Question 1

A 43-year-old man is evaluated during a routine physical examination. He has no current symptoms and no prior medical history. Family history is notable for diabetes mellitus and hypertension in two first-degree relatives. He takes no medications.

On physical examination, initial blood pressure measurement is 144/86 mm Hg; repeat measurement after 5 minutes of rest are 136/86 mm Hg and 134/88 mm Hg. BMI is 32. The remainder of the examination is normal.

Laboratory studies show normal serum creatinine and plasma glucose levels.

In addition to lifestyle modifications, which of the following is the most appropriate next step in the management of this patient's blood pressure?

A
Initiate a low-dose ACE inhibitor

B
Initiate low-dose chlorthalidone

C
Order ambulatory blood pressure monitoring

D
Recheck blood pressure in 1 year

Answer & Critique

Correct Answer: D

Educational Objective: Manage prehypertension.

Key Point

Prehypertension is managed with lifestyle modifications and annual follow-up visits to monitor blood pressure.

In addition to lifestyle modifications, rechecking blood pressure in 1 year is appropriate for this patient with prehypertension. Although the eighth report of the Joint National Committee (JNC) did not address prehypertension, JNC 7 defined prehypertension as a systolic blood pressure of 120-139 mm Hg or a diastolic blood pressure of 80-89 mm Hg in the absence of preexisting end-organ disease (for example, diabetes mellitus, chronic kidney disease, or cardiovascular disease). Lifestyle modifications, including a low salt diet and exercise regimen, can be used to effectively reduce blood pressure in patients with prehypertension. Patients with prehypertension may also adopt the DASH (Dietary Approaches to Stop Hypertension) diet, which emphasizes vegetables, fruits, whole grains, legumes, and low-fat dairy products and limits sweets, red meat, and saturated/total fat, along with dedicated weight loss planning. Appropriate follow-up for those with prehypertension occurs at annual visits. The mean blood pressure in this patient (even accounting for the potential of inaccurate technique upon initial check-in) falls within the prehypertensive range, making lifestyle modifications and follow-up in 1 year the appropriate management. If blood pressures measuring 140/90 mm Hg or greater were documented, this would require repeat measurements for at least three visits over the period of at least 1 week of more to establish a diagnosis of hypertension.

Although there is an increased risk of stroke and cardiovascular disease for every level of blood pressure above 115/75 mm Hg and an increased risk of the development of hypertension, treatment of prehypertension using pharmacologic therapy (such as an ACE inhibitor or diuretic) has not yet been demonstrated to reduce this risk.

Ambulatory blood pressure monitoring records blood pressures periodically during normal activities. It is indicated primarily for diagnosis of suspected white coat hypertension (persistently

elevated blood pressure readings in the office without evidence of end-organ damage) or to confirm a poor response to antihypertensive medication. It may also be useful in assessing for masked hypertension (evidence of end-organ damage without apparent elevated blood pressures) or for evaluating episodic or resistant hypertension. It is not indicated for this patient with evidence of prehypertension.

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Question 2

A 74-year-old woman is evaluated for a 1-week history of intermittent painless gross hematuria. She has a 3-year history of stage G4/A3 chronic kidney disease due to diabetic nephropathy, a 12-year history of type 2 diabetes mellitus, diabetic retinopathy, and hypertension. Medications are lisinopril, furosemide, insulin glargine, and insulin lispro.

On physical examination, temperature is 37.0 °C (98.6 °F), blood pressure is 128/85 mm Hg, pulse rate is 76/min, and respiration rate is 15/min. BMI is 28. The lungs are clear. There are no abdominal masses or costovertebral angle tenderness. There is no edema.

Laboratory studies:

Creatinine	2.6 mg/dL (230 µmol/L)
Estimated glomerular filtration rate	23 mL/min/1.73 m^2
Urinalysis	2+ protein; 25-50 erythrocytes/hpf; 0 leukocytes/hpf; no erythrocyte casts

Which of the following is the most appropriate diagnostic test to perform in this patient?

A
Contrast-enhanced CT of the abdomen and pelvis

B
Gadolinium-enhanced MRI of the abdomen and pelvis

C
Radiography of the abdomen and pelvis

D
Ultrasonography of the abdomen and pelvis

Answer & Critique

Correct Answer: D

Educational Objective: Select the most appropriate imaging modality for a patient with chronic kidney disease.

Key Point

Ultrasonography is an appropriate imaging modality for patients with chronic kidney disease to avoid adverse events such as contrast-induced nephropathy or nephrogenic systemic fibrosis.

Ultrasonography of the abdomen and pelvis is appropriate for this patient with chronic kidney disease (CKD). She requires imaging studies to evaluate her kidneys and genitourinary tract in order to rule out a structural lesion or tumor as the source of gross hematuria. Ultrasonography is an appropriate initial screening test because it can provide necessary information without exposure to the risks associated with the administration of contrast agents in patients with severe CKD who are at increased risk of contrast-induced nephropathy (CIN) and gadolinium-induced nephrogenic systemic fibrosis (NSF).

This patient has risk factors for CIN (older age, elevated serum creatinine, diabetes mellitus); therefore, a contrast-enhanced CT to evaluate for lesions of the kidneys and genitourinary tract as a cause of her hematuria should be performed only if similar information cannot be obtained from tests that entail less risk to the patient.

The use of gadolinium in MRI studies is relatively contraindicated in patients with an estimated glomerular filtration rate of less than 30 mL/min/1.73 m^2 due to the increased risk of NSF. Although most NSF cases have occurred in patients with end-stage kidney disease, there have been isolated case reports occurring in patients with stage G4 CKD. Gadolinium-enhanced MRI is therefore contraindicated in these patients unless there is a compelling clinical indication and the patient is fully informed of the risk of NSF.

Radiography of the abdomen and pelvis may be a reasonable test to rule out nephrolithiasis. However, the patient does not have symptoms suggestive of nephrolithiasis, and a plain radiograph would not provide information to determine whether there are structural lesions in the kidneys or genitourinary tract.

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Answer & Critique

Correct Answer: D

Educational Objective: Select the most appropriate imaging modality for a patient with chronic kidney disease.

Key Point

Ultrasonography is an appropriate imaging modality for patients with chronic kidney disease to avoid adverse events such as contrast-induced nephropathy or nephrogenic systemic fibrosis.

Ultrasonography of the abdomen and pelvis is appropriate for this patient with chronic kidney disease (CKD). She requires imaging studies to evaluate her kidneys and genitourinary tract in order to rule out a structural lesion or tumor as the source of gross hematuria. Ultrasonography is an appropriate initial screening test because it can provide necessary information without exposure to the risks associated with the administration of contrast agents in patients with severe CKD who are at increased risk of contrast-induced nephropathy (CIN) and gadolinium-induced nephrogenic systemic fibrosis (NSF).

This patient has risk factors for CIN (older age, elevated serum creatinine, diabetes mellitus); therefore, a contrast-enhanced CT to evaluate for lesions of the kidneys and genitourinary tract as a cause of her hematuria should be performed only if similar information cannot be obtained from tests that entail less risk to the patient.

The use of gadolinium in MRI studies is relatively contraindicated in patients with an estimated glomerular filtration rate of less than 30 mL/min/1.73 m^2 due to the increased risk of NSF. Although most NSF cases have occurred in patients with end-stage kidney disease, there have been isolated case reports occurring in patients with stage G4 CKD. Gadolinium-enhanced MRI is therefore contraindicated in these patients unless there is a compelling clinical indication and the patient is fully informed of the risk of NSF.

Radiography of the abdomen and pelvis may be a reasonable test to rule out nephrolithiasis. However, the patient does not have symptoms suggestive of nephrolithiasis, and a plain radiograph would not provide information to determine whether there are structural lesions in the kidneys or genitourinary tract.

Question 3

A 45-year-old man is evaluated during a new patient visit. He immigrated to the United States from Serbia 4 years ago and was diagnosed with Balkan endemic nephropathy at that time. His kidney function has remained stable, and his only symptoms are mild nocturia and urinary frequency. Medical history is otherwise unremarkable. He takes no medications.

On physical examination, temperature is 37.1 °C (98.7 °F), blood pressure is 138/82 mm Hg, pulse rate is 76/min, and respiration rate is 12/min. BMI is 26. The remainder of the examination is normal.

Laboratory studies:

Hemoglobin	9.6 g/dL (96 g/L)
Electrolytes	Normal
Creatinine	1.7 mg/dL (150.1 µmol/L)
Glucose	Normal
Estimated glomerular filtration rate	35 mL/min/1.73 m^2
Urinalysis	Specific gravity 1.005; 2+ glucose; 10-20 erythrocytes/hpf

An increased risk of which of the following is most likely in this patient?

A
Diabetes mellitus

B
Intracranial cerebral aneurysm

C
Renal cell carcinoma

D
Transitional cell carcinoma

Answer & Critique

Correct Answer: D

Educational Objective: Identify the increased risk for transitional cell carcinoma in patients with Balkan endemic nephropathy.

Key Point

Patients with Balkan endemic nephropathy are at increased risk for transitional cell carcinomas of the renal pelvis, ureters, and bladder.

This patient has Balkan endemic nephropathy (BEN) and is at increased risk for transitional cell carcinoma. BEN is a slowly progressive tubulointerstitial disease that has recently been linked to aristolochic acid. Aristolochic acid is a nephrotoxic alkaloid from the plant *Aristolochia clematis*, which is endemic to the Balkan region and is sometimes a component of herbal therapies used for weight loss. BEN is believed to be due to exposure to low levels of aristolochic acid over years, compared with more acute toxicity associated with ingestion of herbal preparations. Characteristics of BEN include chronic kidney disease due to tubulointerstitial injury, tubular dysfunction (polyuria and decreased concentrating ability, glucosuria without hyperglycemia, and tubular proteinuria), and anemia. Because aristolochic acid is also mutagenic, patients with BEN are at increased risk for transitional cell carcinomas of the renal pelvis, ureters, and bladder. Therefore, annual surveillance with urine cytology is recommended.

Although this patient has glucosuria, BEN is not associated with an increased incidence of diabetes mellitus. The glucosuria is due to a tubular defect, resulting in glucosuria with normoglycemia.

Intracranial cerebral aneurysms are associated with autosomal dominant polycystic kidney disease, which is characterized by large kidneys with multiple kidney cysts.

Patients with BEN are at higher risk for transitional cell carcinoma, not renal cell carcinoma.

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Question 4

A 64-year-old man is evaluated for a 6-week history of intermittent red-colored urine. He notes fatigue but otherwise feels well. Medical history includes hypertension, mechanical mitral valve replacement due to myxomatous degeneration, and calcium oxalate nephrolithiasis. He is a current smoker with a 60-pack-year history. Medications are amlodipine, warfarin, and aspirin.

