* Gold Standard (Test) for Renal Function is **Creatinine Test**

RENAL SYSTEM- RENAL PHYSIOLOGY

Functions of Renal System:

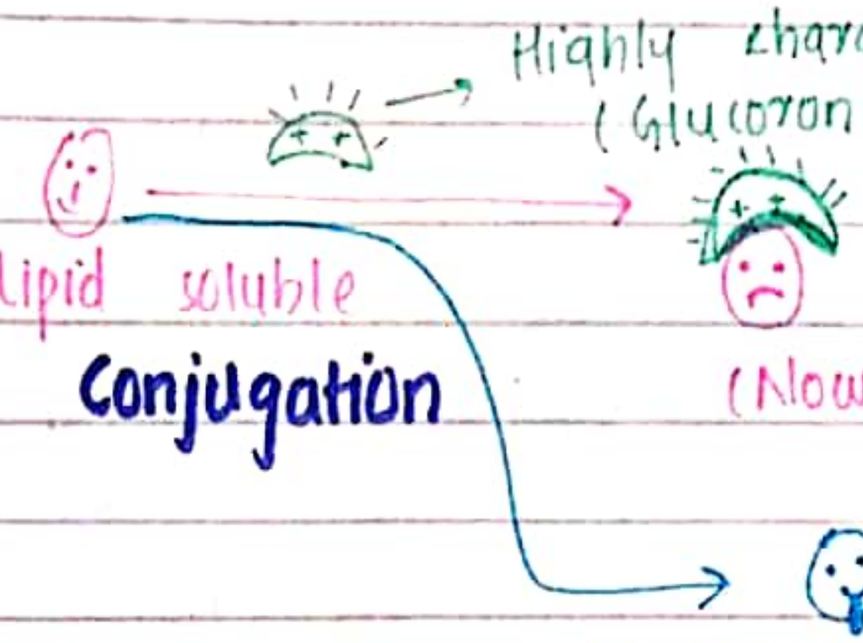
- Excretory Function → Metabolic waste products (urea & creatinine)
  - Drugs
  - Toxins
  - mmol: meq.
- Regulatory Function (Regulate)
  - H_2O Balance
  - Electrolyte Balance
    - Na^+ 140mmol/L
  - Acid, Base Balance
  - Even lesser fluctuation causes critical situation
  - Na^+ = 125-145 meq/L
  - K^+ = 3.5 - 5.5 meq/L
  - (K^+ level is more imp. bcz its lesser fluctuation even causes critical situation)
  - Cl^- = 100 meq/L
  - HCO_3^- = 22-28 meq/L
  - Ca^{++} = 2.5 meq/L
- Endocrine Function
  - Ht (Boton) conc = 40n eq/L
- Metabolic Function

(At level of 7, it is critical)

* When renal failure occurs, urea & creatinine both level high, but urea can also be increased in blood irrespective of kidney even if its function is ok. So, it means only creatinine test is standard for kidney. function.
* Any substances which passes through the kidney must be water soluble. Nephron is made of epithelial cells. Each kidney comprises 1 million Nephron { in both kidneys => 2 millions + Nephrons.
* Lipid soluble substances can pass through the biological membrane (mucosal membrane of GIT, blood brain barrier. { placental membrane)
* Drugs, Harmones (lipid soluble substances) donot pass through the Hepatobiliary { renal system bcz they get absorbed by its membrane. Thatswhy,

Scanned with CamScanner

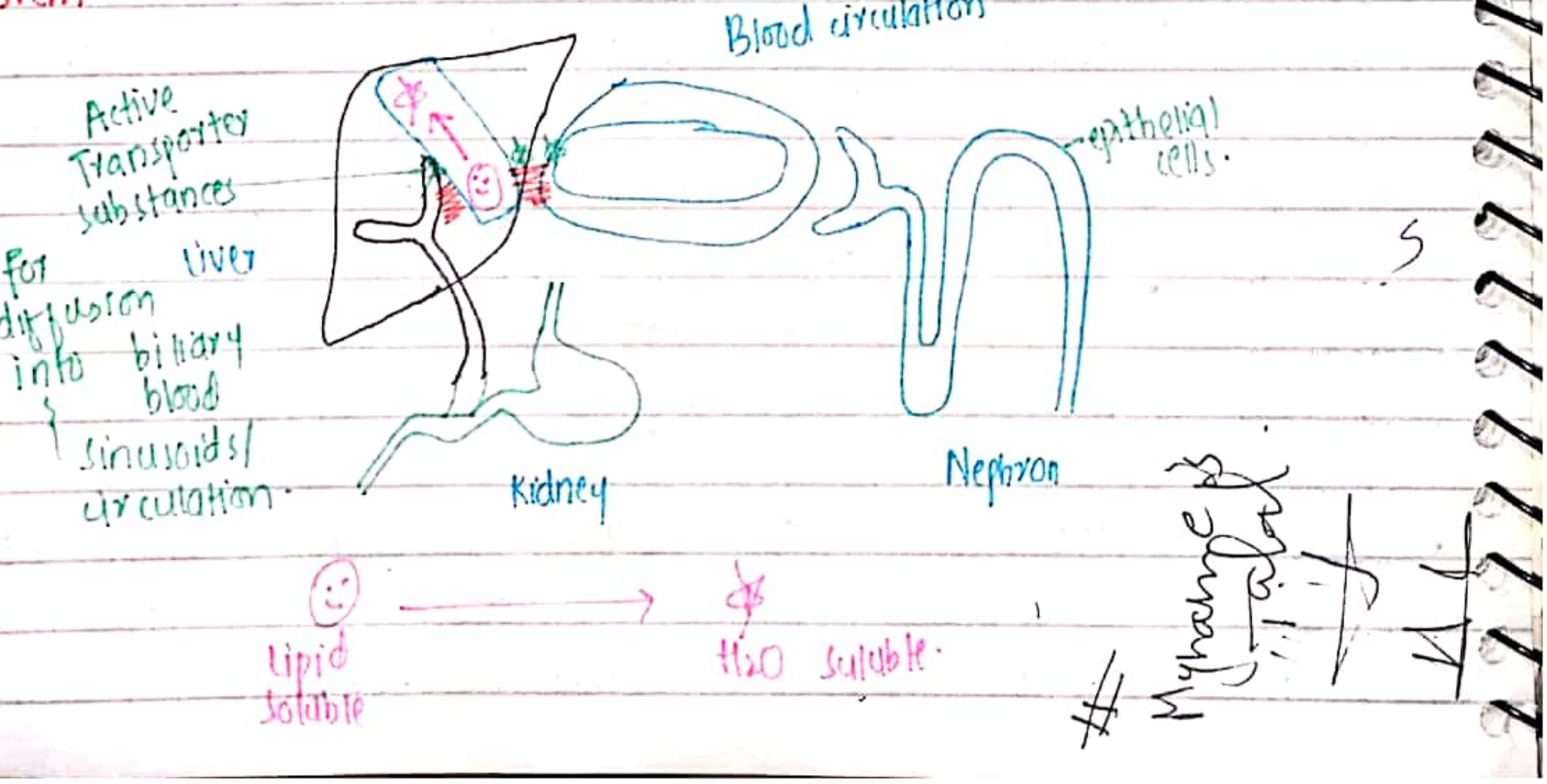
we should need to convert lipid soluble substances into the H_2O soluble. So, that they can pass through urine.



(when drug passes through the Hepatocytes, its charge component moves out { it bcm polar).

Bio Transformation I: Molecule expose their charged part.
Bio Transformation II: charged molecule attached with it.

* When the lipid soluble substance convert into the H_2O soluble in Hepatocytes, cannot diffuse easily needs active transporter for diffusion into biliary system { circulatory System.



* Iron is absorbed at entry point (GIT) while the other extra moved through feral matter.

Endocrine function of Kidney:

(group of cells which produces the substance entering the blood and altering the biological function of another grp of cells)

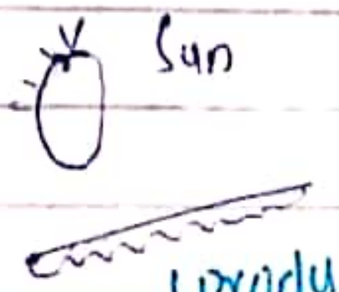
- → **Erythropoetin**
- → **Renin**
  convert Angiotensin I ⟶ II
- → **Prostaglandins**
  (Vasodilator)

* Juxtaglomerular apparatus produces Renin.
* Capillaries around P.C.T & D.C.T are Peritubular capillaries containing Endothelial cells which produces Erythropoetin.

→ form by the modified Renal cells (macula densa) and modified vascular cells (Polkisin) (of afferent vessels) collectively called Juxtaglomerular apparatus.

Metabolic Function of Kidney:

convert Inactive Vit. D ⟶ Active Vit. D.



(produces cholycalciferon)

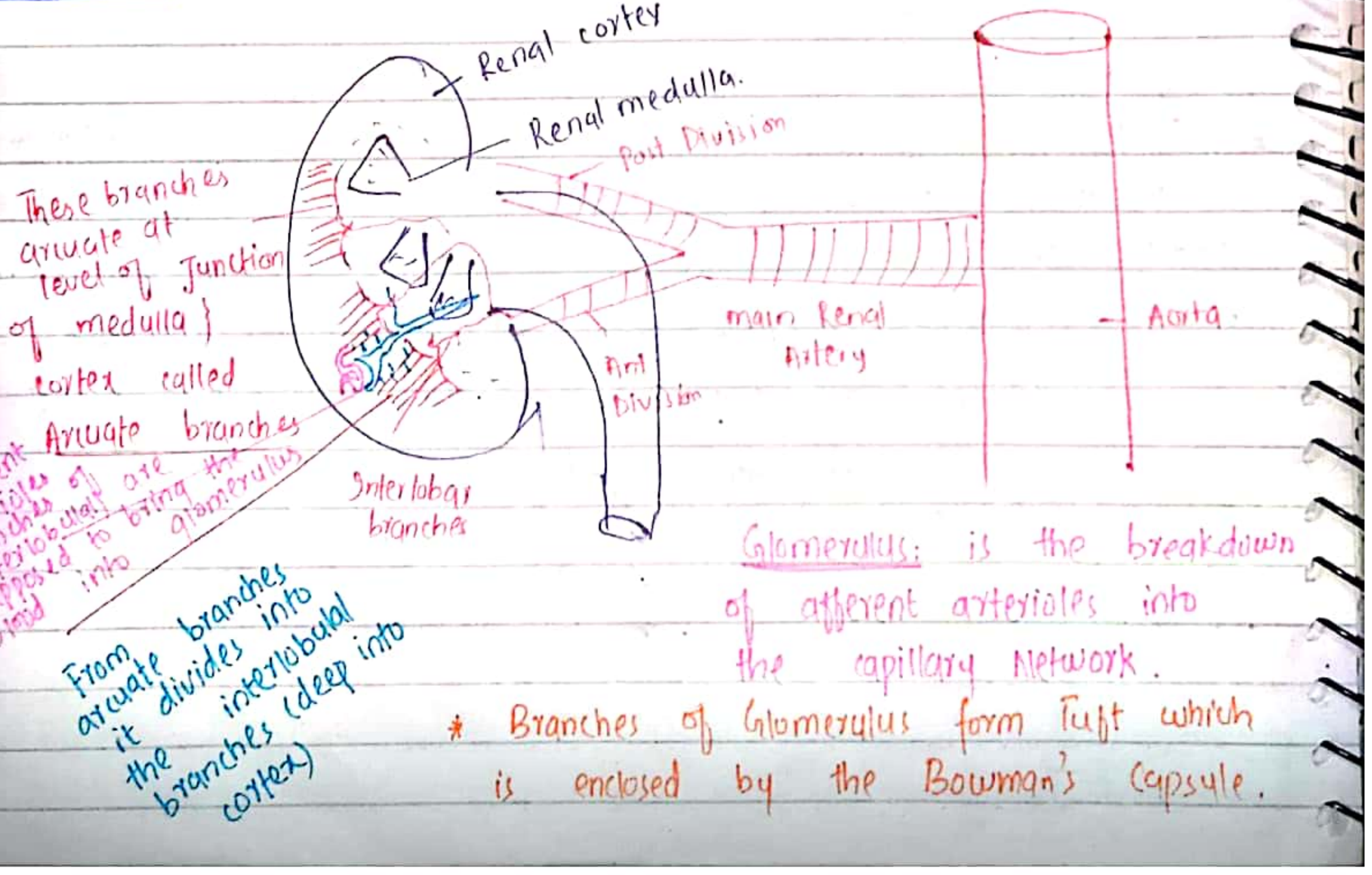
⟶ 25-OH C.C.F ⟶ (Kidney) 1,25 Dihydroxy C.C.F.

enter Liver

Hydroxylation occurs

* Proximal convulated Tubular cells have α-hydroxylase enzymes which convert 25-OH C.C.F into 1, 25 Dihydroxy C.C.F. Parathyroid Harmone act on these cells to produce α-Hydrylase enzymes.

Lecture #2

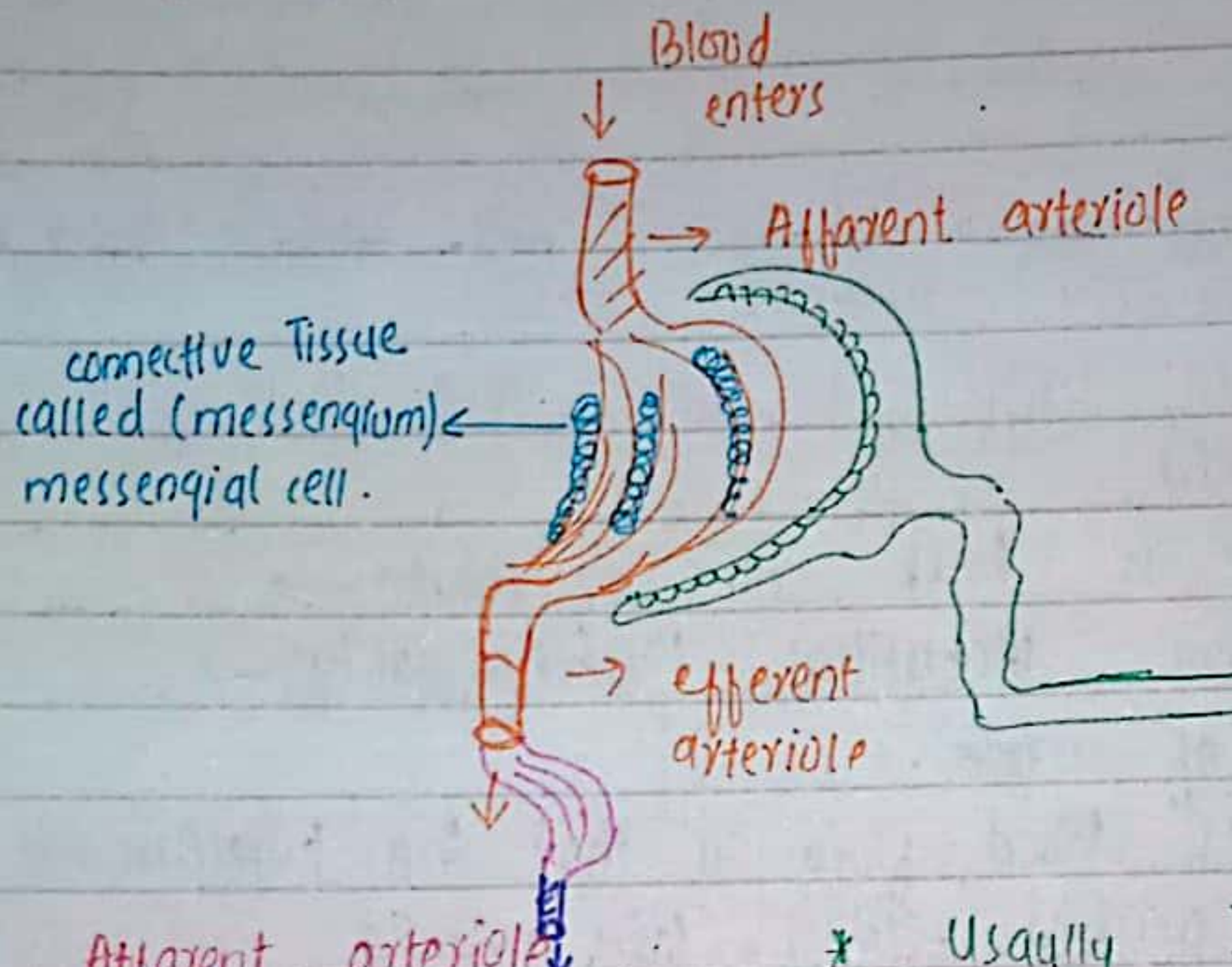


Glomerulus: is the breakdown of afferent arterioles into the capillary Network.

* Branches of Glomerulus form Tuft which is enclosed by the Bowman's Capsule.

* Glomeruli which forms near the junction of cortex & medulla are **Juxtamedullary Glomeruli**. which are only **10-15%**.

* Glomeruli which form away from the junction are **cortical Glomeruli** which are **80-90%**.



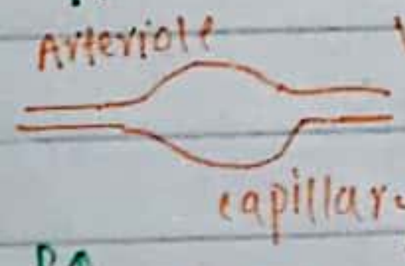
Efferent arteriole will break down into the capillary Network but here it drain into the True veins called peritubular Network surrounded by P.C-T as well as D.C.T.

* Substances which are ~~rec~~ filtered from Glomerulus capillary Network are reabsorbed into peritubular capillary Network (ie Glucose)

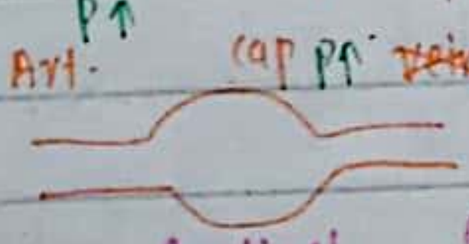
→ 1 Afferent arteriole makes 10-15 loopes of capillaries forming Glomerulus.

* Usually In capillary Network, one side having arteriole & the other side having vein but here is unique at **both sides** of the capillary Network is the **arteriole**.

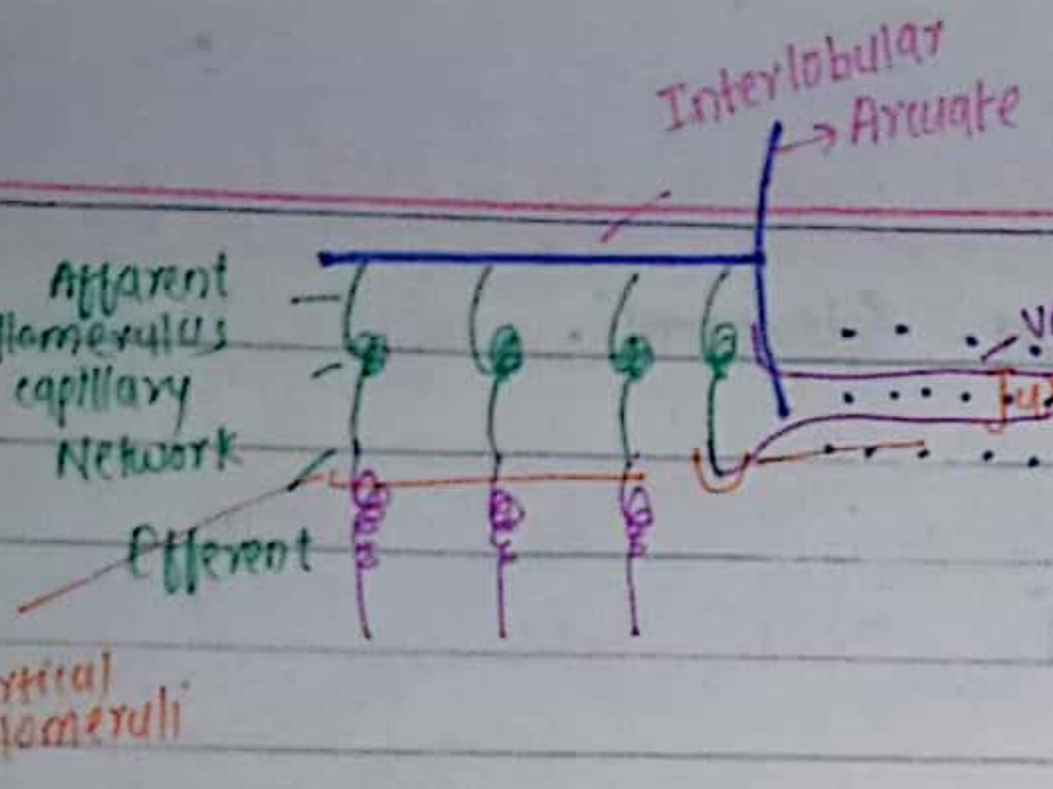
* Glomerulus capillary is high pressure system bcz of also arteriole having high filtration system.



* Venules are low-pressure system while arterioles are high-P system bcz arterioles are high constricted



→ Cortical Structure of Nephron is provided by the 2 capillary Networks. Glomerulus & Peritubular Network.



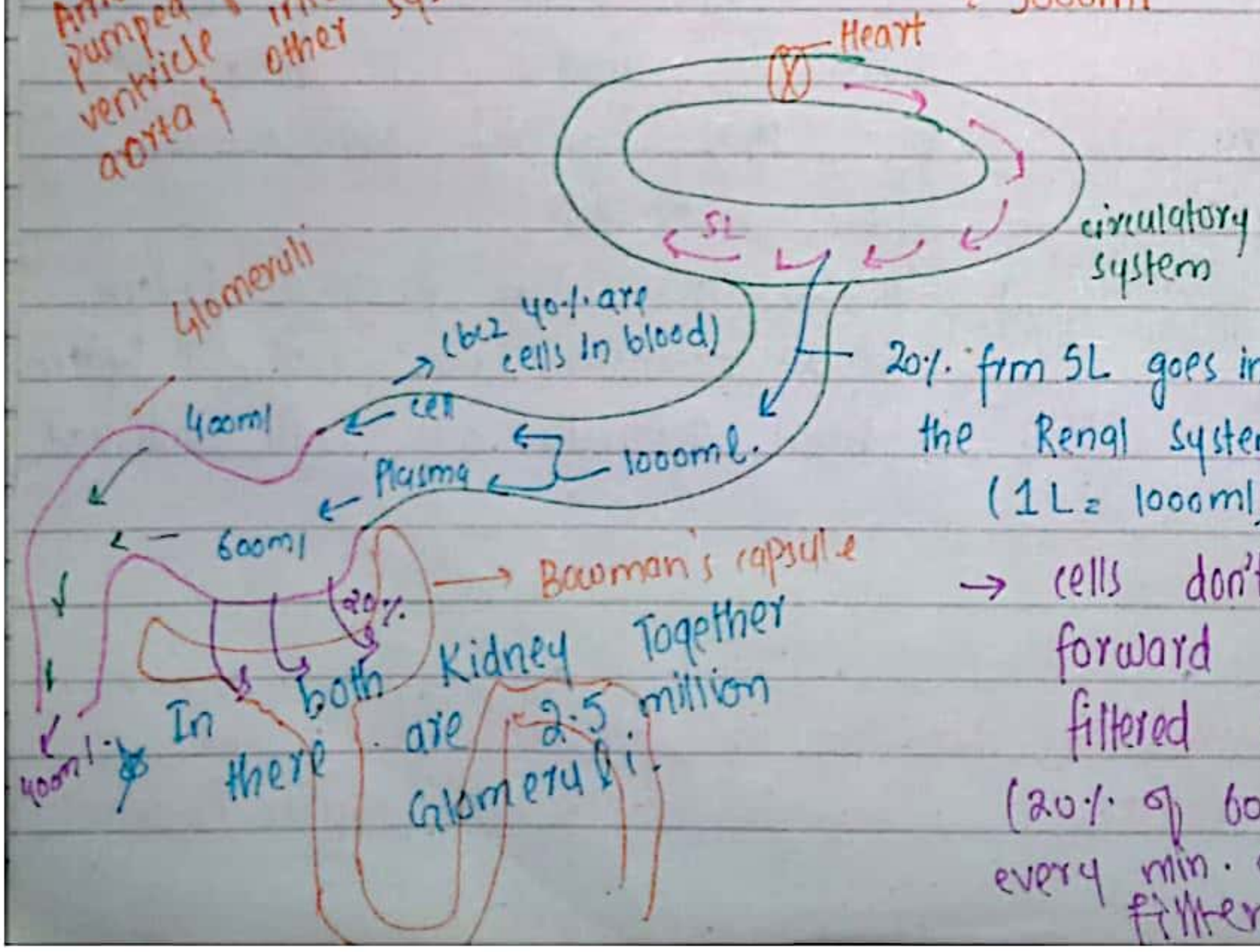
vasa recta (maintaing very little Blood flow in the renal medulla)

Juxtamedullari glomeruli { short P.C.T, D.C.T collecting Tubule
bcz it is near but very long the medulla. Loop of Henle)

* Efferent arterioles frm the cortical Glomeruli breakdown into peritubular capillary Network while in Juxtamedullary it doesnot break & form long loop of capillaries called vasaracta.
* In medulla, there is high conc. of solute → Hyperosmolality (Medullary interstitial Hyperosmolality) → Help in concentration of urine.
* Vasa recta has low blood flow so that the hyperosmolar solute conc. is not washed away frm medulla.

Amount of blood pumped frm left ventricle into aorta & other system.

C.O = Heart rate x Stroke volume. (ejected by the left vent. during resting conditions.
72 x 70
= 5000ml



20% frm SL goes into the Renal System (1L = 1000ml)

→ cells don't filter pass forward while Plasma filtered here except Proteins (20% of 600 filtered) So every min. app. 120ml fluid is fiiltered in Bowman's Capsule.

So among 120ml, (60 ml by each Kidney is filtered)

Among 120ml (suppose 100ml) 65% of H_2O is reabsorbed by the **P·C·T** and 15% by the **loop of Henle** while in Ascending limb (Thick limb) Here no reabsorption occure while in **D·C·T** 15% reabsorb. Now 5% are left in collecting which by the the act of Aldosterone which acts on Na^+ ions etc & ADH which acts on H_2O. only **1 ml urine is produce from both the Kidneys per minute.**

If 1ml urine is present per minute. then how much urine per day?

1 hr = 60 min.
= 24 hr x 60 min
= 1440 min per day.

So, 1440 ml urine produces average person per day.

