Key points revision

Part 1: Introduction

1. The kidney: structural overview

- The kidneys move down on inspiration.
- The nephron consists of a glomerulus and the tubules that leave it.
- Filtrate is formed in the glomerulus and altered in composition and volume by the tubules.
- An afferent arteriole supplies the glomerulus and an efferent arteriole drains the glomerulus.
- The filtration barrier consists of a layer of endothelial cells, a layer of epithelial cells, and a basement membrane between them.

2. The kidney: functional overview

- The bulk of solute and water reabsorption occurs in the proximal tubules.
- Reabsorption in the proximal tubules is iso-osmotic.
- Active transport uses up ATP and can generate concentration gradients and electrical gradients.
- Water cannot be directly pumped and is moved by osmosis.
- The kidney produces hormones and is acted on by hormones.

3. Development of the renal system

- There are three fetal kidneys, the pronephros, the mesonephros, and the metanephros.
- The metanephros forms the final adult kidney.
- The metanephros forms in the pelvis and migrates upward.
- The ureteric bud forms the draining system from the collecting ducts to the bladder.
- Metanephric tissue forms the tubular system from the glomeruli to the distal nephron.
- Capillaries invaginate tubules to form glomeruli.
- The urogenital sinus forms most of the bladder. The urethral folds form the external genitalia.

4. Clinical features of kidney disease

- The history and examination are essential in assessing the patient.
- Always measure the blood pressure.
- Always assess the patients' fluid volume status.
- If renal disease is suspected, dipstick urinalysis should be undertaken.

5. The kidney: laboratory investigation and diagnostic imaging

- The kidney excretes urea and creatinine.
- If there is renal impairment, the plasma levels of these substances rise.
- Glomerular filtration rate can be estimated from the blood creatinine and variables such as age, gender and ethinicity.
- Ultrasound scanning can detect renal obstruction.
- Renal angiography can detect renal artery stenosis.

Part 2: Filtration and blood flow

6. Renal vascular biology

- Afferent arterioles supply the glomerulus.
- Efferent arterioles drain the glomerulus.
- About 20% of renal blood flow is filtered – this is the filtration fraction.
- Afferent arteriole constriction reduces glomerular filtration rate.
- Efferent arteriole constriction increases glomerular filtration rate.
- Renal vasoconstrictors include: angiotensin II, vasopressin, norepinephrine, epinephrine, and endothelin.
- Renal vasodilators include: prostaglandins, nitric oxide.

7. Glomerular filtration

- The filtration barrier consists of the glomerular endothelial cells, the glomerular basement membrane, and the podocytes.
- Filtrate passes through the filtration barrier into Bowman's space and then into the tubules.
- Glomerular endothelial cells are thin and have pores within them.
- Podocytes have foot processes and between the foot processes are the filtration slits.
- Whether a molecule is filtered depends on its size and charge.

8. Renal vascular disease

- Renal artery stenosis is caused by atherosclerosis in most cases.
- In young women patients, fibromuscular dysplasia can be the cause.
- A fall in renal blood flow triggers excess renin production.
- Renin acts through angiotensin II and aldosterone to cause hypertension and sodium retention.
- Clinically there may be hypertension, edema, renal bruits, and renal impairment. Treatment is by balloon dilatation or surgery.

9. Erythropoietin and anemia in renal disease

- Erythropoietin is made in the kidney.
- It stimulates red blood cell production.
- Erythropoietin production is increased in response to hypoxia or anemia.
- Chronic renal disease can cause erythropoietin deficiency which causes anemia.
- This anemia in chronic renal disease can be treated with erythropoietin.

Part 3: Sodium and water

10. Renal sodium handling

- Sodium is the major cation in extracellular fluid.
- Sodium is freely filtered and then reabsorbed, but not secreted.
- Most sodium reabsorption is in the proximal tubule.

- Sodium reabsorption is driven by the $3Na^+/2K^+$ ATPase.
- The common major diuretic drugs inhibit sodium reabsorption and increase sodium and water excretion.