On physical examination, temperature is 37.6 °C (99.7 °F), blood pressure is 112/72 mm Hg, and pulse rate is 98/min. BMI is 30. Examination of the heart reveals a metallic click with a grade 2/6 cardiac systolic murmur that radiates to the axilla. The lungs are clear. There is no costovertebral angle tenderness. The remainder of the examination is unremarkable.

Urinalysis is dipstick positive for 3+ blood, 1+ protein, and no leukocyte esterase or nitrites; on microscopic examination, there are no cells or casts, although calcium oxalate crystals are seen.

Which of the following is the most likely cause of this patient's clinical f indings?

A
Bladder cancer

B
Glomerulonephritis

C
Hemoglobinuria

D
Nephrolithiasis

Answer & Critique

Correct Answer: C

Educational Objective: Diagnose hemoglobinuria.

Key Point

Hemoglobinuria is distinguished from true hematuria by the absence of erythrocytes on urine microscopy.

This patient most likely has hemoglobinuria, possibly due to intravascular hemolysis from his mechanical mitral valve, whose dysfunction is suggested by the finding of mitral regurgitation on physical examination. Fragmentation hemolysis in this setting manifests as a microangiopathic hemolytic anemia with thrombocytopenia and is accompanied by the release of free hemoglobin into the circulation. Free hemoglobin is partially bound by haptoglobin but may also be filtered into the urine, producing a red color. Heme reacts with peroxidase in the urine dipstick, causing a false-positive result for blood. Hemoglobinuria is distinguished from true hematuria by the absence of erythrocytes on urine microscopy. Similar findings on urinalysis will also occur with the release of myoglobin into the circulation, usually from muscle injury (rhabdomyolysis). Myoglobin is a small molecule relative to hemoglobin, is not bound within the circulation by haptoglobin, and is readily filtered through the kidneys, resulting in red-colored urine. It also reacts with peroxidase in the urine dipstick indicating blood, although microscopic examination will also be negative for erythrocytes.

Bladder cancer is a concern in a patient with a significant smoking history presenting with a finding of red urine. However, the urine color change in bladder cancer is due to bleeding into the urinary tract, and erythrocytes would be seen on urinalysis.

Glomerulonephritis may be associated with bleeding into the urine and would be suspected if erythrocytes, particularly acanthocytes (dysmorphic erythrocytes), were found on urine microscopic examination. Proteinuria may also be found in glomerulonephritis, although this patient's proteinuria is relatively mild and may result from tubular damage caused by hemoglobin toxicity.

Nephrolithiasis often presents with true hematuria in association with acute flank pain radiating to the ipsilateral groin, with or without costovertebral angle tenderness. Despite his history of nephrolithiasis, this patient does not have suggestive clinical symptoms and has no evidence of erythrocytes on urinalysis, making this an unlikely diagnosis.

Question 5

A 62-year-old man is evaluated during a follow-up visit for hypertension. His clinic blood pressure readings during the past year have been persistently above 140/90 mm Hg, and home blood pressure readings have been in the range of 150-170/90-96 mm Hg. He reports no symptoms. Medical history is otherwise unremarkable. Medications are maximal doses of lisinopril, nifedipine, and atenolol.

On physical examination, temperature is 36.8 °C (98.2 °F), blood pressure is 168/100 mm Hg in both arms with no orthostasis, pulse rate is 60/min, and respiration rate is 16/min. BMI is 29. Retinal examination shows copper wiring of the arteries. An S_4 is heard on cardiac auscultation. There are no bruits heard over the carotids or abdomen. Neurologic and peripheral vascular examinations are normal. There is no edema.

Laboratory studies:

Creatinine	1.5 mg/dL (132.6 µmol/L)
Potassium	4.1 mEq/L (4.1 mmol/L)
Estimated glomerular filtration rate	45 mL/min/1.73 m^2
Urinalysis	No protein, blood, or cells

Electrocardiogram shows left ventricular hypertrophy with repolarization abnormalities. Kidney ultrasound is normal.

Which of the following is the most appropriate next step in management?

A

Add chlorthalidone

B

Add clonidine transdermal patch

C

Add minoxidil

D

Switch nifedipine to amlodipine

\\\

Answer & Critique

Correct Answer: A

Educational Objective: Treat a patient with uncontrolled hypertension.

Key Point

Diuretics are almost always required to achieve adequate blood pressure control in patients with resistant blood pressure.

The addition of chlorthalidone is the most appropriate next step in management in this patient who has uncontrolled hypertension with evidence of end-organ damage (left ventricular hypertrophy, chronic kidney disease, and retinopathy) despite being on three medications. However, he does not meet the definition of resistant hypertension, which is defined by blood pressure readings not at target despite three agents, one of which must be a diuretic. Persistent volume expansion, even if not sufficient to produce clinically evident edema, contributes significantly to hypertension; because of this, use of diuretics is almost always required to achieve adequate blood pressure control in patients with resistant blood pressure. Therefore, the addition of a diuretic such as chlorthalidone is appropriate for this patient before other drugs are added. Chlorthalidone is often preferred over other thiazide-type diuretics primarily due to its higher potency and longer duration of action.

Although limited data exist regarding the most effective medication regimen for patients requiring multi-drug therapy, a reasonable approach is to use medications recommended by hypertension treatment guidelines that have different mechanisms of action, with consideration of other agents with an antihypertensive effect indicated for treatment of comorbid conditions (such as a β-blocker for atrial fibrillation). For example, in addition to diuretic therapy, the combination of a long-acting dihydropyridine calcium channel blocker with an ACE inhibitor or angiotensin receptor blocker is often effective and generally well tolerated.

Vasodilator agents (hydralazine or minoxidil) and centrally acting agents (clonidine or guanfacine) may be effective, although side effects are common. Therefore, these medications are more commonly used as add-on therapy to other guideline-recommended agents and would not be an appropriate choice in this patient who is not currently on a diuretic. Additionally, minoxidil promotes sodium retention and is almost always given with a diuretic. Its use in this patient who is not taking a diuretic would not be appropriate.

Switching from nifedipine to amlodipine would not be expected to significantly improve blood pressure because both drugs are in the same class.

Question 6

A 68-year-old man is evaluated for a 6-month history of progressive dyspnea on exertion, dizziness on standing, lower extremity edema, and burning pain with numbness in his extremities. He also notes intermittent loose stools up to 6 times daily. Medical history is otherwise unremarkable, and he takes no medications. He is current with scheduled health maintenance screening interventions, and laboratory studies obtained 3 years ago for an insurance physical examination were normal.

On physical examination, temperature is normal, pulse rate is 90/min, and respiration rate is 20/min. Blood pressure is 140/70 mm Hg sitting; upon standing, blood pressure drops to 90/60 mm Hg with dizziness. BMI is 27. Estimated central venous pressure is 7 cm H_2O. Decreased breath sounds are heard at the lung bases bilaterally. Heart examination does not reveal a rub or gallop. Abdominal examination reveals mild hepatosplenomegaly. On neurologic examination, there is impaired touch and vibration sense in a glove and stocking distribution. Bilateral lower extremity edema is noted to the level of the ankles.

Laboratory studies:

Albumin	2.8 g/dL (28 g/L)
Creatinine	1.6 mg/dL (141.4 μmol/L)
Electrolytes	Normal
Fasting plasma glucose	98 mg/dL (5.4 mmol/L)
Urinalysis	3+ protein; no blood or cells
Urine protein-creatinine ratio	4800 mg/g

Which of the following is the most likely diagnosis on kidney biopsy?

A
AL amyloidosis

B
Diabetic nephropathy

C

Myeloma nephropathy

D

Primary focal segmental glomerulosclerosis

Answer & Critique

Correct Answer: A

Educational Objective: Diagnose AL amyloidosis with kidney manifestations.

Key Point

In amyloidosis involving the kidney, glomerular lesions tend to be prominent and present with proteinuria, often in the nephrotic range.

AL amyloidosis secondary to a plasma cell dyscrasia is the most likely diagnosis. Amyloid consists of randomly oriented fibrils composed of various proteins that form organized ?-pleated sheets within the tissues; amyloid resulting from monoclonal lambda or kappa light chains is termed*AL amyloid*. AL amyloid may present with nonspecific systemic symptoms such as fatigue or weight loss, but most commonly presents with symptoms associated with infiltration of different organ systems. These may include restrictive cardiomyopathy, peripheral neuropathy, hepatosplenomegaly, and, less commonly, cutaneous purpura and macroglossia. In amyloidosis involving the kidney, glomerular lesions tend to be prominent and present with proteinuria, often in the nephrotic range. However, amyloid deposits may also be found in tubular basement membranes, the interstitial space, and blood vessels. Findings on biopsy show deposits that stain apple green on Congo red staining under a polarizing microscope; these deposits are also visible on electron microscopy. In this patient, the presence of the nephrotic syndrome, autonomic symptoms (diarrhea and postural hypotension), and sensory neuropathy is highly suggestive of AL amyloidosis.

Although diabetes mellitus may present with similar systemic manifestations, such as autonomic and peripheral neuropathy and the nephrotic syndrome, these manifestations are typically seen after many years of diabetes, and this patient does not have evidence of diabetes on his current laboratory studies or on prior studies.

Myeloma nephropathy results from filtering of myeloma light chains with minimal albumin, with the light chains accumulating in the renal tubule causing tubular injury and typically forming casts (cast nephropathy). Filtered light chains are often not detected on routine dipstick testing and require identification with urine electrophoresis. The degree of albuminuria seen in this patient is less consistent with the findings typically seen in myeloma nephropathy.

Primary focal segmental glomerulosclerosis is a kidney-limited disease and is not associated with the systemic manifestations exhibited in this patient.

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Question 7

A 55-year-old woman is evaluated for persistent hyperkalemia. She is asymptomatic. Medical history is significant for type 2 diabetes mellitus complicated by nephropathy and peripheral neuropathy; she also has hypertension. Medications are insulin, rosuvastatin, amlodipine, amitriptyline, and aspirin.

On physical examination, temperature is 36.3 °C (97.4 °F), blood pressure is 130/72 mm Hg, pulse rate is 64/min, and respiration rate is 18/min. BMI is 32. Estimated central venous pressure is 6.0 cm H_2O. There is hyperesthesia of the feet bilaterally but no edema. The remainder of the examination is unremarkable.

Laboratory studies:

Creatinine	1.9 mg/dL (168 µmol/L)
Electrolytes:	
Sodium	138 mEq/L (138 mmol/L)
Potassium	5.1 mEq/L (5.1 mmol/L)
Chloride	112 mEq/L (112 mmol/L)
Bicarbonate	18 mEq/L (18 mmol/L)
Glucose	142 mg/dL (7.9 mmol/L)
Phosphorus	4.5 mg/dL (1.5 mmol/L)
Estimated glomerular filtration rate	27 mL/min/1.73 m^2
Urinalysis	pH 5.0

Which of the following is the most likely cause of this patient's metabolic findings?