Normal urine Output/Day → 500ml → 3500ml

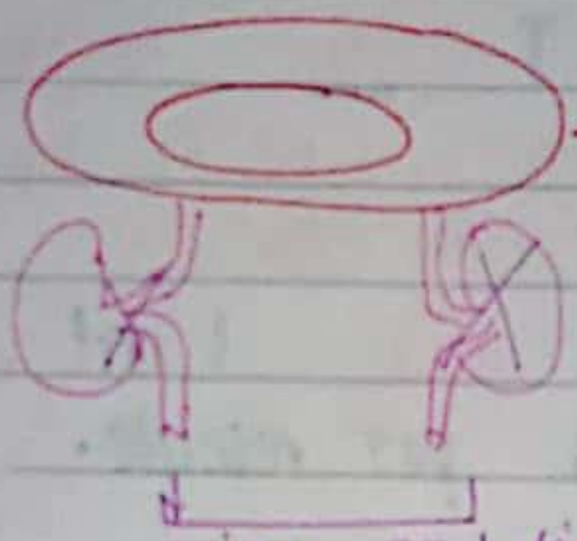
Oliguria → If ↓ 500 ml
Polyuria → If ↑ 3500 ml (bcz of capacity of urinary Bladder)

Norm Human met. waste production 600mosl. → 500ml of H_2O
M.W
1200mOsml → 1000 ml of H_2O

Metabolic waste produce by body
↓
Kidney has the capacity to concentrate it. into H_2O soluble

* In the average adult Human, the Glomerular Filteration Rate is about 125ml/min or 180L/day.

Hypercatabolic state → More metabolic waste ⇒ more production of urea & creatinine.



- Blood circulation (accumulation of urea, K^+, creatinine etc. but they are in balance(mild) doesn't show any disease (Renal failure) can alter the biochemistry only called

↓

Azotemia

urine production (↓ 500ml)

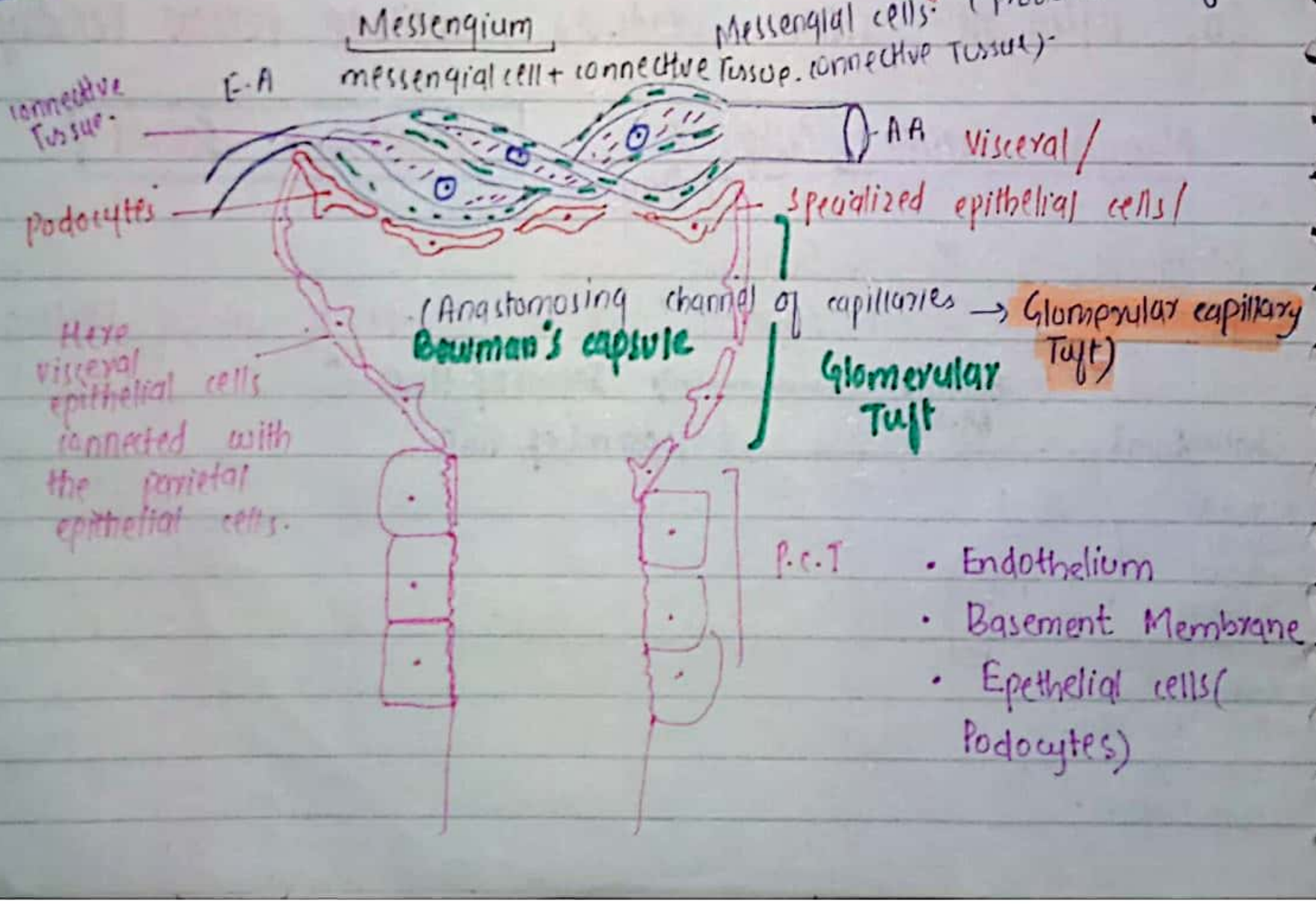
Azotemia + Sign & Symptom of Renal failure (vomiting etc), acid base alts skin dry changes.

↓

Uremia

Lect #3

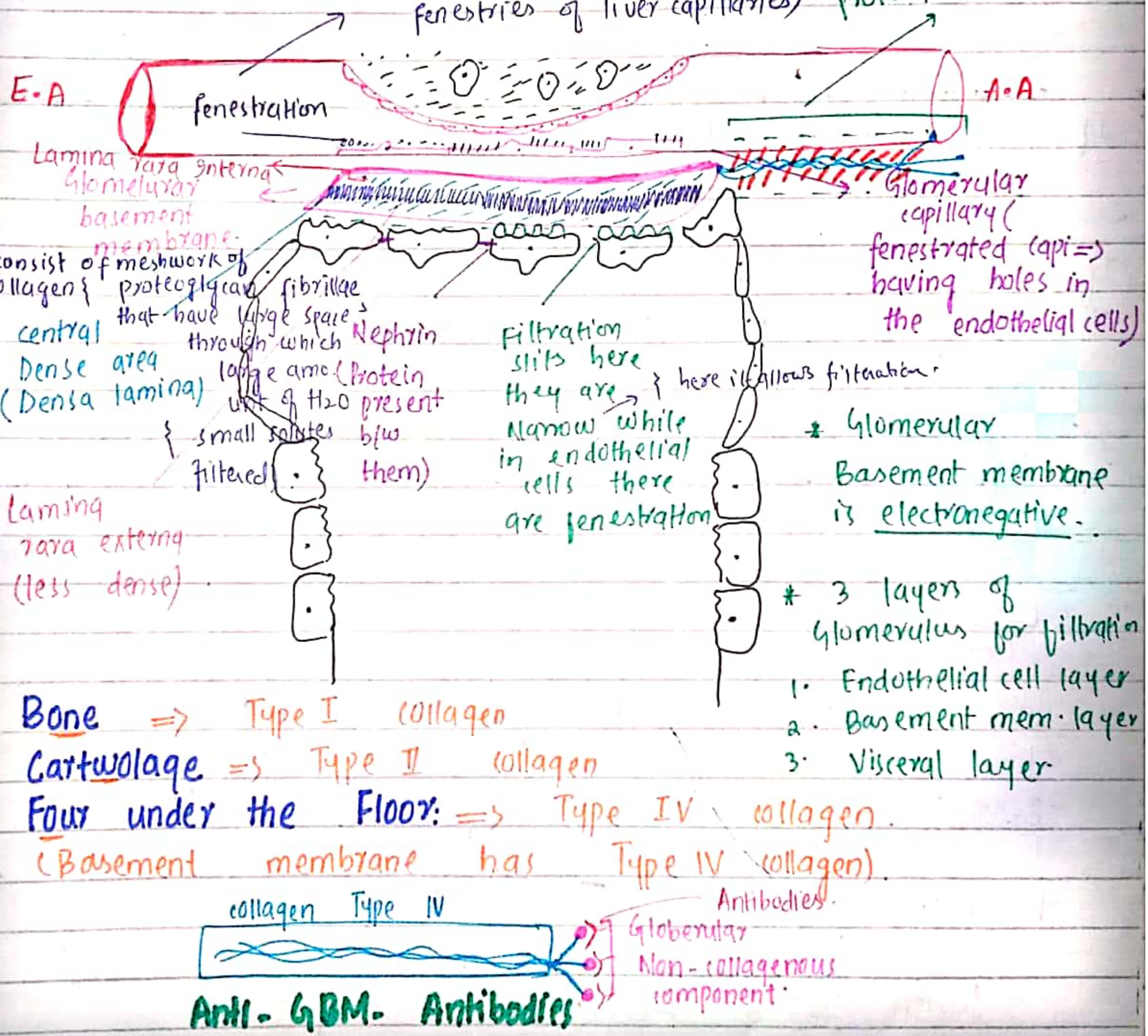
Glomerulus ⇒ Filtration unit for kidney



Glomerulus :

Grp of anastomosing capillaries present in the kidney

invested by the double layer of the epithelial cells making Bowman's capsule & capillaries are embedded within mesengium => Glomerulus functionally → Filtration unit of Nephron where filtration occur.



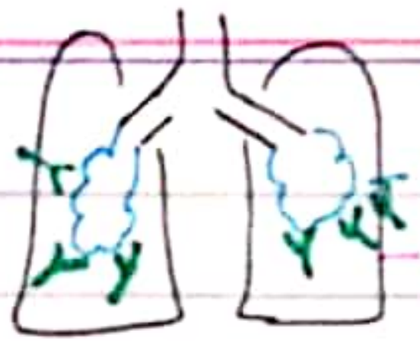
* Glomerular Basement membrane is electronegative.

* 3 layers of Glomerulus for filtration
1. Endothelial cell layer
2. Basement mem. layer
3. Visceral layer

Bone => Type I collagen
Cartwolage => Type II collagen
Four under the Floor: => Type IV collagen.
(Basement membrane has Type IV collagen)

Anti-GBM-Antibodies

* Negative basement membrane. repels the inside plasma protein (having neg. charge) thatswhy provide additional restriction to Plasma protein & permitt rapid filtration of H2O & Solutes.



Anti- ABM- Antibodies.

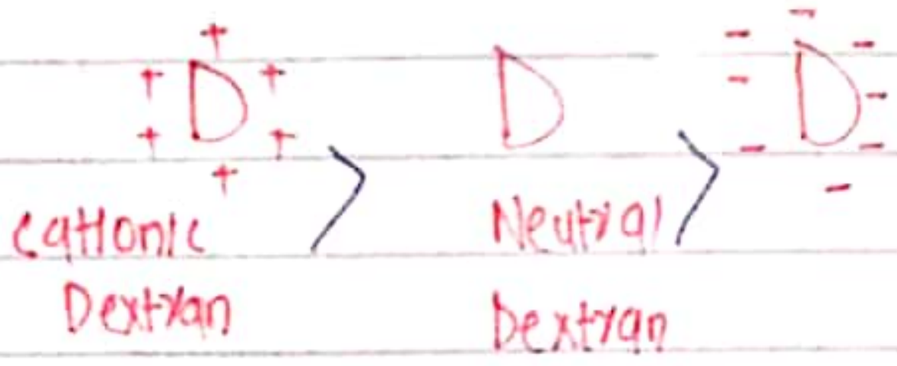
Antibodies coming attack the Kidney and alveoli. On Kidney, it produces Hematuria while on alveoli produces Hemoptysis called good Posture Syndrome

If it damages the Kidney wall called Glomerulus Nephritis

If there is mutation in the α-Helix of the Type IV collagen called Hereditary Nephritis

Glomerular Filteration membrane is a Size Barrier Membrane

* Destrans are polysaccharide.



Cationic Dextran will be more easily filterable bcz Glom. membrane is (-ve) So it will attract it. while Anionic Dextran is worst filterable.

Filteration depends on — [Size, charge]

Small Size } cationic are more filterable.

RBC → 7-8μm WBC (12-14μm) Platelets (1-2μm)

→ All these cannot pass through the Glomerular membrane cz of their large size.

In plasma, Globulin, Fibrinogen doesn't pass through Glom. memb (8nm) bcz of its large size. while (just right to the fenestration point) **Albumin** (6nm) having small size but are **negatively charge.** Thatswhy, cannot pass through it.
(↳ of basement membrane { podocytes)

Minimal Change Glomeruli pathy / Nephropathy:

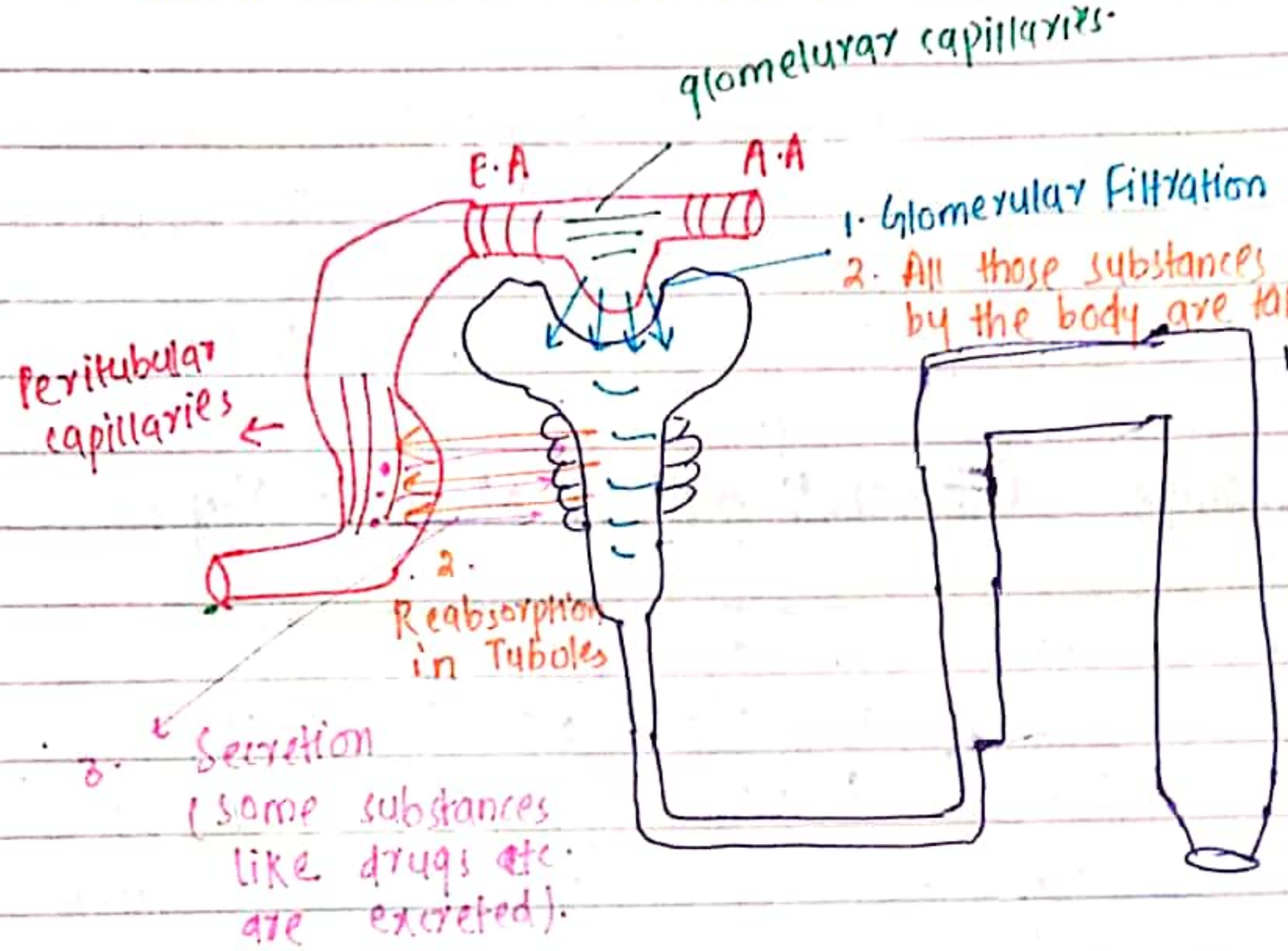
In this, immunological part of the body produces cytokins which neutralizes the electroneg. Glomeruli. So, albumin can pass through fenestration Now. Thatswhy, high albumin urea is produced condition called proteinuria or albumenuria due to immunological response and abnormal T-cell secretion of cytokins that injures the Podocytes.

Messengial cells :
* contractile cells
* Have receptor for Angiotensin II.
* Have phagocystic cell
* can proliferate
* If irritated, can also enhance the inflammation in the Glomeruli.

* Minimal change Nephropathy is more common in children but can also occurs in adults especially in those who have autoimmune disorder.

Lecture # 4

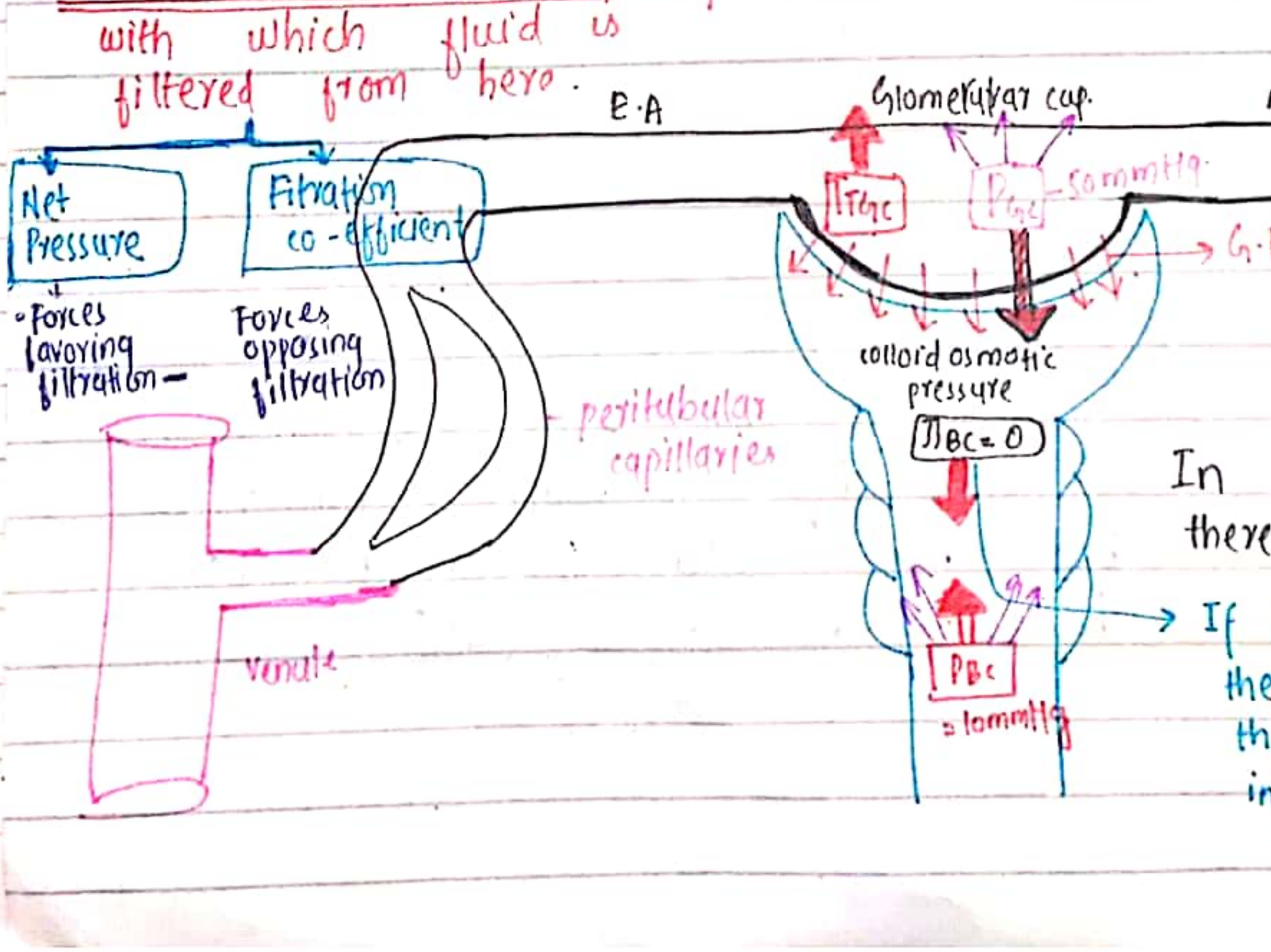
GLOMERULAR FUNCTION



1. Glomerular Filtration
2. All those substances which are required by the body are taken (reabsorb (Glucose is filtered freely then reabsorb by the body).

Urinary Excretion: Glomerular Filtration - Tubular Reabsorption + Tubular Secretion

Glomerular Filteration Rate: Speed with which fluid is filtered from here.



In Bowman's capsule, there is no protein

If they were present, then they will pull the proteins from G. capill. into the Bowman's capsule.

Glomerular cap. are present b/w 2 Arterioles. So, the pressure in these capillaries are high comparable to other.

→ Other capillaries in the body have Hyd. Pressure of about 20-30 mmHg while in Glomerular it is 50mmHg which promote Filteration → Guyton

Forces favoring Filtration

→ Hydrostatic P of Glomerular capillaries (P_G) = 50 (60mmHg)

→ colloid Osmotic P of Bowman's capsule (π_{BC}) = 0 (bcz here (glomerular filterate) protein conc. is so low.

Forces Opposing Filtration

→ colloid osmotic p of G. capillaries = 30mmHg (32mmHg).

→ Hyd. P of Bowman's capsule = 10mmHg (18mmHg) ↓ which oppose Filteration.

Sum = 40mmHg

Net Filtration Pressure = 50mmHg - 40mmHg

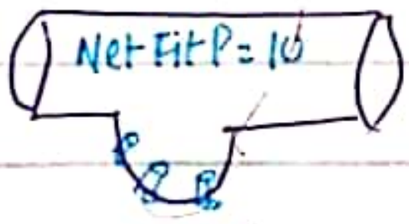
= 10mmHg

(60 - 18 - 32) = +10mmHg

2. Filtration co-efficient K_f

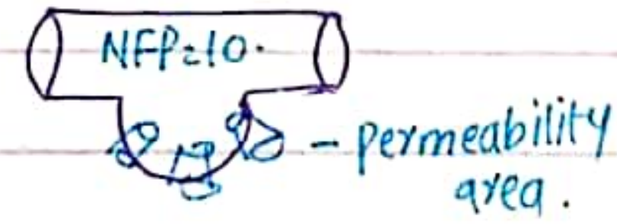
Permeability of filtering membrane (Hydrolic conductivity)

Total surface area of filtration membrane.

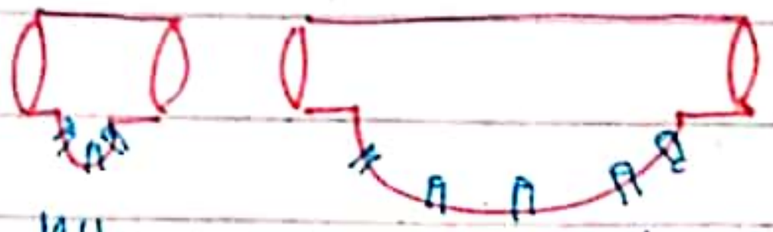


less H.C

(Degree of conductivity by the membrane)



~~less~~ More H.C



less area {pers same.

More per/more area

G·F·R α Net Pressure Filtration

G·F·R α Kf

G·F·R = Net filtration Pressure x Kf

$$Kf = \frac{G\cdot F\cdot R}{Net\cdot F\cdot Pressure\cdot} = \frac{125\ ml/min}{10} = 12.5ml/min.$$

C·O = 5L (Out of which 20·/· / 1100ml/min enters Kidney } 80·/· (4L) to the rest of the body).

Among 20·/· (1L) (1000ml) — 400ml (RBC cells)
— 600ml (Plasma).

* Two Kidneys constitute only about 0.4·/· of the total body weight (They can receive extremely high blood flow as compared to other organs (20·/· of the C·O).

(Among 600ml → 20·/· filtered by the Bowman's capsule i-e 120ml) { remaining passes through the Glomerular capillaries)

Filtration Fraction :

Fraction of Plasma flow which has been filtered.

$$F\cdot F = \frac{G\cdot F\cdot R}{Renal\ Plasma\ Flow} = \frac{120}{600} = \boxed{0.2}$$

$$Kf = \frac{120}{10} = 12\ ml$$ of the fluid is filtered per mmHg/minute/ Total glomeruli in Total renal substance of both Kidneys

(For 10mmHg Pressure they make 120ml of filterate } for 1mmHg 12ml/ of Pressure) per min.

weight of one Healthy Kidney = 150 gram

∴ Both Kidney = 300 gm

If 300 gm of Kidney filtered 12 ml. of Glomerular Substances, then from 100 gm of Kidney substance

300 — 12 . 51 ml/min

100 — 4 : ?

$\frac{100 \times 12}{300}$: ?

4 = x (a value about 400 times as high as the Kf of most other capillary system of the body)

? ($K_f = \frac{12}{3} = 4$ ml.).

Kf (Filtration co-efficient)

diseases which reduces permeability ↓

Hydrolic conductivity or Permeability of G. membrane

Glomerular capillaries is Thickened membrane) ∴ Kf ↓

→ Diabetes Mellitus (protenaceous material is deposited)

→ Hypertension (they destroy capillary Glomeruli → also ↓ surface area) function.

Total area of Gl. capillaries

→ chronic polynephritis (chronic inflammation of Kidney in which many Glomeruli destroy)

→ chronic Glomerulus Nephritis

Hydrostatic P in Bowman's capsule ∝ Glomerular Filteration rate.

Hydronephrosis: Due to pathological condition, the Hydrostatic P of Bowman's capsule inc. causes reduction of G.F.R. due to obstruction of Ca^{2+} or uric acid that lead to formation of stone in urinary tract or ureter (Distention ∴ Dilatation of renal Pelvis ∴ Calyces) can even damage or destroy the Kidney unless obstruction is relieved.

(Renal Blood Flow ∝ G.F.R ∝ N.F.P
G.F.R)

GFR = N.F.P x Kf (almost remains constt)

- $P_{G.C}$ — Hy. Pressure of Glomerulus capillaries
- $\pi_{G.C}$ — colloid osmotic Pressure of Glomerulus capillaries.
- $P_{B.C}$ — antiosmotic pressure
- $\pi_{B.C}$ — They are normally zero.