11. The kidney and water handling

- Water is filtered and then reabsorbed by osmosis.
- The major site of water reabsorption is the proximal tubule.
- In the proximal tubule water is absorbed iso-osmotically with ions. In the loop of Henle, ion and water reabsorption occur in different limbs.
- In the loop of Henle more ions are reabsorbed than water, so the medulla becomes concentrated and the tubular fluid becomes dilute.
- There is no significant water reabsorption in the distal tubule. In the collecting ducts water can leave the ducts to enter the medullary interstitium.
- Vasopressin controls the insertion of aquaporin water channels which are necessary for water reabsorption in the collecting duct.
- The posterior pituitary makes Vasopressin.
- Vasa recta are looped blood vessels which maintain the concentrated nature of the medullary interstitium.

12. Regulation of body sodium and body water

- Body osmolality is controlled by regulating body water content.
- Body volume is controlled by regulating body sodium content.
- Body water content is altered by changes in thirst and renal water excretion.
- Body sodium content is altered by changes in renal sodium excretion.
- Body osmolality is detected by osmoreceptors in the hypothalamus.
- Body volume is detected by stretch receptors mainly in the circulation.
- Osmoreceptors influence vasopressin (antidiuretic hormone, ADH) release. Vasopressin enhances renal water reabsorption.
- Many factors influence renal sodium excretion, especially the renin–angiotensin II–aldosterone system which promotes sodium reabsorption.
- Osmolality will usually be regulated even if this means that body volume will be altered from normal.
- The main exceptions to this rule arise if the regulatory mechanisms are themselves disordered.

13. Disorders of sodium and water metabolism

- Disordered water regulation causes abnormal plasma osmolality.
- Disordered sodium regulation causes abnormal plasma sodium concentration.
- Diabetes insipidus occurs when there is either inadequate vasopressin production (cranial diabetes. insipidus) or a failure of the kidney to respond to vasopressin (nephrogenic diabetes insipidus).
- In either case the result is inadequate water excretion which can cause a rise in plasma osmolality.
- SIAD (syndrome of inappropriate diuresis causes excess vasopressin and a low plasma osmolality.
- Excess aldosterone causes sodium retention.
- Inadequate aldosterone causes sodium loss.
- Hyponatremia (a low plasma sodium) usually reflects hypo-osmolality.
- Hypernatremia (a high plasma sodium) usually reflects hyper-osmolality.

14. Hyponatremia and hypernatremia

- Hyponatremia means a low plasma sodium level.
- Hypernatremia means a high plasma sodium level.
- Hyponatremia typically causes neurological depression.
- Hypernatremia typically causes neurological excitation.
- Both hypernatremia and hypernatremia can ultimately cause fits, coma, and death.
- Hyponatremia can be caused by water retention or loss of both sodium and water followed with replacement mainly with water.
- Hypernatremia can be caused by loss of a dilute fluid such as dilute urine or by inappropriate sodium retention in the kidney.
- Hyponatremia is treated with fluid restriction if body volume is raised and by administration of sodium and water if body volume is low.
- Hypernatremia is treated by water replacement.
- Both hyponatremia and hypernatremia should be corrected slowly with careful monitoring.

15. The edema states: sodium and water retention

- The edema states are characterized by excess sodium and water retention.
- The major factor is inappropriate renal reabsorption of sodium.
- The main causes are congestive heart failure, chronic liver disease, and the nephrotic syndrome.
- There is often perceived hypovolemia (low body volume).
- There is typically excess renin, angiotensin II and aldosterone, excess vasopressin and excess renal sympathetic nervous input which together promote sodium and water retention.
- Clinical signs can include pitting edema, a raised jugular venous pressure, added heart sounds and inspiratory crackles suggesting pulmonary edema.

Part 4: Potassium

16. Renal potassium handling

- Potassium is the major intracellular cation.
- Potassium is pumped into cells by the NKCC2 transporter and then leaks out through potassium channels.
- The potassium gradient across the cell membrane is the main influence on the electrical potential across the membrane and so on the excitability of tissues such as cardiac cells and neurons.
- Potassium is both freely filtered and then reabsorbed and to a lesser extent secreted.
- Potassium excretion is mainly regulated by altering potassium secretion.
- Most potassium reabsorption occurs in the proximal tubule.

17. Regulation of potassium metabolism

- Potassium movement into cells is promoted by insulin, beta 2 agonists, and alkalosis.
- Renal potassium excretion is promoted by aldosterone, loop and thiazide diuretics, increased urine flow rates and vasopressin.
- Amiloride and spironolactone oppose potassium excretion.

