Renal physiology and AKI – Q and A

Q1. What is the reason behind t4 RTA seen in Diabetes - is it because they are on ACE inhibitor? or another etiology ?

Partly due to ACEI/ARB which have the downstream effect of less aldosterone production. But, low plasma renin activity is common in diabetic patients due, in part, to a defect in the conversion of the precursor prorenin to active renin which leads to decrease in aldosterone production.
Of note, spironolactone type of drugs cause aldosterone resistance. All other causes of TYPE 4 RTA are associated with low aldosterone production.

Q2. Can you please explain how lithium & NSAID comes

I am assuming we are asking the renal effects of the two. Lithium causes two effects- a chronic tubulointestinal disease and almost 20-40% develop nephrogenic DI.
Also remember, lithium by its action on the CasR can cause almost an acquired form of FHH- that is high serum calcium due to hypocalciuria (renal effect due to TAL CaSR effected by lithium) and high normal to high PTH (PTH CaSR effected by lithium).

NSAIDs by preventing formation of the vasodilatory prostaglandins predispose to AKI. Under basal conditions, these prostaglandins have no significant role in the regulation of renal perfusion. However, in the setting of hypotension and reduced renal perfusion from any cause, the prostaglandin synthesis is increased to maintain renal perfusion and minimize ischemia/AKI.
Following conditions predispose to AKI secondary to prostaglandins-

- Chronic kidney disease (CKD), especially stage 3 or worse (ie, estimated GFR [eGFR] <60 mL/min/1.73 m^2)
- Volume depletion from aggressive diuresis, vomiting, or diarrhea
- Effective arterial volume depletion due to heart failure, nephrotic syndrome, or cirrhosis
- Older age
- Severe hypercalcemia with associated renal arteriolar vasoconstriction

Q3. How FGF23 causes a decrease in vitamin D production?

It decreases the activity of 1alpha hydroxylase and therefore decreases the production of activated Vit D3

Q4. Is contrast induced neprhopathy something we should actually worry about or a myth when considering whether to give a patient a scan? Have been told the evidence is mixed, and sometimes I see clinicians stopping frusemide or not doing the scans out of fear of contrast kidney injury

Contrast induced nephropathy is a form of ATN, but unlike ATN following prolonged prerenal AKI due to ischaemia/sepsis etc, here the ATN comes quickly (within 48 hours) and also, resolves quickly- by 7 days. It is basically due to the vasoconstrictor effect of the contrast. Try to hold metformin as in case the patient develops AKI< may become acidotic and the metformin will potentiate the acidosis by more production of lactic acid.
Try to hold off all non-critical potential nephrotoxic drugs for 48 hours prior and administer normal saline pre procedure in normotensive/hypotensive patients. Of course, use the lowest volume of lowest osmolality agent.

Q5. Giving fluids pre and post contrast does it prevents the nephropathy and is it evidence based ?
Yes absolutely- normal saline is fine. No need for sodium bicarbonate(some like it) unless patient happens to be acidotic.

Q6. If a certain drug (eg Augmentin) causes AIN, is this now considered an allergy and should not be prescribed again? Or can the patient be retrialled on it later?

Prefer to not use them unless life threatening need.

Q7. What is more specific for AIN? white cell casts or eosinophiluria?
question asked in the written previously

White casts. Eosinophiluria can be seen in many conditions including UTIs/prostatitis/some of the progressive GN/ATN.

Q8. what is the dose of salbutamol used for managing hyperkalaemia?
Use liberally- I don't think there is a prescribed dose.

Q9. I've always wondered regarding the management of postrenal AKI - in the acute setting, if we insert an IDC which is draining good urine - is the renal USS still urgent or can it wait? Thanks!

Ideally do the USG before putting in the IDC or clamp it for few hours before the scan.

CKD – Q and A

Q1. Why are live vaccines contraindicated in CKD?
Patients with ESKD have a reduced response to vaccination because of the general suppression of the immune system associated with uremia. Compared with vaccination in patients without ESKD, for example, dialysis patients have a lower antibody titer and an inability to maintain adequate antibody titers over time.
People with ESRD are immunocompromised with ongoing inflammatory condition and also lose of good globulins (immunoglobulins) in urine due to the accompanying tubule-intestinal disease.