(the arterial Plasma colloid osmotic pressure) ↓ antiosmotic pressure

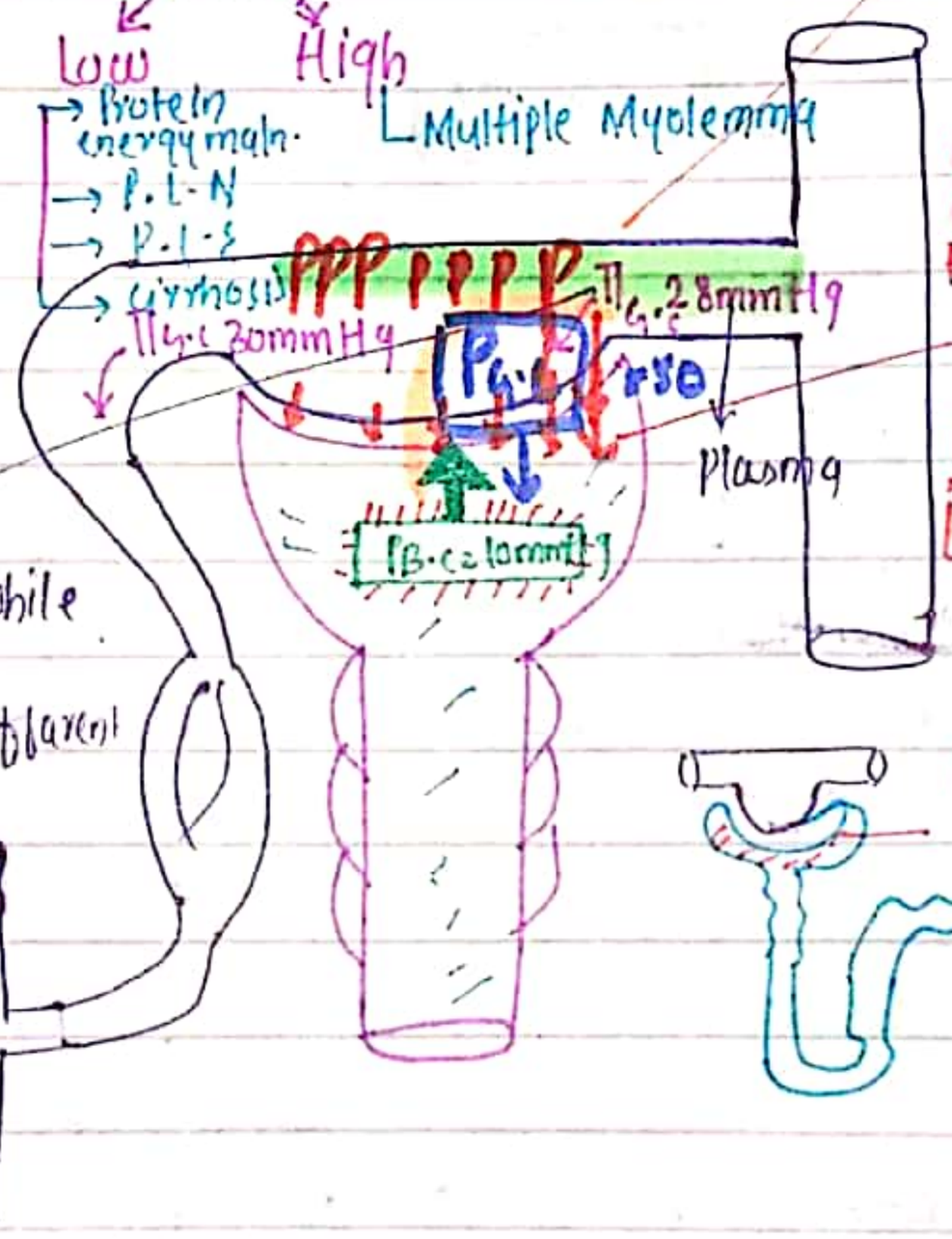
Pressure Filtration

Fraction Filtration

If there is accumulation occurs at urinary drainage then it cause ↑ Hyd-P of Bowman's capsule which ↓ the Tubular flow.

Low
- Protein energy malnutrition
- P.L-N
- P.L-S
- Cirrhosis

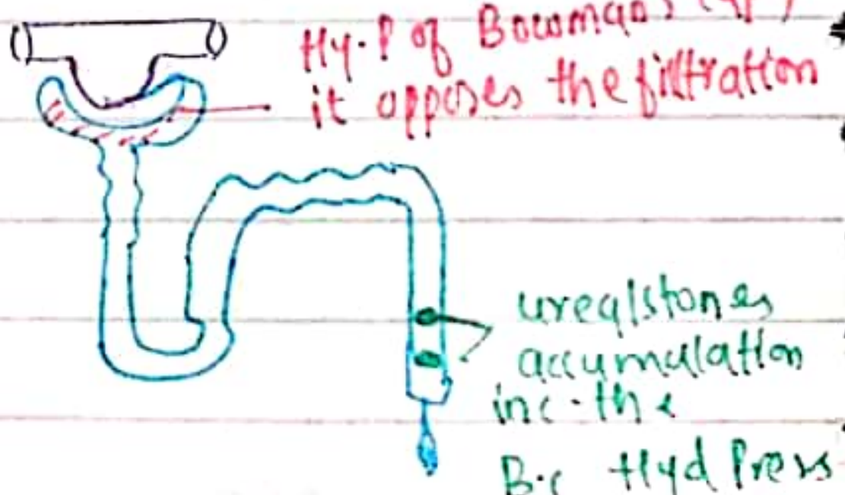
High
- Multiple Myelomma



when blood is entering $\pi_{G.C}$ is 28 but when it leaves it bcm 32.

When there is obstruction back P is coming ⇒ don't allow the filtrate to move forward.
G.F.R ↓ cause Renal Failure ⇒
POST RENAL FAILURE

In Plasma, only fluid is filtered while Plasma protein is not.
(In Gl. capillaries near the efferent more filtration occurs while onward filtration dec. (progressively Plasma protein bcm more concentrated.) so colloidal osmotic P ↑ on E. Art.



Renal failure (3 cause)

⇒ **PreRenal Failure** : (If due to some circulatory shock, Blood doesn't reaches the Kidney, then this is Prerenal failure bcz Kidney is Normal)

⇒ If Nephron is ok, Glomeruli is okay, but urinary drainage ~~subs~~ system doesn't work then it is **Post Renal causes**.

⇒ May be due to Renal causes or prblm due to Renal Substances.

How colloid Osmotic Pressure of Glomerulus capillaries can alter the Glomerulus Filtration Rate?

Normal $\pi_{G.C}$ = 30mmHg (opposing P)

* $\pi_{G.C}$ ↑ then G.F.R will be dec.

Depends on Total Plasma Protein Level.

→ If P.P.L ↑ the G.F.R also ↑.

In **Hypoprotenamia** which causes Cirrhosis => liver is not able to synthesize enough **Plasma Protein.** { grp of diseases called **Protein losing Enteropathy.** (diseases in which proteins are too much lost frm GIT) { this condition patient will develop Hypoproteramic { liver bcm cirrohtic **(Protein loosing Nephropathies)** when G.m is too much permeable.

* If T.P.P ↑ (condition called **Multiple Myolemma**) malignancy of the Plasma cells they produce abnormal protein. Too much abnormal proteins { Normal Protein in Blood causes Myolemma (so Total Plasma Protein will be high. Blood may bcm visious. In this condition, $\pi_{G.C}$ may be high that will oppose G.F.R.

→ If filtration fraction is more, it means out of plasma big amount is filtered, now plasma protein is highly concentrated, more colloid osmotic pressure in G.C that opposes further filtration, if plasma (in which less amount is filtered) less filteration fraction, less $\pi_{G.C}$.

$P_{G.C}$ (Hydrostatic Pressure)

Systemic Blood Pressure / Arterial Pressure

* Whenever S.B.P ↑, the $P_{G.C}$ increases, which ↑ Glomerular (G.F.R) capillaries P.{ by decreasing it ↓.

Resistance offered by Afferent arteriole

→ Due to constrictions less blood will coming through it causes:

↓ G.B. Flow
↓ G.P. Flow
↓ $P_{G.C}$ (Hydro static Glomerular P) [bcz less blood comes in arterioles { capillaries]
↓ N.F.P
↓ G.F.R

Resistance offered by Efferent arteriole.

α_1 (Androgenic Receptors) present (rich) in Afferent arteriole which can be stimulated by Epinephrine { Norepinephrine (Sympathetic Stimulation)

* Epinep + N.Ep.Nep
* Endothelin (also stimulates androgenic receptors).

(Peptide release from damaged vascular endothelial cells of Kidney

Endothelin level in Plasma is also high in.

→ Acute Renal Failure
→ chronic Renal Failure / uremia
→ Pregnancy Induced HyperTension. / Toxemia of Pregnancy.

If Afferent Arteriole Dilation occurs causes:
↑ G.B Flow, ↑ G.P.F, ↑ $P_{G.C}$ F, ↑ N.F.R, ↑ G.F.R.

Dilators are:
→ Bradykinin
→ Prostaglandin
→ NO.

During Stress, In severe Sympathetic Stimulation there is release of Epinep } Nor-epin. which constrict the afferent arteriole.. so powerfully that G.F.R drops (To protect Kidney, it releases prostaglandins which causes some aff. arteriole to dilated so, that G.F.R will not drop { protect Kidney failure. In such patients if we give **NSAIDs** (Non-Steroidal Anti inflammatory Drugs) then such patients not able to produce prostoglandins there will be intense constriction, G.F.R ↓ } kidney failure occur.

Hydrostatic Pressure ($P_{G.C}$) in Glomerulus capillaries is opposed by colloid Osmotic Pressure ($\pi_{G.C}$) of the Plasma Protein Powerful Efferent Art. constricter is **(Angiotensin II)**

Dilation

- ↓ $P_{G.C}$ (bc2 blood moved Towards E.A)
- ↓ G.F.R

+ See Graph on pg(335) Guyton

Constriction

→ Moderately constriction
- ↑ $P_{G.C}$
- ↑ G.F.R.

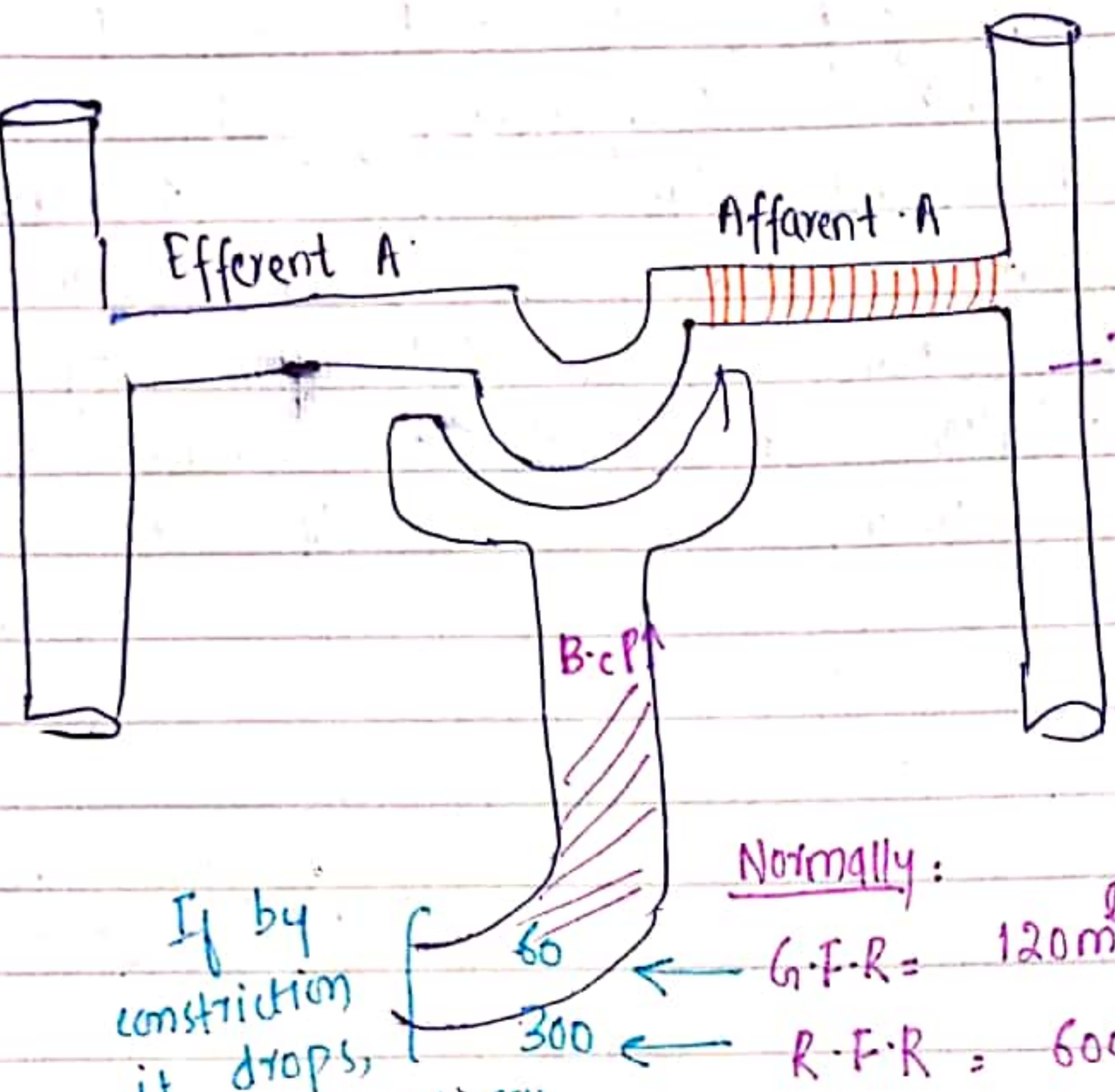
→ Severe condition (constriction more than 3 fold).
- ↑↑ $P_{G.C}$.
- ↑ Filtration Fraction.
- ↑↑↑ $\pi_{G.C}$. (Glomerular Blood flow ↓)
- ↓ N.F.P (due to ↑ $\pi_{G.C}$) (causing a reduction in G.F.R)

Filteration Fraction: From total Plasma, how many percentage of solutes are filtered.

Glomerular Filteration rate : fitered substances (Plasma).

* On a per gram weight basis, Kidney normally absorb oxygen at Twice the rate of brain but have almost seven times the blood flow of brain. (If G.F.R ceases, Renal Na^+ reabsorption also ceases } O_2 consumption ↓ to about one fourth of Normal). **(Graph 27.8 pg 336).**

Lecture #6



If by constriction it drops, then proportional dropping in both occurs that doesn't chang Fitration Fraction.

$= \frac{60}{300}$

$= 0.2$

Normally:

G·F·R = 120ml/mint

R·F·R = 600ml/mint

$F.F = \frac{120}{600} = 0.2$

Parameter	Renal Flow	G·F·R	Filtration Fraction
Aff. Art. constricter (EpiN / Nor. epine)	↓	↓	No. change
Aff. Art. Dilation Eff. Art (const/moderate)	↑ ↓	↑ ↑ (Power P in G. capillari)	No change ↑
Eff. Art const (Severe)	↓	↓↓↓ (Bcz Plasma is already fitered & due to Too much πG·c it not occurs a gain)	↓
ToTal Plasma Protein↑	No. change	↓ (Bcz ↑ colloid osmotic P in G.c which opposes filtration	↓

→ caffeine ↑

a) R·P·F ↑, G·F·R ↑, F·F (No chnge)
B) R·F·F ↓ , G·F·R ↓, F·F (")
c) R·P·F ↑, G·F·R ↓, F·F (chng occur).

→ If G·F·R = 600,
R·P·F = 600
F·F = 60 / 600 = 0·1

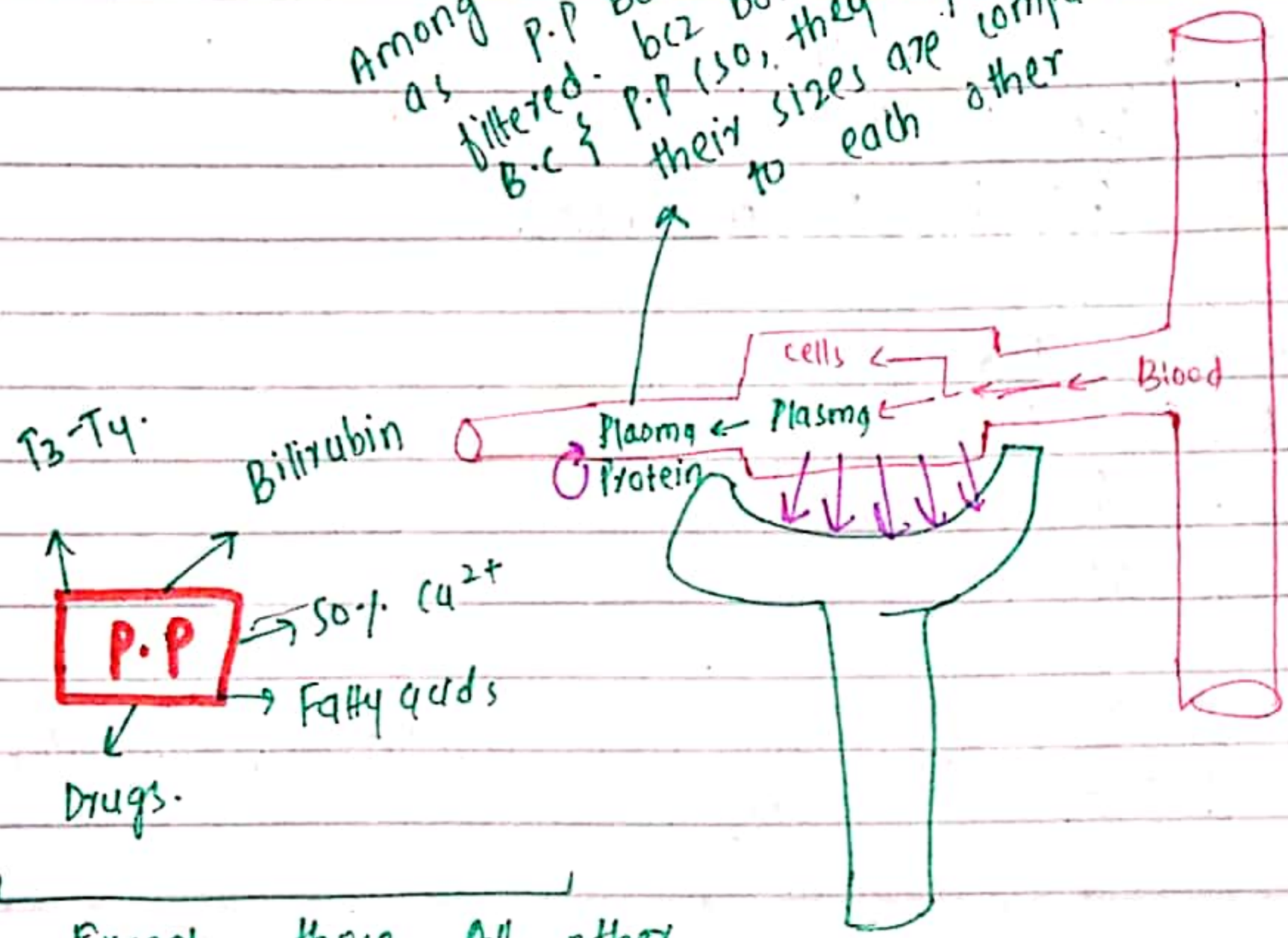
↑F. Fraction = ↑ G·F·R / ↓ R·F [It means more filterate, frm plasma occurs].

Total Plasma Protein ↓	No chng	↑	↑
Ureteric constriction (more P in Bowman's capsule occurs)	No chng	↓ (P in B.C ↑ which is the opposing F for filteration)	↓

Substances Filtered:

(Amout of substances which are fitered from vascular component (G·C) to the Bowman's capsule)

Among Plasma, Plasma Protein as well as P.P bound substances are not filtered. bcz both the neg. charges of B.C & P.P (so, they repel) although their sizes are comparable to each other



Except those All other substances are filtered.

→ H_2O

→ Major Electrolytes → cations → Na^+, K^+, Ionized Mg^{2+}.
→ Anions

→ Metabolic wastes → urea, creatinine

→ Metabolites → Glucose, Amino acids, Organic comp. Ketone Bodies

→ Low Molecular Weigh Protein → Insulin, Haemoglobin.
It moves into the P.C.T from B.C { here it fit breakdown use in formation of glucose (Gluconeoge. nesis → Gluc. formation frm Non-~~carbohydrate~~ carbon (fatty acids etc) compound)

Hb is not present in free form, if RBCs rupture occurs then it freely moves as Diamer & entered P.C.T causes some Renal damisease.

→ Non-Natural Substances ⟶ Inulin, Paramino Hippouric Acid (PAH)

Inulin → use to find G.F.R

PAH → for R.B.F.

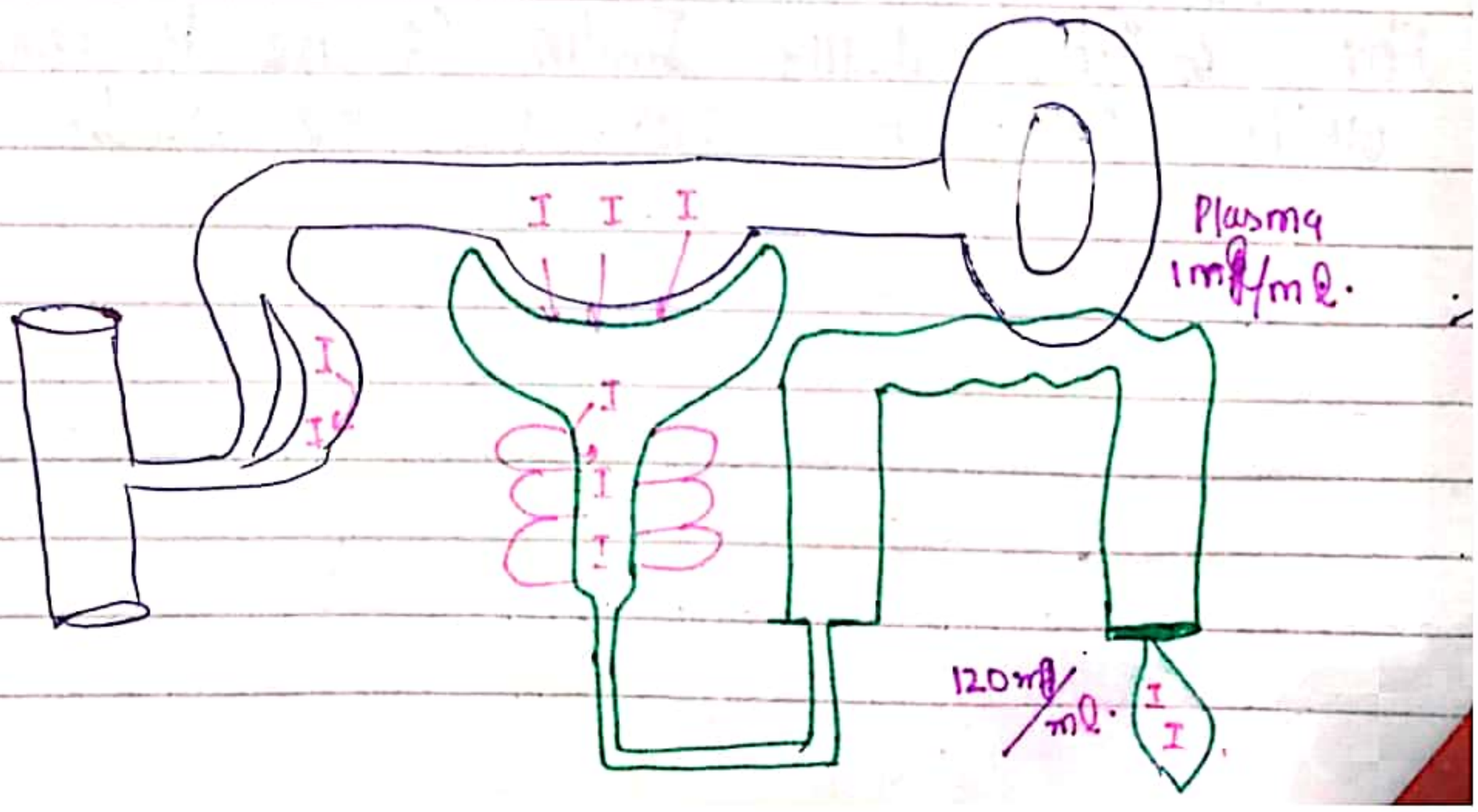
Lect#7

Measurement of G.F.R

By Inulin

→ Non-Toxic Substance
→ No Protein Binding
→ No charged molecule
→ Small molecule.
→ No reabsorption
→ No secretion.

Freely Filterable



Inulin conc. in Plasma Protein

Filtered load of urine = Urinary Excretory load of Inulin

$$P_{[Inulin]} \times G.F.R = [U]_{Inulin} \times V$$

($[U]_{In}$ = urine, Inulin concentration; V = volume of urine in which Inulin present.)

→ Inulin is Neither absorbed, Not secreted Therefore must be equal to each other.