• In the distal tubule, sodium reabsorption and potassium secretion are mechanistically linked.
• Aldosterone, therefore, promotes sodium reabsorption and potassium secretion.

18. Hypokalemia and hyperkalemia

• Both hypokalemia and hyperkalemia can cause cardiac arrhythmias because of their effect on the membrane potential of cardiac cells.
• Hyperkalemia is a medical emergency and can cause sine waves on the electrocardiograph and cardiac arrest due to ventricular fibrillation.
• Treatment of hyperkalemia includes calcium administration, insulin, and removal of the excess potassium by the kidney or by hemodialysis, hemofiltration or oral cation exchange resins.
• Always consider hyperkalemia as a potential cause in a cardiac arrest in a patient with renal impairment or renal failure and consider administering calcium.

Part 5: Acid-base

19. Renal acid-base and buffer concepts

• Metabolism produces acid.
• Buffers prevent this acid causing significant changes in body pH.
• Buffers consist of weak acids or weak bases.
• A rise in plasma carbon dioxide levels increases plasma carbonic acid levels which directly lowers plasma pH.
• A rise in plasma bicarbonate concentration increases plasma pH.

20. Renal acid-base handling

• Bicarbonate is freely filtered and then reabsorbed.
• Hydrogen ions are secreted along the nephron.
• In the early nephron, hydrogen ion secretion contributes to bicarbonate reabsorption.
• In the later nephron, hydrogen ion secretion contributes to net acid excretion.
• Acid is mainly excreted as NH_4^+ and as hydrogen ions associated with other buffers.
• Glutamine is metabolized in the proximal tubule cells to produce NH_3 which enters the tubular fluid.

21. Acid-base regulation and responses to acid-base disturbances

• Plasma pH is determined by the ratio of carbon dioxide to bicarbonate ions.
• An uncompensated metabolic acidosis is associated with a low plasma bicarbonate.
• An uncompensated metabolic alkalosis is associated with a high plasma bicarbonate.
• A respiratory acidosis is associated with a high plasma carbon dioxide level.
• A respiratory alkalosis is associated with a low plasma carbon dioxide concentration.

22. Clinical disorders of acid-base metabolism and metabolic acidosis

In metabolic acidosis, pH is low, plasma bicarbonate is low, and the anion gap is normal or increased.
• The anion gap is the calculated difference between the measured cations (Na^+ and K^+) and the measured anions (HCO_3^- and Cl^-).
• An increased anion gap metabolic acidosis indicates the accumulation of unmeasured anions and, therefore, the accumulation of an acid species, such as ketoacids or lactic acid.
• As electroneutrality is always maintained, the level of cations (potassium and sodium ions) must be increased, resulting in a raised anion gap.
• A normal anion gap metabolic acidosis indicates that the primary effect of the acidosis has been a loss of bicarbonate.
• This is balanced by accumulation of chloride to maintain electroneutrality and as both bicarbonate and chloride are measured, the anion gap is not altered.

23. Metabolic alkalosis, respiratory acidosis, and respiratory alkalosis

• In a metabolic alkalosis, plasma bicarbonate is raised.
• This usually arises from loss of body acid, inappropriate excess renal bicarbonate reabsorption, or administration of alkali.
• Aldosterone excess causes excess renal bicarbonate reabsorption.
• A normal plasma chloride concentration is required for normal renal bicarbonate excretion.
• A rise in plasma carbon dioxide level causes a respiratory acidosis.
• A fall in plasma carbon dioxide level causes a respiratory alkalosis.
• Panic attacks cause transient respiratory alkalosis and transient hypocalcemia.

24. Renal tubular acidosis

• Renal tubular acidosis occurs when the kidney does not adequately reabsorb bicarbonate.
• Bicarbonate loss from the kidney causes acidosis.
• The acidosis can be more severe in distal renal tubular acidosis.
• Proximal renal tubular acidosis is associated with other tubular disorders.
• Distal renal tubular acidosis is associated with multisystem disorders.
• Hypoaldosteronism can cause a renal tubular acidosis because distal tubule hydrogen ion secretion is reduced.

