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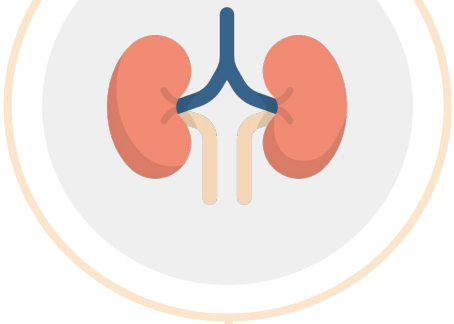

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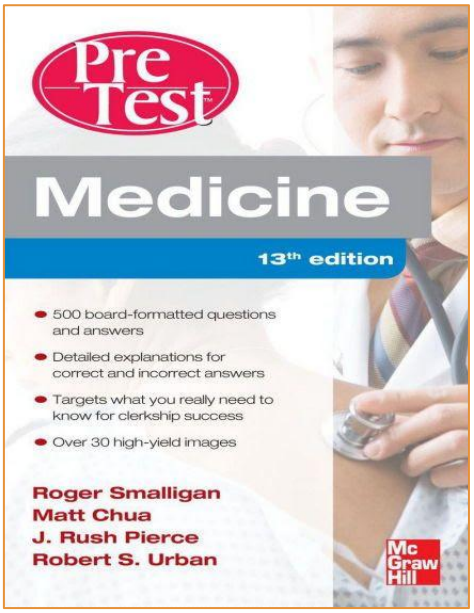
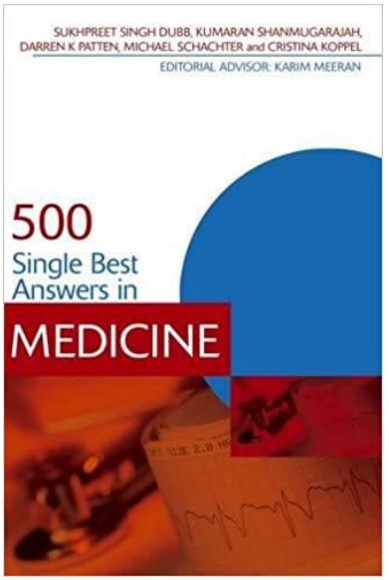
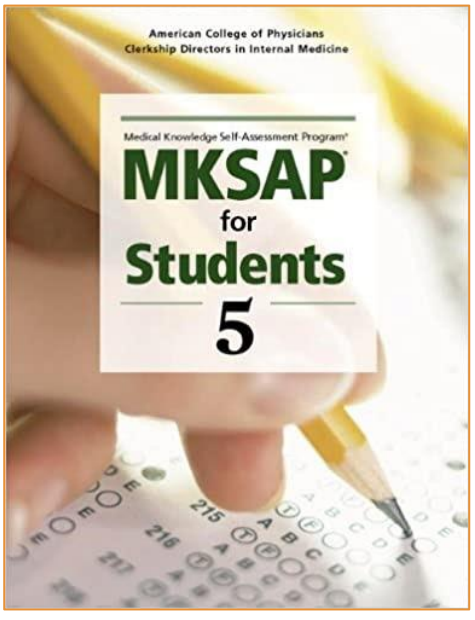






AMBOSS
medical knowledge distilled

Glomerular Diseases

Q1: A 21-year-old man presents with painless haematuria which he has noticed in the last 3 days. He suffers from type 1 diabetes which is well controlled, but is otherwise fit and healthy. The patient has recently recovered from a mild throat infection. Urine dipstick analysis reveals blood and protein in the urine. The most likely diagnosis is:

A. Henoch–Schonlein purpura
B. Benign prostate hypertrophy
C. IgA nephropathy
D. Diabetic nephropathy
E. Urinary tract infection (UTI)

Explanation: Haematuria may be macroscopic with blood evident in the urine or microscopic requiring urine dipstick testing. The anatomical origin of macroscopic haematuria can often be deduced from its presentation in the urine, although this should not be relied upon. Bleeding from the bladder or above usually presents throughout voiding, terminal bladder or prostatic bleeding occurs at the end of voiding, while urethral sites present at the beginning. Microscopic haematuria identified by urine dipstick requires microscopic analysis to confirm red blood cell presence. Red cell casts are red blood cells that have leaked into renal tubules and clump together forming a cast-like structure which is excreted into the urine. The presence of red cell casts are therefore strongly suggestive of glomerular pathology. False-positive results may arise from haemoglobin or myoglobin in the urine. IgA nephropathy or Berger's disease (C) is the most common cause of glomerulonephritis and may present at any age. Haematuria is usually acroscopic and occurs in intervals corresponding with glomerular attacks, infections such as pharyngitis can exacerbate the condition. Henoch– Schonlein purpura (A) differs from Berger's disease through more systemic involvement, often presenting with arthritis of the large joints, abdominal pain and a characteristic purpuric rash of the extensor skin surfaces. The absence of pain and genital symptoms excludes a UTI (E). Diabetic nephropathy (D) typically presents with proteinuria and not haematuria. Benign prostatic hypertrophy (B) occurs in much older patients often alongside poor urine flow.

Q2: A 58-year-old African man presents with pitting oedema of his ankles. He suffers from recently diagnosed hypertension, but is otherwise healthy. Blood results show low albumin and a urine dipstick is positive for protein. The most appropriate initial treatment is:

A. High protein diet
B. Diuretics
C. Prophylactic anticoagulation
D. ACE inhibitor
E. Bed rest

Explanation: This patient has the classic triad of proteinuria, low serum albumin and oedema that occurs in the nephrotic syndrome. This can occur due to a number of disease processes such as diabetes and SLE, as well as those specific to the kidney, including minimal-change nephropathy and focal- segmental glomerulosclerosis. First-line management should include dietary measures to restrict sodium intake and a diuretic (B). Potental diuretics include furosemide which is often required to control any associated severe oedema. High protein diets (A) do not have any benefit to the management of nephritic syndrome, a normal low salt diet should be encouraged. Albumin infusion can be used as adjuncts in patients who are resistant to diuretic therapy but never in isolation as they have transient beneficial effects. Bed rest (E) should also be discouraged in patients since coagulation factors, for example antithrombin, are also lost as part of the proteinuria creating a hypercoagulable state, patients are therefore at risk of thromboembolism, including renal vein thrombosis. Therefore, prophylactic anticoagulation (C) is desirable to protect against hypercoagulation and should always be considered, Angiotensin-converting enzyme (ACE) inhibitors (D) protect against proteinuria by reducing the filtration pressure upon the glomerular capillaries.

Q3: A 17-year-old patient is referred by his GP after presenting with periorbital oedema.
The patient noticed the oedematous eyes 3 days ago, but reports feeling unwell since a throat infection 3 weeks ago with nausea and vomiting in the last week. A urine dipstick is positive for protein and blood while serum creatinine and urea are mildly deranged. The most likely diagnosis is:

A. Nephrotic syndrome
B. Nephritic syndrome
C. Renal failure
D. Glomerulonephritis
E. Von Grawitz tumour

Explanation: This patient is suffering from post-streptococcal glomerulonephritis (D), which forms part of the nephritic syndrome consisting of haematuria (micro- or macroscopic), hypertension, proteinuria and oedema. In severe cases, oliguria and uraemia can also occur. Patients usually suffer from a streptococcal infection 1–3 weeks prior to presenting with the above symptoms or signs of the nephritic syndrome. During this time, immune complexes are formed and deposited in the glomeruli causing damage. The nephrotic syndrome (A) involves albuminuria usually in the order of ≥3.5 g/d in adults causing oedema and is also associated with hyperlipidaemia (increased LDL/HDL ratio). Nephritic syndrome (B) involves haematuria (micro- or macroscopic) alongside hypertension and proteinuria. Renal failure (C) is an abrupt reduction in kidney function, usually ≤48 hours, with an increase in serum creatinine of ≥26.4 µmol/L or reduction in urine output. A Von Grawitz tumour (E), otherwise known as renal cell cancer, typically occur in males (2:1 male to female ratio) originating from the proximal tubular epithelium. The average age of presentation is 50 years with symptoms including pain, haematuria and usually a mass in the flank alongside other symptoms of malignancy such as weight loss.

Answers: Q1: C | Q2: B | Q3: D

Glomerular Diseases

Q4: A 35-year-old woman is evaluated for a 1-month history of progressive bilateral lower-extremity edema. She was diagnosed with type 1 diabetes mellitus 10 years ago. At her last office visit 4 months ago, the urine albumin-creatinine ratio was 40 mg/g. Medications are enalapril, insulin glargine, insulin aspart, and low-dose aspirin. On physical examination, vital signs are normal except for a blood pressure of 162/90 mm Hg (baseline 130/70 mm Hg). Cardiopulmonary and funduscopic examinations are normal. There is 3+ pitting edema of the lower extremities to the level of the thighs bilaterally. On kidney ultrasound, the right kidney is 12.2 cm and the left kidney is 12.7 cm. There is no hydronephrosis, and no kidney masses are seen. Which of the following is the most appropriate next step in this patient's management?

A. Cystoscopy
B. Kidney biopsy
C. Spiral CT of the abdomen and pelvis
D. Observation

Hemoglobin A_{1c}	6.8%
Albumin	3 g/dL (30 g/L)
Serum creatinine	1.1 mg/dL (97.2 µmol/L)
Urinalysis	3+ protein; 2+ blood; 8-10 dysmorphic erythrocytes/hpf; 2-5 leukocytes/hpf; few erythrocyte casts
Urine protein-creatinine ratio	5.2 mg/mg

Explanation: Kidney biopsy would be appropriate for this patient. This study is recommended in patients with features of nondiabetic kidney disease in order to establish a diagnosis and determine the most appropriate treatment. Diabetic nephropathy is characterized by proteinuria, hypertension, and a decline in the glomerular filtration rate in patients with a long-standing history of type 1 diabetes or a 5- to 10-year history of type 2 diabetes. This condition usually progresses from microalbuminuria to macroalbuminuria to an elevated serum creatinine level over a number of years. Although this patient's long-standing history of diabetes and proteinuria is suggestive of diabetic nephropathy, the presence of glomerular hematuria (dysmorphic erythrocytes and erythrocyte casts) and the rapid onset of symptomatic nephrotic syndrome are not consistent with diabetic nephropathy. These findings raise suspicion for primary glomerular disease. Furthermore, patients with diabetic nephropathy often have diabetic retinopathy, which is absent in this patient. Cystoscopy would be considered in an adult with hematuria of uncertain origin in order to exclude bladder cancer. Similarly, imaging studies may help to evaluate urinary tract obstruction, kidney stones, kidney cysts or masses, renal vascular diseases, and vesicoureteral reflux. However, cystoscopy or a spiral CT would not be warranted in a patient with erythrocyte casts seen on urinalysis and dysmorphic erythrocytes, which suggests glomerular hematuria. Observation alone would place this patient at risk for progressive kidney injury if her condition remains undiagnosed and untreated.

Key Point Kidney biopsy is recommended in patients with diabetes mellitus who have features of nondiabetic kidney disease.

Q5: A 25-year-old man is referred to you because of hematuria. He noticed brief reddening of the urine with a recent respiratory infection. The gross hematuria resolved, but his physician found microscopic hematuria on two subsequent first-voided morning urine specimens. The patient is otherwise healthy; he does not smoke. His blood pressure is 114/72 and the physical examination is normal. The urinalysis shows 2+ protein and 10 to 15 RBC/hpf, with some dysmorphic erythrocytes. No WBC or casts are seen. What is the most likely cause of his hematuria?

A. Kidney stone
B. Renal cell carcinoma
C. Acute poststreptococcal glomerulonephritis
D. Chronic prostatitis
E. IgA nephropathy (Berger disease)

Explanation: Dysmorphic erythrocytes and proteinuria suggest a glomerular source of hematuria. The commonest causes of glomerular hematuria in this population are IgA nephropathy (Berger disease) and thin basement membrane disease. Berger disease can cause hypertension or even renal insufficiency; thin basement membrane disease is a benign condition. Berger disease is associated with IgA deposits in the mesangium. Patients with IgA nephropathy often have an exacerbation of their hematuria with intercurrent respiratory illnesses.
Acute glomerulonephritis usually occurs a week or two after the sore throat (ie, to give enough time for vigorous antibody production against the streptococcal antigens). Acute glomerulonephritis is usually symptomatic (hypertension, periorbital edema) and is associated with red blood cell casts and an active urinary sediment. Poststreptococcal GN is now a rare condition in the adult population of developed nations. Although urological cancers, kidney stones, and prostatitis are important causes of hematuria (especially in an older or symptomatic patient), they would not cause dysmorphic erythrocytes or protein in the urine.

Q6: An 18-year-old man presents with general malaise and lethargy for the last 2 weeks, he denies any weight loss and has maintained a good appetite. On examination, there are no abnormalities except for sacral oedema and a polyphonic wheeze. Urine dipstick is positive for protein only and blood pressure is 140/90. The most likely diagnosis is:

A. Nephritic syndrome
B. Nephrotic syndrome
C. Goodpasture's disease
D. Thin-basement membrane nephropathy
E. Minimal change glomerulonephritis

Explanation: Minimal change nephropathy (E) is the most common cause of nephrotic
syndrome in children and young adults. The nephrotic syndrome (B) is likely in this patient with proteinuria resulting in oedema, however, the cause of these symptoms is minimal change glomerulonephritis, hence this is the best answer. The nephritic syndrome (A) consists of haematuria (micro- or macroscopic) which differs from the nephrotic syndrome since in the latter the damaged pores are large enough to allow passage of proteins, but not RBCs. Also, part of the nephritic syndrome is hypertension and proteinuria which causes oedema. Thin basement membrane nephropathy (D) is one of the most common causes of asymptomatic haematuria alongside IgA nephropathy, it is a benign condition characterized by thinning of the glomerular basement membrane which does not impact renal function, hence signs such as sacral oedema would not be present. Goodpasture's disease (C) is the triad of glomerulonephritis, pulmonary damage causing haemorrhage and the presence of anti- glomerular basement membrane antibodies. This is due to a type II autoimmune reaction whereby the anti-GBM antibodies attack type IV collagen of the lungs and the renal glomerulus.

Answers: Q4: B | Q5: E | Q6: E

Glomerular Diseases

Q7: A 6-year-old has a sore throat and has been given antibiotics. Three weeks later, he represents feeling feverish with nausea, vomiting and tea-coloured urine. Urine dipstick confirms haematuria and protein. Blood pressure is 100/60 mmHg. The most likely diagnosis is:

A. Nephritic syndrome
B. UTI
C. Acute tubulointerstitial nephritis
D. Minimal change glomerulonephritis
E. Post streptococcal glomerulonephritis

Explanation:This patient has the typical findings that manifest in a case of poststreptococcal glomerulonephritis (E). The group A streptococcus infection causes deposition of immune complex in the glomeruli. Within this period, the streptococcal organisms themselves are destroyed, hence a UTI (B) coinciding this presentation is not likely. Also, other symptoms suggestive of a UTI are absent, such as dysuria. This patient does not fulfil the triad required for nephritic syndrome (A) since there is no hypertension despite the presence of haematuria and proteinuria. An acute tubulointerstitial nephritis (C) is usually accompanied by fever, skin rashes and painful joints. Minimal change nephropathy (D) is the most common cause of the nephrotic syndrome in children. In this case, haematuria is not a feature of minimal change glomerulonephritis, although proteinuria are present but there is no oedema, which does not fulfil the criteria present in the nephrotic syndrome.

Q8: A 64-year-old woman with type 1 diabetes presents to clinic with several months of sinus problem and a 4-day history of oliguria. Her blood pressure is 137/80, serum results show mildly elevated urea and creatinine, absence of anti-GBM antibodies, while a C-ANCA assay is positive. Red blood cell (RBC) casts are present in the urine and her renal biopsy reveals glomerular crescents. The most likely diagnosis is:

A. Post-streptococcal glomerulonephritis
B. Goodpasture's syndrome
C. Minimal change glomerulonephritis
D. Rapidly progressive glomerulonephritis
E. Wegener's granulomatosis

Explanation: Wegener's granulomatosis (E) is part of the small vasculitides that also includes other diseases such as Churg–Strauss syndrome. Wegener's typically affects the lungs and kidneys although other body systems can be involved. The pathology of Wegener's is automimmune in nature. Antineutrophil cytoplasmic antibodies (ANCAs) attack small to medium-sized blood vessels resulting in necrotizing granulomatous inflammation. There is a broad spectrum of symptoms but specific to the renal system patients can be asymptomatic to presenting with renal failure on presentation. Patients characteristically have a crescentic necrotizing glomerulonephritis with the presence of RBC casts. Minimal change nephropathy (C) most commonly occurs in young children causing the nephrotic syndrome. There is also a high association with asthma and eczema. Rapidly progressive glomerulonephritis (D) is characterized by the presence of RBC casts (dysmorphic RBCs damaged as they pass into the renal tubules) which are present in the haematuria. Patients rapidly develop renal failure over weeks and may have glomerular crescents on histology. There are several common causes of rapidly progressive glomerulonephritis, such as ANCA- associated glomerulonephritis, including Wegener's granulomatosis, Goodpasture's disease and a severe form of lupus nephritis. Goodpasture's disease (B) is due to a type 2 autoimmune reaction with antibodies attacking the glomerular basement membrane and lung membrane. Patients often present with upper respiratory tract complaints such as haemoptysis with renal manifestations, such as anaemia and glomerulonephritis, occuring later. ANCA may be positive but are not a dominant feature. Post-streptococcal glomerulonephritis (A) is usually associated with haematuria and hypertension following a streptococcal infection which leads to an acute nephritis due to deposition of immune complex.

Q9: A 21-year-old man presents with lethargy over the last week, he has periorbital oedema and proteinuria. The patient mentions he has been to hospital a number of times in the past due to the same symptoms as well as mild eczema. Light microscopy of a renal biopsy showed normal morphology. Electron microscopy of the renal biopsy reveals the diffuse effacement of the epithelial podocytes. The most appropriate treatment is:

A. Cyclosporin
B. No treatment
C. Probenecid
D. Renal transplant
E. Oral prednisone

Explanation: This patient is suffering from minimal change disease which is the most common cause of nephrotic syndrome in children but can also present in young adults. Only electron microscopy is able to detect any abnormalities of the glomerulus which typically demonstrates fusion of the podocyte foot processes. Although this finding is not pathognomonic, it is highly predictive in children or young adults with nephrotic syndrome with associated eczema or asthma and its positive response to steroids (E). Since this patient has presented a number of times with the nephrotic syndrome, not providing treatment (B) is not helpful given the good response minimal change disease patients demonstrate to steroids or immunosuppressants. Probenecid (C) is primarily used in the prophylaxis against gout as it acts to increase urinary excretion of uric acid. Renal transplant (D) is the treatment for several chronic kidney diseases or end stage renal function. Cyclosporin (A) is an alternative second-line therapy for patients who are steroid-resistant or continually relapse. Cyclosporin therapy requires longer-term therapy compared to steroids but must be continually monitored as accumulation is nephrotoxic, hence it is not appropriate as first-line therapy when compared to oral steroids.

Answers: Q7: E | Q8: E | Q9: E

Glomerular Diseases

Q10: A 29-year-old man with HIV, on a highly active antiretroviral therapy (HAART) regimen including the protease inhibitor indinavir, presents with severe edema and a serum creatinine of 2.0 mg/dL. He has had bone pain for 5 years and takes large amounts of acetaminophen with codeine, aspirin, and ibuprofen. He is on prophylactic trimethoprim-sulfamethoxazole. Blood pressure is 170/110; urinalysis shows 4+ protein, 5 to 10 RBC, 0 WBC; 24-hour urine protein is 6.2 g. The serum albumin is 1.9 g/L (normal above 3.7). Which of the following is the most likely cause of his renal disease?

A. Indinavir toxicity
B. Analgesic nephropathy
C. Trimethoprim-sulfamethoxazole–induced interstitial nephritis
D. Focal glomerulosclerosis
E. Renal artery stenosis

Explanation:Although many glomerular lesions occur in association with HIV, focal glomerulosclerosis is by far the commonest etiology of this patient's nephrotic syndrome. While focal sclerosis is more common in intravenous drug users with HIV, the lesion is different from so-called heroin nephropathy. Indinavir toxicity may cause tubular obstruction by crystals and is a cause of renal stones, but does not cause nephrotic syndrome. Analgesic nephropathy is a frequently unrecognized cause of occult renal failure. This entity requires at least 10 years of high-level analgesic use and may cause renal colic owing to papillary necrosis. Analgesic abuse nephropathy, however, is an interstitial disease and does not cause nephrotic range proteinuria. Trimethoprim- sulfamethoxazole may cause acute interstitial nephritis, but the patient does not have fever, rash, WBC casts, or eosinophils in the urinalysis. Again, interstitial diseases do not cause high-level proteinuria. Bilateral renal artery stenosis would be rare at this age and is associated with a normal urinalysis.

Match questions 11, 12 & 13 with the options below

Q13: A 50-year-old white man presents with mild hypertension, nephrotic syndrome, microscopic hematuria, and venous thromboses (including renal vein thrombosis). Renal biopsy reveals a thickened glomerular basement membrane with subepithelial immunoglobulin deposition.

