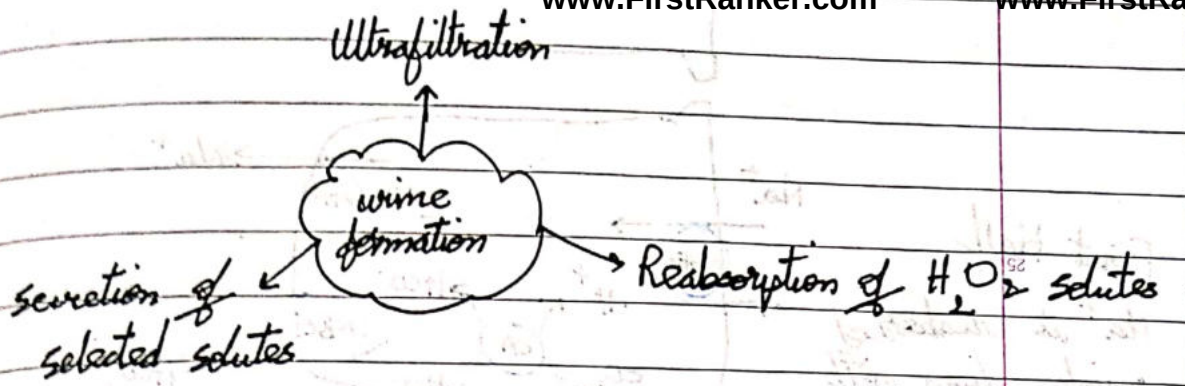
Reabsorption & Secretion :-



By the processes of reabsorption & secretion renal tubules determine the composition and volume of urine

Solute & water Reabsorption along Nephron :-

NaCl & H_2O reabsorption - Major function
25000 mEq/day of Na & 179 L/day of H_2O is reabsorbed

PCT :-

Absorbs 67% of filtered H_2O, Na^+, K^+, Cl^- & many other solutes
Reabsorbs all glucose & aa & most of HCO_3^-
Key element - $Na^+ - K^+$ ATPase in Basolateral membrane.

Reabsorption of Na^+ :-

Reabsorption of Na^+ and Cl^- occurs both by transcellular ($2/3^{rd}$) and paracellular ($1/3^{rd}$) routes

