Perform the analyses to laboratory standard operating procedures on patients with disorders of renal pathology - CB-2-C-2

Renal Homeostasis

The normal human adult has two kidneys 11-14cm long, 5-6cm wide and 3-4cm deep, located at the posterior abdominal wall on each side of the spine (1, 2). The kidneys have major roles in water and electrolyte balance, removal of waste substances (urea, creatinine) and endocrine functions (glucose homeostasis, erythropoietin production). Each kidney is supplied with 25% of the cardiac output via the renal arteries, which branch from the abdominal aorta and drain via the renal veins to the inferior vena cava (1). The renal arteries become the renal arterioles which then feed into the glomerular capillary bed, which drains into glomerular efferent arterioles and then branch into the peritubular capillary network and subsequently the renal veins (2). This blood network is designed around the functional unit of the kidney called the nephron (fig. 1) of which there are around 1 million in each kidney and consist of a glomerulus, proximal convoluted tubule (PCT), loop of Henle, distal convoluted (DCT) tubule and collecting duct (CD) (1, 2). The glomerulus, PCT, DCT and upper segment of the CD traverse the cortex of the kidney whilst the loop of Henle and lower segment of the CD traverse the medulla of the kidney (2).

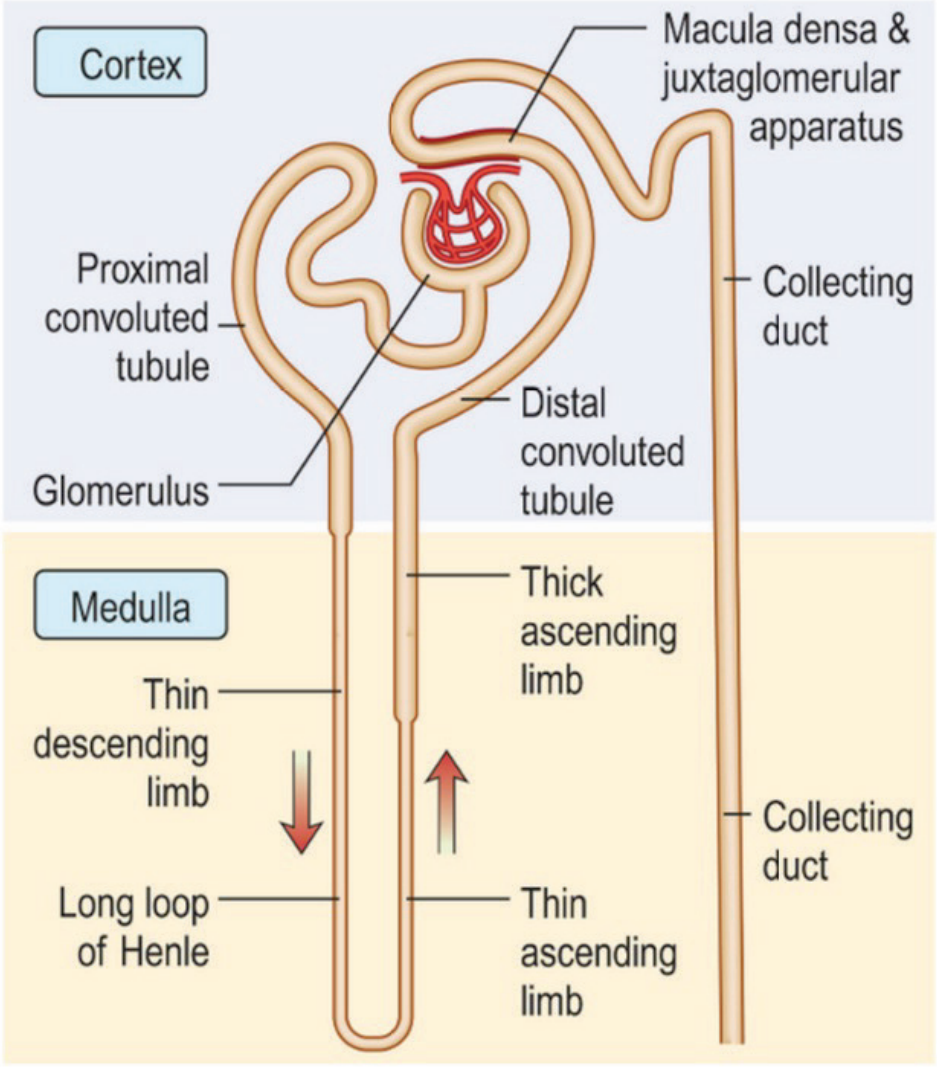

Figure 1 Functional unit within the kidney: the nephron. Taken from (2).

