MBChB Year 2 Renal Tutorial

A phase I clinical trial is being conducted on a new anti-inflammatory drug. Volunteers are given small doses of the drug, to determine how it behaves in the human body. The pharmacokineticists are interested in whether;

(a) the drug is held back by the glomerular filter, or

(b) the drug passes freely through the glomerular filter, or

(c) The drug is actively excreted (secreted) by the tubule cells.

The clinical biochemists provide the following measurements for one volunteer;

- Plasma Creatinine **1mg/dL**
- Plasma Drug = **25mg/dL**
- Urine Creatinine = **0.16mg/mL**
- Urine Drug = **12mg/mL**
- Urine flow rate = **5mL/min**

On the basis of these figures, which of a,b or c is the correct possibility?

Remember I showed you the derivation of the GFR equation;

Glomerular filtration rate

GFR x Plasma [Creatinine] = Urine flow rate x Urine [Creatinine]

amount passing into nephron *amount passing out of nephron*

So…

$$GFR = \frac{UFR \times [C]^{urine}}{[C]^{plasma}}$$

So we can use this to calculate GFR;

$$GFR = \frac{UFR \times [C]^{urine}}{[C]^{plasma}}$$

$$GFR = \frac{5mL/min \times 0.16mg/mL}{0.01mg/mL} = 80mL/min$$

NB converted units

We can use a similar approach to look at the excretion rate of the drug

$$\text{Rate} = \text{UFR} \times [\text{Drug}]^{\text{urine}} = 5\text{mL/min} \times 12\text{mg/mL} = 60\text{mg/min}$$

$$\text{Expected Rate} = \text{GFR} \times [\text{Drug}]^{\text{plasma}} = 80\text{mL/min} \times 0.25\text{mg/mL} = 20\text{mg/min}$$

So passive filtration would give us an excretion rate of 20mg/min but we actually see 60mg/min.

We have an 'excess' secretion of 40mg/min.

Or you could have crunched this into a single algebraic equation before throwing the numbers in;

$$\text{'Excess Secretion'} = UFR \left([Drug]^{urine} - \frac{[C]^{plasma} \times [Drug]^{urine}}{[C]^{plasma}} \right)$$

To answer this question with no numbers, you could have just compared the ratio of urine to plasma creatinine with the ratio of urine to plasma drug.

Quick problem:

What would be the effect on the kidney of someone who keep having panic attacks?

Potassium _flux is sensitive to body pH:

panting

Alkalosis: H^+ out-pumping by intercalated cells reduced, so less K^+ re-uptake (AND apical K^+ channel activity increased in Prinicipal cells and so is the Na^+/K^+ ATPase -> more K^+ loss)

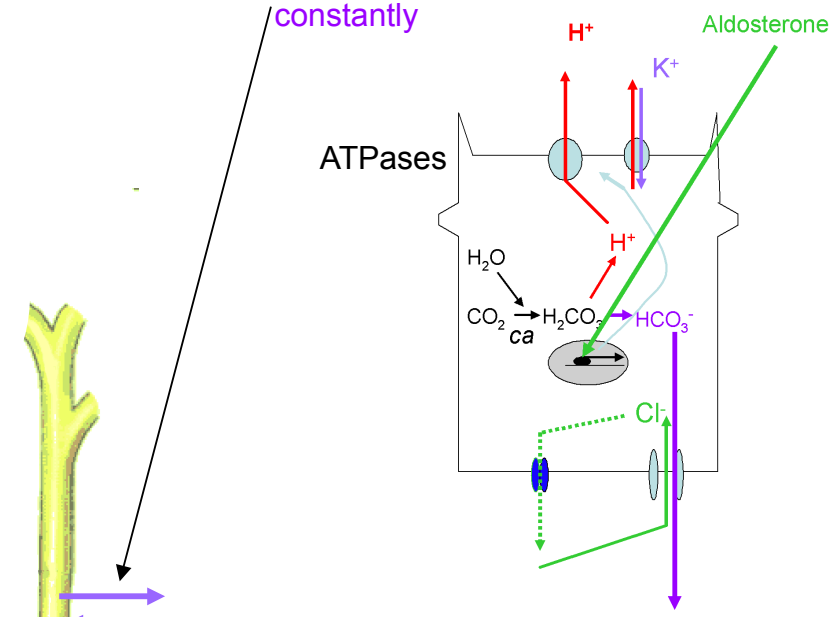
→ hypokalaemia

Acute acidosis: H^+ out-pumping by intercalated cells increases so K^+ reuptake increases. Also, apical K^+ channels on Principal cells less active (by an effect on their intracellular regulation) so K^+ secretion falls.