A Kidney failure
B Type 1 (hypokalemic distal) renal tubular acidosis
C Type 2 (proximal) renal tubular acidosis
D Type 4 (hyperkalemic distal) renal tubular acidosis

Answer & Critique

Correct Answer: D

Educational Objective: Diagnose type 4 (hyperkalemic distal) renal tubular acidosis.

Key Point

Patients with type 4 (hyperkalemic distal) renal tubular acidosis typically present with hyperkalemia, a normal anion gap metabolic acidosis, and impaired urine acidification, but with the ability to maintain the urine pH to <5.5.

Type 4 (hyperkalemic distal) renal tubular acidosis (RTA) is the most likely cause of this patient's metabolic findings. Type 4 (hyperkalemic distal) RTA is caused by aldosterone deficiency or resistance. Primary aldosterone deficiency is seen in primary adrenal deficiency (Addison disease), and relative aldosterone deficiency may be seen in the syndrome of hyporeninemic hypoaldosteronism in which there is diminished renin release by the kidney. This occurs most commonly in patients with mild to moderate kidney disease due to diabetic nephropathy (such as this patient) or chronic interstitial nephritis (such as in systemic lupus erythematosus or AIDS). It may also be associated with acute glomerulonephritis, specific drugs that impair renin release (NSAIDs and calcineurin inhibitors), tubulointerstitial disease, and drugs that reduce aldosterone production (ACE inhibitors, cyclooxygenase inhibitors, and heparin). Patients with type 4 (hyperkalemic distal) RTA typically present with hyperkalemia, a normal anion gap metabolic acidosis, and impaired urine acidification, but with the ability to maintain the urine pH to <5.5. The specific cause can be differentiated by measurement of plasma renin activity, serum aldosterone, and serum cortisol. Initial treatment includes correction of the underlying cause if possible, with discontinuation of offending medications. Replacement of mineralocorticoids with fludrocortisone is indicated for patients with documented deficiency and should be considered for those with hyporeninemic hypoaldosteronism unless hypertension or heart failure is present.

Although kidney failure may cause hyperkalemia and metabolic acidosis, the acidosis associated with kidney failure more commonly reflects an increase in the anion gap with impaired organic acid excretion.

Type 1 (hypokalemic distal) RTA results from a defect in urine acidification in the distal tubule with impaired excretion of hydrogen ions and a normal anion gap metabolic acidosis. However, this tubular defect also results in potassium wasting and hypokalemia, which are not present in this patient.

Type 2 (proximal) RTA involves a defect in regenerating bicarbonate in the proximal tubule and is characterized by hypokalemia, glycosuria (in the setting of normal plasma glucose), low-molecular-weight proteinuria, and renal phosphate wasting, none of which is present in this patient.

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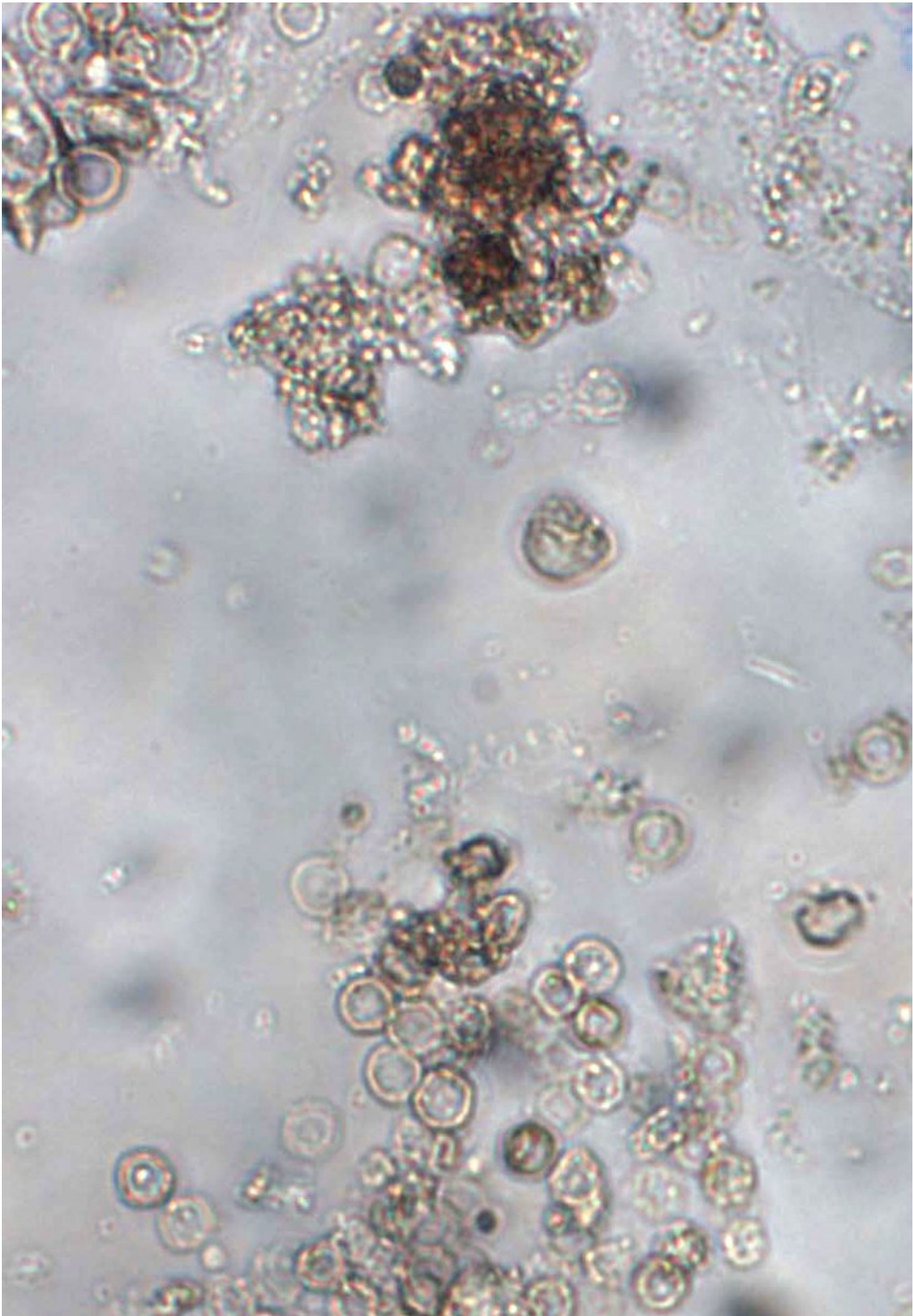
Question 8

A 37-year-old woman is evaluated for an episode of blood in her urine. She notes the passage of red-colored urine that resolved spontaneously and was not associated with her menstrual cycle. She reports having had several similar episodes in the past. She has no other symptoms such as abdominal pain or dysuria. Medical history is otherwise unremarkable, and she takes no medications.

On physical examination, the patient is afebrile. Blood pressure is 128/78 mm Hg, pulse rate is 82/min, and respiration rate is 13/min. Cardiopulmonary and abdominal examinations are normal. There is no flank tenderness to palpation. The remainder of the examination is unremarkable.

Laboratory studies show a normal complete blood count and metabolic profile and a serum creatinine level of 0.9 mg/dL (79.6 μmol/L). Dipstick urinalysis is positive for blood and protein but is negative for leukocyte esterase and nitrites.

Microscopy of the urine sediment is shown.



Which of the following is the most appropriate next step in the evaluation of this patient?

A
Cystoscopy

B
Evaluation for glomerular disease

C
Noncontrast helical abdominal CT

D
Serum creatine kinase measurement

Answer & Critique

Correct Answer: B

Educational Objective: Differentiate between glomerular and nonglomerular hematuria.

Key Point

Glomerular hematuria typically features brown- or tea-colored urine with dysmorphic erythrocytes (or acanthocytes) and/or erythrocyte casts on urine sediment examination.

Evaluation for glomerular disease is the most appropriate next step for this patient. An initial step in evaluating hematuria is assessing whether the likely source of bleeding is from the glomerulus or elsewhere in the urinary tract. Glomerular hematuria is typically characterized by brown- or tea-colored urine with dysmorphic erythrocytes (or acanthocytes) and/or erythrocyte casts on urine sediment examination, although some glomerular disorders may cause gross hematuria. Other findings suggestive of a glomerular source include proteinuria. Nonglomerular bleeding typically presents with isomorphic erythrocytes in the urine without evidence of glomerular dysfunction. Glomerular causes of hematuria include inflammatory processes such as glomerulonephritis that may lead to rapid declines in kidney function but may also include more benign or indolent diseases such as thin glomerular basement membrane disease, IgA nephropathy, and other forms of chronic glomerulonephritis. The clinical presentation in this asymptomatic patient with normal kidney function and apparent recurrent episodes of gross hematuria is consistent with IgA nephropathy as a cause of her hematuria.

Cystoscopy is used to evaluate for lower urinary tract causes of nonglomerular bleeding. It is not an appropriate next step in this patient with evidence of glomerular bleeding and no other risk factors for lower urinary tract pathology.

Noncontrast helical abdominal CT can be used to detect kidney stones or other potential causes of nonglomerular hematuria. However, this patient's presentation is not suggestive of nephrolithiasis, and she has evidence of a glomerular source of her hematuria. Additionally, the preferred method of kidney imaging in younger patients, particularly women of childbearing age, is ultrasonography due to decreased radiation exposure.

Measurement of serum creatine kinase levels is useful in evaluating for rhabdomyolysis. This diagnosis should be suspected when dipstick urinalysis is positive for heme with a negative microscopic urinalysis for erythrocytes; however, this patient has evidence of erythrocytes in her urine. Additionally, she does not have a clinical history consistent with rhabdomyolysis, and her urine studies suggest a glomerular cause of her hematuria.

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Question 9

A 22-year-old woman is evaluated for persistent hematuria initially discovered following treatment of a urinary tract infection. She is asymptomatic. Family history is significant for persistent hematuria in her father and brother without kidney failure. Medical history is unremarkable, and she takes no medications.

On physical examination, temperature is 37.0 °C (98.6 °F), blood pressure is 110/74 mm Hg, pulse rate is 74/min, and respiration rate is 16/min. BMI is 22. Hearing is normal, and examination of the eyes is unremarkable. Cardiopulmonary examination is normal. Skin examination shows no lesions. Neurologic examination is unremarkable.

Laboratory studies:

Blood urea nitrogen	18 mg/dL (6.4 mmol/L)
Creatinine	0.9 mg/dL (79.6 µmol/L)
Urinalysis	pH 5.0; 2+ blood; no protein; 10-20 erythrocytes/hpf

Kidney ultrasound shows normal-sized kidneys without evidence of obstruction or cysts.

Which of the following is the most likely diagnos is?

A
Fabry disease

B
Hereditary nephritis

C
Thin glomerular basement membrane disease

D
Tuberous sclerosis complex

Answer & Critique

Correct Answer: C

Educational Objective: Diagnose thin glomerular basement membrane disease.

