DIURETICS

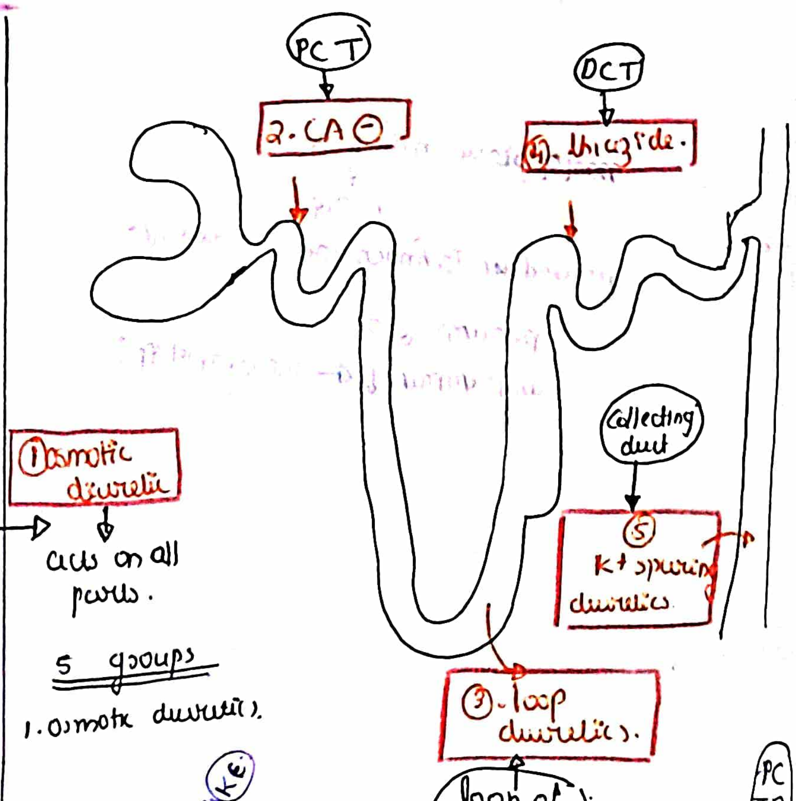
Based on which part of nephron it acts: CD, PCT, DCT, loop, CD

What do u mean by diuretics?

Diuretics → remove both water, Na^+ in urine.

drug only removing water.
↓
aquaretic ✓
not diuretic ($H_2O + Na^+$).

aquaretic → eg: water.



5 groups
1. Osmotic diuretics.

PC LL KC TD. (PCT)(TD)(LL)(KE)

PC TD. LL KC

PC Thomasinte department | Love letterayi KC.

① OSMOTIC DIURETICS.

→ Mannitol
- acts on all parts / any part of nephron.
- → works by osmosis
- Mannitol → high molecular weight.

↓

attracts water to wherever it is
↓
Cause it is osmotically active & attracts water from other compartments to it's own compartment so that osmotic pressure is equal on both sides.

But first-line drug in stable when given topically is {pilocarpine.}

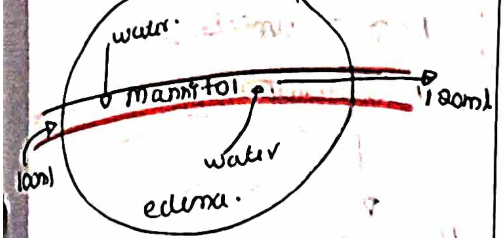
USES

→ ① Acute Congestive glaucoma / acute angle closure glaucoma

In acute attack of narrow angle glaucoma
↓
↑ in IOP
↓
due to ↑ in aqueous humor.
↓
When mannitol is given IV → reach eye vessels.
↓
It attracts water from aq humor into blood vessels.
↓
↓ aq. humour
↓
↓ IOP.

DOC in Acute Congestive glaucoma attack: IV Mannitol

(2) Cerebral Edema.



By osmotic effect, mannitol in blood vessel.

↓

Extract water from cerebral edema.

↓

↓ cerebral Edema.

