Question time for Revise Nephrology 2023

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Q 1

Which of the following does not lead to hypokalaemia with metabolic alkalosis?

a. Bartter syndrome
b. Addison disease
c. Hyperaldosteronism
d. Chronic vomiting
e. Diuretic abuse

Answer is b

ADDISON DISEASE characterised by inability to excrete K+ and H+

How do we differentiate between the rest?

- Hyperaldosteronism will be characterised by hypertension while Bartter and Gitelman will have low to normal BP
- Patient who abuse diuretics will show variable urinary Cl levels depending on the timing of diuretic abuse and in cases of doubt, a urine diuretic screen may be helpful
- Chronic vomiting leads to hypovolemia and associated increased NaCl reabsorption and hence low urinary Cl

Electrolyte abnormality in Addison Disease

- Hyponatremia is found in 70 to 80 % of patients, reflecting both sodium loss and volume depletion caused by mineralocorticoid deficiency and the compensatory increase in vasopressin secretion
- Hyperkalemia, often associated with a mild hyperchloremic acidosis, occurs in up to 40 percent of patients due to mineralocorticoid deficiency

Q 2

What is the unifying mechanistic principle of action of all diuretics?

a. Prevent water reabsorption
b. Prevent Na secretion
c. Prevent Na reabsorption
d. Cause K secretion

Answer is c

- All diuretics act by inhibiting tubular Na reabsorption
- Diuretics cause secondary hyperaldosteronism by causing intra vascular volume contraction
- Raised aldosterone due to loop and thiazide diuretics leads to tubular K and H loss and resultant hypokalemia and metabolic alkalosis
- K sparing diuretics antagonize the actions of aldosterone leading to K and H retention and the resultant hyperkalemia and acidosis

Q 3

The commonest renal disease associated with myeloma is-

a) ATN
b) Fanconi Syndrome
c) Interstitial disease
d) Hypercalcemia induced renal failure
e) Myeloma cast nephropathy

Answer is e.
Hypercalcemia seen in up to 15% can cause AKI by renal vasoconstriction but is not very common as the primary cause of AKI

TUBULAR

- Light chain cast nephropathy (myeloma kidney): 30-50%

- Interstitial nephritis/fibrosis: 20-30%

- Acute Tubular Necrosis: 10%

GLOMERULAR

- Amyloidosis: 10%

- Monoclonal immunoglobulin deposition disease (mostly light chain deposition disease): 5%

- Rare: Cryoglobulinemia, MPGN, DDD, Fibrillary GN and immunotactoid glomerulopathy

Q 4

A 54-year-old man presents with constipation and polyuria. His serum calcium is elevated with the serum PTH suppressed below normal. All of the following might be responsible for these findings, except:

a. Metastatic breast cancer

b. Familial hypocalciuric hypercalcaemia

c. Thiazide abuse

d. Milk-alkali syndrome

e. Addison’s disease

Answer is b

Causes of hypercalcaemia with normal PTH (remember normal PTH is inappropriate for the high serum calcium) or elevated serum PTH include-

- Primary hyperparathyroidism

- Tertiary hyperparathyroidism (there will be history of secondary hyperparathyroidism which would be in the context of CKD or rickets/osteomalacia)