About 67% of NaCl filtered each day is reabsorbed by PCT

Date / /
Page Camlin

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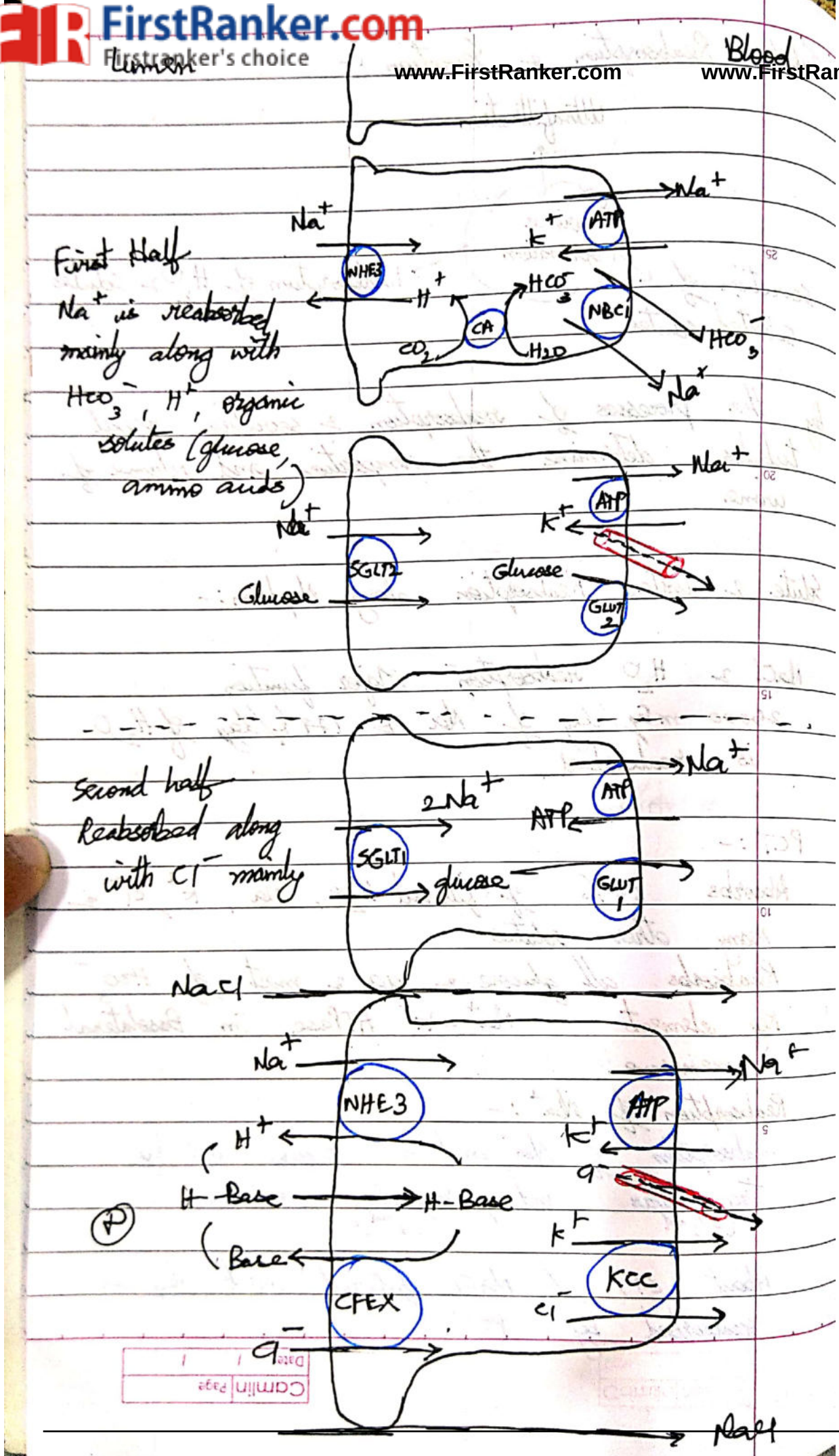


First half	Second half
① Na^+ reabsorbed primarily with HCO_3^- and other solutes (aa, glucose, P_i lactate)	① Na^+ is reabsorbed mainly with Cl^-
② Na^+ reabsorbed more	② less
③ More glucose, aa and other organic solutes are reabsorbed	③ less reabsorbed.
④ Entry of Na^+ through Na^+/H^+ antiport (NHE3) results in reabsorption of $NaHCO_3$	④ Entry of Na^+ through NHE3 is coupled with Cl^-/Base antiport (CFEX) This is equivalent to uptake of NaCl
⑤ Na^+ leaves the cell through Na/K^+ ATPase	⑤ Same.
⑥ Organic solutes leave the cell through symporters passive mechanisms.	⑥ Cl^- leaves the cell through K^+/Cl^- symport (KCC) and Cl^- channel.
⑦ $[Cl^-]$ is less in tubules	⑦ $[Cl^-]$ ④.
⑧ A -ve transepithelial voltage is created across PCT leads to paracellular reabsorption of Cl^-	⑧ A +ve transepithelial voltage generate due to passive diffusion of Cl^- across tight junctions

Date / /
Page
Camlin

Paracellular reabsorption of NaCl in second half due conc gradient of Cl^- generated [Cl⁻] rises along the length of PCT. Diffusion of Cl^- across tight junc into lateral intercellular space leads to +ve transepithelial voltage which causes diffusion of Na^+ into blood.

H_2O reabsorption :-

i) Absorbs 67% of water
ii) The reabsorption of Na^+ along with other solutes (HCO_3^-, Cl^-, glucose, aa, P_i) leads to an transtubular osmotic gradient.
iii) The osmolality of Tubular fluid (T) and that of lateral intercellular space (P).
iv) This leads to reabsorption of water across PCT (osmosis)
Transcellular through Aquaporins (AQP1)
Paracellular through tight junc as they are permeable to H_2O.
v) Accumulation of H_2O in lateral intercellular space leads to (P) in Hydrostatic pressure. This (P) hydrostatic pressure along with elevated prdem oncotic pressure in the peritubular capillaries facilitates reuptake of fluid & solute into capillaries.
vi) Reabsorbed fluid is slightly hyperosmotic relative to plasma.
However it is considered as isoosmotic due to minor osmolality diff.