↓

↑ blood volume
100 → 120ml.

Question: Q

what is the beneficial effect of mannitol in cerebral Edema?

Diuretic effect ✗ No ✓

Here, it's Osmotic effect!!

→ Diuresis is when it reaches kidney!! !

On hemorrhage ✗

mannitol enters brain tissues.

↓

mannitol will accumulate water in brain tissue.

↓

Aggravated Edema CI

Contra Indications

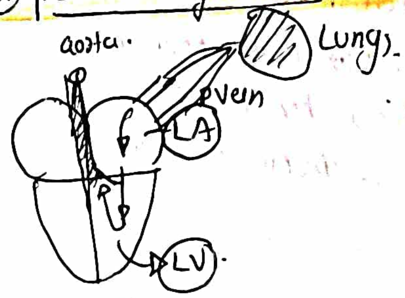
(1) Active cerebral hemorrhage

So we always have to check CT before giving mannitol.

↓

Can only give it after bleeding has stopped.

(2) pulmonary Edema



~~[illegible]~~ L.V → unable to pump blood into aorta.

↓

blood buildup in LV

↓

back pressure on L.A

↓

↑ hydrostatic pressure of pulmonary vein

↓

pulmonary edema.

when we use diuretic - mannitol

↓

↑ blood volume.

↓

↑ Volume in LV

↓

↑ back pressure.

↓

↑ pulmonary edema.

(3) Acute Renal failure

Blood volume ↑↑

↓

But in renal failure, kidney can't filtrate form urine.

↓

So hydrostatic pressure ↑

↓

Edema.

Summary

Contraindications:

→ cerebral hemorrhage.

→ acute renal failure

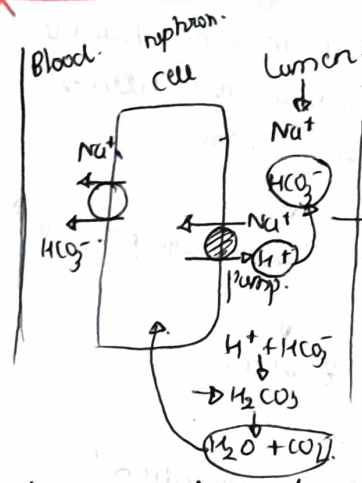
→ pulmonary edema.

Uses:

→ cerebral Edema

→ Acute Congestive glaucoma.

Carbonic Anhydrase Inhibitors



- glomerulus filtered Na^+ & HCO_3^- and they reached lumen.
- Na^+ H^+ pump is present on nephron cell
- It takes in Na^+ & pump out H^+.
- the $H^+ + HCO_3^- \rightarrow H_2CO_3$.
- $H_2CO_3 \rightarrow H_2O + CO_2$

- above 2 reactions are catalysed by Carbonic anhydrase.
- H_2O & CO_2 are passive substance and they can freely enter inside cell.
- Inside cell, they again combine.

$H_2O + CO_2 \rightarrow H_2CO_3$.

& $H_2CO_3 \rightarrow (H^+ + HCO_3^-)$

In net effect, H^+ & HCO_3^- reached inside cell.

- then, HCO_3^- & Na^+ are pumped into blood by $Na^+ + HCO_3^-$ pump

ie, what Na^+ & HCO_3^- that had been filtered, is not reabsorbed into blood because of Carbonic Anhydrase.

→ you don't need to remember all these..... just remember that

→ Carbonic Anhydrase causes Na^+ & HCO_3^- reabsorption into blood

No Need to remember

ie, if we inhibit C.A Na^+ & HCO_3^- will not be reabsorbed

Na^+ & HCO_3^- → Excretion in Urine ↑

along with Na^+, H_2O Excretion also ↑.

due to HCO_3^- → Urinary alkalisation & metabolic (blood) acidification.

C.A ⊖

- Acetazolamide
- Dorzolamide.
- Brinzolamide.

They are Non Competitive ⊖

But Reversible.