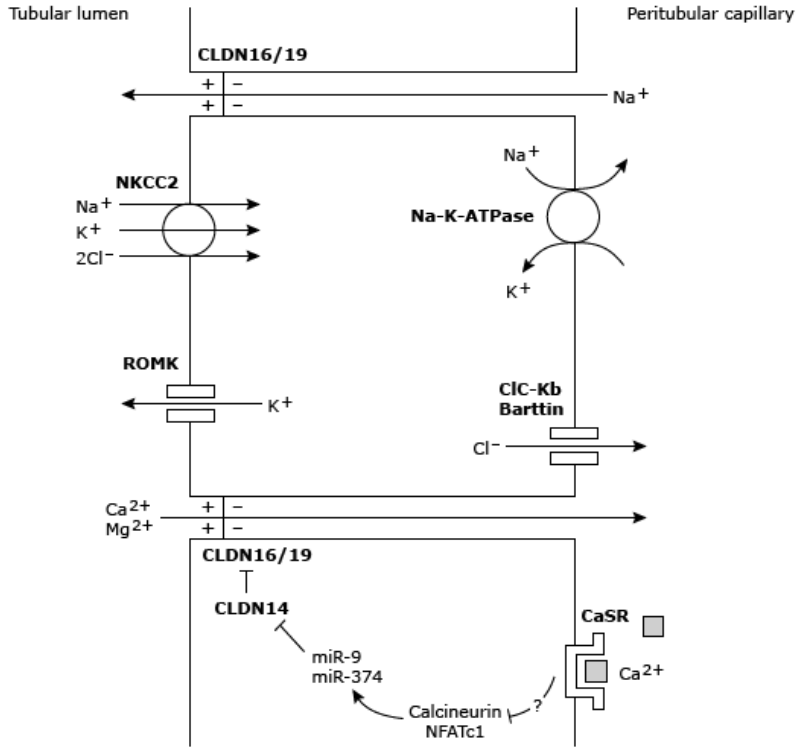
- Lithium-induced hyperparathyroidism

- Familial hypocalciuric hypercalcaemia (FHH)

Ca sensing receptor

- Apart from parathyroid gland also found in basolateral membrane on the cells of the thick ascending limb (TAL) of the loop of Henle
- Ca stimulation of CaSR also leads to decrease in claudrin 16 and 19 which are the carrier proteins for Ca paracellular reabsorption in TAL thus inhibiting calcium reabsorption
- Net result of renal CaSR stimulation by plasma Ca - **Decrease in paracellular Ca (increased urinary Ca loss)**

Calcium reabsorption in TAL



FHH and Lithium

- FHH can be diagnosed by inappropriately suppressed urinary 24 hours Ca or urinary Ca/creatinine ratio < 0.01. Hypercalcemia due to all other causes will lead to the kidneys trying to excrete Ca.
- Both lithium and FHH lead to abnormality in the Ca sensing receptors on both the kidneys (allowing uncontrolled renal Ca reabsorption leading to hypocalciuria and hypercalcemia) AND parathyroid gland (allowing ongoing PTH secretion despite hypercalcemia).

Q 5

Which of the following is the leading cause of AKI in patients with chronic liver disease?

a. Pre-renal AKI

b. Glomerulonephritis

c. AKI associated with infection e.g., sepsis or SBP

d. Hepatorenal syndrome (HRS)

Answer is c

Causes of AKI in patients with chronic liver disease are

- AKI associated with infection e.g., sepsis, SBP- 46%
- Pre-renal AKI- 32%
- HRS- 13%
- Parenchymal renal disease e.g., glomerulonephritis – 9%

HRS presentation in the CLD patient

- Worsening serum creatinine
- No significant haematuria and none or minimal proteinuria (less than 500 mg per day)
- A very low rate of sodium excretion (urine sodium concentration often< 10 mEq/L)
- Oliguria (may take days to develop)
- **Problems with estimating kidney function**: both urea and creatinine low due to liver disease itself, reduced muscle mass and low protein intake
- **Low GFR due to renal vasoconstriction in the face of nitric oxide induced splanchnic vasodilatation**

Two types

Type 1 HRS- Associated with doubling of serum creatinine > 2.5mg/dl (220 umol/l) or a 50% reduction in GFR to < 20ml/min in < 2 weeks.

- Median survival without treatment is 2 weeks.
- Often multiorgan failure and hyponatremia
- Precipitating events: bacterial infections(specially SBP), gastrointestinal bleeding, abdominal paracentesis or NSAIDs

Type 2 HRS- Associated with a much less rapid decline in renal function and mainly presents with refractory ascites. Median survival without treatment is 4-6 months

Diagnosis

- Not pre or post renal failure/ recent nephrotoxic drugs/infections
- Serum creatinine > 133 umol/l
- No significant haematuria(<50 RBC/HPF) and none or minimal proteinuria (< 500 mg/day)
- **No improvement in renal function(to < 133umol/L) after volume expansion with intravenous albumin (1 g/kg of body weight per day up to 100 g/day) for at least two days and withdrawal of diuretics**

Important : HRS is a diagnosis of exclusion

HRS treatment

- Terlipressin with albumin
- Midodrine, octreotide, and albumin where Terlipressin is not available
- Norepinephrine with albumin for hypotensive patient in ICU

Q 6

A 65-year-old male presents with painless hematuria. Urinalysis shows 2+ blood with normal renal function. USG shows left renal cyst with inhomogeneous appearance. What is the next step?

