ↓ Saturation of O_2 (Carbon Monoxide Poisoning, Methhemoglobinemia)



DISSOLVED OXYGEN ⇒ P_{O_2} (mm of Hg)

↓

?? mL/dL

Solubility of O_2 ⇒ 0.003 mL/dL/mm of Hg

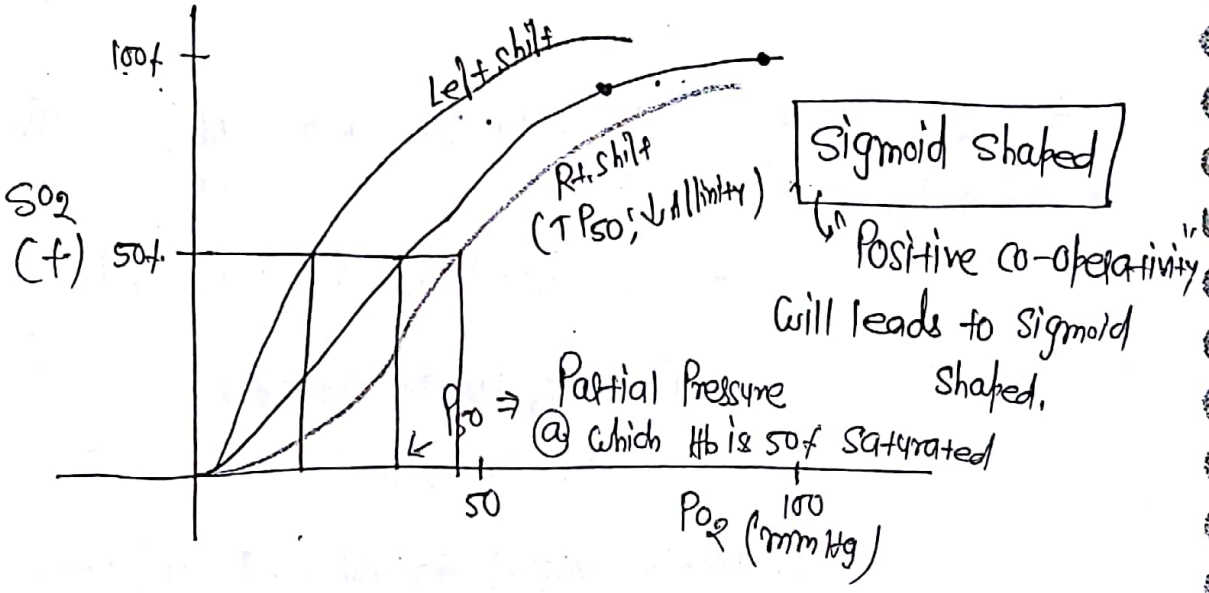
↳ if P_{O_2} is 1 mm of Hg ⇒ Dissolved O_2 is 0.003 mL/dL

So; if P_{O_2} is 100 mm of Hg ⇒ Dissolved O_2 is 0.3 mL/dL

if P_{O_2} is 90 mm of Hg ⇒ Dissolved O_2 is 0.27 mL/dL

if P_{O_2} is 80 mm of Hg ⇒ Dissolved O_2 is 0.24 mL/dL

* Oxygen Hb Dissociation curve ⇒



Sigmoid shaped

↳ "Positive co-operativity" will leads to Sigmoid shaped.

P_{O_2}	Saturation of O_2
95 mm of Hg	97–98%
Hypoxia → 60 mm of Hg	89%
if P_{O_2} is less than 60 mm of Hg. 40 mm of Hg	75%

Deoxy Hb ⟶ Oxy Hb

(Tense configuration) (Relaxed configuration)

T ⟶ R conversion

T ----------> R conversion

P_{50} ⇒ Normally 25–27 mm of Hg
= 3.6 kPa

[1 kPa = 7.5 mm of Hg]

Right Shift of curve ⇒ ↑ P_{50} ↓ Affinity (Favours delivery shift to Right)

Condⁿ ⇒ ↑ PCO_2
↑ H^+
↓ pH
↑ 2,3-DPG
↑ temp.
HbS

caused by

G → Growth Hormone
E → Exercise (Untrained Individual)
T → Thyroid (excess)
A → Anemia
Altitude (high)
Androgen

4 moles of O_2 binds with 1 mole of Hb; but 1 moles of O_2 binds with 1 mole of Hb; but both binds at same place

Left Shift of curve ⇒ ↓ P_{50} ↑ Affinity (Favours affinity shift to Left)

Condⁿ ⇒ ↓ PCO_2
↓ H^+
↑ pH
↓ 2,3 DPG
↓ temp.
HbF

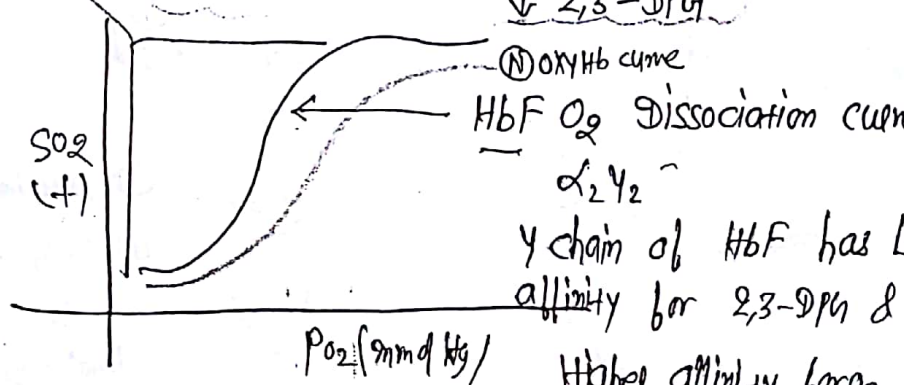
1 mol of Myoglobin binds with 1 mol of O_2

Myoglobin O_2 dissociation curve
⇓
Rectangular hyperbola
(P_{50} = 5 mm of Hg)

HbF ⇒

Myoglobin ⇒ Store house of oxygen in Muscles

Banked blood → Glycolysis
↓ 2,3-DPG



$\alpha_2\gamma_2$
γ chain of HbF has Lower affinity for 2,3-DPG & ∴ Higher affinity for O_2

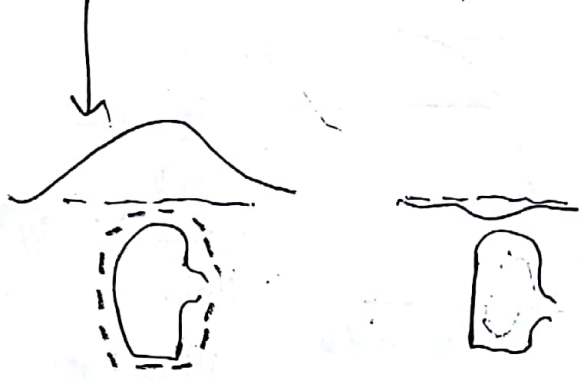
REGULATION OF RESPIRATION

- NEURAL CONTROL
- CHEMICAL CONTROL (Chemoreceptors)

MEDULLA

→ Pacemaker → **PRE BOTTZINGER COMPLEX**

DRG	VRG
Dorsal Respiratory group	Ventral Respiratory group
"I" cells	"I" & "E" cells
Function in (N); Quiet Respiration	Functions whenever Requirement req (eg⇒ Exercise)
DRG ("i" Neurons) → (+) → Phrenic N. Nucleus (cervical spinous cord)	DRG ("i") → (+) → (+)
X	X
X	X



Contraction of diaphragm ⇊ Inspiration

Relaxation of Diaphragm ⇊ Exhiration

DRG → Inspiratory signal..

Receptor for Tidal Receptor ⇒ Muscle spindle of diaphragm & ~~External~~ Internal costal Muscle

PONTINE CENTERS →
- Smooth transition b/w Inspiration & expiration
- control depth of Inspiration

PNEUMOTAXIC CENTER (P.C.)

APNEUSTIC CENTER

(+) (+) → INSPIRATION (DEPTH)

(−) P.C

(−) vagus

Pulmonary Stretch Receptor

HIGHER CENTERS
- → Limbic System ⇒ Emotion & Respiration
- → Cerebral Cortex ⇒ Voluntary control of Respiratory

(a) Vagal Stimulation

↳ ↓ Depth

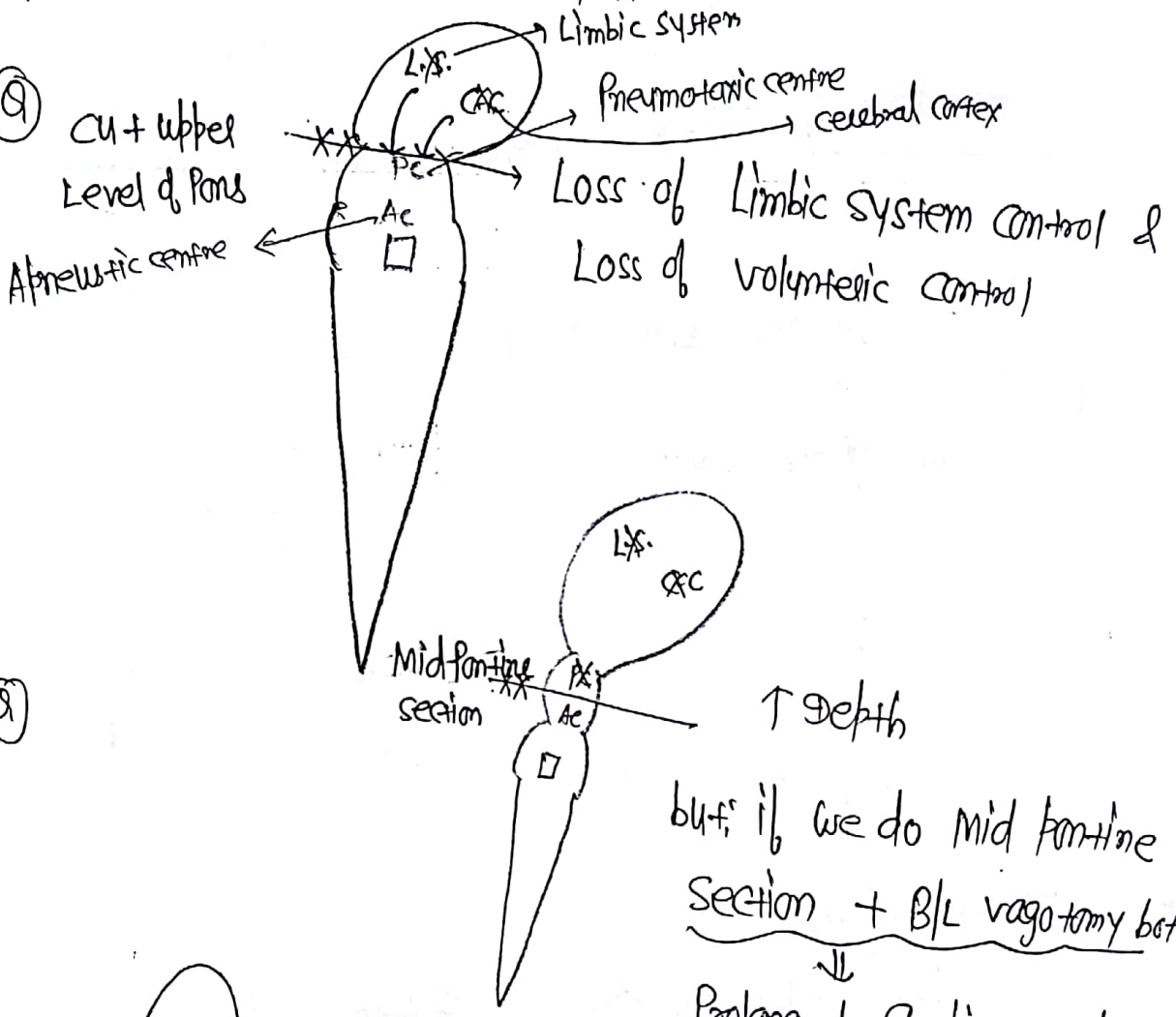
(a) Strong vagal Stimulation

↳ Apnea

(a) B/L Vagotomy

↳ ↑ Depth

(a) Cut upper Level of Pons



Loss of Limbic system control &
Loss of volunteric control

(a)

↑ Depth

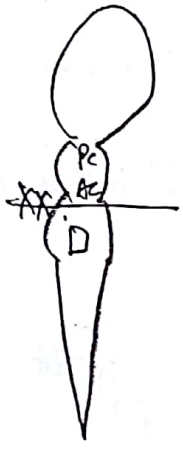
but if we do Mid pontine Section + B/L vagotomy both

↓

Prolonged Inspiratory Spasm

Known as APNEUSES OR APNEUSTIC BREATHING

(a)



Section @ upper border of Medulla.

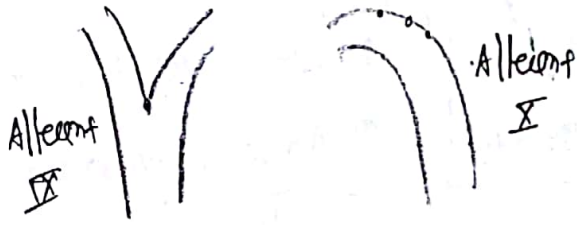
Highly Irregular & Grasping type of breathing

Q. Apnea will seen if section is at :→
(a) Upper pons; (b) Lower pons; (c) Upper Medulla;
(d) ~~Lower~~ Medulla

CHEMICAL CONTROL
↓
By ChemoReceptors

Peripheral chemoReceptor
↓
Carotid & Aortic bodies*

Central chemoReceptors
↓
on the surface of Medulla



Stimuli for Peripheral chemoReceptors ⇒

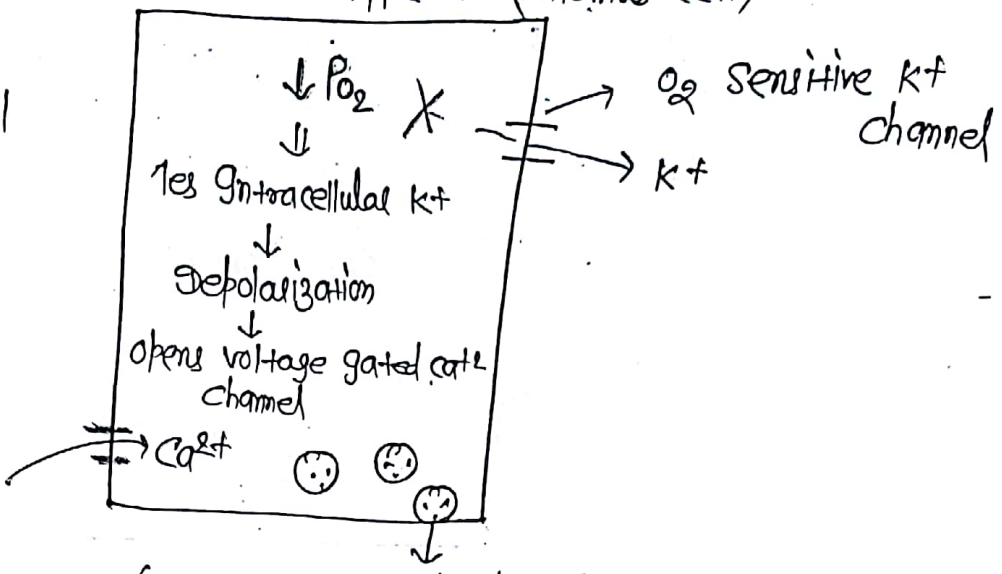
i) ↓P_{O_2} ← Most potent stimuli for Peripheral chemo Receptors
ii) ↑P_{CO_2}
iii) ↑H^+
iv) ↓PH
v) ↑Lactic acid
vi) ↑K^+ (severe exercise)
vii) ~~Severe~~ cyanide

(Q) Peripheral chemo Receptors stimulated by
(a) ↑P_{O_2}
(b) ↓P_{CO_2}
(c) ↑PH
(d) ~~Cyanide~~ Cyanide poisoning

CAROTID BODY

Type-II
⇓
Supporting cell

Type-I (Glomus cell)



CENTRAL / MEDULLARY CHEMORECEPTORS (C.C.R)

(Q) Most potent & direct stimulation for C.C.R

⇓

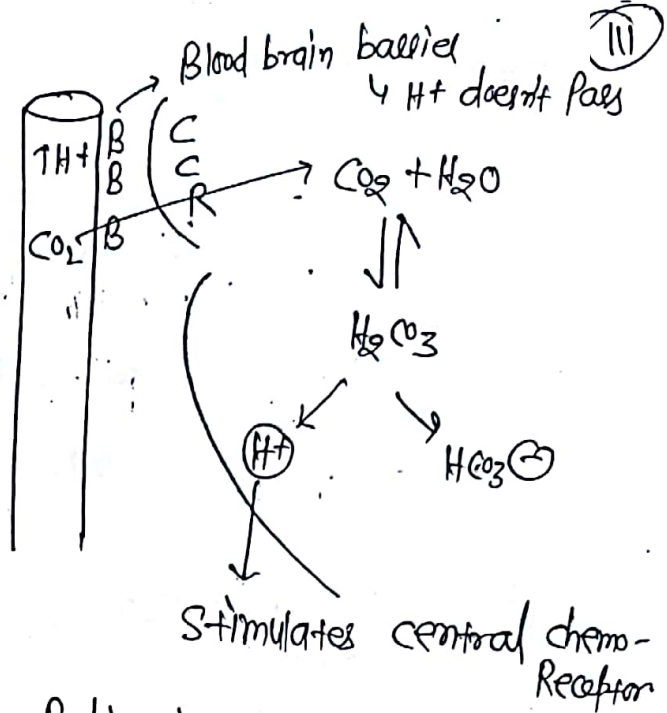
$H^{\oplus}$

Q. Most potent Stimulus for C.C.R in blood ⇒

(a) ↑H⊕ ; (b) ~~↑Pco_2~~

Q. Most potent Stimulus for C.C.R in CSF ⇒

(a) ~~↑H⊕~~ ; (b) ↑PCO_2



Q. Most potent Stimulus for Respiration

(a) ↓PO_2 ; ~~(b) ↑PCO_2~~ → Stimulate both

↓ ⊕ ⊕ 30% ⊕ 70%

Only Peripheral Chemo Receptors

Central Chemo Receptors

RESPIRATORY REFLEXES

(1) HERING BREUR INFLATION REFLEX ⇒

If Lung Inflation ≥ 1–1.5L ⇒ Stimulate Pulmonary stretch Receptors (⊕ @ Tracheo-bronchial tree)

↓ vagus

↓ Depth & ↑ Expiration time.

② HERING BREUR DEFLATION REFLEX :→

↓

↑ Depth of Inspiration
&
↓ Expiration time

↳ It prevents " Atelectasis of Lungs "**

③ HEAD'S PARADOXICAL REFLEX :→

Inflation causes further Inflation of Lungs.

Significance ⇒ Newborn's → 1st breath is d/t it.

④ J-RECEPTOR REFLEX :→ J ⇒ Juxtacapillary

↓

by Dr. A.S. PAINTAL

⊕ In Alveolo capillary Junction

Stimuli for J-Receptor ⇒ Hyper Inflation
Pulmonary congestion
Pulmonary Edema
Pulmonary Embolism

Responses ⇒ Apnea (Transient) – Rapid Shallow ventillation QQ
– Hypotension
– Bradycardia.

Q) In Exercise → ↑ Rate; ↑ Depth

Which Resptor Stimulate ⇒ ⓐ Pulmonary Stretch Receptor
In exercise (Mild to Moderate) ⓑ J-Receptor
P_{O_2}, P_{CO_2}, pH ⊆ in ⓝ Limits ← ⓒ chemoReceptor
~~ⓓ~~ Joint Proprio Receptors

Joint:- Proprio ceptors

(+) → Vaso Motor centre

(+) → Respiratory centre

* but; In Severe exercise ; ↓ P_{O_2}, ↑ P_{CO_2}, ↑ H+, ↓ K+ ⇒ Joint Proprioceptors + Chemo Receptors both works

CYANOSIS – Bluish discolouration of skin & Mucosa

. Deoxy Hb ≥ 4.0 gm/dL

So; Severe Anemia will Not prt. with cyanosis

While; In Polycythemia patient present ∈ cyanosis (May be)

. Meth Hb ≥ 1.5 gm/dL

. Sulph Hb ≥ 0.5 gm/dL

HYPOXIA ⇒ O_2 deficiency at tissue Level

1. HYPOXIC HYPOXIA ⇒ P_{O_2} < 60mm of Hg, S_{O_2} < 89%

"M/c type of Hypoxia"

Cyanosis (+)

M/c type of Hypoxia
Cyanosis (+)

Causes ⇒ High Altitude — High Altitude

Hypoventilation — Hypoventilation

Gulleian - Baare Syndrome — Gulleian - Baare synd

Bulbal infarct — Bubal infact

Peripheral chemoReceptor ⇒ (+)

Peripheral chemo-receptor stimulation — stimulation

2. ANEMIC HYPOXIA ⇒ either Hb ↓ or Saturation of O2 ↓ — Anemic Hyoxia — either Hb Decrease or satuation of O2 decrease

Cyanosis = (-) — Cynosis - (-)

Hb → ↓

SO_2 → ↓

P_{O_2} → (N) (b/c there is No problem Regarding the exchange of O2 here)

PeriPheral chemoReceptor ⇒ (-)

stimulation

eg ⇒ Met Hb

CO Poisoning

3. STAGNANT HYPOXIA ⇒ ↑ Arterio-Venous O2 difference — also "Hypoperfusion hypoxia"

Stagnant hypoxia — Cyanosis (+)

b/c of Sluggish blood Flow

eg: CHF or circulatory shock.