{Normally Competitive ⊖ are non-reversible}

⇒ They are poor Diuretic

Cause they are Self limiting

y?

Cause, as we said before, it causes metabolic acidosis & Urinary alkalosis

after some time, kidney will try to Compensate for metabolic acidosis.

Inhibit HCO_3^- Excretion in Urine.

So where are they used?

If not as Diuretics

Uses:

G - glaucoma ✓

A - alkalinization of urine ✗

M - mountain sickness ✓

E → Epilepsy ✗

glaucoma

D.OC in Angle closure glaucoma.

↓

ie, in normal time, we use CA ⊖ so that IOP won't be increased

but when there is sudden ↑ IOP → it's called

↓

acute Congestive glaucoma

Emergency!

↓

then we give mannitol

alkalinization of urine

not that preffered, cause we can give Na_2CO_3.

& there is acidosis of blood so not that good.

Epilepsy

- used earlier...
- Now we have better ones.

MOUNTAIN SICKNESS

IMPT!

DOC is CA ⊖

- at height → PO_2 ↓
- So hyperventilation occurs.
- ↓ CO_2. $[CO_2 + H_2O \rightarrow H_2CO_3]$
- So respiratory alkalosis occurs.
- we know, CA ⊖ causes ↑ HCO_3^- urine excretion, so PH normal!

It is DOC to prevent & treat Mountain Sickness

treatment

① give O_2

② acetazolamide DOC

③ steroids for pulmonary edema. {not digoxin & all cause it's not heart's fault}

④ Descend down. Not Impt

Cardiac valve drugs have no role in treating pulmonary edema due to acute mountain sickness.

So. Must remember Uses!

- Glaucoma
- Mountain Sickness

Side effects S/E.

① Metabolic acidosis

② hypokalemia. ★

{maximal hypokalemia compared to other diuretics}

③ paraesthesia

④ (kidney stones). ★

{calcium crystallize in alkaline medium}

⑤ Liver failure ★

C/I

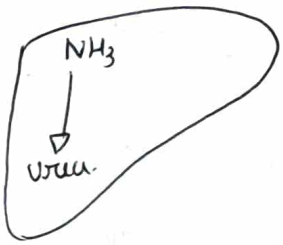
↓

Coma of hepatic coma.

↓

Why?

Lemme tell you hon!



Normally, Liver converts NH_3 → urea.

cause NH_3 is back

when there is liver failure, kidney does it.

$NH_3 + H^+$

↓

NH_4^+

Charged....

so can't be reabsorbed

↓

Urine excretion

But for that we need H^+

H^+ is in acidic urine.

not in alkaline urine.

CA⊖ alkalyes urine..
So NH_3 can't be removed
↓
So now kidney also can't
↓
NH_3↑ – reach brain.
↓
Causes Coma ∴

So Don't give CA⊖ to Liver failure patients.

C/I of CA⊖
↓
Liver failure

X ⟶ X

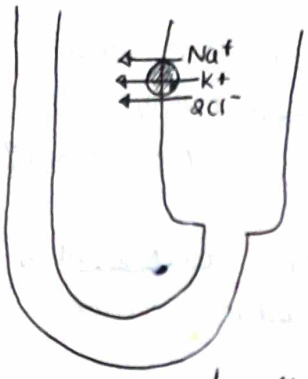
CA⊖ – Impt

① DOC in angle closure glaucoma
② DOC in AMS & prevention of Mountain Sickness.
③ Max Hypokalemia
④ Kidney stone s/e
⑤ Liver failure c/I.

③ Loop Diuretics

- Furosemide
- Torsemide
- Bumetanide.

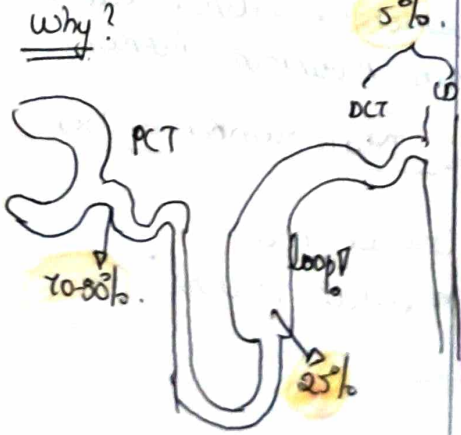
They act on:
LOOP OF HENLE
↓
on thick ascending limb.