Some solutes like K^+ & Ca^{2+} are entrained in absorbed fluid and absorbed by process of solvent drag.

Protein reabsorption

Peptide hormones, small proteins and small amt of large proteins like albumin are filtered through glomerulus.

Filtered pr = GFR × Pr in ultrafiltrate
= 180 L/day × 40 mg/L
= 7.2 g/day

Multiligand endocytic Receptors ←

Reabsorbed as intact or partially degraded pr
They are then completely degraded in the PCT cells by enzymes to aa which are transported to cells.
This sys is effective - pr completely reabsorbed
disruption of filtration barrier - proteinuria

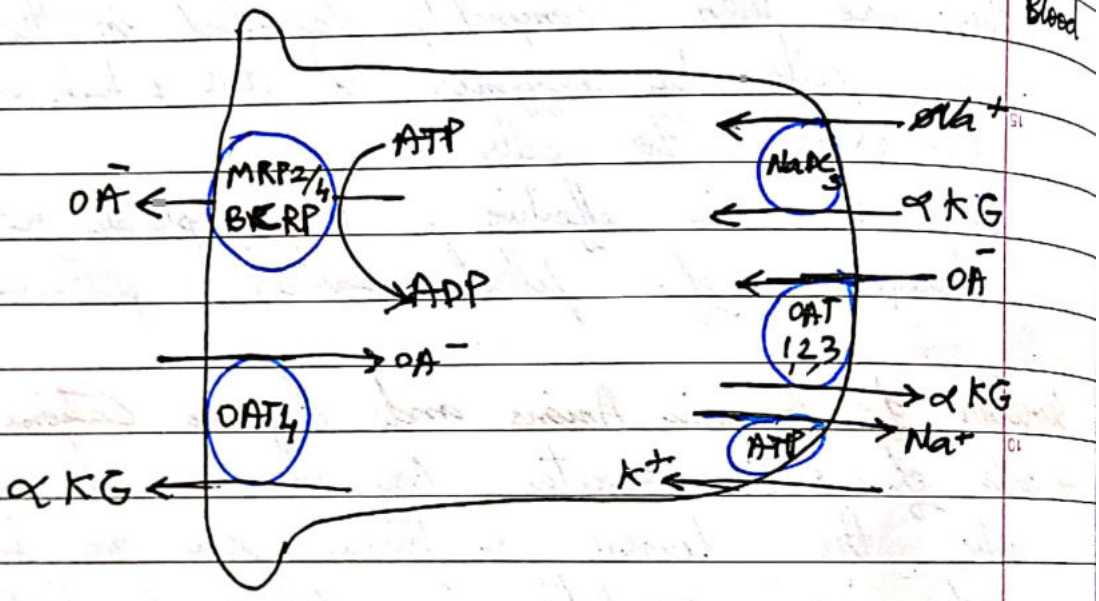
Secretion of Organic Anions and Organic Cations :-

→ cells of PCT secrete Org anions and cations into the lumen & hence play an impt role in regulation of plasma xenobiotics (drugs - antibiotics, diuretics, antiviral, NSAID's)
→ Also secrete toxic subs derived from endogenous and exogenous sources
→ Many of them - metabolic end prod
→ Only a small fraction secreted - many are bound to plasma pr.
→ These sub removed by both filtration & secretion

eg of Anions (OA^-) :-
endogenous — cAMP, cGMP, Bile salts, malate, PGE2, $PGF_{2\alpha}$, urate, oxalate, Ascorbate, folate.
drugs — Salicylate, NSAID's

eg of cations (Oc^+) :-
endogenous :- creatinine, dopamine, Epinephrine, norepinephrine
drugs — morphine, Atropine