Peripheral chemo-Receptor ⇒ Very very very high Rate of blood flow (2-3 gm)

⇒ 2000 ml/min/100gm

In Brain ⇒ 52 ml/min/100 gm

if there is ↓ in blood flow Rate

↳ ↓ Total Volume of blood & therefore O2 delivered to Peripheral chemoReceptors in cardiac arrest or Low

④ **HISTOTOXIC HYPOXIA** ⇒ ↓ Arterio-Venous O_2 difference

eg ⇒ ~~Cyanide Poisoning~~ Cyanide Posining

Peripheral chemoReceptor → ⊕ Stimulation

ACCLIMATIZATION ↱ Minm time Required * ↳ 2-3 days

- ~~Development of compensatory Mechanism to ward off ill effects of Low Barometric pressure.~~
- i) ↑ Renal excretion of bicarbonates → Leads to Polyuria (More loss of water) b/c Solutes comes ↓ ↑↑ Solvent.
  ↓
  pH tends to Normalize (So, Respiratory Alkalosis ; further Nf inhibit the Peripheral chemo-RR Receptor)
  ↓
  ↓P_{O_2} → Les Respiratory Drive
- ii) ↓P_{O_2} → ↑ Erythropoietin → comes from kidney → ↑ Red cell Mass (Polycythemia)
- iii) Shifts oxygen-Hb dissociation curves to Right (Least helpful) ⇒ ↓↑ Les O_2 delivery to tissue
  ↳ ↓↑ Les in 2,3-DPG

* In Natives of High Altitude ⇒ iv) ↑ Capillary density at tissue Level
v) ↑ Mitochondria ; ↑ Cytochrome enzyme

HIGH ALTITUDE PHYSIOLOGY

(↓P_{O_2}) Hypoxic Hypoxia → Stimulate Peripheral chemo Receptor → ↑ Rate of ventilation
↑ Depth of ventilation
⇓
⊖ "CO_2 washout" ⇐ Hyperventilation
↳ Respiratory Alkalosis

$P_{CO_2} \propto \frac{1}{V_A}$

* ↓P_{O_2}
↓
Peripheral chemo (R)

VMC → Sympathetic Discharge
Respiratory centre → ↑ Rate of Ventilation, ↑ Depth of ventilation

→ CVS changage 1st to Normalize in Acclimatization

* Physical activity during Acclimatization → Rate of Ascent → ACUTE MOUNTAIN SICKNESS ⇒ Individual Susceptibility alter 1st 24 hrs. (1-3 days)
⇒ In few clin Few hours

Mild Altitude Sickness ⇒ Headache; Sleep disturbance; Irritability.

HACE ⇒ High altitude Cerebral edema

↓ P_{O_2}

↓

Cerebral vasodilation

↓

↑ P_c

↓

↑ Tissue fluid formation

R_x ⇒ give O_2 & evacuate

Prevention ⇒ Acetazolamide

↳ Produces Metabolic acidosis & Acidosis's Res. Respiratory drive

HAPE ⇒ High altitude Pulmonary edema

↓ P_{O_2}

↓

Pulmonary vasoconstriction

(Patchy vasoconstriction) ← Not Uniform vasoconstriction

↑ Flow in those Areas where there is little or No vasoconstriction.

↓

↑ P_c

↓

↑ Tissue Fluid formation

CHRONIC MOUNTAIN SICKNESS

↳ MONGE'S DISEASE

↳ occur in Fully Acclimatized patient

↓ P_{O_2}

↓

Pulm. vasoconstriction

↓

Pulm. Hypertension

↓ P_{O_2}

↓

↑ Red cell Mass

↓

↑ Blood viscosity

↓

↑ Resistance to flow

Right heart Failure

⇓

Congestive Cardic Failure

↳ Pulmonary edema

GIT

Smooth Muscle

- Unstriated
- Involuntary
- Actin
  Myosin
  Tropomyosin
  Troponin
- Ca++ binding Protein
  - Calmodulin

QQ- Gatekeeper in the GIT ⇓ Epithelial calcium channel.

RMP of Smooth Muscle ⇓ -60 mv to -30 mv

Ca++ binding protein

Calmodulin

Smooth Muscle

Single Unit

Single unit

Gap Junction (+)

- Walls of Hollow viscera (GI tract, Ureter, Urinary bladder, Uterus)

Multi-Unit

Multi- Unit

No Gap junction

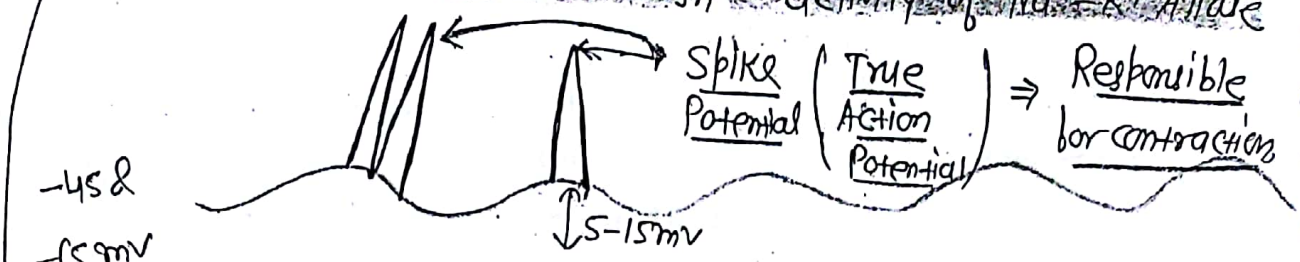
- Iris
  - constrictor pupillae
  - dilator pupillae
- Ciliaris

* Vasaylal Smooth Muscle ⇒ has both Single & Multi-unit type of Smooth Muscle

* Electrical activity ⇓ PaceMaker ⇒ Interstitial cells of CAJAL ⇓ BER (Basal electrical Rhythm)

* Basal electrical Rhythm

↳ Variation of Membrane potential d/t oscillation in activity of Na+-K+ ATPase



Frequency → Variable

Maxm → ~~Duodenum~~ – ~~12/min~~ 12/min

Minm → ~~Cecum~~ – ~~2/min~~ 2/min

Duodenum

cecum

↳ It is Not Responsible for contraction,

Depolarization ⇒ Ca^{+2} influx (Not Na+ influx)

Q. ↑ frequency of Spike potential in All except ⇒

↳ ↑ Contractile Activity

(a) Parasympathetic

(b) Ach

(c) Stretch → Opening of Mechano-Sensitive Ca^{2+} channel.

~~(d) Adrenaline~~

Mech^{n} of Smooth Muscle contraction ⇒

Increase In Sarcoplasmic ca+2

↑ In Sarcoplasmic Ca^{2+}

↓

Ca^{2+} binds ē Calmodulin

↓

Ca^{2+} – Calmodulin complex

↓

Activates "MLCK" (Myosin light chain kinase)

↓

Phosphorylates Myosin Light chains in Myosin head

↓

Activates Myosin ATPase

↓

Actin – Myosin cross-bridge "formation"

↓

Actin – Myosin cross-bridge "cycling"

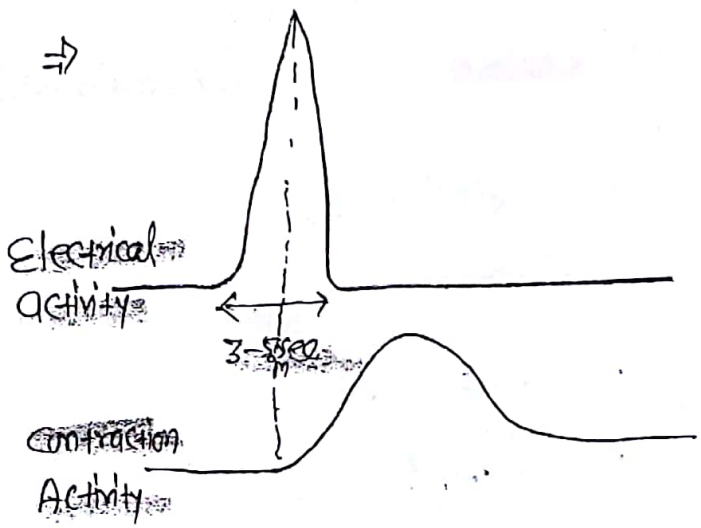
Relaxation by

↓

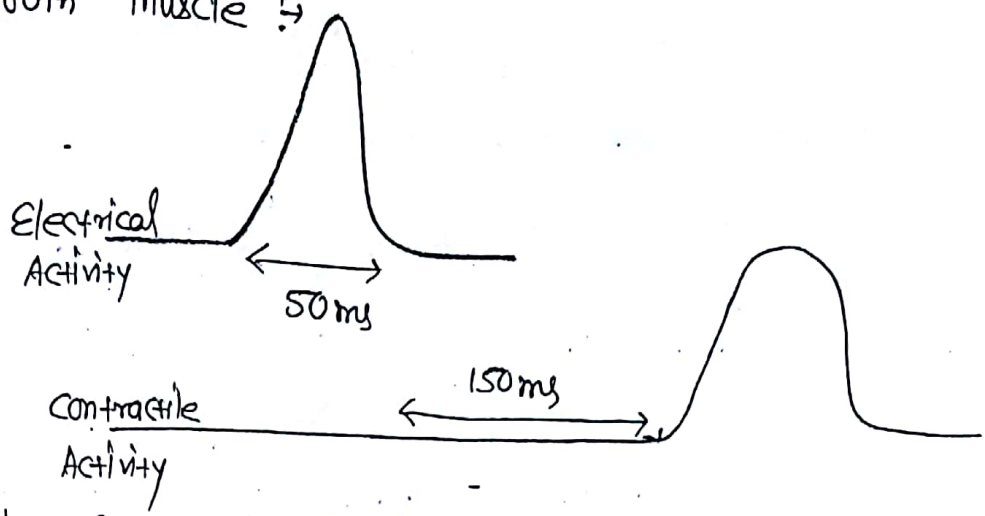
Phosphatase

LATCH MECHANISM ⇒ Slower Actin-Myosin cross bridge cycling.

In Skeletal Muscle ⇒



* In Smooth Muscle :-



* GI Transplant done Rarely; b/c Intestine is Rich in Lymphoid tissue; so! chance of its Rejection is very high.

CONTROL OF SMOOTH MUSCLE (GI Tract)

- **NEURAL CONTROL** — Neural control
  - ⇓
  - **Enteric Nervous System** — Enteric Nervous system
    - Intrinsic nervous system → **INTRINSIC NERVOUS SYSTEM**
      - Found in b/w the Longitudinal & circular Muscle Layers
      - **MYENTRIC OR AUERBACH'S PLEXUS**
        - ⇓
        - Controls GUT Motility
      - **SUB MUCOSAL OR MEISSNER'S PLEXUS**
        - ⇓ controls
        - Secretory Activities
        - Blood supply
    - Extrinsic nervous system → **Extrinsic Nervous System**
      - Modify the activity of Intrinsic
      - → Symphathetic
        - ↑ Contraction of sphincter
        - ↓ the contractile activity
        - ↓ Secretory activities
      - Parasymphathetic
        - ↑ Contractile activity of gut
        - Relaxation of sphincter
        - ↑ Secretory activities
- **HORMONAL CONTROL** — Hormonal control

HORMONAL CONTROL OF GI Tract

STOMACH

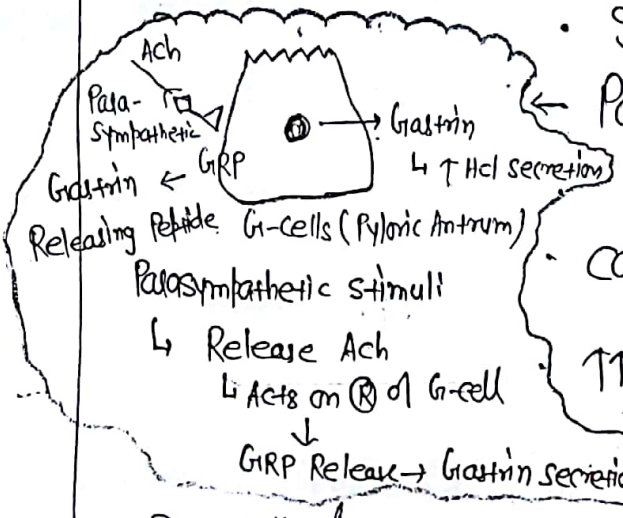
↳ G cells (Antrum) → Gastrin → ↑ HCl secretion

G cells (Antrum)

Gastrin

Increase HCl secretion

- Distension
- Parasympathetic - Stimulation
- Ach
- Ca^{+2} (Intraluminal & Blood borne)
- ↑↑ Adrenaline



Parasympathetic stimuli
↳ Release Ach
↳ Acts on (R) of G-cell
↓
GRP Release → Gastrin secretion.

↳ D_1 cells (FUNDUS) → GHRELIN → also by Epsilon cells of Pancreas

c"C cell" of pancrease

GHRELIN

- orexigenic (↑↑ Appetite)
- Mobilizes fats & ↑↑ Fat deposition

Mobilizes fats & increase fat deposition

- Modifies choice of Food

Modifies choice of food

- Enhances Memory
- Sleep deprivation (↑ Ghrelin secretion
- Anorexia → (N) OR High Ghrelin
- ↑ Growth hormone secretion.

Small intestine

SMALL INTESTINE

↳ "I" cells ⇒ CCK

- ↑ Gall bladder contraction
- ↑ Pancreatic Enzyme Secretion
- Potentiates action of secretin

QQ Most imp. Stimulation for Secretion of CCK ?

(A) Fatty acids; (B) Products of Protein Digestion

CHOLERETICS Choleretics

↑es synthesis of Bile salts

Increase synthesis of bile salts

↓

∴ ↑ Secretion of Bile

Increase secretion of Bile

Eg ⇒ Bile salts

Biles salts

CHOLEGOGUES Cholegogues

↑ Gall bladder contraction

Increase Gall Bladder contraction

↓

∴ ↑ Secretion of bile

Increase secretion of Bile

CCK

CCK

"S" cells of Small Intestine ⇒ SECRETIN

"S" cells of small intestine

↳ ↑ HCO_3^- Content of bile & Pancreatic Juice

Increase HCO- content of bile & pancreatic juice

↳ delays gastric emptying

delays gastric emptying

QQ Most alkaline Secretion ?

Saliva → 6.0 - 8.0 (7-8 usually)

Bile → 7.0 - 8.0

Pancreatic Juice → upto 8.8

Brunner's gland → upto 9.3

Secretion ↳ ⊕ in duodenum

"K" cells of Small Intestine ⇒ GIP ⇒ Glucose dependent Insulinotropic peptide

k cells of small intestine

Glucose dependent Insulinotropic peptide

Incretin

Incretin

↑ Insulins

Increase Insulins

"L" cells of Small Intestine → GLP-1 ⇒ Glucagon like peptide-2

"L" cells of small intestine

GLP - 1

Glucagon like peptide

GIP ⇒ ↑ Insulin

GIP - 1

⇒ Also known as Physiologic β-cell stimulating hormone of GI tract

Physiology Beta- cell stimulating hormone of GI tract

S cells of Small Intestine — Somatostatin

Somatostatin

- ↓ Gastric Motility & secretion

Decrease - Motility & Secretion

- ↓ Intestinal "

Decrease Intestinal motility & secretion

M cells of Small Intestine — Motilin

- When a Meal is ingested, secretion of Motilin is suppressed until digestion & Absorption are complete
- Migratory Motor Complexes
- ↑ GUT Motility (99)

Erythromycin combines to Motilin

HORMONES OF GI Tract

Hormones of GI Tract

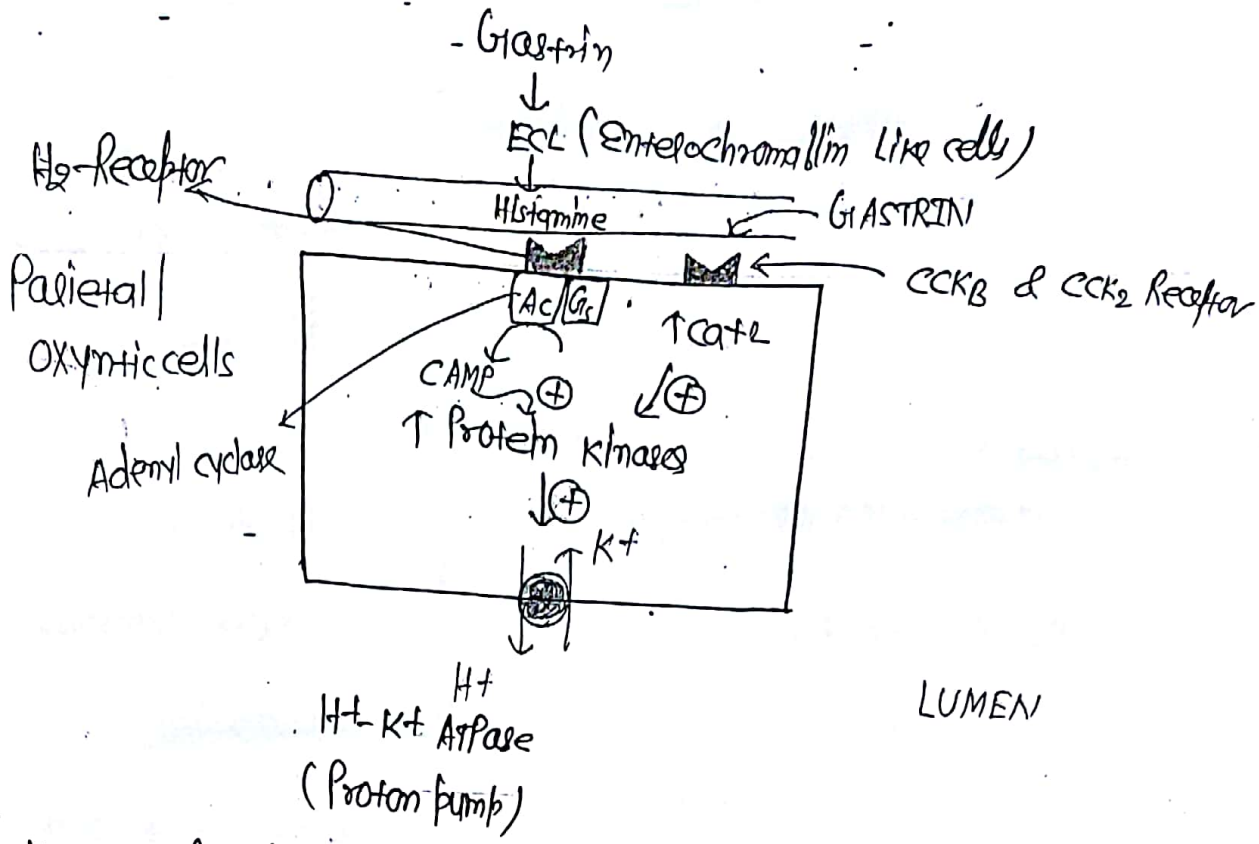
Gastrin family

- Gastrin
- CCK

Structural Similarity

Secretin family

- Secretin
- GIP
- GLP-1
- Somatostatin
- Motilin



* Gastrin acts on entero-chromaffin cells

↓

Histamine secretion

↓

Acts on H_2 Receptor

↳ acts on G_s Protein

↳ Activates Adenyl cyclase

↳ ↑ cAMP & ↑ Protein kinase

Increase cAMP &
Increase Protein kinase

SECRETION OF GI TRACT

SALIVA ⇒ 800 - 1200 ml/Day

pH = 6.0 - 8.0 (usually 7.0 - 8.0)

- 3 Pairs of Major salivary gland
  - → Parotid → Largest gland
  - → Submandibular + Maxm contribution to Saliva
  - → Sublingual

3 Phases

↳ CEPHALIC ⇒ Most Important ; b/c Thought; Sight
ORAL → by Sour Maxim , Smell
GASRTIC activated

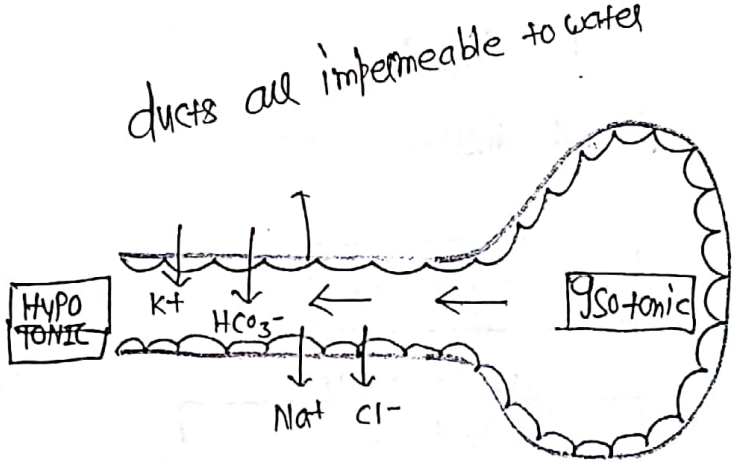
3 Enzymes

↳ S. Amylase

Lysozyme

Lingual Lipase ⇒ Secreted by 'EBNER's GLANDS ON DORSUM OF GLAND.