↓ Actually, they are.
⊖ Na+ K+ 2Cl⁻ pump
Inhibitor

They are:
High Ceiling Diuretics
↓
ie, they can remove max Na+ & Liters of water!!

Why?



- 70-80% water reabsorption occurs from PCT.
- So if we are giving blockers at PCT ie, CA⊖, shouldn't that be high ceiling?

The thing is-...

① Even though we give CA⊖, we can block reabsorption from PCT... but still it has many places to go... loop, DCT, CD etc... So it can still be reabsorbed

② due to metabolic acidosis it's very limiting.

Meanwhile... at loop there is only 25% reabsorption but by giving loop diuretics we can block that Completely!! pukka and also there isn't much to go after loop...

∴

High Ceiling
⇒ Loop Diuretics

Not CA⊖ @ PCT!! ✗
(70-80%)

USES of loop diuretics

- Edema.
- hypertensive Emergency.
- Br^- & I^- poisoning ★
- hypercalcemia (loop loses calcium)

pulmonary Edema

→ we give furosemide.

→ before Even it's diuretic action, patient will get ruby cause it's vasodilatory.

→ for pulmonary Edema, furosemide gives fastrelief due to it's

→ vasodilatory action ★

→ diuretic ✗ action needs time to work.

S/E

Loop & Thiazides.

↓ Na
↓ K
↓ Mg
↓ H. - metabolic alkalosis

↑ Glucose
↑ Uric acid.
↑ Lipids.

difference

loop ↓ Ca^{2+} (loop loses calcium)

Thiazides ↑ Ca^{2+}

④ thiazides

→ Thiazides Inhibit Na^+-Cl^- pumps on Early part of DCT.

→ Impt to remember

① thiazides	thiazide-like
Chlorthiazide	• metolazone.
hydrochlorthiazide	• Indapamide.
polythiazide.	• Chlorthalidone

Uses

① hypertension.

② metolazone - renal failure.
{no other thiazides are used in renal failure}

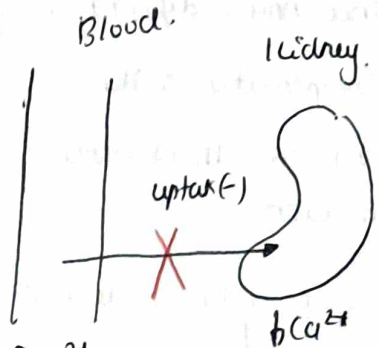
③ Edema

④ Br & I^- poisoning.

⑤ bg. osteoporosis (thiazide ↑ Ca^{2+})

⑥ Renal recurrent stones (↓ Ca^{2+} in kidney)

⑦ diabetes insipidus.



* thiazides - ↓ Ca^{2+} in blood & decrease Ca^{2+} inside kidney. ★

So, it is used in Osteoporosis to ↑ Ca^{2+} (blood) & in kidney stone to ↓ Ca^{2+} (in kidney.)

Looks paradoxical.

⇒ thiazides are hypercalcemic so don't get confused why are we using hypercalcemic in stones?

In DI insipidus

→ there is ADH deficiency.

→ it retains only water ↓ not Na function of ADH.

→ if ADH is deficient... water only will not be retained.

→ so plasma osmolarity ↑

→ stimulates thirst centre

→ ADH ↑

→ Since ADH is deficient...

→ Compensation solely depends on thirst centre activation.

→ so polydypsia develops.

→ as a result polyuria also occurs

Q) how does thiazide works in this ?

- as we go down in medulla, urine becomes more concentrated.
- dilution occurs at DCT.
- on giving thiazide, dilution is blocked.
- so thiazide causes excretion of concentrated urine...

ie, plasma osmolarity ↓

ADH deficiency - Db Insipidus

↓

↑ water excretion alone.