Key Point

Diagnosis of thin glomerular basement membrane disease is usually based on the history of persistent hematuria, normal kidney function, and positive family history of hematuria without kidney failure.

The most likely diagnosis is thin glomerular basement membrane (GBM) disease, an inherited type IV collagen abnormality that causes thinning of the GBM and results in hematuria. The disorder may affect up to 5% of the population, and 30% to 50% of patients report a family history of hematuria. The disease is characterized by microscopic or macroscopic hematuria that may be first discovered in young adults. Diagnosis is usually based on the history of persistent hematuria, normal kidney function, and positive family history of hematuria without kidney failure; biopsy is not typically required. Long-term prognosis for kidney function is excellent, with rare progression to chronic kidney disease (CKD).

Fabry disease is a rare X-linked inherited disorder in which there is deficiency of ?-galactosidase A (an enzyme in the glycosphingolipid pathway) that leads to progressive deposit of globotriaosylceramide (Gb3) in lysosomes. This disorder may present as CKD in young adulthood. Other associated clinical features include premature coronary artery disease, severe neuropathic pain, telangiectasias, and angiokeratomas. Because Fabry disease is X-linked and this patient has no other clinical findings of this disorder, it is not a likely diagnostic consideration.

Hereditary nephritis (also known as Alport syndrome), also a heritable disorder of type IV collagen, is a rare cause of end-stage kidney disease with a prevalence of 0.4% among adult U.S. patients. Most cases are X-linked (80%) and are associated with sensorineural hearing loss and lenticonus (conical deformation of the lens), with proteinuria, hypertension, and kidney failure developing over time. The remaining cases are autosomal recessive (15%) or autosomal dominant (5%) and may also be associated with hearing loss. Female carriers variably develop kidney disease depending on activity of the X chromosome in somatic renal cells. The prevalence of this disorder and the patient's gender make this a less likely possibility.

Tuberous sclerosis complex (TSC) results from mutations in genes coding for proteins that have a tumor-suppressing effect. Disruption of these gene products allows abnormal cell proliferation in different tissues, including the skin, brain, lung, liver, and kidney. Mild TSC may be detected in adulthood. Renal angiomyolipomas are a characteristic kidney lesion in TSC and occur in 75% of patients on imaging. The lack of evidence of other lesions suggestive of TSC and her normal kidney ultrasound make this an unlikely diagnosis in this patient.

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Question 10

A 51-year-old man is evaluated during a follow-up visit for management of newly diagnosed hypertension and diabetes mellitus. He has started a program of lifestyle modification for his diabetes but has not yet started antihypertensive therapy. He is currently taking no medications.

On physical examination, blood pressure is 148/92 mm Hg, and pulse rate is 76/min. BMI is 33. The remainder of the examination is unremarkable.

Laboratory studies show a serum creatinine level of 1.5 mg/dL (132.6 μmol/L) (estimated glomerular filtration rate of 52 mL/min/1.73 m^2) and a serum potassium level of 4.2 mEq/L (4.2 mmol/L); a urine dipstick demonstrates no hematuria or proteinuria, and a spot urine protein-creatinine ratio is 50 mg/g.

Which of the following is the most appropriate antihypertensive treatment for this patient?

A
Hydrochlorothiazide

B
Lisinopril

C
Lisinopril and amlodipine

D
Lisinopril and hydrochlorothiazide

E
Lisinopril and losartan

Answer & Critique

Correct Answer: B

Educational Objective: Treat stage 1 hypertension in a patient with diabetes mellitus and chronic kidney disease.

Key Point

The eighth report of the Joint National Committee recommends an ACE inhibitor or angiotensin receptor blocker for patients with hypertension and chronic kidney disease, with or without diabetes mellitus.

The ACE inhibitor lisinopril is appropriate antihypertensive therapy for this patient. He was recently diagnosed with diabetes mellitus and stage 1 hypertension (defined as a systolic blood pressure of 140-159 mm Hg and/or a diastolic blood pressure of 90-99 mm Hg) and is now noted to have chronic kidney disease (CKD). There is evidence that in patients with hypertension and CKD, regardless of diabetes status, renin-angiotensin system agents (ACE inhibitor or angiotensin receptor blocker [ARB]) have a protective effect on kidney function. Based on this evidence, the eighth report of the Joint National Committee (JNC 8) recommends the use of these agents in patients with hypertension and CKD, with or without diabetes. The blood pressure goal recommended by the JNC 8 and the American Diabetes Association is <140/90 mm Hg for adult patients with hypertension and diabetes.

Recommendations for more aggressive blood pressure goals of <130/80 mm Hg in this population have recently been tempered by the lack of efficacy in reducing mortality with lower blood pressure goals and an increase in adverse events related to antihypertensive agents. Thus, initial combination therapy is not warranted in this case. Furthermore, the combination of two renin-angiotensin system agents for antihypertensive management in the setting of diabetes and moderately increased albuminuria (formerly known as microalbuminuria) has not been shown to improve outcomes and is associated with higher rates of hyperkalemia and other adverse events.

Question 11

A 73-year-old man is evaluated during a routine examination. He feels well but notes a gradual weight gain of 9.1 kg (20 lb) over the past 5 years. He reports his blood pressure to be around 155/85 mm Hg on several determinations at his local pharmacy. Medical history is significant for mild benign prostatic hyperplasia, gout, and hyperlipidemia. Medications are atorvastatin and as-needed colchicine.

On physical examination, blood pressure is 158/87 mm Hg, pulse rate is 85/min, and respiration rate is 12/min. BMI is 29. Cardiac examination is normal, and the remainder of the physical examination is unremarkable.

Laboratory studies show a normal chemistry panel; a urine dipstick demonstrates no blood or protein.

An electrocardiogram shows no evidence of left ventricular hypertrophy.

Which of the following is the most appropriate next step in management?

A

Doxazosin

B

Hydrochlorothiazide

C

Metoprolol

D

Lifestyle modifications

E

Repeat blood pressure determination in 6 months

Answer & Critique

Correct Answer: D

Educational Objective: Recommend lifestyle modifications in a patient with newly diagnosed hypertension.

Key Point

Lifestyle modifications are indicated for all patients with hypertension, which can produce reductions in blood pressure that are equivalent to antihypertensive agents.

Lifestyle modification is the most appropriate next step in management for this 73-year-old patient with likely stage 1 hypertension based on consistently elevated blood pressure determinations. He has no evidence of end-organ manifestations on history or physical examination. Therefore, lifestyle modifications, including a low sodium diet; a diet such as DASH (Dietary Approaches to Stop Hypertension) that emphasizes vegetables, fruits, whole grains, legumes, and low-fat dairy products and limits sweets, red meat, and saturated/total fat; weight loss irrespective of diet; and exercise, are the most appropriate initial management strategies. The most effective lifestyle modification is salt restriction to 1500 mg/d, which lowers blood pressure by an average of 7/3 mm Hg. The eighth report of the Joint National Committee (JNC 8) recommends a blood pressure goal of <150/90 mm Hg for those ≥60 years of age. Because his blood pressure measurements have been around 155/85 mm Hg, salt restriction alone as part of lifestyle modifications may be enough to avoid the use of medications to achieve the treatment goal for this 73-year-old patient.

Although the α-blocker doxazosin may be considered for its dual blood pressure–lowering effect and its effect on urinary frequency, its use as first-line therapy for persistent hypertension following lifestyle modification should be decided while considering its adverse effect profile (such as orthostatic hypotension) and its increased incidence of heart failure that was noted in the Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial (ALLHAT).

This patient may ultimately require medical treatment; because he has gout, the angiotensin receptor blocker (ARB) losartan may be preferred not only for its benefits in lowering blood pressure but also for its uricosuric effect. This is in contrast to thiazide diuretics such as hydrochlorothiazide, which increases serum urate.

β-Blockers such as metoprolol are no longer recommended as primary initial therapy for hypertension given their side-effect profiles, which includes higher cardiovascular-related events and mortality compared with ARBs.

Because this patient has evidence of persistently elevated blood pressures and likely stage 1 hypertension, a 6-month follow-up of his blood pressures without intervention is not appropriate.

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Question 12

A 24-year-old man is evaluated in the hospital for progressively worsening kidney function. He was admitted 5 days ago with fevers and was diagnosed with endocarditis with methicillin-resistant*Staphylococcus aureus*. Intravenous vancomycin was started and adjusted daily to target levels of 15 to 20 µg/mL (10.4-13.8 µmol/L). Since admission, his fevers have resolved, but his serum creatinine level has gradually increased. Medical history includes two previous admissions for staphylococcal endocarditis treated with prolonged courses of antibiotics. He has occasionally used injection drugs, including heroin, during the past 4 years. His only medication is vancomycin.

On physical examination, temperature is 37.3 °C (99.2 °F), blood pressure is 110/70 mm Hg, pulse rate is 92/min, and respiration rate is 18/min. BMI is 22. Cardiac examination is notable for a soft diastolic murmur along the left sternal border. There is trace lower extremity edema. There is no skin rash or arthritis.

Laboratory studies:

C3	Low
C4	Normal
Creatinine	2.8 mg/dL (247.5 µmol/L) (1.5 mg/dL [132.6 µmol/L] on admission)
Cryoglobulins	Negative
Urinalysis	3+ blood; 2+ protein; 30-40 erythrocytes/hpf; 10-15 leukocytes/hpf; erythrocyte casts

Transthoracic ultrasound shows moderate aortic regurgitation without vegetations (confirmed on transesophageal ultrasound). Kidney ultrasound shows normal-sized, mildly echogenic kidneys. Doppler study of the renal arteries and veins is normal.

Which of the following is the most appropriate management?

A

Initiate glucocorticoids

B

Schedule a kidney biopsy

C

Switch vancomycin to daptomycin

D

Continue current therapy

Choose an Answer Above

Answer & Critique

Correct Answer: D

Educational Objective: Manage infection-related glomerulonephritis.

Key Point

Management of infection-related glomerulonephritis typically only consists of treatment of the underlying infection.

The most appropriate management for this patient is to continue current therapy. This patient with methicillin-resistant *Staphylococcus aureus* endocarditis is found to have worsening kidney function since hospitalization. The differential diagnosis includes infection-related glomerulonephritis (IRGN), drug-induced nephrotoxicity, acute interstitial nephritis (AIN), and septic emboli. The finding of a nephritic urine sediment (erythrocytes, erythrocyte casts, and proteinuria) in an azotemic patient with an active infection suggests IRGN. IRGN is an immune complex–mediated disease most frequently associated with nonstreptococcal infections, with the antigen in the immune complex derived from the infectious agent. Immune complexes deposit in the subepithelial area and activate complement with recruitment of inflammatory cells, leading to a proliferative GN. The likelihood of IRGN is high in this patient given the low C3 complement, the absence of cryoglobulins, and the lack of clinical findings suggestive of other causes on the differential diagnosis.