→ Chloride ion (Cl^-) Require to activation of S. Amylase
↳ Not H^+; HCO_3^-



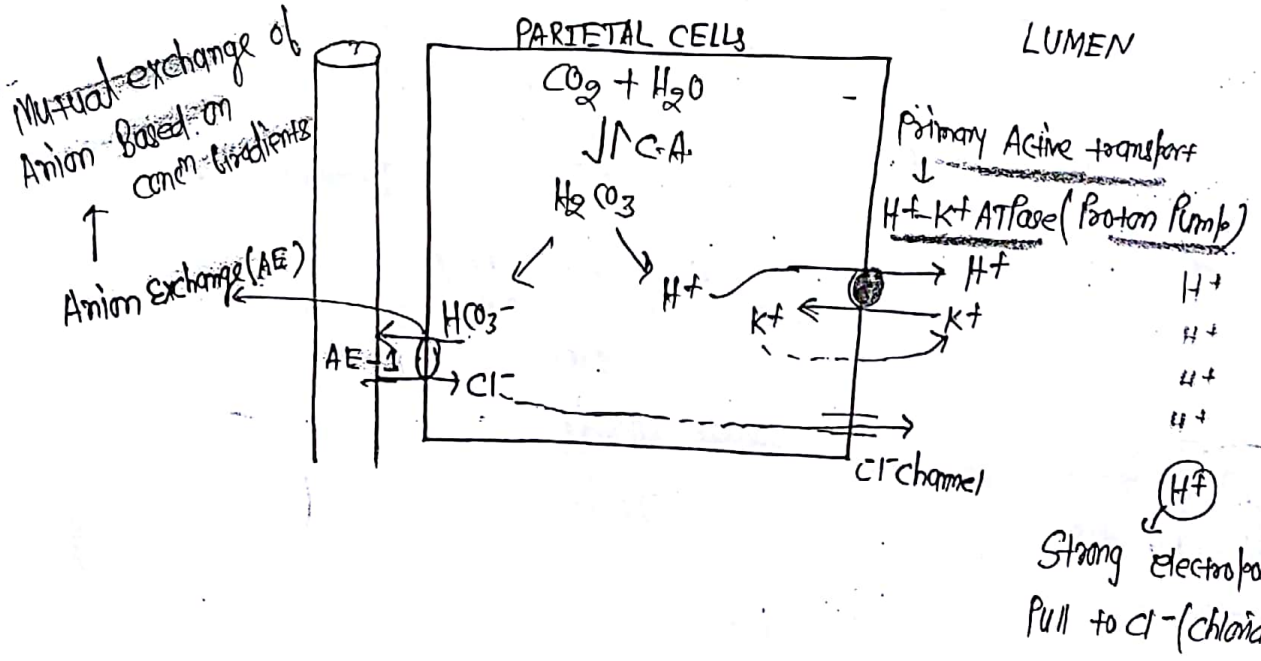
Na^+, Cl^- Reabsorption > K^+, HCO_3^- Secretion into saliva

* Aldosterone Receptors are present here
↳ In Collecting duct
Salivary glands
Sweat glands
Colon
Hippocampus

GASTRIC SECRETION ⇒

- 2,000 / 2,500 mL / Day ← Maximum
- pH = 2-3
- 3 Phases
  - Cephalic
  - **Gastric** ← Neural + Hormonal ⇓ by Gastrin
  - Intestinal
- Oxyntic / Parietal cells
  - Secreted HCl
  - Intrinsic Factor
- Chief / Peptic cells
  - Pepsin
  - Gastric Lipase

HCl Secretion



Strong electropositive Pull to Cl⁻ (chloride).

Function of Hcl ⇒ i) Bactericidal Agent

pH of Pure Hcl ⇒ 1-2.

ii) Solubilizes the Iron salts

Fe^{+3} —vit c→ Fe^{2+}

↳ only absorbable form of Iron

iii) Activation of Pepsinogen to form Pepsin.

PANCREATIC SECRETION ⇒ 1500 mL/Day

↳ pH = upto 8-8

↳ Very Rich in enzyme

↳
- Pancreatic Amylase
- Trypsin
- Chymotrypsin
- Carboxypeptidase
- Elastase
- Nucleotidase
- Lipases
  - ↳ Colipase Dependent Pancreatic Lipases
  - ↳ Bile Salt activated Pancreatic Lipases

INTESTINAL SECRETION ⇒ 1500 mL/Day

- pH = 7.0–8.0
- Secrete Enzymes

⇓

- Enterokinases

Trypsinogen → Trypsin

⇓

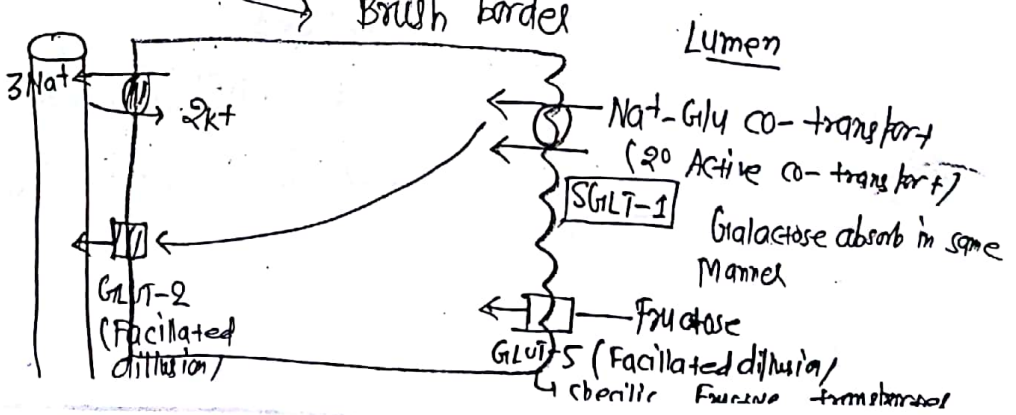
Activates all other Pancreatic enzyme to their active forms

- Disaccharidases
  - Lactases
  - Sucrases
  - Maltases
- Di & Tri-peptidases

DIGESTION & ABSORPTION

(A) CARBOHYDRATE → Luminal

→ Brush border



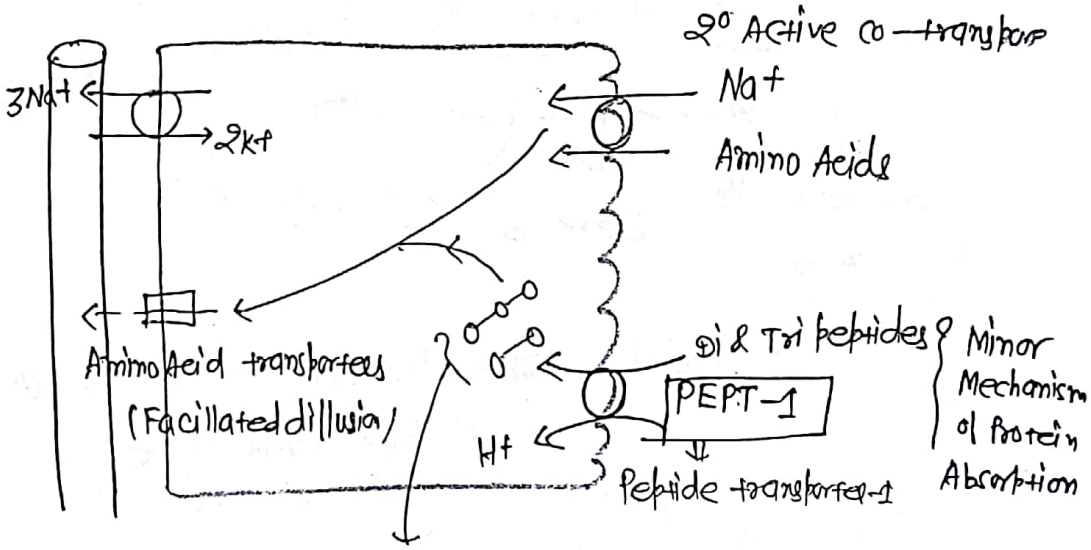
Glucose is absorbed by :-

a) ~~Facillated~~ diffusion ; b) ~~2°~~ Active co-transport

(B) PROTEINS DIGESTION :-

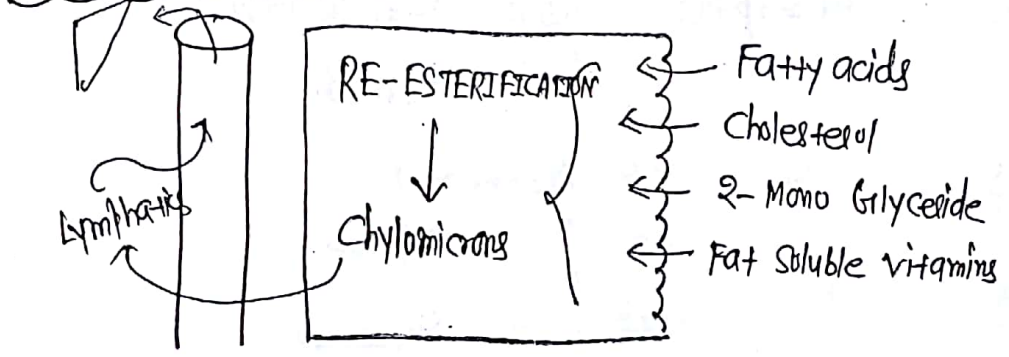
- Luminal digestion
- Brush border digestion
- Intracytoplasmic Digestion (Di & Tri peptidase (+))

Absorption ⇒

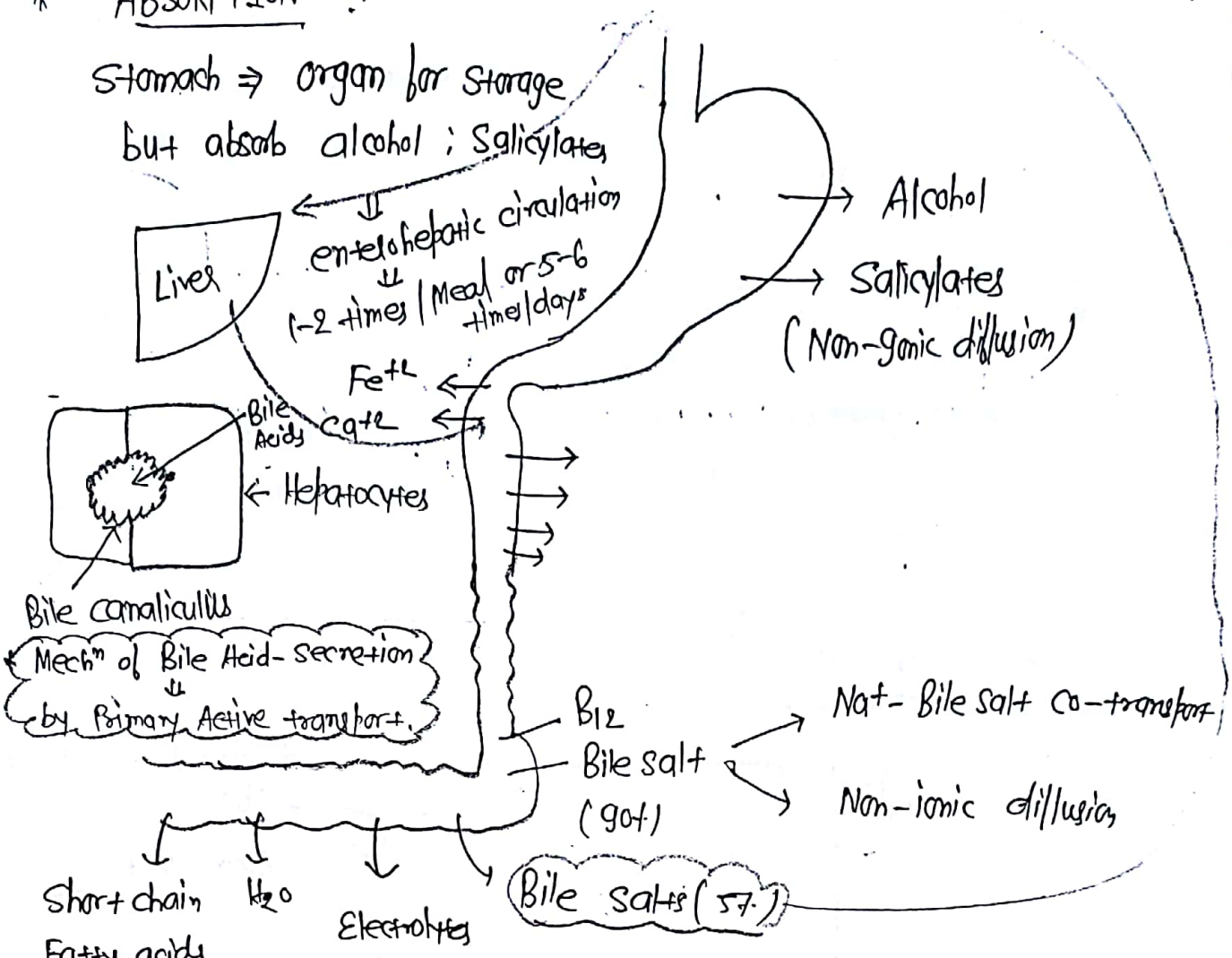


done by Intracytoplasmic Di & Tri peptidases

(C) FATS ABSORPTION :-



* ABSORPTION :-



↳ Produced by colonic bacteria by Action on dietary fibers; complex carbohydrate

eg ⇒ Acetate 60%
Propionate 25%
Butyrate 15%

QQ: Absorption alcohol starts in ??
↳ Stomach

QQ Maxm Alcohol Absorption ??
↳ Jejunum

QQ Fe+2 absorption ⇒ Duodenum

Q. Maxm Ca^{2+} ⇒ Jejunum

Q. B_{12} ⇒ Distal ileum

Q. Fatty acids ⇒ Jejunum

Q. Bile ~~Acids~~ Salts ⇒ Distal ileum

Q. Short chain fatty acids ⇒ Colon

Q. Long chain fatty acids ⇒ Jejunum

Q. Maxm water absorption ⇒ 9000 ml enters in ~~Gall~~ Small Intestine.

Jejunum	⟶	5500 mL (Maxm)
Ileum	⟶	2000 mL
Colon	⟶	1300 mL
Feces	⟶	200 mL

Q. Maxm Na+ absorption ⇒ Jejunum

Q. Maxm K+ is secreted by :- Salivary glands

Q. Maxm K+ conc^{n} is in ⇒ Colonic fluid

SDA (Specific Dynamic Action of Food) ⇒

↳ Obligatory Expenditure of Energy for Digestion & Absorption of Food

eg ⇒

	Proteins	Carbohydrate	Fats
	↓↓ ⊗ amount	↓↓ ⊗ amount	↓↓ ⊗ amount
	100 Kcal energy generated	100 Kcal energy generated	100 Kcal energy Generated
To digest & assimilate ⇒	30 Kcal expend	6 Kcal	5 Kcal

QQ SDA is Maxm for ⇒ Proteins

BASAL METABOLIC RATE

depends on ⇒ ~~Body~~ Surface Area

~~Lean~~ Body Mass

MOVEMENTS OF GI TRACT

,Movements of GI Tract

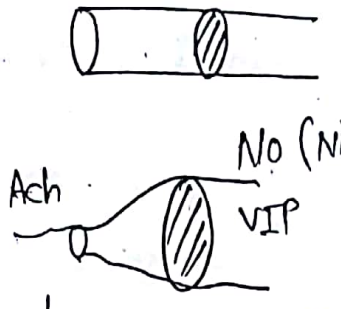
* When food prt. in Small Intestine

↳ first Movement ⇒ i) Segmentation Contraction ⇒

- Mixing contraction
- Alternate contraction & Relaxation in the segment of Intestine

ii) Peristalsis :→ Local Neural activities

↳ Mediated by Parasympathetic & Sympathetic



Ring of contraction behind Food

Relaxation in front of Food

Gn Esophageal Peristalsis

- 1° ⇓ Mediated by vagus during Swallowing
- 2° ⇓ ib Primary fails to Move food forward ⇓ Secondry (2°) is Mediated by Local plexus

Gn B/L vagotomy

↳ Loss of 1° Esophageal Peristalsis

iii) Migratory Motor Complexes (MMC)

Migratory motor complexes (MMC)

↳ ⊕ Gn Gastric Digestive Period

↳ Not a Neural activity; it is Hormonal activity ⇓ by Motilin (M cells)

↳ Ring of contraction which starts from body of Stomach goes upto Distal Ileum

↳ Kl as "HOUSEKEEPING CONTRACTION"

Housekeeping contraction

, 1st MMC ⇒ 90–120 min after Last Meal

↓ then

occur in cycles of 90 mins

- Phases of MMC
  - I ⇒ Quiescent Phase
  - II ⇒ Phase of irregular electrical & Motor activity
  - III ⇒ Phase of Regular electrical & Motor activity

Total duration ⇒ 90 min

- MMC ⇒ 5 cm/min

  (Peristalsis ⇒ 5–25 cm/sec)

- GI prevents Reflux of colonic contents into ileum. and also clearing the tract.

GI REFLEXES

* Receptive Relaxation of Stomach

Receptive relaxation of stomach

- Relaxation of Fundus during Swallowing
- Mediated by vagus

* Gastro colic Reflex ⇒

Food ⊕ in Stomach ⇒ Defecation

In Infants it is Prt.; Abolished in Adults.