The glomerulus is designed for ultrafiltration of the blood and is a unit of capillaries especially designed with particular contact with epithelial cells and basement membrane to form its filtering abilities. The endothelial cells of the glomerular capillaries are fenestrated to allow anything in the blood < 50kDa in size to move across a basement membrane supported by epithelial cells called podocytes (1). The podocytes have foot like processes, which allow the ultrafiltrate to move through and into the Bowman space, which is surrounded by parietal epithelial cells that are continuous with the epithelial proximal tubule cells forming the lumen of the nephron (1, 2). A combination of difference across afferent and efferent glomerular arteriole pressure, osmotic pressure between blood and ultrafiltrate and hydrostatic pressure in the Bowman space contribute to the rate at which the glomerulus filters the blood i.e. glomerular filtration rate (GFR) (1).

The PCT is connected to the loop of Henle in a continuous fashion but differentiated by the epithelial cells that line the lumen (1). The proximal tubule epithelia have a luminal brush border of microvilli to enhance the surface area across which reabsorption of components of the ultrafiltrate occurs. The PCT is responsible for 60-80% of sodium and water reabsorption along with the majority of filtered potassium, bicarbonate, glucose and amino acids (1). Reabsorption occurs via co-transporters, ion channels, exchangers, endocytosis and pumps dependent on the reabsorption component (1). There is also ammonium and hydrogen excretion by these cells, which along with bicarbonate reabsorption contributes to acid-base balance (3).

The loop of Henle is composed of the thin descending limb, thin ascending limb and the thick ascending limb and is responsible for concentration of the urine by a counter-current system that involves each of the limbs, the medullary interstitium, collecting duct and blood vessels surrounding the system (2). At the thick ascending limb sodium and chloride are actively transported out of the lumen causing the interstitium to become hypertonic and the filtrate to become hypotonic (with respect to plasma). This in turn causes water to diffuse out of the lumen at the thin descending limb (1). The result is hypotonic filtrate reaching the DCTs and reabsorption of a further 15% of water from the loop of Henle along with sodium (1).

The DCT is the site of hormonal regulation of electrolyte reabsorption. The epithelia of the DCT express receptors to a number of hormones that alter the balance of sodium, potassium, phosphate, calcium, hydrogen and bicarbonate that is excreted or reabsorbed dependent on the needs of the body (1). Aldosterone is responsible for regulating sodium reabsorption and indirectly potassium excretion. Aldosterone is released as part of the renin-angiotensin-aldosterone axis. Sodium depletion, hypotension and β-adrenergic nerve activity cause macula densa cells (found in DCT) to release renin, which initiates an enzymatic cascade to form angiotensin II in the circulation (3). The result of this is stimulation of the adrenal glands to release aldosterone, which acts on nuclear minerocorticoid receptors in the DCT cells leading to sodium uptake from the DCT and efflux into the surrounding blood vessels (3). Aldosterone also indirectly acts on potassium levels by its action on the Na^+/K^+ ATPase on the basolateral membrane in principle tubule cells whilst the α-intercalated cells exchange potassium for hydrogen ions (4). Parathyroid hormone (PTH) is released in response to low serum calcium levels and acts on PTH receptors in the DCT resulting in the increased expression of calcium channels e.g. TRPV5 resulting in an increased reabsorption of calcium from the urine. PTH also causes a reduction in phosphate reabsorption leading to increased excretion (1). Phosphate is also linked to the control of hydrogen and bicarbonate reabsorption/excretion primarily because at physiological pH phosphate forms the inorganic ions HPO_4^- and $H_2PO_4^-$ at a ratio of 4:1, this helps to remove the excess hydrogen produced by the body without over acidification of the urine (fig. 2). Bicarbonate ions cannot be directly reabsorbed by the DCT cells and as such there is an indirect mechanism for reabsorption. Excreted hydrogen reacts with the filtered bicarbonate in the distal lumen to form carbon dioxide, which diffuses into the DCT cells. In the renal tubular cells carbonic anhydrase combines carbon dioxide with water to form carbonic acid, which dissociates into bicarbonate and hydrogen ions (fig. 2). The bicarbonate is exchanged for chloride on the basolateral membrane and therefore replenishes the bicarbonate levels in the blood (4).