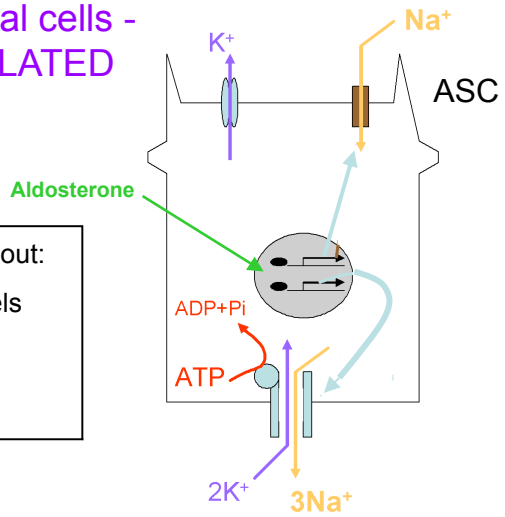
→ hyperkalaemia

(Chronic acidosis; Na pump less efficient in PCT, so urine more copious and helps flush K^+ away)

Re-absorption by intercalated cells constantly



Excretion by principal cells - REGULATED



1)	High tissue K^+ increases K^+ flow into cells thence out:
2)	Low K^+ diets ►tyrP of apical K^+ channels ►channels removed from membrane
3)	High K^+ diets cause loss of tyrP and channels accumulate in membrane

Data from Giebisch GH. (2002) A trail of research on potassium. Kidney Int. 62:1498-512

Quick problem:

What would be the effect on the kidney and then the whole body of having renal arterial stenosis?

How does the macula densa work?

NOTE: this is the slide I showed you in the lectures, which follows what happens if pressure is elevated: in this story, everything is the other way round.

Elevated glom blood pressure

Filtrate flows faster

Less time for solute recovery

More NaCl remains in the distal tubule

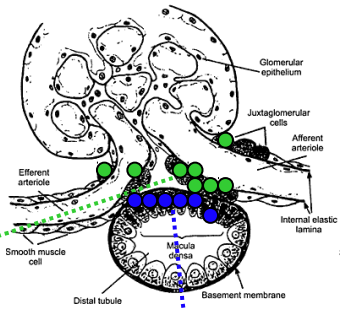
Macula densa cells pump out more NaCl than they usually can

(because there is more available)