a. Renal biopsy
b. Non contrast CT
c. CT with contrast
d. PET scan

Answer is c

- In most cases, CT can accurately diagnose RCC. It also provides information on function and morphology of the kidneys, tumour extension, venous involvement, lymph node involvement and surrounding structures.
- A change of more than 15 Hounsfield Units with contrast is significant and suggests a malignant process

Q 7

Which of the following is true about membranous nephropathy (MN)?

a. It is a common cause of nephrotic syndrome and ESRF in children
b. It is caused by auto-antibodies to C3 convertase called C3 nephritic factor
c. The characteristic biopsy finding is presence of “spikes” in the GBM on silver methenamine stain.
d. Immunosuppressive treatment is recommended in those with persistent sub-nephrotic range proteinuria.
e. It is the commonest cause of nephrotic syndrome in people of African origin.

Answer is c

- Idiopathic MN is common in Caucasian males and quite uncommon in children.
- C3 nephritic factor is involved in the pathogenesis of mesangiocapillary GN (MCGN/MPGN).
- More than 70% of idiopathic MN have circulating auto-antibodies against phospholipase A2 receptor 1(PLA2R1) located on the surface of podocytes.
- The characteristic abnormality on light microscopy is diffuse global capillary wall thickening due to subepithelial immune-complex deposition which appears as “spikes” in silver methenamine stain.
- Patients with sub-nephrotic range proteinuria are treated with ACEI or ARB alone and immunosuppressive therapy is only indicated in those with persistent high-grade proteinuria > 4 g/daily despite the use of ACEI or ARB.
- FSGS is the commonest cause of nephrotic syndrome in people of African origin

Q 8

Dialysis treatment in acute kidney injury is indicated in the following except:

a. Pulmonary oedema
b. Rising level of creatinine from 700 to 980 µmol/L
c. Metabolic acidosis
d. Hyperkalaemia resistant to medical treatment
e. Pericarditis presumed to be uremic

Answer is b

Dialysis treatment is not guided by absolute level of urea or creatinine.

The indications of acute dialysis are:

- metabolic acidosis refractory to medical management
- hyperkalaemia refractory to medical management
- pulmonary oedema
- uremic pericarditis
- uremic symptoms (mainly encephalopathy)

Q 9

The commonest clinical manifestation of PAN is-

a. Abdominal pain
b. Testicular pain
c. Haemoptysis
d. Hypertension
e. Peripheral neuropathy

Answer is e

- PAN is a systemic necrotizing vasculitis that typically affects medium-sized muscular arteries with characteristic absence of involvement of veins, smaller arteries or capillaries and is ANCA negative
- Peripheral neuropathy may be seen in up to 75% of cases with PAN
- Gastro-intestinal symptoms with abdominal pain or blood in stool may be seen in up to 40%.
- Hypertension seen in 35%
- Orchitis in up to 20%
- Pulmonary involvement is uncommon in PAN