Q. Maxm Postprandial ↑ in tone & Motility is ⊕ in which Segment of colon ?

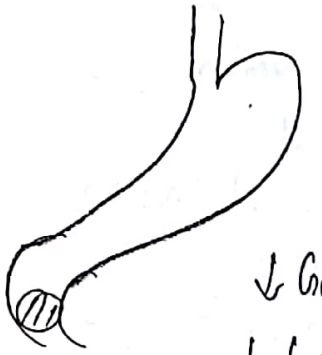
a) Ascending colon

~~b)~~ Descending colon

~~c)~~ Sigmoid colon

* ENTEROGASTRIC REFLEX ⇒ Neural + Hormonal

↳ Mainly Somatostatin



↓ Gastric Motility

↓ Gastric secretion

Stimuli that Inhibit ⇒ ① - Distension M.Imp

Gastric Motility

② Type of Food ⊕

Fats > Proteins > Carbohydrate

③ Acidity of Gastric chyme

More Acidity of Gastric chyme

↳ greater Inhibition

④ Osmolality of Gastric chyme

DEFECATION REFLUX ⇒ 1st Urge ⇒ 18 mm of Hg

Evacuation ⇒ 55 mm of Hg

MICTURATION REFLUX ⇒ 1st Urge ⇒ 150 ml

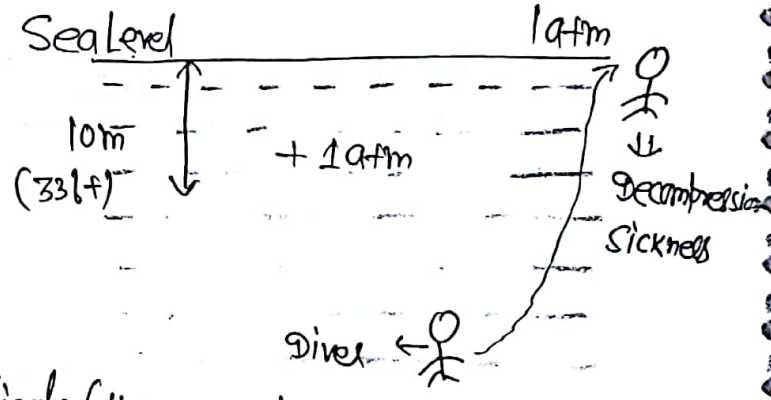
Uncontrollable ⇒ 400 ml

DEEP SEA PHYSIOLOGY

Deep Sea Physiology

(a) At 100 ft ⇒ 4 atm Pressure

At 100 m ⇒ 11 atm



Diver

↓

100% O_2 → ↑↑ Solubility of O_2

⇓

Generation of Free Radicals (H_2O_2, O_2^-)

⇓

O_2 TOXICITY – Symptoms ⇒ Choking

~~Coughing~~ coughing

So; O_2 ± Inert gas given

↳ $O_2 - N_2$

Under water ⇒ ↑↑↑ Solubility of N_2 ⇒ ↑ N_2 Dissolution in plasma, Myelin; Cell Membrane

⇓

Alters Ionic Conductivity ⇐ N_2 Narcosis → "RAPTURES OF DEPTHS". OR "MARTINI Effect".

↳ Symptoms ⇒ Similar to Alcohol Intoxication.

TO Avoid N_2 Narcosis ⇒ Oxygen – He Mixture preferred

⇓

b/c He is less soluble
less Narcotic
less dense ⇒ Breathing is easier

Decompression Sickness

DECOMPRESSION SICKNESS ⇒ K/as "Dysbarism"
Dysbarism
OR
"CAISSON'S DISEASE"
Caisson's disease

Gas embolism (+)

M/c Symptoms ⇒ BENDS (Painful Joint & Muscle) → M/c symptom

Pulmonary symptoms

Cerebral symptoms

Coma

death

(+)ve "g" Forces

↑ Peripheral pooling of blood

⇓

"Black out"

Prevention ⇒ "Anti-"g" Suits"

(−)ve "g" forces

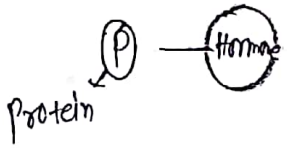
⇓ ↑ Flow towards head ends

Red out ⇒ ↑es conjunctival & scleral congestion

ENDOCRINE SYSTEM

LIPID SOLUBLE HORMONES	⇒	WATER SOLUBLE HORMONES
• Steroids • Thyroid		• Amines • Peptides
* Synthesize as & when Needed (No Storage). ↳ except ⇒ Thyroid		• Synthesize & Stored
• Transported ∈ Proteins except ⇒ DHEA Adrenal Androgen		• Transported as such except ⇒ [gGF-1] ↳ a/w growth hormone ↳ Longer half life than growth hormone
• Cytoplasmic / Nuclear Receptors		• Membrane Surface Receptor • Need 2nd Messengers (except → Insulin) ↳ b/c Insulin Receptor itself has Tyrosine kinase activity.
• Mech^n of Action ⇒ Synthesis of New proteins (enzyme)		– Act by Modifying Action of Pre-existing enzyme
• Longer half Life		• Shorter half Life

Total Hormone = Bound hormone + Free hormone



[Activity (Responsible for Activity as well as for One feedback

* Liver Induces ⇒ ↑ Hepatic output of Proteins

- Estrogen
- Barbiturates
- opioids
- Major Tranquilizers

⇓

↑ Bound hormones ; & ↓ free hormone (Transient change)

⇓

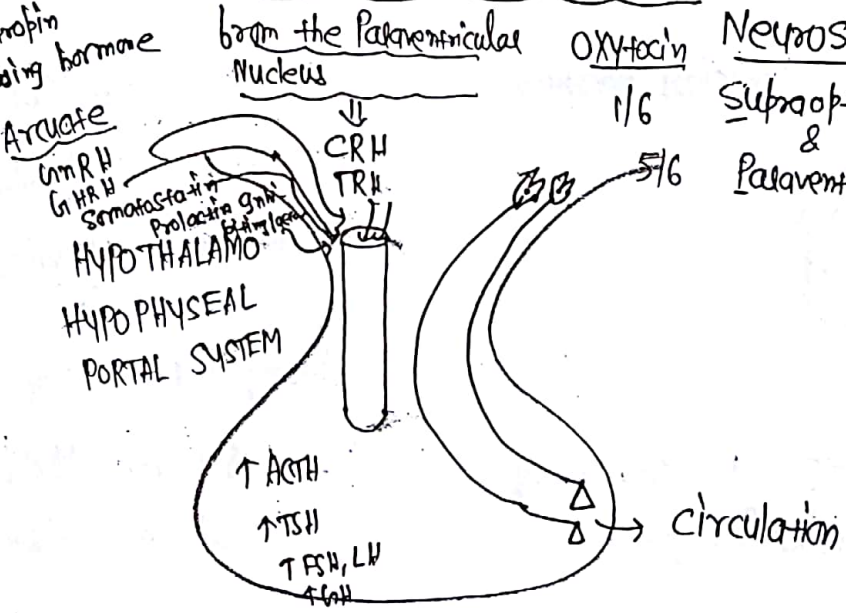
↑ total hormones ; ↑ Bound hormone ; Free hormones (N)

Q. In a heroin Addict

↳ Total thyroid ⇒ ↑
Bound thyroid ⇒ ↑
Free T_3, T_4 ⇒ (N)

HYPOTHALAMIC PITUITARY AXIS

CRH = corticotropin Releasing hormone



Neurosecretion

Oxytocin		ADH
1/6	Supraoptic	5/6
5/6	& Paraventricular	1/6

HYPOTHALAMUS		ANTERIOR PITUITARY
CRH	⊕ →	ACTH
TRH	⊕ →	TSH
GnRH	⊕ →	LH, FSH

HYPOTHALAMUS → ANT. PITUITARY

GHRH ⊕ → GH

Somatostatin ⊖ → GH

Prolactin inhibiting factor (Dopamine) ⊕⊖ → Prolactin

"STALK Effect" ⇒ ↑es in Prolactin

↳ Thrombus in Hypothalamo Hypophyseal Portal system

* All Hypothalamic hormone are secreted in Pulsatile fashion ⇒ except ⇒ TRH.

* Low frequency Pulse of GnRH ⟶ ↑ FSH.
  High frequency Pulse of GnRH ⟶ ↑ LH

QQ Continous infusion of GnRH

↳ ↓ FSH ; ↓ LH (down Regulation of GnRH happen in continous infusion)

* Pulsatile secretion prevents down Regulation of GnRH Receptor in Anterior Pituitary

ANTERIOR PITUITARY

Acidophils ⇒ Somato-tropes ⇒ GH
- Maxim in No.
- Lacto-tropes ⇒ Prolactin

Basophils ⇒ Cortico-tropes ⇒ ACTH
- Gonado-tropes ⇒ FSH, LH
- Thyro-tropes ⇒ TSH
  - Minm in No.

GROWTH HORMONE

Stimuli which tes GH ⇒
- Fasting ;
- Starvation ;
- Hypoglycemia ; – Most potent stimulation
- Stress hormone
- Emotion
- Sleep (NREM III, IV)
  - [In REM sleep ⇒ ↓ Growth hormone]
- Arginine ; Leucine
- Exercise
- Ghrelin

Stress Hormone
- ↑ Energy Substrates

eg ⇒
- Catecholamines
- Growth hormones
- Glucocorticoids
- Glucagon
- ADH
- Thyroid ±

ACTIONS OF GROWTH HORMONE

DIRECT ACTIONS

- ↑ Blood glucose level (Anti-insulin action)
- ↑ Free Fatty acids (Lipolysis)
- ↑ Protein synthesis
- Na^+; K^+; Ca^{2+}; Phosphorus Retention

INDIRECT ACTIONS

GH → Liver → IGF-1 (Source → Liver) (Somatomedin-C)

- ↓ Blood glucose
- Lipogenesis
- Protein synthesis
- Chondrogenesis (Growth of epiphyseal plate control)

IGF-1 → Responsible for "Growth Spurt @ Puberty"

IGF-1 Secretion is Maxm in ⇒ Adolescence > Children > Adults > Elde

Growth hormone → ↑IGF-1 Receptor on Cartilage

IGF-1 Synergistic Action ≅ Growth hormone

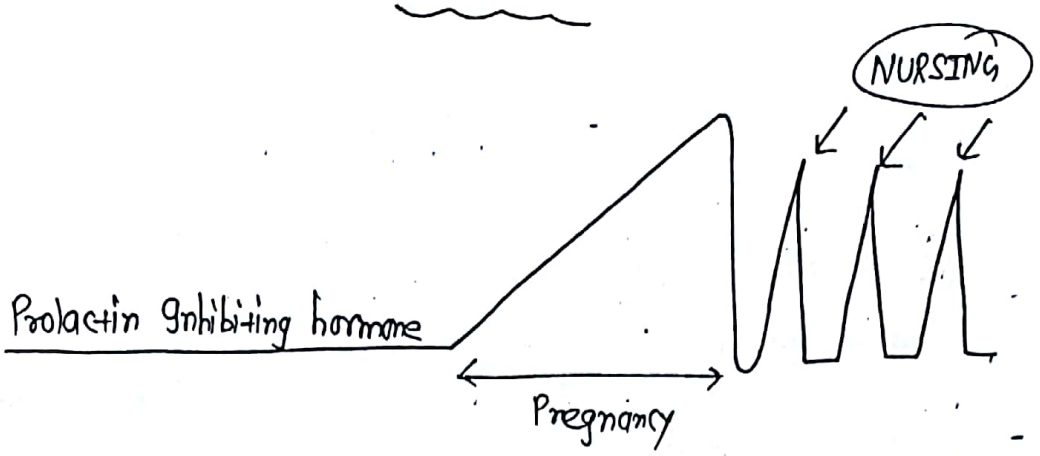
Direct Action (Independent Action)

→ CARTILAGE

⇒ Estrogen causes fusion of growth plate.

* only IGF-1 in short stature child

PROLACTIN



Stimuli for Prolactin :- New PET SHOP

New ⇒ Nursing
P ⇒ Pregnancy
E ⇒ Estrogen
T ⇒ TRH (Hypothyroidism → Galactorrhea)
S ⇒ Stress
Sternous exercise
Sleep (NREM)
S ⇒ Sexual Intercourse
H ⇒ Hypothyroidism
O ⇒ Opiates
P ⇒ Phenothiazines

Stimulation Test ⇒ TRH Stimulation test ⇒ TSH, PRL
GnRH " ⇒ FSH; LH
Insulin Infusion test ⇒ GH; ACTH

POSTERIOR PITUTARY

ADH

* Stimuli which Tes ADH ⇒ ① ↑ Plasma Osmolality; (Tes of 5 mosm) ↑ Most potent stimulus
② ↓ Blood volume (10-15%)
③ Stress;
④ Emotions;
⑤ Pain;
⑥ Trauma;
⑦ Surgery;
⑧ Nausea;
⑨ Vomiting;
⑩ Exercise;
⑪ Prolonged standing;
⑫ Clofibrate; carbamezepine
⑬ Angiotensin II

* Stimuli which Ves ADH ⇒ ① ↓ Plasma Osmolality
② ↑ Blood volume
③ Alcohol
④ Weightlessness

* Receptors for ADH ⇒
- V_1 | V_1A Receptors
- V_2 Receptors
- V_3 | V_1B Receptors

Secondry Messangers

$V_1 | V_{1A}$ — GPCR — IP_3 & Ca^{2+} ⇒ Vascular Smoot Muscle → Vasospasm
Liver → Glycogenolysis
Area Prostrema → ↓ Cardiacoutput.

V_2 — GPCR — CAMP ⇒ Collecting duct ⇒ ↑ Insertion of Ak-2 on Luminal Membrane

$V_3 | V_{1B}$ — IP_3 & Ca^{2+} ⇒ Ant. Pituitary ⇒ ↑ ACTH secretion

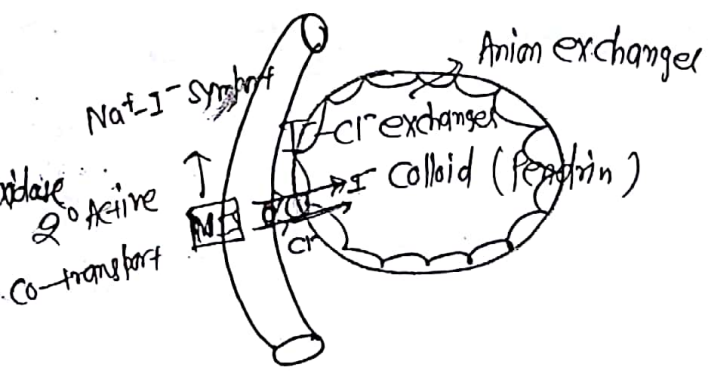
THYROID HORMONES

Hypothalamus → TRH
TRH → (+) TSH
TSH → (+) T_4, T_3
T_4, T_3 → (−) TRH
T_4, T_3 → (−) TSH

Steps in Synthesis of Thyroid hormone :- ① IODIDE TRAPPING :-
In Thyroid cells

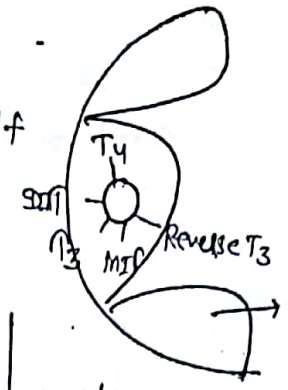
In Colloid :-

- oxidation of
  $I^- \xrightarrow{TPO} I_2$
  Enzyme: Thyroid Peroxidase (TPO)
- Iodination of Tyrosine
  - MIT — TPO
  - DIT — TPO
- Coupling RXn
  DIT + DIT → T_4 — TPO
  MIT + DIT → T_3 — TPO



- Storage :-

When gland Stimulated
↳ Endocytosis of part of colloid



- Secretion of ⇒ T_4
T_3
← Reverse T_3

In decreasing Conc.

In traces Amount

Thyroid cells itself ⇓ have Microsomal deiodinase ⇓ Deiodinates the MIT, DIT ↳ Iodine is Recycled

* If Microsomal deiodinase deficiency
↳ Hypo-thyroidism symptom ⊕
↳ MIT, DIT ⊕ In Urine & plasma

	T_4	T_3
Secretion by thyroid gland ⇒	↑ (More than T_3)	
Binding ē ⇒ Protein i) TBG ii) Albumin iii) Transthyretin	99.98% T_4 is Maximally bound ē TBG	99.8% T_3 is Maximally bound ē Albumin
Binding ē Receptors		↑ (binds More avidly ē Receptors)
Half-life	Longer than T_3 (6 days)	1 days

RT_3 ← 5-Delodinase — T_4 — 5'-Delodinase → T_3

RT_3	T_4	T_3
3, 3', 5'	3, 5, 3', 5'	3, 5, 3'
Tri Iodo thyronine	Tetra Iodo thyronine	Tri Iodo thyronine

Reverse T_3

Q. RT_3 in circulation — Main Source

(a) Secretion

(b) ~~Peripheral~~ conversion of $T_4 \rightarrow RT_3$

Condⁿ in which $RT_3 > T_3$ (Advantage) ↳ Conserves calories

- Starvation
- Prolonged illness
- Chronic kidney disease
- Febrile Illness
- Burns
- "Se" deficiency
- Drugs which Inhibit Delodinase

* Action of Thyroid hormone :⇒

① ↑ O_2 consumption { ↑es BMR, ↑es body temp. ; Loss of body weight }

Increase O2 consumption (Increase BMR, Increase Body Temp. ; Loss of body weight)

⇒ except ⇒ except

- Pituitary ;
- Spleen ;
- Lymph Node ;
- Ovaries ;
- Testis.

(2) Hypothyroid ⇒ Carotenemia (+)
Hypothyroid — Carotenemia +

b/c; Carotene → Thyroid → Vitamin A
Carotene — Thyroid — Vitamin A

(3) Hypothyroid → ↑ Serum cholesterol
Hypothyroid — increase serum cholesterol

b/c; Thyroid → ↑ No. of LDL Receptor
Thyroid — Increase of LDL receptor

↳ So, ↓ Serum cholesterol
So, decrease serim cholesterol

(4) Protein Metabolism → Protein Anabolic effect; but in Large dose Protein catabolic effect.

* TR_α; TR_{α_2}; TR_β; Receptors are widely distributed; TR_{β_2} is found only in the brain.

ADRENALS **

* Layers of Adrenal Cortex :⇒

		Hormone Secretion **
Zona glomerulosa	→	Aldosterone (Mineralocorticoids)
Zona Fasciculata	→	Glucocorticoids (cortisol; cortisosterone); & Some amounts of Androgen
Zona Reticularis	→	Sex steroids (Androgens); & Some amounts of Glucocorticoids

* Hormone Secreted by Adrenal Medulla :⇒ Epinephrine, Norepinephrine
(Epinephrine > Norepinephrine)
(90:1)

* After Hypophysectomy
↳ Zona glomerulosa will be intact (RAAS); while
Zona Fasciculata, Zona Reticularis → Atrophied.

* Comprises 285 A.A Residues & serve as precursor of many proteins.

← POMC (Pro-Opio Melano cortin) → Synthesize in Pituitary,

cleaved

- ACTH (Adrenocorticotropic Hormone)
- β-Lipotropin
  - α-MSH
  - β-MSH
- β-endorphin

- Cushings ⇒ Hyperpigmentation
  - ↳ ↑↑ ACTH (S. ACTH itself has Melanocyte Stimulating hormonal activity).

* Deficiency	Aldosterone	Glucocorticoids	Androgens
• 21 β hydroxylase (95% of CAH) No Mineralocorticoid Activity	↓	↓	↑↑ (Virilizing symptoms)
• 11 β hydroxylase (5% of CAH)	↓	↓	↑↑

• Mineralocorticoid Activity

How to differentiate ⇒ ↑B.P. ↓K+] Seen in 11β hydroxylase deficiency ⇒ Hypo Aldosteronic Hypertension

↓

* 11 Deoxy corticosterone ↑↑

↓ 11β hydroxylase (XX)

Corticosterone

↓

Aldosterone Synthase

↓

Aldosterone (X)

(Excess) 11-Deoxy corticosterone has Mineralocorticoids Activity

↓↓

↑ Na+

↑ B.P.

↓ K+

* Deficiency	Aldosterone	Glucocorticoids	Androgens
• 17,20 Lyase deficiency	↑	↓	↓
** 17,α hydroxylase deficiency	↑	↓	↓

* GLUCO-CORTICOIDS ACTION :⇒

Gluco-corticoids ↓es ⇒ B ⇒ Basophils
E ⇒ Eosinophils
L ⇒ Lymphocytes
→ By promoting their Migration from blood into tissues

Gluco-corticoids ↑es ⇒ Neutrophils
Monocyte
RBC
Platelets

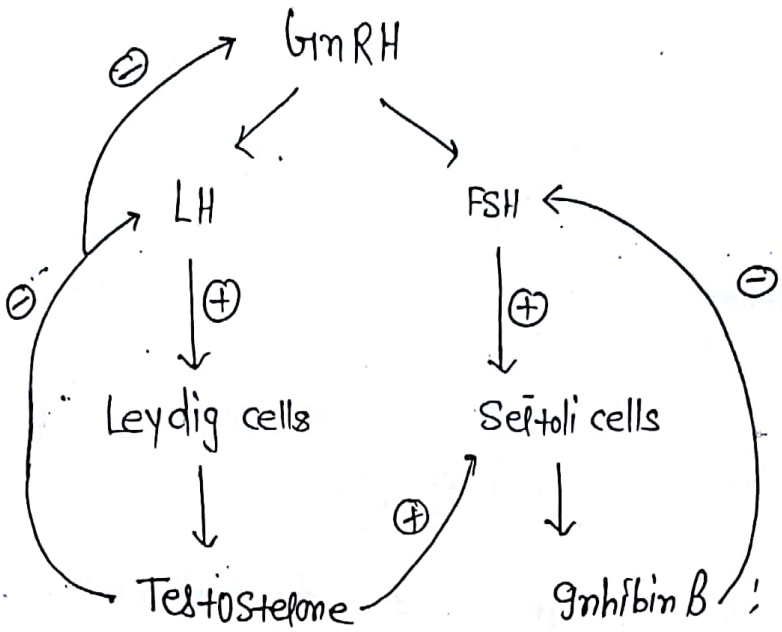
Permissive Action ⇒ It enhances the action of other hormone.

on Glucagon → • Glycogenolysis in Liver ; but Not in Muscle in general ; but when cortisol is ⊕n+ Glucagon, do glycogenolysis in Muscle too.
• Lipolysis

on catecholamine (Adrenal Medulla hormone) → Glycogenolysis;
Lipolysis;
Vasoconstriction;
Bronchodilation.