1 ml of Blood containing 1 ml of Inulin.

$$G.F.R = \frac{[U]_{Inulin} \times V}{[P]_{Inulin}}$$

$$= \frac{120\,mg/ml \times 1}{[1\,ml)}$$

$$= 120\,ml/mint.$$

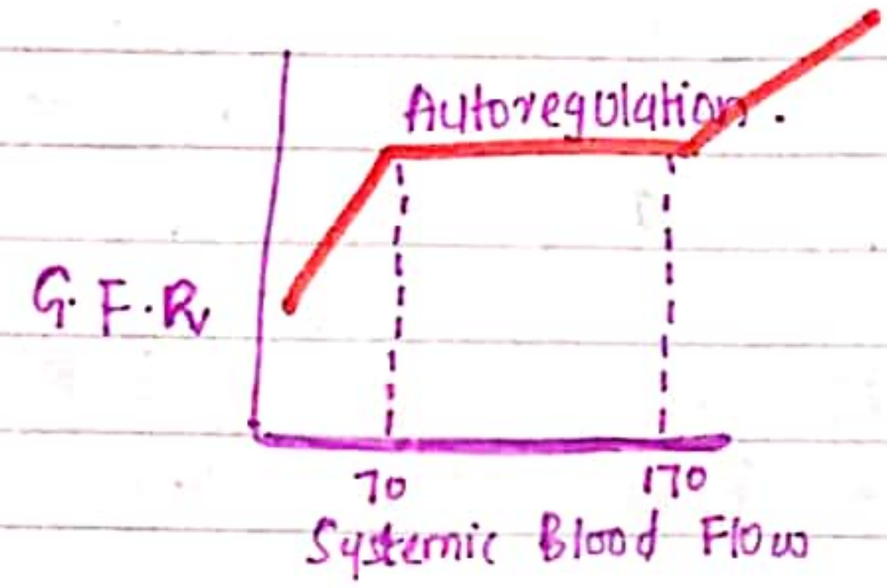
But if, amount of Inulin is 2 ml per ml of blood the G.F.R is 60 ml/min.

$$= \frac{120 \times 1}{2} = 60ml/mint.$$

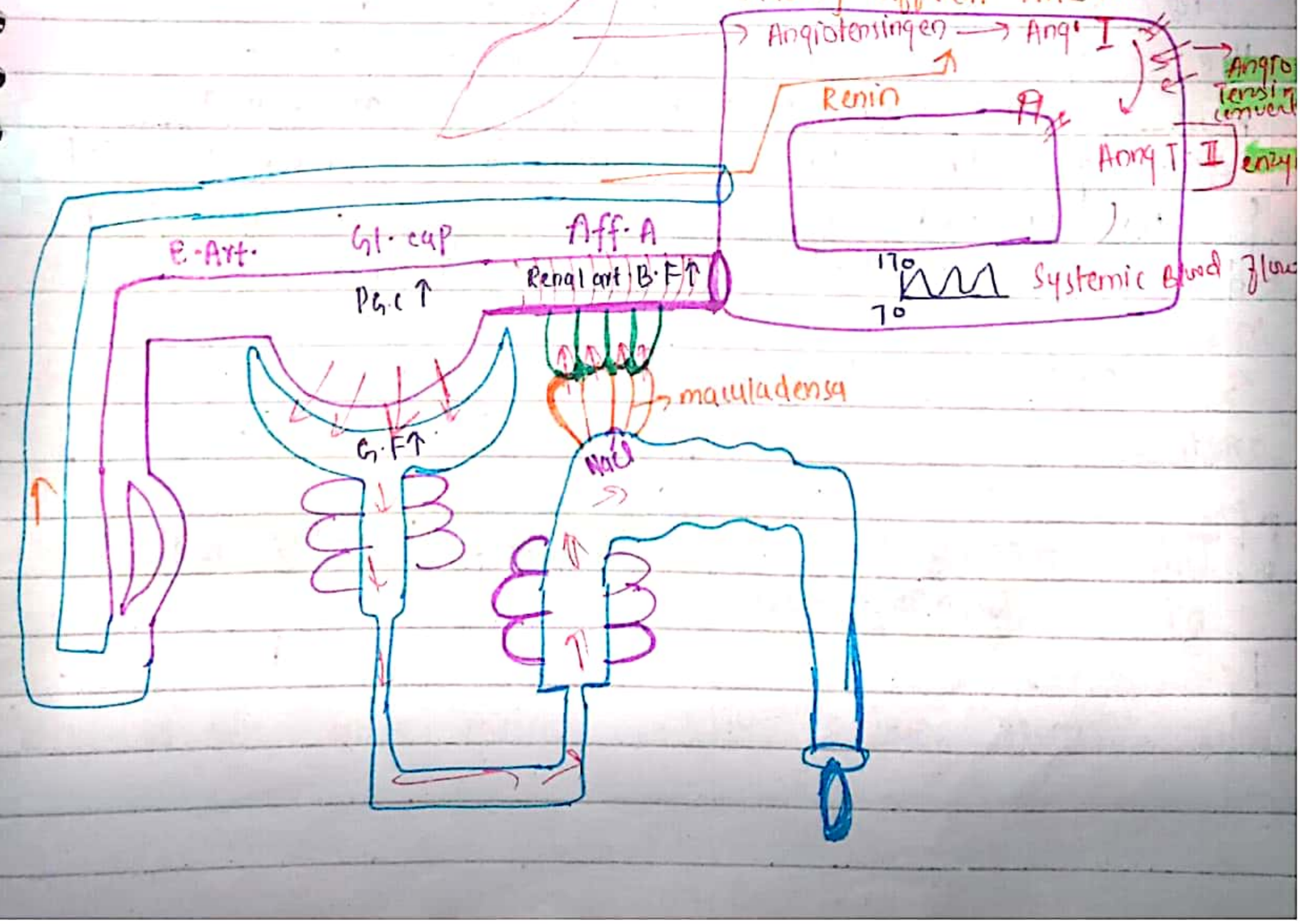
For G.F.R, ideally Inulin is use to measure, while creatinine can also be used.

Autoregulation of GFR & Renal Blood Flow

Acc. to us, when Systemic B.P ↑ the R.B.B.Flow ↑ { Glomerular Filtration ↑ same in case of dec. but actually when Systemic Blood P ↑ from 70 - 170 then G.F.R constant while below 70 it dec. { above 170 it increases.



* In the begining, G.F.R also ↑ but for immediate effect due to which Tubular flow ↑ but there is less extraction of solutes P.C.T as well as Ascending limb due to which at the start of D.C.T NaCl accumulates which causes. excretion of product frm macula dense causing Afferent Arteriole constricti



By macula Densa product, Afferent arteriole constriction occurs as well as the efferent art. Dilation occurs by reduce production of Renin due to less Angiotensin II. ~~less~~ dilation of efferent art. occurs. causes the G.C pressure as well as G.F.R to Normal.

* In the beginning when A. arteriolar constriction occurs, then the smooth smooth muscle surrounding the A. Arteriole also constrict by calcium moving inside through Ca^{2+} sensitive gates present in smooth muscles. called myogenic mechanism.

Similarly, all mechanism reverse in dropping B.P instead of A. arteriole constriction Now A. arteriole Dilation occurs.

→ When Systemic B.P ↓, A. Renal artery B. flow ↓, P.G.C ↓ due to which ↓ G.F.R by ↓ G.F.R the speed of Tubular flow will be decreased { more solute (NaCl) extraction frm P.C.T as well as Ascending limb so no accumulation of NaCl at D.C.T } No production of any substance frm macula densa But more production of renin occurs. which flows into the systemic circulation cause more production of Angiotensin II which further constricted efferent arteriole { P.G.C become Normal ↑ } ↑ G.F.R also ↑ } process revise again.

[This mechanism is or **Autoregulation**]

Tubulo-Glomerular Balance

Person Taking more meat, then it cause ↑ G.F.R (bcz more amino acids), amino acids can be

reabsorb with the Na+, co Transport occur. Due to which No accumulation of Nacl occur. The glucose also excreted by co. Transport with Na+.

Lec # 8

Processing of Glomerular Filterate

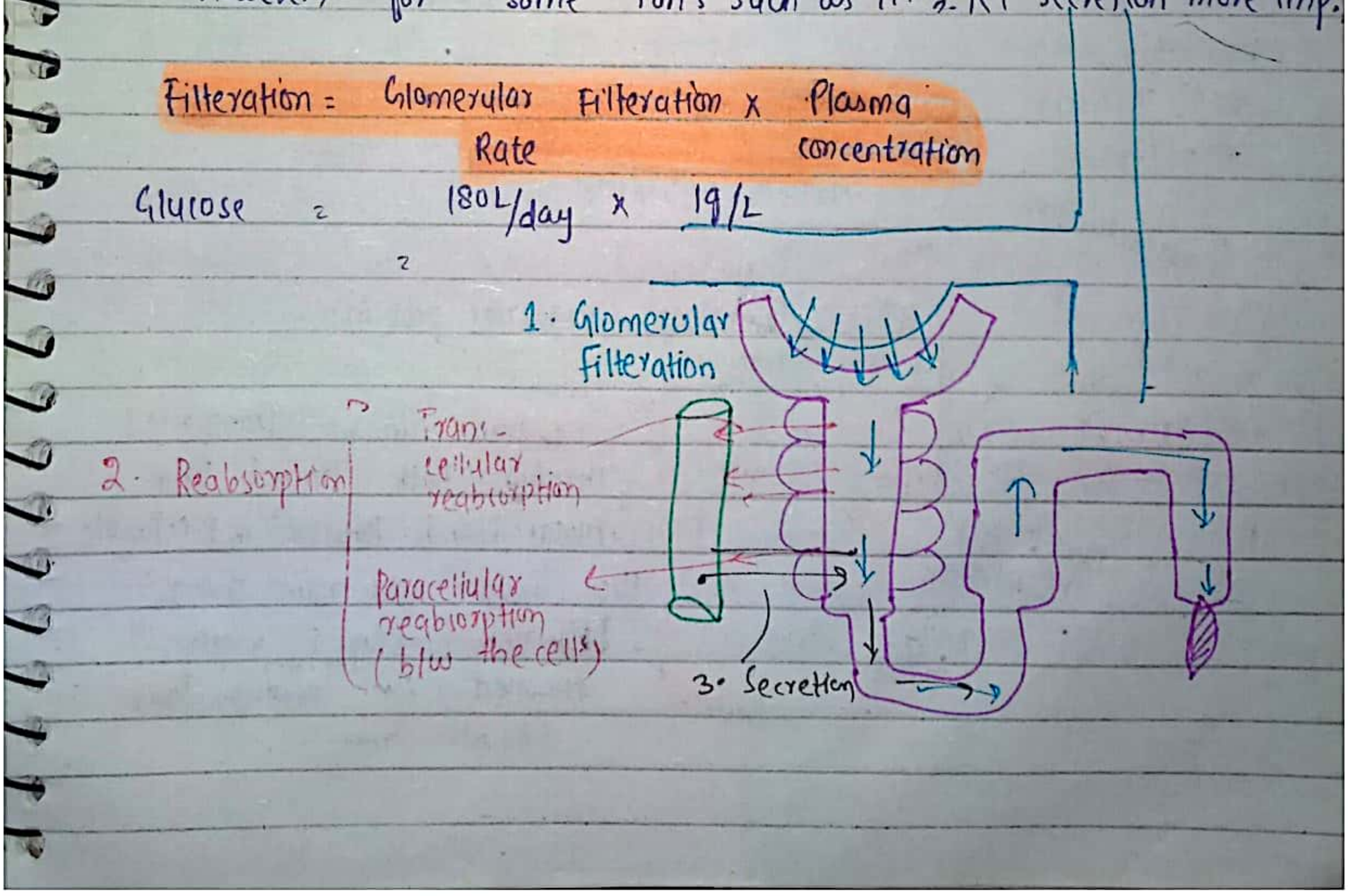
First step in urine formation is
1) Glomerular Filteration
2) Tubular reabsorption
3) Tubular secretion.

Urine Excretion = Glomerular Filteration − Tubular reabsorption + Tubular secretion

* Tubular reabsorption plays an important role than Secretion, However, for some ions such as H+ & K+ secretion more imp.

Filteration = Glomerular Filteration Rate × Plasma concentration

Glucose = 180L/day × 1g/L



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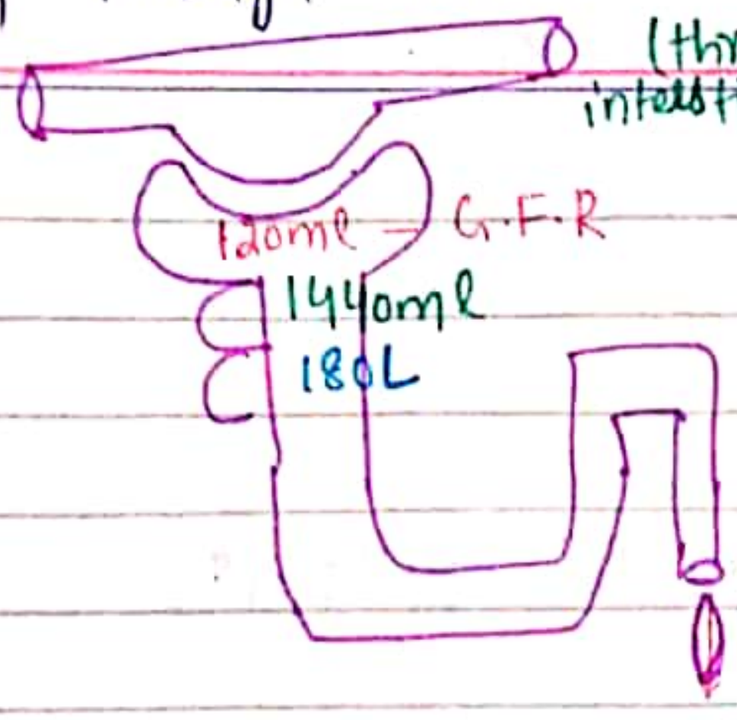
Reabsorbtion

1) from Tubular epithelial membrane into the renal interstitium
2) through Peritubular capillary membrane back into Blood. Transport into (through A Trans/Para cellular interstitium } then through Bulk flow into the Blood.



G.F.R = 120 ml/mint → (ultrafiltration)

Q: How much in ONE Day? ↓

1 Day = 24 hrs
1 hr = 60 mint

Day = 24 x 60 = 1440

G.F.R = 120 x 24 x 60
= 1440 x 120
= 172800 ml/Day
= 172 L/Day.

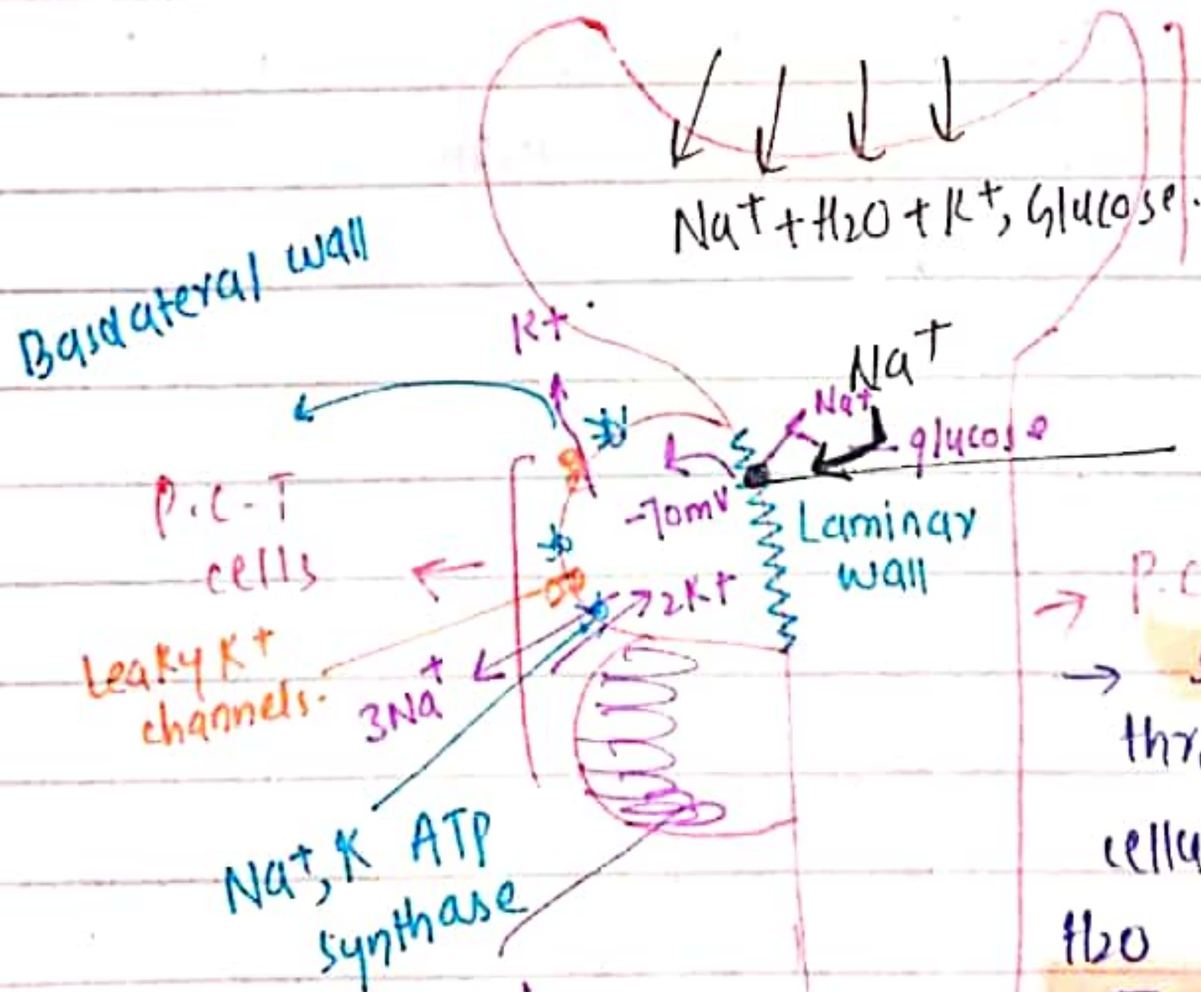
(facilitated by Hydrostatic } colloid osmotic pressure.

120 ml/mint.
144 ml/mint
144 ml/mint

Average G.F.R 125 - 180 L/Day 1.5L

For 180L = 1.5 L
less than 1.5L → oligouria
More than 1.5L → Polyuria.

It means 99% of Glomerular filterates are reabsorb while only 1% are excreted through urine.



→ P.C-T

→ Sodium can be Transported through both Trans { Para-cellular memb. However, in P.C. Tubule H2O reabsor max. occurs through Transcellular membrane { water dissolved ions (K+ } Cl-) through Para cellular mem

Trans-

* 65% of the Gl-Filterate is reabsorb in P.C.T.

* If 100ml G.F then 65ml reabsorb here.
* Here 100% reabsorption of ~~NaCl~~ & aminoacids { Glucose occur. while 65% of ~~glu~~ NaT along with chlorine and H_2O occurs!

→ P.C.T cells have luminar wall containing Brush like ~~mic~~ bodies for more absorption { also have Basolateral wall containing **Na^+, K^+ ATPase.** (having capability of binding Na^+, K^+ { breakdown of ATP)

(**Primary A. Transport**) ATP —< **Primary A. Transp** (By direct use of ATP)
Sec. A. Transport (Indirect use).

→ By Na^+, K^+ Atpase. Na^+ moves outside from the intracellular area against the concentration gradient. while K^+ move inside. more electroneg. take place leading to constipation, while thre is also K^+ leaky channels in Basolateral wall through which few K^+ also moves out.

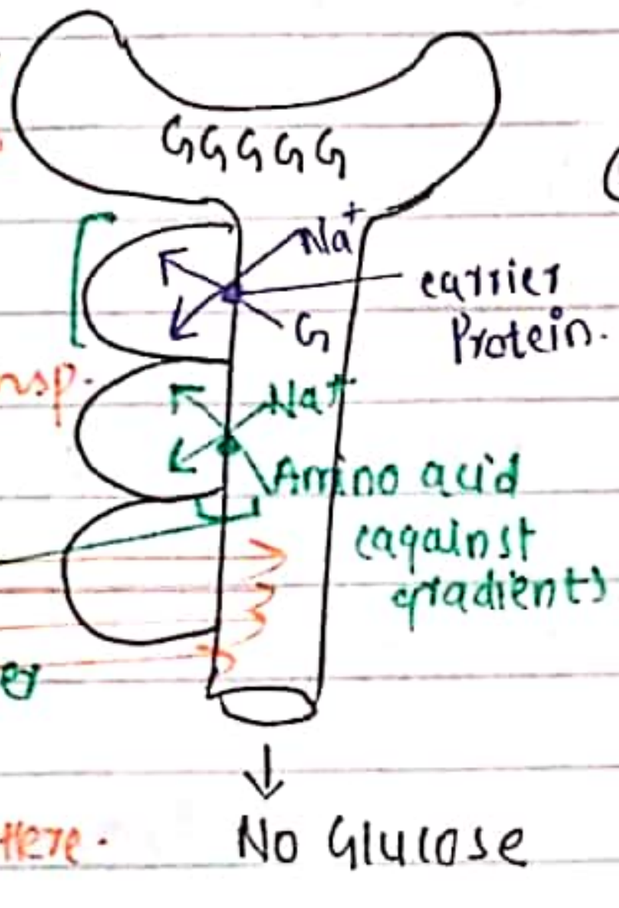
-> However, in the P.C.T the Na^+ conc. is more which can be Transported through the laminar wall into the P.C.T cells. bcz it is along the conc. gradient { 2ndly it is (+ve) charge which can be attracted by the negative intracellular cell. But laminar wall doesnot allow it directly with the help of carrier protein it will move inside through **facilatated Diffusion.** with the co Transp. ort of Glucose.

65% Na^+, 65% H_2O, 100% Glucose | 100% A.A, Cl^- almost 60-65% | Reabsorb by Proximal con. Tubules

Na^+ carrier protein → Passive Transport → No ATP.

Na^+, K^+ ATP Synthase → Active Transport → ATP

Probenecid (Drug) block the cellular Transporter due to which Na^+, Glucose no Transporter Penicillin is Transp. in the Lumen.



Glucose reabsorby the P.C.T cells, so, many of them are present in P.C.T cells and less conc. in Tubular area so, it needs energy for its Transport along with Na^+, coTransport But the energ for this is coming from the Na^+, when moving inside release energy by see. active Transport.

→ Mitochondria present in Basolateral wall has which provides energy for the Na^+, K^+ ATPase.

→ For Glucose, Amino acids Transportation from the P.C.T cells, channels are present that allow it to move in any direction. but due to higher conc. inside so it will moving outward. called. facilatated Diffusion.

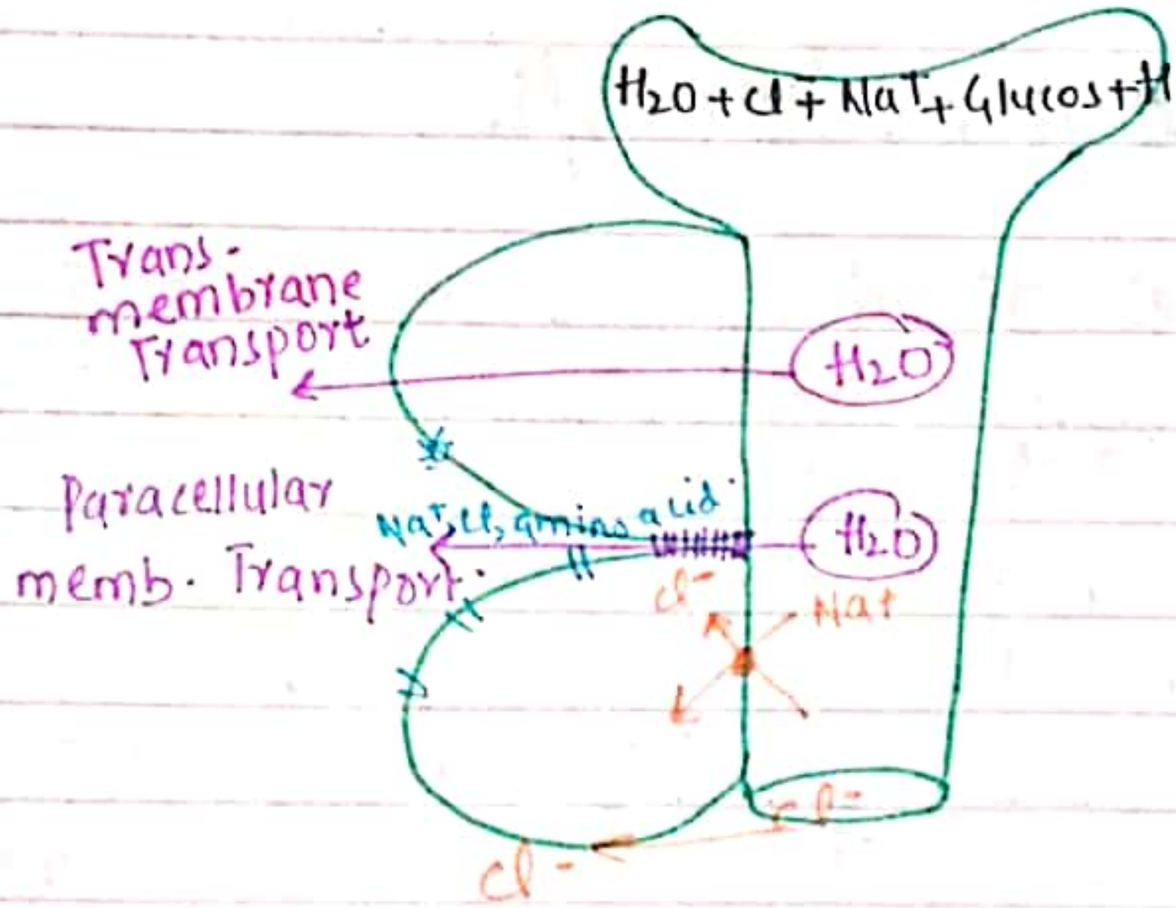
Na^+ → from Tubule into P.C.T cells by carrier Protein (facil. Diff.)

from P.C.T C into interstitial cells (extracellular fluid) → Primary Active Transport (Na^+, K^+ ATPase)

Phosphate reabsorption ~~is~~ stop by Harmone (Parathyroid Harmone) & calcium.

Glucose/Amino acids → frm Tubule into P.C.T (by Sec. Active Transport) frm P.C.T. cells → Int. Flwd by (Facilitated diffusions/channels)

The first part of the P.C.T is bcz in taking Na^+ with Glucose while the latter part can take Na^+ with Cl^- & till last part the Tubular procen bcm concentrated. Now Cl^- moved through passive Transp.



* Along with H_2O, moving inside the cell, some of the solute present in tubular cells ~~moved~~ in interstitial cells along with H_2O called **Bragg solvent Mechanism**

Cl^- → Secondary Active Transport (co-Transport with Na^+)

passive Transport (In the End part)

Na^+ → Primary Active Transport (frm P.C.T → Int. cell)

K^+ → (frm Int. cell → P.C.T)

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Lecture 79

HCO_3^- (alkali) is use to maintain the normal pH = 7.4

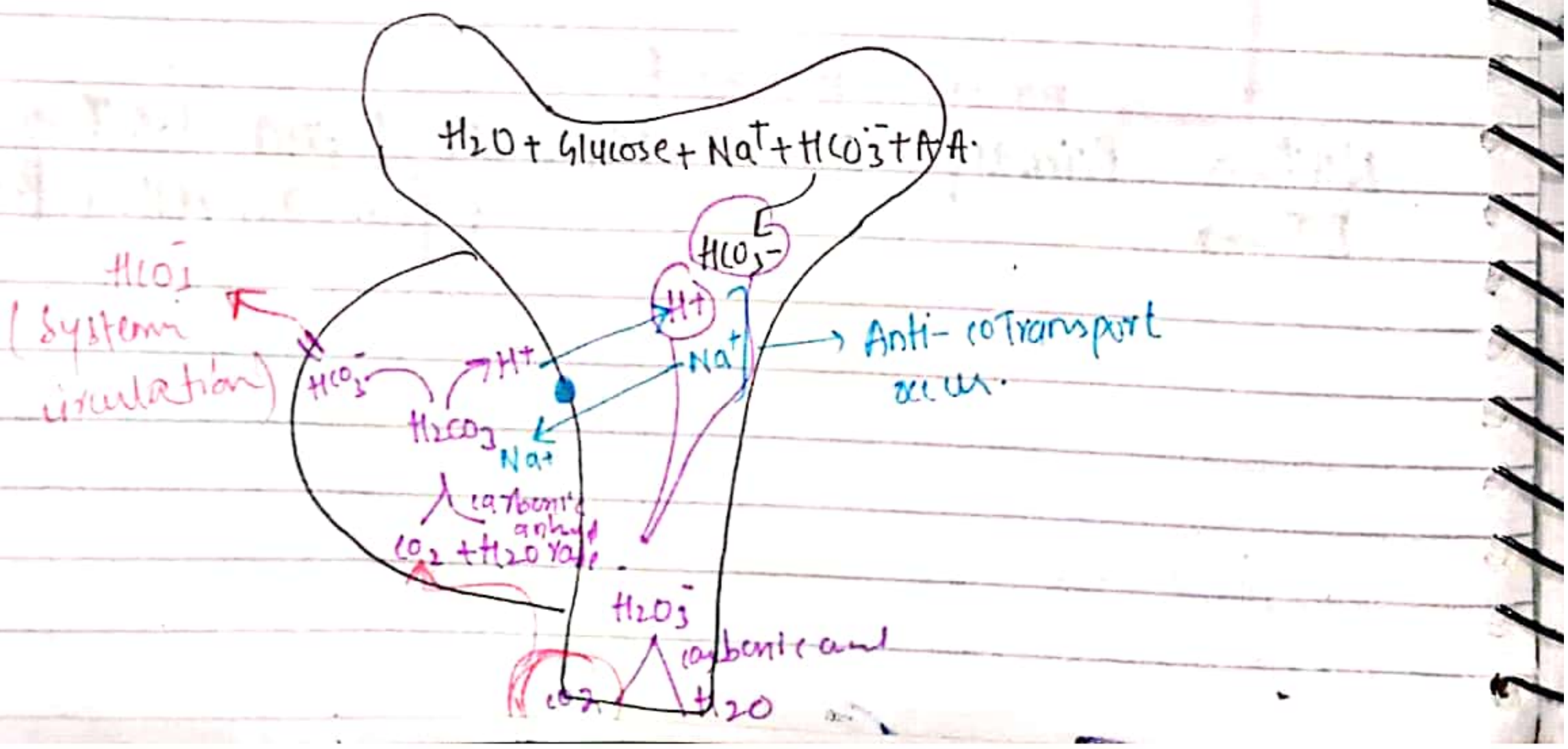
Why it is necessary to maintain pH?

pH is use to maintain the protein structure. ↑ H^+ conc. destroy the protein folding while ↓ H^+ conc. } ↑ $-OH^-$ causes abnormal folding. Due, to which we can't get normal enzyme for functioning.