At the collecting ducts the fine tuning of water balance is controlled by the hormone antidiuretic hormone (ADH/vasopressin. The epithelial cells of the collecting duct are normally impermeable to water, however ADH is capable of instigating aquaporin-2 expression at the plasma membrane allowing water to diffuse across into the interstitium (1). The release of ADH is controlled by the hypothalamus, where neurons containing osmoreceptors sense increased serum osmolality and sodium concentration and secrete ADH (4). This process regulates the osmolality of the urine as only water is reabsorbed, however, there is the capability for further sodium reabsorption in exchange of potassium or hydrogen (1).

During normal homeostasis over a 24h period around 1.5-2L of urine is produced and should be composed as follows: osmolality of 50-1200 mmol/Kg, sodium 40-220 mmol/24h, potassium 24-125 mmol/24h, phosphate 15-50 mmol/24h, calcium 2.5-7.5 mmol/24h, protein 0.1-0.14 g/24h, urea 430-710 mmol/24h and creatinine 7.1-17.7 mmol/24h. Disturbances in renal function both directly at the kidneys and in the whole body water and electrolyte homeostasis can result in a number of conditions some of which are discussed here.

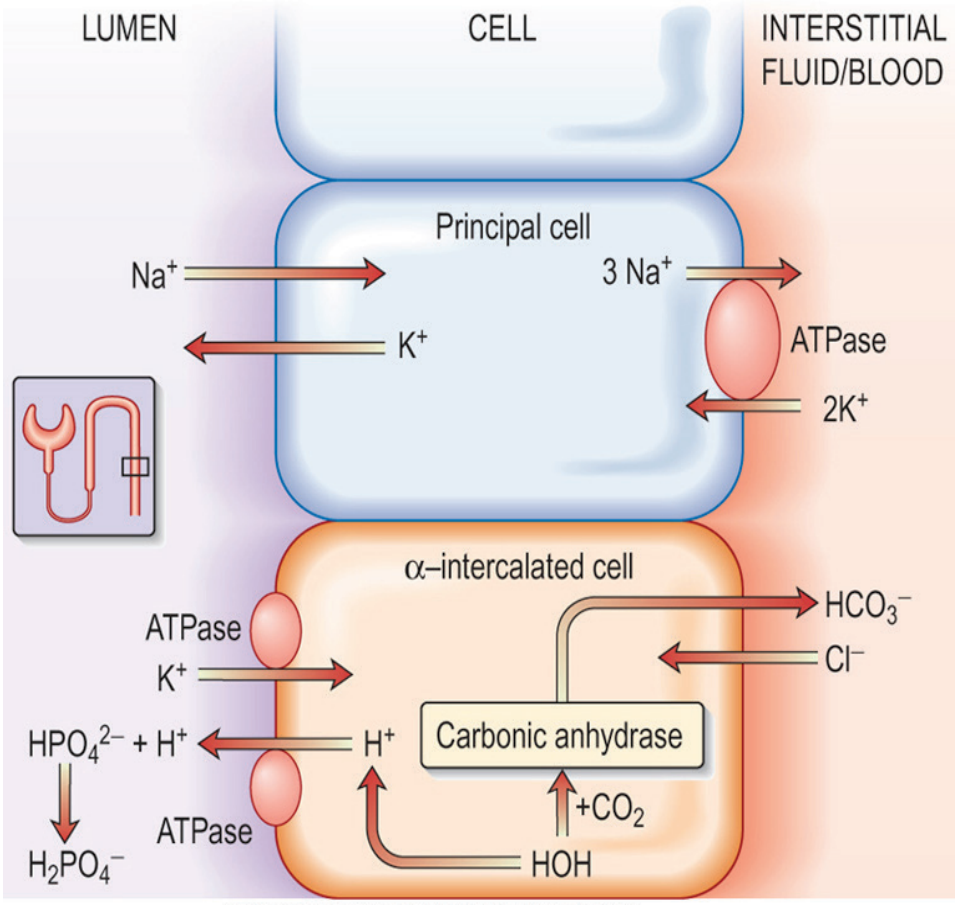

Figure 2 Relationship between sodium, phosphate, hydrogen and bicarbonate ion reabsorption in the distal convoluted tubule. Taken from (4).