Part 6: Divalent ions

25. Calcium, phosphate, and magnesium metabolism

• Calcium and phosphate precipitate as calcium phosphate if their concentration is too high
• Both calcium and phosphate can bind proteins.
• Calcium or phosphate which is not bound to proteins is freely filtered in the glomerulus.
• Along the nephron, calcium and phosphate are both reabsorbed but not secreted.
• Most reabsorption of calcium and phosphate is in the proximal tubule.
• Phosphate is reabsorbed by co-transport with sodium in the proximal tubule.

• Calcium is reabsorbed by a paracellular route in the proximal tubule, calbindins bind calcium and transport it across distal tubular cells.
• Magnesium that is not protein bound is filtered in the glomerulus and reabsorbed along the tubules.

26. Regulation of divalent ions and disorders of phosphate and magnesium

• Parathyroid hormone (PTH) is a peptide hormone.
• Parathyroid hormone is released by the parathyroid gland in response to a fall in ionized calcium.
• Parathyroid hormone promotes renal reabsorption of calcium and renal excretion of phosphate.
• It also promotes vitamin D synthesis and bone resorption.
• Vitamin D is finally metabolized in the kidney.
• Vitamin D promotes calcium and phosphate reabsorption in the kidney and absorption in the gut and release from bone.
• FGF23 is made in bone and inhibits renal phosphate reabsorption and vitamin D production.
• The major cause of hyperphosphatemia is renal failure.

27. Hypocalcemia and hypercalcemia

• Excess PTH causes a high plasma calcium.
• Inadequate PTH causes a low plasma calcium.
• Hypocalcemia can cause tetany and spasm and Chvostek's sign and Trousseau's sign may both be positive.
• Hypercalcemia can cause dehydration, mood and neurological change, abdominal symptoms, and renal stones and tissue calcification.
• The commonest causes of hypercalcemia are primary hyperparathyroidism, malignancy and renal failure with tertiary hyperparathyroidism.
• The QT interval on the electrocardiograph is lengthened in hypocalcemia and shortened in hypercalcemia.

Part 7: Drugs and genetic disorders

28. Drug and organic molecule handling by the kidney

• The kidney is a major site of drug excretion.
• Renal impairment can cause drugs to accumulate to toxic levels.
• If a drug is renally excreted then its dose and the frequency of administration may need to be reduced if there is renal impairment.
• Drugs can be filtered and secreted in the kidney.
• The proximal tubule is the major site of drug secretion.

29. Renal pharmacology: diuretics

• Diuretics reduce water reabsorption and increase urine volume.
• Loop diuretics such as furosemide (frusemide) inhibit the NKCC2 co-transporter in the loop of Henle.
• Thiazide diuretics inhibit the NaCl co-transporter (NCC) in the distal tubule.
• Amiloride inhibits the ENaC (epithelial sodium channel) in the collecting duct.
• Spironolactone is an aldosterone antagonist.
• Mannitol is an osmotic diuretic.
• Acetazolamide inhibits carbonic anhydrase.
• Of the commonly used diuretics, loop diuretics and thiazide diuretics increase potassium excretion, whereas amiloride and spironolactone reduce potassium excretion.

30. Hereditary disorders of tubular transport

• Mutations which inhibit the activity of transporters can have the same effects as diuretic drugs which inhibit the same transporters.
• Mutations which inactivate the NKCC2 transporter in the loop of Henle mimic the effects of furosemide.
• Mutations which inactivate the NaCl cotransporter (NCC) in the distal tubule mimic the effects of thiazides.
• Mutations which inactivate the ENaC transporter mimic the effects of amiloride.
• Fanconi syndrome refers to proximal tubule dysfunction which causes a failure of reabsorption of substances including sodium, glucose, phosphate, and bicarbonate.

The disorders discussed in this chapter are not common, but are important because they tell us much about the function of the molecules which they affect. Do not try to remember the details of the diseases; just try to use them to help you to further understand the function of the tubules.

31. Polycystic kidney disease

• Autosomal dominant polycystic kidney disease (ADPKD) is the commonest form of polycystic kidney disease and usually affects adults.
• The disease is characterised by cysts in the kidneys and often in the liver and pancreas. Subarachnoid hemorrhage can occur.
• Clinical features can include hypertension, progressive renal failure, renal stones and infection.
• 85% of cases of ADPKD arise from mutations in PKD1 gene which encodes the polycystin-1 protein.