* Secretion of gluco corticoid is Regulated by ⇒ Anterior Pituitary gland through ACTH (corticotropin)

* MALE REPRODUCTIVE - HORMONE

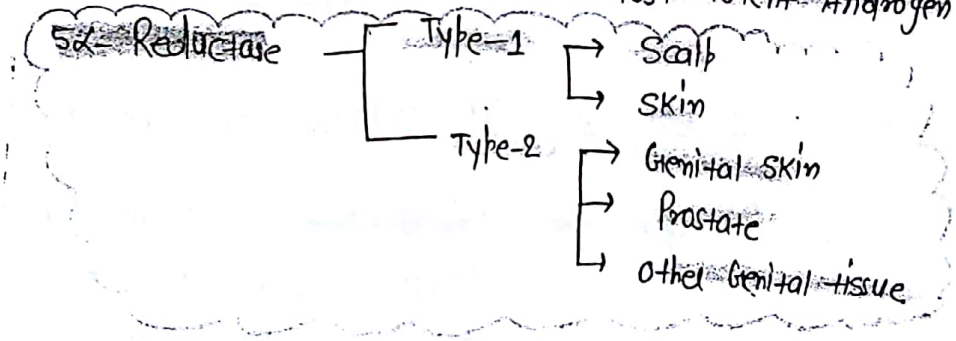


- DHT
- DHEA (dehydro-epiandrosterone)
- Androstendione

Androgen binding Protein (ABP);
Mullerian Inhibiting Substance.

* Testosterone —5α-Reductase→ Dihydro-testosterone (DHT)

Most Potent Androgen



* Action of different Androgens ⇒

	Testosterone	DHT
Fetal Life ⇒	Development of Male type of Internal Genitalia	• Male type of external Genitalia
	• Male type of Brain	

Testosterone

DHT

Post Pubelty ⇒ Spermatogenesis;
Gonadotropin Regulation;
Tes Muscle Mass;
Development of sexual drive

2° sexual characters
Prostate growth

QQ. Before Pubelty castration done ?:-
~~(a) Tall~~; (b) Dwarf; (c) Normal
↳ d/t Lack of Estrogen (No Physeal fusion).

* Function of Sertoli cells ⇒ Supportive cells;
↳ as blood testis barrier;
↳ secrete Androgen Binding Protein;
↳ also secrete Inhibin 'B'; MIS (Mullerian Inhibiting substance)
↳ contains Aromatase

Testosterone —AROMATASE→ Estrogen

* SPERMATOGENESIS ⇒

74 days

SPERMATOGONIA
↓
1° SPERMATOCYTE
↓
2° SPERMATOCYTE
↓
SPERMATIDS
↓ SPERMIOGENESIS
MATURE SPERMS (SPERMATOZOA)

Androgen Independent

? ⇒ FSH / Androgen-dependent
⇓
Testosterone Acting on sertoli cells

V.V.G. ☆

CLASSIFICATION OF HORMONE

GROUP I :- Hormones acting on Intracellular Receptor;

GROUP II :- Hormones acting on Membrane Receptor;

IIA :- Hormones acting through cAMP;

IIB :- Hormones acting through cGMP;

IIC :- " " " IP_3 - DAG Ca^{2+} system

IID :- " " " kinases (Tyrosine kinase ; JAK-STAT kinase)

* TYPE OF RECEPTORS

1) G-protein coupled Receptor (GPCR) :- Mech^m of Action :-

(a) Via Adenylyl cyclase (AC) :- Activation of Adenylyl cyclase Results in Tes synthesis & Intracellular accumulation of cAMP.

example ⇒ CRH :- Corticotropin Releasing Hormone

LH^{φ}, FSH^{φ};

TSH ;

ACTH ; (corticotropin$^{\varphi}$)

ADH ;

Vasopressin (V_2 Receptor)

Para-thormone ;

Catecholamines (β_2^{φ}, α_2) eg ⇒ Adrenaline ;

Glucagon$^{\varphi}$

hCG

calcitonin ;

Somatostatin ;

Ach (M_2) ;

Dopamine$^{\varphi\varphi}$ (D_1, D_2) ;

Angiotensin II (epithelial cells) ;

Gastrin : Histamine (H_2^{φ})

(b) Phospholipase IP_3 - DAG System :⇒

IP_3 → Mobilizes Ca^{2+} from Intracellular organelles → ↑ cytosolic Ca^{2+}

Ca^{2+} acts as "3rd Messanger" @ here ← "DAG" enhances protein kinase "C" activation by Ca^{+2}

* Protein kinase "C" = Phosphorylates various Intracellular proteins (Threonine, Serine or Tyrosine Residue).

Protein kinase "C" = phosphorylates various intracellular proteins

eg ⇒ GHRH (Growth hormone Releasing hormone); TRH; GnRH; ADH/ Vasopressin (V_1 Receptor); Oxytocin; Cholecystokinin; PDGF; Gastrin; Catecholamines; Angiotensin II (Vascular Smooth Muscle); Substance-P; Histamine (H_1); Muscarinic (M_1, M_3).

(c) Channel Regulation :⇒ eg ⇒ i) ↑ Ca^{+2} - β_1 - Adrenergic; ii) ↓ Ca^{+2} - Dopamine D_2; $GABA_B$; iii) ↑ K^+ - Adrenergic - α_2; Muscarinic M_2; Dopamine D_2; $GABA_B$.

2. Receptors ≡ Intrinsic Ion channels - Fastest acting Receptors; - Cell Surface Receptor/ Ligand gated Ion - channel (for Na^+; K^+; Ca^{2+}; Cl^-;

eg ⇒ Nicotinic cholinergic, $GABA_A$; $5HT_3$ (all other 5HT Receptor are GPCR).

3. Enzyme Linked Receptor - (a) Intrinsic enzyme (R) (Tyrosine kinase (R) :⇒ Insulin; Epidermal growth factor (EGF), PDGF; FGF.

(b) JAK- STAT KINASE BINDING (R) ⇒ eg ⇒ Growth hormone; Prolactin

(c) Guanylyl cyclase ⇒ Result in Intracellular accumulation of cGMP

eg ⇒ Atrial Natriuretic peptide & Nitric oxide

4. Receptors Regulating Gene expression (Transcription factors) :→
Slowest Acting.

a) Cytoplasmic Receptors → Glucocorticoids; Mineralocorticoids; Androgens; Progestins.

b) Nucleual Receptors → Estrogen, T_3, T_4, Retinoic acid; Vit D

SECOND MESSENGERS

- Molecules that Relay signals from the Membrane Receptors to Target Molecules inside the cells.

eg ⇒ cAMP; cGMP; Phosphatidylinositol; Diacylglycerol (DAG); IP_3; Ca^{2+}; NO; CO; H_2S.

NEET PG ★ So, NO acts as both 1° Messenger, through cGMP; as well as secondary Messenger

So, No acts as both 1' messenger , through cGMP; as well as secondary messenger

CNS

* Receptor → Biological transducer

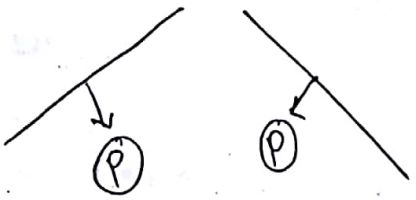
- Adequate stimulus ⇒ Stimulus to which a Receptor is Most Sensitive or to which a Receptor Respond @ Low energy Level

* Sensory coding → Receptor codes for 4 attribute of stimulus →
  i) Site / Location of stimulus ;
  ii) Modality (fine | crude) ;
  iii) Intensity ;
  iv) Duration .

* ADAPTATION → Stimulus ⊕ ; but Response ↓es over a Period of time

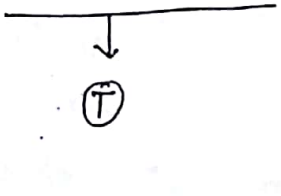
PHASIC Ⓡ
aka → "Rapidly Adapting Ⓡ"
- usually encapsulated Nerve endings
- Can detect Rate of change of Stimulus

TONIC Ⓡ
aka → "Slowly Adapting Ⓡ"
- Expanded or free Ⓝ Nerve Ending
- Can detect steady stimulus



Steady stimulus

Phasic stimulus



Tonic stimulus

PHASIC ® — "Aβ"

eg :→ PACINIAN CORPUSCLES :→

- Fnt in Joint capsules (128 Hz) & Deep in Muscle
  Fnt in Joint capsules (128 Hz) & Deep in muscles
- Very Rapidly Adapting Touch Reception.
  Very rapidly adapting touch receptor
- Specific to Fast Vibration (upto 800 cycles/sec)
  Specific to fast vibration
  upto 800 cycles / sec
- Deep Pressure (POKING)
  Deep pressure (Poking

"Aβ"

MEISSNER'S CORPUSCLES :→
Meissner's corpiscles

- Located at No hairy parts of skin
  Located at No hairy parts of skin
- Finger tips (++)
  Fingers tips ++
- Slow vibration upto 80 cycle/sec
  Slow vibration upto 80 cycle/sec
- Texture (Rough/Smooth)
  Texture (Rough/ smooth
- Topognosis (Topography of any Area, Localize by fingers)
  Topognosis
  topography of any area: localize by fingers
- BRAILLE (Writing system used by People, who are blind or have Low vision)
  BRAILLE (writing system used by people who all blind or have low vision

HAIR END's ORGAN :→

- Detect light Movement on the skin
  Detect light movement on the skin

TONIC ®

"Aβ"

eg :→ MERKEL's DISC :→

- Fine well Localized touch
- Location ⇒ At Finger tips.
- Texture.

RUFFINI's ENDING :→

- Fine & well Localized touch
- Prolonged Pressure
- Receptors for Sense of Position

C — MECHANO RECEPTORS :→

- Crude touch (Diffuse)
- Pressure.

JOINT CAPSULE RECEPTORS :→

- Muscle spindles
- Golgi tendon organs

} JOINT's POSITION SENSE (PROPRIOCEPTION).

BARORECEPTORS :→

- Adaptation time ⇒ 2 days

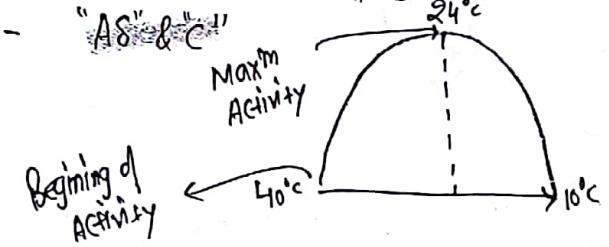
THERMORECEPTORS :→

Detection of skin temperature

S

COLD

- More Numerous
  More numerous
- More cold Sensitive Spots
  More cold-sensitive spot
- "Aδ" & "C"



WARMTH
warmth

- Less in No.
  less is no.
- "C"
- Can detect temp. upto 30-46°c (>46°c ⇒ Tissue damage, Pain ® will stimulate)
  can detect temp. upto 30-46 'c (>46'c => Tissue damage pain R will stimulate

30- 40 'C

30 - 40°C → Warm Receptor Activity is More

Warm - receptor activity is more

Cold receptor activity is more

Cold Receptor Activity is More

Overlap b/w Cold & Warmth Receptors

overlap b/w cold & warmth receptors

Other eg of Tonic ® ⇒ - NOCICEPTORS

- Free Nerve endings for Pain → Mechanical
  → Thermal
  → Chemical
  → Polymodal

- very Poorly Adapting OR Not at all.

- CHEMO RECEPTORS

Never Adapt (b/c they give information about potentially life threatening situation)

eg ⇒ Taste buds; OSmo Receptors ; Olfactory ®: glucoReceptors.

QQ Don't Adapt at all

i) Chemo ®; ii) Noci ®

qmp

TRANSIENT RECEPTOR POTENTIAL (TRP) CHANNELS

→ These all a family of excitatory channels.

Family of excitatory channels

→ Sub family

① VANILLOID ® → Noxious Heat (Painful heat)

H+

capsaicin (Vanillin group of compounds)

Capsicin (Vanillin group of compounds

TRPV1 ⇒ H+ capsaicin

H+ capsaicin

TRPV3 ⇒ detect temp b/w 35-39°C

Detect temp b/w - 35-39'c

TRPV4 ⇒ detect temp upto 34°C

Detect temp upto 34'C

② Acid sensing ion channels → detection of H^+

H^+ → TRPV1, ASIC (Acid sensing ion channels)

③ ANKYRIN ® → Kla "TRPA1"
- Pain

④ PURINERGIC ® → Kla "P_{2X}, P_{2Y}"
- for Pain

Pain → TRPA1; Pain —ATP→ P_{2X}, P_{2Y}

⑤ MENTHOL ® → Kla "$TRPN_3$"
- for Moderate cold
- also Kla "CMR-I" Receptors
  - cold & Menthol Sensitive Receptor-1

* TRP channels → Temperature → Noxious heat, Moderate cold
→ H^+
→ Capsaicin
→ Pain
→ Taste

* Mechano-tropic ®

GPCR (G-Protein coupled Receptor) → Sweet, Bitter, Umami (eg ⇒ Fish; Meat; Mushroom)

* Taste Receptors
  - IONOTROPIC
    - Salt
    - Sour
  - MECHANO TROPIC GPCR
    - Sweet
    - Bitter
    - Umami → Glutamate Receptor
    - TRP Channel

NEUROTRANSMITTER

SMALL MOLECULE RAPIDLY ACTING NEUROTRANSMITTER

I → Ach

II → Amines
- Nor epinephrine
- epinephrine
- Dopamine
- Seloronin
- Histamine

III → Amino Acids
- Glutamate ; Aspartate
- Glycine ; GABA

IV → Gas
- Nitric oxide (NO)

LARGE MOLECULE SLOWLY ACTING NEUROTRANSMITTER

- Pituitary Peptides
  - ADH
  - ACTH
- Hypothalamic Peptides
  - GnRH
  - CRH
- Gut Peptides
  - cholecystokinin (CCK)

* LAW OF SENSORY PHYSIOLOGY :⇒

I. Bell - Magendie Law :⇒

(Posterior) Dorsal Horn ⟶ Sensory

(Anterior) Ventral Horn ⟶ Motor

* DRG (Dorsal Root Ganglion) :⇒ Contains the cell body (Soma) of Sensory Neuron coming from Receptors.

II. Muller's Doctrine of Specific Nerve Energy :⇒

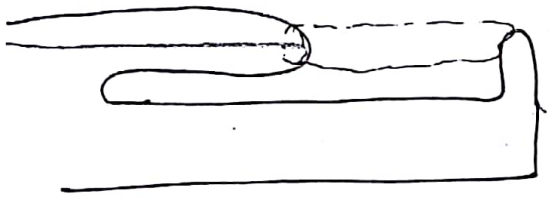
Muller's Doctrine of specific nerve energy

- Receptor
- Pathway
- Area of Brain Stimulated

} ⇒ Specific for Each Sensation.

III. Law of Projection :⇒ "PHANTOM LIMB"

- if a Nerve Pathway is stimulated Anywhere in its course; the Sensation appear arising from site of Receptor.



⇒ d/t Cortical Plasticity

Thalamus & cortex → Have ability to form New Synapses.

IV. Law for Intensity Discrimination of a Stimulus ⇒

Ⓐ WEBER FECHNER LAW ⇒ Sensation felt α Log (Intensity of Stimulus)

Sensation felt 2 log (Intensity of stimulus)

$\Rightarrow$ $S = K \log I$

(B) STEVEN'S POWER LAW :$\Rightarrow$ Sensation felt $\propto I^a$

$S = KI^a$ (K, a $\Rightarrow$ constant).

S = KI a

TYPES OF INHIBITION

I. Direct / Post-synaptic Inhibition :$\Rightarrow$

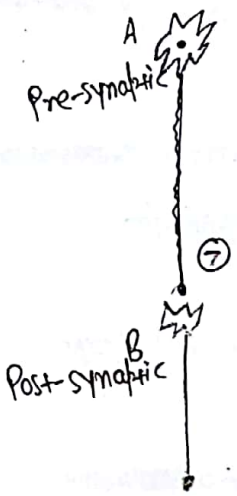
Neuron (A) $\longrightarrow$ Releases Inhibitory Neurotransmitter (Glycine)

$\downarrow$

Produce IPSP (Inhibitory Post-synaptic potentials)

$\downarrow$

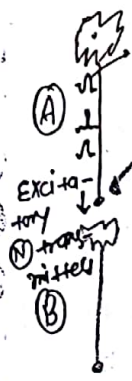
Inhibit Neuron (B)



* "Strychinine" can antagonize this type of Inhibition

II. Pre-synaptic / Indirect Inhibition :$\Rightarrow$

Neuron (A) $\longrightarrow$ (+) Neuron (B)



Neuron (C) $\rightarrow$ Inhibitory Neuron

↳ Forms Axo-Axonal Synapse c pre-synaptic Neuron (Neuron A)

GABA Release

(Hyperpolarization)

$\Downarrow$

$\downarrow$ (N) Excitatory Neurotransmitter

* GABA Receptor on Pre-Synaptic Membrane

GONOTROPIC RECEPTOR

METALLOTROPIC RECEPTOR

$GABA_A$ $GABA_C$

$GABA_B$

they ↑es Cl⁻ conduction

they ↑ K⁺ conductance

Hyperpolarization of Pre-Synaptic Membrane (Neuron-A)

↓

↓es the Secretion of excitatory Neuro-transmitter

(So; Indirect Inhibition)

Advantage ⇒ Prevent Excessive Excitation of LMN

↓

Fine & Well controlled Movement

Fine and well controlled movement

Lateral corticospinal tract (Pyramidal Tract)

Glutamate

GABA

Secretion; Not completly stopped; only ↓es.

Spinal Motor Neuron / Anterior Horn cell / Ax Motor Neuron / LMN

* Tetanus toxin

↳ Inhibit Secretion of GABA;
Inhibit secretion of Glycine;
Inhibit Synapto-brevin

↓

excitation

↓

↑↑ Glutamate Release

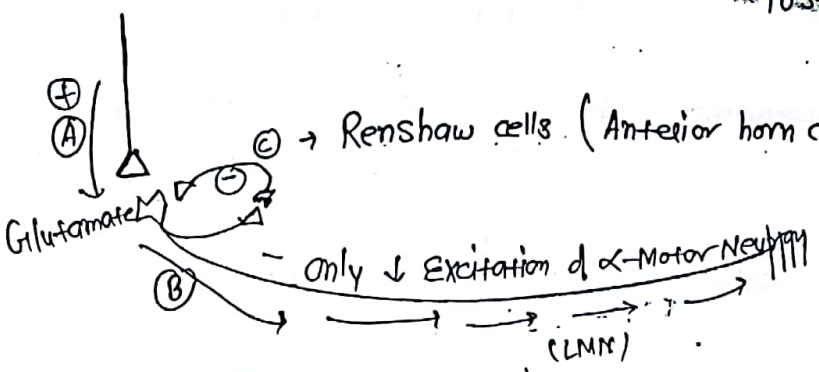
↓

Spastic Paralysis

d/t → Hyperpolaris'n of Pre-synap.

III. FEEDBACK INHIBITION (RENSHAW CELL INHIBITION) ⇒

↳ Postsynaptic type of inhibition



UMN → ⊕ LMN → Stimulate Muscle cells; but some impulse goes to Renshaw cell; which will inhibit UMN

↳ "Feedback inhibition"

Advantage ⇒ Precise well control; Well Regulated Movement.
Prevent excessive excitement of LMN.