Q14: A 19-year-old white man presents with hypertension, nephrotic syndrome, mild renal insufficiency, RBC casts in urine, and depressed third component of complement (C3). Renal biopsy shows thickened basement membranes and increased cellular elements. Electron microscopy shows dense deposits within the basement membrane.

Q15: A 43-year-old woman complains of fatigue and swelling of her legs. She has been taking several ibuprofen tablets daily for recurrent headaches. She has no history of lymphadenopathy, night sweats, or weight loss. On examination she has a slightly puffy face and her blood pressure is 150/95. She has no adenopathy, her lungs are clear, her heart is normal, and she has 2+ pitting edema to the mid-calf bilaterally. Her creatinine is 0.8 and her urinalysis shows 3+ protein, some amorphous material, and eosinophils. Her 24-hour urine protein is 3.9 g. Renal biopsy results show normal light microscopy and no deposits by immunofluorescent microscopy. Electron microscopy shows effacement of the foot processes.

A. Minimal change disease
B. IgA nephropathy
C. Focal and segmental glomerulosclerosis
D. Anti-glomerular basement membrane disease
E. Membranous nephropathy
F. Membranoproliferative glomerulonephritis

Explanation: Glomerular diseases present with proteinuria and sometimes an active urinary sediment (dysmorphic red cells, white blood cells, and red cell casts). Many patients have the nephrotic syndrome. Patients who present with an active sediment, hypertension, and worsening renal function without nephrotic-range proteinuria and hypoalbuminemia are said to have the nephritic syndrome. Finally, some patients (eg, the usual patient with IgA nephropathy) will have asymptomatic proteinuria or hematuria. Serological studies, complement levels, and, often, renal biopsy will be necessary to establish a definite diagnosis and to adequately plan treatment. **Membranous nephropathy** is the commonest cause of idiopathic nephrotic syndrome in adults. One-third of cases improve spontaneously, one-third remain stable, and one-third progress to end-stage renal disease if untreated. The condition is fairly responsive to corticosteroid and cytotoxic therapy. **Membranoproliferative glomerulonephritis** is an uncommon cause of idiopathic nephrotic syndrome in adults. Depressed C3 is caused by an autoantibody that directly activates the third component of complement. A progressive clinical course and erratic response to therapy are typical. **Minimal change disease** is the cause of nephrotic syndrome in about 15% of adults and 70% to 90% of children. While it often presents as primary renal disease, it is also seen in association with other conditions like NSAID use with concomitant interstitial nephritis and Hodgkin disease. Clinically, patients present as described with sudden onset of edema, nephrotic syndrome, and amorphous urinary sediment on the urinalysis. Most (80%-85%) adults achieve remission of the disease with the use of prednisone, cyclophosphamide, chlorambucil, or mycophenolate mofetil. Relapses can occur but are less common in adults than in children. While children often do not require a biopsy if they respond to high- dose steroids, most adults do undergo biopsy to confirm the etiology. Renal biopsy and electron microscopy are exactly as described in the question. **IgA nephropathy** is the commonest glomerular disease in adults but rarely causes nephrotic syndrome. Focal and segmental glomerulosclerosis is often associated with drug use or AIDS. Anti-glomerular basement membrane (anti-GBM) disease causes a nephritic picture with hematuria and rapidly progressive renal insufficiency. Light microscopy often reveals crescent formation, and immunofluorescence shows linear IgG staining of the GBM..

Answers: Q10: D | Q11: E | Q12: F | Q13: A

Acute Kidney Injury

Q1: A 16-year-old boy presents with a low-grade fever which started 1 week ago. The patient also reports feeling fatigued and indicates pain in his joints. His parents mention that he has been visiting the toilet more often than usual. A urine dipstick shows trace proteins, while a blood test shows raised eosinophils. The most likely diagnosis is:

A. Acute tubulointerstitial nephritis
B. Renal failure
C. Diabetes mellitus
D. UTI
E. Reactive arthritis

Explanation: The majority of tubulointerstitial nephritis (A) is due to drug hypersensitivity reactions, most commonly penicillin or non-steroidal anti-inflammatory drugs which are commonly given. Patients typically present with fever, skin rashes and may also have painful joints. Blood results will often have raised eosinophils. Eosinophils are involved in allergic responses, such as asthma and drugs, parasitic infection and also tissue inflammation. Renal failure (B) is the sudden loss of renal function which in the acute phase is reversible, plasma urea and creatinine typically increase due to the loss of filtering function of the kidney and patients tend to be oliguric rather than polyuric. In diabetes (C), although patients would tend to visit the toilet more due to hyperglycaemia causing an osmotic diuresis, other important features would include weight loss, polydipsia and the presence of glucose and possibly ketones on urine dipstick. A UTI (D) is characterized by features that include dysuria, elevated white cell count and raised leukocytes and nitrites in the urine. Reiter's disease (E) is a sterile synovitis that typically follows an infection and involves the classical triad of urethritis, arthritis and conjunctivitis.

Q2: A 58-year-old man presents with breathlessness, he reports feeling unwell over the last three months with nausea, vomiting and difficulty breathing. You notice his ankles are swollen and he has bruises on his arms. The patient mentions he has not been urinating as often as normal. The most appropriate investigation is:

A. Urine microscopy
B. Renal ultrasound
C. Serum electrolytes, urea and creatinine
D. Renal biopsy
E. Chest x-ray

Explanation: This patient is suffering from symptoms of renal failure which is defined as an abrupt, reversible deterioration in renal function causing uraemia and often associated with oliguria. The uraemia can result in non-specific symptoms such as nausea and vomiting, failure to excrete H+ results in acidosis causing hyperventilation. Oedema can also result as the kidney loses its diuretic ability, erythropoietin is also produced by the kidney. With increasing impairment there is also reduced haemostatic function causing easy bruising. Serum electrolytes, urea and creatinine (C) is the first-line investigation in this case in order to determine the current level of renal function. Biochemical impairment is reflected by sodium, potassium (increased in renal failure), urea (increased in renal failure) and creatinine (increased in renal failure). The RIFLE criteria (risk, injury, failure, loss, end-stage renal disease) is useful in determining the difference between an acute, chronic or acute-on-chronic presentation of renal failure which can otherwise be difficult in clinical practice. The patient does not have typical features of a UTI, therefore a urine microscopy (A) is not appropriate although it may show evidence of red cell casts to support the blood investigations. Oliguria and easy bruising deviates away from respiratory pathology which would be revealed using a chest x-ray (E). A renal ultrasound scan (B) would reveal the degree of gross damage to the kidneys and structure problems, such as dilatation of the urinary tract due to obstruction, while a biopsy would show histological changes (D). However, these tests are more useful for determining the cause of renal failure and are not appropriate as first-line investigations until the diagnosis of renal failure has been established.

Answers: Q1: A | Q2: C

Acute Kidney Injury

Q3: A 62-year-old woman is evaluated for acute oliguric renal failure. She was admitted to the hospital 7 days ago for sepsis due to methicillin-sensitive Staphylococcus aureus; intravenous cefazolin was begun and she quickly improved. Today, her urine output is 10 mL/h. On physical examination, temperature is 37.5°C (99.5°F), blood pressure is 138/88 mm Hg, pulse rate is 78/min, and respiration rate is 12/min. A macular erythematous rash is present over her anterior chest and abdomen. The remainder of the physical examination is normal. Renal ultrasonography shows normal kidney size without hydronephrosis. Which of the following is the most likely diagnosis?

	Day 1	Day 7
Blood urea nitrogen	8 mg/dL (2.9 mmol/L)	20 mg/dL (7.1 mmol/L)
Creatinine	0.6 mg/dL (53.0 µmol/L)	1.8 mg/dL (159.1 µmol/L)
Urinalysis	Normal	Dipstick: pH, 5; protein, 1+; blood, negative. Microscopic: 15-20 white blood cells per high power field; many leukocyte casts
Urine culture		No growth

A. Acute interstitial nephritis
B. Acute tubular necrosis
C. Cholesterol crystal embolization
D. Prerenal azotemia

Explanation: The most likely diagnosis is acute interstitial nephritis. This patient has acute kidney injury (AKI), as evidenced by the sudden onset of oliguria and an increase in her blood urea nitrogen (BUN) and serum creatinine values. Her urine (normal upon admission) is positive for leukocytes and leukocyte casts, but the culture is negative (sterile pyuria). This clinical picture is most consistent with tubulointerstitial inflammation caused by acute interstitial nephritis. Drugs, particularly β-lactam antibiotics, are the most common etiology of acute interstitial nephritis. Patients may also have fever, rash, and eosinophilia, although only a minority of patients will have all three features. Acute tubular necrosis (ATN) is the most common form of intrarenal disease that causes acute kidney injury in hospitalized patients. Onset of this condition usually occurs after a sustained period of ischemia or exposure to nephrotoxic agents. Urinalysis in approximately 75% of patients with acute tubular necrosis reveals muddy brown casts; leukocytes and leukocyte casts are not associated with ATN. Cholesterol crystal embolization may cause AKI in patients with aortic atherosclerotic plaques. This condition may occur spontaneously but most often develops after coronary or kidney angiography or aortic surgery. Kidney injury in patients with cholesterol crystal embolization usually has a subacute onset with a stuttering course over several weeks. Cutaneous manifestations develop in approximately 10% to 15% of patients and may include livedo reticularis, skin ulceration, and nodules. Patients with cholesterol crystal embolization typically have a bland urine sediment but may have dysmorphic hematuria and erythrocyte casts. The absence of orthostatic hypotension, tachycardia, and the normal BUN-creatinine ratio of approximately 10:1, argue against prerenal azotemia as the cause of AKI.

Key Point Acute interstitial nephritis is characterized by acute kidney injury, sterile pyuria, and leukocyte casts

Q4: An 18-year-old man is evaluated in the emergency department after his mother found him unconscious in his bed at home. She reported that her son had gone to a party 24 hours ago, but she was not sure when he returned home. When she checked on him, he was unarousable. He has no significant medical history and takes no medications. In the emergency department, he is afebrile, blood pressure is 110/70 mm Hg, pulse rate is 50/min, and respiration rate is 6/min; he is intubated. Complete blood count, alkaline phosphatase, bilirubin, and albumin are normal. Urine dipstick is 4+ positive for occult blood, negative for erythrocytes. Blood alcohol level is 0.8 g/dL (174 mmol/L). Toxicology testing is positive for opiates and cocaine. Bladder catheterization reveals only 30 mL of brown urine. Which of the following is the most likely cause of the acute kidney injury?

Creatinine	3.2 mg/dL (282.9 µmol/L)
Aspartate aminotransferase	80 U/L
Alanine aminotransferase	46 U/L
Creatine kinase	18,400 U/L
INR	1.2

A. Hemolytic anemia
B. Hemolytic-uremic syndrome
C. Hepatorenal syndrome
D. Rhabdomyolysis

Explanation: This patient most likely has rhabdomyolysis, which is caused by skeletal muscle damage that leads to release of intracellular components into the circulation. The syndrome was first identified in patients with traumatic crush injuries, but there are nontraumatic causes, such as alcohol (due to hypophosphatemia), drug use, metabolic disorders, and infections. The classic triad of findings includes muscle pain, weakness, and dark urine. The diagnosis is based on clinical findings and a history of predisposing factors (such as prolonged immobilization or drug toxicity) and confirmed by the presence of myoglobinuria, an increased serum creatine kinase level, and, in some cases, hyperkalemia. A positive urine dipstick for blood in the absence of erythrocytes also suggests rhabdomyolysis. The disorder usually resolves within days to weeks. Treatment consists of aggressive fluid resuscitation; fluids should be adjusted to maintain the hourly urine output at least 300 mL until the urine is negative for myoglobin. Acute kidney injury resulting from acute tubular necrosis occurs in approximately one third of patients. Dialysis is sometimes necessary. Although fulminant hepatic failure may result in coma, dark urine, and renal failure, other tests of synthetic liver function in this patient are normal. Hemolytic anemia would not explain the patient's elevated creatine kinase level and usually does not cause renal failure. Hemolytic uremic syndrome is not consistent with the normal complete blood count, clinical findings of polysubstance overdose or the laboratory finding of the elevated serum creatine kinase level.

Key Point Rhabdomyolysis is associated with muscle pain, weakness, and dark urine; laboratory findings include an elevated serum creatine kinase level and positive urine dipstick for blood in the absence of erythrocytes.

Answers: Q3: A | Q4: D

Acute Kidney Injury

Q5: A 72-year-old man is evaluated in the emergency department for a 2-day history of suprapubic abdominal pain. He has had difficulty urinating for the last 6 months, including urinary frequency and difficulty starting his urinary stream. He has nocturia four to five times per night. Medical history is otherwise nonsignificant, and he takes no medications. On physical examination, the patient is uncomfortable. Temperature is 37.0°C (98.6°F), blood pressure is 162/90 mm Hg, pulse rate is 92/min, and respiration rate is 12/min. Suprapubic fullness to palpation is noted. Which of the following is the best diagnostic test for this patient?

A. Kidney arteriography
B. Kidney biopsy
C. Kidney ultrasound
D. Urine dipstick for protein

Blood urea nitrogen	30 mg/dL (10.7 mmol/L)
Creatinine	2.2 mg/dL (194.5 µmol/L)
Electrolytes	
Sodium	136 meq/L (136 mmol/L)
Potassium	5.2 meq/L (5.2 mmol/L)
Chloride	100 meq/L (100 mmol/L)
Carbon dioxide	20 meq/L (20 mmol/L)

Explanation: The best diagnostic test for this patient is kidney ultrasound to evaluate for urinary obstruction. The patient has lower urinary tract symptoms with difficulty voiding and suprapubic fullness. This is consistent with bladder outlet obstruction from prostatic hypertrophy. Obstruction can cause intrarenal vasoconstriction, ischemic tubular injury, and interstitial fibrosis that may lead to end-stage kidney disease if uncorrected. Although patients with complete obstruction have significantly decreased urine output, those with partial obstruction may have polyuria caused by loss of tubular function or excretion of excess retained solute. Kidney ultrasound in most patients with obstruction reveals hydronephrosis. Patients with acute kidney injury (AKI) caused by urinary tract obstruction have a favorable prognosis when obstruction is relieved within 1 week of onset. A kidney ultrasound would reveal a distended bladder and possible hydronephrosis. Insertion of a Foley catheter is initial treatment. Kidney biopsy should be considered when the diagnosis of AKI remains unclear after excluding prerenal and postrenal disease. Biopsy is warranted to help guide therapy or provide prognostic information. Ultrasound duplex arteriography, CT arteriography, MRI, and angiotensin-converting enzyme inhibitor renography are used to evaluate renal vasculature in the presence of disrupted arterial or venous blood flow. In this patient with voiding symptoms and suprapubic fullness, noninvasive kidney ultrasoundy is the diagnostic test of choice. Albumin is the only protein detected on dipstick urinalysis, and nothing in the patient's presentation suggests he has a primary glomerular disease causing AKI; dipstick evaluation would add little to this case. Quantitative measurements, rather than dipstick methodology, are recommended to detect albumin excretion less than 300 mg/24 h.

Key Point Kidney ultrasound is indicated for all patients with acute kidney injury to define kidney anatomy and to exclude hydronephrosis.

Q6: A 29-year-old woman comes for a follow-up office visit. Six months ago, she underwent double-lung transplantation for cystic fibrosis. She was diagnosed with Pseudomonas bronchitis 14 days ago and began oral ciprofloxacin and intravenous tobramycin at that time. Today, she states that her cough has resolved, she has not had fever, and she feels well. Additional medications are acyclovir, mycophenolate mofetil, prednisone, tacrolimus, and trimethoprim-sulfamethoxazole. On physical examination, temperature is 36.6°C (97.8°F), blood pressure is 132/80 mm Hg, pulse rate is 90/min, and respiration rate is 18/min. Cardiopulmonary examination is normal. Cutaneous examination is normal. There is no asterixis. There is no edema. Urine sediment findings are shown. Kidney ultrasound shows normal-sized kidneys and no hydronephrosis. Which of the following is the most likely cause of this patient's findings?

A. Acute interstitial nephritis
B. Acute tubular necrosis
C. Thrombotic thrombocytopenic purpura
D. Urinary tract obstruction

Hemoglobin	12.0 g/dL (120 g/L)
Leukocyte count	8400/µL (8.4×10^9/L)
Platelet count	335,000/µL (335×10^9/L)
Serum creatinine	2.3 mg/dL (203.3 µmol/L) (1.2 mg/dL [106.1 µmol/L] 6 weeks ago)
Urinalysis	Specific gravity 1.011; pH 5.5; 1+ protein; no blood; 2-5 erythrocytes/hpf; no leukocyte esterase

Explanation: This patient's elevated serum creatinine level, minimal proteinuria, and muddy brown casts on urinalysis are most consistent with acute tubular necrosis. This condition usually develops after a sustained period of ischemia or exposure to nephrotoxic agents such as cisplatin, intravenous aminoglycosides, or radiocontrast. Acute interstitial nephritis most commonly develops after exposure to certain medications, including trimethoprim. Manifestations of this condition may include rash, pruritus, eosinophilia, and fever. Urine sediment findings include pyuria, leukocyte casts, microscopic hematuria, and tubular-range proteinuria. These features are absent in this patient. Manifestations of the thrombotic microangiopathies, including thrombotic thrombocytopenic purpura, may include acute kidney injury that is usually accompanied by microangiopathic hemolytic anemia and thrombocytopenia. Approximately 50% of patients have low C3 levels. The urine sediment usually shows minimal or no abnormalities and is nondiagnostic; rarely, erythrocyte or muddy brown casts may be seen. This patient's normal hemoglobin concentration and platelet count exclude a thrombotic microangiopathy as the cause of the acute kidney injury. Kidney ultrasonography in most patients with obstruction reveals hydronephrosis, which is absent in this patient. Furthermore, the urinalysis in patients with obstruction is benign and is not associated with the muddy brown casts found in this patient's urine.

Key Point Acute tubular necrosis usually develops after a sustained period of ischemia or exposure to nephrotoxic agents and is associated with muddy brown casts on urinalysis

Answers: Q5 :C | Q6: B

Acute Kidney Injury

Q7: A 65-year-old man with a history of stage 4 chronic kidney disease and hypertension comes for a follow-up examination. Two days ago, he was discharged from the hospital after a 4-day stay for pneumonia. During his hospitalization, his blood pressure averaged 130/70 mm Hg and he was not exposed to radiocontrast agents. He was treated with ceftriaxone and azithromycin; on discharge, these agents were discontinued and he began oral levofloxacin. Since his discharge, he has had nausea, vomiting, and anorexia. He believes that his urine output over the past day has been less than 500 mL. Additional medications are lisinopril, calcium carbonate, and low-dose aspirin.
On physical examination, temperature is 35.8°C (96.4°F), blood pressure is 110/50 mm Hg standing and 100/80 mm Hg supine, pulse rate is 108/min standing and 96/min supine, and respiration rate is 16/min. The remainder of the examination is normal except for crackles heard at the base of the lungs bilaterally. Which of the following is the most likely cause of this patient's acute kidney injury?

Serum creatinine	6.0 mg/dL (530.4 µmol/L) (2.5 mg/dL [221.0 µmol/L] in the hospital)
Urinalysis	Specific gravity 1.016; no protein or blood; occasional hyaline casts

A. Acute interstitial nephritis
B. Acute tubular necrosis
C. Prerenal azotemia
D. Renal vein thrombosis

Explanation: The most likely cause of this patient's acute kidney injury is prerenal azotemia. Prerenal azotemia develops when autoregulation of kidney blood flow can no longer maintain glomerular filtration rate (GFR). This condition generally occurs in patients with a mean arterial pressure below 60 mm Hg but may occur at higher pressures in individuals with chronic kidney disease (CKD) or in those who take medications that can alter local glomerular hemodynamics, such as NSAIDs. Patients with prerenal azotemia may have a history of fluid losses and decreased fluid intake accompanied by physical examination findings consistent with extracellular fluid volume depletion, such as postural hypotension. However, these findings are absent in up to 50% of patients with this condition. Nausea, vomiting, and anorexia accompanied by relatively low blood pressure in the absence of edema or urine sediment abnormalities strongly suggest prerenal azotemia. Acute interstitial nephritis may be caused by use of certain drugs, including antibiotics and NSAIDs, and classically manifests as pyuria, leukocyte casts, or eosinophils on urinalysis. Fever, rash, and blood eosinophilia also may be present. The urine sediment in acute tubular necrosis usually shows muddy brown casts or tubular epithelial cell casts. Renal vein thrombosis is an uncommon cause of acute kidney injury associated with hematuria and nephrotic-range proteinuria. This condition is most often associated with membranous nephropathy, malignancy, trauma, or hypercoagulable states. The normal urinalysis helps exclude acute interstitial nephritis, acute tubular necrosis, and renal vein thrombosis as the cause of this patient's renal decompensation.

Key Point Prerenal disease is usually associated with relative low blood pressure, oliguria, and normal urinalysis.

Q8: An 85-year-old man who resides in a nursing home presents with a 3-day history of lower abdominal pain and increasing fatigue and lethargy. He is afebrile, his BP is 160/92, and RR 16. His lungs are clear and his heart examination normal. There is diffuse abdominal tenderness on palpation and a large area of fullness and dullness to percussion starting just below the umbilicus and extending to the suprapubic area. His serum sodium is 130 mEq/L, potassium 4.9 mEq/L, BUN 75 mg/dL, and creatinine is 3.5 mg/dL. His baseline BUN and creatinine were 25 and 1.3 respectively as recently as 1 month ago. A Foley catheter is placed and 1200 cc of urine is obtained. What will be the likely clinical course for this patient with regard to his renal function?