Normal H^+ (proton) conc. = 40neq/L

Kidney is the master gland for production of Bicarbonate (HCO_3^-) as well as its conservation also take place here.

→ HCO_3^- present in Blood are always in threat of destruction bcz CO_2 removed from our cells in body form carbonic acid (H_2O_3) with H_2O which is split by carbonic anhydrase } its (H^+) then again combine with. bicarbonate



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Na^+ → from P.C.T cell → To Tubular cells] Passive Transport
Facilated Diffusion

H^+ → from P.C.T cell → Tubular cells] See. Active Transport

Na^+ / H^+] Anti. Co-Transporter

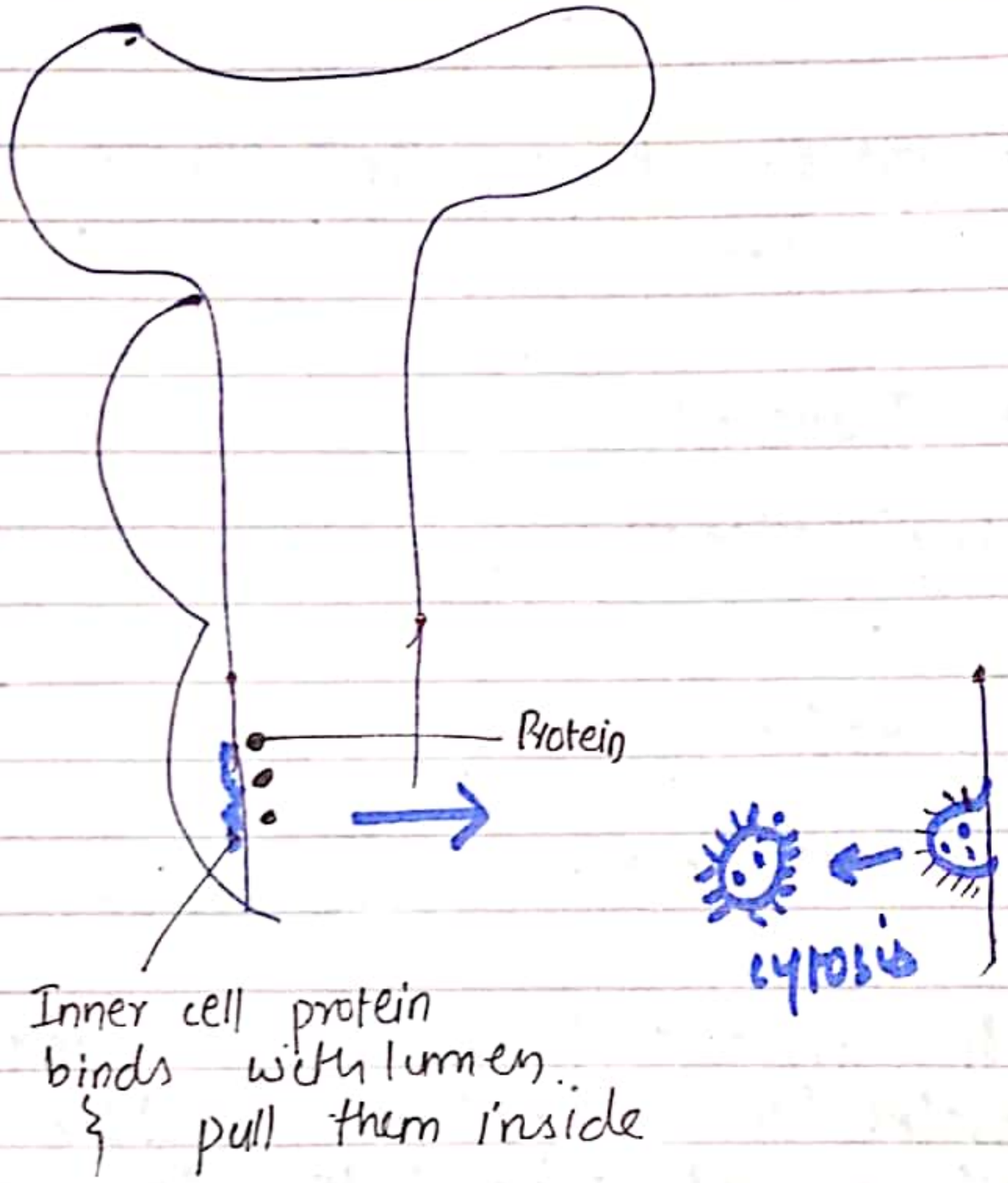
HCO_3^- → moves out frm P.C.T cells to interstitial cells]
Passive Transport

- Active Transport
  - → Primary active Transport
  - → 2ndry Active Transport
    - → Cytosis (Endocytosis) (Pinocytosis)

Kidney has major function in catabolism of low molecular weight protein (like Insulin etc.) which catabolise to Glucose moves into the body.

→ In Normal Human urine, almost negligible protein is present in abnormal state when protein enters it totally reabsorb by proximal cells.

In case of Hb, (rupture of RBC) then Hb also filters through Bowman's capsule, when it passes through the P.C.T it passes into the P.C.T cells. the Fe^{+} of Hb destroy mitochondria causes destruction of P.C.T cells.



* Some substances which are reabsorb frm lumen to the cellular side of P.C.T attain the condition of Transport maximum (at which further capability of lumen to Transport extra solutes / substances vanishes. In case of Diabetes mellitus, Further Glucose is not reabsorb by P.C.T (above its limit) then some glucose

passes through the urine.

Nat doesnot have only one way to reabsorb like Glucose which can reabsorb only through the co-Transport with the the Nat while can reabsorb through multiple way by.

Na+, Glucose.
Na+, Aminoacids
Solvent Drag etc.

It doesn't depend on Tmax like Glucose. 97 at one point it is unable to reabsorb it can then reabsorb by another.

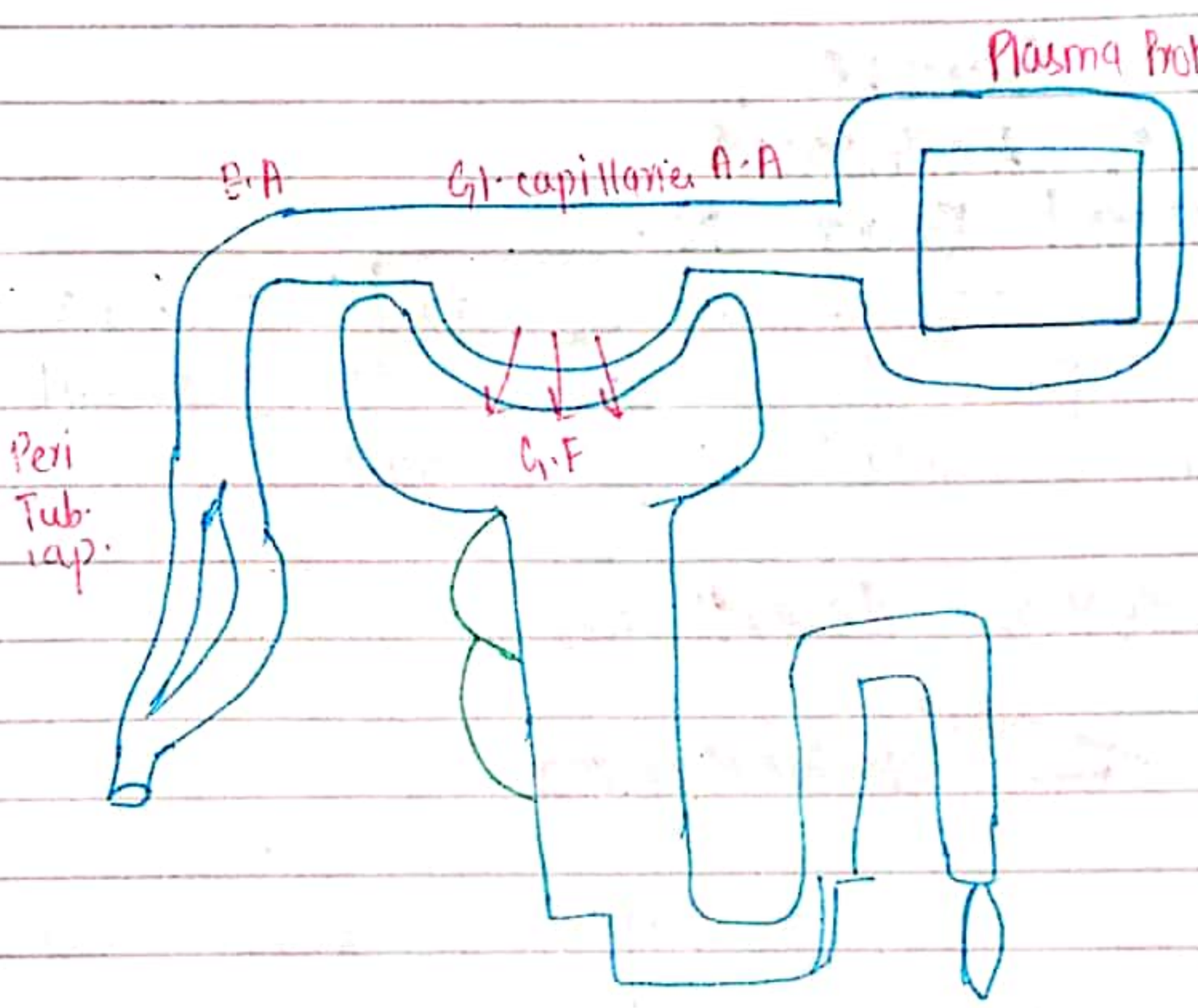
Na+ absorption depends on

→ Gradient ← conc electrochemical
→ Timing

(Bcz when Glomerul Fultration flows rapidly when it is in more conc. then it is less extracted by P.C.T cells) while when its conc.↓ then more NaT are extracted while in Glucose rather the Timing/conc. is more or less they will be totally extracted into P.C.T. cells from lomeru to pals interstitial cells.

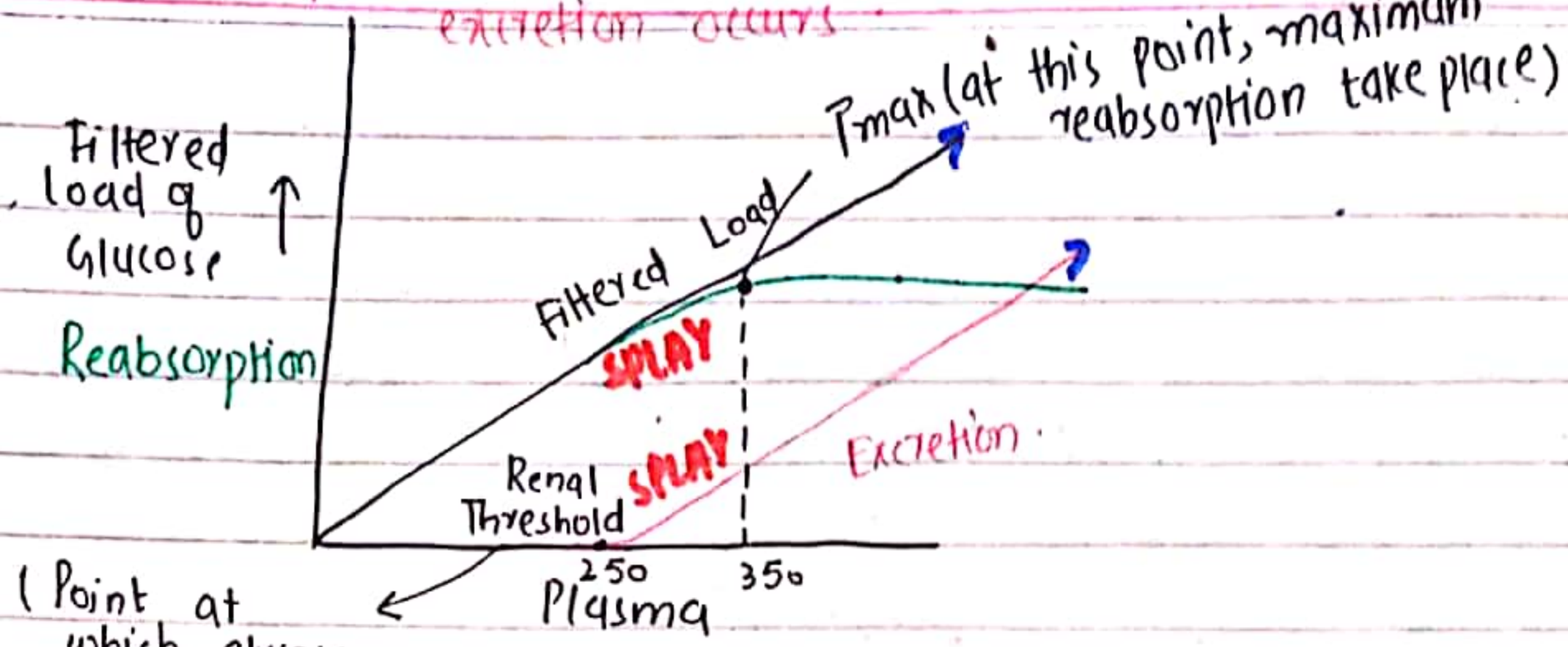
Lect #10

Glucose Titration Curve & Transport maximum (Tmax.)
(Relationship b/w Plasma glucose conc. with Filtered glucose, reabsorbed & excreted glucose)



* In Normal person, all the glucose present in systemic circulation are reabsorb by proximal convoluted Tubular cell through Na^+, glucose co Transporter
* But in abnormal situation, when Glucose conc. is too much high, a point reaches when further glucose frm glomerular filterate is not reabsorb bcz of Na^+, Glucose co-Transporters are saturated (booked). So in this case these extra glucose will pass through the excretion.

Plasma Glucose conc. ∝ Glomerular Filteration.
At certain point, Reabsorption not occur.
After a certain limit, when reabsorption stops then excretion occurs.



* The amount of Na^+, Glucose Transporter varies in each Nephron. Each one has different capability for Reabsorption..
→ Due to diff. capability of Nephron, the Renal Threshold is less than Tmax.

Reason of Splay
→ Heterogenity of Nephron
→ affinity of affinity Transp } some of the glucose deattaches from NaTG then attach to another one →.

Filtered load = [G] x G.F.R
glucose conc. in plasma protein.

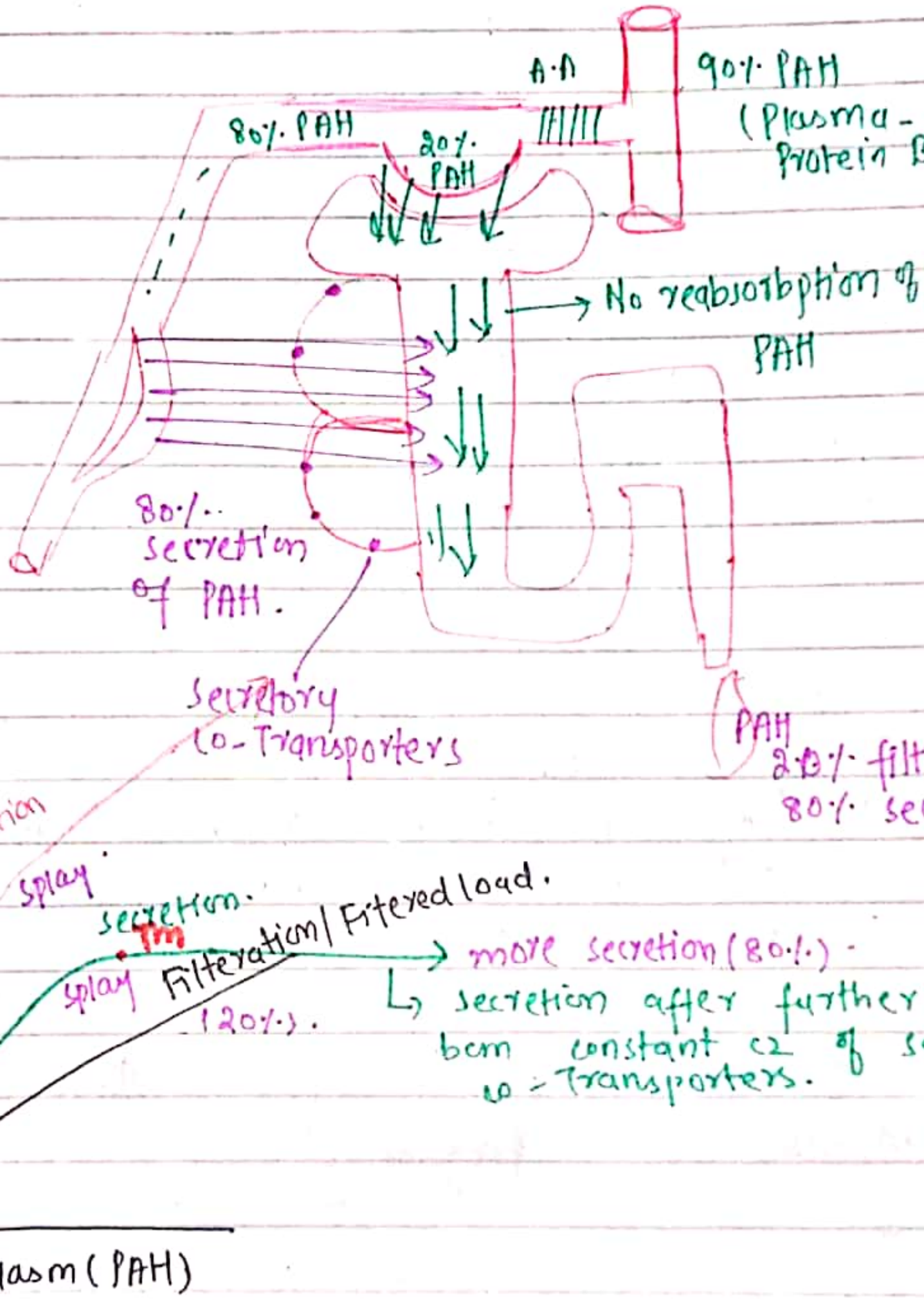
↑Filtered load = [G]↑ x G.F.R
Diabetes Mellitus const.

↑F.Load = [G] x G.F.R↑
Normal
Pregnancy

Filtered Load = [G] x G.F.R
(Normal) Norm Norm

* Here also glucose excreted in Urine ∵ of dyf. capability of Nephron here Renal Threshold is less than 250. ∵ less Na^+, glu ↓ Transporter

Para Amino Hippuric acid -> An example of excretory Substances (PAH)



* If there is too much conc. of PAH in plasma protein then some of it will also passes into Renal vein. & it is most imp. point to measure the Renal Blood Flow.

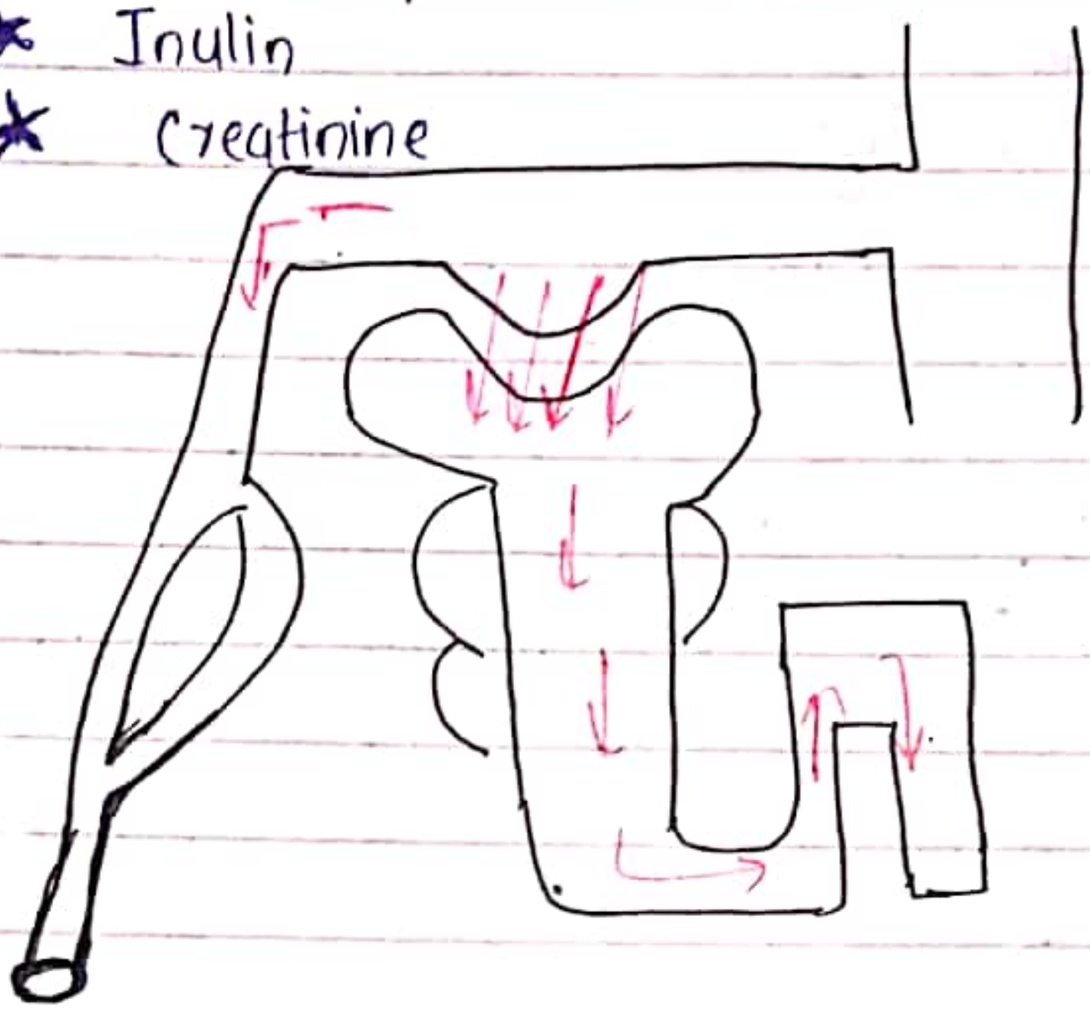
Net effects of reabsorption & secretion.

1. **Filteration** (No reabsorption & No secretion)
   Filtered Load = ×(Secretory)/ Excretory Load

Example:

Inert compounds like

* Inulin
* creatinine



2. **Reabsorption:**
   (As well as filteration, Reabsorption also occurs).
   Filtered Load > Excretory load.

Example:

* Glucose
* Amino Acids
* Na^+
* Cl^-

3. **Secretion**
   (Not reabsorption, only filteration & secretion occurs).
   Excretory load > Filtered load.

* All organic Acids
* PAH.

* Para Thyroid Harmone reabsorb calcium frm Distal convoluted Tube. It is (P·T·H) phosphate Trashing Harmone, it stops reabsorption of phosphate in P·C·T.

* **AngioTensin - II** also works on P·C·T due to which it ↑ Na^+ reabsorption, it is Vasoconstricter, produces/secrete Aldosterone & too many other functions.

* **Activation of Vitamin D**

Inactive Vit·D frm Skin then activate in P·C·T & then moved Towards Blood.