OA^- secretion

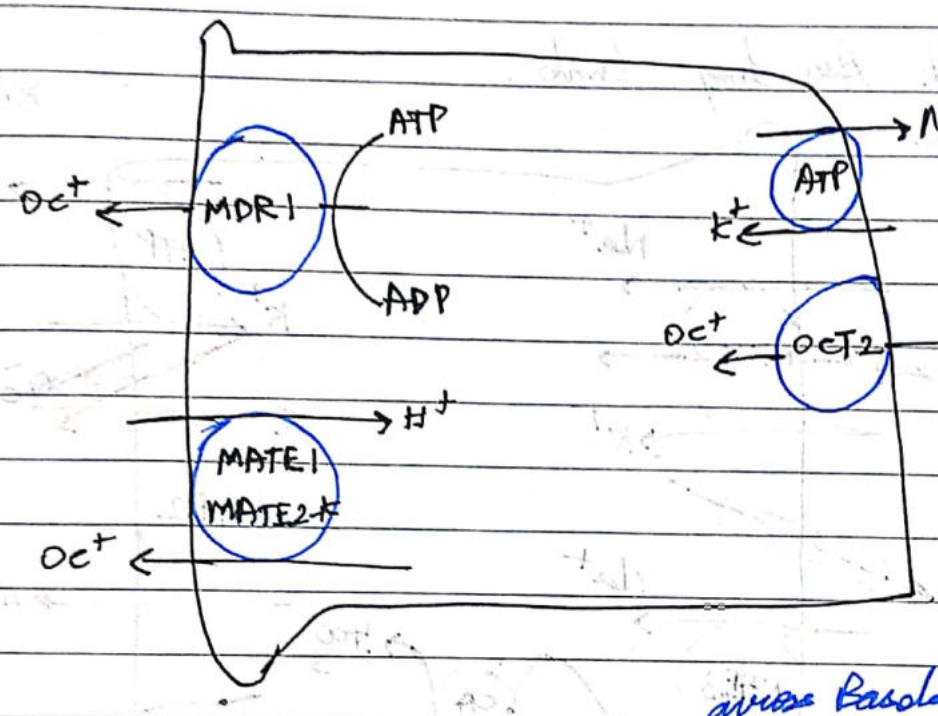


OA^- enter the PCT cell through $OA^-/\alpha KG$ antiporter (OAT 1 / OAT 2 / OAT 3)
OA^- moves against conc gradient into cell
αKG moves out of the cell
αKG accumulated in cell through $Na^+/\alpha KG$ symporter (NaDC3) against its conc gradient

OAT 3 - dicarboxylate transporter 3
The α KG recycles across the basolateral membrane on the OATS in exchange for OH^-
OA^- leaves the cell through ATP dependent Multi drug resistant pr 2/4 (MRP 2/4) and Breast cancer Resistant pr (BCRP).

OAT 4 transports organic anion urate into the cell.

OC^+ secretion



across Basolateral mem

OC^+ Transported by OCT 2 / against their conc gradient, this transport is driven by cell -ve pot diff
ATP dependent.

MDR1 - multi drug resistant pr - 1
MATE - multi drug and toxin transporter
↳ transports OC^+ into tubular fluid in exchange for H^+