A. His creatinine will continue to rise slowly for 2 to 3 more days.
B. His creatinine will return to 1.3 over the next week.
C. He will require dialysis within 24 hours.
D. He will produce minimal urinary output for at least 3 days.
E. His renal function is unlikely to show any improvement in the future and 3.5 will be his new baseline.

Explanation: This patient has obstructive uropathy. With relief of the obstruction due to an enlarged prostate, which was causing bilateral obstruction, it is very likely that renal function will return to baseline over the ensuing week. If an obstruction has been present for 1 to 2 weeks, recovery may be only partial. Obstruction that has lasted several weeks often causes irreversible damage. A nuclear medicine renal scan performed following relief of the obstruction may give an indication of the prognosis. Relief of bilateral obstruction is associated with a post obstructive diuresis. Urine output in this situation can be brisk and may require careful attention to volume status of the patient. In most patients, however, this is associated with appropriate excretion of excess salt and water.

Answers: Q7: C | Q8: B

Acute Kidney Injury

Q9: A 76-year-old man presents to the emergency room. He had influenza and now presents with diffuse muscle pain and weakness. His past medical history is remarkable for osteoarthritis for which he takes ibuprofen, and hypercholesterolemia for which he takes lovastatin. Physical examination reveals blood pressure of 130/90 with no orthostatic change. The only other finding is diffuse muscle tenderness. Laboratory data include Which of the following is the most likely diagnosis?

A. Nonsteroidal anti-inflammatory drug-induced acute kidney injury (AKI)
B. Volume depletion
C. Rhabdomyolysis-induced acute kidney injury
D. Urinary tract obstruction
E. Hypertensive nephrosclerosis

BUN: 30 mg/dL
Creatinine: 6 mg/dL
K: 6.0 mEq/L
Uric acid: 18 mg/dL
Ca: 6.5 mg/dL
PO_4: 7.5 mg/dL
UA: large blood, 2+ protein. Microscopic study shows muddy brown casts and 0 to 2 rbc/hpf (red blood cells/high power field).

Explanation: Rhabdomyolysis-induced AKI is characterized by hyperkalemia, hyperphosphatemia, and hyperuricemia, all caused by release of intracellular muscle products. The high phosphorus level causes hypocalcemia. The BUN/creatinine ratio, normally 10/1, is reduced because of release of muscle creatine, which is converted to creatinine. The load of creatinine to be excreted by the failing kidney therefore exceeds the urea load, which is little changed. The presence of "blood" on the dipstick determination is caused by myoglobinuria. The dipstick registers red blood cells, hemoglobin (eg, from intravascular hemolysis), and myoglobin as "blood." Trauma, medications (especially statins), infectious processes (influenza, sepsis), and extreme muscular exertion (seizures, exertional heat stroke) are common causes. All nonsteroidal agents may cause decreased renal function. Usually this is attributed to decreased blood flow—less commonly, to drug-induced interstitial nephritis. The laboratory abnormalities in this case do not suggest decreased blood flow or interstitial nephritis. However, stopping the ibuprofen would be prudent. The absence of orthostatic hypotension makes the diagnosis of volume depletion very unlikely. Nothing on history, physical examination, or electrolyte abnormalities suggests obstruction. However, in a 76-year-old man, a renal sonogram to rule out occult obstruction would be reasonable. Hypertensive nephrosclerosis causes chronic rather than acute renal insufficiency and would not account for the electrolyte abnormalities.

Q10: A 60-year-old diabetic woman develops angina and will need a coronary angiogram for evaluation of coronary artery disease. She has a creati-nine of 2.2. Which of the following is the most effective in reducing the risk of contrast induced nephropathy?

A. Administer mannitol immediately after the contrast is given.
B. Perform prophylactic hemodialysis after the procedure.
C. Give IV hydration with normal saline or sodium bicarbonate prior to and following the procedure.
D. Indomethacin 25 mg the morning of the procedure.
E. Dopamine infusion before and after the procedure.

Explanation: Contrast agents harm the kidney by causing the production of oxygen radicals and by causing vasoconstriction, both of which can lead to acute tubular necrosis. Patients with underlying kidney disease at baseline, those with diabetes, congestive heart failure, multiple myeloma, and dehydration are at greatest risk of this complication. Prehydration with IV normal saline or bicarbonate has been proven to decrease the risk of contrast nephropathy. N-acetylcysteine is also used by some clinicians for prevention, though studies have not been as convincing as those using saline or bicarbonate. Mannitol, dopamine, and prophylactic hemodialysis have been studied and found ineffective in preventing contrast nephropathy. Indomethacin would cause further vasoconstriction and is contraindicated in patients with renal insufficiency.

Q11: A 73-year-old man undergoes abdominal aortic aneurysm repair. The patient develops hypotension to 80/50 for approximately 20 minutes during the procedure according to the anesthesia record. He received 4 units of packed red blood cells. Postoperatively, his blood pressure is 110/70, heart rate is 110, surgical wound is clean, and a Foley catheter is in place. Over the next 2 days his urine output slowly decreases. His creatinine on post-op day 3 is 3.5 mg/dL (baseline 1.2). His sodium is 140 mEq/L, K 4.6 mEq/L, and BUN 50 mg/dL. Hemoglobin and hematocrit are stable. Urinalysis shows occasional granular casts but otherwise is normal. Urine sodium is 50 mEq/L, urine osmolality is 290 mosmol/L, and urine creatinine is 35 mg/dL. The FeNa (fractional excretion of sodium) based on these data is 3.5. What is the most likely cause of this patient's acute renal failure?

A. Acute interstitial nephritis
B. Acute glomerulonephritis
C. Acute tubular necrosis
D. Prerenal azotemia
E. Contrast induced nephropathy

Explanation: This patient with known atherosclerotic disease and a minimally elevated baseline creatinine has suffered a brief period of hypotension and hence renal hypoperfusion. By calculating the fractional excretion of sodium (FeNa) using the data that have been provided (FeNa = Urine sodium • plasma creatinine • 100/plasma sodium • urine creatinine), one can feel more comfortable distinguishing between prerenal azotemia and acute tubular necrosis. If the FeNa is less than 1, the patient likely has prerenal azotemia. If it is over 2, it is more likely that the patient has acute tubular necrosis or some other intrinsic renal disease. The clinical scenario of this patient, along with the high FeNa and the granular (sometimes called "muddy brown") casts in the urine, all point toward acute tubular necrosis (ATN). Interstitial nephritis more commonly occurs in patients following exposure to certain medications and typically is associated with white blood cells (especially eosinophils) in the urine. This patient may have had recent exposure to a contrast agent, but that has not been mentioned. Glomerulonephritis is unlikely due to the hypotension and the lack of red cell casts on the urinalysis.

Answers: Q9: C | Q10: C | Q11: C

Acute Kidney Injury

Q12: A 53-year-old man with HIV suffers a ruptured aortic aneurysm and is rushed into theatre, he undergoes a successful operation and is recovering on the wards in a stable condition. One day after the operation, he becomes oliguric with mildly elevated urea and creatinine. After 1 week, he becomes polyuric with a GFR of 30. The most likely diagnosis is:

A. Haemolytic–uraemic syndrome
B. Acute tubular necrosis
C. SIADH
D. HIV nephropathy
E. Acute renal failure

Explanation: Acute tubular necrosis (B) is most commonly due to renal ischaemia, as in this case, though direct pharmacological toxicity can also be the cause among many others including haemorrhage, diuretics, contrast during radiological procedures and heart failure. The clinical course is dependent on the offending factor and degree of damage but most commonly early oliguria followed by recovery of renal function with an increase in renal output. GFR, however, may remain low due to tubular damage. Full renal capacity is usually regained within 6 weeks of the initial stressor. Haemolytic uraemic syndrome (HUS) (A) defines the acute injury to the kidney from RBC fragmentation which usually originates from thrombosis within arteries. HUS is therefore the triad of microangiopathic haemolysis, thrombocytopenia and acute renal injury. The syndrome of inappropriate anti-diuretic hormone (C) (SIADH) is the result of inappropriately elevated levels of ADH causing the acute retention of water. As a result, there is hyponatraemia and reduced serum osmolality which is not present in this patient. In severe cases, patients can become very agitated and at risk of seizures. HIV nephropathy (D) is a common occurrence in HIV sufferers and can be due to direct HIV infection. Features include nephritic range proteinuria, large kidneys on ultrasound scan and typically collapsing focal segmental glomerulosclerosis on renal biopsy. In this acute case, the impact of renal hypoperfusion is the likely cause of the patient's presentation. Although this is an example of acute renal failure (E), the specific cause is the most appropriate answer.

Match questions 13, 14 & 15 with the options below

Q13: A patient is admitted to the hospital with a nursing-home–acquired pneumonia. His blood pressure is normal and the extremities well-perfused. Admission creatinine is 1.2 mg/dL. UA is clear. The patient is treated on the floor with piperacillin/tazobactam and improves clinically. On the fourth hospital day, the patient notes a nonpruritic rash over the abdomen. The creatinine has risen to 2.2 mg/dL. The urinalysis shows 2+ protein, 10 to 15 WBC/hpf, and no casts or RBCs.

Q14: A 62-year-old man is admitted with pneumonia and severe sepsis. Vasopressors are required to maintain peripheral perfusion, and mechanical ventilation is needed because of ARDS. Admission creatinine is 1.0 mg/dL but rises by the second hospital day to 2.2 mg/dL. Urine output is 300 cc/24 h. UA shows renal tubular epithelial cells and some muddy brown casts. The fractional excretion of sodium is 3.45.

Q15: A 76-year-old man is admitted with pneumonia. He has a history of diabetes mellitus. Admission creatinine is 1.2 mg/dL. He responds to ceftriaxone and azithromycin. He develops occasional urinary incontinence treated with anticholinergics, but his overall status improves and he is ready for discharge by the fifth hospital day. On that morning, however, he develops urinary hesitancy and slight suprapubic tenderness. The creatinine is found to be 3.0 mg/dL; UA is clear with no RBCs, WBCs, or protein.

A. Prerenal azotemia because of intravascular volume depletion
B. Ischemia-induced acute tubular necrosis
C. Nephrotoxin-induced acute tubular necrosis
D. Acute interstitial nephritis
E. Postrenal azotemia because of obstructive uropathy
F. Postinfectious glomerulonephritis

Explanation: Acute kidney injury in adults usually occurs during hospitalization for other illness. The history (in particular, exposure to nephrotoxins including intravenous contrast agents), physical examination (in particular, assessment of volume status and search for allergic manifestations such as skin rash), and urine studies will usually establish the diagnosis. The fractional excretion of sodium may demonstrate renal underperfusion if this is not clear from the clinical setting. If the kidneys are underperfused from volume depletion, third space losses, or poor cardiac output, the kidneys will retain salt and water, and the fractional excretion of sodium (FENa) will be low. In the cases presented here, the clinical setting suggests the diagnosis.
Interstitial nephritis typically occurs as an allergic reaction to antibiotics, particularly beta-lactams and sulfa derivatives. So-called tubular proteinuria is modest (< 1g/24 h), albuminuria is minimal, and the nephrotic syndrome does not occur. Pyuria and eosinophiluria are usually present. The commonest cause of acute renal failure is acute tubular necrosis. The FENa is usually above two and muddy brown cases may be present on the urinalysis. Ischemia (often owing to sepsis) and nephrotoxins are the usual causes. Obstructive uropathy can occur acutely, particularly in the setting of bladder outlet obstruction (BPH) or neurogenic bladder (as can occur in diabetes). The patient will often have difficulty voiding and the urinalysis will be unremarkable. Complete anuria or fluctuations from oliguria to polyuria also suggest the diagnosis. Bladder catheterization or renal sonography are diagnostic. Glomerulonephritis rarely occurs during hospitalization for unrelated acute illness.

Answers:Q12: A | Q13: D | Q14: B | Q15: E

Chronic Kidney Disease

Q1: A 60-year-old man is evaluated during follow-up for chronic kidney disease secondary to autosomal dominant polycystic kidney disease. He reports no chest pain, dyspnea, changes in his mental status, or excessive sleepiness. He has no anorexia, nausea, vomiting, weight loss, or itching. His medications are lisinopril, furosemide, low-dose aspirin, calcitriol, sevelamer, and ferrous sulfate. He has several family members who are being evaluated as potential kidney donors. Estimated glomerular filtration rate (GFR) 2 months ago was 18 mL/min/1.73 m2. On physical examination, he is mentally alert. Temperature is 37.0°C (98.7°F), blood pressure is 125/75 mm Hg, pulse rate is 75/min, and respiration rate is 14/min. Cardiac rhythm is normal without murmurs, extra sounds, or rubs. The estimated central venous pressure is 8 cm H2O. The lungs are clear to auscultation. His abdominal examination is significant for large, nontender bilateral flank masses. No bleeding, ecchymosis, or petechiae is evident. He scores 29/30 on the Mini-Mental State Examination and no asterixis is evident. He has 1+ pretibial edema. Which of the following is the most appropriate next step in the management of this patient's disease?

A. Initiation of dialysis
B. Increase the dose of lisinopril
C. Ultrasonography of the abdomen
D. No change in management

Hemoglobin	13.0 g/dL (130 g/L)
Albumin	3.9 g/dL (39 g/L)
Blood urea nitrogen	60 mg/dL (21.4 mmol/L)
Calcium	8.4 mg/dL (2.1 mmol/L)
Creatinine	4.9 mg/dL (433.1 micromol/L)
Electrolytes	
Sodium	140 meq/L (140 mmol/L)
Potassium	5.3 meq/L (5.3 mmol/L)

Chloride	100 meq/L (100 mmol/L)
Carbon dioxide	21 meq/L (21 mmol/L)
Phosphorus	5.2 mg/dL (1.7 mmol/L)
Estimated GFR	13 mL/min/1.73 m^2

Explanation: At this time, no change in the management of this patient's disease is required. Patients with stage 5 chronic kidney disease (glomerular filtration rate [GRF] <15 mL/min/1.73 m2 or receiving dialysis) often develop signs of uremia and require kidney replacement therapy. Absolute indications include uncontrollable hyperkalemia, uncontrollable hypervolemia, altered mental status or excess somnolence, pericarditis, or bleeding-diathesis secondary to uremic platelet dysfunction. Relative indications include nausea, vomiting, and poor nutrition caused by decreased appetite; severe metabolic acidosis; mild changes in mental status such as lethargy and malaise; asterixis; and worsening of kidney function with GFR less than 15 mL/min/1.73 m2. However, the timing of hemodialysis in patients without fluid overload, hyperkalemia, metabolic acidosis, or uremic symptoms, such as this patient, is unclear. A recent study suggests early initiation of hemodialysis does not improve patient outcomes. Kidney transplantation is the treatment of choice for uremia. Transplantation in patients who have not yet been treated with hemodialysis is associated with better patient and allograft outcomes. This patient has several family members who are willing kidney donors, and it is possible that he could receive a transplant in the near future; therefore, the best course of action would be to follow the patient closely to ensure he does not develop uremic signs or symptoms or other indications for dialysis and strive for transplantation rather than dialysis. No indication exists for increasing the lisinopril, especially with controlled blood pressure and a borderline high serum potassium level. Likewise, no reason exists to perform an abdominal ultrasound, because the bilateral flank masses are expected physical findings in a patient with enlarged kidneys secondary to polycystic kidney disease and are currently asymptomatic.

Key Point Kidney replacement therapy for patients with stage 5 chronic kidney disease who are not hypervolemic, hyperkalemic, acidotic, or uremic may be delayed.

Q2: A 49-year-old woman attends your clinic suffering from chronic renal failure due to progressive glomerular disease. She appears well and her blood pressure is 141/92 mmHg. Blood tests reveal elevated phosphate, serum creatinine and urea, while calcium levels are low. Her estimated glomerular filtration rate is 35 mL/min/1.73 m2. You also notice the patient's cholesterol levels are moderately raised. The most appropriate management is:

A. Sevelamer
B. Parathyroidectomy
C. Oral vitamin D
D. Cinacalcet
E. Renal dialysis

Explanation: This patient is suffering from secondary hyperparathyroidism due to renal failure which explains the abnormal calcium and phosphate levels. Hyperphosphataemia can cause vascular calcification and should be treated as soon as possible. Gut phosphate binders such as sevelamer (A) binds to ingested phosphate within the gut, thereby lowering serum phosphate levels. It also lowers calcium and lowers cholesterol. Parathyroidectomy (B) is reserved for patients refractive to medical therapy and should not be used as first-line therapy. Oral vitamin D therapy (C) is useful in early renal disease as it lowers PTH levels, however it is not appropriate as first-line therapy since it increases calcium and phosphate reabsorption and so can inadvertently exacerbate the patient's symptoms. Once phosphate levels have been lowered, vitamin D therapy is then beneficial. Calcimimetics such as cinacalcet (D) are successful in treating secondary hyperparathyroidism through PTH suppression which then lowers calcium and phosphate levels. The first stage of management is with correction calcium, phosphate by appropriate use of oral phosphate binder and then vitamin D therapy. Renal dialysis (E) is not necessary in this case since adequate medical treatments are available to treat hyperphosphataemia.

Answers: Q1: D | Q2: A

Chronic Kidney Disease

Q3: A 33-year-old woman comes for follow-up examination for a left fibula fracture due to a fall 1 week ago. She has hypertension and stage 5 chronic kidney disease treated with home hemodialysis. Medications are lisinopril, sevelamer, epoetin alfa, paricalcitol, and multivitamins. On physical examination, temperature is normal, blood pressure is 130/70 mm Hg, pulse rate is 88/min, and respiration rate is 12/min. BMI is 29. Cardiopulmonary examination is normal. An arteriovenous fistula is present in the left forearm. Except for a cast on her left leg, musculoskeletal examination is normal and reveals no bone pain. Which of the following is the most likely cause of this patient's bone disease?

Hemoglobin	10.3 g/dL (103 g/L)
Albumin	3.5 g/dL (35 g/L)
Phosphorus	5.8 mg/dL (1.9 mmol/L)
Calcium	8.4 mg/dL (2.1 mmol/L)
Parathyroid hormone	700 pg/mL (700 ng/L)
Alkaline phosphatase	330 U/L

A. Adynamic bone disease
B. Osteonecrosis
C. Osteoporosis
D. Secondary hyperparathyroidism

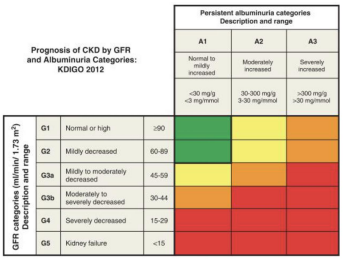
Explanation: The most likely cause of this patient's bone disease is secondary hyperparathyroidism. Chronic kidney disease (CKD) is associated with progressive alterations in mineral and bone metabolism that can cause bone disease. In patients with end-stage kidney disease (ESKD), the kidney's inability to excrete phosphorus leads to hyperphosphatemia. Loss of kidney function also is associated with 1,25-dihydroxyvitamin D deficiency. Hyperphosphatemia along with decreased 1,25 dihydroxyvitamin D levels result in hypocalcemia, which leads to direct stimulation of parathyroid hormone secretion. Furthermore, decreased 1,25 dihydroxyvitamin D levels cause increased production of parathyroid hormone. Therefore, bone disease due to secondary hyperparathyroidism, the most common bone pathologic finding seen in patients with ESKD, develops. This patient's hyperphosphatemia, hypocalcemia, and elevated serum parathyroid hormone and alkaline phosphatase levels are consistent with secondary hyperparathyroidism.
Adynamic bone disease commonly occurs in patients with ESKD and may cause fractures. However, unlike bone disease associated with secondary hyperparathyroidism, adynamic bone disease is often associated with hypoparathyroidism caused by excess vitamin D intake and/or calcium loading. This condition usually manifests as bone pain accompanied by a serum parathyroid hormone level below 100 pg/mL (100 ng/L) and a normal alkaline phosphatase level. Osteoporosis is defined by low bone mass, which is associated with reduced bone strength and an increased risk of fractures. Osteoporosis occurs most commonly in postmenopausal women but may develop secondary to drugs such as corticosteroids and anticonvulsants. Osteoporosis does not affect the concentrations of serum calcium, phosphorus, parathyroid hormone, or alkaline phosphatase.
Osteonecrosis is caused by transient or permanent lack of blood supply to bone, which causes death of bone and bone marrow infarction that results in mechanical failure. Patients typically present with chronic bone pain, not fracture, and normal concentrations of calcium, phosphorus, and parathyroid hormone.

Key Point Bone disease due to secondary hyperparathyroidism commonly occurs in patients with end-stage kidney disease and may be associated with elevated serum parathyroid hormone and alkaline phosphatase levels, hyperphosphatemia, and hypocalcemia.

Q4: At a routine checkup, a 42-year-old male with diabetes is found to have an eGFR of 32 ml/min/1.73 m2. When repeated 3 months later, it is 35 ml/ min/1.73 m2. His albumin:creatinine ratio (ACR) is 35 mg/mmol (310 mg/g). Macroalbuminuria is defined as ACR >30 mg/mmol (>300 mg/g). What stage of CKD does he have?