IV. FEED FORWARD INHIBITION ⇒

A neuron is connected through two pathway

A Neuron is connected through two pathways, one excitatory & one inhibitory

One: Excitatory and one Inhibitory

Neuron A → ⊕ Neuron B

↓ ⊖

Neuron C

- typically seen in "cerebellum"

Cerebellum

Cerebellum

↓

Granule cells

↓ ⊕

Basket cells

↓ ⊖

Purkinje cells

Granule cells

↓ ⊕

Stellate cell

↓ ⊖

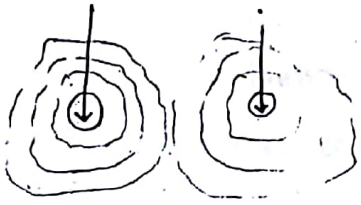
Purkinje cells

V. LATERAL INHIBITION ⇒ 2 Point Discrimination,

* if 2 points Inhibit Simultaneously
↓
Inhibit Surrounding ®

* Min^m Separable → At finger tips (2mm)
So; Braille → 2-5mm

- Max^m Separable → At back (65mm)



ASCENDING TRACTS (Sensory System)

Posterior Column
- Fine Touch
- vibration
- consious Proprioception
- Localization
- 2 point discrimination
- Stereognosis
- Ability to judge different degree of Pressure

Spino-thalmic Tract
- Lateral Spino-thalmic Tract (STT)
  - Pain
  - Temperature
- Anterior Spino-thalmic Tract (STT)
  - Crude Touch
  - Itch
  - Tickle
  - Sexual Sensation
  - detection of Pressure (Barognosis)

Spino-cerebellar Tract
- Unconsious Proprioception
  - Dorsal → Uncrossed
  - ventral → crossed

Q Posterior column lesion; What will happen to Barognosis ?? (detection of "Pressure") [done by anterior STT]

~~Pain~~
~~Temp~~

Graphesthesia (Localize the touch) is absent.

~~Proprioception is carried to Spinal cord by Aα Sensory Neuron, while other Sensation (Fine touch, Kinesthesia) are carried out by Aβ (type II) Sensory Neurons.~~

POSTERIOR COLUMN

3,1,2
Sensory cortex

3rd order sensory Neuron

THALAMUS

VPL Nucleus OR Ventrobasal complex

Ventero-Postero Lateral

Medial Leminiscus (Fibers of 2nd order sensory Neuron)

2nd order sensory Neuron

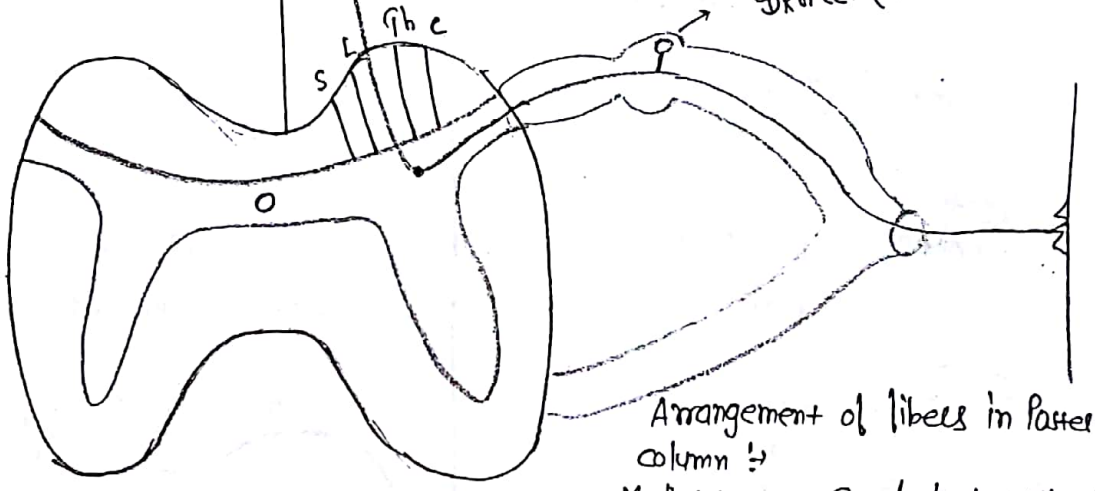
Medulla (GoLL)

N. Gracilis → Sacral; Lumbar fiber

N. cuneatus → Thoracic; cervical fiber

(BURDACH)

1st order sensory Neuron
DRG cell (Pseudounipolar)



Arrangement of fibers in Posterior column :-

Medial Most ⇒ Sacral > Lumbar > Thoracic > Ce Co

Fasciculus gracilis Tract of (GoLL)

Fasciculus cuneatus

Sensory cortex ⇒
- Posterior central Gyrus ;
- Area 3,1,2
- Sensory Homunculus (Physical Representation of Human body ; Located c/in Brain)

⇓

Grotesque Figure of Penfield & Rasmussen

Largest cortical Representation ⇒ Face Including Lips

Smallest cortical Representation ⇒ Trunk & Back

CEREBRUM ⇒ 6 Histological Layers ⇒ I, II, III, (IV), V, VI

(IV) ← Bulk of Sensory Information.

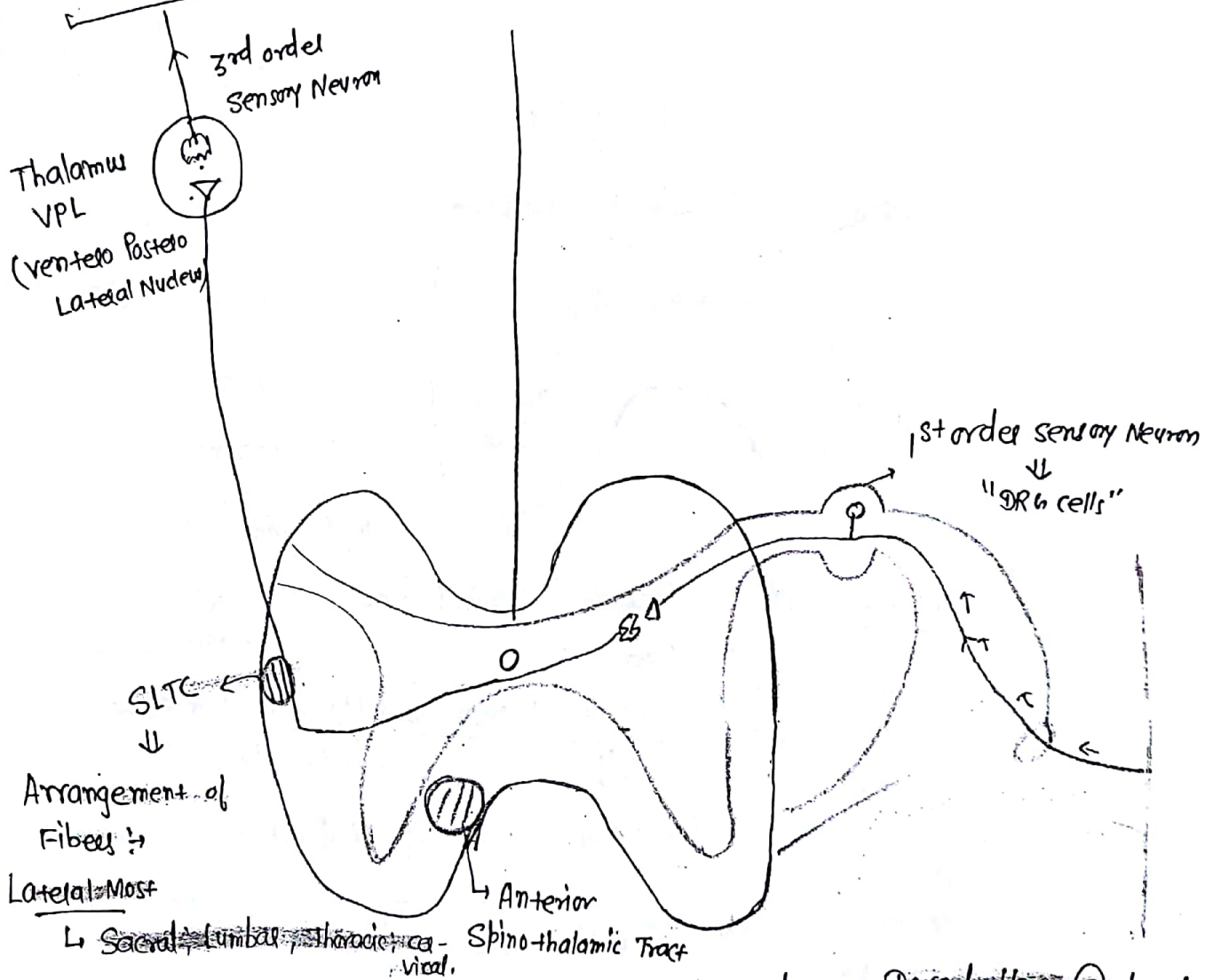
Tract Specific for Stereognosis ⇒ Fasciculus cuneatus

QQ. Stereognosis Lost in lesion of → ⓐ Fasciculus gracilis
⇓ ⓑ Fasciculus cuneatus
Ability to identify an object ⓒ Cortex.
by feeling it.

* Fasciculus gracilis ⇒ Fibers from Lower part of body

Fasciculus cuneatus ⇒ Fibers from upper part of body

SPINOTHALAMIC TRACT



1st synapse → Dorsal Horn @ Level of Entry into Spinal cord or 1-2 Level above

* FAST PAIN PATHWAY / EPICRITIC PAIN
↳ evolved Later

- Sharp pain; well localized
- Pricking Sensation
  Stabbing Sensation
-
- "Good Pain"
  ⇓
  (Responsible for Flexor withdrawl Reflex.)
- Carried by → "A_δ"
- Felt $\bar{c}$ in 0.1 sec
- Velocity → 12-30 m/sec
- Stimulus → Mechanical / thermal
- Neurotransmitter → Glutamate
- Synapse - I / V (Lamina)

SLOW PAIN PATHWAY / PROTOPATHIC PAIN
↳ earlier evolved

Dull Pain; diffuse Pain

- Aching Pain
  Burning Pain
  Throbbing Pain
  Nauseous Pain
  "Bad Pain"
  ⇓
  (Autonomic symptom a/w Slow Pain Pathway)

"C"

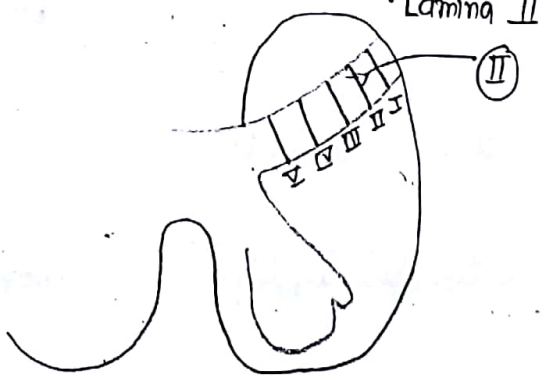
Felt after 1 sec

Velocity → 0-5 m/sec

Chemical

Substance-P

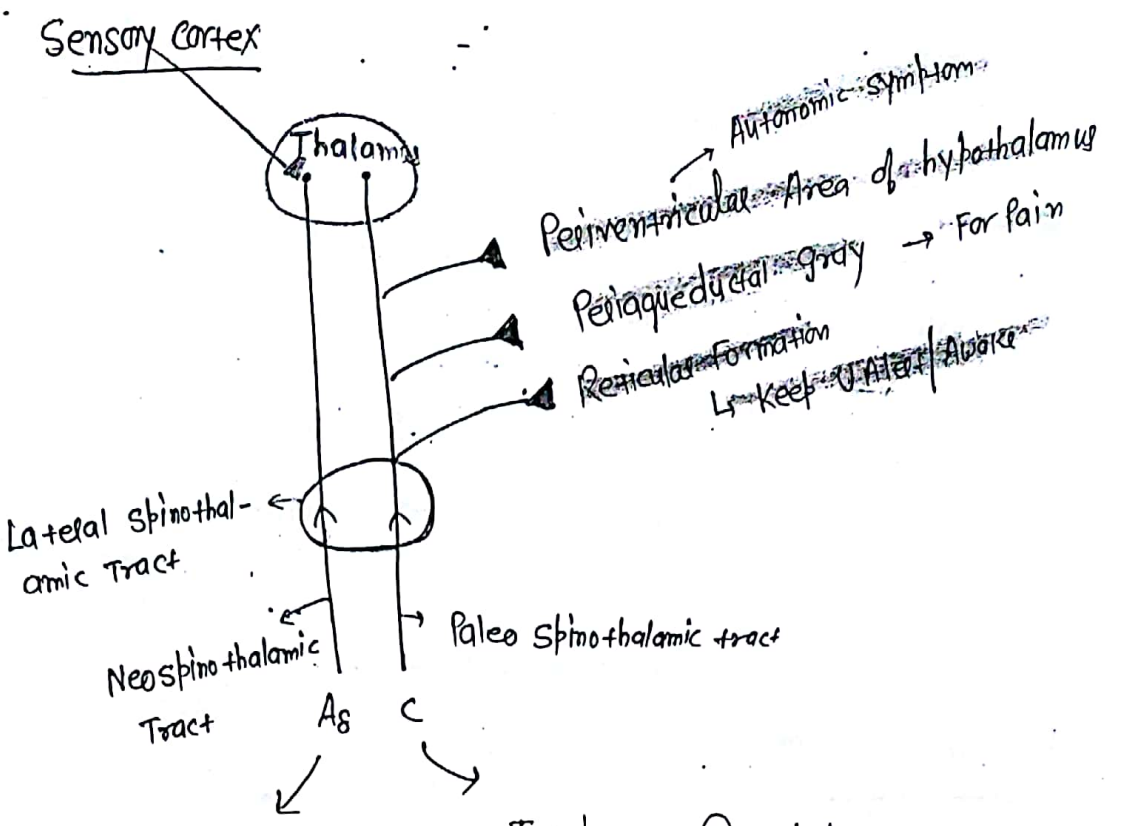
- Posterior Horn divided into 5 Laminae
  (Whole grey Matter → 9 Lamina)
- Lamina II → Substancia Gelatinosa of Rolando



A_δ Fibre → Klas "Neo-Spino-thalamic Tract".

C Fibre → Klas "Paleo-Spino-thalamic Tract" (Lateral Spino-thalamic Tract)

Both go to the thalamus → 3rd order sensory Neuron → S. Cortex.



- Terminates @ Sensory cortex
- No branching

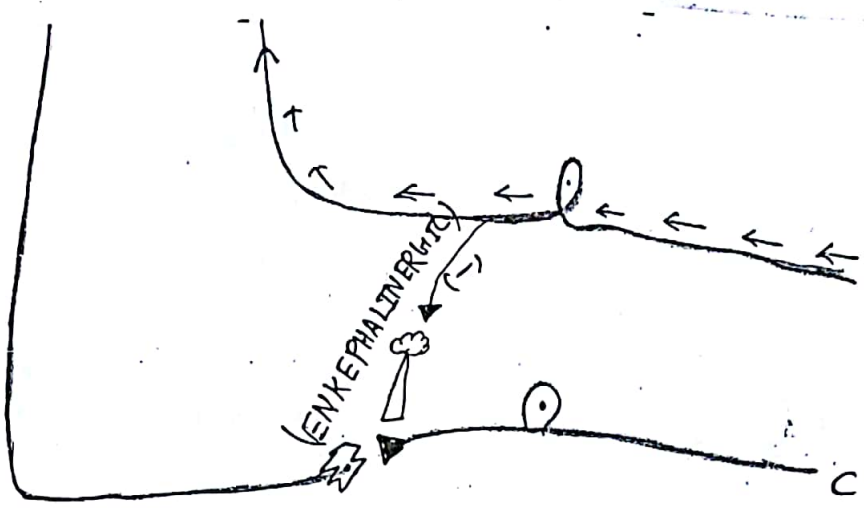
- Terminates @ Thalamus
- Gives branches (collaterals on the way)

• ENDOGENOUS ANALGESIA SYSTEM :⇒

1. Gate control theory of MELZAC & WALL :⇒

By Rubbing the Area → Large diameter Myelinated touch fibres excited

- Gives a Small collaterals → Synapse @ Inhibitory Neuron → Pre-Synaptic ⊖ of Pain Pathway.
- Aβ → they enter in Spinal cord & Ascends upward



(Aβ) on Rubbing ↓ Pain

C Pre-synaptic Inhibition of Pain pathway ⇓ ↓ Pain.

TENS → Trans-cutaneous Electrical Nerve Stimulation;

↳ based on Gate control theory of Melzac & wall;

↳ For Intractable Pain (cancer Pain) (Stimulate Aβ fiber) ⇓ By Transcutaneous Electro

2. DESCENDING PAIN INHIBITION PATHWAY ⇒

• It Starts from "Peri-aqueductal Gray (PAG)"

Slow Pain pathway ⊕→ PAG ⊕← cortex, ⊕← Hypothalamus, ⊕← Limbic system

they project to RAPHE MAGINUS NUCLEUS (In PONs)

↳ these all Serotonergic

↳ Means Serotonin Secreting Neurons.

Neurons descends down, Secret Serotonin ↓ Synapses E-enkephalinegic Neurons in dorsal horn of Spinal cord

Causes (Inhibit transmission of pain) by Pre & Post synaptic inhibition of pain pathway

Causes (Inhibition of transmission of Pain) by Pre & Post synaptic Inhibition of Pain Pathway.

De-cerebrate Rigidity

→ Severe extensor Rigidity

Neck
Upper Limb ⇒ Extended
Lower Limb

* Lesion @ Upper border of Pons

De-corticate Rigidity

→ Moderate Rigidity
Upper Limb → Flexion
Lower Limb → extension

* Lesion above Mid brain

* In Decerebration → Lesion Above the Pons ; Both cortex & Midbrain Lost ;

↳ cortico-Reticular fibres are destroyed

So; Inhibitory fibre for Medullary R.F lost ; only excitatory fibre to Pontine R.F. from collaterals fnt.

Which develop ⟶ TT tone @ extension
Severe (extensor Rigidity)

* In Decortication → Lesion Above Midbrain ; Mid brain give Some excitation (only cortex is gone)

- Some amount of Inhibitory fibres to Medullary Reticular fibre will be Intact
- excitatory fibre will be More ; but these will Moderate Ter of tone (Moderate extensor Rigidity)

THALAMUS

- It is a "Grand Sensory Relay Nuclei"

Sensory Relay Nuclei

Non-specific
- Midline
- Intra Laminar

Specific
- For Somatic Sensation
  - ↳ VentroPosterior Lateral
- For Visual Pathway
  - ↳ LGB
- For Auditory Pathway
  - ↳ MGB
- For Taste Pathway
  - ↳ VentroPosterior Medial
- For olfaction
  - ↳ Medio dorsal thalamic OR Dorso Medial

* Motor Nucleus of Thalamus — Ventro Anterior Nucleus
Ventro Lateral Nucleus

PAPEZ CIRCUIT — Involved in
- Memory
- Learning
- Emotion

↳ Interconnected closed circuit forms by various Nuclei of Limbic system.

↳ It starts from Hippocampus of Brain
↳ It convert Short term Memory → Long term Memory.

AIIB

Hippocampus → Mamillary body of Hypothalamus

Hippocampus

↓ Mamillo thalamic tract OR Tract of vicq d'Azyr.

Anterior Thalamic Nucleus

Anterior Thalamic Nucleus

↓

Pre-frontal cortex

↓

Basal Forebrain (Nucleus basalis of MEYNERT) ⇒ Destroy ↳ in Alzheimer disease

Nucleus basalis of Meynert

AMYGDALA (Window of the Limbic system) → high emotional content Memory.

Amygdala

Neo-cortex

NEO-CORTEX (For Storage)

AIIS ⇒ Every thalamic Nuclei except → Reticular Nuclei sends axon to different part of cortex.

REFLEXES

- Based on No. of synapses.

① Asynaptic Reflex ⇒ Axon Reflex

↳ It is a part of Triple Response (Blunt Injury) ** b/c of histamine > Axon Reflex

⇓

a) Red Reaction ⇒ b/c of Release of histamine,

b) Flare Response ⇒ b/c of Axon Reflex;

c) Wheal Response ⇒ d/t histamine & bradykinin

Axon Reflex ⇒ Blunt Injury over skin

↓

excite the Pain fibre

↓

Impulse goes to Spinal cord ; K/as "ORTHODROMIC CONDUCTION".

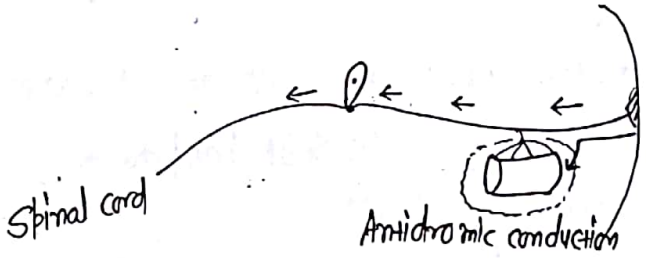
- These fibre also Receive branches from Blood vessels supplying these areas.
- Some fibres goes in "Antidromic conduction" of impulses to the blood vessels supplying the Area

↓

Arteriolar dilatation

↳ Spreading Redness

↳ K/as ⇒ "Flare Response" ***



(2) **MONOSYNAPTIC REFLEX ⇒** Deep tendon Jerks ;
Stretch Reflex / MYOTACTIC Reflex.