MDR1 also known as P - glycoprotein

Henle's Loop :-

Reabsabs 25% of filtered NaCl
15% of filtered H_2O

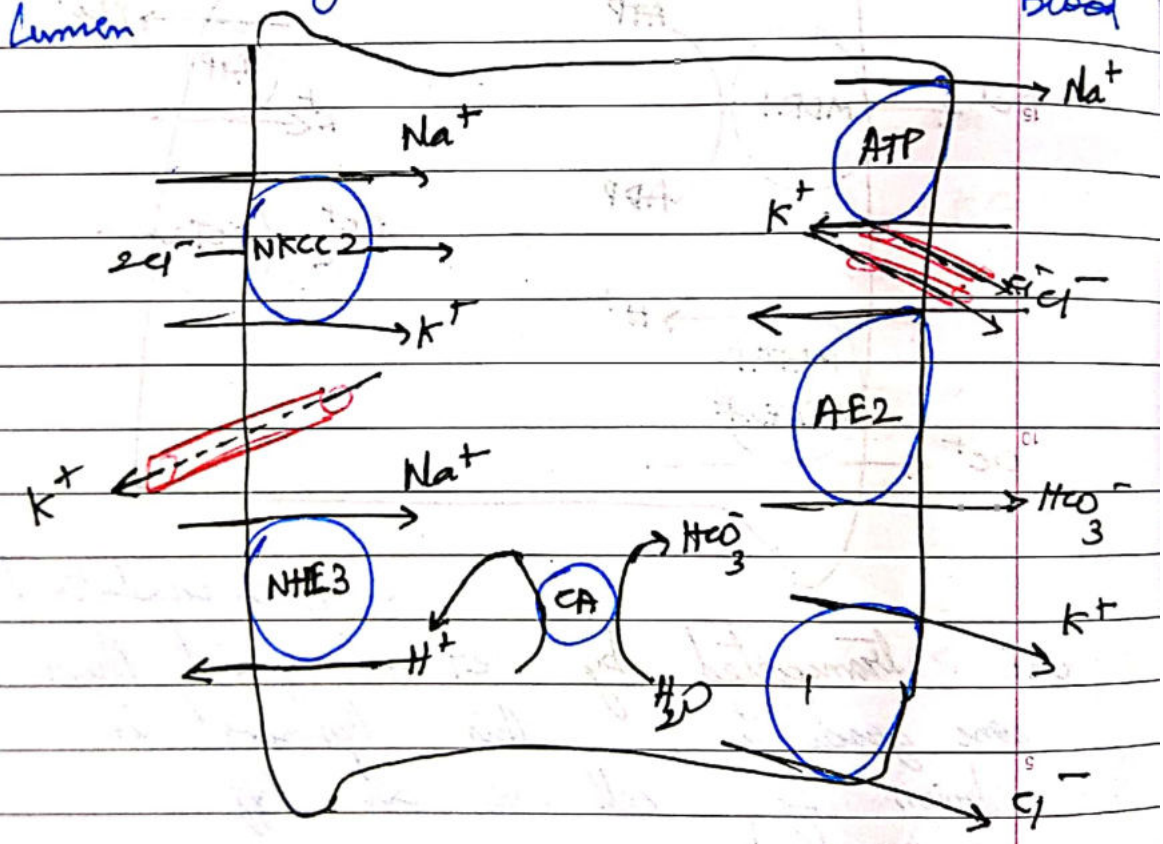
Reabsorption of NaCl occurs in both thin and thick ascending limbs.

Water reabsorption in Thin descending through AQP1 – Passive reabs.

Reabsorption of NaCl through Thin ascending limb is Passive

[NaCl] ⓟ in Thin Ascending due to reabsorption of H_2O in descending limb

Thick Ascending Limb.



K⁺ ATPase plays an important role
↳ provides chemical gradient for Na from tubular fluid to cell by maintaining low intracellular Na^+ concentration.

$1Na^+/1K^+/2Cl^-$ symporter (NKCC2) transports Na^+ and Cl^- across the apical membrane. The potential energy generated helps in transport of K^+ against it's conc gradient.

ROMK and Maxi K are K^+ channels move K^+ out to maintain K^+ conc in tubular fluid for the func of NKCC2