Acute Kidney Injury

Symptoms

Acute kidney injury (AKI) was previously known as acute renal failure (ARF) and occurs rapidly, usually within 7 days (5). Patients may initially be asymptomatic with mild oligouria but can rapidly exhibit nausea, vomiting, confusion, dehydration, abdominal pain, high blood pressure (B.P) and oedma (6). Furthermore there are a number of risk factors associated with development of AKI in adults, which must be considered, these include (7):

- Chronic kidney disease (CKD)
- Other chronic illnesses such as cardiac failure, liver disease, diabetes
- Age >65
- Nephrotoxic drugs such as: diuretics, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor antagonists (ARBs) or non-steroidal anti-inflammatory drugs (NSAIDs).
- Neurological/cognitive impairment or disability limiting intake of fluids.
- Sepsis
- Urological obstruction
- Hypovolemia

In children the above factors should be considered along with:

- Severe diarrhoea
- Haematological malignancy
- Hypotension
- Nephritis

AKI occurs when any of the above risk factors lead to a reduction in glomerular filtration rate (GFR) and a subsequent build-up of creatinine and urea. Reduced GFR can occur due to damage to the glomeruli, tubules, interstitium or intrarenal blood vessels (8).

Diagnosis

There was a lack of standardization prior to the introduction of the clinical definition of AKI and it was recognized that an international definition was required including staging of the injury (9). Patients exhibiting any of the above symptoms or within the described at risk groups should be investigated for AKI (7).

NICE guidelines specify that AKI should be diagnosed if:

- Serum creatinine rises >26 µmol/L in 48hr
- >50% increase in creatinine within 7 days
- Oliguria of <0.5 ml/kg/hr for >6hrs adults, >8hrs children.
- >25% decrease estimated GFR (eGFR) in children within 7 days.

Staging of AKI levels 1-3 is defined as seen in table. 1.

Stage	Serum creatinine (SCr) criteria	Urine output criteria
1	increase ≥ 26μmol/L within 48hrs or increase ≥1.5 to 1.9 X reference SCr	<0.5 mL/kg/hr for > 6 consecutive hrs
2	increase ≥ 2 to 2.9 X reference SCr	<0.5 mL/kg/ hr for > 12hrs
3	increase ≥3 X reference SCr or increase ≥354μmol/L or commenced on renal replacement therapy (RRT) irrespective of stage	<0.3mL/kg/hr for > 24hrs or anuria for 12hrs

Table 1 Criteria for staging severity of AKI taken from (7)

At the RSCH there are clear guidelines (Local Clinical Protocols and Referrals Procedures Policy) for treating suspected AKI, in the first instance a urine dipstick should be used to test for proteinuria and/or presence of haemoglobin. This should be followed up with liver function tests (LFTs), creatinine kinase (CK), platelets and blood film as well as, importantly, urea and electrolytes (U&Es - urea, Na^+, K^+, creatinine). A gold top vacuette is required for serum creatinine measurement, clinicians should treat AKI as a medical emergency and so samples should be marked as urgent and therefore turnaround time should be 1hr. The Winpath system now has an algorithm employed to identify AKI staging based on previous creatinine measurements and appears in the urgent phoning queue with a comment describing the stage of AKI, for levels 2 and 3 the clinician should then initiate the care pathway.