Knee Jerk – Strike over Patella Tendon

↓

Tendon Indent

↓

Jerk in Muscle length

↓

Increase in Muscle length

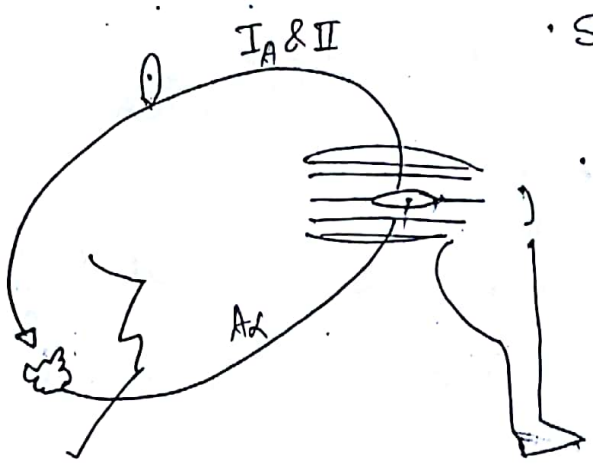
Muscle Spindles get Stretched

↓

Sensory fibres I_A & II enters into spinal cord

↓

In Spinal cord synapse ē Aα fibres



- Stimulus for stretch Reflex
  - ↳ ↑ in Muscle Length.
- Receptor for Reflex
  - ↳ Muscle spindle
- Afferent fibres
  - ↳ I_A & II
- Centre for stretch Reflex
  - ↳ Spinal cord
- efferent fibres for Reflex
  - ↳ Aα
- Response of Reflex
  - ↳ Muscle contraction
- No. of Synapses
  - ↳ 01 (one).

* During a stretch Reflex ⇒ Dynamic Response > Static

Nuclear bag (dynamic) >> Nuclear bag (static) & Nuclear chain fibre

* When a Muscle spindle is excited (↑ Muscle Length, ↑ Aγ discharge)

↓

Cause Muscle contraction

* Aγ Motor Neurons are Not powerful enough & Not strong enough to produce Muscle contraction

⇓

So; they ↓ Muscle tone

QQ. Which tract control Aγ Motor Neuron??

⇓

Reticulo-Spinal Tract

QQ Which tract control Aα Motor Neuron??

⇓

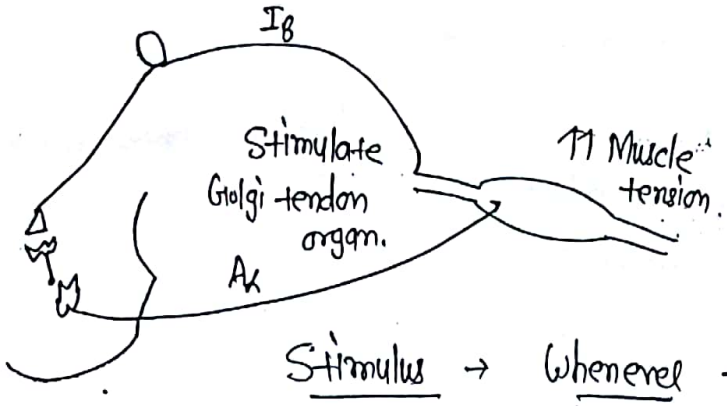
Cortico-Spinal Tract

Aγ Motor Neuron discharge ← ⊖ Medulla / Inhibitory Reticulospinal tract

↑ ⊕

Pontine / Excitatory Reticulospinal Tract.

③ BISYNAPTIC REFLEX ⇒ Inverse Stretch Reflex (Muscle Relaxation)



Stimulus → Whenever there is ↑es in Muscle tension; it stimulates Golgi tendon organs (Receptors)

↓ Nerve fibres Ib

Synapse ⊂ Inhibitory Neuron

↓

Inhibits Aα Motor Neurons going to particular Muscle

* There are 3-25 Muscle fibers | Golgi tendon organ.
* Golgi tendon organs acts as "Muscle tension-detector".

* Stimulus ⇒ ↑↑ Muscle tension;
* Receptor ⇒ Golgi tendon organ (G.T.O.);
* Afferent Fibre ⇒ Ib ;
* Centre ⇒ Spinal cord;
* Efferent Fibre ⇒ Aα
* Response ⇒ Muscle Relaxation
* No. of Synapse ⇒ 02 (Two) NEET 16

* When Muscle spindle excites ⇒ Muscle Contraction (at Moderate stretch)
* When Golgi tendon organ excites ⇒ Muscle Relaxation (on excessive stretch OR ↑ Muscle tension) → It has high threshold for stretch.

④ Polysynaptic Reflex ⇒ Most Reflexes

- Flexor withdrawal Reflex
- Crossed Extensor Reflex
- Micturation Reflex
- Defecation Reflex
- Sexual Reflex

} Higher centre control

DESCENDING TRACTS (MOTOR PATHWAYS)

Medial

- Control Axial Muscles (Tone & Posture)

- Anterior corticospinal Tract
- Vestibulo spinal Tract
- Tecto-spinal Tract
- Reticulo-spinal Tract
  - Pontine Reticulo-spinal Tract
  - Medullary Reticulo-spinal Tract

} ↑ especially Lower Limb Extension

} ↑↑ especially Lower Limb Extension.

Lateral

- Control Distal Muscles (Fine; Skilled Movements).

- Lateral cortico-spinal Tract (Pyramidal Tract)
- Rubrospinal Tract (Alternate Pathway) → (Extrapyramidal Tract; Similar acting Pyramidal Tract)

⇒ ↑↓ especially in Upper Limb flexion.

* CORTICOSPINAL TRACT

Origin → ① Primary Motor cortex ⇒ Contributes 30% fibres of corticospinal Tract;
↳ Located in Pre-central Gyrus; Area 4

Motor Homanculas

↳ Largest cortical Representation *

↳ More complicated Movement.

∴ Largest – Muscle of Vocalization ; (Max^m)
Muscle of Mastication ; (2nd Max^n)
Muscle of Thumb

Smallest cortical Representation – Muscle of Trunk / Back.

② Pre-Motor | Supplementary Motor Area :⇒ Area 6 ++

↳ Contributes 30% of the fibres.

③ Sensory cortex ⇒ contributes 40% of the fibres (So; there are 40% sensory fibres in corticospinal tract).

↳ Area 3, 1, 2

I
II
III
IV → bulk of incoming sensory information (Layer IV)
V → Motor output (Majority of Motor fibre).
VI

Histological Layer of cerebrum.

Pyramidal cells of BETZ

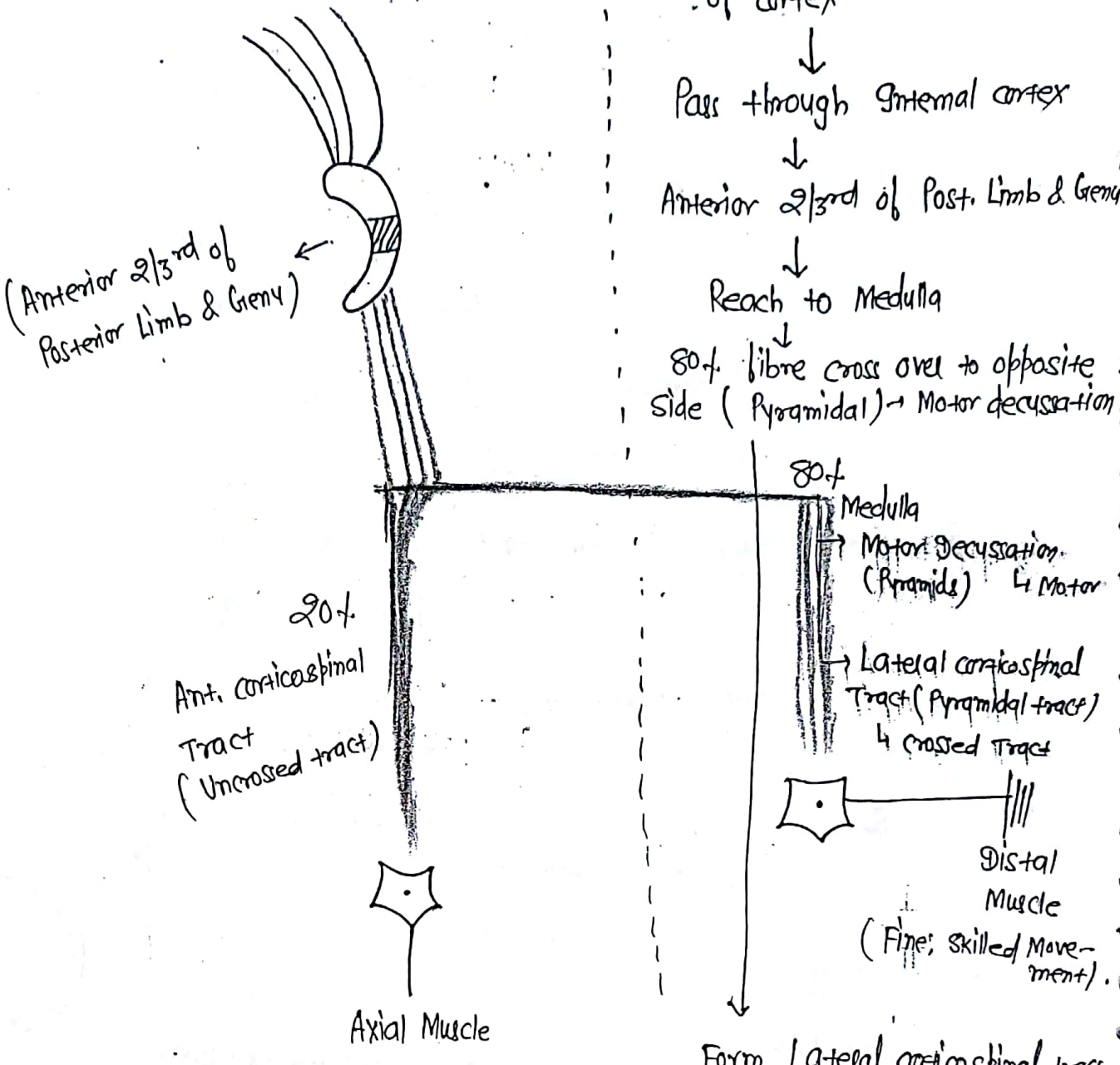
Betz cells

↓

Large (16 µm) Myelinated fibre originated from "Giant Pyramidal cells".

– Found in Primary Motor cortex.

* CORTICO - SPINAL TRACT - COURSE



Fibres from different Areas of cortex

↓

Pass through Internal capsule

↓

Anterior 2/3rd of Post. Limb & Genu

↓

Reach to Medulla

↓

80% fibre cross over to opposite side (Pyramidal) → Motor decussation

Form Lateral corticospinal tract (Pyramidal tract)

20% Fibre ; which Not cross

↓

Form Anterior corticospinal Tract (Uncrossed)

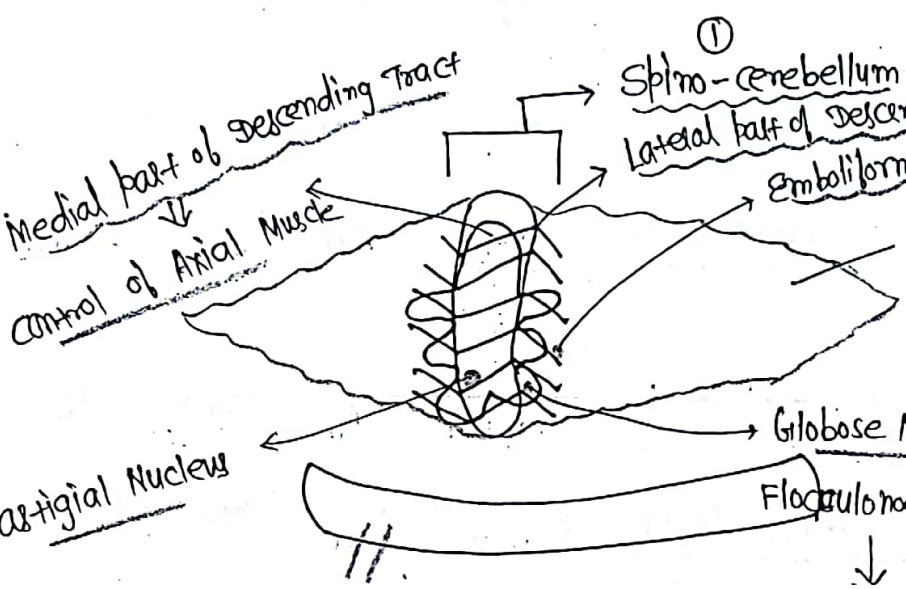
↓

For Axial Muscles.

CEREBELLUM

- 3 parts ;
- 4 Nucleus (4 pair) ⇒ Collection of Gray Matter.
- 5 cells ;

Collection of Gray Matters



① Spino-cerebellum → Motor co-ordination.
→ Distal Muscle contro

dentate Nucleus (Largest Nucle

② cerebrocerebellar
(Neo-cerebellum)
↳ involved in Motor planning.

Flocculonodular Lobe (oldest part)
↳ No Nucleus.
↓
aka " Vestibulo-cerebellum "
⇓
this part is Responsible for
- Balance
- eye Movements.

To vestibular Nuclei

QQ Most imp. function of cerebellum :-
a) Motor co-ordination;
b) Motor planning.

* 4 Nucleus → Medial to Lateral
① Fastigial Nucleus → Medial part of Spinocerebellum
② Globose Nucleus → Lateral "
③ Emboliformis Nucleus → Lateral "
④ Dentate Nucleus → Neo-Cerebellum,
↳ Largest Nucleus.

* 5- cells →
  i) Granule cells → excitatory;
  ii) Basket cells
  iii) Stellate cells
  iv) Golgi cells
  v) Purkinje cells
  → Inhibitory;
  Purkinje cells → Largest cells.

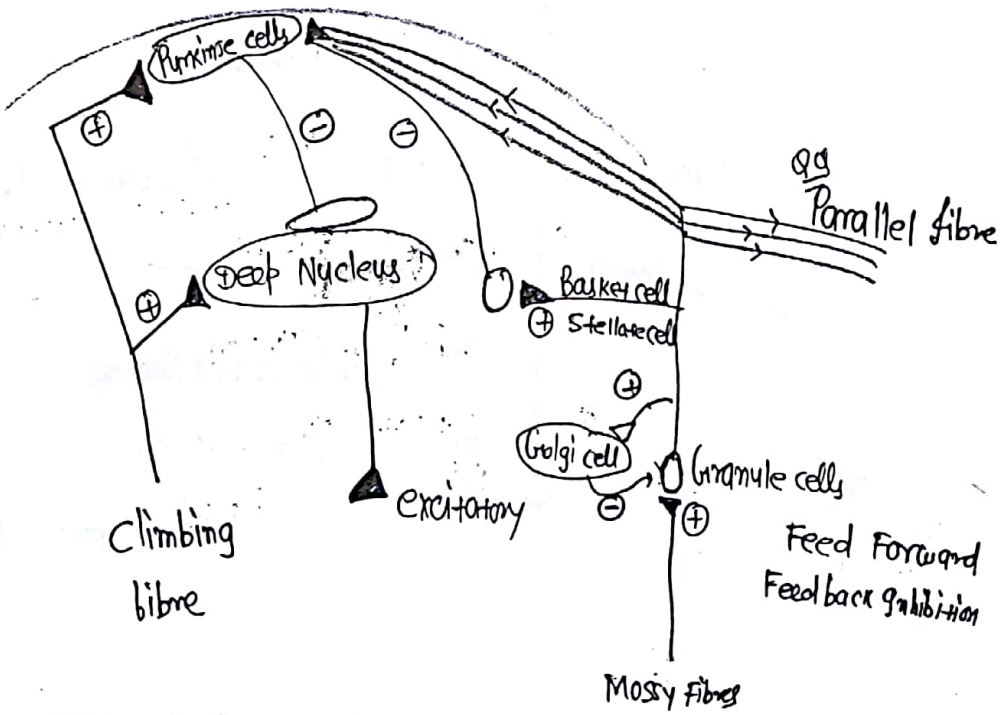
* Cerebellar cortex arranged in three Layer ⇒

① External Molecular Layer ⇒ Contains Basket cells & stellate cells;

② Middle Purkinje cells ⇒ Contains Purkinje cells;

③ Inner Granular Layer ⇒ Contains Granule cells & Golgi cells

* OUTPUT OF CEREBELLUM ⇒ From deep Nucleus (excitatory output)
  ↳ Purkinje cells inhibit the output of deep Nuclei.
  * Output of cerebellar cortex → Purkinje cells.



INPUT INTO CEREBELLUM :- via 2 types of fibre

CLIMBING FIBRE

- Strong excitatory input ;
- Formed by fibres of the olivo-cerebellar tract (it brings proprioceptive impulses from whole body)

* climbing fibre → ⊕ Deep Nucleus
So; it is 1st excitatory then it is also give ⊕ stimulus to Purkinje cells; so; Later on it is inhibitory.

** "climbing fibres" brings information only from "inferior olivary Nuclei"

MOSSY FIBRES

- Weak excitatory input
- Rest all fibres.

Mossy FIBRES → They synapse ⊂ Granule cells

- ⇓ Parallel fibres travel into cortex
  ⇓ Synapse ⊂ Multiple Purkinje cells
  ⇓ Inhibit deep Nucleus
- ↓ excite basket cells (or stellate cells)
  ↓ ⊖ Purkinje cells

* Granule cells excite a Golgi cells
Golgi cells → Inhibits → Granule cells

* ROMBERG SIGN – ⊕ In Posterior column lesion
a/k/a ⇒ "Sensory Ataxia"
↳ When eye closes → Ataxia
open → Stable (good balance)

BASAL GANGLIA

- Involve In Motor Planning
- Co-ordination of Autonomic and Associat. Movement
↓
↳ Swinging of Arms while walking
Facial expression while talking
↓
cycling.

- To kill a Fly (Insect)
↓ we Need
Cerebellum control
⇓
Rate
Range
Force
direction
} of Voluntary Movement

caudate Nucleus
⇓
Major Role in cognitive control of Motor activity

- Components – 1. caudate Nucleus
2. Putamen
} Striatum ↑ Receives Most of the afferent Input coming to the basal Ganglia.
⇓
95% of Neuron Secrete ⇒ GABA
5% of Neuron Secrete ⇒ Ach
Somatostatin

3. Globus Pallidus → In Athetosis; Mainly affected part
   ↳ cond^n in which abnormal Muscle contraction causes Involuntary writhing Movements.
   - External segment ⇓ GABA Secrete
   - Internal segment ⇓ GABA Secrete

4. Substantia Nigra → Principal output Nuclei i.e the efferent arises from these
   - Substantia Nigra Pars Reticulasis ⇓ GABA Release
   - ~~Substantia Nigra~~ Pars ~~compacta~~ ⇓ Dopamine Release → destroy in Parkinsonism.

5. Subthalamic Nucleus of Lewis → if affected "BALLISM" may cause.
   ↳ Release Glutamate ⇒ Excitatory Neurotransmitter

PATHWAYS ⇒
① Striato Pallidal GABAergic Pathway;
② Striato Nigral GABAergic Pathway;
③ Intra-striatal Cholinergic Pathway;
④ Nigro-striatal Dopaminergic Pathway;
⑤ Subthalamic Nucleus of Lewis → Glutamate → Globus Pallidus External segment, Glutamate → Globus Pallidus Internal segment.