A. Stage 1
B. Stage 2
C. Stage 3
D. Stage 4

Explanation:



Answers: Q3: D | Q4: C

Chronic Kidney Disease

Q5: A 55-year-old woman comes to the physician because of a 6-month history of worsening shortness of breath on exertion and fatigue. She has type 1 diabetes mellitus, hypertension, hypercholesterolemia, and chronic kidney disease. Her mother was diagnosed with colon cancer at the age of 65 years. Her blood pressure is 145/92 mm Hg. Examination shows conjunctival pallor. Laboratory studies show:

Hemoglobin	9.2 g/dL
Mean corpuscular volume	88 μm^3
Reticulocyte count	0.6 %
Serum	
Ferritin	145 ng/mL
Creatinine	3.1 mg/dL
Calcium	8.8 mg/dL

A. Autoantibodies against the thyroid gland
B. Chronic occult blood loss
C. Malignant plasma cell replication
D. Deficient vitamin B12 intake
E. Hematopoietic progenitor cell mutation
F. Decreased erythropoietin production

Explanation: This patient's normocytic anemia is most likely due to her underlying CKD. The etiology of anemia of chronic kidney disease is multifactorial, but primarily driven by low erythropoietin. Erythropoietin is produced and released by the interstitial cells in the peritubular capillaries and stimulates erythroid proliferation in the bone marrow. In CKD, there is decreased production of erythropoietin, leading to a decrease in RBC proliferation, and subsequent normocytic anemia with a low reticulocyte count. CKD may also manifest with iron deficiency, however, this patient's high ferritin indicates normal iron stores.

Q6: A 62-year-old woman with type 2 diabetes mellitus comes to the physician because of a 3-month history of fatigue and weakness. Her hemoglobin A1c concentration was 13.5% 12 weeks ago. Her blood pressure is 152/92 mm Hg. Examination shows lower extremity edema. Serum studies shown below, Which of the following is the most appropriate parameter for early detection of this patient's renal condition?

K^+	5.1 mEq/L
Phosphorus	5.0 mg/dL
Ca^{2+}	7.8 mg/dL
Urea nitrogen	60 mg/dL
Creatinine	2.2 mg/dL

A. Urinary red blood cell casts
B. Serum total protein
C. Urinary albumin
D. Serum creatinine

Explanation: Microalbuminuria is the earliest diagnostic sign of diabetic nephropathy. Progression of glomerular damage (nodular glomerulosclerosis) leads to increased urinary loss of albumin, which can manifest as nephrotic syndrome. The extent of albuminuria in patients with diabetic nephropathy also correlates with the risk of future cardiovascular events. ACE inhibitors can prevent the progression of albuminuria in patients with diabetic nephropathy.

Q7: A 44-year-old woman is brought to the emergency department after she was found lying in the park mumbling to herself. She is lethargic and disoriented. She has a 2-week history of increasing weakness, nausea, and vomiting. She denies any recent alcohol or drug use. She has a history of systemic lupus erythematosus but stopped taking methotrexate many years ago. Her temperature is 37.3°C (99.1°F), pulse is 89/min, and blood pressure is 154/91 mm Hg. On mental status examination, she is confused and only oriented to person, but not to place or time. She is unable to name the days of the week backwards. She exhibits moderate generalized weakness. Physical exam shows jugular venous distention and pitting edema in the lower extremities. Laboratory studies show:

Serum	
Na^+	137 mEq/L
K^+	5.5 mEq/L
Cl^-	102 mEq/L
Bicarbonate	15 mEq/L
Urea nitrogen	94 mg/dL
Creatinine	5.5 mg/dL
Glucose	92 mg/dL

A. Administer haloperidol
B. Administer lactulose
C. Hemodialysis
D. Fluid restriction

Explanation: Patients with uremia are at risk of pericarditis, seizures, coma, and hemorrhage due to platelet dysfunction, and require urgent hemodialysis to remove uremic toxins. Hemodialysis is also the most effective and definitive treatment option for hyperkalemia and volume overload in patients with renal failure.

Answers: Q5: F | Q6: C | Q7: C

Chronic Kidney Disease

Q8: A 52-year-old woman comes to the physician because of intense retrosternal chest pain for the last 3 days. The pain is worse with breathing or coughing, and improves while sitting upright. She also reports a mild fever and shortness of breath. She was diagnosed with chronic kidney disease secondary to lupus nephritis 12 years ago and has been on hemodialysis since then, but she missed her last two appointments because of international travel. She also underwent a percutaneous coronary intervention 8 months ago for a myocardial infarction. She takes azathioprine after hemodialysis. Her temperature is 37.8°C (100°F), pulse is 110/min, and blood pressure is 130/84 mm Hg. The lungs are clear to auscultation bilaterally with normal breath sounds. Cardiac examination reveals a high-pitched scratching that obscures both heart sounds. The remainder of the examination is unremarkable. Cardiac enzyme levels and anti-DNA antibodies are within normal limits. An x-ray of the chest shows no abnormalities. An ECG shows Q waves in the anterior leads. Which of the following is the most likely cause of these findings?

A. Low serum levels of thyroid hormone
B. Adverse effect of medication
C. Serositis from an immunologic reaction
D. Infarction of myocardial segment
E. Purulent exudate in the pericardial space
F. Elevated serum levels of nitrogenous waste

Explanation: Uremia is the most likely cause of this patient's findings given the history of CKD and missed dialysis sessions. Uremic pericarditis does not present with the classic diffuse ST-elevations seen on ECG as in other types of pericarditis. Uremic pericarditis is an indication for urgent hemodialysis.

Q9: A 55-year-old woman comes to the physician because of a 6-month history of worsening fatigue. During this time, she has noted a decrease in her exercise capacity and she becomes short of breath when walking briskly. She has had occasional streaks of blood in her stools during periods of constipation. She was diagnosed with type 1 diabetes mellitus at the age of 24 years and has a history of hypertension and hypercholesterolemia. She does not smoke or drink alcohol. Her current medications include insulin, lisinopril, aspirin, and atorvastatin. Her diet mostly consists of white meat and vegetables. Her pulse is 92/min and blood pressure is 145/92 mm Hg. Examination shows conjunctival pallor. Cardiac auscultation shows a grade 2/6 midsystolic ejection murmur best heard along the right upper sternal border. Sensation to pinprick is decreased bilaterally over the dorsum of her feet. The remainder of the examination shows no abnormalities. Laboratory studies show:

A. Decreased erythropoietin production
B. Hematopoietic progenitor cell mutation
C. Increased hepcidin production
D. Chronic occult blood loss

Hemoglobin	9.2 g/dL
Leukocyte count	7200/mm^3
Erythrocyte count	3.06 million/mm^3
Mean corpuscular volume	84 μm^3
Platelets	250,000/mm^3
Reticulocyte count	0.6 %
Erythrocyte sedimentation rate	15 mm/h
Serum	
Na^+	142 mEq/L
K^+	4.8 mEq/L
Ca^{2+}	8.1 mEq/L
Ferritin	115 ng/mL
Urea nitrogen	48 mg/dL
Creatinine	3.1 mg/dL

Explanation: Given her long-standing history of type 1 diabetes and hypertension, this patient's elevated markers of kidney function suggest a diagnosis of chronic kidney disease (CKD). Normocytic anemia in a patient with CKD occurs because of decreased production of erythropoietin (EPO) by renal peritubular cells. Diabetes can also lead to microvascular damage in the bone marrow, which results in a reduced response to EPO. As a result, erythropoiesis is reduced and normocytic anemia with a low reticulocyte count develops.

Answers: Q8: F | Q9: A

Chronic Kidney Disease

Q10: A 67-year-old man comes to his family physician because of a 4-month history of increasing fatigue, weakness, and numbness in both of his feet. More recently, he has also experienced intermittent nausea and loss of appetite. He has hypertension and type 2 diabetes mellitus and has been taking ramipril and metformin for more than 10 years. He reports that he has difficulty following his medication regimen. His pulse is 80/min and blood pressure is 145/84 mmHg. Physical examination shows conjunctival pallor. There is a flapping tremor when the hands are outstretched. Serum studies shown below, Which of the following is the most likely explanation for this patient's increase in blood urea nitrogen?

A. Urinary tract obstruction
B. Increased tubular reabsorption
C. Decreased glomerular filtration
D. Increased protein breakdown
E. Impaired urea cycle
F. Decreased plasma volume

Potassium	5.2 mEq/L
Phosphorus	5.2 mg/dL
Urea nitrogen	53 mg/dL

Explanation: Decreased glomerular filtration rate (GFR) due to CKD is the most likely cause of this patient's elevated BUN. Decreased GFR results in impaired filtration and excretion of BUN (as well as potassium and phosphorous) by the kidneys. Uncontrolled hypertension (due to medication nonadherence) and diabetes mellitus are the most common causes of CKD, respectively.

Answers: Q10: C

Na - Water Balance

Q1: A 74-year-old type 2 diabetic woman undergoes a bowel resection for cancer of the colon. She is well prior to the operation with well–controlled diabetes and no other underlying disease. The operation is successful and the patient is given postoperative insulin and IV dextrose. Two days after the operation she becomes very agitated. The most likely cause of the hyponatraemia is:

A. Addison's disease
B. Syndrome of inappropriate anti-diuretic hormone (SIADH)
C. Diabetic nephropathy
D. Excess insulin
E. Water overload

Sodium	124	(135–145)
Potassium	3.3	(3.5–5.0)
Urea	3.1	(3.0–7.0)
Glucose	7.2	(2.5–6.0)
Serum osmolality	265	(275–295)
Urine osmolality	150	

Explanation: This patient has a significant hyponatraemia with a mildly low potassium level and low osmolality. Sodium homeostasis involves insensible and obligatory loss followed by the dominant influence of the kidney. Factors controlling sodium reabsorption include the renin-angiotensin-aldosterone system, natriuretic peptides and indirectly anti-diuretic hormone (ADH). Hyponatraemia arising from water overload (E) often occurs in patients following surgical procedures with inappropriate fluid management. In this case, excess dextrose solution causes dilutional hyponatraemia resulting in acute delirium. Addison's disease (A) results in a deficiency of mineralocorticoid activity causing an accumulation of potassium and reduced sodium reabsorption which is not reflected in the patient's biochemistry results. The SIADH (B) is due to inappropriately elevated levels of ADH which leads to increased retention of water causing hyponatraemia and reduced serum osmolality. The syndrome does not typically cause hypokalaemia and the urine would be more concentrated due to water reabsorption. Diabetic nephropathy (C) is a progressive disease that arises in diabetic patients, pathology is characterized by an initial increase in glomerular filtration rate and glomerular basement membrane hypertrophy. As the disease progresses, glomerulosclerosis occurs as a result of accumulation of extracellular matrix and destroying the filtering ability of the glomerular membrane. This allows protein leakage. Severe diabetic nephropathy may present with symptoms of the nephrotic syndrome and acute derangement of biochemistry does not occur. Excess insulin injection (D) would cause hypoglycaemia and a reduction in potassium due to a shift of potassium to the intracellular compartment. Patients become irritable, sweat and eventually can fall into a coma.

Q2: A 56-year-old woman is evaluated for a 1-week history of right upper-quadrant abdominal pain, anorexia, nausea, and vomiting and a 3-day history of increasing lethargy and weakness. She also has dark-colored urine and a decreased urine output. One year ago, she was diagnosed with stage IV breast cancer treated with mastectomy and hormonal and chemotherapy. Current medications are tamoxifen and trastuzumab. On physical examination, temperature is normal, blood pressure is 90/50 mm Hg, pulse rate is 100/min, and respiration rate is 18/min. Cardiopulmonary examination is normal. The mucous membranes are dry. Abdominal examination reveals hepatomegaly. There is no edema. On abdominal ultrasound, the right kidney is 9.6 cm and the left kidney is 9.1 cm. There is no hydronephrosis, and no renal calculi or focal solid masses are seen. There is hepatomegaly with multiple liver metastases. Which of the following is the most appropriate next management step?

A. Dialysis
B. Isotonic saline
C. Midodrine and octreotide
D. Rasburicase

Sodium	124 meq/L (124 mmol/L)
Potassium	5.7 meq/L (5.7 mmol/L)
Chloride	94 meq/L (94 mmol/L)
Bicarbonate	12 meq/L (12 mmol/L)
Uric acid	9.2 mg/dL (0.54 mmol/L)
Phosphorus	5.8 mg/dL (1.9 mmol/L)
Calcium	10.1 mg/dL (2.5 mmol/L)
Blood urea nitrogen	105 mg/dL (37.5 mmol/L)
Serum creatinine	5 mg/dL (442 µmol/L) (1 mg/dL [88.4 µmol/L] 1 month ago)
Urinalysis	Specific gravity 1.022; pH 5; trace protein; rare amorphous crystals
Urine sodium excretion	4 meq/L (4 mmol/L)

Explanation: This patient most likely has prerenal azotemia, and the most appropriate next step in management is isotonic saline. Acute kidney injury in patients with malignancy is often due to prerenal disease, obstruction, or use of nephrotoxic agents. The presence of hypotension, hyponatremia, and a decreased urine sodium excretion accompanied by a bland urine sediment raises suspicion for prerenal azotemia. Dialysis would be indicated if the azotemia persisted or worsened after correction of the hypovolemia, particularly if other uremic complications such as encephalopathy or refractory hyperkalemia were present. Dialysis is not indicated before this patient has undergone a trial of adequate volume replacement. Therapy with midodrine and octreotide may be effective and safe for the treatment of hepatorenal syndrome in some patients. However, the absence of ascites or other signs of portal hypertension are not consistent with hepatorenal syndrome. Tumor lysis syndrome may manifest as hyperkalemia, hyperphosphatemia, and hyperuricemia. Tumor lysis syndrome most likely occurs in patients with extremely rapidly progressive lymphoid neoplasms and in those who have bulky lymphoid neoplasms that respond rapidly to treatment. Rasburicase can be used to treat malignancy-related hyperuricemia in order to prevent tumor lysis syndrome in high-risk patients or as a component of therapy for established tumor lysis syndrome and associated hyperuricemia. However, this patient's serum electrolyte, phosphorus, and uric acid level abnormalities are most likely a result of hypovolemia and associated kidney dysfunction and should improve with volume repletion; therefore, rasburicase therapy would not be warranted.

Key Point The presence of hypotension, hyponatremia, and a decreased urine sodium excretion accompanied by a bland urine sediment should raise suspicion for prerenal azotemia.

Answers: Q1: E | Q2: B

Na - Water Balance

Q3: A 63-year-old man alcoholic with a 50-pack-year history of smoking presents to the emergency room with fatigue and confusion. Physical examination reveals a blood pressure of 110/70 with no orthostatic change. Heart, lung, and abdominal examinations are normal and there is no pedal edema. Laboratory data are as follows: Which of the following is the most likely diagnosis?

A. Volume depletion
B. Inappropriate secretion of antidiuretic hormone
C. Psychogenic polydipsia
D. Cirrhosis
E. Congestive heart failure

Na: 110 mEq/L
K: 3.7 mEq/L
Cl: 82 mEq/L
HCO_3: 20 mEq/L
Glucose: 100 mg/dL
BUN: 5 mg/dL
Creatinine: 0.7 mg/dL
Urinalysis: normal
Specific gravity: 1.016

Explanation: Inappropriate secretion of antidiuretic hormone is suggested in a patient without clinical evidence of volume depletion or an edematous (ie, salt-retaining) condition. This syndrome may be idiopathic, associated with certain pulmonary and intracranial pathologies, resulting from endocrine disorders (eg, hypothyroidism), or drug-induced (eg, many psychotropic agents). Volume depletion is unlikely in the absence of orthostatic hypotension. Psychogenic polydipsia requires the ingestion of huge quantities of water to overcome the kidneys' ability to excrete a free-water load and would be associated with a very dilute urine (ie, urine specific gravity of 1.001 or 1.002). Cirrhosis is unlikely in the absence of ascites and edema. Congestive heart failure can cause hyponatremia but would be associated with edema and evidence of venous congestion.

Q4: A 66-year old man is evaluated in the emergency department for a 6-week history of dyspnea on exertion and a 3-day history of orthopnea. He reports no chest pain or palpitations. He has a 45-pack-year history of cigarette smoking. He takes no medications. On physical examination, temperatures is 37.2°C (99.0°F), blood pressure is 150/90 mm Hg, pulse rate is 108/min, and respiration rate is 26/min. Oxygen saturation by pulse oximetry is 88% on ambient air. The patient has jugular venous distention to the angle of the jaw when sitting upright. A prominent S3 and bibasilar crackles are heard on auscultation of the lungs, and pitting edema to the knees is present. Which of the following best describes this patient's plasma tonicity and serum sodium status?

A. Hyperosmolar hyponatremia
B. Hyposmolar hyponatremia
C. Normal osmolar hypernatremia
D. Normal osmolar hyponatremia
E. Normal osmolar pseudohyponatremia

Blood urea nitrogen	56 mg/dL (20 mmol/L)
Creatinine	1.7 mg/dL (150.3 µmol/L)
Electrolytes	
Sodium	120 meq/L (120 mmol/L)
Potassium	5.3 meq/L (5.3 mmol/L)
Chloride	100 meq/L (100 mmol/L)
Carbon dioxide	22 meq/L (22 mmol/L)
Glucose	180 mg/dL (6.5 mmol/L)

Explanation: This patient has hyposmolar hyponatremia. Osmolality is defined as the number of solute particles per kilogram of solution. Plasma osmolality can be directly measured by an osmometer or calculated using the following equation: Plasma osmolality (mosm/kg = 2 serum [Na+] (meq/L) + blood urea nitrogen (mg/dL)/2.8 + plasma glucose (mg/dL)/18 Using this formula, the calculated plasma osmolality is 252 mosm/kg (normal, 275-295 mosm/kg [275-295 µmol/kg]). Therefore, the patient is hyposmolar and hyponatremic. Hyponatremia can be caused by a decrease in effective arterial blood volume, which results in baroreceptor stimulation of antidiuretic hormone (ADH) secretion, which impairs water excretion. Consequently, distal delivery of filtrate to the tip of the loop of Henle decreases. A decrease in effective arterial blood volume may be associated with low extracellular fluid volume (hypovolemic hyponatremia) or high extracellular fluid volume in edematous patients (hypervolemic hyponatremia), including heart failure, cirrhosis, and nephrotic syndrome. True hyponatremia may be associated with an elevation in the plasma concentration of an effective osmole, such as glucose. This elevation results in an increase in plasma osmolality (hyperosmolar hyponatremia), which causes water to leave the cells and results in a diluted serum sodium concentration. Hyponatremia that occurs in the absence of a hyposmolar state (pseudohyponatremia) is generally caused by an increased serum concentration of an effective osmole. Common causes of pseudohyponatremia include hyperglobulinemia and hypertriglyceridemia. Because these conditions are associated with a decrease of plasma water relative to plasma solids in the blood, the amount of sodium in a given volume of blood also decreases.

Key Point Hyponatremia can be caused by a decrease in effective arterial blood volume, which results in baroreceptor stimulation of antidiuretic hormone (ADH) secretion.

Answers: Q3: B | Q4: B

Na - Water Balance

Q5: A 73-year-old woman is brought to the emergency department after falling at home. Her family states that she has been very confused and disoriented over the past 2 days and that she began therapy with a new medication 4 days ago. She has type 2 diabetes mellitus, hypertension, and glaucoma. A bag containing the patient's medications includes glyburide, metformin, hydrochlorothiazide, acetazolamide, and enalapril. On physical examination, temperature is 37°C (98.6°F), heart rate is 68/min, respiration rate is 12/min, and blood pressure is 115/65 mm Hg. She is confused and unable to answer questions appropriately. Cardiac examination is normal. The lungs are clear. There is no edema. Which of the following drugs is most likely responsible for the patient's findings?

Blood urea nitrogen	17 mg/dL (6.1 mmol/L)
Creatinine	1.1 mg/dL (97.2 µmol/L)
Sodium	107 meq/L (107 mmol/L)
Potassium	3.9 meq/L (3.9 mmol/L)
Chloride	76 meq/L (76 mmol/L)
Bicarbonate	24 meq/L (24 mmol/L)

A. Acetazolamide
B. Glyburide
C. Hydrochlorothiazide
D. Metformin

Explanation: Hydrochlorothiazide is a common cause of hyponatremia in the outpatient setting. It is especially common in the elderly. Early signs of symptomatic hyposmolality may be very nonspecific, such as nausea, vomiting, and headaches (hyponatremic encephalopathy). Worsening of brain swelling then causes decreased mental status and seizures. Diuretic-induced hyponatremia most commonly occurs in patients taking thiazide diuretics. Elderly women with low body mass indices who tend to increase fluid intake after initiation of therapy with these agents are often affected. Thiazide diuretics work at the level of the convoluted tubule and collecting segment. Therefore, these agents maintain urinary concentrating capacity but not diluting capacity, which makes them prone to cause hyponatremic encephalopathy. By inducing relative volume depletion, antidiuretic hormone secretion is stimulated, which leads to urine concentration and water retention. Treatment includes stopping the diuretic and infusing normal saline (for mildly symptomatic patients) or 3% saline (for significantly symptomatic patients). Acetazolamide acts in the proximal tubule as a carbonic anhydrase IV inhibitor. Blocking this enzyme in the proximal tubule impairs bicarbonate reabsorption but not diluting capacity and is most often associated with hypokalemia and metabolic acidosis. Acetazolamide is not associated with the development of hyponatremia. Metformin and glyburide do not affect fluid and electrolyte balance.