Glucocorticoids are not typically used in IRGN because there is usually improvement with control of the associated infection.

A kidney biopsy is not indicated because the probability of IRGN is high. However, biopsy would be appropriate if this patient's kidney function fails to improve with treatment of the underlying infection.

Drug-induced tubular toxicity (for example, with vancomycin) typically occurs after 7 to 10 days of antibiotic therapy and the urine sediment does not show cells, unlike in this patient. Antibiotic-induced AIN is typically associated with mild proteinuria, erythrocytes, leukocytes, and leukocyte casts on urinalysis. Eosinophiluria, recurrence of fevers, rash, and peripheral eosinophilia may also be seen and typically occur after 7 to 10 days of therapy, none of which is present in this patient. Therefore, switching vancomycin to daptomycin is not appropriate.

Question 13

A 58-year-old man is evaluated during a follow-up visit for a 15-year history of hypertension. Medical history is significant for hypertensive nephropathy. He states that he feels well and is without current complaints. Medications are lisinopril and hydrochlorothiazide.

On physical examination, the patient is afebrile, blood pressure is 138/82 mm Hg, pulse rate is 83/min, and respiration rate is 12/min. BMI is 29. Cardiovascular examination is unremarkable. The lungs are clear. There is no peripheral edema.

Laboratory studies are significant for a serum creatinine level of 1.7 mg/dL (150.3 µmol/L) and a urine albumin-creatinine ratio of 200 mg/g.

Which of the following is the most appropriate management?

A

Add losartan

B

Increase lisinopril dose

C

Replace lisinopril with amlodipine

D

Continue current medications

Choose an Answer Above

Answer & Critique

Correct Answer: D

Educational Objective: Treat a patient who has chronic kidney disease and hypertension.

Key Point

For patients with chronic kidney disease, the eighth report from the Joint National Committee recommends a blood pressure target goal of <140/90 mm Hg using a medication regimen that includes an ACE inhibitor or angiotensin receptor blocker.

The most appropriate management for this patient with hypertension and chronic kidney disease (CKD) is to continue the current medication regimen. Although hypertension is a common cause of CKD, hypertension is also highly prevalent in patients with CKD not caused by hypertension. The presence of hypertension in CKD promotes progression of underlying kidney disease and increases cardiovascular risk. Therefore, optimal management of hypertension is an important component of evaluating and treating all patients with CKD. For patients with CKD, the eighth report from the Joint National Committee (JNC 8) recommends a blood pressure target goal of <140/90 mm Hg using a medication regimen that includes an ACE inhibitor or angiotensin receptor blocker (ARB). In general, there is insufficient evidence to justify lower blood pressure goals unless patients have severely increased albuminuria, usually defined as >300 mg/g (stage A3), which is not present in this patient. His hypertension is currently at target goal, and he is taking an ACE inhibitor. Therefore, no changes to his medications are needed at this time.

The addition of the ARB losartan is inappropriate because the patient is already at goal blood pressure. Furthermore, studies have demonstrated that combination ACE inhibitor/ARB therapy worsens clinical outcomes and should not be used to treat patients with CKD.

Increasing this patient's lisinopril dose is unnecessary at this time because the patient is already at goal blood pressure.

Replacing lisinopril with amlodipine is not indicated because the JNC 8 guidelines recommend the use of an ACE inhibitor (such as lisinopril) or ARB as first-line therapy for hypertension in patients with CKD, and not dihydropyridine calcium channel blockers, which have a lower renoprotective effect. Additionally, this patient is at the recommended blood pressure goal.

Question 14

A 20-year-old woman is evaluated during a new-patient visit for persistent dipstick-positive hematuria initially discovered 2 years ago when she was evaluated for a possible urinary tract infection. Two subsequent urinalyses have shown dipstick-positive hematuria and 10-15 erythrocytes/hpf on microscopic examination without other abnormalities. She has not noted any episodes of gross hematuria or other urinary tract symptoms. She reports no fever, rash, or arthritis. Family history is notable for her mother and maternal aunt who have hematuria; there is no family history of kidney disease. Medical history is otherwise negative, and the patient takes no medications.

On physical examination, the patient is afebrile, blood pressure is 118/78 mm Hg, pulse rate is 64/min, and respiration rate is 14/min. BMI is 22. The remainder of the physical examination is normal.

Laboratory studies:

Complements (C3 and C4)	Normal
Creatinine	0.6 mg/dL (53 µmol/L)
Hepatitis B and C serologies	Negative
Antinuclear antibodies	Negative
ANCA	Negative
Urinalysis	2+ blood; no protein; 10-15 erythrocytes/hpf; no casts
Urine protein-creatinine ratio	110 mg/g

Kidney ultrasound is normal.

Which of the following is the most appropriate management?

A

Abdominal CT with contrast

B

Cystoscopy

C

Kidney biopsy

D

Serial kidney function and urine protein determinations

E

Urine cytology

Choose an Answer Above

Answer & Critique

Correct Answer: D

Educational Objective: Manage isolated hematuria.

Key Point

Patients with isolated hematuria with a family history of hematuria may require serial measurements of kidney function and urine protein because kidney failure may occur later in life.

Serial kidney function and urine protein determinations are appropriate for this young patient with asymptomatic microhematuria. The evaluation of asymptomatic hematuria is somewhat different in younger patients as compared with older patients. In the former, hematuria is likely from mild glomerular disease (such as IgA nephropathy and genetic disorders such as collagen mutations). In older patients, structural changes, stones, infection, and cancers predominate. This young patient presents with asymptomatic microhematuria and has a family history of hematuria (without kidney failure) on her mother's side. Serologic and imaging studies are normal, there are no structural abnormalities of the kidney (such as kidney stones), and infection is unlikely based on the urinalysis. She likely has a familial hematuric syndrome, which is typically associated with either X-linked or somatic mutations of type IV collagen. In female carriers of X-linked hereditary nephritis (Alport syndrome), kidney failure may occur later in life. Thus, annual measurements of blood pressure, kidney function, and urine protein are reasonable (although there are no consensus guidelines defining the frequency of testing).

Cystoscopy is usually performed in patients with hematuria who are older than 35 years of age or who have risk factors for lower urinary tract malignancy (such as smoking, aniline dye, or cyclophosphamide exposure). This patient is at low risk for urinary tract malignancy and therefore does not have an indication for cystoscopy or urine cytology. Similarly, an abdominal CT could identify a renal malignancy that might have been missed on kidney ultrasound, which is not indicated in this young patient.

A kidney biopsy is often performed in a patient with unexplained abnormalities on urinalysis (such as hematuria or proteinuria) in the presence of evidence of kidney failure in order to establish the diagnosis and guide therapy. However, this patient has normal kidney function and stable microhematuria without other clear risk factors for progressive kidney disease. Therefore, kidney biopsy is not currently indicated.

Question 15

A 48-year-old woman is evaluated during a follow-up visit for hypertension. Blood pressure measurements taken at the past three visits have been in the range of 135 to 146 mm Hg systolic and 86 to 92 mm Hg diastolic. Twenty-four hour ambulatory blood pressure monitoring shows an overall mean blood pressure of 136/84 mm Hg; daytime readings average 138/85 mm Hg, and nighttime readings average 130/82 mm Hg. She has no other pertinent personal or family history. She takes no medications.

On physical examination, blood pressure is 146/92 mm Hg, and pulse rate is 76/min. BMI is 29. The remainder of the examination is unremarkable.

Laboratory studies show a normal chemistry panel; a urine dipstick demonstrates no protein.

Which of the following is the most appropriate next step in management?

A

Begin lisinopril

B

Begin melatonin

C

Recheck blood pressure in the office in 6 months

D

Recheck blood pressure in the office in 1 year

E

Repeat 24-hour ambulatory blood pressure monitoring in 1 year

Answer & Critique

Correct Answer: A

Educational Objective: Treat a patient with hypertension based on ambulatory blood pressure monitoring.

Key Point

Blood pressure averages ≥135/85 mm Hg by ambulatory blood pressure monitoring or home monitoring meet most consensus panels' definition of hypertension and should be treated with pharmacologic therapy.

Initiation of a low-dose ACE inhibitor with follow-up in 2 weeks is appropriate for this patient with hypertension. Lower thresholds for the definition of hypertension exist for measurements obtained in the ambulatory setting. In general, blood pressure averages ≥135/85 mm Hg by ambulatory blood pressure monitoring or home monitoring meet most consensus panels' definition of hypertension, and nighttime hypertension is defined by average values >125/75 mm Hg. This is to reflect the typical blood pressure drop from daytime to nighttime (during sleep) of approximately 15%, noted in both normotensive and hypertensive patients. A lack of blood pressure drop of at least 10% (“non-dipping”) is independently associated with left ventricular hypertrophy, cardiovascular events, moderately increased albuminuria (formerly known as microalbuminuria), and a more rapid rate of decline in glomerular filtration rate. This patient has hypertension defined by ambulatory readings and is a non-dipper with nighttime hypertension; therefore, pharmacologic therapy is indicated.

Although it has been shown that melatonin release is diminished in non-dippers and in small studies melatonin can lower nighttime blood pressure, there are no large trials with cardiovascular end points to recommend this therapy.

Observation is appropriate in the setting of prehypertension or white coat hypertension; however, this patient has confirmed hypertension and requires pharmacologic therapy.

Question 16

A 36-year-old man is evaluated following his second episode of nephrolithiasis. His initial kidney stone occurred 6 months ago and passed spontaneously. The stone was recovered and on analysis was found to be a pure uric acid stone. He was advised to increase his urine output to at least 2 L/d and has been adherent to this recommendation. His second episode occurred last week. He again passed the stone spontaneously, which was submitted for analysis and shown to be a pure uric acid stone. Medical history is significant for type 2 diabetes mellitus, but he has never had evidence of gout. Medications are metformin and rosuvastatin.

On physical examination, temperature is 36.9 °C (98.5 °F), blood pressure is 135/87 mm Hg, pulse rate is 78/min, and respiration rate is 12/min. BMI is 31. There is no costovertebral angle tenderness. No joint abnormalities or gouty tophi are noted.

Laboratory studies:

Electrolytes	Normal
Kidney function studies	Normal
Urate	7.6 mg/dL (0.45 mmol/L)
Urinalysis	pH 5.8; no blood; no cells or crystals
24-Hour uric acid excretion	850 mg/24 h (5 mmol/24 h)

In addition to continuing oral hydration, which of the following is the most appropriate next step in therapy?

A

Allopurinol

B

Cholestyramine

C

Hydrochlorothiazide

D

Urine alkalinization

Answer & Critique

Correct Answer: D

Educational Objective: Manage uric acid nephrolithiasis with adequate urine output and urine alkalinization.