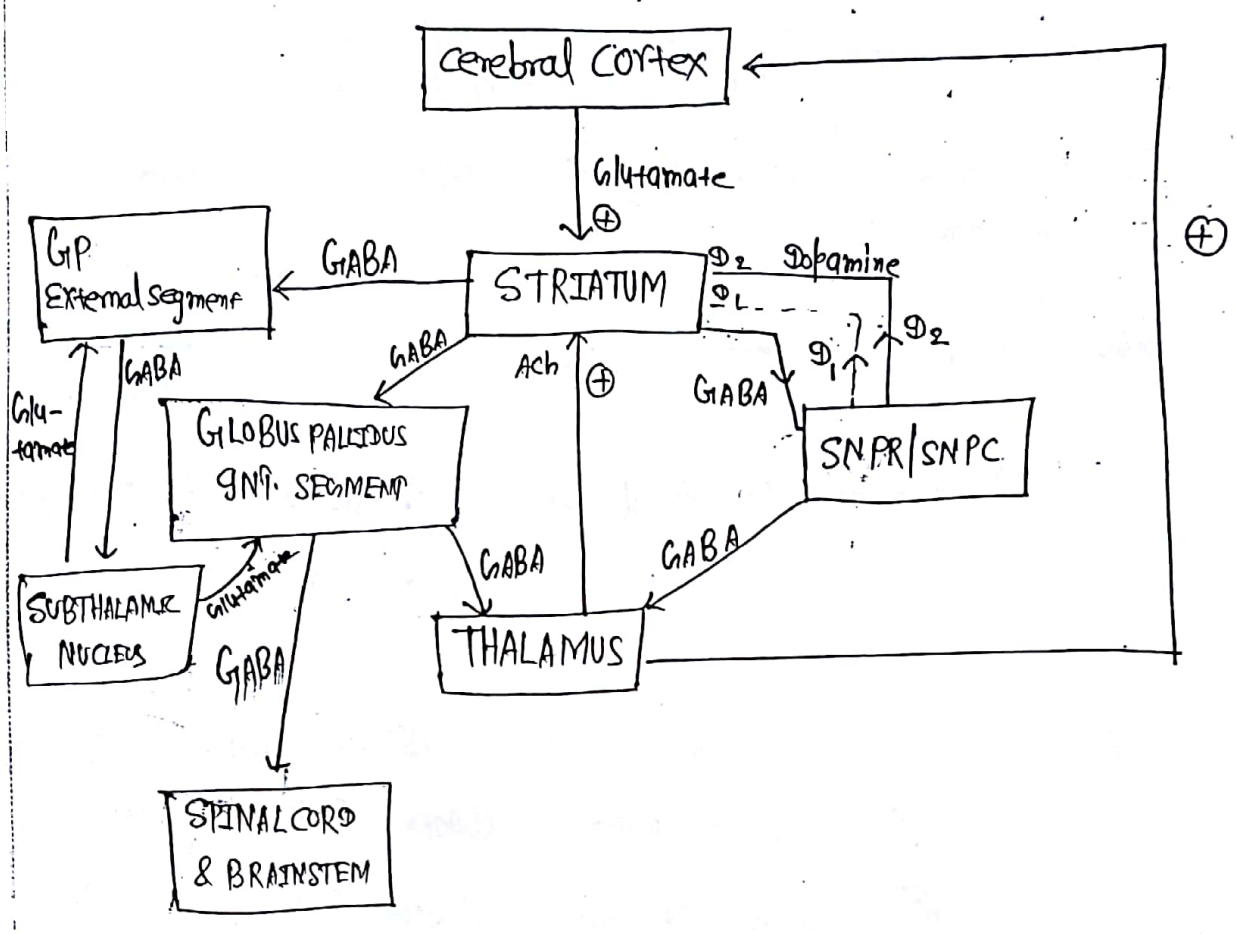
* In Huntington chorea ⇒ Mainly "striatum" part Involved (~~caudate~~ Nucleus; ~~Putamen~~)
   ↳ Loss of Intrastriatal GABAergic & cholinergic Neurons occurs.
   ↳ Both cholinergic & GABAergic Neuron Involved.

* Dopamine Receptor ⊕nt in → Striatum

D_1 → Excitatory

D_2 → Inhibitory

* CONNECTIONS ⇒



POSTURAL REFLEX

POSTURE ⇒ Static position of Any part of the body.

• This Reflex helps to Maintain posture.

Mainly of Four types ⇒ i) Spinal; ii) Medullary; iii) Midbrain; iv) cortical.

A. SPINAL POSTURAL REFLEX ⇒ 1. Stretch Reflex (Basic Postural Reflex) ;

→ Stimulus of Stretch Reflex is Passive stretch

2. Inverse spinal Reflex :

3. ⊕ve Supporting Reaction : Kla "Magnet Reflex"

Receptor → Touch Ⓡ on foot Pad

↓

Extension of Limb.

4. ⊖ve Supporting Reaction : if foot pad contact Move from ground ⟶ Flexion of Limb.

5. Standing :

6. Walking :

7. Galloping :

B. MEDULLARY POSTURAL REFLEX ⇒ 1. TONIC NECK REFLEXES → changes in posture ; d/t Movement of Neck ;

Receptor ⇒ Neck Proprioceptors.

* Neck flexion → Flexion of Forelimb
  → extension of Hindlimb.

* Neck extension → extension of Forelimb
  → Flexion of Hindlimb.

2. Vestibular / Labyrinthine Reflex :→

Keeps the head horizontal w.r.t. ground

Receptors → Otoliths (in Semi-circular canal).

C. MID BRAIN REFLEXES :→

- All Righting Reflex — Except — Visual Righting Reflex
(correction of Body Posture) ↳ centre ⊕ in cortex.

• Vestibular Righting Reflex
eg → Head on Body Righting Reflex ↳ centre ⊕ in Medulla.

Body on Body Righting Reflex.

D. CORTICAL REFLEXES :→ Hopping Reflex

Placement Reflex.

* CSF

→ 150 mL

→ Daily Secretion ⟶ 550 ml/day / 0.38 ml/day

→ Secreted by "choroid plexus"

→ circulate by "Subarachnoid space" & Absorb by "Arachnoid villi"

→ It is Secreted & Absorb ⟶ 3.7 times per day
(once every 6 hr)

→ Ⓝ CSF pressure ⇒ 70-180 mm H_2O
8-12 mm of Hg

* Rate of CSF Secretion ⇒ Independent of CSF Pressure;
* Rate of CSF Absorption ⇒ Dependent on CSF Pressure.

* At CSF Pressure

112 mm H_2O ⟹ Secretion = Absorption

> 112 mm H_2O ⟹ Absorption ↑

< 112 mm H_2O ⟹ Absorption ↓

< 68 mm H_2O ⟹ No Absorption.

* TRANSMISSION ON AUTONOMIC GANGLION

FAST RESPONSE

↓

Fast EPSP

↓

d/t Ach acting on Nicotinic ®

· Response time ⇒ mSec

SLOW RESPONSE

Slow EPSP	Slow IPSP	Late slow EPSP
↓	↓	↓
Ach acting on M_1 Receptor	Ach acting on M_2 Receptor	GnRH Receptor
Response time = Sec	Sec	(Min.)

HYPOTHALAMUS

→ Vegetative Brain;

· Hunger Centre ⟶ Lateral Hypothalamus

Satiety Centre ⟶ Ventromedial Hypothalamus

Thirst Centre ⟶ Lateral Superior Hypothalamus

Circadian Rhythms ⟶ Suprachiasmatic Nucleus.

* Regulation of Thirst ⇒

① ↑ Plasma Osmolality ⟶ Stimulate osmo-Ⓡ (Anterior Hypothalamus)

* Ineffective osmoles (glucose & urea) don't induce osmoⓇ.

Thirst center (Lateral Hypothalamus) → ↓ Ters water intake → Osmolality Restored

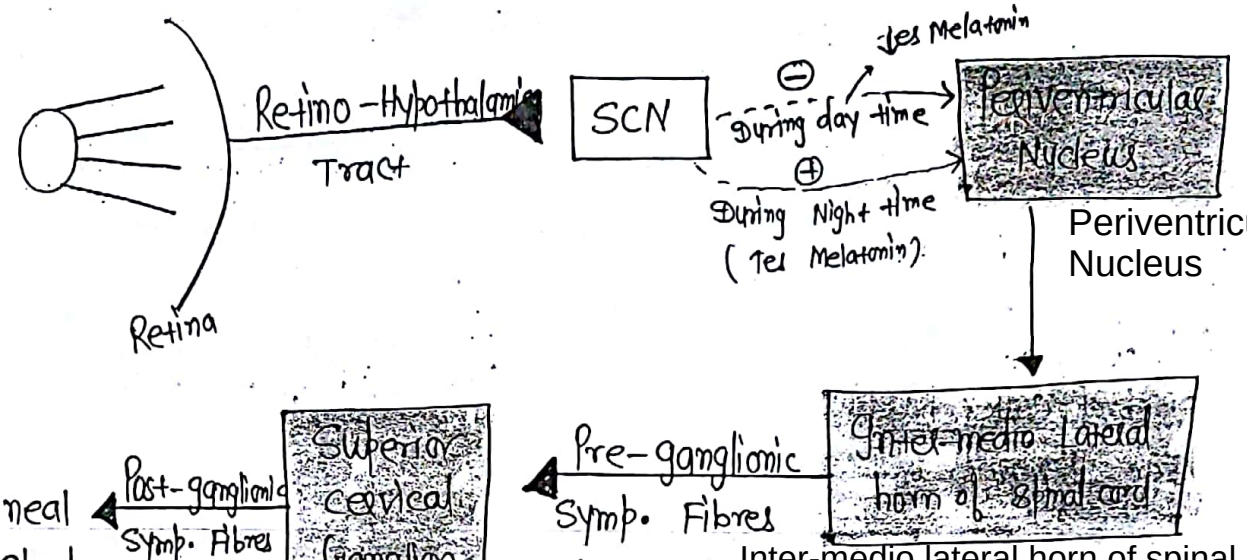
Supraoptic Nucleus (ADH Release) → ↓ Vers Urine Volume → Blood volume Restored

② Hemorrhage ⟶ Hypovolemia

Renin-Angiotensin System → ↓ Angiotensin II → ↓ Subfornical organ (OVLT) → ↓ Thirst center (Lateral Hypothalamus) → ↓ Ters water intake → ↓ Osmolality Restored

Baroreceptors in heart & blood vessels → ↓ SUPRAOPTIC NUCLEUS (ADH Release) → ↓ Vers Urine Volume → ↓ Blood volume Restored

* Circadian Rhythm - Supra-chiasmatic Nucleus is involved,
  ↓
  believed to contain the "Biological clock"



* If SCN is deprived of Light & darkness Informa.
  ⇓
  Precision of circadian Rhythm is disturbed but an approximately 24 hours Rhythm is still Maintained.

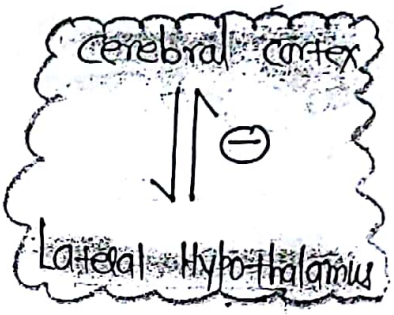
* RAGE CENTRE → Lateral Hypothalamus (Aggressive)
* REWARD CENTRE (Flaccid) → Medial Forebrain bundle
  Nucleus Accumbens (Drug Addiction)
  Ventro-medial hypothalamus.
* PUNISHMENT CENTRE → Posterior Hypothalamus & Dorsal Mid-brain;
* AVERSIVE RESPONSE → Learned Negative/Undesired Reaction to an Unpleasant event.
  ↳ Peri-aqueductal-gray (PAG)
* SELF STIMULATION EXPERIMENT → Experiment Animal kept in a cage.
  ↳ electrodes are placed in different Areas of brain & they are connected to a Lever; when he presses the Lever → Response

* It is Most effective ; if electrode is placed at Medial Forebrain Bundle.

* SHAM RAGE ⇒ Sham Means False.

Seen in Decorticate Animals

Animals whose whole cerebral cortex has been Removed.



* Slight provocation to Animal ⟶ Goes into Rage (B/c No Inhibition to Lateral Hypothalamus).

* This Rage is Not ** Goal directed

* Sexual Responses ⇒ Anterior Most & Posterior Most portion of Hypothalamus
  - Anterior Hypothalamus (especially Medial Pre-optic Nucleus) is More Important.
  - In Males Additional Area ⇒ Piriform cortex.

*

TEMPERATURE REGULATION (PRE-OPTIC REGION)

Posterior Hypothalamus
(Heat gain centre)
↓
Response to cold (winter)
i) ↑ Sympathetic discharge
↳ Peripheral Vaso-constriction

Anterior Hypothalamus
Including pre-optic Nucleus
(Heat Loss centre)
↓
Response to warm (Summer)
i) Peripheral Vasodilation;
ii) Sweating
(Sympathetic cholinergic fibres)

Posterior Hypothalamus

ii) Non-Shivering thermogenesis

↑ Sympathetic discharge → Nor-epinephrine → β_3 ® (Brown fat)

↓

Uncoupling of oxidative Phosphorylation

(∵ the help of UCP-1)

⇓

Uncoupling protein-1

→ Heat produced

⇓

only 10-15% of total heat is produced by this Mechanism.

→ ⊕nt in → Interscapular Region; Subscapular Region; Around the Neck; Axilla; b/w shoulder blades; kidney, Adrenal gland; Around Thoracic abdominal great vessels.

iii) Shivering

** Radiation is Major Mech^n for Heat gain & Heat loss.

* Dominant / Categorical Hemisphere :⇒ Left hemisphere is klas "Dominant hemisphere"

dominant for Language in over 95% of Rt. handers & in over 60-70% of Left handers; so)

In 95% Person → Left side

· B/c Wernicke's & Broca's Area is More developed in Left side → "Calculation"

So; if Left hemisphere damage ⇒ Acalculia.

* Non-Dominant / Visuo-Spatial Hemisphere :→ Rt. side

Involve in Fine Art; Creativity; Dance; Music

Rt. Inferior temporal Lobe ⇒ Recognition of Faces

↳ Loss → PROSOPAGNOSIA / FACE BLINDNESS

QQ. Temporal Lobe functions are all except :⇒

a) Memory ;

b) Healing ;

c) Behaviour → Ant. Most part of Frontal & temporal Lobe (Mainly Motivation)

d) ~~Spatial~~ orientation
↳ completly Parietal Lobe function.
↳ GPS of Brain *

* CIRCUMVENTRICULAR ORGAN (OUTSIDE BBB) :⇒

Structure in the brain that are characterized by their extensive vasculature & Lack of Normal BBB.

① OVLT (organum vasculusum of Lamina terminalis) ;

② S.F.O. (Subfornical organ) ;

③ Median eminence ;

④ Area - Postrema → control → CTZ (chemoReceptor Trigger Zone)
→ CVS
→ Medullary Structures in the brain that controls vomiting.

⑤ Posterior Pituitary (Neurohypophysis)

EEG (ELECTROENCEPHALOGRAPHY)

Delta wave (S-wave) ⇒ Origin = cortex ;
↳ Occur Independent of activity in Lower Areas.

NREM

* Also "Synchronized sleep"
OR
"Quiet sleep"
OR
"orthodox sleep". QQ

- Events ⇒
  - SOMNAMBULISM (Night walking)
  - SOMNILOQUY (Sleep talking)
  - NOCTURNAL ENURESIS
  - BRUXISM (Teeth grinding)
  - NIGHT TERRORS (Pavor Nocturnus)

  → NREM (III & IV)

REM

- Spontaneous Awakening occurs in REM Sleep.
- This is period of Autonomic Instability
  - HR
  - BP
  - RR

  ] Irregular.

* ~~PGO spikes~~ are seen
(Ponto-geniculo-occipito)

PONS ⇒ PGO on cells

- Ach Release

Events ⇒ NIGHT MARES ;

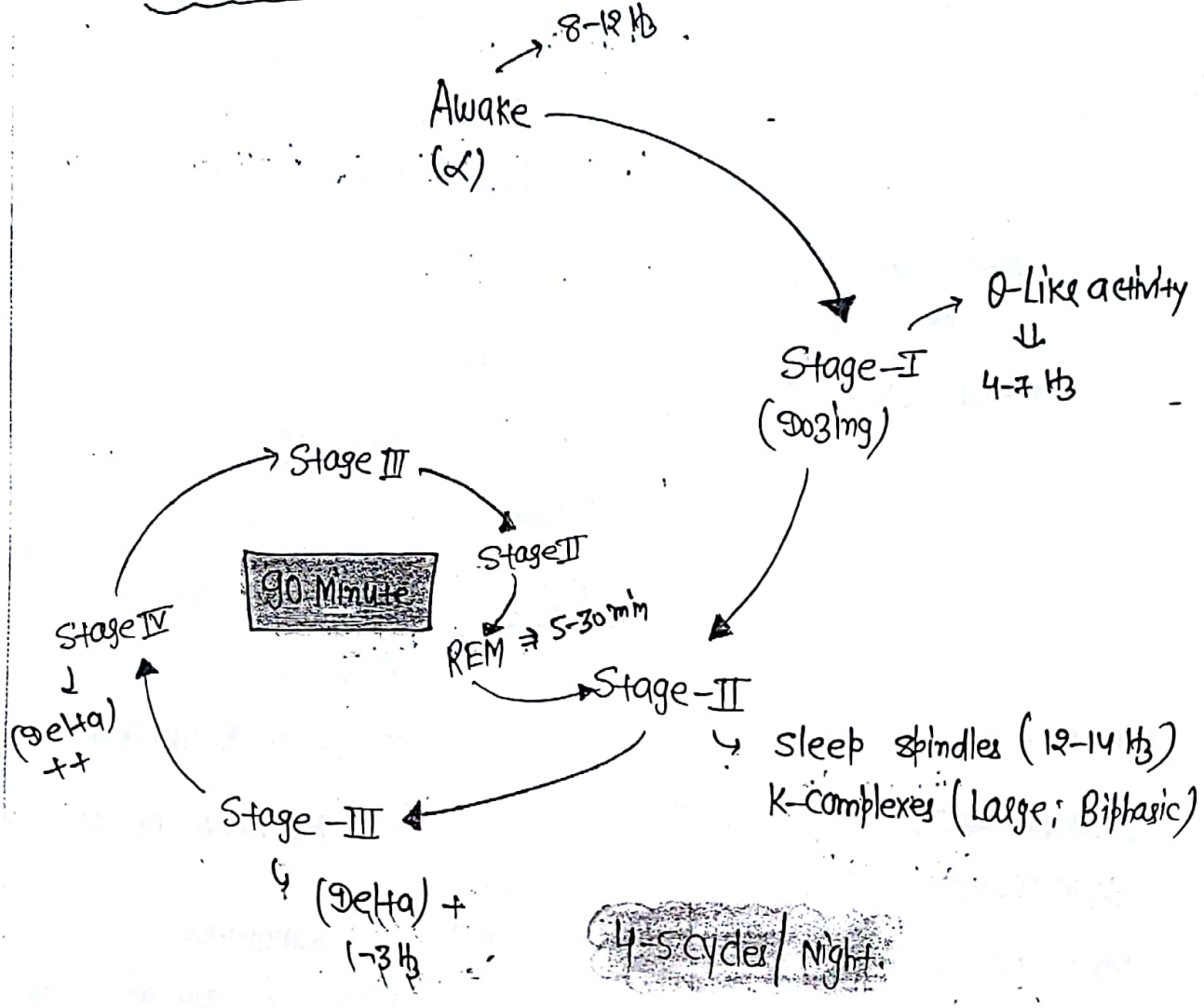
- NOCTURNAL PENILE TUMESCEN
- NARCOLEPSY
  (excessive day time sleep)
  ↳ q/w Cataplexy (↓es in Muscle tone).
  Hypnagogic hallucination
  Sleep paralysis

* Saw tooth waves (Low voltage fast activity);
Reappearance of α-wave

* Tone of Neck Muscle is Markedly Reduced in REM sleep
(Other Muscles Retain their tone)

* Locus ceruleus Mediated Relative Paralysis ⇒ in REM sleep.

* Sleep cycle ⇒



Most difficult to Arouse ⇒ Stage III & IV

↳ Deep sleep or Slow wave Sleep; high Arousal threshold

* Total time spent in REM Sleep ⇒

Preterm ⟶ 80% of Sleep time

Term ⟶ 50% "

Adults ⟶ 25% "

Elderly ⟶ 15% "

* On an average; REM Sleep occupies 20-30% of Total Sleep.

NREM Sleep occupies 60-70% of Total Sleep.

Time spent by different stages of NREM sleep :-

- Stage I ⇒ 5-10%
- Stage II ⇒ 40-50%
- Stage III & IV ⇒ 15-20%

Total ⇒ 60-70% ↓ NREM sleep.

RAS (Reticular Activating System)

- ~~Ascending Polysynaptic Pathway~~
- ~~Non-specific system~~ ; which can be ~~excited by Any sensation~~
- on (Arousal from sleep) the EEG pattern changes to high frequency low voltage activity (β-wave) from high voltage slow wave (δ-wave) of sleep ⇒ "δ-block"

→ ***Activation of RAS is Responsible for Arousal from sleep.**