Part 8: Glomerular and tubulointerstitial disease

32. Glomerular disease: an overview

• Glomerulonephritis can be classified according to the clinical syndrome it produces, the pathological appearance on a renal biopsy, or if known, the underlying cause or disease.
• Clinical features can include hematuria, proteinuria, hypertension, edema, and renal impairment.
• A focal glomerulonephritis affects some but not all the glomeruli, a diffuse glomerulonephritis affects all the glomeruli.
• A segmental glomerulonephritis affects just a portion within the affected glomeruli, a global glomerulonephritis affects all portions of affected glomeruli.

33. Glomerular pathologies and their associated diseases

• Minimal change nephropathy causes childhood nephrotic syndrome and has a good prognosis.
• Focal segmental glomerulosclerosis has a poor prognosis and is associated with HIV infection.
• Membranous nephropathy is a common cause of nephrotic syndrome in the elderly and is associated with malignancies.
• Mesangiocapillary glomerulonephritis is rare and has a poor prognosis.
• IgA nephropathy is common and can cause recurrent frank hematuria.
• Henoch–Schönlein purpura causes hematuria, abdominal pain, and a rash, usually in children.
• Diffuse proliferative glomerulonephritis occurs following streptococcal or other infections and has a good prognosis.

• Crescentic glomerulonephritis represents substantial renal damage and can be superimposed on other patterns of glomerular disease or associated with systemic disorders such as vasculitis.

34. Specific diseases affecting the glomeruli

• Antibodies to glomerular basement membranes (AGBM) occur in Goodpasture's disease.
• Antibodies to neutrophil cytoplasmic contents (ANCA) occur in primary systemic vasculitis.
• p-ANCA against myeloperoxidase occurs in microscopic polyangiitis.
• c-ANCA against proteinase 3 occurs in granulomatosis with polyangiitis.
• In systemic lupus erythematosus, there are antibodies to dsDNA, complement levels are low, the ESR is high, and the CRP is low.
• Hepatitis C causes cryoglobulinemia and mesangiocapillary glomerulonephritis.
• Myeloma can cause cast nephropathy, light chain deposition disease, and amyloidosis.
• Amyloidosis can arise in chronic inflammation (AA amyloid) or if there is excess immunoglobulin in the form of a paraprotein (AL amyloid).
• Gold and penicillamine cause membranous nephropathy.
• Alport's disease is an X-linked mutation in the alpha 3 chain of collagen type 4 and causes renal disease and deafness.

35. Proteinuria and the nephrotic syndrome

• Proteinuria can result from glomerular disease, tubular disease of excess plasma proteins.
• Nephrotic syndrome occurs if proteinuria is heavy and plasma albumin falls.
• In nephrotic syndrome, the kidneys retain sodium and water causing edema.
• Nephrotic syndrome can be complicated by infection, hyperlipidemia, renal impairment, and edema.
• Proteinuria in pregnancy can be a sign of pre-eclampsia.

36. Tubulointerstitial disease

There are many causes of tubulointerstitial nephritis as most causes of renal tissue damage can cause tubulointerstitial damage.
• Tubulointerstitial nephritis is often just termed interstitial nephritis.
• Major causes of acute interstitial nephritis include the drug groups: analgesics, especially nonsteroidal antiinflammatory drugs, proton-pump inhibitors diuretics and antibiotics.
• A major complication of chronic disease is papillary necrosis and disordered tubular function, especially the ability to concentrate urine.

Part 9: Systemic conditions and the renal system

37. Hypertension: causes and clinical evaluation

• Hypertension is common and important.
• Treatment improves the likelihood of complications such as stroke.
• Causes include excess aldosterone, renal artery stenosis, renal disease and drugs, especially the contraceptive pill.
• Obesity and a high alcohol intake may contribute to hypertension.
• Most hypertension is idiopathic.
• In a hypertensive patient assess end-organ damage, particularly to the retina, the kidneys, and the heart.