Key Point

Management of uric acid nephrolithiasis includes adequate urine output, urine alkalinization, and xanthine oxidase inhibitors if needed to decrease uric acid production.

Urine alkalinization is the most appropriate treatment for this patient with uric acid nephrolithiasis not adequately treated with increased urine output. Uric acid is an uncommon cause of nephrolithiasis (approximately 10% of cases). It is more common in hot arid climates where low urine output and acidic urine (low urine pH) are more likely. These two factors, particularly low urine pH, markedly increase the risk of uric acid stones by favoring the development of insoluble uric acid from the relatively soluble urate salt. Elevated serum urate levels, gout, and associated hyperuricosuria are other risk factors, although many patients with uric acid stones do not have these risk factors. Other comorbid risk factors for uric acid stones include diabetes mellitus, the metabolic syndrome, and chronic diarrhea. Oral hydration to maintain a urine output of at least 2 L/d is the mainstay of therapy. If this is inadequate, the next treatment is urine alkalinization (usually with potassium citrate or potassium bicarbonate) to increase the solubility of uric acid.

Treatment with xanthine oxidase inhibitors such as allopurinol to lower uric acid production is usually reserved for patients with refractory disease despite adequate urine output and urine alkalinization or those with very high 24-hour urine uric acid levels (>1000 mg/24 h [5.9 mmol/24 h]). Therefore, allopurinol is not the next treatment of choice in this patient with mild uricosuria who has not undergone a trial of urine alkalinization.

Cholestyramine binds bile salts and oxalate in the gut and is sometimes used as a treatment for kidney stones related to hyperoxaluria but would likely not benefit this patient with uric acid stones.

Thiazide diuretics, such as hydrochlorothiazide, decrease hypercalciuria by increasing proximal sodium reabsorption and passive calcium reabsorption in the kidney. However, this is a strategy for treating calcium-based nephrolithiasis and is not effective for uric acid stones.

Question 17

A 45-year-old man is evaluated during a routine follow-up visit. Medical history is significant for difficult-to-control hypertension, type 2 diabetes mellitus complicated by proliferative retinopathy and sensory and autonomic neuropathy, and chronic kidney disease. He has no new symptoms. Medications are lisinopril, amlodipine, hydrochlorothiazide, and insulin.

On physical examination, temperature is 36.9 °C (98.4 °F), blood pressure is 180/100 mm Hg in both arms, pulse rate is 66/min, and respiration rate is 14/min. BMI is 34. There is bilateral lower extremity edema to the mid calf.

Laboratory studies are significant for a serum creatinine level of 2.2 mg/dL (194.5 µmol/L), a serum potassium level of 4.2 mEq/L (4.2 mmol/L), and a urine protein-creatinine ratio of 4000 mg/g.

Which of the following is the most appropriate treatment?

A

Add aliskiren

B

Add clonidine

C

Add minoxidil

D

Switch hydrochlorothiazide to furosemide

Answer & Critique

Correct Answer: D

Educational Objective: Treat resistant hypertension by switching a thiazide diuretic to a loop diuretic in a patient with chronic kidney disease.

Key Point

In the setting of chronic kidney disease stage 4 and greater (glomerular filtration rate <30 mL/min/1.73 m^2), thiazide diuretics lose potency, and loop diuretics may often be required.

Switching hydrochlorothiazide to furosemide is the most appropriate next step in this patient. Uncontrolled hypertension in a patient who is already on three drugs, one of which is a diuretic, is defined as resistant hypertension. The approach to patients with resistant hypertension centers around lifestyle changes (particularly salt reduction and optimizing medication adherence) and choosing appropriate drug combinations. In patients with diabetic nephropathy and chronic kidney disease (CKD), ACE inhibitors or angiotensin receptor blockers should be used as an initial therapy given the established benefit of these agents in patients with diabetes mellitus and proteinuria. Most patients will require a second medication, and diuretic therapy is typically used in patients with CKD because persistent volume expansion contributes significantly to hypertension. Although thiazide diuretics are frequently used as initial therapy, they are generally less effective when the glomerular filtration rate drops below 30 mL/min/1.73 m^2. When this occurs, loop diuretics tend to be more effective and should be used instead of (or added to) thiazide diuretics. The dosage of loop diuretics depends on the sodium intake and the severity of CKD. Generally, furosemide doses of 40 to 80 mg once or twice daily is initiated with a salt-restricted diet and adjusted according to the response.

Adding a second inhibitor of the renin-angiotensin system such as aliskiren increases the risk of acute kidney injury and hyperkalemia without any benefit on renal and cardiovascular end points; therefore, combination therapy with renin-angiotensin inhibitors should not be used.

The centrally acting agent clonidine and the vasodilator minoxidil are potent antihypertensives sometimes used in cases of resistant hypertension if maximal doses of more conventional agents are unsuccessful. However, this patient is not currently on optimal triple therapy, and both agents also increase the risk of orthostatic hypotension in those with autonomic neuropathy, such as this patient. Moreover, the use of minoxidil without adequate diuresis will worsen salt and water retention and should be avoided.

Question 18

An 85-year-old man arrives with his daughter to discuss options for end-stage kidney disease (ESKD) management. He has stage G5/A3 chronic kidney disease due to diabetic nephropathy and hypertension. History is also significant for a 3-year history of Alzheimer disease and heart failure with a left ventricular ejection fraction of 35%. Medications are aspirin, losartan, furosemide, carvedilol, and calcium acetate. The patient is a resident of a nursing facility.

On physical examination, the patient appears comfortable but is not oriented to place or time. Temperature is 37.0 °C (98.6 °F), blood pressure is 142/70 mm Hg, pulse rate is 82/min, and respiration rate is 18/min. BMI is 21. The lungs are clear. There is trace bipedal edema. The remainder of the examination is unremarkable.

Laboratory studies are notable for a blood urea nitrogen level of 82 mg/dL (29.3 mmol/L), a serum creatinine level of 5.1 mg/dL (450.8 µmol/L), and an estimated glomerular filtration rate of 9 mL/min/1.73 m^2.

Which of the following is the most appropriate recommendation for management of this patient's ESKD?

A Hemodialysis in a dialysis unit

B Hemodialysis at the nursing facility

C Nocturnal peritoneal dialysis

D Non-dialytic therapy

Answer & Critique

Correct Answer: D

Educational Objective: Recommend non-dialytic therapy for a very elderly patient who has end-stage kidney disease and a high burden of comorbid conditions and poor functional status.

Key Point

Very elderly patients who have end-stage kidney disease with a high burden of comorbid conditions and poor functional status may live as long or longer with non-dialytic therapy that is focused on alleviating symptoms and maximizing quality of life.

The most appropriate next step in the management of this patient's end-stage kidney disease (ESKD) is to recommend non-dialytic therapy. Dialysis may be beneficial in prolonging life with a good quality in many older patients; therefore, age itself is not always an absolute limiting factor in deciding whether dialysis is appropriate for a specific older patient. However, studies have shown that very elderly patients with a high burden of comorbid conditions and poor functional status may live as long or longer with non-dialytic therapy that is focused on alleviating symptoms and maximizing quality of life. Moreover, most nursing facility residents have a progressive decline in functional status after starting dialysis. Therefore, in this very elderly resident with multiple comorbidities who lives in a nursing facility, pursuing non-dialytic therapy is the most appropriate recommendation. The option of non-dialytic care should not be seen as refusal to provide care or provision of a lower level of care than those receiving dialysis, but rather as an appropriate recommendation based on expected outcomes in these patients. Palliative medicine and hospice services can be helpful in managing patients who choose this mode of therapy.

In older patients who choose to pursue dialysis, there are few definitive data regarding outcomes with hemodialysis versus peritoneal methods, although hemodialysis is typically chosen more frequently by older adults. However, neither modality is appropriate in the patient given his advanced age and other clinical circumstances.

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Question 19

A 48-year-old woman is evaluated during a follow-up visit for newly diagnosed hypertension, confirmed by multiple measurements at home and in the office. Medical history is notable for hyperlipidemia, for which she takes atorvastatin. Lifestyle modifications have been recommended.

On physical examination, blood pressure is 160/92 mm Hg, and pulse rate is 64/min. BMI is 32. The remainder of the examination is unremarkable.

Laboratory studies show a serum creatinine level of 1.1 mg/dL (97.2 μmol/L), a fasting plasma glucose level of 114 mg/dL (6.3 mmol/L), and a serum potassium level of 4.0 mEq/L (4.0 mmol/L); a urine dipstick demonstrates no blood or protein.

Which of the following is most likely to be effective in controlling this patient's hypertension?

A

Amlodipine

B

Lisinopril

C

Losartan

D

Lisinopril and amlodipine

E

Losartan and lisinopril

Answer & Critique

Correct Answer: D

Educational Objective: Treat a patient with stage 2 hypertension using combination therapy.

Key Point

Combination antihypertensive therapy is appropriate for patients who are >20/10 mm Hg above their target blood pressure goal.

Combination therapy with the ACE inhibitor lisinopril and the calcium channel blocker (CCB) amlodipine is appropriate for this patient with stage 2 hypertension, which is defined as a systolic blood pressure ≥160 mm Hg and/or a diastolic blood pressure ≥100 mm Hg. There is general agreement among hypertension societies that a single agent is unlikely to control blood pressure in patients who are >20/10 mm Hg above target blood pressure. In this circumstance, initial therapy may include a combination of two agents either separately or in a fixed-dose pill. A combination of two agents at moderate doses is often more successful at achieving blood pressure goals than one blood pressure agent at maximal dose and minimizes the side effects that are more commonly noted at higher doses. Several combination regimens are appropriate, including the combination of a thiazide diuretic with an ACE inhibitor or angiotensin receptor blocker (ARB), or an ARB with a CCB; these combinations have been supported by both the eighth report from the Joint National Committee (JNC 8) and the European Society of Hypertension as reasonable approaches to management. However, there is evidence from the Avoiding Cardiovascular Events in Combination Therapy in Patients Living with Systolic Hypertension (ACCOMPLISH) trial that a reduced rate of cardiovascular events may occur with the combination of an ACE inhibitor and CCB compared to an ACE inhibitor and thiazide. The combination of a thiazide and CCB is also an effective strategy for blood pressure lowering, although there is less evidence of the effectiveness of this regimen compared with other combination therapies.

There is general consensus that the dual use of renin-angiotensin-aldosterone agents (ACE inhibitor, ARB, or the direct renin inhibitor aliskiren) should not be used because of evidence showing that combining these medications is not associated with improved cardiovascular or renal end points and results in increased adverse events, including hypotension and hyperkalemia.

Given this patient's degree of hypertension (measurement of 160/92 mm Hg at her current visit), it is unlikely that a single agent will achieve her treatment goal of <140/90 mm Hg. Therefore, combination therapy is indicated as initial treatment.