The reference ranges for creatinine at RSCH are as follows (SPS-SOP-003 Appendix 4):

- <30days 27 – 87 μmol/L
- <2years 14 – 34 μmol/L
- <8years 23 – 48 μmol/L
- <12years 28 – 63 μmol/L
- <14years 40 – 72 μmol/L
- Adult – male: 64 – 104 μmol/L, female 49 – 90 μmol/L

Management

Dependent on the underlying cause of AKI, this must be treated accordingly e.g. hypovolemia should be treated with fluids, sepsis according to microbiological origin etc. Furthermore patients should be monitored daily for U&Es with particular attention to creatinine levels (Local Clinical Protocols and Referrals Procedures Policy). Complications arising from AKI must also be monitored. These can include:

- Hyperkalaemia
- Acidosis
- Fluid overload
- Uraemic coma

Following an AKI incident, patients should be examined for development of CKD for 2-3 years after an AKI (7).

Chronic Kidney Disease

Symptoms

Chronic kidney disease (CKD) was previously known as chronic renal failure or insufficiency and is a progressive long-term (> 3 months) impaired structure or renal function (2). Patients can be asymptomatic or exhibit similar indications as in AKI such as: haematuria, high B.P, oedema, confusion, nausea dehydration etc (11). Also in similarity to AKI, CKD is related to a number of risk factors for its development (2, 12):

- Genetic e.g. polycystic kidney disease, medullary cystic disease
- Diabetes
- Hypertension
- AKI
- Cardiovascular disease e.g. heart failure, Wegner's granulomatosis
- Urinary tract obstruction e.g. renal calculi, prostatic disease
- Multisystem disease e.g. system lupus erythematosus (SLE), systemic sclerosis
- Nephrotoxic agents e.g. drugs, free light chains in multiple myeloma

CKD arises when any of the above risk factors lead to a reduction GFR for > 3 months, this is defined by a GFR < 60 ml/min/1.73m^2 on two separate occasions > 90 days apart (with or without markers of kidney damage) (12).

Some patients can develop the uraemic syndrome, which affects multiple systems and some examples of its manifestations include: hypertension, pericarditis, pruritus, sexual dysfunction, glucose intolerance, nausea, vomiting, anorexia, anaemia, peripheral neuropathy, confusion, coma, pulmonary oedema, nocturia and thirst (1). This often occurs at the point of renal failure due to the inability of the body to remove uraemic toxins such as urea, peptides (β_2-microglobulin, PTH), oxalate, polyamines, guanidines etc (1).

Diagnosis

There was a lack of standardization prior to the introduction of the clinical definition of CKD and it was recognized that an international definition was required including staging of the disease (13). Patients exhibiting any of the above symptoms or within the described at risk groups should be investigated for CKD (12).

NICE guidelines specify that CKD should be diagnosed if:

- Abnormal kidney structure or function for > 3 months i.e. with markers of kidney damage such as albuminuria (> 3 mg/mmol), electrolyte imbalance histological and imaging abnormalities of kidney structure.
- GFR < 60 ml/min/1.73m^2 at 2 intervals over at least 90 days

Staging of CKD with GFR and albumin:creatinine ratio (ACR) levels is defined as seen in table. 2.

The GFR is often estimated in clinical laboratories using the CKD Epidemiology Collaboration (CKD-EPI) equation for eGFR with correction for those of African-Caribbean origin. It is also possible to measure GFR by cystatin C measurement, however, this method although more accurate, is considerably more expensive than creatinine and as such is not routinely offered. In cases of patients with an eGFR of 45-59 ml/min/1.73m^2 at two intervals in at least 90 days with no proteinuria or other markers of kidney impairment a cystatin C measurement should be offered (12).

Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012

GFR categories (ml/min/ 1.73 m²) Description and range				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk.

Table 2 Criteria for staging severity of CKD based on GFR and ACR. Taken from (13).

Management

Patients that fall into the at risk groups should be monitored for CKD on a case-by case basis dependent on the presence of any indications of CKD and if diagnosed with CKD monitored dependent on the severity of their CKD as described in table. 3 (13). Those taking nephrotoxic drugs should be monitored at least annually (12).

Furthermore investigations (renal ultrasound) should be initiated to determine the cause of CKD and where possible underlying conditions should be treated. However, for most patients CKD is a life-long condition and as such should be monitored for disease progression.