38. Hypertension: complications and therapy

• In the kidney, hypertension initially causes proteinuria then glomerulosclerosis.
• In the heart it causes atherosclerosis and left ventricular hypertrophy.
• If grade 3 or 4 retinopathy is present (hemorrhages, exudates, or papilledema), the hypertension is potentially dangerous and requires close supervision and control.
• In black patients, calcium channel blockers, alpha 1 adrenergic blockers, and diuretics are useful.
• In diabetics, angiotensin-converting enzyme inhibitors may be beneficial and effective. Beta blockers may blunt the awareness of hypoglycemia and worsen symptoms of peripheral vascular disease.
• Alpha 1 antagonists may improve urine flow rates in men with prostatic hypertrophy.

39. Pregnancy and the renal system

• During pregnancy the placenta produces prostaglandins.
• These prostaglandins cause blood vessel dilatation.
• This vasodilatation reduces blood pressure, but increases renal blood flow.
• Glomerular filtration rate increases.
• There is marked sodium and water retention.
• Pre-eclampsia occurs in late pregnancy and typically includes water retention, hypertension, and proteinuria.
• Urinary tract infection in pregnancy is important as there is an increased risk of the infection ascending the dilated ureters to affect the kidney.

40. Diabetes mellitus and the kidney

• Diabetes mellitus (both insulin dependent and noninsulin dependent) is a major cause of renal disease.
• An early sign is microscopic albuminuria.
• Good glycemic control and good blood pressure control may reduce the rate of progression of renal disease.
• Angiotensin-converting enzyme inhibitors may also have a beneficial effect.
• Retinopathy is usually present if there is nephropathy. In the long term, glomerulosclerosis occurs.

Part 10: Acute kidney injury and chronic kidney disease

41. Acute kidney injury: pathophysiology

• Acute kidney injury is serious and carries a high morbidity and mortality.
• Causes can be prerenal, renal, or postrenal.
• Most cases are prerenal in origin causing renal ischemia.

- Tubular toxins, especially drugs are important causes.
- Acute tubular necrosis describes injury causing death of the tubular epithelium.

42. Acute kidney injury: clinical aspects

- A full history and examination are essential in acute kidney injury.
- Look especially for toxic drugs and evidence of volume depletion.
- Always exclude obstruction by ultrasound scanning.
- Always dipstick and microscope the urine for signs of intrinsic renal disease.
- Be vigilant for the complications of hyperkalemia, acidosis, and pulmonary edema.
- Treatment with renal replacement therapy should be initiated to prevent these complications whenever possible.
- Hemodialysis or hemofiltration are generally used for acute renal failure.

43. Chronic kidney disease and kidney function in the elderly

- Chronic kidney disease is common and the prevalence rises with age.
- Chronic kidney disease is associated with an increased risk of vascular disease.
- eGFR (estimated glomerular filtration rate) is calculated from plasma creatinine and other variable such as the patient's age.
- eGFR falls as plasma creatinine values rise.
- Blood pressure control is important with chronic kidney disease.

44. Severe chronic kidney disease and renal bone disease

- The major complications of acute renal failure arise because of deficient excretory or endocrine function of the kidney.
- Phosphate accumulation contributes to renal bone disease.
- Vitamin D deficiency contributes to renal bone disease.
- Erythropoietin deficiency causes anemia.
- Renal bone disease is best prevented by control of plasma phosphate and administration of vitamin D.
- Plasma phosphate is controlled by reducing dietary phosphate intake and taking oral phosphate binding substances which inhibit gut absorption of phosphate.

45. Severe chronic kidney disease: clinical complications and their management

- Erythropoietin deficiency causes anemia.
- Impaired platelet function causes a prolonged bleeding time which may be improved by administration of synthetic vasopressin (DDAVP).
- Fluid balance must be controlled by fluid intake and dialysis.
- Hypertension must be controlled by correct fluid balance and if necessary drugs.
- Vascular disease and infection are common problems.

46. Treatment of kidney failure with dialysis

- End-stage renal disease is usually treated with hemodialysis, peritoneal dialysis, or renal transplantation.
- Hemodialysis machines and peritoneal dialysis employ both dialysis and hemofiltration.
- Dialysis describes the equilibration of substances across a semipermeable membrane.
- Hemofiltration describes the bulk flow of water and soluble substances with it, across a membrane, under the influence of hydrostatic or osmotic pressure differences across the membrane.
- Hemodialysis requires blood access.
- Acute complications include hypotension, hypoxemia, cramps, headache, and initially dialysis disequilibrium.
- Chronic complications include infection, access problems, and dialysis amyloid (containing beta 2 microglobulin).