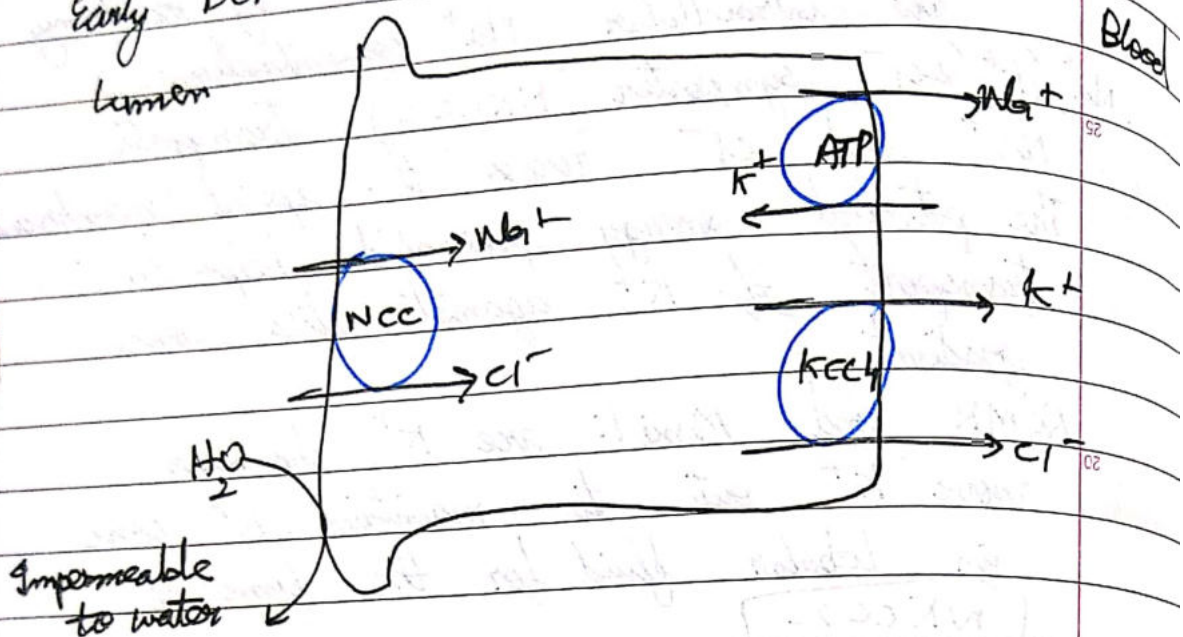
NHE3 also move Na^+ into the cell. The intracellular Na moves out through Na K ATPase in Basolateral mem HCO_3^- generated inside moves out through Cl^-/HCO_3^- antiport (AE3)
K^+, Cl^- leave through sep channels and symport

Reabsorption of NaCl leads to +ve charge in tubular fluid This helps in paracellular reabsorption of cations eg Na^+, K^+, Ca^{2+}, Mg^{2+}

Reabsorption of NaCl and other solutes - ⓓ in osmolality of tubular fluid to < 150 mOsm/kg H_2O.
Hence called diluting segment.