Key Point Hydrochlorothiazide can cause severe hyponatremia.

Q6: A 44-year-old man comes to the emergency department with polyuria and polydipsia. Overt Physical examination is normal. Admission laboratory results included serum sodium of 155 meq/L (155 mmol/L), plasma glucose of 150 mg/dL (8.3 mmol/L), and urine osmolality of 117 mosm/kg (117 µmol/kg). He has significant increase in urine osmolality (greater than 50%) within 1 to 2 hours after injection of arginine vasopressin. What is the most likely cause of the hypernatremia?

A. Central diabetes insipidus
B. Diabetes mellitus
C. Nephrogenic diabetes insipidus
D. Primary polydipsia

Explanation: The most likely cause of this patient's hypernatremia is central diabetes insipidus. This patient is clearly hyperosmolar, as estimated by multiplying the serum sodium level by 2 (310 mosm/kg [310 µmol/kg]; normal, 275-295 mosm/kg [275-295 µmol/kg]). The appropriate renal response to hyperosmolality is to maximally concentrate the urine (generally to greater than 800 mosm/kg [800 µmol/kg]). This response is not seen in this patient. Thus, he has either diabetes insipidus or a solute diuresis. A solute diuresis is most often caused by hyperglycemia. This patient does have a plasma glucose level of 150 mg/dL (8.3 mmol/L); however, this degree of elevation is unlikely to cause significant solute diuresis because the renal threshold for glucose reabsorption in most persons is 200 to 225 mg/dL (11.1 to 12.5 mmol/L). Furthermore, solute diuresis is usually characterized by isotonicity of the urine, whereas this patient has a markedly hypotonic urine. Consequently, diabetes mellitus is unlikely. Hyperosmolar patients without glucosuria who have submaximally concentrated urine have diabetes insipidus by definition. Distinguishing between central and nephrogenic diabetes insipidus in a patient who is already hyperosmolar can be done by measuring plasma arginine vasopressin (AVP) (patients with central diabetes insipidus have an inappropriately low level, whereas patients with nephrogenic diabetes insipidus have a normal to elevated level); or by evaluating the response to administered AVP (5 U subcutaneously) or, preferably, the selective AVP V2 receptor agonist desmopressin (arginine vasopressin, 1 to 2 µg subcutaneously or intravenously). A significant increase in urine osmolality (greater than 50%) within 1 to 2 hours after injection indicates insufficient endogenous AVP secretion, and, therefore, central diabetes insipidus, whereas a lack of response indicates renal resistance to the effects of AVP and, therefore, nephrogenic diabetes insipidus. Patients with primary polydipsia also manifest polyuria and polydipsia but do not become hypernatremic and hyperosmolar. These patients may develop hyponatremia and typically have clearly identifiable psychiatric illness.

Key Point Hyperosmolar patients without glucosuria who have submaximally concentrated urine have diabetes insipidus by definition.

Answers: Q5: C | Q6: A

Na - Water Balance

Q7: A 60-year-old man is brought in by ambulance and is unable to speak. The EMS personnel tell you that a neighbor informed them he has had a stroke in the past. There are no family members present. His serum sodium is 118 mEq/L. Which of the following is the most helpful first step in the assessment of this patient's hyponatremia?

A. Order a chest x-ray
B. Place a Foley catheter to measure 24-hour urine protein
C. Clinical assessment of extracellular fluid volume status
D. CT scan of head
E. Serum AVP (arginine vasopressin) level

Explanation: The first step in the clinical assessment of hythorough history and physical examination, including assessment of extracellular fluid status. Increased ECF in the setting of hyponatremia may be caused by heart failure, hepatic cirrhosis, nephrotic syndrome, or renal insufficiency. A normal ECF in the same setting would indicate a disorder such as SIADH,mwhereas a decreased ECF would prompt a search for the cause of the hypovolemia (GI or renal losses being the most common). In hypovolemic states, ADH release is stimulated by the decreased ECF volume status and leads to free-water retention. MRemember that, even when ECF volume is decreased, hyponatremia almost always indicates free-water excess (hypotonicity). Determination of plasma osmolality is helpful in the setting of hyponatremia to confirm the presence of hypotonicity. Most patients with hyponatremia will have a low-plasma osmolality. A high-plasma osmolality usually indicates hyperglycemia, and a normal-plasma osmolality can indicate "pseudohyponatremia" caused by disorders such as hyperproteinemia and hyperlipidemia. In this case, determination of ECF status from the physical examination (history would be limited owing to patient's inability to communicate) would be the best first step. You would not wait for the plasma osmolality before beginning assessment and development of an initial differential diagnosis. Helpful laboratory assessment in the face of hyponatremia includes plasma osmolality, urine osmolality, and urine K and Na concentration. The plasma AVP assay is difficult to perform, and the result would not be available in time to help the patient. Proteinuria does not cause hyponatremia unless overt nephrotic syndrome is present. Chest x-ray and CT scan of the head are indicated if the patient is found to have SIADH (euvolemic hyponatremia), but SIADH cannot be diagnosed until the volume status is determined.

Q8: A 39-year-old woman is admitted to the gynecology service for hysterectomy for symptomatic uterine fibroids. Postoperatively the patient develops an ileus accompanied by severe nausea and vomiting; ondansetron is piggybacked into an IV of D5 ½ normal saline running at 125 cc/h. On the second postoperative day the patient becomes drowsy and displays a few myoclonic jerks. Stat labs reveal Na 118, K 3.2, Cl 88 HCO3 22, BUN 3, and creatinine 0.9. Urine studies for Na and osmolality are sent to the lab. What is the most appropriate next step?

A. Change the IV fluid to 0.9% (normal) saline and restrict free-water intake to 600 cc/d.
B. Change the ondansetron to promethazine, change the IV fluid to lactated Ringer solution, and recheck the Na in 4 hours.
C. Start 3% (hypertonic) saline, make the patient NPO, and transfer to the ICU.
D. Change the IV fluid to normal saline and give furosemide 40 mg IV stat.
E. Make the patient NPO and send for stat CT scan of the head to look for cerebral edema.

Explanation: The patient has acute symptomatic hyponatremia, a life- threatening condition. Although some controversy persists as to whether chronic hyponatremia should be rapidly corrected, acute symptomatic hyponatremia should be rapidly treated with hypertonic saline. This patient is at high risk of seizure and respiratory arrest, the main cause of permanent CNS damage in hyponatremia. ICU care, with frequent monitoring of the serum sodium level and CNS status, is critical. Once the Na has risen 4 to 8 mEq/L and the symptoms have improved, the rate of hypertonic saline infusion can be decreased. Less aggressive methods of treating her free-water overload, such as fluid restriction alone or in combination with furosemide, are not appropriate for this acute emergency. Isotonic fluids such as normal saline and lactated Ringer solution are useful in volume depletion but will not treat this patient's free-water excess. Postoperative hyponatremia is particularly common in premenopausal women. The nausea and pain sometimes associated with surgery are very potent stimulators of vasopressin (ADH) release by the neurohypophysis. If hypotonic fluids are used at all in this setting, the serum sodium level should be closely monitored, and isotonic fluids used if there is any trend toward free-water retention (ie, hyponatremia).

Answers: Q7: C | Q8: C

Na - Water Balance

Q9: A 44-year-old man is brought to the emergency department 45 minutes after being involved in a high-speed motor vehicle collision in which he was the restrained driver. On arrival, he has left hip and left leg pain. His pulse is 135/min, respirations are 28/min, and blood pressure is 90/40 mm Hg. Examination shows an open left tibial fracture with active bleeding. The left lower extremity appears shortened, flexed, and internally rotated. Femoral and pedal pulses are decreased bilaterally. Massive transfusion protocol is initiated. An x-ray of the pelvis shows an open pelvis fracture and an open left tibial mid-shaft fracture. A CT scan of the head shows no abnormalities. Laboratory studies show the following, The patient is taken emergently to interventional radiology for exploratory angiography and arterial embolization. Which of the following is the most likely explanation for this patient's hyponatremia?

Hemoglobin	10.2 g/dL
Leukocyte count	10,000/mm^3
Platelet count	<250,000/mm^3
Prothrombin time	12 sec
Partial thromboplastin time	30 sec
Serum	
Na^+	125 mEq/L
K^+	4.5 mEq/L
Cl^-	98 mEq/L
HCO_3^-	25 mEq/L
Urea nitrogen	18 mg/dL
Creatinine	1.2 mg/dL

A. Renal tubule injury
B. Pathologic ADH (vasopressin) secretion
C. Physiologic ADH (vasopressin) secretion
D. Physiologic aldosterone secretion
E. Pathologic aldosterone secretion

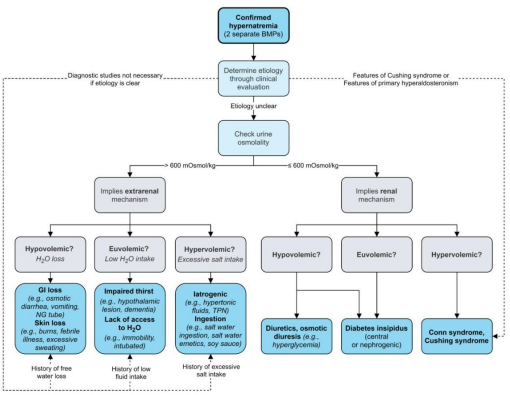
Explanation: When baroreceptors detect decreases in effective arterial volume, such as after massive blood loss, they cause antidiuretic hormone (ADH) to be released from the pituitary gland to increase renal reabsorption of free water, diluting serum sodium levels and causing hyponatremia. Management of hypovolemic hyponatremia includes volume repletion with normal saline. Correction of hypovolemia removes the stimulus to release ADH, causing free water excretion by the kidneys, which leads to rapid correction of serum sodium levels. Accordingly, volume repletion with normal saline must occur at a slow rate, because rapid correction of hyponatremia can cause central pontine myelinolysis.

Q10: A 75-year-old man comes to the physician because of a 7-day history of nausea and vomiting. Over the past 2 days, he has also been feeling weak and tired. When standing up after sitting for a while, he feels dizzy. He says he has to go to the bathroom more often than usual, and that he is urinating "a normal amount" each time. He has not had diarrhea. He has hypertension, for which he has been taking hydrochlorothiazide for the past 6 months. He drinks 9 glasses of water per day and takes his medication regularly. He is 168 cm (5 ft 6 in) tall and weighs 90 kg (198 lb); BMI is 32 kg/m2. His temperature is 36.5°C (97.7°F), blood pressure is 106/54 mm Hg, and pulse is 92/min. Physical examination shows whitening of the tongue. Skin that is pinched on the back of the hand retracts after 5 seconds. On mental status examination, his speech is slowed; he is oriented to person, place, and time. Laboratory studies show the following, Which of the following is the most likely explanation for these findings?

Serum	
Na^+	150 mEq/L
Cl^-	97 mEq/L
K^+	3.6 mEq/L
HCO_3^-	30 mEq/L
Osmolality	354 mOsmol/kg H_2O
Hemoglobin A_{1C}	10.5%
Urine	
Osmolality	400 mOsmol/kg H_2O

A. Insufficient production of antidiuretic hormone
B. Gastroinstestinal fluid loss
C. Excess production of aldosterone
D. Osmotic diuresis
E. Diuretic overdose

Explanation: This patient most likely has hyperosmotic hyperglycemic syndrome (HHS), as a result of undiagnosed diabetes mellitus, as evidenced by his hemoglobin A1C, polyuria, orthostatic hypotension, and dehydration. Patients with HHS often present with mild hyponatremia because elevated serum glucose concentrations increase serum osmolality, pulling water out of cells and reducing the serum sodium concentration. However, patients with highly elevated serum osmolality can also experience marked water excretion due to osmotic diuresis, in which water loss exceeds sodium loss, which worsens volume depletion and increases the serum sodium concentration.



Answers: Q9: C| Q10: D

K-Ca Imbalance

Q1: A 21-year-old woman complains of urinary frequency, nocturia, constipation and polydipsia. Her symptoms started 2 weeks ago and prior to this she would urinate twice a day and never at night. She has also noticed general malaise and some pain in her left flank. A urine dipstick is normal. The most appropriate investigation is:

A. Serum phosphate
B. Serum calcium
C. Parathyroid hormone (PTH)
D. Plasma glucose
E. Serum potassium

Explanation: This patient has symptoms of hypercalcaemia, the major causes of which can be divided into primary, secondary and tertiary disorders. Primary usually includes malignancies such as adenomas producing PTH, secondary conditions are due to a compensatory increase in parathyroid hormone due to low serum calcium, such as in vitamin D deficiency. Secondary conditions can eventually become tertiary disorders with autonomous PTH production, such as in renal failure. The symptoms of hypercalcaemia can vary depending on severity, patients may be asymptomatic or suffer a number of features affecting different organ symptoms. General symptoms include malaise, abdominal pain and depression. Renal tubule impairment can lead to polyuria, polydipsia and nocturia. Bone pain occurs due to the effect of PTH upon bone metabolism, renal stones can also form due to increased serum calcium and dehydration. Serum calcium (B) must be measured first as this will be able to confirm an abnormal level of calcium in the body. Measuring PTH (C) may or may not provide useful diagnostic information, for example in a tumour producing excess calcium the PTH would be low. Serum phosphate (A) is useful to measure in patients with anorexia, weight loss and osteoporosis as this suggests deficiency, although this is very rare due to an abundance in natural foods. Plasma glucose (D) would be useful in a patient with suspected diabetes, however flank pain and constipation are not typical presentations and urine dipstick would reveal the presence of glucose and ketones. Derangement of serum potassium (E) does not produce the symptoms described in this patient. Hyperkalaemia predisposes to cardiac arrhythmias (loss of p-waves, widened QRS complex and tented T-waves) and muscle weakness, while in severe hypokalaemia there is muscle weakness, atrial and ventricular ectopics.

Q2: A 47-year-old HIV-positive man is brought to the emergency room because of weakness. The patient has HIV nephropathy and adrenal insufficiency. He takes trimethoprim-sulfamethoxazole for PCP prophylaxis and is on triple-agent antiretroviral treatment. He was recently started on spironolac-tone for ascites due to alcoholic liver disease. Physical examination reveals normal vital signs, but his muscles are diffusely weak. Frequent extrasystoles are noted. He has mild ascites and 1 + peripheral edema. Laboratory studies show a serum creatinine of 2.5 with a potassium value of 7.3 mEq/L. An EKG shows peaking of the T waves and QRS duration of 0.14. What is the most important immediate treatment?

A. Sodium polystyrene sulfonate (Kayexalate)
B. Acute hemodialysis
C. IV normal saline
D. IV calcium gluconate
E. IV furosemide 80 mg stat

Explanation: This patient has life-threatening hyperkalemia as suggested by the ECG changes in association with documented hyperkalemia. Death can occur within minutes as a result of ventricular fibrillation, and immediate treatment is mandatory. Intravenous calcium is given to combat the membrane effects of the hyperkalemia, and measures to shift potassium acutely into the cells
must be instituted as well. IV regular insulin 10 units and (unless the patient is already hyperglycemic) IV glucose (usually 25 g) can lower the serum potassium level by 0.5 to 1.0 mEq/L. Nebulized albuterol is often used and is probably more effective than IV sodium bicarbonate. It is crucial to remember that measures to promote potassium loss from the body (Kayexalate, furosemide, or dialysis), although important in the long run, take hours to work. These measures will not promptly counteract the membrane irritability of hyperkalemia. IV normal saline will not lower the serum potassium level.
This patient's hyperkalemia is a result of the combination of CKD and several medications (trimethoprim, spironolactone), which can cause hyperkalemia. Adrenal insufficiency could be playing a role as well. An important aspect of the management of CKD is avoiding drugs that can worsen kidney function or the metabolic effects (hyperkalemia, hyper-phosphatemia, metabolic acidosis) of renal failure.

Q3: A 27-year-old alcoholic man presents with decreased appetite, mild generalized weakness, intermittent mild abdominal pain, perioral numbness, and some cramping of his hands and feet. His physical examination is initially normal. His laboratory returns with a sodium level of 140 mEq/L, potassium 4.0 mEq/L, calcium 6.9 mg/dL, albumin 3.5 g/dL, magnesium 0.7 mg/dL, and phosphorus 2.0 mg/dL. You go back to the patient and find that he has both a positive Trousseau and a positive Chvostek sign. Which of the following is the most likely cause of the hypocalcemia?

A. Poor dietary intake
B. Hypoalbuminemia
C. Pancreatitis
D. Decreased end-organ response to parathyroid hormone because of hypomagnesemia
E. Osteoporosis caused by hypogonadism

Explanation: One of the commonest causes of hypocalcemia is impaired parathormone (PTH) production. Hypomagnesemia causes decreased production of PTH as well as decreased end-organ response to the hormone. Alcohol causes increased urinary losses of magnesium which then leads to the mentioned effects on PTH and ultimately to hypocalcemia. While pancreatitis can cause hypocalcemia, this patient's presentation does not suggest the condition. Osteoporosis and poor dietary intake do not lead to hypocalcemia unless the patient has vitamin D deficiency. Routine calcium levels are not accurate in the setting of a low albumin. To estimate the true calcium level, one may add 0.8 mg/dL to the observed calcium level for every 1 g reduction in the albumin level (from 4 used as normal). In this case, the albumin is not far from 4 and hence the calculation would change the low calcium level very little. An ionized calcium level is consistent and accurate regardless of the albumin level of a patient.

Answers: Q1: B | Q2: D | Q3: D

K-Ca Imbalance

Q4: A 55-year-old man is seen during a routine evaluation. He was diagnosed with type 2 diabetes mellitus 15 years ago. He also has hypertension and a 1-year history of right knee osteoarthritis that is well controlled with maximal-dose ibuprofen. His other medications are losartan, metformin, and pravastatin. On physical examination, temperature is 37.2°C (98.9°F), blood pressure is 146/92 mm Hg, pulse rate is 70/min, and respiration rate is 14/min. Cardiopulmonary examination is normal. There is bilateral lower-extremity edema to the mid shin. Urine protein-creatinine ratio 0.46 mg/mg Urinalysis Specific gravity 1.015; 3+ protein; 2+ glucose; no casts Which of the following is the most appropriate initial management step?

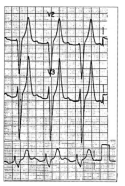
Glucose (nonfasting)	230 mg/dL (12.8 mmol/L)
Sodium	142 meq/L (142 mmol/L)
Potassium	5.9 meq/L (5.9 mmol/L)
Chloride	108 meq/L (108 mmol/L)
Bicarbonate	18 meq/L (18 mmol/L)
Serum creatinine	2.5 mg/dL (221 µmol/L)

A. Begin hydrochlorothiazide
B. Begin spironolactone
C. Discontinue ibuprofen and begin furosemide
D. Substitute lisinopril for losartan

Explanation: Discontinuation of ibuprofen and initiation of furosemide are the most appropriate next steps in the initial management of this patient's chronic kidney disease. This patient's long-standing history of diabetes mellitus, hypertension, proteinuria, and elevated serum creatinine level are consistent with diabetic nephropathy. Aggressive blood pressure control, particularly with pharmacologic modulators of the renin-angiotensin-aldosterone system, would help to slow the progression of this patient's disease but will likely worsen his hyperkalemia. Until the glomerular filtration rate decreases to less than 15 mL/min/1.73 m2, chronic kidney disease usually does not cause hyperkalemia without other mitigating factors. These factors include use of medications that interfere with the renin-angiotensin-aldosterone system and NSAIDs. Use of the NSAID ibuprofen is most likely contributing to this patient's hyperkalemia and reduced glomerular filtration rate and should be discontinued. However, discontinuing ibuprofen alone would most likely not help to lower this patient's blood pressure, control volume overload, or fully correct his hyperkalemia; the addition of a loop diuretic is therefore warranted. If needed, additional interventions to help decrease the risk of hyperkalemia include adherence to a low-potassium diet and use of sodium bicarbonate. Thiazide diuretics are largely ineffective in individuals with an estimated glomerular filtration rate below 30 mL/min/1.73 m2. The addition of losartan would worsen this patient's hyperkalemia and would not be recommended. Spironolactone has been shown to further decrease urine protein excretion when added to either angiotensin-converting enzyme inhibitors or angiotensin receptor blockers in patients with diabetic nephropathy. However, this agent impairs kidney potassium excretion and also would further exacerbate this patient's hyperkalemia.

Key Point Discontinuation of medications that interfere with the renin-angiotensin-aldosterone system, including NSAIDs and, if needed, angiotensin-converting enzyme inhibitors and angiotensin receptor blockers, is warranted to help correct significant hyperkalemia in the setting of chronic kidney disease.

Q5: A 30-year-old man with type 1 diabetes mellitus and chronic kidney disease (serum creatinine, 5.3 mg/dL [468.5 µmol/L]) is evaluated in the emergency department for a 2- day history of muscle weakness and recent onset of light headedness. An electrocardiogram taken in the emergency department is shown. Which of the following is the best immediate treatment option?