Patients with a change of GFR > 25% or GFR group within 12 months or > 15 ml/min/1.73m^2 per year are at greater risk of progression to renal failure and as such should be closely monitored (12).

It is also important for CKD patients to maintain their B.P below 140 mmHg over 90 mmHg and where patients fall into the groups below antihypertension drugs should be prescribed (12):

- Diabetes and ACR ≥ 3 mg/mmol
- Hypertension and ACR ≥ 30 mg/mmol
- ACR ≥ 70 mg/mmol

Guide to Frequency of Monitoring (number of times per year) by GFR and Albuminuria Category				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–300 mg/g 3–30 mg/mmol	>300 mg/g >30mg/mmol
GFR categories (ml/min/1.73 m²) Description and range	G1	Normal or high	≥90	1 if CKD	1	2
	G2	Mildly decreased	60–89	1 if CKD	1	2
	G3a	Mildly to moderately decreased	45–59	1	2	3
	G3b	Moderately to severely decreased	30–44	2	3	3
	G4	Severely decreased	15–29	3	3	4+
	G5	Kidney failure	<15	4+	4+	4+

Table 3 Criteria for monitoring of CKD based on GFR and ACR. Taken from (13)

Care must be taken when selecting drugs due to adverse effects of some drugs on renal function. The first choice should be a renin-angiotensin system antagonist (ACE inhibitors) and before dosing serum potassium should be tested and if > 5 mmol/L ACE inhibitors should not be used (12). CKD patients receiving ACE inhibitors should have serum potassium routinely measured to avoid hyperkalaemia.

CKD patients are at an increased risk of cardiovascular disease (CVD) and to prevent cardiovascular complications dosing with oral anticoagulants such as apixaban (as opposed to warfarin) or antiplatelet drugs should be considered only in CKD patients with (12):

- History of stroke or TIA
- > 75 years old
- Hypertension
- Diabetes
- Heart failure (symptomatic)

Furthermore CKD patients should also be offered statins for the preventions of CVD (12).

Patients with high grade CKD who are close to or in renal failure (CKD group G4 or G5) may have complications of bone metabolism and anaemia as well as symptoms and complications seen with AKI (13). The kidneys are responsible for vitamin D production and contain receptors for PTH and severe renal dysfunction results in a loss of bone homeostasis leading to an increased risk of osteoporosis (12). The kidneys are also responsible for erythropoietin production and as such the formation of new red blood cells, those with moderate to severe CKD (G3b, G4 & G5) are at risk of anaemia and as such should be monitored for haemoglobin levels and treated appropriately (12).

Those with advanced CKD are also at risk of metabolic acidosis and as such should have their bicarbonate levels monitored accordingly and treated with oral sodium bicarbonate as necessary (12).

Renal Replacement Therapy & Transplantation

Renal replacement therapy (RRT) is an umbrella term for the variety of dialysis procedures available for patients with renal failure (2). The major RRTs available are haemodialysis, haemofiltration and peritoneal dialysis. The other option available to those in renal failure is a kidney transplant (2).

Haemodialysis involves pumping the patient's blood through a semipermeable membrane, which has a countercurrent flow of dialysate that has a similar electrolyte composition to normal human plasma (2). This causes the blood composition to change along its concentration gradient towards that of the dialysate thus correcting disturbances in electrolytes and removing urea and other waste products (2).

Haemofiltration differs from haemodialysis by the method in which the plasma constituents are rebalanced. The patient's plasma is removed by convective flow across a semipermeable membrane and then replaced with a solution containing the desired electrolyte concentrations (2). This method is used in haemodynamically unstable patients who are not suitable for haemodialysis (2).

Peritoneal dialysis involves placing a tube into the peritoneal cavity and infusing the space with dialysate. This then causes diffusion of urea and other toxins along their concentration gradient much like the electrolytes (2). The advantage of this technique it is possible to maintain this over a long period of time by regularly changing the dialysate (2). However there is an increased risk of peritonitis and/or infection at the tube site (2).