Q 10

Fanconi syndrome should be suspected in-

a. Hyperuricemia

b. Hyperphosphatemia

c. Hypophosphatemia

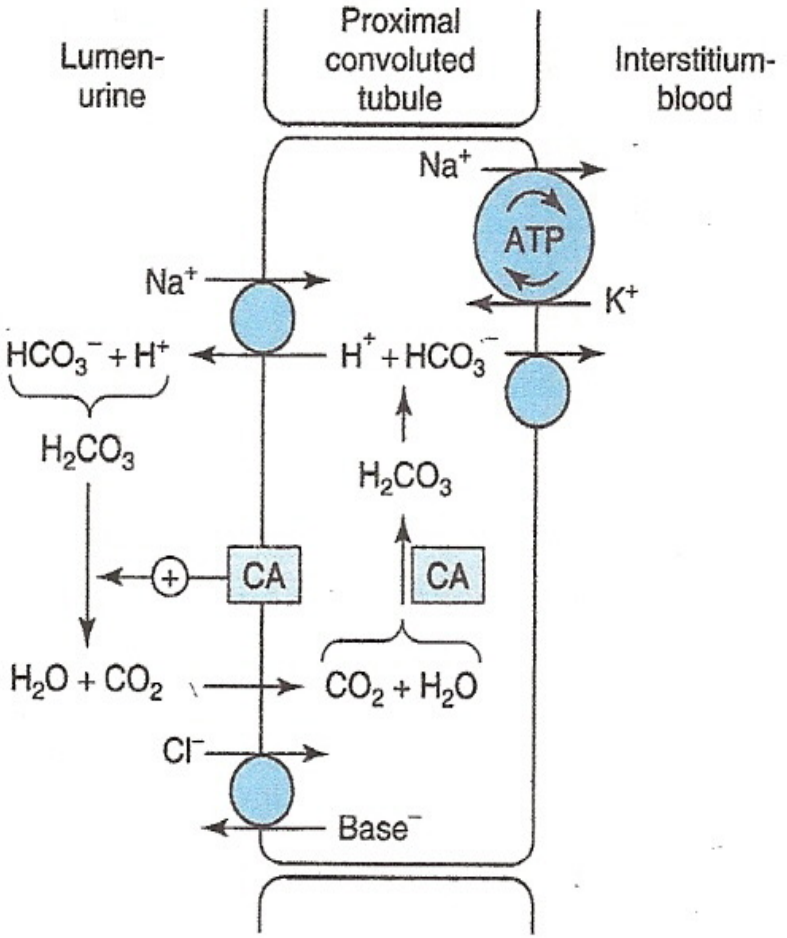
d. Hyperkalaemia

e. Alkalosis

Answer is c

- Type 2 RTA is due to a proximal tubular defect in the reabsorption of $HCO3^-$ leading to urinary loss of $HCO3^-$ and metabolic acidosis with hypokalaemia
- The absorption of HCO3- in this segment is normally linked to the reabsorption of Na^+.
- As the reabsorption of Na^+ is linked to the reabsorption of glucose, amino acids, phosphate and uric acid, the patient may present with glycosuria, hypophosphatemia and hypouricemia (due to urinary losses of phosphate and uric acid respectively) and this condition is termed as Fanconi syndrome.

PCT- Role of Carbonic Anhydrase (CA)



RTA 1 and 2

DISTAL RTA

- Inability to secrete H+
- **Urine pH >5.5 (no H+ in urine)**
- Proximal tubules reabsorb all alkali including citrate which normally keeps Ca in urine soluble and so…. nephrolithiasis, nephrocalcinosis
- **No Fanconi syndrome**
- Sjogren's syndrome, SLE, PBC, autoimmune hepatitis
- Treat with alkali and K+ replacement

PROXIMAL RTA

- Inability to reabsorb HCO3
- **Urine pH < 5.5 (distal tubules secrete excess H+)**
- No renal stones
- **Fanconi syndrome -**glycosuria,phosphaturia, uricaciduria and aminoaciduria
- Myeloma,drugs- tenofovir, acetazolamide
- Same treatment…..needs bigger doses of alkali though…..

Q 11

A 40-year-old male presents to ED with a sudden onset severe headache. On examination, he has abdominal fullness, haematuria and proteinuria. What is the most likely diagnosis?

A. Autosomal Dominant Polycystic Kidney Disease

B. IgA Nephropathy

C. Medullary Sponge Kidney

D. Polyarteritis Nodosa

E. Cirrhosis

Answer is A

Cerebral aneurysm is the most dreaded complication of ADPKD and may be seen in up to 8% of patients with ADPKD.

However, the prevalence may be as high as 16% in those with family history of cerebral aneurysm.

Screening is not indicated in every patient with ADPKD as most cerebral aneurysms found on pre-symptomatic screening are small and have a low risk to rupture with the risks associated with surgery clearly outweighing risk of rupture.

Indications for screening with MRI are-

- Family history of cerebral aneurysm or sub arachnoid haemorrhage
- Previous aneurysmal rupture
- Preparation for surgery with potential for hemodynamic instability
- High risk occupations e.g., airline pilots
- Patients who require chronic anticoagulation e.g., those with DVT or AF

If the initial scan is negative in the above group of patients, then most clinicians re-screen them every five years

Q 12

The following electrolyte profile may be associated with both thiazide and loop diuretics-

a. Hyperkalaemia with metabolic alkalosis
b. Hypokalaemia with metabolic alkalosis
c. Hyperkalaemia with metabolic acidosis
d. Hypokalaemia with metabolic acidosis
e. Hyperkalaemia

Answer is b

- All diuretics act by inhibiting the tubular reabsorption of Na^+.
- With more Na^+ flowing to the distal nephron, the tubular cells try to reclaim the excess Na^+ leading to decrease in positive charge within the lumen. The tubular epithelial cells try to compensate for this by secretion of the positively charged K^+ and H^+ into the lumen.
- Also, intravascular volume contraction because of the diuretics cause activation of the renin-angiotensin-aldosterone (RAS) which in turn leads to the urinary K^+ and H^+ losses under the influence of aldosterone.