Sunlight ⟶ Fall on skin (Production of cholicalceferol) ⟶ goes to general circulation (Taken by liver) ⟶ In Hepatocyte there is enzyme it add -OH to the 25-Position of ascholecalciferol it is inactive

Blood ⟵ 1,25-OH cholcalcy· ⟵ Kidney P·C·T ⟵ α-1-Hydoxylase

Lecture:

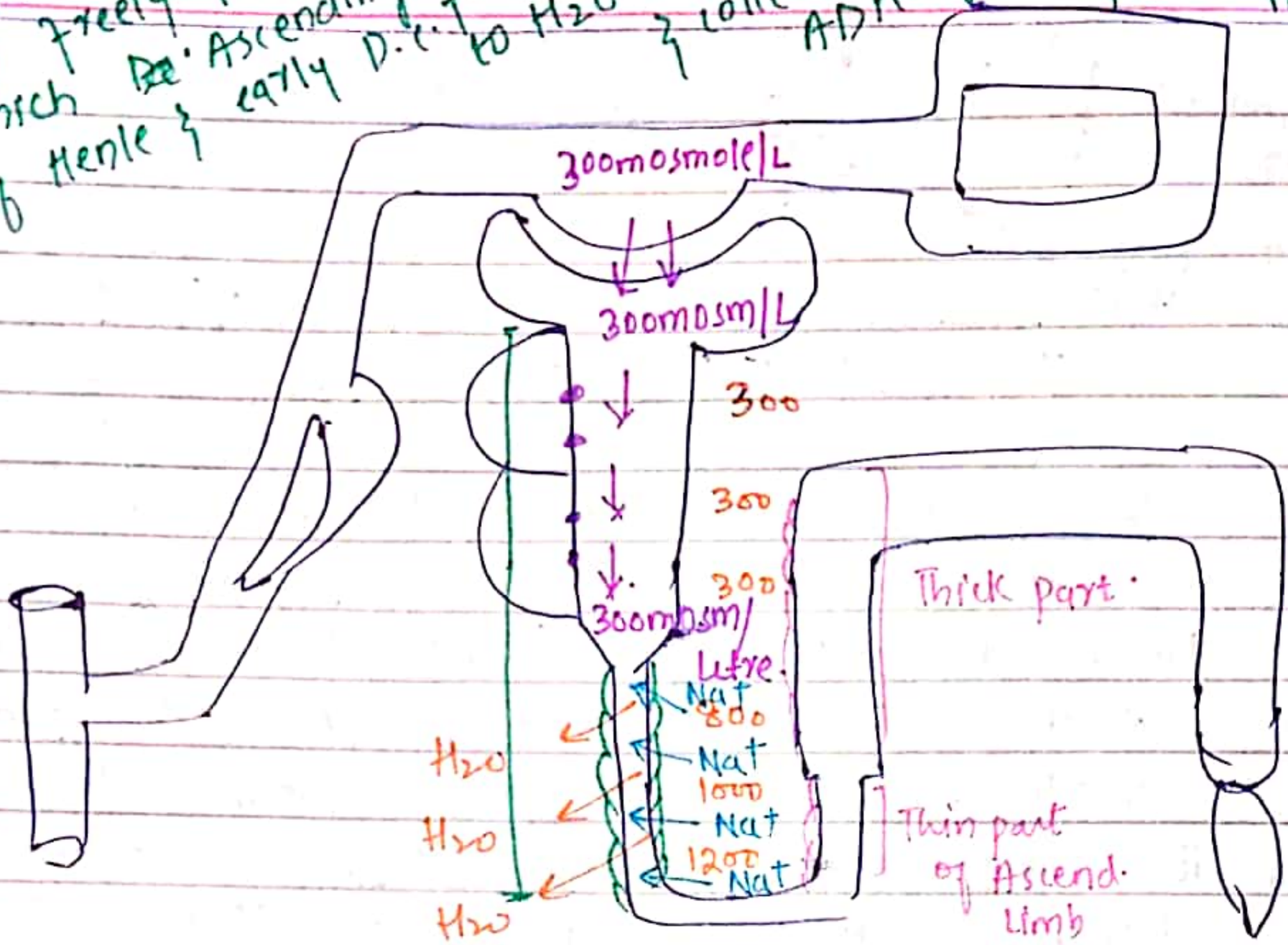
Normal Osmolarity: 280 miliosmol/litre.

But for our convenience we consider it as 300 milios/litre

The Osmolarity of the Plasma in the G·C is 300mOS/litre when it filtered the Gl·filterate also have 300mOsmo/litre in the proximal part of P·C·T as well as the distal part of P·C·T. Bc2, the amount of solute which reab. the H_2O also reabsorb with solute. Therefore,

Imp Note :-

- P.C.T ⇒ Descending part of loop of Henle is freely permeable to H_2O which ~~is~~ Ascending part of loop of Henle ⇒ early D.C.T are not permeable to H_2O. while late D.C.T ⇒ collectables are regulated by ADH if it is present then it is permeable if not then not permeable.

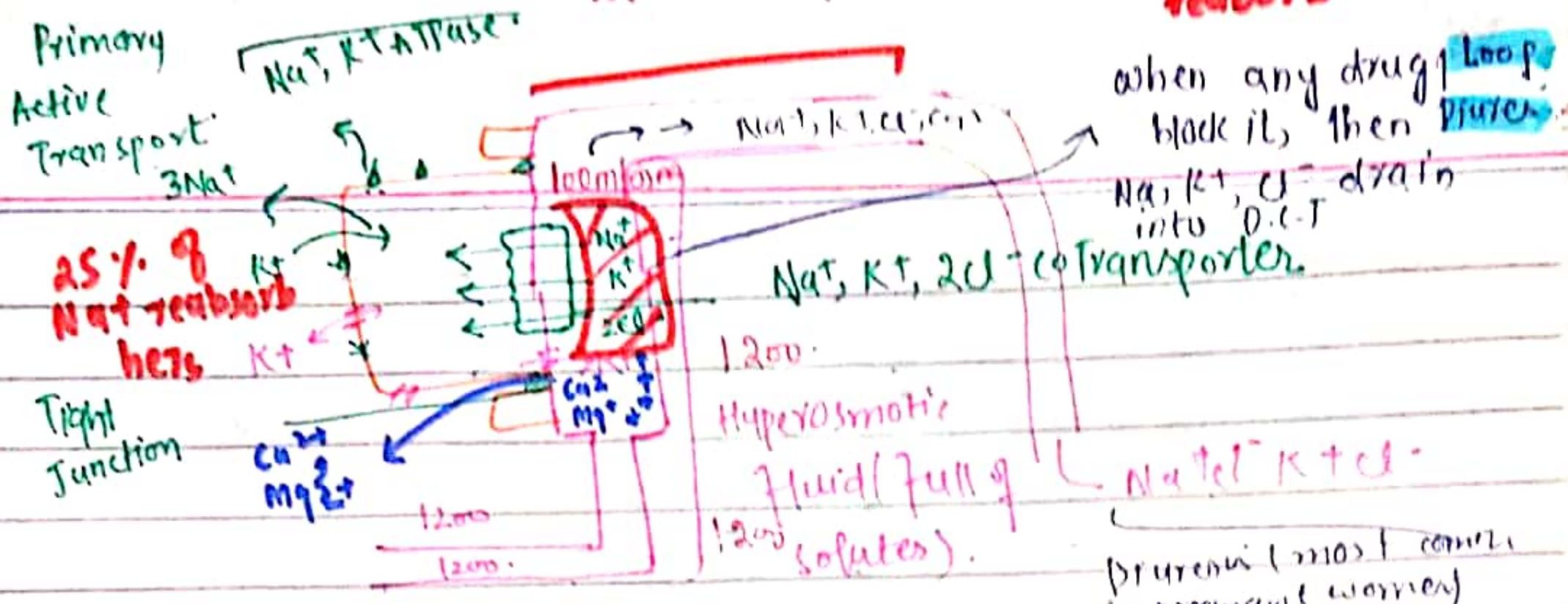


the conc. of solution ⇒ solvent will be same but its amount will be decrease. like, in start if 10ml of solute present in 20ml solv. then now 5ml solute will be present in 10ml solvent. The Osmolarity will be less tha 300 when it bcm diluted ⇒ on concent. the osmolarity will be more than 300. **(Isosmotic absorption)**

occurs in P.C. Tubule.

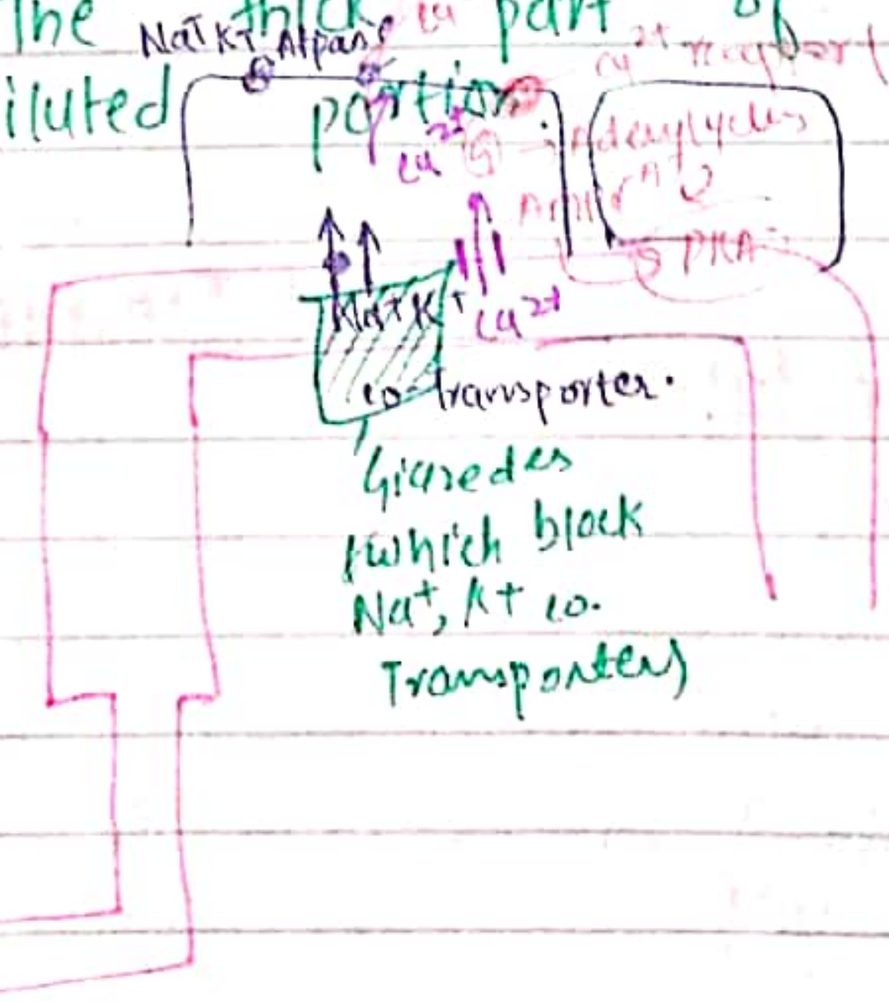
* 65% H_2O reabsorbtion occurs at P.C.T while 20% at Descending loop of Henle. when moving down into the medullary part it bcm concentrated ⇒ osmolarity ↑ frm 300 - 1200. The thick Desc. loop of Henle is permeable to H_2O but partially Permeable for Nat. So when H_2O reabsorption occurs. Nat also moves inward ⇒ osmol. ↑.

Till distal part almost 90% Na^+ reabsorb.



* Due to too much, accumulation of K^+ inside the P.C.T cells, there are some leaky channels in the lumen as well as in the basolateral membrane through which K^+ moves out { prevent it from its accumulation. When it moves inside the lumen, it causes its potential to be electropositive { the divalent cations present here (Ca^{2+}, Mg^{2+}) attaches through it { by membrane it rushes outside. Due to which, the interstitium is hyperosmotic too much solutes here, while inside the glomerulus fluid is hyposmotic → The thick part of loop of Henle is the most diluted portion.

Paracellular Transp

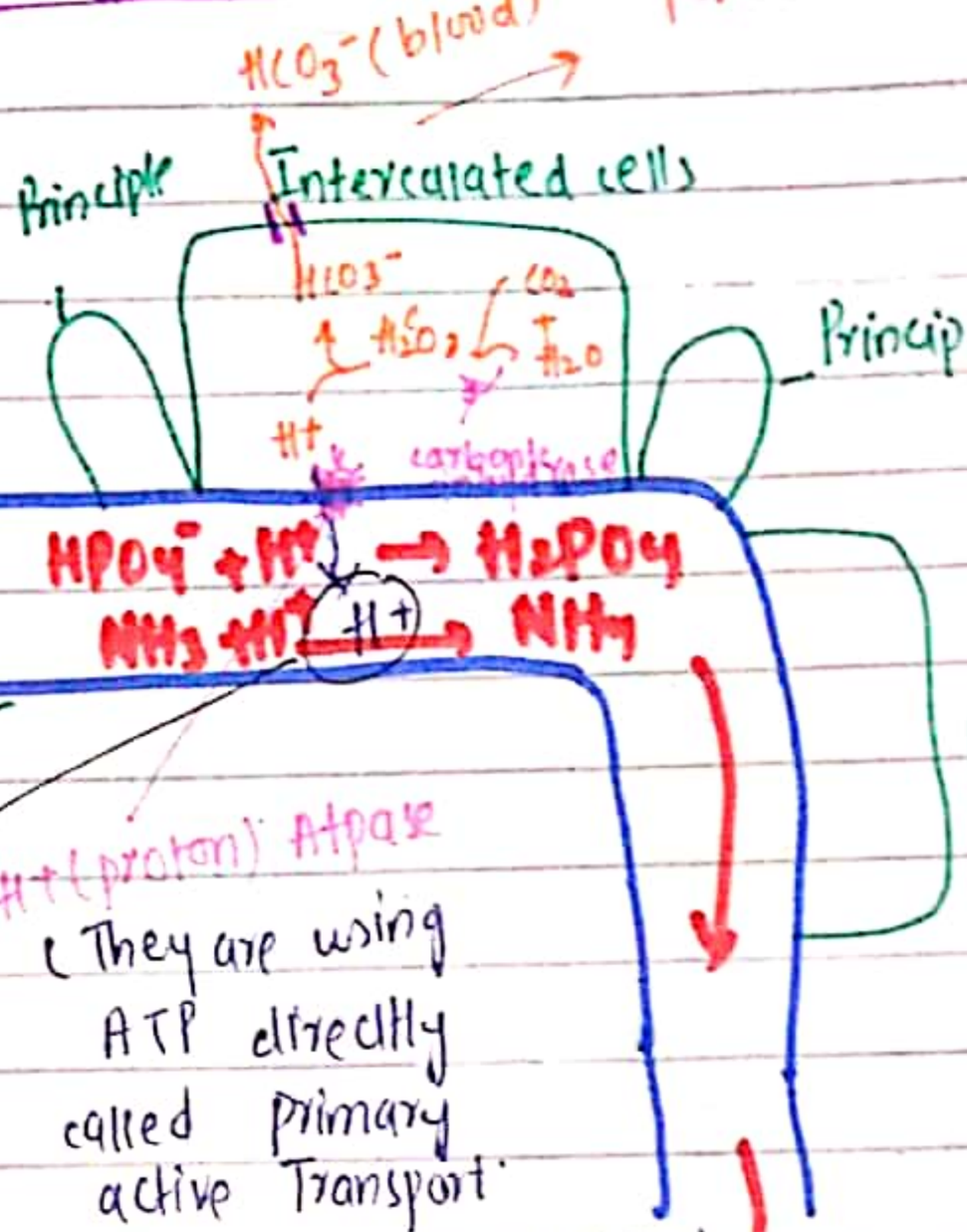


Here, Ca^{2+} is reabsorb by Transcellular membrane having PTH receptor here. The PH receptor attach with intracellular G-protein which stimulates Adenylyclase & convert ATP → cAMP which produces Protein kinase Adenyl (PKA). The PKA will do phosphorylation of Ca^{2+} Synthase & Ca^{+} Na coTransporter, through which more reabsorption of Ca^{2+} occurs from D.C.T cells into the interstitium. Due to less amount of Ca^{2+} here, the inside the Tubular cells due to Ca^{2+} leaky channels the Ca^{2+} will also moves from here to outside for reabsorption.

* Thiazedes will block the Na^{+}, Cl^{-} reabsorption then these will excrete, they not only produce Nitrouresis as well as Diuresis.
* Loop diuresis loop excrete out Ca^{2+}/Mg^{2+} also → also aggravate osteoporosis
c2 no K^{+} enters through leaky channels no electropositive potential inside the Tubule so no Ca^{2+}, Mg^{2+} reabsorption occur. while, in case of the D.C.T the Ca^{2+} reabsorption take place in a different way it dec. the Ca^{2+} losses through urine.

→ Thiazides are hypocalciuric drug c2 it inc. the Ca^{2+} reabsorbtion due to thiazedes it blocks Na^{+}, K^{+} coTransporters, so, there will be no Transp. inside the D.C.T so, there will be shortage of Na^{+} here which can be fulfilled by using Ca^{+}, Na^{+} Transporter trough which max. Transp. of Na^{+} occurs from interstitium inside the cell. max. Ca^{2+} reabsorption occurs in interstitium

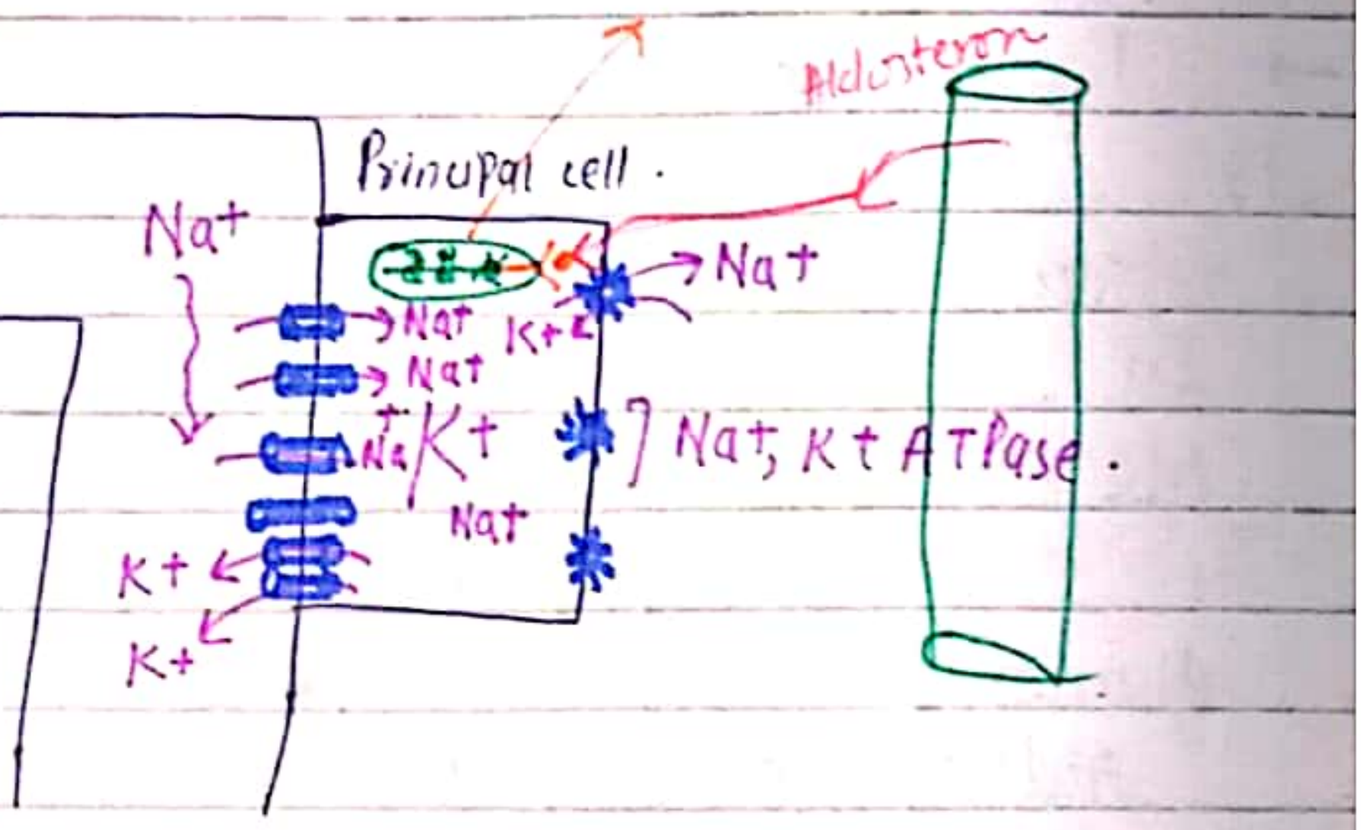
→ Loop diuresis are Hypercalciuretic



This proton is dangerous which can even destroy the ~~other substances~~ this area } will go back. So, we will put it into a basket which will come frm G.F.R.

* Monobasic } Dibasic phosphate (HPO_4^-, $H_2PO_4^-$) frm G.F.R passes into the D.C.T } here the (H^+) of intercalated disc combine with it, also this H^+ combine with the NH_3 to form the NH_4^+.
In case of acidosis (more H^+) outside in interstitium more HCO_3 bind with H^+ } ~~Bicarbonat~~ carbonic acids form which can be again through carbonic anhydrase split } again H^+ pump

Lecture :



* Na^+ due to Na^+, K^+ Atpase moves into the interstitium while K^+ inside the cell. Due to which inside K^+ conc. is more while Na^+ conc. is less. } by K^+ leaky channels K^+ moves inside the lumen while Na^+ moves into the cellular body by Facilitated diffusion } through primary Active Transport into the interstitium.
* The activity of the principal cells can be enhanced by Aldosterone. Aldosterone secreted by the glomerular adrenal cortex it is lipid soluble easily pass through the principal cell } here it binds with the receptor forming Aldosterone Receptor complex. which convert these gene containg inside Nucleus into mRNA ⟶ Protein } then $Na^+ K^+$ Atpase. So, more Na^+, K Atp will form on basolateral layer } more Na^+ reabsorbed along with H_2O } more K^+ secretion take place..

under influence of aldosterone, principal cells retain Na+/salt } water } maintains the blood volume.

→ Those diseases in which aldosterone level is high in the blood then salt } H_2O retain which K^+ (more) excreted in urine.

In cardiac failure, shock, Hypokteimic patient => Aldosterone level is high.

In conn's syndrome ; Tumour present at glomerulosa, Too much production of glomerul Aldosterone occurs, causing Na^+/H_2O reabsorbtion } K^+ is excreted in Urine.

65% Na^+ absorb by → P.C.T
25% Na^+ by Thick loop of Henle
7-3% ⟶ Early part of D.C.T
3-7% ⟶ by Principle cells (last part of Nephron)

* Due to Diuretics loop Diuretics intake more K^+ are excreted in urine (Hypokelemia)

→ Acetazolamide can block the enzyme carbonic anhydrase in the proximal convulated Tubule. then cell will not secrete proton H^+ (frm carbonic acid) } ~~these~~ b bicarbonate frm G.F.R move through the distal convuleted Tube (late) } here it accumulates.

* The Diuretics present in P.C.T, Thick part of loop of Henle, early D.C.T causes accumulation of the

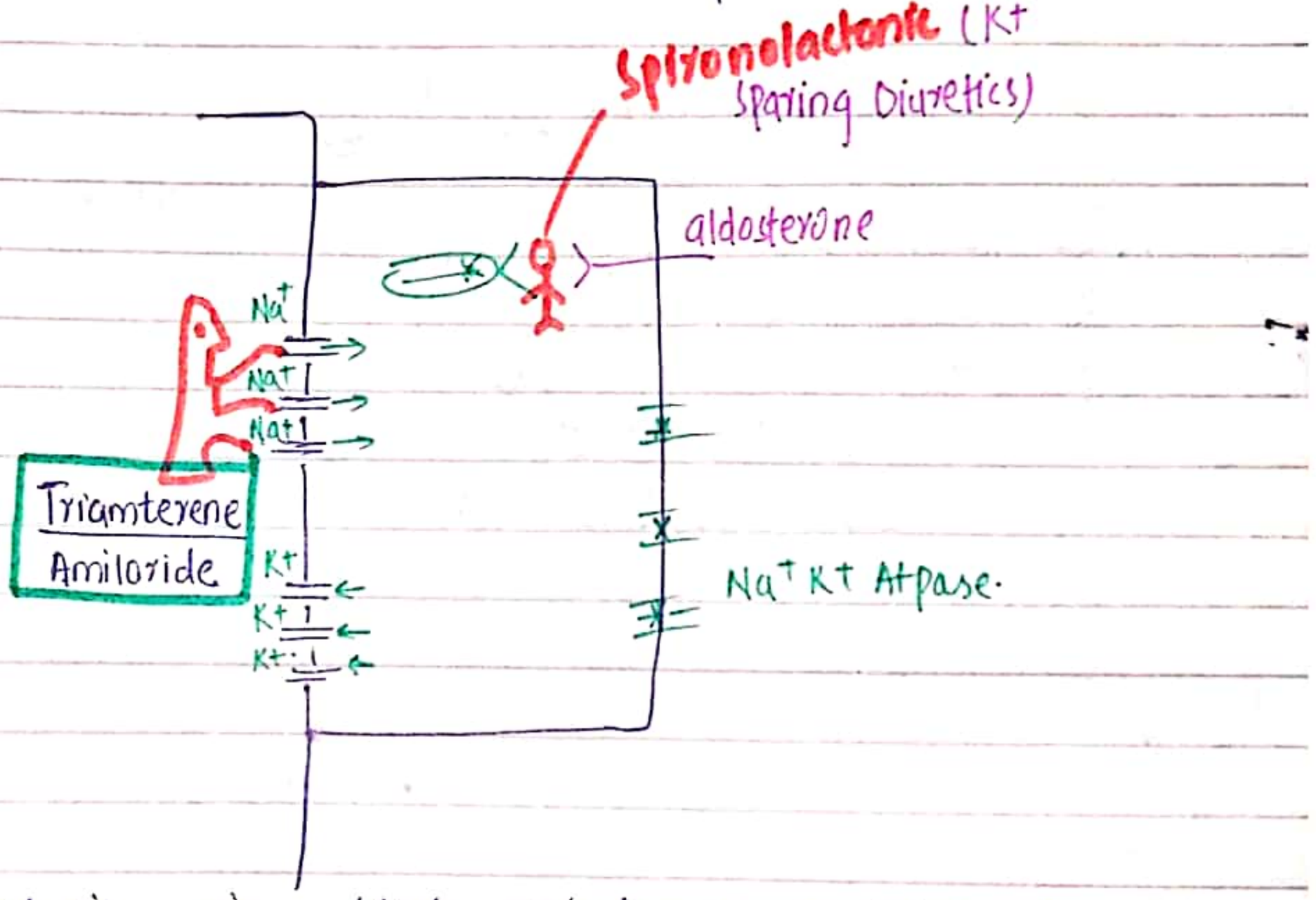
. Positive ions (Na^+), neg. ions (Cl^-, K^+) } HCO_3^- ↑ (H_2O)

principal cells.

→ All diuretics which work proximal to the principal cells are the K^+ wasting Diuretics. Thiswhy, person taking diuretics having more chances of Hypokelemia (more K^+ wastage in urine).

=> K^+ accumulation causes its more loss as well as K^+ present in lumen from interstitial cells also wasted.

→ HCO_3^- attracts K^+ into lumen { more K^+ moves outs.