In patients where dialysis no longer becomes safe (due to increased cardiovascular risk and amyloidosis) or where it is not suitable, the only other option is a kidney transplant (2). This can be from a live donor or someone recently deceased. Since it is almost impossible to get a genetically identical kidney patient's require immunosuppressive drugs to prevent transplant rejection (2). There are a number of risks associated with transplant, the most obvious being rejection but others include: infections (bacterial and viral), acute tubular necrosis (ATN), lymphoproliferative disorders (associated Epstein-Barr virus), malignancies (immunosuppression increases melanoma incidence), CVD, osteoporosis and recurrent kidney disease (2).

Clinical Indications

Evidence suggests a benefit for CKD patients with a GFR < 30 ml/min/1.73m^2 should be advised of the options of RRT and transplantation available to them to prevent mortality and co-morbidities (13).

Patients with AKI and complications including: hyperkalaemia, metabolic acidosis, uraemia, fluid overload and pulmonary oedema who do NOT respond to treatment of these should be immediately referred for RRT to avoid mortality and co-morbidities (7).

Monitoring

Patients receiving RRT should have their blood tested before and after dialysis for U&E's, osmolality, LFTs, bone profile (vitamin D and PTH where appropriate) and a full blood count (FBC), to ensure dialysis has been successful. Patients with suspicion of amyloidosis should have their β_2-microglobulin levels measured.

Common practice involves calculating urea kinetics to determine the adequacy of dialysis (1, 2):

Urea reduction ratio (URR) or equilibrated urea clearance = eKt/V where K – dialyser clearance (total urea clearance), t – time in minutes of dialysis and V is the urea distribution volume (estimated by total body water) (2).

Transplant patients will also need regular testing as above but also monitoring of immunosuppressive drugs.

Renal Tubular Acidosis

Symptoms

Renal tubular acidosis (RTA) is an acid-base disorder caused by renal impairment of either hydrogen excretion or bicarbonate reabsorption. RTA is grouped into 3 different syndromes: RTA I, RTA II and RTA IV (3, 14). Each is caused by different pathologies and arises as result of different mechanisms.

Distal renal tubular acidosis (RTA I) is caused by a loss of the hydrogen ion gradient between the blood and the lumen (14). Its pathogenesis involves either: down regulation/loss of the H^+-ATPase or increased luminal hydrogen ion permeability. There are a number of causes including (4):

- Primary = genetic, idiopathic, Marfan's syndrome, Sickle cell anaemia etc
- Hypergammaglobulinaemia = amyloidosis, cyroglobulinaemia, liver disease etc
- Autoimmune = primary biliary cirrhosis, autoimmune hepatitis, Sjögren's syndrome, SLE etc
- Drugs = lithium, NSAIDs, amphotericin B etc
- Other = chronic hypercalcaemia, renal transplant rejection, nephrocalcinosis

Proximal renal tubular acidosis (RTA II) is caused by a loss of bicarbonate reabsorption and is very rare (4, 14). Pathogenesis involves loss or impairment of either the proximal tubule Na^+/H^+ antiporter or Na^+/HCO_3^- co-transporter (4). Extremely rare cases show a carbonic anhydrase isoform II deficiency syndrome (15). Often RTA 2 is seen alongside general proximal tubule dysfunction along with glycosuria and amino aciduria in Fanconi syndrome (14, 15). Causes can include (3):

- Metabolic disease = tyrosinosis, cystinosis, fructose intolerance, Wilson disease.
- Drugs/toxins = acetazolamide, lead, mercury
- Other = multiple myeloma, Sjögren syndrome, amyloidosis

Hyperkalaemic, hypoaldosterone renal tubular acidosis (RTA IV) is a result of resistance/reduction of aldosterone (4, 14). The lack of response to aldosterone or reduced levels leads to an inability of the kidneys to excrete hydrogen and potassium leading to a hyperkalaemic acidosis (4). There are a number of causes of hypoaldosteronism (14):

- Adrenal failure = congenital adrenal hyperplasia, Addison's disease etc.
- Renal disease = diabetic nephropathy, tubulointerstitial disease, lupus nephritis
- Drugs = NSAIDS, spironolactone, indomethacin

The symptoms of RTA are often dependent on the underlying cause of and type RTA. Symptoms consistent with all types of RTA include confusion, fatigue, increased breathing rate, bone pain (rickets and osteomalacia) and muscle pain/weakness (16, 17).