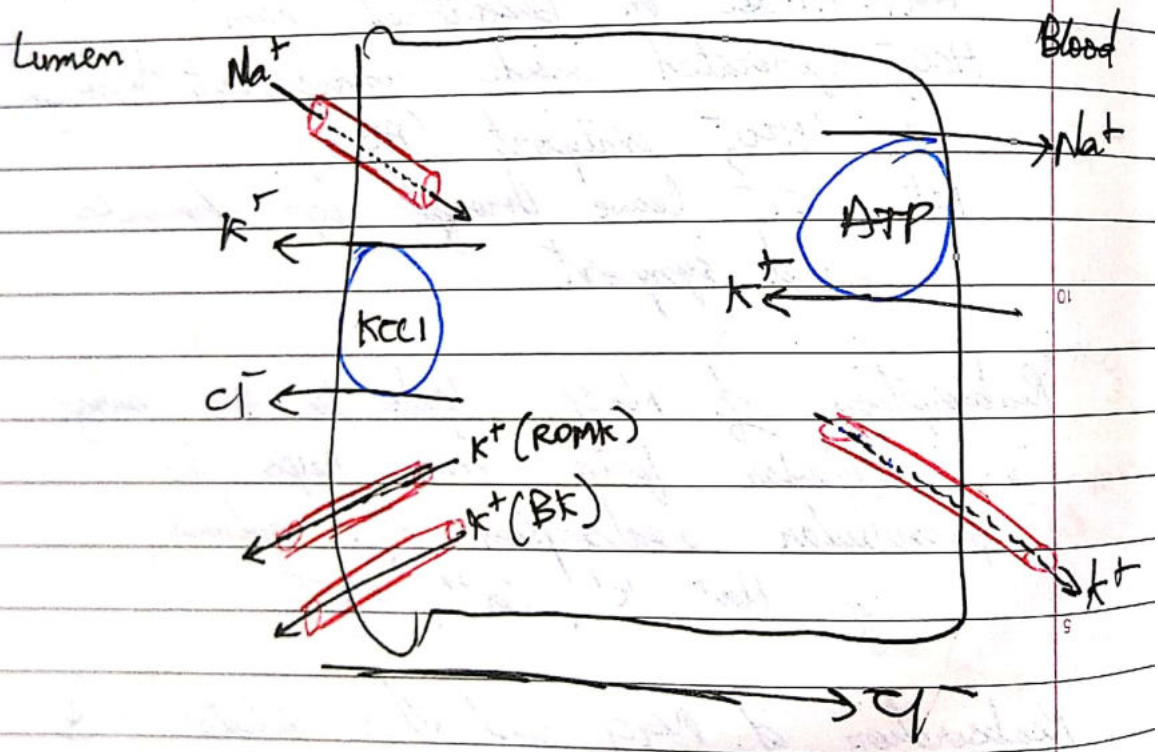
DCT and collecting duct :-

Early DCT

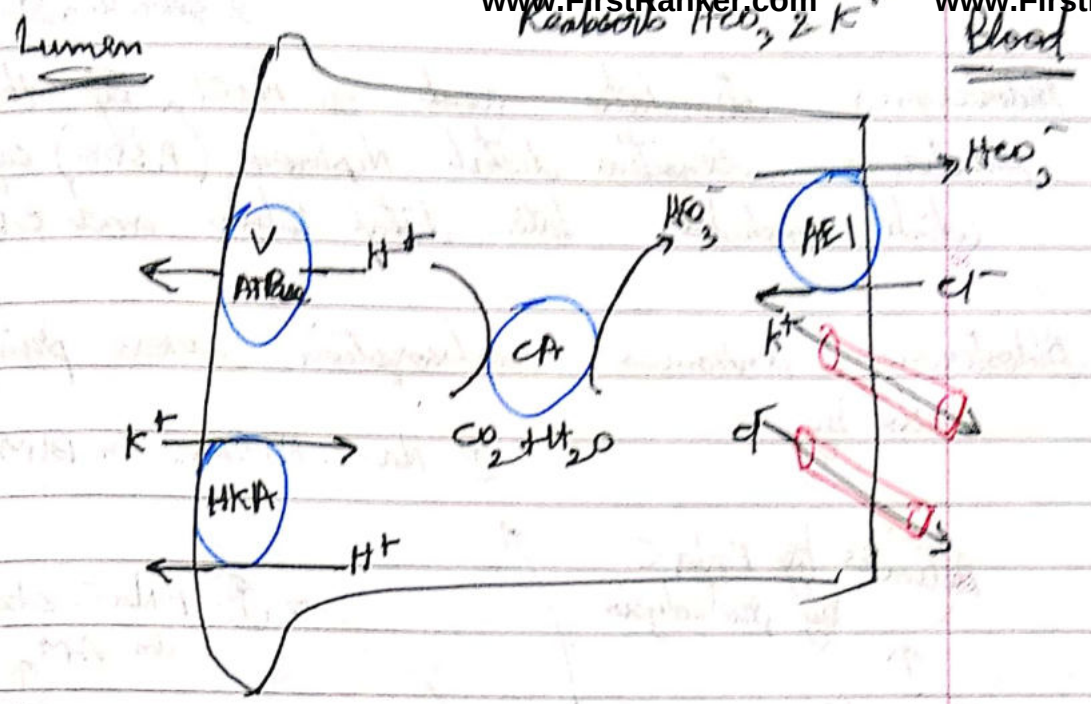


Late DCT

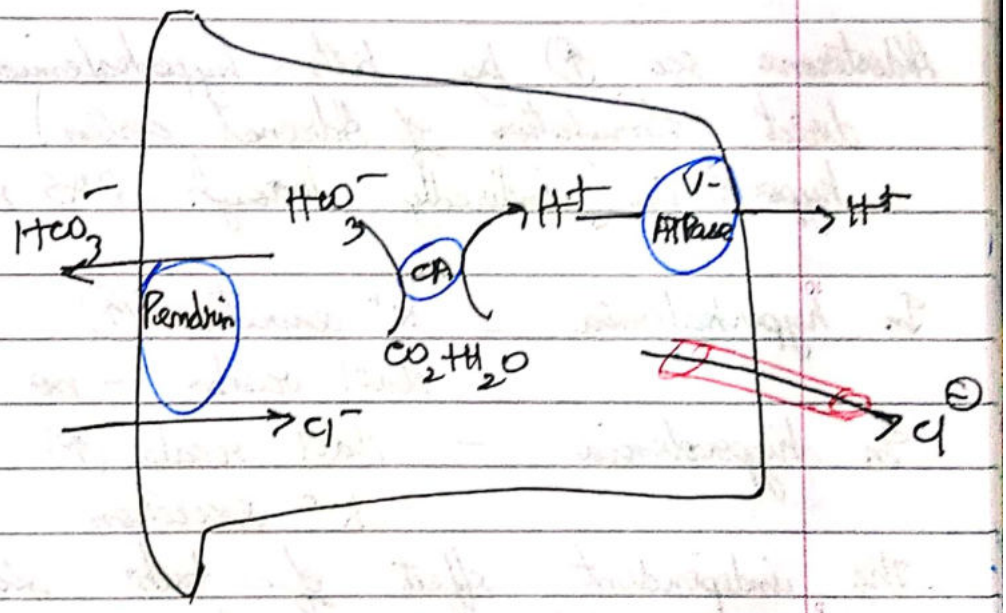
(a) Principal cells :-



a intercalated cells :- Secrete H^+
Reabsorbs HCO_3^- & K^+



b intercalated :- Secrete HCO_3^-
Reabsorbs H^+ and Cl^-



Aldosterone Paradox :-

Aldosterone stimulates reab of NaCl & secretion of K^+ by the Aldosterone Sensitive distal Nephron (ASDN) segments which includes late distal tubule and CD.

Aldosterone enhances reabsorption across principal cells by

↑ Na-K ATPase in BLM

Activates ENaC by proteolysis

↑ stimulating CAP1 a serine protease

Aldosterone

↑ ENaC channel in AM

↑

Elevating SgK1 which

Aldosterone sec ↑ by both hyperkalemia (through direct stimulation of Adrenal cortex) and hypovolemia (indirectly through RAS mech)

In hyperkalemia - K^+ excretion ↑
NaCl reabs - no change

In hypovolemia - NaCl reab ↑
K^+ excretion - no change

The independent effect of ~~both~~ aldosterone on urinary Na^+ & K^+ excretion is called the Aldosterone Paradox.

	ECFV depletion	Hyperkalemia
①	Aldosterone ↑	same
②	Angiotensin II ↑	Not here

③ Angiotensin II stimulates NaCl Reabs by PCT & by by Early DCT by activating with no lysine Kinase (WNK)
↓
enhances NCC (Na/Cl Sym)

Aldosterone stimulates Na^+ reab by ↑ ENaC by ↑ Sgk1 – ↑ ENaC in Apical membrane of Principal cells