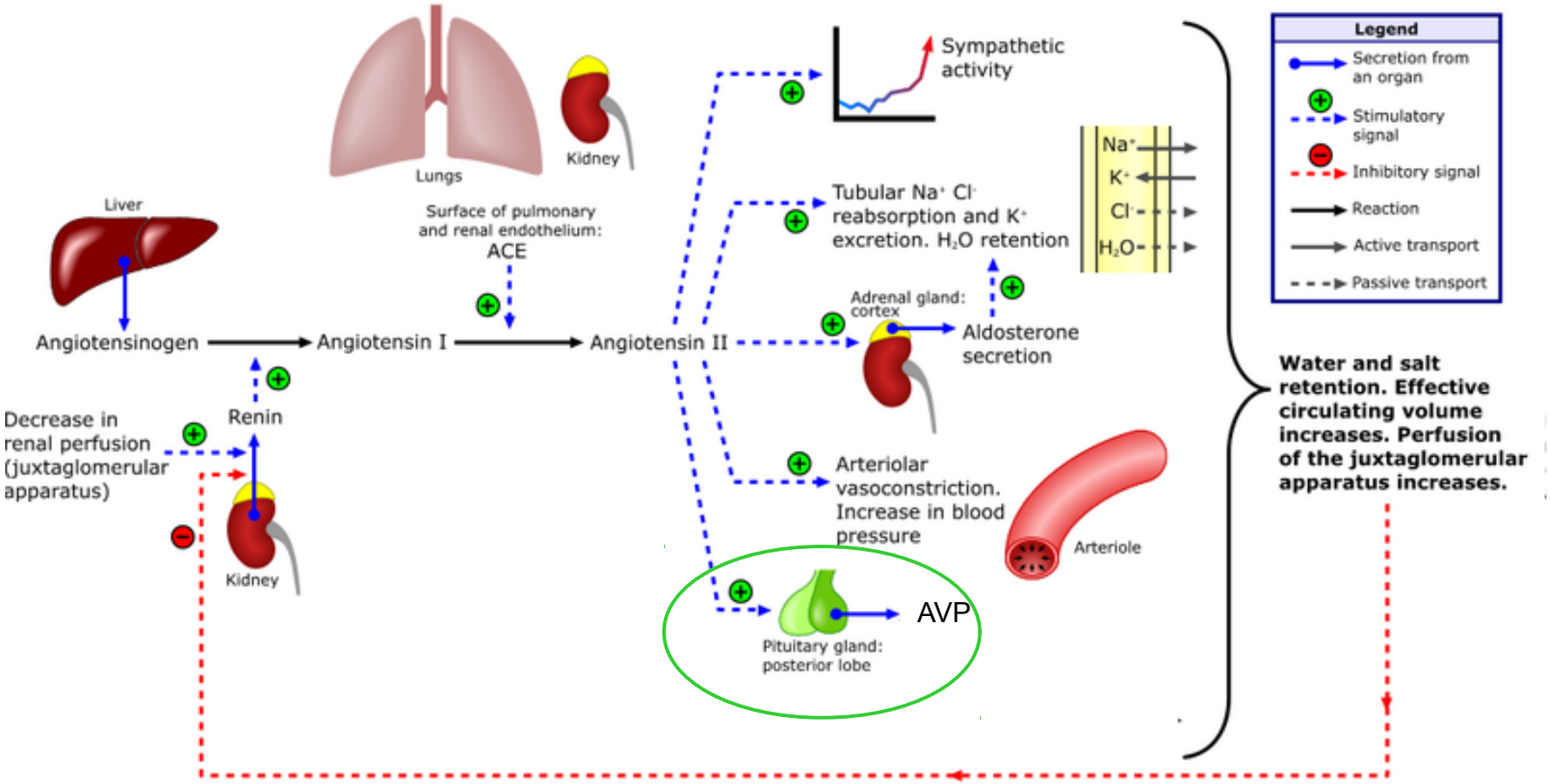
Juxtaglomerular cells release renin

Afferent arteriole constricts in response to adenosine

Juxtaglomerular cells release adenosine



Renin-angiotensin-aldosterone system



Low renal blood flow – kidney makes more renin – elevates systemic pressure to compensate (5% of hypertensives are due to Renal Artery stenosis)

Wikipedia commons

Quick problem:

A 20yr old man presents with dizziness and weakness. He has had TB in the past. On examination he was

-dehydrated

-had low bp (70/40)

- Plasma Na^+ 125mM (low)
- Plasma K^+ 6mM (high)
- Plasma glucose 3mM (low)

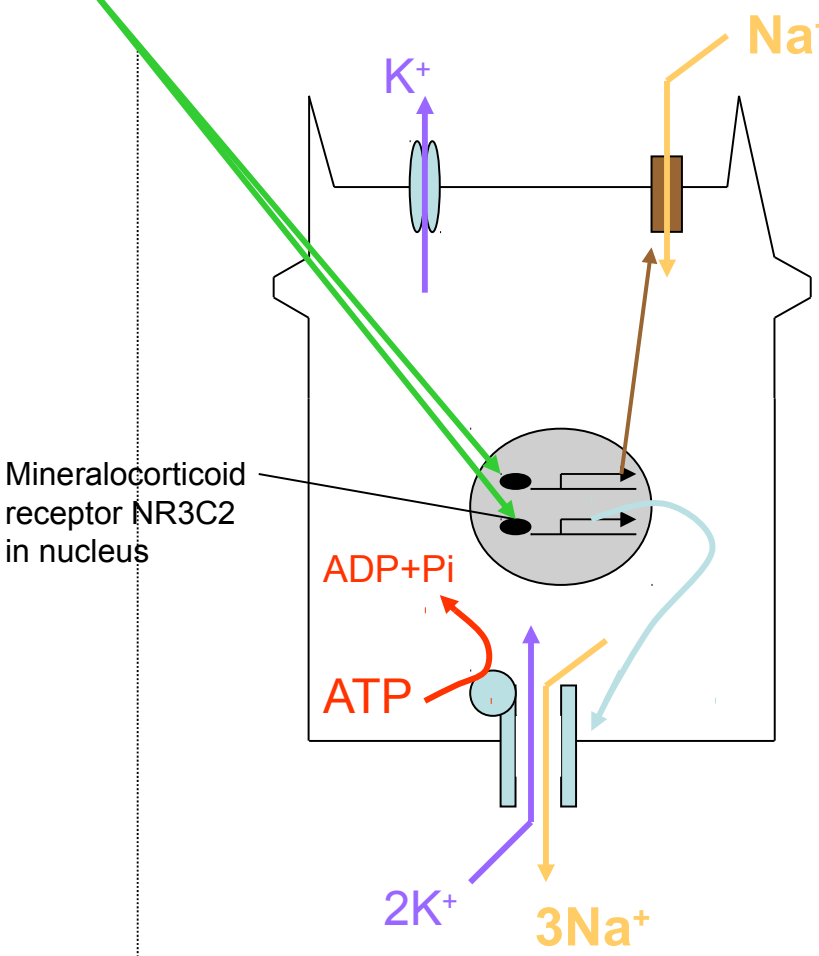
What's the most likely diagnosis?

Action of Aldosterone on kidney cells:

Aldosterone

Not made if adrenal is missing

Coll duct Principal cell:



TB can destroy the adrenal cortex; this also reduces glucocorticoids hence hypoglycaemia .

-> aldosterone means more Na recovery and K secretion