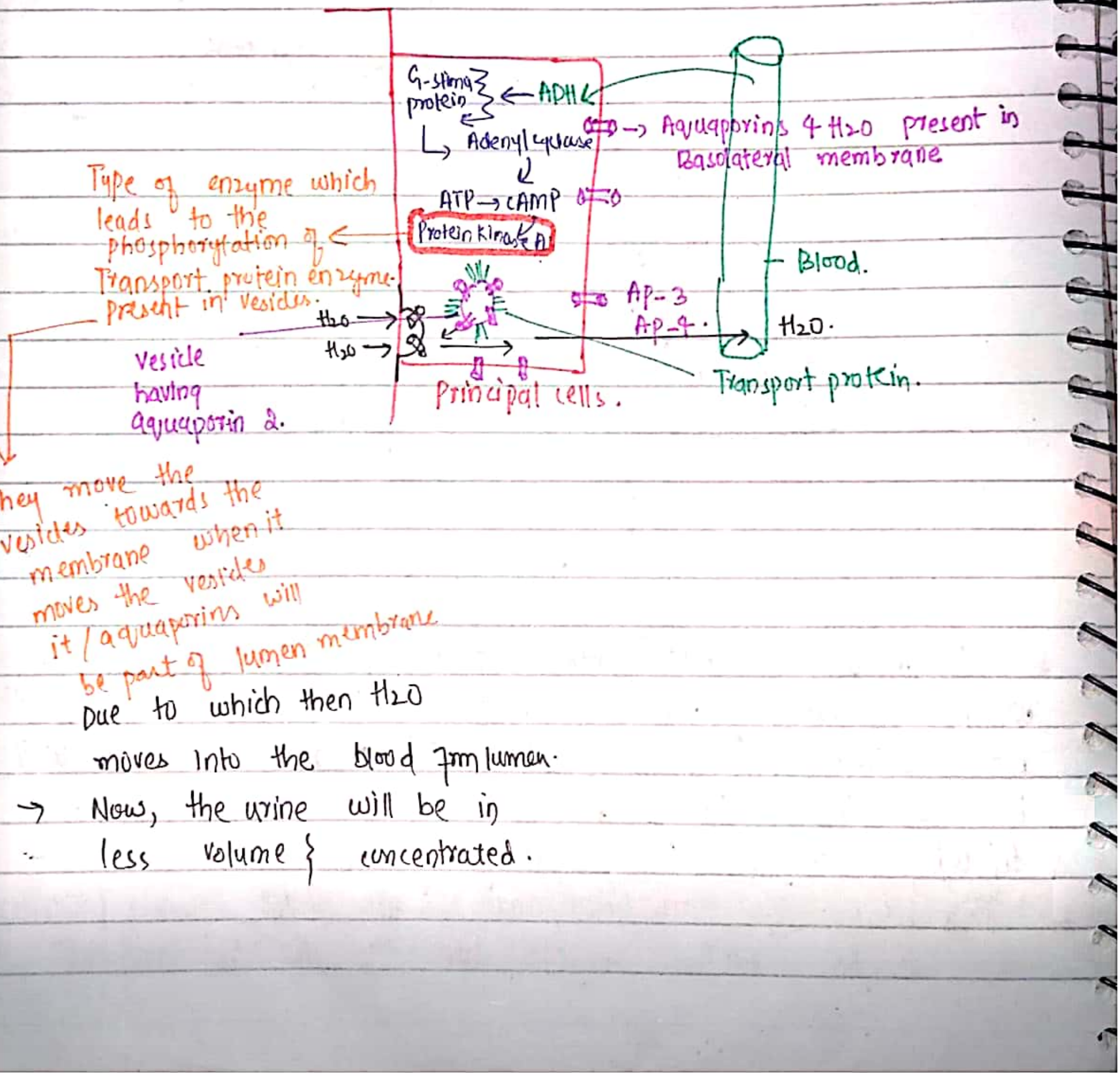
* Spironolactonic will block aldosterone receptors due to which aldosterone (which causes Na^+, H_2O) retention will not occurs { less Na^+, K^+ Atpase less K^+ will be in the lumen, so less K^+ will moves out. thiswhy it is K^+ Sparing Diuretics.

* Triamterene { Amiloride are also (K^+ Sparing Diuretics) it blocks Na^+ channels due to which no Na^+

enters & less Na, K+ activity due to this reason less K+ enters the lumen & less K+ wasted.

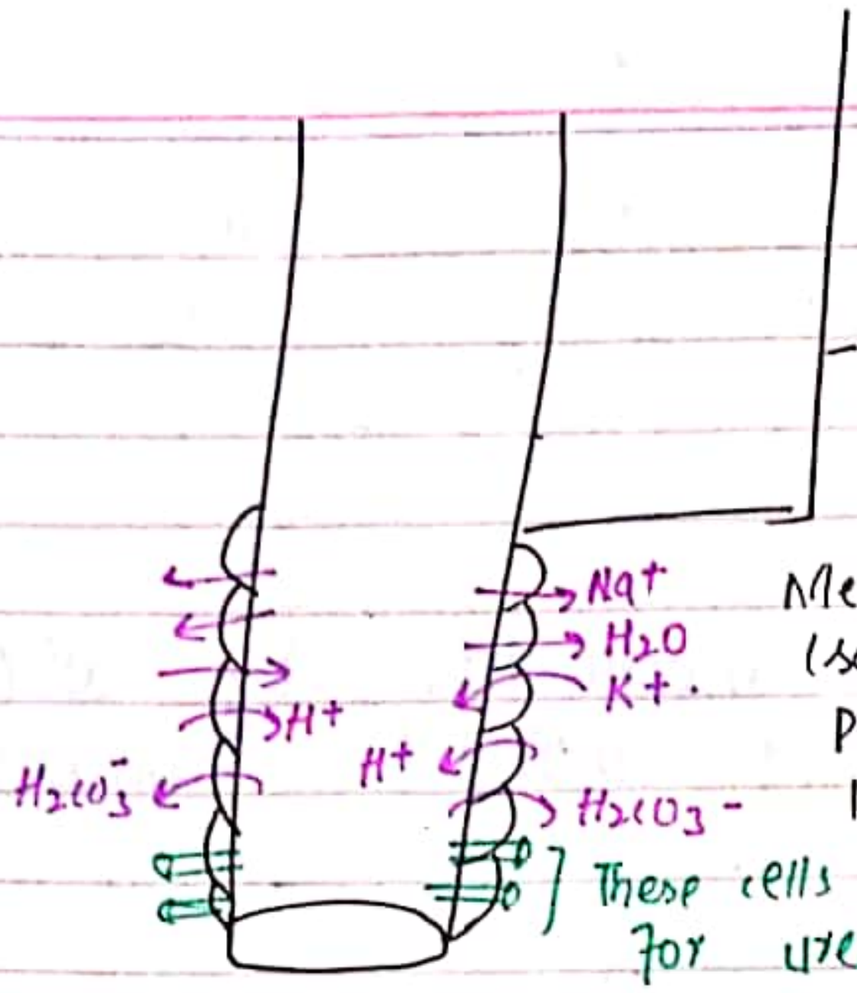
How ADH works on principal cell?

→ Due to presence of ADH, last part of Nephron is permeable to H_2O & due to its absence it will not be permeable to ~~ADH~~. H_2O.



Due to which then H_2O moves into the blood from lumen.

→ Now, the urine will be in less volume & concentrated.



Medullary collecting Duct.
(some function are like principle cells & some are like intercalated cells)

These cells have special receptors for urea reabsorption.

Urea Transporter-1 & UT-2.

Only medullary collecting duct are highly permeable to urea which there is no reabsorption of urea in other parts of Nephron. bcz here it bcm concentrated

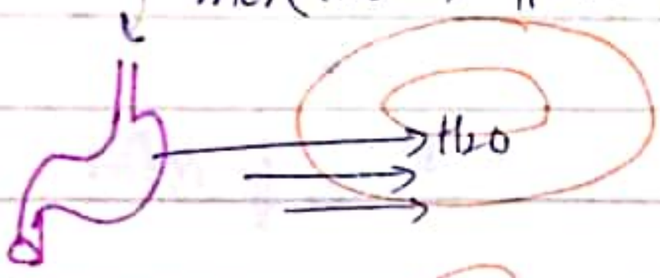
~~no~~ ~~H~~.

Lecture: 15

Why Kidney should produce sometimes dilute urine & sometimes concentrated urine?

Normal Osmolarity is 290 mOsm/Litre ≈ 300 mOsm/Litre

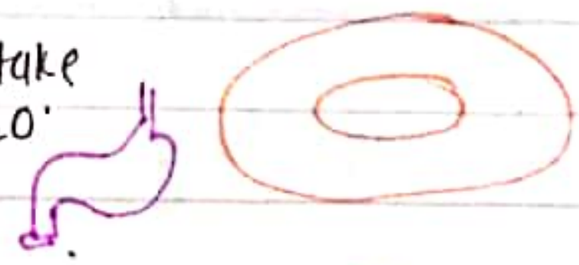
By drinking more H_2O → Hyposmolarity

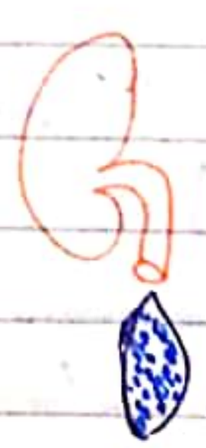


Normal metabolic waste Osmolarity is 600 mOsm/L

Hyposmolaro urine (dilute urine)

No intake of H_2O.



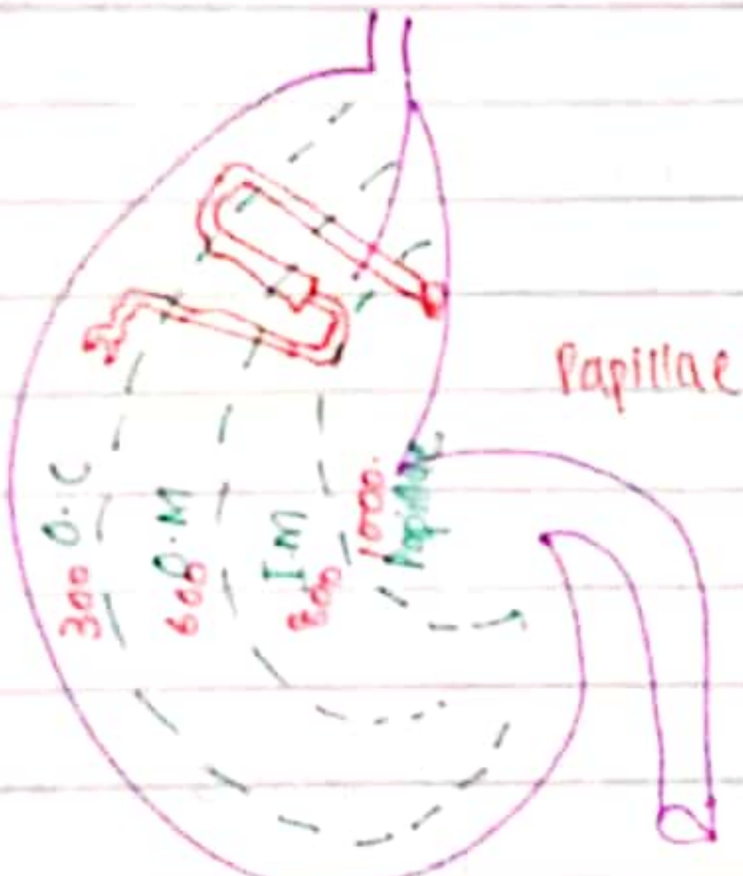


→ Here urine production is less & Solute conc. is concentrated but same in both

By sweating & by respiration some metabolic waste removed & some through urine.

→ By drinking more water, to become Osmolarity of the urine Kidney normal, Kidney produces more urine { deprived of H_2O, Kidney Osmolarity increases { conserve more H_2O to bcm Osmolarity to normal less urine is produce.

Q. what are the mechanism by which Kidney can dilute urine { concentrate urine?



Papillae bcm Hyperosmolar.

Mechanism of Urine concentration

→ HyperOsmolar Renal medullary Interstitium (cortico papillary Gradient)

→ Osmotic Role of ADH

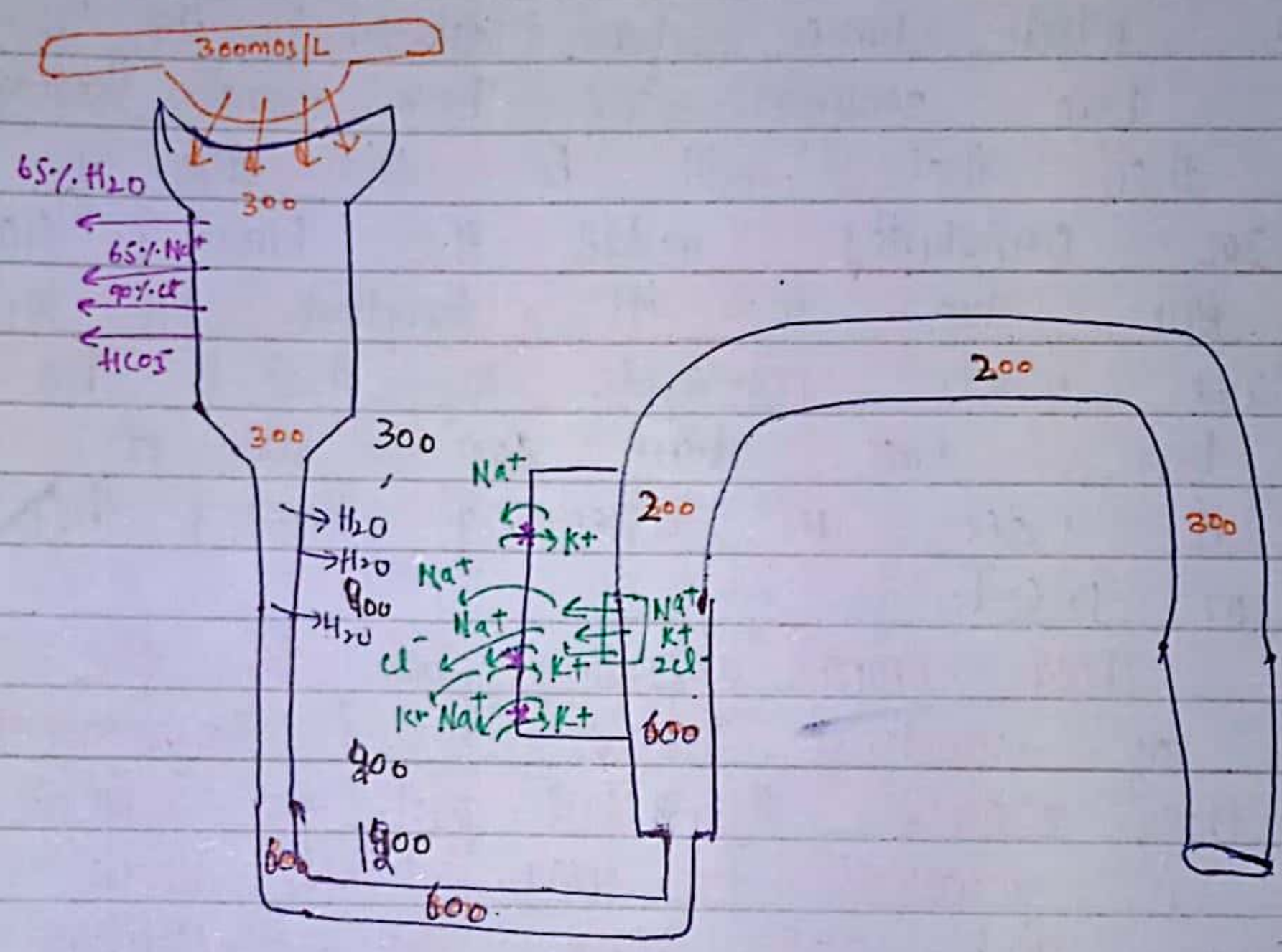
→ How M.I.H is produced?
Counter Current Multiplier (loop of Henle)

→ Urea Recycling in Renal medullary cortex.

↳ **How M.I.H is maintained?**

Vasa Recta.

as counter current Exchanger. [Fig 29.4 pg 369 ch # 29].



P.C.T is Isoosmotic bz Osmolarity remains same amount of solute & H_2O reabsorption occur.

→ If nephron is straight then their will be only diff. of 200 blw the Tubular flow & Interstitium.

Lecture # 16

URINE CONC. & DILUTION

The Osmolarity of the P.C.T remains same as 300 bz equal amount of solute & H_2O reabsorption occurs. while in case of Ascending limb of loop of Henle which is impermeable to H_2O the solutes moves into the interstitium by the Na^+, K^+ ATPase & Na^+, K^+, $2Cl^-$ Transporter- Due to which lumen bcm diluted & its osmolarity bcm changes. If there were straight Nephron then their will be the diff. of only 200 Osmolarity inside the lumen & 400 outside. But due to its bending, the loop of Henle which permeable to H_2O & the lumen bcm conc. bcm 600 → 800 etc. while it dec. in ascending limb & then further in D.C.T.

* For urea from ascending limb to the 2/3rd of collecting Tubule, it is impermeable 4 Urea. while the last part of collecting Tubule is permeable for urea. which allow Urea reabsorption and also causes the interstitium HyperOsmolar. & some reabsorption also occurs in loop of Henle. In this way, recycling of urea occurs.

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* ADH also increases/amplify the activities of counter current multiplier & urea recycling.

→ Counter Current Multiplier.

⇒ occurs in loop of Henle

⇒ It is active Transport System

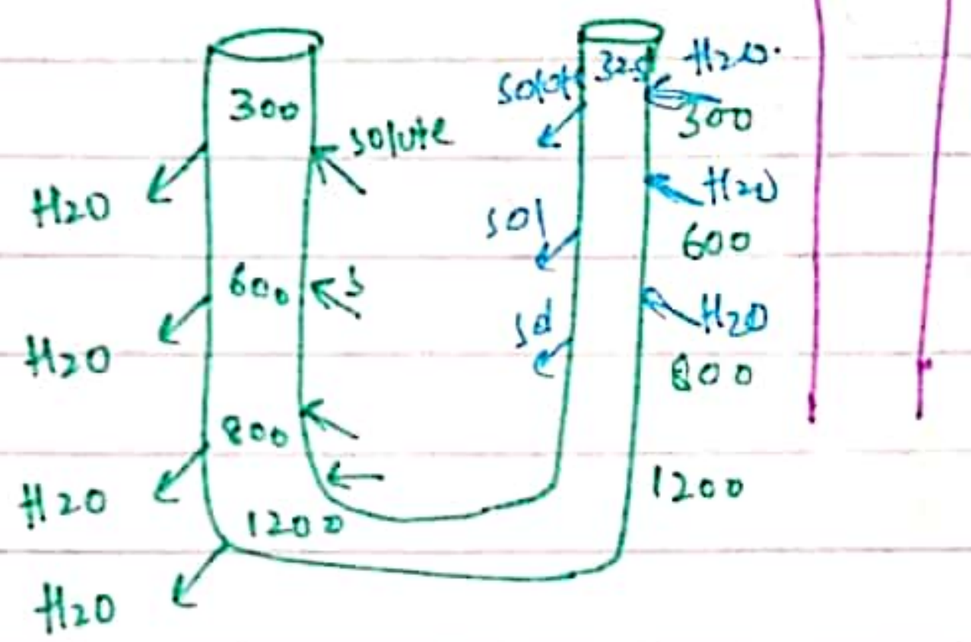
⇒ It make Hyperosmolarity.

Counter Current Exchanger:

→ Take place in Vasa recta.

→ Passive Transport System

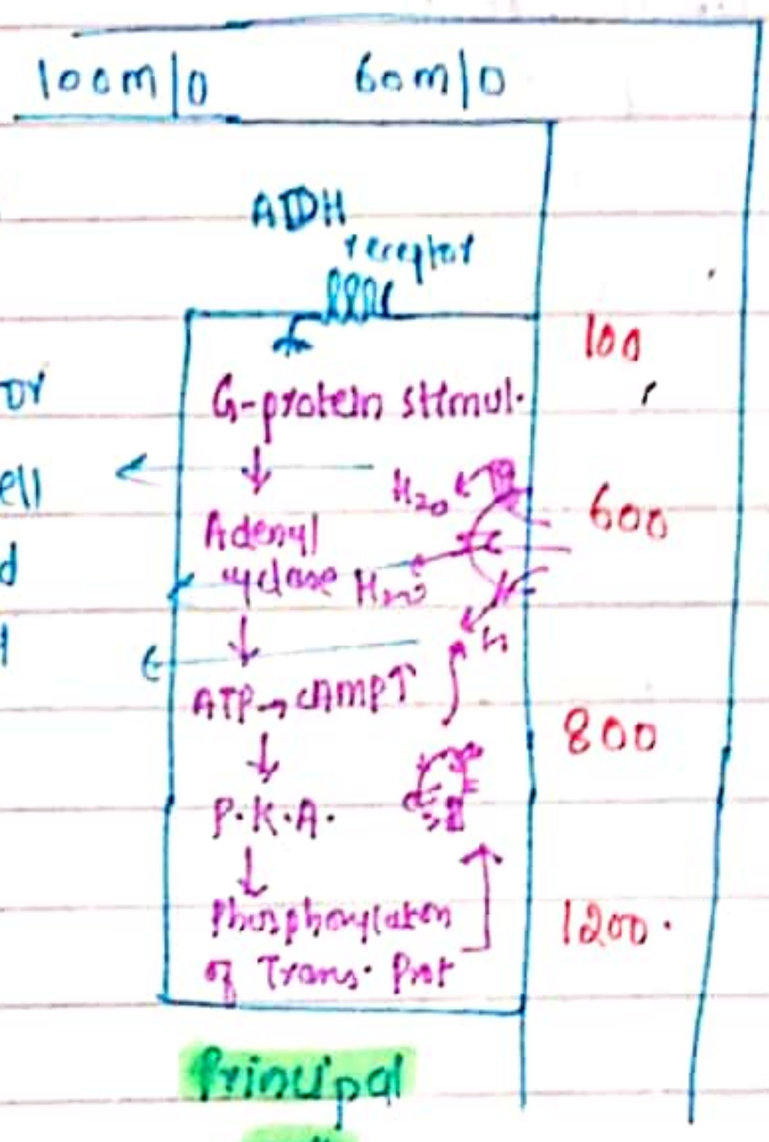
→ maintains Hyperosmolarity



→ Rate of Blood flow in cortex is more than the medullary, as it deepens down less solute washes out with Blood.

Principle cells present in cortical collecting Tubule as well as medullary C.T → controlled by ADH as well as Aldosterone { Na^+ { H_2O reabsorption occur while K^+ moves inside the lumen by influence of Aldosterone. But for influence of ADH, only H_2O reabsorption occur.

→ If there is no ADH, then no H_2O reabsorption in late distal part as well as cortical { medullary collecting part.



ADH receptor present in Basolateral membrane. while Aldosterone receptor present inside the cell ∠ they are lipid soluble while ADH (peptide) not lipid soluble.

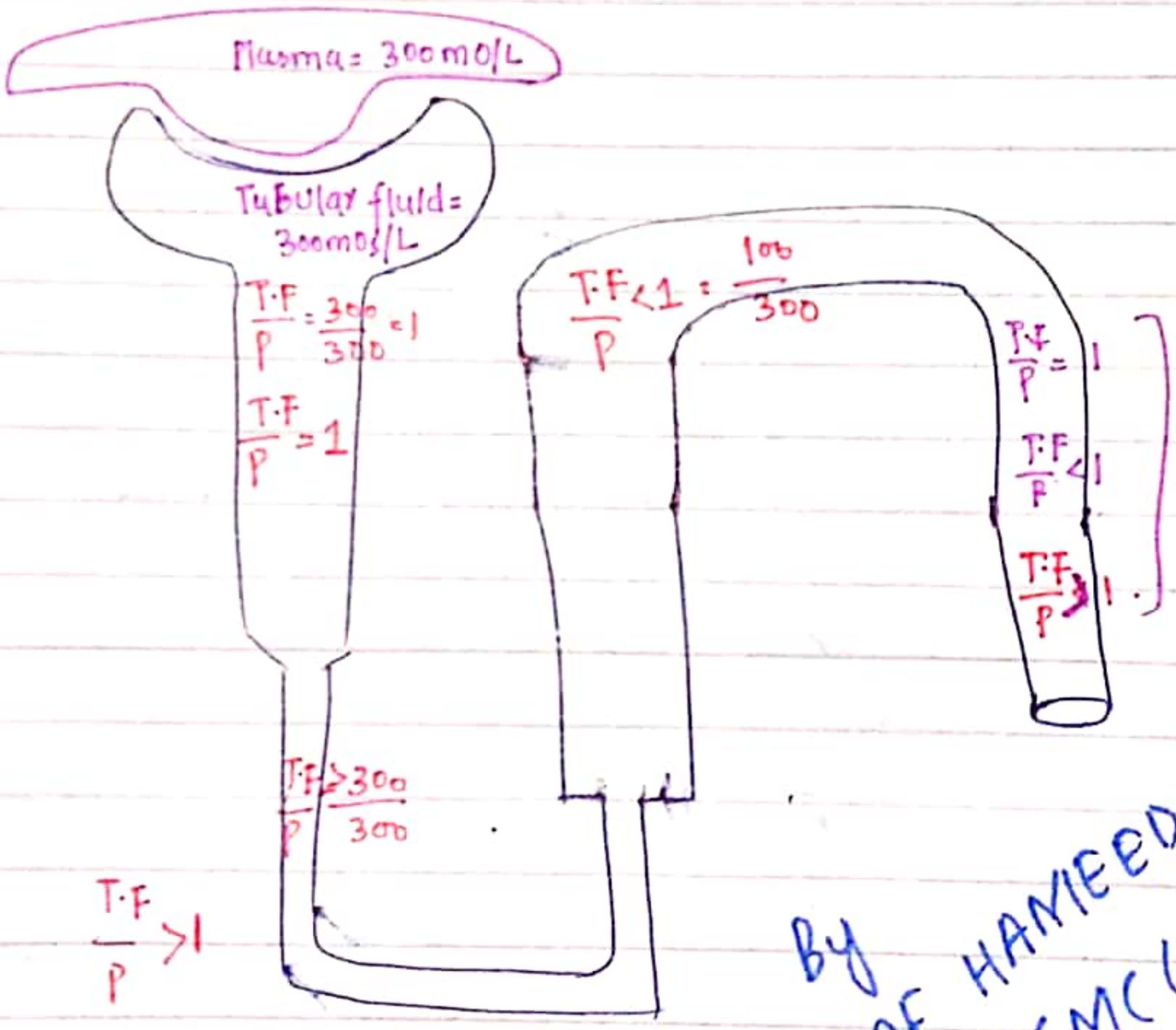
→ If ADH absent the Hyposmolar (Diluted urine) produces, but due to its presence reabsorption occur { concentrated urine produces. (Hyperosmolar

ADH also increases the Kidney interstitum Hyperosmolarity by counter current multiplier (↑ Na^+ Transport into the interstium) { urea recycling.

Q: when Someone lost in desert?

Due to deprieved H_2O, the Osmolarity of blood increases which activates the Osmoreceptor { the optic nucleus present in Hypothalamus produces ADH it is moved towards post-pituatary

where it stores & secretes by activating Osmoreceptors then ADH acts on principle cells allow aquaporin in luminar membrane due to which H_2O reabsorption occur & concentrated (less volume) urine produces. ADH also acts on the ascending loop of henle more solutes reabsorbption takes place Solutes & the interstitum bcm hyperOsmolas.



BY KASHAF HAMEED KHATTAK KGMC (2nd yr)

THE END

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TOPICS FROM BOOK chap # 26 & 27

DETERMINANTS OF RENAL BLOOD FLOW

Renal Blood Flow is determined by the pressure gradient across the renal vasculature (the difference between renal artery and renal vein hydrostatic Pressure) divided by the total renal vasular resistance.

$$RBF = \frac{(\text{Renal artery Pressure} - \text{Renal vein Pressure})}{\text{Total renal vascular resistance}}$$

* Renal artery Pressure is about equal to the systemic arterial Pressure and renal Vein pressure averages about 3-4 mmHg.
* Most of renal vascular resistance, reside in three segments; interlobular arteries, afferent arteriol and efferent arteriole.
* Resistance of these is controlled by Sympathetic Nervous System, various Harmones.