Q2. What's "firstline" to suppress PTH in CKD? When we try suppress the PTH, do we measure PTH and see how the patient responds to our interventions?
Lower the phosphate with phosphate binders and check PTH 6- monthly. In case of tertiary hyperparathyroidism, cinacalcet or sometimes parathyroidectomy especially after transplant

Q3. Why /how Alluminium causes osteomalacia ?
Aluminum toxicity is now uncommon because aluminum is removed from water used for dialysis and because nonaluminum-containing phosphate binders are widely available. Osteomalacia is characterized by low bone turnover in combination with abnormal mineralization. Osteomalacia, which is now uncommon, was due primarily to aluminum deposition in bone at a time when aluminum-containing antacids were used as phosphate binders. Basically as aluminium deposits itself over the bone, it prevents the usual turnover.

Q4. You note that we should use calcitriol to reduce PTH, but then also noted that we should aim for PTH to be 7x higher for adynamic bone disease. Can you please further explain this?
Aim to keep the PTH in 2-7 times the upper limit of normal. Less predisposes to low turnover bone disease (adynamic bone disease) and more can lead to high turnover bone disease. People use calcitriol as Vit D has a direct inhibitory effect on PTH, but many like myself do not use it. The reason being calcitriol causes Ca absorption from the intestines and as CKD progresses, many of them tend to have Ca in the upper end. Also, remember with the high phosphate, there is increased calcium/phosphate deposition in the tissues including blood vessels making them stiffer, narrowed, and increasing the chances of calciphylaxis.

Q5. What is the logic of giving calcium with food instead of without food?
Calcium binds to phosphate in the food and they are lost in the stool with minimum intestinal absorption. The idea is to prevent phosphate absorption from the food.

Q6. I thought urea was freely filtered across the osmotic membrane (i.e. not an osmole) - how does this factor into the brain swelling?
I think you are talking about dialysis disequilibrium syndrome. Urea takes time to move across membranes- could be hours while water moves quickly.

Q7. Past Exam Question (Wasn't sure about):
What is the earliest physiological change seen in diabetic nephropathy?
A. Microalbuminuria B. Decreased glomerular filtration rate C. Increased glomerular filtration rate D. Anaemia E. Hyperkalaemia

The toss here is between A and C. I would choose C. The increased intraglomerular pressure due to RAAS activation causes increased albumin loss in the urine.

Q8. My understanding is that recent evidence supports ongoing use of SGLT2 inhibitor into ESRF if it were already commenced prior to eGFR falling < 30?

Yes- I am told the TGA now says can continue dapagliflozin.

Q9. Can you clarify your point about not adding ARB/ACE in DM associated proteinuria and CKD. At what point do we not add/avoid it? Do you mean we continue but don't add it? Or we cease at a certain GFR/level proteinuria?

Use either ACEI or ARB to decrease the intraglomerular pressure but please do not add both. Significantly increases chances of AKI and hyperkalemia.
When you start either, pick a small dose and check EUC in 5-7 days. As long as not jumped by >20%, keep using. If all OK then slowly titrate upwards.

Q10. Why does hypokalemia worsen initially with alkali therapy in prox RTA?
As you replace alkali as sodium bicarbonate in proximal RTA, because the nature of the disease (inability to reabsorb the bicarbonate), the sodium bicarbonate which is freely filtered across the glomeruli is lost in the urine. The CD cells realise that the urine is full of Na, they do not like this and try to reclaim the Na. In exchange then they lose K and so more hypokalemic. So can recommend potassium-based alkali e.g., potassium citrate.

The same mechanism leads to hypokalemia on loop and thiazide diuretics.

Peritoneal Dialysis – Q&A

Q1. Do you mind explaining what APD is and the difference between APD and CAPD, as well as then where CCPD/NIPD? Thanks

CAPD - Continuous Ambulatory PD: PD exchanges are conducted manually by the patient (and without a cycler/machine)
APD – Automated PD with the use of a cycler/machine to perform PD exchanges
Patients using the cycler (APD) – typically connect their PD catheters to the machine that performs PD exchanges for them at night, when they are asleep. When patients get up in

the morning – when they disconnect the machine, they can either have no PD fluid in the peritoneal cavity during the day (NIPD – Nocturnal intermittent PD) or have PD fluid in the peritoneal cavity during the day time (CCPD – Continuous cycler PD).