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Question 20

A 55-year-old woman is evaluated during a follow-up visit for elevated blood pressure noted on several previous clinic visits. She checks her blood pressure at home with a device checked in the clinic for accuracy and reports measurements typically in the “120s over 80s.” She is asymptomatic except for occasional palpitations associated with episodes of anxiety. Medical history is notable for depression, for which she takes citalopram.

On physical examination, blood pressure is 152/88 mm Hg, and pulse rate is 88/min. BMI is 24. The remainder of the examination is unremarkable.

Laboratory studies show a normal chemistry panel; a urine dipstick demonstrates no blood or protein.

A resting electrocardiogram is normal.

Which of the following is the most appropriate diagn ostic test to perform next?

A 24-Hour ambulatory blood pressure monitoring

B 24-Hour urine testing for fractionated metanephrines

C Ambulatory electrocardiography

D Echocardiography

E Plasma aldosterone-plasma renin ratio

Answer & Critique

Correct Answer: A

Educational Objective: Diagnose white coat hypertension using ambulatory blood pressure monitoring.

Key Point

Ambulatory blood pressure monitoring is useful to evaluate patients for white coat hypertension.

Ambulatory blood pressure monitoring (ABPM) is appropriate to evaluate this patient for white coat hypertension. ABPM is accomplished with a device that typically measures blood pressure every 15 to 20 minutes during the day and every 30 to 60 minutes at night. White coat hypertension is defined as blood pressure readings in the office ≥140/90 mm Hg and out-of-office readings that average <135/85 mm Hg. Prevalence may be as high as 10% to 20% of patients diagnosed with hypertension. This patient's blood pressure measurements have been elevated in the office but normal at home and require further documentation with 24-hour ABPM. If she has normal blood pressure at home, her blood pressure would be classified as white coat hypertension, which does not pose an increased risk of cardiovascular events but does increase her risk of future development of hypertension. Conversely, hypertension documented by ABPM is associated with a higher risk of cardiovascular death compared with hypertension determined in the office or at home. A summary of interpretation of office-based, ABPM, and self-recorded blood pressure readings is shown.

Interpretation of Blood Pressure Readings

Blood Pressure Category	Office-Based Readings (mm Hg)	24-Hour Ambulatory Readings (mm Hg)	Self-Recorded (mm Hg)
Hypertension (Nonelderly)	Systolic ≥140 or diastolic ≥90	≥135/85	≥135/85

Interpretation of Blood Pressure Readings

Blood Pressure Category	Office-Based Readings (mm Hg)	24-Hour Ambulatory Readings (mm Hg)	Self-Recorded (mm Hg)
White Coat Hypertension	≥140/90	<135/85	<135/85
Masked Hypertension	<140/90	>135/85	>135/85

Urine testing for fractionated metanephrines is used to evaluate for pheochromocytoma as a secondary cause of hypertension. Pheochromocytoma is generally suspected in patients with the symptom triad of episodic headache, sweating, and tachycardia associated with coincident increases in blood pressure. Similar symptoms may be seen with episodes of anxiety and panic attacks, which occur with increased frequency in patients with depression, as is present in this patient. However, these symptoms are not associated with significant blood pressure elevations when caused by anxiety or panic attacks. Documentation of consistent symptoms with accompanying blood pressure elevations would increase consideration of pheochromocytoma; however, testing for this diagnosis would not be indicated in the absence of this relationship, and further assessment for anxiety and panic attacks would be indicated.

Ambulatory electrocardiography or echocardiography would not be the appropriate next steps given the lack of other cardiovascular examination findings; palpitations are common and a nonspecific finding in possible hypertension.

Plasma aldosterone-plasma renin ratio would not be appropriate given this patient's normal laboratory findings and the lack of a firm diagnosis of hypertension.

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Question 21

A 65-year-old man is hospitalized for an ischemic, nonhealing right lower extremity ulcer with associated biopsy-proven osteomyelitis. On hospital day 1, he was started on cefazolin and underwent angiography and stenting of the iliac artery using a low osmolar contrast agent. On day 2, he became febrile and was switched to vancomycin and gentamicin based on culture sensitivity data. On day 3, his fever resolved and his serum creatinine was at baseline (1.5 mg/dL [132.6 µmol/L]). On day 10, his serum creatinine increased to 3.0 mg/dL (265.2 µmol/L) with a urine output of 0.5 mL/kg/h. Medical history is notable for type 2 diabetes mellitus, hypertension, dyslipidemia, coronary artery disease, and chronic kidney disease. Medications are rosuvastatin, amlodipine, carvedilol, aspirin, insulin, vancomycin, and gentamicin.

On physical examination, blood pressure is 150/78 mm Hg, and pulse rate is 72/min. There is no rash. The lower extremities have decreased peripheral pulses. The right foot has a 1-cm clean-appearing ulcer on the tip of the second toe. The remainder of the physical examination is normal.

Laboratory studies on day 10:

Hemoglobin	11.2 g/dL (112 g/L)
Leukocyte count	8500/µL (8.5 × 10^9/L) with 58% polymorphonuclear leukocytes, 20% lymphocytes, 3% eosinophils
Creatinine	3.0 mg/dL (265.2 µmol/L) (baseline, 1.5 mg/dL [132.6 µmol/L])
Urine sodium	40 mEq/L (40 mmol/L)
Fractional excretion of sodium	2.1%
Urinalysis	Specific gravity 1.012; pH 5.5; trace blood; trace protein; 1-3 normal-appearing erythrocytes/hpf; granular casts; tubular epithelial cells

Kidney ultrasound is normal.

Which of the following is the most likely cause of this patient's acute kidney injury?

A

Cefazolin

B

Cholesterol emboli

C

Contrast

D

Gentamicin

Choose an Answer Above

Answer & Critique

Correct Answer: D

Educational Objective: Diagnose aminoglycoside-induced nephrotoxicity.

Key Point

Aminoglycoside-induced acute kidney injury typically presents as nonoliguric acute tubular necrosis with granular casts in the urine sediment and a fractional excretion of sodium >1%, and the serum creatinine characteristically rises 5 to 10 days after starting therapy.

This patient has developed acute kidney injury (AKI) from gentamicin. Aminoglycoside-induced AKI typically presents as nonoliguric acute tubular necrosis (ATN) with granular casts in the urine sediment and a fractional excretion of sodium >1%. The serum creatinine characteristically rises 5 to 10 days after starting therapy. Hypokalemia and hypomagnesemia can also occur with aminoglycoside toxicity due to kidney potassium and magnesium wasting. Recognizing drug-induced ATN is important because eliminating the nephrotoxic agent often leads to renal recovery. Incidence increases in older patients and in patients with decreased effective blood volume, chronic kidney disease, or concomitant nephrotoxin exposure.

Cephalosporins, such as cefazolin, can cause AKI from acute interstitial nephritis. Urine findings include leukocytes, erythrocytes, and leukocyte casts. Fever, maculopapular rash, peripheral eosinophilia, and eosinophiluria can also occur. Onset of AKI after drug exposure ranges from 3 to 5 days with a second exposure, to as long as several weeks to months with a first exposure. This patient does not have any features of acute interstitial nephritis. Furthermore, cefazolin was discontinued prior to the elevation in serum creatinine.

Cholesterol embolism occurs in patients with atherosclerotic disease after undergoing an invasive vascular procedure or receiving an anticoagulant or thrombolytic agent within the past several months. Emboli from ruptured atheromatous plaques occlude small and medium arterioles, causing ischemia and inflammation with organ dysfunction. Clinical features include rash (livedo reticularis), AKI, purple discoloration of the toes, bowel ischemia, neurologic manifestations, and eosinophilia. This patient does not have findings of embolic phenomena.

Iodinated contrast can induce vasospasm and cause ischemic injury or direct damage to the kidneys. Low osmolar contrast is thought to be safer than high osmolar contrast. Contrast-induced nephropathy (CIN) is defined as either an increase in serum creatinine of 0.5 mg/dL (44.2 µmol/L) or an increase in serum

creatinine of 25% from baseline at 48 hours after contrast administration. This patient had no change in the serum creatinine level at 48 hours, making CIN an unlikely diagnosis.

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Question 22

A 59-year-old man is evaluated during a follow-up visit for a 6-year history of end-stage kidney disease and a 20-year history of hypertension. He had a kidney transplant 3 months ago with an unremarkable postoperative course. Current medications are tacrolimus, mycophenolate mofetil, nifedipine, losartan, valganciclovir, and prednisone, 5 mg/d.

On physical examination, temperature is 37.0 °C (98.6 °F), blood pressure is 165/95 mm Hg, pulse rate is 86/min, and respiration rate is 14/min. BMI is 28. There are no oral lesions. There is no jugular venous distention. Heart sounds are normal. The lungs are clear. The abdomen is nontender with no bruits. There is a well-healed scar in the right lower abdomen over the kidney allograft. There is 1+ peripheral edema.

Laboratory studies are notable for a serum creatinine level of 1.0 mg/dL (88.4 μmol/L).

Monitoring for which of t he following complications is indicated in this patient?

A

Hyperphosphatemia

B

Hyperthyroidism

C

Hypoparathyroidism

D

New-onset diabetes mellitus and dyslipidemia

Answer & Critique

Correct Answer: D

Educational Objective: Monitor complications of immunosuppressive medications used in kidney transplantation.

Key Point

Kidney transplant recipients require lifelong immunosuppression and must be monitored for metabolic complications such as diabetes mellitus and dyslipidemia.

New-onset diabetes mellitus and dyslipidemia should be monitored in this patient. Although kidney transplant recipients have improved clinical outcomes compared with patients who remain on dialysis, they require lifelong immunosuppression to prevent rejection of the transplanted kidney. In addition to increasing the risk of hypertension, infection, and certain malignancies, these medications can predispose patients to metabolic complications that should be anticipated by clinicians. Kidney transplant recipients are predisposed to new-onset diabetes after transplantation (often referred to as NODAT). Medications that promote development of NODAT include glucocorticoids, tacrolimus, and the mammalian target of rapamycin (mTOR) inhibitors sirolimus and everolimus. Dyslipidemia is also a common complication posttransplantation, and commonly used immunosuppressive medications that promote dyslipidemia include cyclosporine and mTOR inhibitors. Because cardiovascular disease is the leading cause of death among kidney transplant recipients, it is important to aggressively treat modifiable cardiac risk factors, including diabetes and dyslipidemia. It is important to emphasize that many medications, including some statins, can significantly alter the pharmacokinetics of immunosuppressant medications. Clinicians should therefore never change medication regimens in kidney transplant recipients without ensuring that there will be no adverse drug interactions.

Although hypophosphatemia is commonly observed in the posttransplant period, which is due in part to residual secondary hyperparathyroidism, hyperphosphatemia is not commonly observed unless there is severely impaired allograft function.

Hyperthyroidism is not a common complication of kidney transplantation or of immunosuppressive medications typically used in kidney transplant recipients.