Diagnosis

Patient's presenting with the above symptoms and suspicion of any of the underlying causes should have the following tests completed: U&E's (particularly potassium), blood gas analysis especially bicarbonate and blood pH, urine pH, ammonia, urine electrolytes (can calculate urine anion gap) and where appropriate serum renin and aldosterone or investigations into inborn errors of metabolism (i.e. cystinosis etc) (15). The different results for these tests dependent on RTA type can be seen below in table. 4.

RTA Type	Diagnostic features of testing
I	Urine pH>5.5 Positive urine anion gap Hypokalaemia Hypercalciuria Systemic acidosis (blood pH <7.35)
II	Urine pH<5.5 Low serum bicarbonate Hypo/normokalaemia Hypophosphataemia Hyperphosphaturia Glycosuria, amino aciduria (i.e. Fanconi syndrome)
IV	Urine pH<5.5 Positive urine anion gap Hyperkalaemia Hypoladosteronism Hyporeninism

Management

Treatment of the underlying cause helps towards correcting any tubular acidosis, however acute treatment for all types involves giving sodium bicarbonate. For RTA I thiazide diuretics can help to increase proximal bicarbonate reabsorption whilst fludrocortisone is used in RTA IV (4).

Renal Calculi

Renal calculi, renal stones and nephrolithiasis are all terms used to describe the formation of mineral deposits within the kidneys (2, 14).

Formation is normally preceded by metabolic disturbances that are responsible for deposition (14).

The symptoms of the presence of renal stones are often severe pain and haematuria although abdominal X-rays often detect them in asymptomatic patients (14).

The composition of renal stones fall into a number of types with varying occurrence and can be seen in table. 5.

Stone Composition	Occurrence (% of total cases of stones)
Calcium oxalate	60
Uric acid	17
Magnesium ammonium phosphate & calcium phosphate	12
Calcium phosphate	10
Cystine	1

Table 1 Types of renal stone and their frequency in cases of stones. Taken from (14).

The formation of calculi is a logical process, the kidney must conserve water in a number of instances and as such components of urine that are less soluble tend to precipitate out (14). This often occurs due to increased excretion of calculi components, chronic dehydration, increased or decreased urine pH, urinary obstruction and some infections (14).

The most common renal stone, calcium oxalate, is formed often as a result of hypercalcaemia and/or hyperoxaluria (14). A small number of hypercalciuria patients also have hypercalcaemia as a result of hyperparathyroidism whilst most patients are normocalcaemic and can be classed into 3 different groups (14): skeletal reabsorption, renal wasting and dietary absorption. Diseases where skeletal reabsorption is increased such as Paget's disease and some drugs therapies (prolonged steroid use) cause increased amounts of calcium to be processed by the kidneys, which can lead to stone formation (14). Patient's consuming increased dietary calcium along with vitamin D and calcium supplements will also cause an increased amount of calcium to be processed in the kidneys. Renal wasting occurs when patients have other pathologies such as medullary sponge kidney, tubular acidosis, and chronic loop diuretic therapy (14).

Hyperoxaluria has recently been found to contribute considerably towards calcium oxalate stone formation (14). In rare cases this is a genetic defect leading to excessive production of oxalate whilst secondary causes include excessive vitamin C ingestion, ingestion of ethylene glycol and infection with Aspergillus (14).

Treatment of calcium oxalate stones involves increasing water intake so as to produce 2-3L urine daily, dietary intervention by removal of oxalate and excess calcium (14). In some cases an operation may need to be formed to remove stones.

Uric acid stones can form due to hyperuricaemia and hypouricaemia as well as those with normal serum and urate levels (14). This is because most patients with uric acid stones tend to produce

concentrated urine with a low pH (<5.5), which supports stone formation. Therefore treatment is simply to encourage an alkali urine often with potassium citrate dosing. Patients with hyperuricaemia due to gout should reduce dietary purine intake and take allopurinol (14).

Those presenting with symptoms of renal stones should have an abdominal X-ray along with serum urea, creatinine, electrolytes, bicarbonate, uric acid and calcium as well as urine pH, albumin, oxalate and calcium to identify stones and investigate any underlying metabolic disturbances (2, 14).

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