A. Calcium gluconate, intravenously
B. 50% glucose, intravenously
C. Hemodialysis
D. Sodium polystyrene sulfonate in sorbitol, rectally

Explanation: The best immediate treatment option is intravenous calcium gluconate. The electrocardiogram shows spiking of the T waves and widening of the QRS complexes, findings that indicate hyperkalemic cardiotoxicity in this patient with chronic kidney disease. The choice of treatment for hyperkalemia and the aggressiveness of its implementation depend largely on the severity of the hyperkalemia as well as on electrocardiographic and neuromuscular manifestations. The approximate relationship between electrocardiographic changes and the serum potassium concentration is substantially modified by changes of other cations in the serum and the acid-base status. (For example, with the simultaneous presence of hyponatremia, hypocalcemia, and acidemia, even modest degrees of hyperkalemia may result in serious and potentially fatal electrical disturbances.) Urgent therapy of hyperkalemia consists of antagonism of the membrane effects of hyperkalemia and induction of intracellular potassium shift. Removing potassium from the body (for example, by sodium polystyrene sulfonate, hemodialysis, peritoneal dialysis) is important, but the effects cannot be accomplished with the necessary urgency. Therefore, the first step in treating urgent hyperkalemia is to administer calcium gluconate to antagonize hyperkalemic cardiac toxicity, an effect that usually begins within 2 to 3 minutes of administration of intravenous calcium gluconate. Sodium bicarbonate and β-antagonists such as albuterol and glucose (with or without insulin) would facilitate intracellular potassium shift. However, their effect is slower (10 minutes for sodium bicarbonate, 15 to 30 minutes for albuterol, and 30 minutes for glucose and insulin). Hypertonic glucose should not be administered without insulin when treating a patient with diabetes. Dialysis, 50% glucose, and sodium polystyrene sulfonate are all helpful therapeutic steps in managing urgent hyperkalemia, but none is the ideal first step.

Key Point The first step in treating urgent hyperkalemia is to administer calcium gluconate to antagonize hyperkalemic cardiac toxicity.

Answers: Q4: C | Q5: A

K-Ca Imbalance

Q6: A 17-year-old girl is evaluated for weakness. On physical examination, the blood pressure is 124/74 mm Hg with no orthostatic changes, pulse rate 72/min, and respiration rate 15/min. BMI is 18. The rest of the physical examination is unremarkable. Blood urea nitrogen and serum creatinine are normal. A spot urine potassium concentration is 8 meq/L (8 mmol/L). Which of the following is the most likely diagnosis?

Sodium	140 meq/L (140 mmol/L)
Potassium	2.8 meq/L (2.8 mmol/L)
Chloride	110 meq/L (110 mmol/L)
Bicarbonate	21 meq/L (21 mmol/L)

A. Laxative abuse
B. Primary hyperaldosteronism
C. Primary hypoaldosteronism
D. Surreptitious diuretic use

Explanation: This patient likely has been abusing laxatives. This is supported by the serum electrolyte pattern suggesting hypokalemia and a metabolic acidosis. In the absence of a cellular shift, a low serum potassium concentration can be caused by losses via the gastrointestinal tract, skin or kidney, or due to inadequate dietary intake of potassium. A urine potassium concentration of less than 20 meq/L (20 mmol/L) is suggestive of extrarenal losses, whereas a concentration higher than this value is suggestive of kidney losses. Therefore, this patient has a hypokalemic disorder associated nonrenal potassium loss. Gastrointestinal disorders are the most common clinical cause of extrarenal potassium losses. Diarrhea leads to fecal potassium wastage and is associated with a normal anion gap acidosis due to increased gastrointestinal loss of bicarbonate. Her low serum bicarbonate is consistent with metabolic acidosis but without an arterial blood gas, the acid-base disorder cannot be determined. Villous adenoma and laxative abuse are two such conditions that can cause gastrointestinal potassium losses. The fact that the patient is an underweight adolescent female, in whom eating disorders are common, suggests the possibility of surreptitious laxative abuse in an effort to control weight. Although primary hyperaldosteronism may result hypokalemia, it is typically associated with hypertension and high urinary potassium concentration, both of which is absent in this patient. Hypoaldosteronism is associated with hyponatremia and hyperkalemia, which are not compatible with this patient's findings. Surreptitious diuretic abuse can cause of hypokalemia; however, it is associated with metabolic alkalosis and high urinary potassium concentration, findings not seen in this patient.

Key Point In a patient with hypokalemia, a urine potassium concentration of less than 20 meq/L (20 mmol/L) is suggestive of extrarenal losses, whereas a concentration higher than this value is suggestive of kidney losses.

Q7: A 55-year-old woman is evaluated in the emergency department for a 2-day history of severe midepigastric pain radiating through to her back and of nausea with vomiting. Before this, she was well and had no medical problems; she does not take any medications or drink alcohol. On examination, she is in distress from pain. Temperature is 37.8°C (98.9°F), blood pressure is 155/97 mm Hg, and pulse rate is 104/min. BMI is 29. Midepigastric tenderness to palpation is marked. An abdominal ultrasound reveals a dilated common bile duct and multiple gallstones. Laboratory evaluation reveals elevated alkaline phosphatase, amylase, and lipase levels; total calcium level is 6.8 mg/dL (1.7 mmol/L). What of the following is the most likely cause of the hypocalcemia?

A. 1,25-dihydroxy vitamin D deficiency
B. Autoimmune hypoparathyroidism
C. Calcium chelation with free fatty acids
D. Parathyroid gland injury

Explanation: The most likely cause of the patient's hypocalcemia is calcium chelation with free fatty acids liberated by pancreatic enzymes during an episode of acute gallstone pancreatitis. When the pancreas is injured, the secretion of pancreatic enzymes is blocked, which leads to an autodigestive injury to the gland. The pancreatic enzymes are then released within the peritoneum and digest fat; the generated free fatty acids avidly chelate insoluble calcium salts, resulting in hypocalcemia and deposition of calcium salts in the pancreatic bed. This process is known as saponification and can lead to symptomatic hypocalcemia and calcium deposits identifiable on plain films of the abdomen. Pancreatic calcification identified by imaging studies is a diagnostic sign of chronic pancreatitis. 1,25-hydroxy vitamin D deficiency is most commonly seen in chronic kidney disease and is due to decreased activity of the 1α-hydroxylase enzyme responsible for converting 25-hydroxy vitamin D to the active form. This patient does not have a history of chronic kidney disease. This patient has no history of previous thyroid surgery, which is the most common reason for parathyroid injury and hypoparathyroidism and is related to incidental removal or vascular injury to the parathyroid glands. Autoimmune destruction of the parathyroid gland usually occurs in the setting of other autoimmune disorders (polyglandular autoimmune syndrome) including adrenal insufficiency and mucocutaneous candidiasis, which are not present in this patient.

Key Point Acute pancreatitis can generate free fatty acids that avidly chelate insoluble calcium salts in the pancreatic bed, resulting in hypocalcemia.

Answers: Q6: A | Q7: C

K-Ca Imbalance

Q8: A 45-year-old man with stage 1 pulmonary sarcoidosis (hilar lymphadenopathy) is evaluated for abdominal pain and distention. He has chronic constipation, and his last bowel movement was 6 days ago. On physical examination, temperature is 36.8°C (98.2°F), blood pressure is 152/80 mm Hg, pulse rate is 78/min, and respiration rate is 12/min. Bowel sounds are present but diminished. Tenderness to palpation is present and most prominent in the left lower quadrant without guarding. Rectal examination reveals firm stool but no masses. Serum calcium level is 11.6 mg/dL (2.9 mmol/L); the reminder of the laboratory evaluation is normal, including thyroid-stimulating hormone level and free thyroxine. A plain film of the abdomen shows marked colonic distention with stool but no free air under the diaphragm or evidence of mechanical bowel obstruction. Enemas and laxatives are prescribed. Which of the following is the most appropriate additional treatment for this patient?

A. Cinacalcet
B. Hydrochlorothiazide
C. Intravenous normal saline
D. Prednisone

Explanation: This man presents with severe constipation due to hypercalcemia in the setting of sarcoidosis. Sarcoidosis is a multisystem, granulomatous, inflammatory condition of unknown cause that occurs in young adults of both sexes. The temporal pattern of disease progression ranges from asymptomatic to acute systemic presentations with fever, erythema nodosum, polyarthralgia, and hilar lymphadenopathy (Lofgren syndrome). Approximately 90% of patients have pulmonary involvement at the time of presentation. Hypercalcemia and hypercalciuria in sarcoidosis are caused by unregulated production of 1α-hydroxylase by activated macrophages in the granuloma tissue. Increased 1α-hydroxylase activity increases the production of 1,25 [OH]2 vitamin D. Increased amounts of vitamin D3 result in increased gastrointestinal absorption of calcium, resulting in hypercalcemia. Corticosteroid therapy decreases vitamin D3 production by decreasing the number of activated macrophages. Cinacalcet binds to the parathyroid calcium-sensing receptor, leading to decreased release of parathyroid hormone. This therapy is indicated only in refractory secondary hyperparathyroidism of chronic kidney disease (low serum calcium and elevated parathyroid hormone levels) or tertiary hyperparathyroidism (elevated serum calcium and elevated serum parathyroid hormone levels), neither of which applies to this patient. Hydrochlorothiazide indirectly inhibits calcium excretion by the kidney, leading to calcium retention, and may cause hypercalcemia. Although this patient's blood pressure is elevated, it should be remeasured after his constipation is relieved and hypercalcemia is resolved; regardless, hydrochlorothiazide would be an inappropriate medication because of its propensity to cause hypercalcemia.
Measures taken to treat acute symptomatic hypercalcemia include increasing urinary excretion of calcium. Urine calcium excretion can be attained by inhibition of proximal tubular and loop sodium resorption, which is best achieved by volume expansion using intravenous normal saline infusion (1-2 L for 1 hour). This therapy is generally reserved for symptomatic patients with moderate calcium elevation (>12 mg/dL [3.0 mmol/L]) and is unnecessary in this patient.

Key Point Sarcoidosis causes hypercalcemia through increased production of 1α-hydroxylase and can be treated with prednisone.

Q9: A 45-year-old man is evaluated for a 3-month history of fatigue, constipation, and polyuria. He also has a 5-year history of hypertension. Current medications are losartan and diltiazem. Physical examination findings, including vital signs, are normal. Measurement of which of the following levels should be done next?

Calcium	11.4 mg/dL (2.9 mmol/L)
Creatinine	1.1 mg/dL (97.2 µmol/L)
Glucose, fasting	88 mg/dL (4.9 mmol/L)
Phosphorus	2.2 mg/dL (0.71 mmol/L)
Thyroid-stimulating hormone	1.2 µU/mL (1.2 mU/L)

A. Calcitonin
B. 25-Hydroxy vitamin D
C. Parathyroid hormone
D. Parathyroid hormone-related protein

Explanation: This patient's parathyroid hormone (PTH) level should be determined next. Primary hyperparathyroidism is the most common cause of hypercalcemia in the outpatient setting. The first step in the diagnosis of hypercalcemia is determination of the PTH level with an assay for intact PTH. If the PTH level is high or "inappropriately" normal, primary hyperparathyroidism is the diagnosis. If the PTH level is suppressed, a search for other entities that cause hypercalcemia must be conducted. Calcitonin is secreted by thyroid parafollicular C cells. This serum level is elevated in patients with medullary thyroid cancer or C-cell hyperplasia. Calcitonin tends to lower the calcium level by enhancing cellular uptake, renal excretion, and bone formation. The effect of calcitonin on bone metabolism is weak and only relevant in pharmacologic amounts. Measurement of serum calcitonin is not indicated in a patient with hypercalcemia. One of the ways in which PTH increases the serum calcium level is by up-regulation of the 1α-hydroxylase enzyme, which stimulates conversion of vitamin D to its most active form, 1,25-dihydroxy vitamin D. This form of vitamin D increases the percentage of dietary calcium absorbed by the intestine. Body stores of vitamin D are assessed by measuring the 25-hydroxy vitamin D level, which has a long half-life. Measurement of this patient's 25-hydroxy vitamin D and 1,25-dihydroxy vitamin D levels may be appropriate if the parathyroid hormone level is suppressed. At this time, however, such measurement is not indicated. Humoral hypercalcemia of malignancy results from the systemic effect of a circulating factor produced by neoplastic cells. The hormone most commonly responsible for this syndrome is parathyroid hormone-related protein (PTHrP). This peptide's N-terminal shares many homologic features with PTH and most, if not all, of the metabolic effects of PTH. Tumors that elaborate PTHrP are most commonly squamous cell carcinomas, such as those of the lung, esophagus, and head and neck. This patient has no evidence of cancer. The diagnosis of humoral hypercalcemia of malignancy can often be made in the absence of PTHrP measurements if a compatible malignancy, hypercalcemia, and suppressed PTH level are present.

Key Point The most common cause of hypercalcemia in the outpatient setting is hyperparathyroidism.

Answers: Q8: D | Q9: C

Acid-Base Disorders

Q1: A 32-year-old builder presents in accident and emergency in a distressed state. He reports suffering from chest pain for the last 2 weeks, the pain is sharp and only occurs when he moves heavy objects. He has a family history of cardiovascular disease and is worried about a heart attack. His blood gas findings are as follows: pH = 7.47; PCO2 = 3.3; PO2 = 15.3; bicarbonate = 17.53. The most likely diagnosis is:

A. Respiratory acidosis with metabolic compensation
B. Acute metabolic acidosis
C. Respiratory alkalosis with metabolic compensation
D. Metabolic acidosis with respiratory compensation
E. Acute respiratory alkalosis

Explanation: The history in this case suggests the patient's chest pain is due to muscular injury rather than anything more sinister. The patient's anxiety about cardiovascular morbidity has ultimately resulted in hyperventilation causing an acute respiratory alkalosis (E). Acid base abnormalities can be solved by either considering the Henderson–Hasselbach equation ($CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$), whereby change in the product(s) on one side of the equation is balanced by a shift in equilibrium. For example, in this case the patient's hyperventilation causes a reduction in CO_2, in order to increase the CO_2 the equilibrium shifts towards $CO_2 + H_2O$ which causes a reduction in H^+ (alkalosis) and HCO_3^-. This process occurs in respiratory alkalosis with metabolic compensation (C). If the patient had a true cardiac arrest it would cause a surge in lactic acidosis hence H^+ concentration increases causing a metabolic acidosis (B). In order to balance this change, the equilibrium shifts away from H^+ and causes increased CO_2 production which can manifest as an increased respiratory rate, otherwise called 'metabolic acidosis with respiratory compensation' (D). In a respiratory acidosis with metabolic compensation (A) scenario, a patient may have a respiratory abnormality such as chronic hypoventilation. The accumulation of CO_2 which leads to increased H^+ is compensated for by bicarbonate which is subsequently reduced. In more chronic conditions, the bicarbonate becomes elevated.

Q2: A 61-year-old man is evaluated in the emergency department because of a 3-day history of cough productive of yellow sputum. He has chronic obstructive pulmonary disease and he routinely uses supplemental oxygen, 2 L/min. He states that he is now short of breath at rest. Physical examination shows that he is using accessory muscles of respiration and pursed-lipped breathing. He has prolonged expiratory-to-inspiratory phase on exhalation and scattered wheezes. He has tachycardia and bilateral pitting edema of the extremities. His oxygen saturation is 91% on supplemental oxygen. Chest radiograph shows changes consistent with emphysema, but is otherwise unchanged from baseline. His arterial blood gas values are PO2, 59 mm Hg (7.8 kPa); PCO2, 64 mm Hg (8.5 kPa); and pH, 7.32. Other pertinent laboratory values include sodium, 140 meq/L (140 mmol/L); chloride, 100 meq/L (100 mmol/L); potassium, 3.5 meq/L (3.5 mmol/L); and bicarbonate, 32 meq/L (32 mmol/L). Which of the following acid-base disorders is most likely present?

A. Metabolic acidosis
B. Respiratory acidosis
C. Respiratory acidosis and metabolic acidosis
D. Respiratory alkalosis

Explanation: This patient's acid-base disorder is respiratory acidosis. Respiratory acidosis is produced by any process associated with primary retention of carbon dioxide. In this patient, the pH is less than 7.38 and the PCO2 is >40 mm Hg (5.3 kPa), indicating the presence of a respiratory acidosis. Renal compensatory response occurs in respiratory acidosis. Persistent hypercapnia stimulates the secretion of protons at the level of the distal nephron. The urinary pH decreases, and excretion of urinary ammonium, titratable acid, and chloride is enhanced. Consequently, the reabsorption of bicarbonate throughout the nephron is enhanced. The predicted increase in serum bicarbonate is calculated as 1 meq/L (1 mmol/L) for each 10 mm Hg (1.3 kPa) increase in PCO2 (acute) or 4 meq/L (4 mmol/L) for each 10 mm Hg (1.3 kPa) increase in PCO2 (chronic). Because this patient with chronic obstructive pulmonary disease probably has chronic retention of carbon dioxide, an increase in the serum bicarbonate by at least 8 meq/L (8 mmol/L) is expected. This is consistent with the measured serum bicarbonate level. Therefore, there is appropriate compensation for the respiratory acidosis and no evidence for a coexisting metabolic acidosis. Respiratory alkalosis is not consistent with the observed decrease in the serum pH.

Key Point In respiratory acidosis, the predicted increase in serum bicarbonate is calculated as 1 meq/L (1 mmol/L) for each 10 mm Hg (1.3 kPa) increase in PCO2 (acute) or 4 meq/L (4 mmol/L) for each 10 mm Hg (1.3 kPa) increase in PCO2 (chronic).

Answers: Q1: E | Q2: B

Acid-Base Disorders

Q3: A 20-year-old man presents with obtundation. Past medical history is unobtainable. Blood pressure is 120/70 without orthostatic change, and he is well perfused peripherally. The neurological examination is nonfocal. His laboratory values are as follows: Which of the following is the most likely acid-base disorder?

A. Pure normal anion-gap metabolic acidosis
B. Respiratory acidosis
C. Pure high anion-gap metabolic acidosis
D. Combined high anion-gap metabolic acidosis and respiratory alkalosis
E. Combined high anion-gap metabolic acidosis and respiratory acidosis

Na: 138 mEq/L
K: 4.2 mEq/L
HCO_3: 5 mEq/L
Cl: 104 mEq/L
Creatinine: 1.0 mg/dL
BUN: 14 mg/dL
Ca: 10 mg/dL
Arterial blood gas on room air: PO_2 96, PCO_2 15, pH 7.02
Blood glucose: 90 mg/dL
Urinalysis: normal, without blood, protein, or crystals

Explanation: The first step in analyzing an acid-base disturbance is simply to look at the pH. This patient has an acidosis. Then look at the HCO3 and the PCO2 to determine the primary disturbance; that is, is it a metabolic acidosis or a respiratory acidosis? The serum HCO3 has decreased from 24 to 5 mEq/L, so this must be a metabolic acidosis. The PCO2 is below the normal value of 40 mm, so this cannot be a respiratory acidosis (the PCO2 would be above 40 in a respiratory acidosis). The first two steps are straightforward and unambiguous. The third (and most difficult) step is to assess the compensatory response. This patient has a metabolic acidosis, so you need to assess the respiratory compensation. That is to say, has the PCO2 decreased appropriately to compensate for the metabolic acidosis? The normal compensatory response in metabolic acidosis is for the PCO2 to decrease by 1 to 1.5 mm Hg for each 1-mEq decrease in HCO3. This patient's 19 mEq/L drop in bicarbonate is matched by a 25-mm drop in the PCO2. Hence, this is a compensated metabolic acidosis. Another method of assessing compensation in a metabolic acidosis is to use the Winters formula, which says that the appropriate PCO2 equals 1.5 (HCO3) + 8. This would give an appropriate PCO2 of 15.5, very close to the measured PCO2. Again, the compensatory response is appropriate for the degree of acidosis; the patient does not have a respiratory acid-base disorder. The fourth step is to calculate the anion gap. The normal anion gap in this case the value is 29 mEq/L. Therefore, this is an anion-gap metabolic acidosis with appropriate respiratory compensation. A brief differential of anion-gap metabolic acidosis is as follows:
Diabetic ketoacidosis Lactic acidosis Alcoholic ketoacidosis Toxic alcohol (methanol, ethylene glycol) ingestion Salicylate intoxication Renal failure

Q4: A 17-year-old man is brought to the emergency room with confusion and incoordination. He is uncooperative and refuses to provide further history. Physical examination reveals an RR of 30; the vital signs are otherwise normal as is the general physical examination. Laboratory values are as follows: Which of the following is the most likely cause of the acid base disorder?