47. Peritoneal dialysis and continuous hemofiltration

- In peritoneal dialysis, the semipermeable membrane is the peritoneal membrane.
- Water is removed by an osmotic gradient between the dialysis fluid and the plasma.
- Other substances are removed by dialysis and also by bulk movement with the water.
- The major complication is infection with skin- or gut-derived organisms.
- In hemofiltration, blood is forced through a semipermeable membrane and water and small molecules are filtered out of the blood.
- Hemofiltration is slower and less physiologically disturbing than hemodialysis and is used in intensive care units on very sick patients.
- Plasma exchange works in the same way, but the pores in the membrane are larger and larger molecules including antibodies and clotting factors are removed.
- Plasma exchange is used to remove unwanted proteins such as antiglomerular basement membrane antibodies.
- Hemoperfusion involves passing blood over a substance such as charcoal which can bind toxins or drugs. The blood is then returned to the body.

48. Renal transplantation

- Renal transplantation is the best treatment for end-stage renal disease.
- HLA matching reduces the chance of rejection. Immunosuppression also reduces the chance of rejection.
- The major drugs are steroids, azathioprine, ciclosporin, mycophenolate, tacrolimus, and sirolimus.
- Complications of immunosuppression include infection, skin tumors, and specific effects of the drugs, especially osteoporosis from steroids.

49. Global kidney medicine

- AKI affects younger patients in poorer countries.
- Obstetric and infectious causes of AKI are important in poorer countries.
- Obesity, diabetes mellitus, hypertension, and vascular disease are major contributors to CKD in richer countries.
- There is often only limited provision for renal replacement therapy in poor countries because it is relatively expensive.
- Renal stone disease is more common in hot dry countries.

Part 11: Stones, infection and cancer

50. Urinary tract infection

- Urinary tract infection is common.
- The incidence is higher in women, probably due to the shorter female urethra.
- The major organisms are *Escherichia coli, Klebsiella,* and *Proteus* species.
- Lower tract infection is usually superficial with no long term consequences.
- Upper tract infection can involve the deep renal tissues and cause renal damage.
- Static urine or a focus for infection, such as a stone, can cause recurrent infection.
- Pregnancy dilates and lowers the tone of the ureters which increases the risk of upper tract infection.
- In small children vesicoureteric reflux can cause upper tract obstruction and renal damage.

51. Urinary tract stones

- Renal tract stones are common.
- They arise when the concentration of stone-forming substances in the urine is high.
- Predisposing factors include infection, urinary stasis, and metabolic abnormalities.
- High urine levels of calcium, oxalate, urate, and cystine promote stone formation.
- Low urine levels of citrate promote stone formation.
- Calcium-containing stones including infection stones are radio-opaque.
- Cystine stones are weakly radio-opaque, but urate stones are not radio-opaque.
- Stones can cause referred pain anywhere from the loin to the external genitalia.
- Stones tend to lodge in the ureter at the pelvi-ureteric junction or where the ureter enters the bony pelvis or as it enters the bladder.

52. Urinary tract cancer

- All renal tract cancers can cause hematuria.
- In older patients with hematuria, renal tract cancer must be excluded.
- In younger patients, cancer is less likely than renal disease such as glomerulonephritis.
- In adults, the kidneys can give rise to renal cell carcinoma.
- This is often associated with systemic features such as night sweats and weight loss.
- In children, the kidneys can give rise to Wilms' tumor. This is associated with mutations in a transcription factor involved in renal development.
- Bladder cancer is associated with smoking, schistosomiasis, and dye industry toxins.
- Bladder cancers spread locally.
- Prostate cancer is common and can interfere with urinary flow and cause urinary obstruction.
- Symptoms include hesitancy, poor stream, terminal dribbling, frequency, nocturia, and urinary retention.
- A rectal examination may indicate a large, hard, craggy prostate.
- Plasma levels of prostate-specific antigen are often raised in prostate cancer.