→ Blood Flow in renal medulla accounts for only 1 - 2% (due to vasa recta) of maximum blood flow occurs in Renal cortex.

(See Table 27.2 & 27.4)

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KGMC

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Random Imp. Points

* The determinant of GFR is most variable & subject to physiological control is Glomerular Hydrostatic Pressure. The variable in turn is influenced by Sympathetic Nervous system, Harmones, autocoids/ vasoactive substances that are released in the Kidney & act locally) & other feedback control.

Strong Sympathetic Nervous System Activation Decreases Glomerular Filteration Rate

* Affarent & Efferent arterioles richly innervated by Sympathetic Nervous fibers.
* Strong activation of Renal Sympathetic Nerves can constrict renal arterioles & decrease renal Blood Flow and G.F.R
* Reflex activation of Sympathetic Nervous System resulting from moderate decrease in pressure at the carotid sinus or baroreceptor has little influence on renal blood flow or GFR.

Angiotensin II: powerful vasoconstricter, considered to be a circulating harmone & locally produced autocoid or paracrine Harmone. (2 it is formed in Kidney & Systemic circulation.

→ Affarent arterioles are strongly protected from Angiotensin due to presence of vasodilators Nitric oxide & prostaglandins which counteract their function.

→ AngioTensin-II induced efferent arteriole constriction increase Tubular reabsorption of Sodium & Water. which helps restore blood volume & blood pressure.

Endothelial Derieved Nitric Oxide:

→ An autocoid that decreases the renal vascular resistance and is released by vascular endothelium throughout the body is called. →.

→ Therefore, administration of drugs that inhibit Nitric oxide increases renal vascular resistance and decreases GFR and urinary sodium excretion causing High Blood Pressure.

→ In Hypertensive patients, damage to endothelial cells occur cause vascular resistance no Nitric oxide production } elevated BP.

Prostaglandins and Bradykinins decrease Renal Vascular Resistance (Vasodilator) which inc. GFR } Renal Blood flow.

* Normal GFR = 180L/Day
  Reabsorbtion: 178.5L/Day
  Excretion => 1.5L/Day.
* In the absence of autoregulation, small increase in blood pressure (from 100-125mmHg) would cause similar 25% increase in GFR (from 180-225 L/day)
* If Tubular reabsorbtion remains constant, urine flow would increase to 46.5L/day (a Total inc. of urine is more than 30-fold).

Tubuloroglomerular Feedback Mechanism;

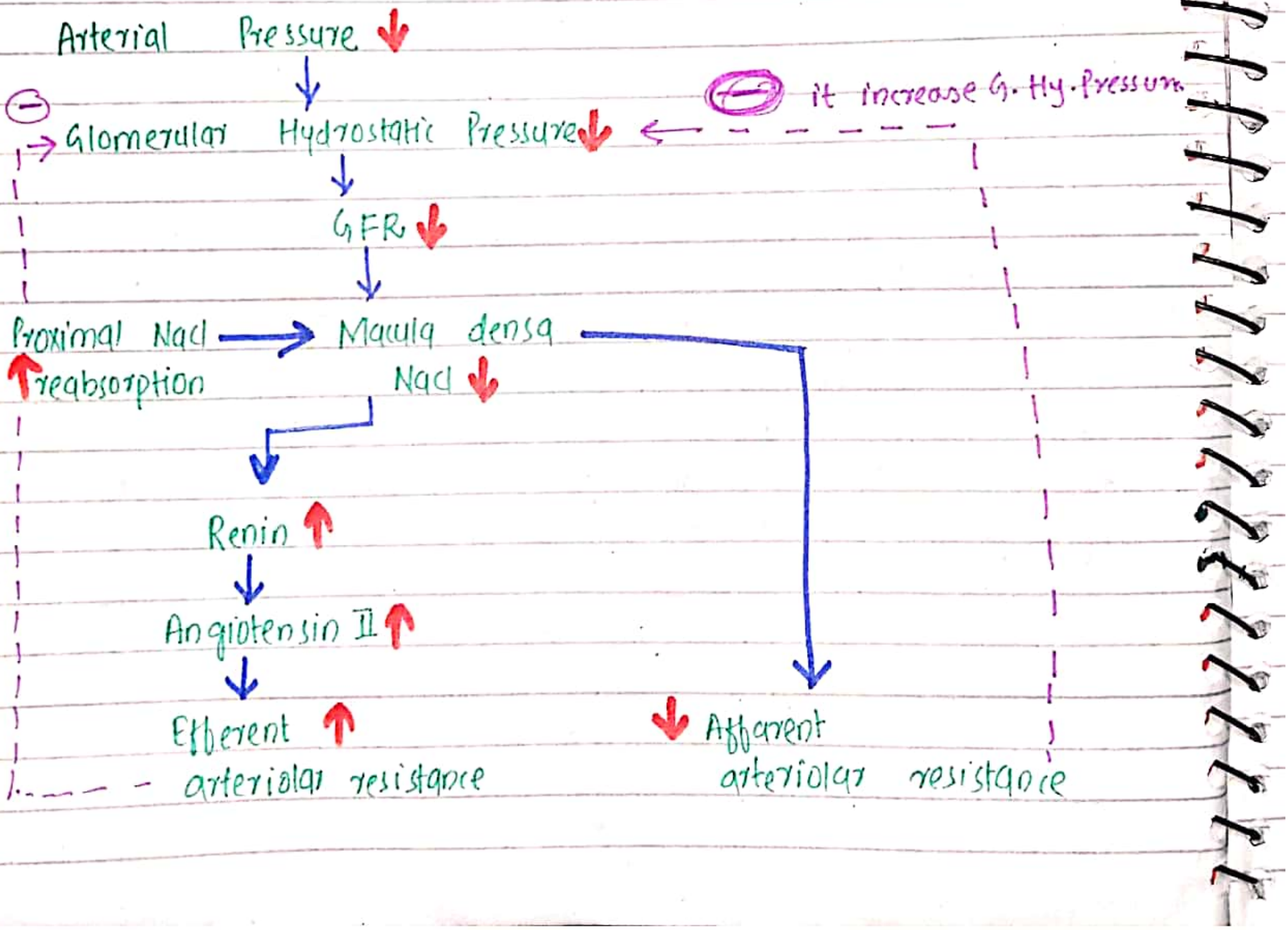
Two components that act Together.

→ Affarent arteriolar Fecdback Mechanism

→ Efferent " "

These feedback mechanism depends on special anatomical arrangment of Juxtaglomerular complex.

The JuxtaGlomerular complex consist of macula densa cells in initial portion of distal Tubule } Juxtaglomerular cells in the wall of affarent } efferent arterioles.



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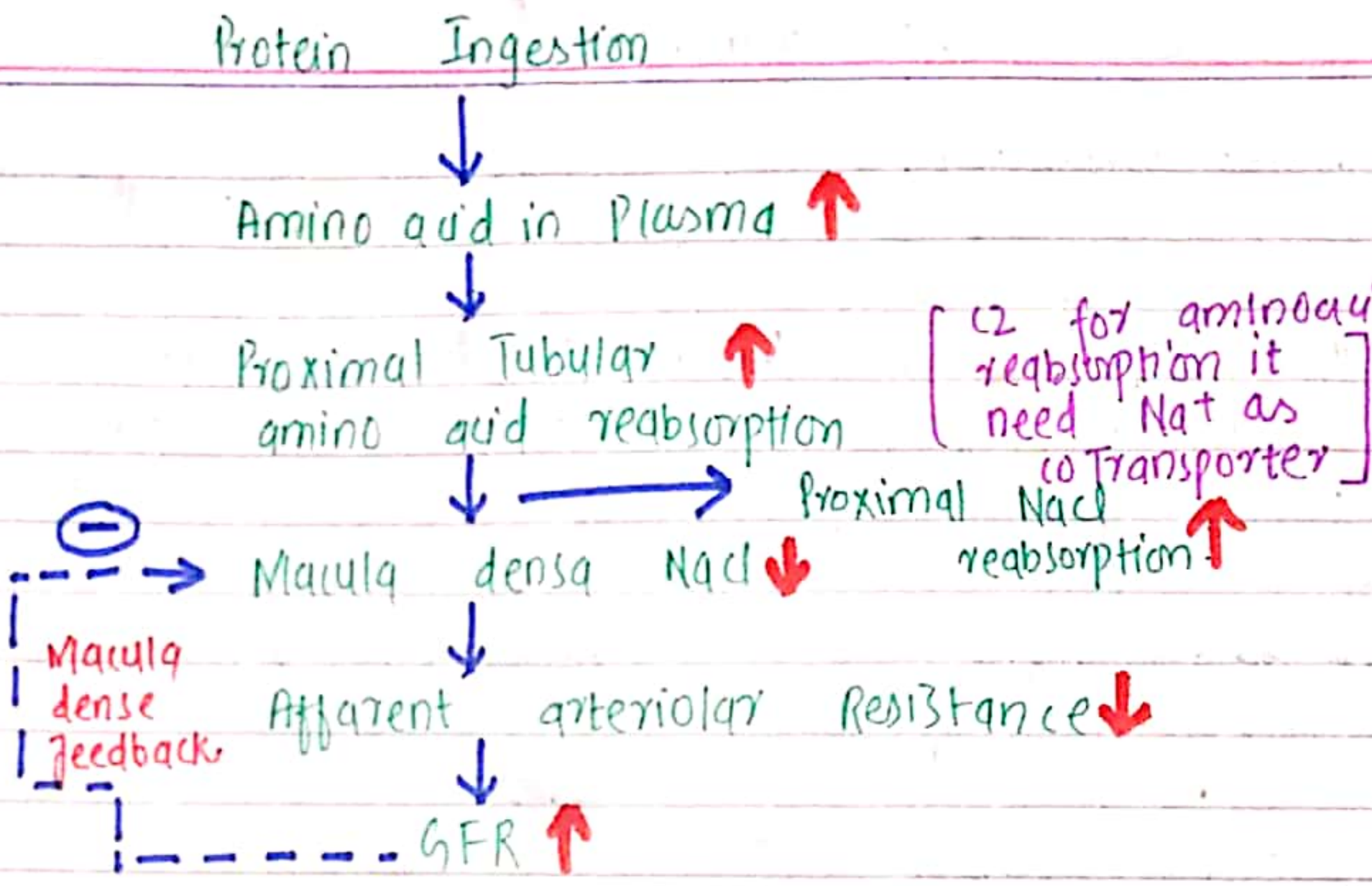

CHAPTER 28

Random Notes:

* Primary Active Transporters in Kidney:
  $Na^+ - K^+$ ATPase, Hydrogen ATPase, H-K^+ ATPase, Calcium ATP
* Maximum Glucose reabsorb by body 375mg/min, Normally 125mg/min, However, when it exceeds maximum then Glucose excretion occurs in urine → Diabetes Mellitus
* Substances actively reabsorbed i-e Glucose, Phosphate, Sulfate, Aminoacids, Urate, Lactate, Plasma Protein.
* Transport maximum for actively Secreted Substances → Creatinine, Para-amino hippuric acid.
* In Proximal convuluted Tubule, Urea are passively reabsorb while Transporter for Urea are present in medullary collecting ducts.

Na^+ reabsorption ↑

↓ Lumen Negative Potential ↑

↓ Passive Cl^- reabsorption

↓ H_2O reabsorption ↑

↓ Luminal Cl^- ↑ concentration

↓ Passive Cl^- reabsorption

↓ Luminal Urea ↑ concentration.

↓ Passive Urea reabsorption

* In mammals, more than 90% of waste Nitrogen, mainly generated in liver as a product of protein metabolism, is normally excreted by Kidneys as Urea.
* Creatinine is even larger molecule than Urea, none of the creatinine is reabsorb, so all the creatinine filtered by glomerulus is excreted in Urine.

→ Proximal Tube epithelial cells are Highly metabolic, have large number of mitochondria to support powerful active Transport Process.

→ P.C.T have an extensive brush border on the luminar (apical) side of membrane

→ In first half of P.C.T, Nat is reabsorb with Glucose} aminoacids } other solutes. Second Half of Proximal Tubule has relatively high concentration of chloride (140 mEq/L) compared with the early Proximal convulated Tubule (105mEq/L)

→ The Proximal Tubule is imp for secretion of organic acids and bases such as bile salts, oxalate, urate and catecholamines (end product of metabolism). The secretion of these substances into the P.C.T { filteration by Gl.c. { total lack of reabsorption, all combined contribute to rapid excretion in urine.

→ Penicillin { Salicylates, rapid clearence by the Kidney maintain therapeutically.

→ Paraminohepuric acid rapidly secreted by P.C.T.

* The thin ascending { descending limb of loop of Henle, have thin epithelial membrane with no brush border, few mitochondria { minimum level of metabolic activity.
* The descending part is highly permeable to H_2O.

See Graph 28.7.

* Loop Diuretics which block (Sodium Potassium 2 chloride Co-Transporter) are furosemide, ethacrynic acid and bumetanide
* Also significant Paracellular reabsorption of cations such as Mg^{2+}, Ca^{2+}, Na^+ { K^+ in the thick loop of Henle (ascending limb). as a result of the slight positive charge of the tubular lumen relative to interstitial fluid.
* The Tubular fluid in the thick ascending limb is very dilute (2 of no reabsorption of H_2O here.

→ Thiazide Diuretics which are widely used to treat disorders such as hypertension, Heart failure, inhibit Sodium chloride Co-Transporters. in Distal Tubule.

* Intercalated cells reabsorb K+ ions } secrete H+ ions into the lumen

* Principle cell reabsorb sodium } water from the lumen } Secrete Potassium ions into the lumen.

→ Potassium Sparing Diuretics are Spironolactone, eplerenone → amiloride and Triamterene.

→ Spironolactone and eplerenone are mineralocorticoid receptor antagonist that compete with aldosterone for receptor sites in the principal cells } therefore inhibit stimulatory effect of aldosterone on Na+ reabsorption } K+ secretion.

→ Amiloride and Triamterene are Sodium channel Blocker that inhibit the entry of Na+ into the Na+ channels of luminal membrane } therefore reduce amount of Na+ that can be transported across basolateral memb by Na+, K+ ATPase.

→ For this reason, Na+ channel Blockers, as well as aldosterone antagonist, decreases urinary excretion of K+ } act as K+ spring Diuretics.

Type A Intercalated cells: Secrete hydrogen ions by H-ATPase Transporter into the Tubular lumen } reabsorb bicarbonate ion. in acidosis.

Type B Intercalated cells:

secrete bicarbonate ion into Tubule and reabsorb H+.

* chloride-Bicarbonate Transporter present on apical (basolateral) membrane is called pendrin.

Acidosis inc. Type A cells while alkalosis inc-Type B cells.

ADH → Vassopressin.

→ Reabsorption increases in response to ↑ Tubular flow increase

if GFR inc. from 125 ml/min to 150 ml/min instead of 8(ml/n (65%) the 97 ml/min (65% reabsorption will take place.

→ Peritubular capillaries hydrostatic pressure is influenced by arterial pressure and resistance of affarent and efferent arterioles.

* ↑ in arterial Pressure tend to raise peritubular capillaries hydrostatic Pressure and decrease the reabsorption rate.

* ↑ in resistance of affarent or efferent arteriole
↓ peritubular capillary hydrostatic pressure. } tend to increase reabsorption rate.

→ colloid Osmotic pressure of peritubular capillaries is determined by;
- Systemic Plasma colloid Osmotic Pressure (more Protein content
- (the filteration fraction

→ Some renal Vasoconstricters such as Angiotensin II, increase peritubular capillary reabsorption by decreasing RPF { ↑ filteration rate.

→ When peritubular capillary reabsorption is reduced, there is increased interstitial fluid hydrostatic pressure { tendency for greater amount of solute { water to leak back into the tubular lumen, thereby reducing the net reabsorption rate.

→ Forces that ↑ the peritubular capillary reabsorption ↑ reabsorption from renal Tubule. Conversely, hemodynamic changes that inhit Peritubular reab also inhibit reabsorp. (Tubular) of solute { H_2O.

Table 28.2

Pressure Natriuresis and Diuresis

"Small ↑ in arterial Pressure can cause marked increase in urinary excretion of Sodium and H_2O phenomeno Pressure Natriuresis or Pressure Diuresis?"

- ↑ arterial Pressure causes increase in GFR
- ↑ in renal interstitial Fluid hydrostatic P causes backleak of Na^+ into the Tubular lumen, thereby reducing the net reabsorbtion of Na^+ & H_2O ↑ the rate of urine output.
- Reduced Angiotensin II formation (angiotensin II itself ↑ Sodium reabsorption by tubules & stimulate aldosterone secretion which further ↑ Na^+ reabsorption.
- Internalization of Sodium Transporter Proteins from apical membrane to Tubular lumen.

See Table 28.3 pg 358.

Addison's Disease: Due to adrenal destruction, conc. of aldosterone decrease.

Conn disease:

Aldosterone concentration increases.

Angiotensin II

- stimulate → aldosterone secretion
- → constrict efferent arteriole
- → directly stimulate Sodium reabsorption in Proximal Tubule, loop of Henle, Dista Tuble & collecting Tubule.

↑ Na^+, H_2O reabsorption.

→ Directly Stimulate Na^+, K^+- ATPase Pump
→ Stimulate Sodium- Hydrogen Exchange
→ Sodium Bicarbonate co-Transport in Basolateral membran.

Diabetes Insipidus: In the absence of ADH, permeability to H_2O of Distal Tubule & collecting duct is low. causing Kidney to secrete large amount of dilute urine.

→ Sympathetic Nervous System stimulation increases Renin release and also increases Sodium reabsorption & decrease sodium urinary excretion.

Use of clearence method Pg. 360. (ch 7 p 28)

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ACID - BASE BALANCE (Lect # 1)

Normal conc. of $[H^+]$ in Normal Human Beings, extracellular Fluid = 4×10^{-7} Eq/L

$[H^+]$ = 40n Eq/L

Taking +ve log on both sides

$+\log [H^+] = +\log [4 \times 10^{-7}]$

$= -7.4$

Taking (-ve) log on both sides

$-\log [H^+] = -(-7.4)$

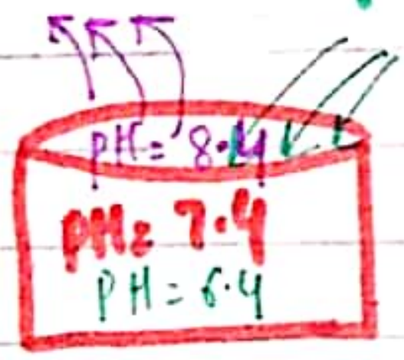
Power of Hydrogen = 7.4

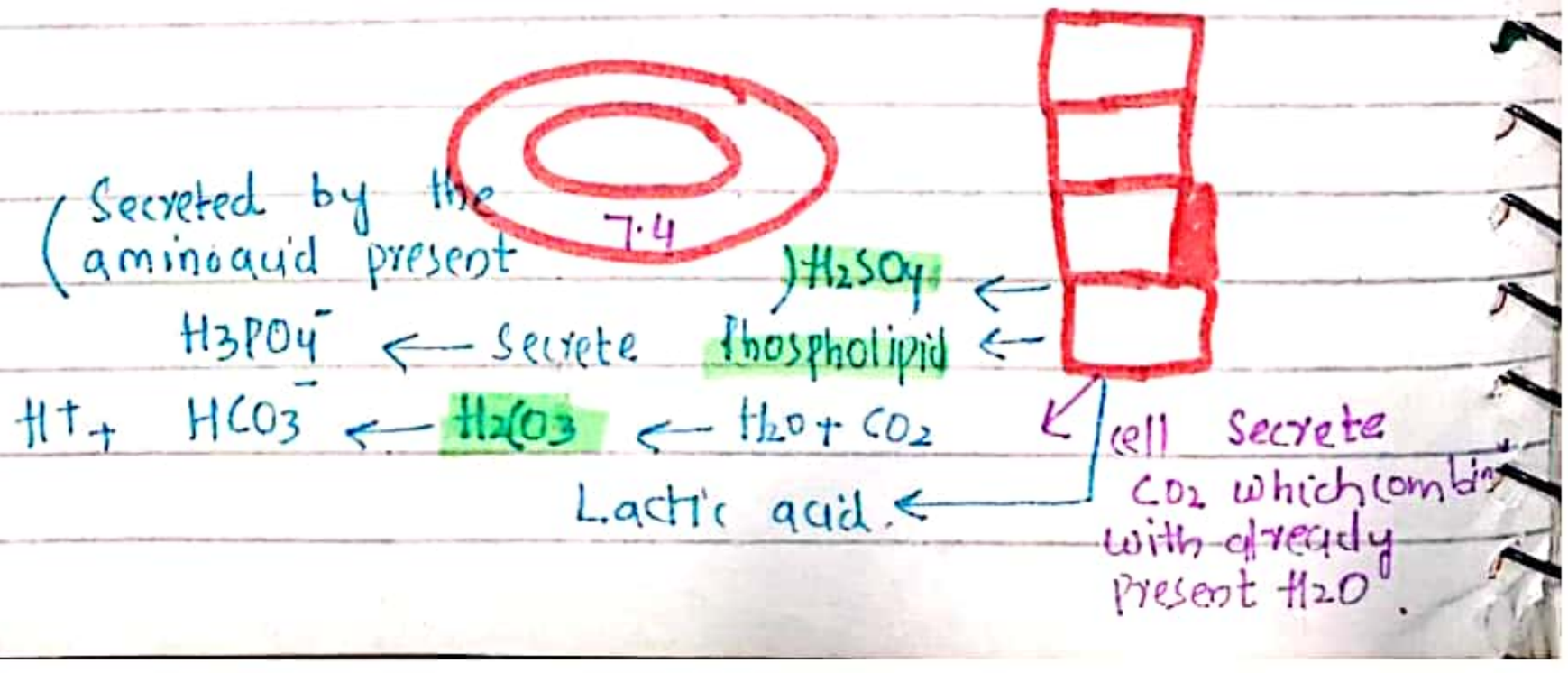
pH = 7.4

Power of Hydrogen concentration

$[H^+]$ = 0.00000004 Eq/L (40n Eq/L)

$pH \propto \frac{1}{[H^+]}$ → If (H^+) conc. inc. 10 Times then pH bcm 6.4 instead of 7.4 & when $[H^+]$ b/w $1/10^{th}$ then pH bcm 8.4.

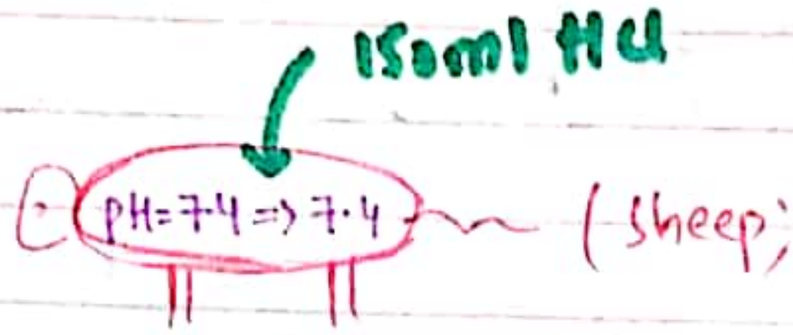




→ pH plays an important role in protein structure (Peptide folding) Due to pH abnormality, Folding of protein structure disturb).

Buffer: Resist change in PH.

"Special system of molecules which has the capability of binding as well as releasing the proton"



→ Due to biological molecules which are already present here resist change in pH ⇒ Buffer.

Lecture #2

Hasselback equation

$$HA \underset{K_2}{\overset{K_1}{\rightleftharpoons}} [H]^+[A]^-$$

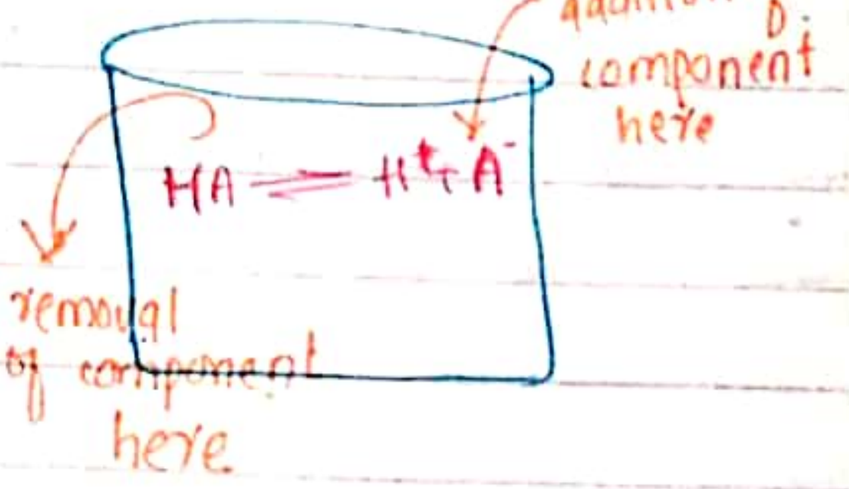
$$K_1[HA] = K_2[H^+][A^-]$$

$$\frac{K_1}{K_2} = \frac{[H^+][A^-]}{[HA]}$$

$$\frac{K_1}{K_2} = K$$

$$K_2 = \frac{[H^+][A^-]}{[HA]}$$

$$K\frac{[HA]}{[A]} = [H^+]$$



$-\log K - \log \frac{HA}{A} = -\log (H^+)$

$\downarrow$ pk $\qquad\qquad$ $\downarrow$ pH

$$pk - \log \frac{[HA]}{[A]} = pH$$

$$pk + \log \frac{[A]}{[H][A]} = pH$$

Equation is applied to a solution having Buffer molecule

$$S = 6 + \log \frac{A}{HA}$$

$$S - 6 = \log \frac{A}{HA}$$

$$-1 = \log \frac{A}{HA}$$

$$1/10 = \log \frac{A}{HA}$$

when Buffer system has equal number of associated & Dissociated molecules, then pH of Buffer System = pK.

$$HA \rightleftharpoons H + A^-$$

1000 $\qquad$ 1000.

$$7.4 = pK + \log 1000/1000$$

$$7.4 = pK.$$

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Buffer System ideally work when pH is near to pKa.
it doesnot work when it is far away from pKa.

pH = ~~P~~ (7) Best Buffer on b/w 6-8

When pH = 5.

i) HA ⇌ $H^+ + A^-$ 4
ii) HA ⇌ $H^+ + A^-$ 5 ✓ → This one is in best Buffer solution.
iii) HA ⇌ $H^+ + A^-$ 7

when pk is

$HA \rightleftharpoons H^+ + A^-$

if pK = 5 (it means than at pH of 5, Half of these buffer molecules are protonated and Half of these are unprotonated.