↓

↑ plasma osmolarity & thirst ⊕ due to thirst centre ⊕.

give thiazides

↓

Con urine form.

↓

↓ plasma osmolarity

↓

no activation of thirst centre

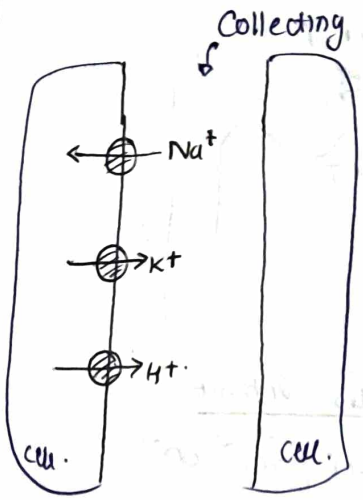
↓

no polydypsia.

↓

no polyuria.

K+ sparing Diuretics



* 3 pumps. - Separate pumps.

that does Na^+ absorption

K^+, H^+ excretion

* But the boss is Na^+.

ie, due to working of Na^+ pump, there is ↑ Na^+ inside cell

↓

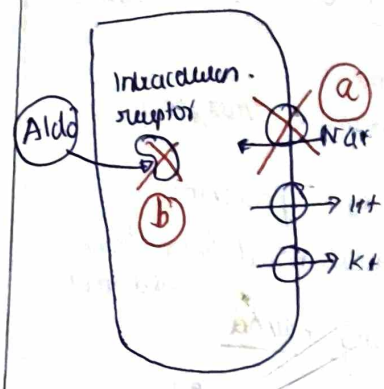
and because of ↑ positivity the remaing two (+) K & H are pushed out.

ie, if Na^+ pump doesn't work K & H will not be pushed out...

It like Cause & effect.

If Na pump works - rest works

If not - rest won't.



Aldosteron from blood... acts on its intracellular receptor and activate all.

3 pumps

ie, ↓ ↑ causes

Na^+ retention

K^+, H^+ excretion.

ⓐ epithelial sodium channel blocker.

ⓑ Aldosterone receptor Inhibitor

ⓐ & ⓑ →

ⓐ → block Na^+ reabsorption

ie, ↑ Na, water excretion

↓

Diuresis.

epithelial Na channel blocker

↓ causes

Diuresis

But we know Na is lost, since Na X
K+ & H+ also Excretion X

leads to
Hyperkalemia & metabolic acidosis

all other diuretics → K+ ↓ hypokalemia.
K+ sparing Diuretics → K+ ↑ hyperkalemia

(b) leads to block of 3 pumps again.
↓
Diuresis.
Hyperkalemia
acidosis

(a) & (b) both
- Diuresis
- HYPERKALEMIA
- acidosis

(a) e Na+ blocker.
↓
Amiloride.
Triamterene.

(b) Aldo.R. block
↓
Spironolactone.
Eplerenone.

K+ sparing Diuretics

P – pott sparing.
A – Amiloride.
S – spironolactone
T – Triamterene.
E – Eplerenone.

Uses.

- Uses of aldo R antagonist ie, spironolactone & Eplerenone.
- Cirrhosis edema
- Resistant Hypertension.
- ↓ LVH ypertrophy in Congestive heart failure.

Cirrhosis → ↑ aldosteron, so use Ald rec(−)

S/E

DISCO drug.

- gynaecomastia, menstrual problm, (male) b.test rec(−)

Di – digoxin
S – spironolactone.
C – Cimetidine + ketoconazole.
O – oestrogen.

- Eplerenone X doesn't cause gynaecomastia. Impt. diff
↓
only ald rec (−)
not testosterone recep (−)

Impl stuff.

- all other diuretics need to get filtered into tubule & then act on luminal side of lining cell.
- but aldosterone receptor blockers comes from blood & act through Basolateral side ... not from luminal side.

ie, spironolactone act from basolateral side.