A. Metabolic acidosis
B. Proximal renal tubular acidosis
C. Disorder of the renin-angiotensin system
D. Distal renal tubular acidosis
E. Respiratory acidosis

Na: 135 mEq/L
K: 2.7 mEq/L
HCO_3: 15 mEq/L
Cl: 110 mEq/L
Arterial blood gases: PO_2 92, PCO_2 30, pH 7.28
Urine: pH 7.5, glucose—negative
Ca: 9.7 mg/dL
PO_4: 4.0 mg/dL

Explanation: The patient has a metabolic acidosis. Respiratory compensation is appropriate, and the anion gap is normal. Therefore, he has a hyperchloremic (normal anion gap) metabolic acidosis. Common causes include renal tubular acidosis, bicarbonate loss owing to diarrhea, and mineralocorticoid deficiency. In a metabolic acidosis, the urine pH should be low (ie, the patient should be trying to excrete the excess acid). This patient's high urine pH is therefore diagnostic of renal tubular acidosis (RTA). Proximal RTA is associated with glycosuria, phosphaturia, and aminoaciduria (Fanconi syndrome). Since the serum phosphorus is normal and glycosuria is absent, proximal RTA is unlikely. GI loss of bicarbonate caused by diarrhea would be associated with an appropriately acidic urine (pH < 5.5). Disorders of the renin-angiotensin-aldosterone system are associated with hyperkalemia, not hypokalemia. The low PCO2 excludes respiratory acidosis. So this patient has a distal RTA, probably because of toluene inhalation (glue sniffing). Toluene can lead to life-threatening metabolic acidosis and hypokalemia.

Q5: A 73-year-old woman with arthritis presents with confusion. Neurologic examination is nonfocal, and CT of the head is normal. Laboratory data include: What is the acid-base disturbance?

A. Respiratory alkalosis with appropriate metabolic compensation
B. High anion-gap metabolic acidosis with appropriate respiratory compensation
C. Combined metabolic acidosis and respiratory alkalosis
D. No acid-base disorder
E. Hyperchloremic (normal anion gap) metabolic acidosis with appropriate respiratory compensation

Na: 140 mEq/L
K: 3.0 mEq/L
Cl: 107 mEq/L
HCO_3: 12 mEq/L
Arterial blood gases: PO_2 62, PCO_2 24, pH 7.40

Explanation: This patient's normal pH would initially suggest a normal acid-base status. However, the PCO2 is significantly low, indicating a respiratory alkalosis. If the pH is normal, there must be a superimposed metabolic acidosis; that is, metabolic compensation would not return the pH all the way back to 7.4. Indeed the serum bicarbonate is too low for a compensatory response (metabolic compensation for respiratory alkalosis rarely drops the HCO3 below 17 mEq/L) and the anion gap is elevated at 21. The only cause of a substantially elevated anion gap is metabolic acidosis (the AG can be elevated to 16 or 17 in alkalosis). Therefore, this patient has a combined (mixed) disturbance, that is, combined respiratory alkalosis and metabolic acidosis.
This is the classic acid-base disturbance associated with salicylate intoxication. Aspirin stimulates central respiratory drive; in addition, several metabolic substances (salicylic acid and lactic acid due to suppression of oxidative phosphorylation, among others) build up to widen the anion gap. Choices a, b, and e are wrong because compensation never normalizes the pH.

Answers: Q3: C | Q4: D | Q5: C

Acid-Base Disorders

Q6: A 28-year-old man is brought to the emergency department with the sudden onset of dyspnea following a stressful interview at work. On physical examination, temperature is 36.7°C (98°F), heart rate is 99/min, respiration rate is 32/min, and blood pressure is 156/80 mm Hg. He is weak and in moderate respiratory distress. Cardiovascular and pulmonary examinations are normal. Which of the following best characterizes the patient's acid-base disorder?

A. Mixed anion gap metabolic acidosis and respiratory alkalosis
B. Mixed metabolic alkalosis and respiratory alkalosis
C. Respiratory acidosis
D. Respiratory alkalosis

Sodium	140 meq/L (140 mmol/L)
Potassium	4.9 meq/L (4.9 mmol/L)
Chloride	110 meq/L (110 mmol/L)
Bicarbonate	22 meq/L (22 mmol/L)

Arterial blood gas studies (on ambient air):	
pH	7.49
PCO_2	30 mm Hg (4.0 kPa)
Po_2	99 mm Hg (13.2 kPa)

Explanation: This patient has a pure respiratory alkalosis. The presence of an alkaline pH with a low PCO2 is compatible with respiratory alkalosis. Furthermore, there is appropriate metabolic compensation for the respiratory alkalosis. In acute respiratory alkalosis, for each 10 mm Hg (1.3 kPa) decline in PCO2 the expected decline in serum bicarbonate is 2 meq/L (2 mmol/L). Since his PCO2 declined by 10 mm Hg (1.3 kPa) to 30 mm Hg (4.0 kPa), the expected decline in the serum bicarbonate is 2 meq/L (2 mmol/L); this matches the measured serum bicarbonate concentration exactly. Because the decline in the serum bicarbonate level is appropriate for the degree of respiratory alkalosis the patient cannot have a metabolic acidosis or metabolic alkalosis. And since his anion gap is normal, there is no possibility that the acid-base disturbance is an anion-gap metabolic acidosis. The anion gap is 8, calculated as [Na+] - ([Cl-] + [HCO3-]). Normal anion gap is 12 ± 2.
Because the PCO2 is depressed rather than elevated, the diagnosis cannot be respiratory acidosis.
There are many potential causes of respiratory alkalosis, and the physical examination is often helpful in identifying the correct diagnosis. Common causes of respiratory alkalosis include psychogenic (for example, hyperventilation associated with anxiety), normal pregnancy, pulmonary vascular disease (for example, pulmonary hypertension or pulmonary embolism), pulmonary parenchymal disease (for example, pneumonia and pulmonary fibrosis), heart failure, sepsis, and cirrhosis.

Key Point In respiratory acidosis, the predicted increase in serum bicarbonate is calculated as 1 meq/L (1 mmol/L) for each 10 mm Hg (1.3 kPa) increase in PCO2 (acute) or 4 meq/L (4 mmol/L) for each 10 mm Hg (1.3 kPa) increase in PCO2 (chronic)

Q7: A 56-year old man with a history of alcoholism is found lying on the street. On arrival at the emergency department, he is confused. On physical examination, temperature is 36.1°C (97.0°F), blood pressure is 126/80 mm Hg, and pulse rate is 70/min. Funduscopic examination shows no papilledema. Cardiac, pulmonary, and abdominal examinations are normal. Which of the following is the most likely diagnosis?

A. Alcoholic ketoacidosis
B. Diabetic ketoacidosis
C. Ethylene glycol poisoning
D. Lactic acidosis

Glucose (fasting)	86 mg/dL (4.8 mmol/L)
Blood urea nitrogen	45 mg/dL (16.1 mmol/L)
Serum creatinine	2.8 mg/dL (247.5 µmol/L)
Sodium	138 meq/L (138 mmol/L)
Potassium	5.4 meq/L (5.4 mmol/L)
Chloride	98 meq/L (98 mmol/L)
Bicarbonate	14 meq/L (14 mmol/L)
Plasma osmolality	336 mosm/kg (336 µmol/kg)
Urinalysis	Calcium oxalate crystals

Arterial blood gas studies (with the patient breathing ambient air)	
pH	7.32
PCO_2	29 mm Hg (3.9 kPa)
PO_2	80 mm Hg (10.6 kPa)

Explanation: This patient has ethylene glycol poisoning, which may manifest as acute kidney injury associated with an increased anion gap metabolic acidosis and an increased osmolal gap. The osmolal gap is the difference between the calculated plasma osmolality and measured plasma osmolality. In this patient, the osmolality is calculated using the following formula:
2 × [Sodium] + [Glucose]/18 + [Blood Urea Nitrogen]/2.8 = 296 mosm/kg (296 µmol/kg) Where sodium is meq/L and glucose and blood urea nitrogen are mg/dL.
The difference between the measured and calculated osmolality is 40 mosm/kg (40 µmol/kg). The normal osmolal gap is approximately 10 mosm/kg (10 µmol/kg). An elevated osmolal gap suggests the presence of an unmeasured osmole that is most commonly ethanol but can be ethylene glycol or methanol. However, only ethylene glycol is associated with kidney injury and calcium oxalate crystals in the urine.
Although alcoholic and diabetic ketoacidosis and lactic acidosis can cause an anion gap metabolic acidosis, none of these conditions is associated with an osmolal gap.

Key Point Ethylene glycol poisoning is associated with an anion gap metabolic acidosis, an increased osmolal gap, kidney injury, and calcium oxalate crystals in the urine.

Q8: A 39-year-old man is evaluated in the emergency department because of severe left flank pain and hematuria after playing softball. The pain is sharp and radiates to the groin. He vomited eight times before presentation. He has a nonobstructing, calcium-containing kidney stone at the ureteropelvic junction on the left side. On initial evaluation, his blood pressure was 130/90 mm Hg, respiratory rate was 30/min, and pulse rate was 110/min. Which of the following best describes this patient's acid-base disorder?

A. Metabolic acidosis and respiratory alkalosis
B. Metabolic alkalosis
C. Metabolic alkalosis and respiratory acidosis
D. Metabolic and respiratory alkalosis

Serum sodium	141 meq/L (141 mmol/L)
Serum potassium	4.0 meq/L (4.0 mmol/L)
Serum chloride	100 meq/L (100 mmol/L)
Serum bicarbonate	34 meq/L (34 mmol/L)
Arterial blood gases	pH, 7.60; PCO_2, 36 mm Hg (4.8 kPa)

Explanation: Arterial blood gas values demonstrate a mixed metabolic and respiratory alkalosis. Metabolic alkalosis is indicated by the high serum bicarbonate level and a pH greater than 7.4. Respiratory compensation for the metabolic alkalosis is not appropriate; the PCO2 would be expected to increase in compensation for the elevated serum bicarbonate level, but instead, the PCO2 has decreased to 36 mm Hg (4.8 kPa), indicating the presence of a respiratory alkalosis. In most patients, for each 1 meq/L (1 mmol/L) increase in serum bicarbonate, the PCO2 can be expected to increase by 0.7 mm Hg (0.09 kPa).
The anion gap is 7, calculated as (141 - [100 + 34]); thus, there is no hidden anion-gap metabolic acidosis (normal anion gap < 12 ± 2). The respiratory alkalosis is most likely due to pain-induced hyperventilation from the kidney stone, and metabolic alkalosis is probably a result of vomiting.

Key Point A mixed metabolic and respiratory alkalosis is suggested by an elevated pH and serum bicarbonate concentration and a PCO2 concentration that is lower than expected for the degree of alkalosis.

Answers: Q6: D | Q7: C | Q8: D

Acid-Base Disorders

Q9: A 54-year-old man is brought to the emergency department by his wife because of high fever and confusion for the past 10 hours. His wife reports that 1 week ago during a trip to Guatemala he underwent an emergency appendectomy. His temperature is 40.1°C (104.2°F), pulse is 132/min, and blood pressure is 74/46 mm Hg. He is oriented only to person. Physical examination shows a surgical wound in the right lower quadrant with purulent discharge. The skin is warm and dry. Serum studies show a sodium concentration of 138 mEq/L, potassium concentration of 3.7 mEq/L, and lactate concentration of 3.5 mEq/L (N = 0.5–2.2). Arterial blood gas analysis on room air shows:

A. Salicylate toxicity
B. Primary adrenal insufficiency
C. Respiratory fatigue
D. Diabetic ketoacidosis

pH	7.21
pCO_2	36
HCO_3^-	12
O_2 saturation	87%

Explanation: Per the Winter formula, a pCO2 of 24–28 mm Hg would reflect an appropriate respiratory compensation for this patient's metabolic acidosis. Instead, this patient's pCO2 is 36 mm Hg, which indicates the presence of a respiratory acidosis in addition to the metabolic acidosis. Respiratory acidosis is caused by hypoventilation (e.g., from respiratory fatigue in critically ill patients), which leads to carbon dioxide retention.

Q10: A 46-year-old woman comes to the emergency department with nausea and abdominal pain for 1 day. Her last bowel movement was 6 days ago. She has not passed flatus for 12 hours. She has a history of multiple surgeries for endometriosis. Vital signs are within normal limits. Examination shows a distended and diffusely tender abdomen with no rebound or guarding. Rectal examination shows an empty rectum. An x-ray of the abdomen shows a dilated cecum and right colon and preservation of the haustra. The patient is kept NPO (nothing by mouth). A nasogastric tube is inserted for continuous decompression and 900 ml (30 oz) of gastric fluid is drained. This intervention is most likely to lead to which of the following sets of serum findings?

A. A
B. B
C. C
D. D
E. E

	pH	HCO_3^-	K^+	Cl^-
A	↓	↓	unchanged	unchanged
B	↑	↑	unchanged	unchanged
C	Unchanged	unchanged	↓	unchanged
D	↑	↑	↓	↓
E	↓	↓	↓	↑

Explanation: This set of findings is consistent with metabolic alkalosis caused by a loss of gastric acid (e.g., due to nasogastric suction or vomiting). Since gastric acid mainly consists of hydrogen chloride (HCl), hypochloremia is expected. Although small quantities of potassium chloride (KCl) are also lost with the gastric fluid, volume depletion, which leads to secondary hyperaldosteronism and, consequently, stimulation of renal potassium excretion is the main cause of hypokalemia associated with continuous nasogastric decompression. Moreover, renal loss of hydrogen ions leads to an increased formation of bicarbonate (HCO3-).

Answers: Q9: C | Q10: D

Diabetic Nephropathy

Q1: A 55-year-old woman is seen in clinic, she has a ten-year history of type 2 diabetes treated with glibenclamide. Her blood pressure is 148/93 with new onset proteinuria, her serum results show elevated lipid levels, glycated haemoglobin of 5.5 per cent and fasting glucose of 6.0 mmol/L. A renal biopsy shows the presence of Kimmelstiel–Wilson lesions. The most appropriate management is:

A. Increase oral hypoglycaemic dosage
B. ACE II antagonists
C. Start cholesterol lowering therapy
D. Start ACE inhibitors
E. Start renal dialysis

Explanation: The mainstay of treatment in diabetic patients with new onset proteinuria is to aggressively control blood pressure, ideally below 130/80 mmHg. ACE inhibitors (D) are therefore first-line therapy, angiotensin receptor blockers can also be used. Oral hypoglycaemic (A) agents should be avoided since they are excreted by the renal system. ACE II antagonists (B) are second- line treatment if there are contraindications to ACE inhibitor use. In patients with persistent proteinuria due to diabetic nephropathy, ACE and ARB may be combined together provided the patient is monitored regularly under specialist care. Renal dialysis (E) is only needed if the patient has progressive end stage renal failure. Cholesterol-lowering therapy (C) would be useful in lowering patient's cardiovascular risk factor but does not help in improving impaired renal function.

Q2: A 19-year-old man is recently diagnosed with type 1 diabetes and attends your clinic to ask about possible complications in the future. He mentions an uncle who has end-stage renal disease due to poorly controlled diabetes and specifically enquires about testing for early signs of renal impairment. The most appropriate investigation is:

A. Blood pressure
B. Microalbuminuria
C. Serum creatinine
D. Serum electrolytes
E. Urine dipstick for glucose

Explanation: Diabetic nephropathy is an insidious complication of diabetes which is often missed since renal compensation can cause patients to present only when they are close to end-stage renal failure. Detection of microalbumin (B) in the urine has been shown to be a good marker for identifying patients most likely at risk of further renal damage. Urine dipsticks are not sensitive enough to detect microalbumin which normally should not be present in the urine. Measurement of blood pressure (A) is a broad marker of cardiovascular integrity. It can both cause and be the product of renal impairment and is not appropriately specific to monitor loss of renal function. Similarly, serum electrolytes (D) such as sodium and potassium can be abnormal due to a number of causes not necessarily related to loss of renal function due to diabetes, for example SIADH. Elevation in serum creatinine (C), which is usually excreted by the kidney, is a late marker of function renal impairment and not appropriate for early risk identification. Urine dipstick for glucose (E) is a screening test for glycaemic control, however, it does not predict specific increased risk for nephropathology but simply increases the likelihood of all diabetic complications.

Q3: A 50-year-old diabetic woman presents for follow-up of her hypertension. Her blood pressure is 152/96 in the office today and she brings in readings from home that are consistently in the same range over the past month. Her current medications are amlodipine 5 mg daily and hydro-chlorothiazide 25 mg daily. The diuretic was added when she developed peripheral edema on the amlodipine; now she has only trace peripheral edema. A spot urine specimen shows 280 µg of albumin per mg creatinine (microalbuminuria is present if this value is between 30 and 300 µg/mg). What would be the best next therapeutic step in this patient?

A. Add clonidine.
B. Add a beta-blocker.
C. Increase the thiazide diuretic dose.
D. Add an alpha-blocker.
E. Add angiotensin-converting enzyme inhibitor or angiotensin receptor blocker.

Explanation: By a variety of mechanisms, angiotensin-converting enzyme inhibitors and angiotensin receptor blockers help to preserve renal function in diabetes. Both classes of medication can cause hyperkalemia, so it is important to monitor serum potassium after initiation. A significant increase in serum creatinine may suggest the presence of renovascular hypertension. A common side effect of ACE inhibitors is a dry cough. A less frequent side effect would be angioedema. Clonidine has not been shown to slow the progression of diabetic renal disease, and often causes orthostatic hypotension, constipation, and erectile dysfunction. Although many diabetic patients receive beta-blockers because of coronary disease, these are not first-line drugs for preventing progression of renal failure. Because of low cost and proven efficacy, thiazide diuretics remain a good choice for the general population, but do not have a specific effect on the progression of renal disease. Short-acting dihydropyri-dine calcium-channel blockers (eg, nifedipine) may increase the incidence of stroke and myocardial infarction, and have no role in the treatment of hypertension.

Answers: Q1:D | Q2: B | Q1: E

Hypertension

Q1: You evaluate a 48-year-old man for chronic renal insufficiency. He has a history of hypertension, osteoarthritis, and gout. He currently has no complaints. His medical regimen includes lisinopril 40 mg daily, hydrochlorothiazide 25 mg daily, allopurinol 300 mg daily, and acetaminophen for his joint pains. He does not smoke but drinks 8 oz of wine on a daily basis. Examination shows BP 146/86, pulse 76, a soft S4 gallop, and mild peripheral edema. There is no abdominal bruit. His UA reveals 1+ proteinuria and no cellular elements. Serum creatinine is 2.2 mg/dL and his estimated GFR from the MDRD formula is 42 mL/minute. What is the most important element is preventing progression of his renal disease?

A. Discontinuing all alcohol consumption
B. Discontinuing acetaminophen
C. Adding a calcium channel blocker to improve blood pressure control
D. Obtaining a CT renal arteriogram to exclude renal artery stenosis
E. Changing the lisinopril to losartan

Explanation: This patient has stage III chronic kidney disease (estimated GFR 30-60 mL/minute). At this stage it is crucial for the internist to prevent progression to end-stage renal disease. Blood pressure control, with a target blood pressure of less than 130 systolic and less than 80 diastolic, is a critical element in his management. The patient is on maximal doses of thiazide and angiotensin-converting inhibitor (ACEI), so the addition of a calcium channel blocker is appropriate. Other important management issues include avoiding nephrotoxins (such as NSAIDs and IV contrast agents), if possible, modest dietary protein restriction, and atherosclerotic risk factor management. If the patient progresses to stage IV CKD (estimated GFR 15-30 mL/minute), he should be referred to a nephrologist.
Modest ethanol consumption is not a renal or cardiovascular risk factor and need not be modified unless you believe the patient is consuming much more alcohol than he admits. Acetaminophen in usual therapeutic doses is the safest agent to control DJD pain and certainly is preferable to nonsteroidals. Angiotensin receptor blockers (such as losartan) can be substituted for ACEIs if side effects such as cough occur, but ARBs have no advantage over ACEIs in preventing progression of CKD. The critical element is tighter blood pressure control.

Q2: A 48-year-old woman has been diagnosed with essential hypertension and was commenced on treatment three months ago. She presents to you with a dry cough which has not been getting better despite taking cough linctus and antibiotics. You assess the patient's medication history. Which of the following antihypertensive medications is responsible for the patient's symptoms?

A. Amlodipine
B. Lisinopril
C. Bendroflumethiazide
D. Frusemide
E. Atenolol

Explanation: ACE inhibitors (e.g. lisinopril (B)) commonly cause a dry cough in some patients. If this occurs, patients are usually taken off the ACEI and started on either an ARB (e.g. irbesartan, losartan, telmisartan) or different class of antihypertensive. Amlodipine (A), bendroflumethiazide (C), frusemide (D) and atenolol (E) do not commonly cause a dry cough as a side effect.

Q3: A 44-year-old woman presents with episodes of headaches, associated with anxiety, sweating and a slow pulse rate. At the time of her initial consultation, her blood pressure was 150/95 mmHg seated, but 24 hour ambulatory monitoring shows a peak of 215/130 mmHg, associated with the symptoms described above. Which of the following would be your initial diagnostic procedure?

A. Magnetic resonance imaging (MRI) scans of the abdomen and pelvis
B. Measurement of random plasma catecholamines
C. Measurement of urinary metanephrines over several 24 hour periods
D. Glucose tolerance test
E. Pharmacological provocation using clonidine

Explanation: Although there is some debate on this issue, the general consensus is that
the best answer is option (C), which is highly sensitive and specific, with levels as much as ten-fold greater than normal. Option (B) may be normal between episodes, option (D) may well be abnormal but would not be diagnostic, and option (E) is not recommended or necessary. Option (A) will be essential once the diagnosis is definite or highly probable.

Answers: Q1: C | Q2: B | Q3: C

Hypertension

Q4: A 57-year-old man is reviewed in a hypertension clinic, where it is found that his blood pressure is 165/105 mmHg despite standard doses of amlodipine, perindopril, doxazosin and bendroflumethiazide. Electrolytes and physical examination have been, and remain, normal. Which of the following would be your next stage in his management?