Q 13

Which of the following conditions is least likely to lead to rapidly progressive glomerulonephritis (RPGN)?

a. Lupus nephritis

b. IgA nephropathy

c. Membranous nephropathy

d. Microscopic polyangiitis

e. Anti-GBM antibody disease

Answer is C

- **Membranous nephropathy is associated with nephrotic syndrome and NOT glomerulonephritis and hence does not lead to RPGN.**
- RPGN refers to the clinical syndrome of nephritis along with rapid deterioration in kidney function over days to weeks and is histologically characterised by crescents in the glomeruli (crescentic GN)
- Normally Bowman’s space has a single layer of parietal and visceral epithelial cells each. Crescents are defined by the presence of two or more layers of proliferating parietal epithelial cells in Bowman's space; they are essentially a marker of severe glomerular inflammation.

RPGN causes

- Pauciimmune RPGN: Causing more than 50% of all RPGN, this group is due to ANCA-associated vasculitis i.e., GPA, MPA, and rarely EGPA
- Anti-GBM antibody disease associated RPGN: Characterised by the presence of anti-GBM antibodies and linear staining of the GBM on IF, this leads to 20% of all RPGN.
- Immune complex mediated RPGN: about 25% of all RPGN is immune complex mediated and may be due to lupus nephritis (commonest in this group), IgA nephropathy, infectious GN, or mesangiocapillary glomerulonephritis (MCGN).

Q 14

Dialysis disequilibrium syndrome refers to neurological symptoms and signs during or shortly after dialysis. The pathogenesis of dialysis disequilibrium is due to:

A. Relative hypotension

B. Cerebral oedema

C. Uremic platelet dysfunction

D. Aberrant calcium and phosphate metabolism

e. Insufficient dialysis

Answer is b

- Dialysis disequilibrium syndrome (DDS) is characterized by neurologic symptoms that affect patients on haemodialysis, particularly when they are first started on dialysis or dialyse after having missed consecutive sessions.
- Haemodialysis rapidly removes small solutes such as urea. The rapid decline in the blood urea content in patients significantly lowers plasma osmolality, while the neurons with a higher urea concentration have a high intracellular osmolality. This gradient leads to water shift into neurons that produces cerebral oedema
- To prevent the development of DDS, haemodialysis is initiated in shorter sessions using low blood flow initially.

Last one… Q 15

A 52-year-old woman of African origin with chronic hepatitis managed with tenofovir presents to ED feeling generally unwell. Blood tests reveal metabolic acidosis with a normal anion gap and hypokalaemia. Her urinary pH is 5.2. The rest of the blood tests including phosphate and uric acid are normal. What could have led to this condition-?

a) Sickle cell anaemia
b) Sjogren's syndrome
c) Autoimmune hepatitis
d) Diabetes mellitus
e) Use of tenofovir

Answer is e

- This patient has proximal RTA (type 2 RTA) induced by tenofovir; does not have Fanconi syndrome as phosphate and uric acid normal in the blood
- The combination of normal anion gap metabolic acidosis with hypokalaemia is suggestive of RTA types I (distal) or 2 (proximal)
- While metabolic acidosis due to any cause will lead to renal compensation by losing extra H^+ which leads to an acidic urine, the urine pH is typically more than 5.5 in distal RTA due to the nature of the tubular defect i.e., inability to excrete H^+.
- Sjogren's syndrome, autoimmune hepatitis, primary biliary cirrhosis, rheumatoid arthritis and drugs (amphotericin B, lithium and ibuprofen) are some of the causes of distal RTA.
- Causes of proximal RTA include multiple myeloma, Wilson's disease, Lowe syndrome, cystinosis and drugs (tenofovir and other antiretroviral drugs, Carbonic anhydrase inhibitors – Acetazolamide, topiramate and aminoglycosides).

It is not that I am so smart; it is just that I stay with problems longer

- ALBERT EINSTEIN