Angiotensin II stimulates WNK in Principal cells which inhibits ROMK preventing ↑ in K^+ secretion

Aldosterone stimulates ROMK mediated K^+ secretion by principal cells by activating WNK

Bcoz of absence of Angiotensin II basal levels of WNK in early DCT is low – ↓ NaCl reabsorption via NCC.

Aldosterone escape :-

In hyperaldosteronism ~~or when~~ the ↑ Na^+ ~ H_2O reabsorption by renal tubules leads to an ↑ in ECF volume & hypertension
However after 10–15% ↑ in ECF pressure diuresis occurs ie excretion of Na and H_2O in urine is ↑d inspite of continued action of aldosterone
This is probably due to ANP

Starling forces :-

Forces that favour movt of solutes & fluid from interstitium to Peritubular capillaries are

P_i - hydrostatic pressure of interstitium

Π_{pc} - oncotic " of peritubular capillaries

$$J = k_f\left[P_i - P_{pc}\right] + \sigma\left[\Pi_{pc} - \Pi_i\right]$$

Starling forces do not effect transport by Henle's loop, DCT and CD as they are relatively less permeable to H_2O

dilation of efferent arteriole - ↑ P_{pc}

The importance of starling forces - glomerulo tubular balance.

↳ spontaneous changes in GFR do not alter Na^+ excretion in urine or Na^+ balance when ECFV is normal bcoz of G-T balance.

↓

Reabsorption of Na^+ and H_2O ↑ in proportion to ↑ in GFR & filtered amt of Na^+

Thus a const fraction of filtered Na^+ is reabsorbed despite variations in GFR