A. Arrange for his medication to be given under direct observation
B. Add spironolactone to his medication
C. Arrange urinary catecholamine assays
D. Request an adrenal CT scan
E. Add verapamil to his medication

Explanation: Poor adherence to therapy (A) is probably the most common cause of apparent resistance to hypertensive therapy. In cases where this occurs despite good adherence, spironolactone (B) is often highly effective, although it is not clear why. Verapamil (E) is very occasionally added to a dihydropyridine in severe hypertension. If he is already a patient of the hypertension clinic, one can presume that he has been screened for possible secondary causes (C and D), so this is very likely to be primary hypertension.

Q5: A 57-year-old male is admitted complaining of headaches and blurring of vision. His blood pressure is found to be 240/150 mmHg and he has bilateral papilloedema, but is fully orientated and coherent. He had been known to be hypertensive for about five years and his blood pressure control had been good on three drugs. However, he had decided to stop all medication two months before this event. Which of the following would be your preferred parenteral medication at this point?

A. Glyceryl trinitrate
B. Hydralazine
C. Labetalol
D. Sodium nitroprusside
E. Phentolamine

Explanation: It is generally agreed that in situations where relatively rapid bloodpressure lowering is indicated, sodium nitroprusside (D) is the most effective and reliable drug. However, it can only be used safely if there are facilities for continuous intra-arterial blood pressure monitoring, since it can produce very rapid drops in blood pressure which can lead to acute cerebral, cardiac or optic hypoperfusion. GTN (A), hydralazine (B) and labetalol (C) have also been used in hypertensive emergencies but are less reliable, GTN is the drug of second choice. They may be preferred if intensive monitoring is not available. Phentolamine (E) is used in phaeochromocytoma-caused hypertensive crises. It should be noted that the evidence base for the management of hypertensive emergencies is still under review.

Q6: A 55-year-old African American woman presents to the ER with lethargy and blood pressure of 250/150. Her family members indicate that she was complaining of severe headache and visual disturbance earlier in the day. They report a past history of asthma but no known kidney disease. On physical examination, retinal hemorrhages are present. Which of the following is the best approach?

A. Intravenous labetalol therapy
B. Continuous-infusion nitroprusside
C. Clonidine by mouth to lower blood pressure
D. Nifedipine sublingually to lower blood pressure
E. Intravenous loop diuretic

Explanation: Malignant hypertension occurs when diastolic blood pressure above 130 is associated with acute (or ongoing) target-organ damage. This patient shows evidence of damage, namely hypertensive encephalopathy (headache, visual disturbance, and altered mental status). Immediate therapy with nitroprusside in the ICU setting is indicated, although renal insufficiency would be a contraindication. Other options include intravenous nitroglycerin, fenoldopam, or enalapril. Intravenous labetalol is often used in hypertensive urgencies but, as a nonselective beta- blocker, is relatively contraindicated in asthma. An oral medication such as clonidine would be slow- acting and difficult to administer in a lethargic patient. Sublingual nifedipine is no longer advised because of increased potential for overshoot hypotension with adverse cardiovascular events such as MI, stroke, or ischemic optic neuropathy. Loop diuretics do not lower blood pressure rapidly.

Answers: Q4: A | Q5: D | Q6: B

Hypertension

Q7: A 30-year-old construction worker continues to have elevated blood pressure of 180/100 despite of four antihypertensive medications. He was found to be hypertensive at age 17 during a routine physical examination. He has a BMI of 23; the rest of the physical examination is unremarkable. He is taking no over-the-counter medications. Routine blood chemistry are shown below. Which of the following is the best next step?

Sodium: 145 mEq/L
Chloride: 110 mEq/L
Potassium: 3.0 mEq/L
HCO_3: 30 mEq/L
Glucose: 90 mg/dL

A. Add a fifth antihypertensive medication and monitor blood pressure closely.
B. Urinary VMA, metanephrines, and catecholamines.
C. Bilateral renal artery Doppler ultrasound.
D. Polysomnography.
E. Plasma aldosterone concentration to plasma renin activity ratio.

Explanation: This patient likely has secondary hypertension caused by hyperaldosteronism. Resistant hypertension and unprovoked hypokalemia especially in the young should raise this suspicion. In a hypertensive patient with unprovoked hypokalemia (ie, unrelated to diuretics, vomiting, or diarrhea), the prevalence of primary aldosteronism approaches 40% to 50%. Other metabolic derangements such as mild hypernatremia and metabolic alkalosis are sometimes seen. The ratio of plasma aldosterone to plasma renin activity (PA/PRA) is a useful screening test. These measurements are preferably obtained in ambulatory patients in the morning. A ratio greater than 30:1 in conjunction with a plasma aldosterone concentration of greater than 555 pmol/L (20 ng/dL) has a sensitivity of 90% and a specificity of 91%. Urinary VMA, metanephrines, and catecholamines are tests for pheochromocytoma. Patients with pheochromocytoma often present with episodes of palpitations, headaches, and sweating. Bilateral renal artery Doppler is used to diagnose bilateral renal stenosis. Hypertension due to obstruction of a renal artery is a potentially curable form of hypertension. The mechanism of hypertension is generally related to activation of the renin-angiotensin system. Two groups of patients are at risk for this disorder: older arteriosclerotic patients who have a plaque obstructing the renal artery and younger patients, usually female, with fibromuscular dysplasia. Hypertension due to obstructive sleep apnea is increasing in frequency. The severity of hypertension correlates with the severity of sleep apnea. Obesity is an important risk factor. Hypertension related to obstructive sleep apnea should also be considered in patients with drug-resistant hypertension and in patients with a history of snoring. The diagnosis can be confirmed by polysomnography.

Q8: You are seeing for the first time a 45-year-old female patient of your partner. A review of the patient's medical record shows that her systolic blood pressure was greater than 140 mm Hg at both of her last clinic appointments. Her medical history is significant only for diabetes mellitus. Her blood pressure today is 164/92. What is the best next step in her blood pressure management?

A. Ask the patient to keep a written record of her blood pressure and bring with her to a return appointment.
B. Advise the patient to begin a heart healthy, low-sodium diet and refer to a nutritionist.
C. Prescribe an ACE inhibitor in addition to heart healthy diet.
D. Prescribe a dihydropyridine calcium-channel blocker in addition to a heart healthy diet.
E. Arrange for echocardiogram to assess for end-organ damage.

Explanation: Hypertension is defined as elevated blood pressure on two or more separate readings. In a patient with stage 1 HTN and no other cardiac risk factors, consideration may be given to a therapeutic trial of diet and lifestyle modification. This patient, however, has diabetes mellitus. Both the American Diabetes Association and JNC-7 recommend a target blood pressure of 130/80 or lower in patients with diabetes. It is unlikely that the patient will be able to reach target blood pressure with diet and lifestyle modification alone, although these interventions will be important adjunct therapies. The JNC-7 recommends a thiazide diuretic as initial therapy for most patients with hypertension. Patients with diabetes and hypertension, however, benefit more from an ACE inhibitor, especially if they have signs of renal damage (elevated creatinine or proteinuria). There is no contraindication to the use of calcium- channel blockers, but their increased expense without increased benefit would prevent answer d from being correct. Evidence of end-organ damage, such as left ventricular hypertrophy on an echocardiogram, is unlikely to change your initial management.

Q9: A 65-year-old African American man comes to the physician for a follow-up examination after presenting with elevated blood pressure readings during his last visit. He has no history of major medical illness and takes no medications. He is 175 cm (5 ft 9 in) tall and weighs 68 kg (150 lb); BMI is 22 kg/m2. His pulse is 80/min and blood pressure is 155/90 mm Hg. Laboratory studies show no abnormalities. Which of the following is the most appropriate initial pharmacotherapy for this patient?

A. Valsartan
B. Chlorthalidone
C. Captopril
D. Spironolactone
E. Metoprolol

Explanation: According to the American College of Cardiology (ACC) and American Heart Association (AHA), as well as the Eight Joint National Committee (JNC-8), chlorthalidone is a preferred first-line drug for African American patients with isolated hypertension. Thiazide diuretics are considered especially effective antihypertensive agents because impaired salt excretion and subsequent intravascular volume expansion are thought to be the primary drivers of hypertension in this patient group. Valsartan, along with other angiotensin receptor blockers, is indicated for the treatment of hypertension in patients with diabetes mellitus, renal disease, ischemic heart disease, and/or heart failure who do not tolerate ACE inhibitors. This patient does not meet these criteria. As such, valsartan is not a recommended treatment for this patient.

Answers: Q7: E | Q8: C | Q9: B

Hypertension

Q10: A 26-year-old woman, gravida 2, para 1, at 28 weeks' gestation comes to the physician for a prenatal visit. She feels well. Pregnancy and delivery of her first child were uncomplicated. Her temperature is 37.2°C (99°F) and blood pressure is 163/105 mm Hg. Her blood pressure 10 weeks ago was 128/84 mm Hg. At her last visit two weeks ago, her blood pressure was 142/92 mm Hg. Pelvic examination shows a uterus consistent in size with a 28-week gestation. A complete blood count and serum concentrations of electrolytes, creatinine, and hepatic transaminases are within the reference range. A urinalysis is within normal limits. Which of the following is the most appropriate next step in management?

A. Magnesium sulfate therapy
B. Lisinopril therapy
C. Low-dose aspirin therapy
D. Hydralazine therapy
E. Dietary salt restriction

Explanation: Antihypertensive therapy is indicated in all pregnant women with severe gestational hypertension (systolic BP ≥ 160 mm Hg or a diastolic BP ≥ 110 mm Hg). Antihypertensives that can be used during pregnancy include hydralazine, labetalol, methyldopa, and nifedipine. In a patient such as this one, at < 37 weeks of gestation with gestational hypertension but no preeclampsia, treatment can be continued on an outpatient basis. Patients treated on an outpatient basis should be evaluated twice weekly with blood pressure measurement, a urine dipstick test, and blood analysis to rule out preeclampsia. Electronic fetal monitoring (cardiotocography/nonstress test) should be performed weekly, and a transabdominal ultrasound should be performed every 3–4 weeks. ACE inhibitors such as lisinopril and angiotensin receptor blockers are absolutely contraindicated during pregnancy because they can cause permanent renal damage in the fetus as well as congenital malformations of the cardiovascular system and/or CNS.

Answers: Q10: D

General Nephrology

Q1: A 64-year-old man is undergoing treatment for polycythaemia vera with chemotherapy, he has no other medical problems. Shortly after starting treatment, the patient becomes lethargic, feels unwell and suffers weight loss. He attributes this is to the chemotherapy. After 2 weeks, the patient becomes oliguric, complains of bilateral flank pain and becomes oedematous. The most likely diagnosis is:

A. Analgesic nephropathy
B. Renal infarction
C. Hyperuricaemic nephropathy
D. Acute tubulointerstitial nephritis
E. Chronic renal failure

Explanation: Acute hyperuricaemic nephropathy (C) is a common finding in patients suffering from hyperuricaemia. This is a common occurrence in patients with increased cell turnover, such as myeloproliferative disorders or following chemotherapy. Uric acid crystallizes within the renal system causing obstructions which can manifest as flank pain, oliguria, hypertension, oedema and uraemic symptoms. Analgesic nephropathy (A) is usually due to chronic NSAID intake causing papillary necrosis and tubulointerstitial nephritis. Presentation can include anaemia, urinary tract infections and haematuria. Acute tubulointerstitial nephritis (D) is a drug hypersensitivity reaction, usually due to penicillin or NSAID medication. Patients typically present with fever, skin rashes and joint pain alongside an eosinophilia. Renal infarction (B) can be a difficult diagnosis to make due to the broad clinical presentation that can result, dependent on the degree of ischaemia and necrosis that may occur. In moderate to severe arterial occlusion, patients may present with pain affecting the back, abdomen or flanks. Patients will often have several cardiovascular risk factors that predispose them to thromboembolism, such as atrial fibrillation, clotting abnormalities, etc. In this patient, polycythaemia alone is unlikely to have caused a severe acute renal infarction in both kidneys and, given the recent commencement of chemotherapy, an acute hyperuricaemic nephropathy is more likely. Another potential differential is renal vein thrombosis. Chronic renal failure (E) occurs as a long-standing illness causing significant reduction in renal function, usually in an insidious manner rather than the abrupt situation in this case.

Q2: A 55-year-old man with a 15-year history of type 2 diabetes mellitus and hypertension is evaluated during a new-patient visit. He reports no symptoms other than ankle edema. A review of his medical records documents the presence of microalbuminuria 5 years ago. His medications are amlodipine, chlorthalidone, simvastatin, metformin, and glargine insulin.On physical examination, temperature is 37.1°C (97.8°F), blood pressure is 150/95 mm Hg, pulse is 80/min, and respiration rate is 12/min. Cardiopulmonary examination is normal. He has trace pretibial edema. The patient is prescribed losartan 25 mg/d. He returns in 3 weeks for a repeat blood pressure check. The average of two blood pressure recordings is 145/88 mm Hg. The serum potassium level is 4.4 meq/L (4.4 mmol/L) and the serum creatinine level is 2.0 mg/dL (177 µmol/L). Which of the following is the most appropriate next step in this patient's management?

A. Add lisinopril
B. Discontinue losartan
C. Increase the dose of losartan
D. Schedule a renal biopsy

Potassium	4.2 meq/L (4.2 mmol/L)
Creatinine	1.8 mg/dL (186 µmol/L)
Urine protein-creatinine ratio	1 mg/mg

Explanation: The most appropriate next management step is to increase the dose of the losartan. Uncontrolled hypertension and proteinuria are important modifiable risk factors for progressive kidney disease. Lowering blood pressure is critical regardless of the underlying disease. For patients with chronic kidney disease, guidelines recommend blood pressure targets of less than 130/80 mm Hg or less than 125/75 mm Hg when significant proteinuria is present. Angiotensin-converting enzyme inhibitors, such as lisinopril, and angiotensin receptor blockers (ARBs), such as losartan, are the preferred agents in chronic kidney disease and slow progression of kidney disease in patients with diabetes. These agents reduce efferent arteriolar resistance and lower intraglomerular pressure and, therefore, may be associated with increases in serum creatinine in patients with a reduced glomerular filtration rate. An increase in creatinine of up to 30% is acceptable. In this patient, blood pressure remains elevated and he has significant proteinuria. The most logical next step would be to increase losartan. It is not necessary to discontinue losartan, because the increase in creatinine is not unexpected and his potassium remains at an acceptable level. Results from a recent study, which involved elderly patients at high risk for cardiovascular events, indicate the use of combination ACE inhibitor and ARB therapy does not reduce morbidity and mortality and furthermore increases adverse side effects compared with the use of ACE inhibitors alone. Further studies are warranted before combination therapy can be recommended. The clinical course and long-standing diabetes progressing to microalbuminuria and then to overt proteinuria and loss of kidney function over a period of years strongly suggests diabetic nephropathy. Kidney biopsy would be unlikely to change the long-term management in this patient.

Key Point In patients with proteinuria and chronic kidney disease, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers should be used to lower blood pressure, decrease proteinuria, and slow disease progression.

Answers: Q1: C | Q2: C

General Nephrology

Q3: A 56-year-old man presents with hypertension and peripheral edema. He is otherwise healthy and takes no medications. Family history reveals that his father and a brother have kidney disease. His father was on hemo-dialysis before his death at age 68 of a stroke. Physical examination reveals BP 174/96 and AV nicking on funduscopic examination. He has a soft S 4 gallop. Bilateral flank masses measuring 16 cm in length are palpable. Urinalysis shows 15 to 20 RBC/hpf and trace protein but is otherwise normal; his serum creatinine is 2.4 mg/dL. Which is the most likely long-term complication of his condition?

A. End-stage renal disease requiring dialysis or transplantation
B. Malignancy
C. Ruptured cerebral aneurysm
D. Biliary obstruction owing to cystic disease of the pancreas
E. Dementia

Explanation: This patient has adult polycystic kidney disease (APCKD), an autosomal dominant condition. It is the commonest genetic renal disease causing ESRD and often presents with hypertension, hematuria, and large palpable kidneys. Imaging studies would confirm the diagnosis by showing numerous bilateral renal cortical cysts. Cysts are often seen in the liver and pancreas but rarely cause symptoms. Most patients progress to end-stage renal disease despite meticulous blood pressure control with ACE inhibitors or angiotensin receptor blockers.
About 10% of patients with adult PCK disease harbor berry aneurysms in the circle of Willis; a ruptured berry aneurysm may have accounted for his father's stroke. APCKD patients also have an increased incidence of abdominal and thoracic aneurysms as well as diverticulosis. The abnormal gene, on chromosome 16 in 85% of patients, appears to encode a structural protein that helps keep the renal tubules open and unobstructed. This same protein provides strength to the walls of arteries and other epithelial structures (pancreatic ductules, bile ductules, colon). Malignancy and dementia are not seen with increased incidence in APCKD patients.

Q4: A 65-year-old diabetic man with a creatinine of 1.6 was started on an angiotensin-converting enzyme inhibitor for hypertension and presents to the emergency room with weakness. His other medications include atorvastatin for hypercholesterolemia, metoprolol and spironolactone for congestive heart failure, insulin for diabetes, and aspirin. Laboratory studies include: Which of the following is the most likely cause of hyperkalemia in this patient?

A. Worsening renal function
B. Uncontrolled diabetes
C. Statin-induced rhabdomyolysis
D. Drug-induced effect on the renin-angiotensin-aldosterone system
E. High-potassium diet

Explanation: The syndrome of hyporeninemic hypoaldosteronism occurs in older diabetic patients, particularly males with congestive heart failure. The syndrome often presents when aggravating drugs are added. Beta-blockers impair renin secretion; ACE inhibitors decrease aldosterone levels; and spironolactone competes for the aldosterone receptor. Combined with diabetes and mild renal insufficiency, the result may be life-threatening hyperkalemia. Moderate renal insufficiency per se is unlikely to cause such severe hyperkalemia. Hypertonicity caused by hyperglycemia could aggravate hyperkalemia, but a blood glucose of 250 mg/dL should not cause severe hyperkalemia. Statin drugs may cause muscle injury and rhabdomyolysis, but a CK of 400 IU/L is a modest elevation (probably caused by the renal insufficiency) and would not cause severe hyperkalemia. A high-potassium diet may contribute modestly to hyperkalemia but is rarely a major factor by itself.

Q5: A 21-year-old man complains his urine has turned a faint red in the last week. He denies any significant changes in his diet or lifestyle and has no other medical problems except for sensorineural deafness diagnosed when he was young. On examination, you notice retinal flecks and urine dipstick confirms protein and blood.
The most likely diagnosis is:

A. Alport's syndrome
B. Benign familial haematuria
C. Wolfram syndrome
D. IgA nephropathy
E. Down's syndrome

Explanation: Alport syndrome (A) is caused by a genetic defect in type IV collagen
synthesis causing the triad of herediatary nephritis, sensorineural deafness and ocular abnormalities which can include cataracts and macular retinal flecks. Renal abnormalities are progressive in such patients and include proteinuria, haematuria and eventually renal failure. Thin basement membrane nephropathy or benign familial haematuria (B) is a common cause of asymptomatic haematuria. Apart from glomerular basement membrane thinning, there are no other associated abnormalities and patients have an excellent prognosis. IgA nephropathy (D) is the most common cause of glomerulonephritis and one of the most common causes for asymptomatic haemauria. Glomerular attacks occur episodically and, during these, haematuria presents. Features such as retinal flecks are not present. Wolfram syndrome (C) is a rare genetic disease that causes diabetes insipidus, diabetes mellitus, optic atrophy and deafness. This is not likely given the absence of glucose on urine dipstick. Patients suffering from Down's syndrome (E) have a range of abnormalities and are often recognized from their characteristic facial appearance. The kidney, however, tends to be spared in such patients. Brushfield spots may be mistaken for retinal flecks in such patients and while sensorineural deafness can occur in Down's syndrome, this is not congenital as occurs in Alport's syndrome.

Answers: Q3:A | Q4:D | Q5:A

General Nephrology

Q6: A 63-year-old woman presents in accident and emergency with a 3-day history of worsening abdominal pain and mild flank pain. Examination reveals pain in the suprapubic region, but otherwise the abdomen is soft with no masses. The patient denies any other symptoms, such as dysuria, but mentions she has had difficulty passing urine in the last week and is only able to provide a small urine sample which is odorous and bloody. She has no other medical problems, but admits to being a long-term smoker. An ultrasound scan of renal system is most likely to show:

A. Bladder dilation
B. Ureteral stricture
C. Bilateral hydronephrosis
D. Renal cysts
E. Renal cancer

Explanation: This patient is suffering from acute urinary retention most likely due to bladder malignancy. The obstruction to urine outflow causes urine to accumulate within the bladder and then create a back-pressure upon the kidneys resulting in bilateral hydronephrosis (C). In comparison, the bladder is a strong muscular organ which requires a significant build up of pressure before it becomes dilated (A). A ureteral stricture (B) is more likely to be painful and cause asymmetrical dilation of kidney. Renal cancer (E) presents characteristically with a palpable mass with pain normally localized to the flanks. Renal cysts (D) are usually asymptomatic and also do not normally cause suprapubic pain.

Answers: Q6: C | Q4:D | Q5:A