Q2. What is limiting factor for PD efficacy - ? Fibrin ? Constipation ? Recurrent PD Peritonituis

If the question is why PD is less efficacious than HD:
Dialysis efficiency is based on 3 main factors:

1. Blood Flow rates: The peritoneal membrane is perfused by arterial blood flow - between 50-100 mL/min and cannot be increased – as compared to HD where we are able to increase blood flow rates up to 300mls/min
2. Surface area of semipermeable membrane: In PD the surface area of the peritoneal membrane is fixed and approximates the patient's body surface area. In addition, only up to 60% of the available peritoneal membrane is recruited /in contact with the PD fluid in the abdomen. In HD, we can increase the surface area of the dialyser to match patients' needs.
3. Dialysis fluid (Dialysate) flow rate: In PD – limited by the number of PD exchanges/day and the volume of fluid administered in each bag – Usually 8-10 litres a day. Whereas in HD the standard dialysate flow rate is around 600mls/min.

If the question is what factors limit PD efficacy: Many!!
Chronic: Loss of residual kidney function, Loss of peritoneal membrane function over time, prescription mismatch with peritoneal membrane transport characteristics, recurrent PD peritonitis, etc..
Acute: Inability to do PD: Constipation, Catheter migration, omental wrapping, peritoneal adhesions, noncompliance etc etc

Q3. Would complications restrict use of PD in future?
Loss of peritoneal membrane function overtime
Loss of Aquaporins over time – Ultrafiltration failure
Sclerosing peritonitis
Fungal peritonitis
TB peritonitis
Recurrent pseudomonas peritonitis
Intractable hernias
Recurrent pleuro-peritoneal leaks
Major abdominal surgeries

MCQ Discussion on NS, GN and Dialysis – Q and A

Q1. What is the difference between SLED and CRRT? Thanks
SLED is essentially standard haemodialysis but with a slower blood flow rate and dialysate flow rate. A SLED session occurs over about 6 – 8 hours whereas a normal HD session would be about 4 – 5 hours. SLED therefore uses a combination of diffusion and convection. CRRT however is reliant predominantly on conversion only.

Q2. In the question about IgA nephropathy mx, would the patient benefit from immunosuppression given that they have persistent proteinuria? Makes sense to up the perindopril first though
Generally, immunosuppression is reserved for patients with proteinuria > 1g despite RAS blockade so in this case because the level is still lowish and the RAS blockade has not been maximised it is a little premature to be immunosuppressing them.

Q3. Does ATTR amyloidosis also present with kidney involvement most commonly?
I apologise that I am not sure if this is the case!

Q4. 90% aa amyloidosis affects kidney, but not necessarily Nephrotic Syndrome
right as in the question?

I agree that it affects the kidney but may not necessarily be nephrotic syndrome. For the purpose of this question however I would still answer nephrotic syndrome

Q5. So MPGN/MCGN/RPGN/mesangioproliferative are histological patterns of kidney disease, but IGA/post infections/cryo/SLE nephritis etc are disease pathologies that cause these patterns?

That is exactly right. A patient with SLE for example may have MPGN, RPGN or mesangioproliferative appearance on renal biopsy because they have different classes of lupus nephritis, but the cause is still lupus and the diagnosis is lupus nephritis. Membranoproliferative = mesangiocapillary; mesangioproliferative is not the same as MPGN and MCGN

Q6. What is dense deposit disease in the MPGN framework? Are the 2 types immune complex or complement mediated?
Dense deposit disease is C3 only in the MPGN framework

Q7. Are SGLT2 inhibitors relevant to management of IgA nephropathy and if so how much is it being used in clinical practice?

SGLT-2 inhibitors are still be defined in IgA nephropathy and in fact at Westmead we are participating in a clinical trial looking at the role of SGLT-2 in these patients. I suspect they could be used in patients who have proteinuria despite RAS blockade but have already received a course of immunosuppression for example.

Q8. What are the indications for intermittent dialysis?

Chronically… Uraemic symptoms as per the IDEAL study and chronic fluid overload/hyperkalaemia/acidosis that cannot be managed by medication (less common)

Q9. Why is PD preferred in congestive heart failure?

It is a slower treatment (24 hours a day, 7 days a week rather than 5 hours 3 times a week) which results in less dramatic fluid shifts and less severe cardiovascular demand.

Q10. What is the difference between SLED and CRRT? Thanks

See above