Many patients have residual hyperparathyroidism after transplant that can be slow to resolve; hypercalcemia is relatively commonly observed posttransplant but hypocalcemia is uncommon. Therefore, hypoparathyroidism is unlikely in this patient.

Question 23

A 36-year-old man is evaluated in the emergency department for right flank pain of 2 days' duration and an episode of gross hematuria. He reports no fever, nausea, or gastrointestinal symptoms. He has no other pertinent medical history, and he takes no medications. Family history is notable for a father with kidney stones.

On physical examination, the patient is in moderately painful discomfort. Temperature is 37.1 °C (98.7 °F), blood pressure is 123/76 mm Hg, pulse rate is 78/min, and respiration rate is 12/min. BMI is 21. There is no costovertebral angle tenderness. The abdomen is normal without rebound or guarding. The remainder of the examination is unremarkable.

Laboratory studies show a normal complete blood count, electrolyte panel, and kidney function. Urinalysis is significant for large blood on dipstick and >50,000 erythrocytes/hpf.

Noncontrast abdominal CT scan reveals a 12-mm stone in the right renal pelvis.

Which of the follow ing is the most appropriate management?

A

Mechanical stone removal

B

Nifedipine

C

Oral glucocorticoids

D

Tamsulosin

Answer & Critique

Correct Answer: A

Educational Objective: Recommend mechanical stone removal for a patient with a large (>10 mm) kidney stone.

Key Point

Mechanical stone removal is appropriate for patients with large (>10 mm) kidney stones or those with smaller stones who have failed medical management or have complicated nephrolithiasis (urosepsis, acute kidney injury, anuria, refractory pain).

Mechanical removal is the most appropriate management of this patient's 12-mm kidney stone located in the right renal pelvis. Large (>10 mm) stones are less likely than smaller stones to pass on their own, with or without use of medications to facilitate stone passage. Mechanical stone removal in the renal pelvis is often achieved with shock wave lithotripsy. Stones in the ureter may be addressed with either shock wave lithotripsy or ureteroscopy (often with ureteroscopic lithotripsy), usually depending on the specific location and size of the stone. Percutaneous antegrade ureteroscopy or retroperitoneal laparoscopy is generally reserved for impacted stones or other situations in which less invasive techniques would likely not be successful. Currently, open stone removal is rarely performed. Other indications for mechanical stone removal include stones <10 mm in size that have failed to pass with medical therapy. Involvement of a urologist is recommended for patients with nephrolithiasis who have urosepsis, acute kidney injury, anuria, or refractory pain, as well as those who are at high risk of complications such as having a single kidney, because more invasive interventions may be required in these situations.

Uncomplicated kidney stones <10 mm in size may usually be treated with conservative management (including hydration, analgesia, observation, and periodic re-evaluation) and medical expulsive therapy, which usually consists of either an α-blocker (such as tamsulosin) or calcium channel blocker (such as nifedipine). Although some clinicians may also treat with glucocorticoids in addition to medical expulsive therapy to decrease inflammation and swelling to facilitate stone passage, the effectiveness of this approach has not been documented.

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Question 24

A 54-year-old woman is evaluated for fatigue, anorexia, polyuria, and nocturia of several weeks' duration. She had otherwise felt well until the onset of her current symptoms. Medical history is significant for autoimmune pancreatitis diagnosed 1 year ago, treated with a prednisone taper that was completed 8 months ago with resolution of her symptoms. She takes no medications.

On physical examination, temperature is 36.2 °C (97.2 °F), blood pressure is 110/58 mm Hg, pulse rate is 72/min, and respiration rate is 16/min. BMI is 25. Estimated central venous pressure is 7 cm H_2O. The lungs are clear. There are no murmurs or extra heart sounds. Abdominal examination is unremarkable. There is no edema.

Laboratory studies:

Blood urea nitrogen	56 mg/dL (20 mmol/L)
Creatinine	5.2 mg/dL (459.7 µmol/L)
Serum free light chain ratio	Normal
Urinalysis	pH 5.0; 1+ protein; 3-5 erythrocytes/hpf; 5-10 leukocytes/hpf; occasional leukocyte casts

Chest radiograph is normal. Kidney ultrasound shows slightly enlarged kidneys without evidence of obstruction.

Which of the following is the most likely diagnosis?

A

ANCA-associated vasculitis

B

Anti–glomerular basement membrane antibody disease

C

IgG4-related interstitial nephritis

DLupus nephritis

Answer & Critique

Correct Answer: C

Educational Objective: Diagnose IgG4-related interstitial nephritis.

Key Point

IgG4-related disease is characterized by infiltration of different organs by lymphoplasmacytic infiltrates of IgG4-positive plasma cells with resultant fibrosis associated with elevated serum IgG4 levels.

The most likely diagnosis is IgG4-related interstitial nephritis. This patient has a history of autoimmune pancreatitis and now presents with acute kidney injury. Her urinalysis is most consistent with a tubulointerstitial pattern, with mild proteinuria and the presence of inflammatory cells. This history and clinical presentation suggest the possibility of IgG4-related interstitial nephritis. Systemic IgG4-related disease is an uncommon disorder characterized by infiltration of different organs by lymphoplasmacytic infiltrates of IgG4-positive plasma cells with resultant fibrosis associated with elevated serum IgG4 levels. Autoimmune pancreatitis is one form of IgG-related disease, although other organs such as the kidney may be affected, most commonly as interstitial nephritis. IgG4-related interstitial nephritis may present with acute or chronic kidney failure as well as renal mass–like lesions on imaging. As with other IgG4-related diseases, almost all patients with IgG4-related kidney disease will have elevated serum IgG4 levels, and the kidneys may be diffusely enlarged on imaging due to cellular infiltration. Definitive diagnosis requires kidney biopsy with staining for IgG4-positive plasma cells. Treatment is similar to other IgG4-related diseases using immunosuppression with glucocorticoids.

ANCA-associated vasculitis and anti–glomerular basement membrane antibody disease typically cause rapidly progressive glomerulonephritis with significant proteinuria and hematuria in the sediment, occasionally with erythrocyte casts, none of which is present in this patient.

Lupus nephritis is primarily a glomerular lesion with significant proteinuria in the context of other clinical findings suggestive of systemic lupus erythematosus. This patient's clinical presentation is therefore less consistent with this diagnosis.

Question 25

A 46-year-old woman is evaluated in the emergency department for fatigue and weakness of 5 days' duration. The patient also reports recurrent lower extremity swelling. She is vague when asked about medication or drug use.

On physical examination, blood pressure is 108/62 mm Hg, pulse rate is 98/min, and respiration rate is 16/min. Upon standing, systolic blood pressure decreases by 15 mm Hg, and pulse rate increases by 10/min. BMI is 26. The remainder of the examination is unremarkable, with no evidence of lower extremity edema.

Laboratory studies:

Serum bicarbonate	29 mEq/L (29 mmol/L)
Serum creatinine	1.2 mg/dL (106.1 µmol/L)
Serum potassium	3.1 mEq/L (3.1 mmol/L)
Urine chloride	53 mEq/L (53 mmol/L)
Urine potassium	25 mEq/L (25 mmol/L)
Urine sodium	42 mEq/L (42 mmol/L)

Which of the following is the most appropria te diagnostic test to perform next?

A
24-Hour urine free cortisol excretion

B
Plasma aldosterone-plasma renin ratio

C
Serum thyroid-stimulating hormone level

D
Urine diuretic screening

Answer & Critique

Correct Answer: D

Educational Objective: Diagnose diuretic-related metabolic alkalosis.

Key Point

Diuretic use can mimic the metabolic alkalosis findings of inherited kidney disorders of sodium and chloride handling such as Bartter and Gitelman syndromes.

Urine diuretic screening is appropriate for this patient. The first step when assessing a patient with metabolic alkalosis is to clinically assess the patient's volume status. This patient has metabolic alkalosis as implied by the elevated serum bicarbonate and is hypovolemic as evidenced by the orthostatic blood pressure and pulse changes. Such a patient would be expected to have low urine concentrations of sodium and chloride. However, this patient's urine electrolytes show increased excretion of sodium and chloride despite the evident hypovolemia. These findings suggest the presence of active diuretic use or a renal tubular defect that impairs handling of sodium and chloride, such as Bartter and Gitelman syndromes. These rare autosomal recessive genetic disorders of renal sodium and chloride transporters clinically mimic loop diuretic and thiazide diuretic use, respectively, but should be considered only after diuretic use has been eliminated with negative urine diuretic screening.

Measurement of 24-hour urine free cortisol excretion is a standard test for diagnosing Cushing syndrome, which is characterized by proximal muscle weakness, hypokalemia, hypertension, and diabetes mellitus. These findings are not present in this patient.

Plasma aldosterone-plasma renin ratio is unlikely to be helpful in this situation. Although primary hyperaldosteronism is characterized by hypokalemia and metabolic alkalosis, the absence of hypertension makes this diagnosis unlikely. Finally, diuretics and Gitelman and Bartter syndromes are associated with various degrees of volume contraction and secondary hyperaldosteronism. Plasma aldosterone and renin activity levels will not differentiate these disorders.

Thyroid dysfunction is not associated with acid-base abnormalities and may be associated with hypokalemia only in rare and severe cases such as thyrotoxic periodic paralysis, in which attacks of profound generalized weakness occur suddenly with preserved consciousness.

Question 26

A 77-year-old woman is evaluated 4 months following a left middle cerebral artery ischemic stroke. The severity of her stroke required prolonged initial hospitalization and a 3-month stay in a rehabilitation center before returning home. Residual deficits include dense right-sided hemiparesis and dysphagia requiring oral feeding with thickened liquids. Medical history is otherwise significant for hypertension and diabetes mellitus. Current medications are aspirin, chlorthalidone, lisinopril, tolterodine, and insulin.

On physical examination, temperature is 37.2 °C (99.0 °F), blood pressure is 136/86 mm Hg, and pulse rate is 86/min. BMI is 18. The general medical examination is unremarkable. Neurologic examination reveals dysarthria, left-sided facial droop, 1/5 strength in the right arm and leg, and bilateral distal sensory neuropathy.

Laboratory studies:

Hemoglobin A_{1c}	7.2%
Albumin	2.4 g/dL (24 g/L)
Blood urea nitrogen	12 mg/dL (4.3 mmol/L) (4 months ago: 28 mg/dL [10 mmol/L])
Creatinine	0.8 mg/dL (70.7 µmol/L) (4 months ago: 1.4 mg/dL [123.8 µmol/L])
Urinalysis	Normal

Which of the following is the most likely cause of this patient's decreased serum creatinine level?

A

Decrease in muscle mass

B

Improvement in diabetic kidney disease

C

Initiation of chlorthalidone

DInitiation of lisinopril

Answer & Critique

Correct Answer: A

Educational Objective: Identify decreased muscle mass as a cause of decreased serum creatinine.

Key Point

Any condition that results in decreased muscle mass would be expected to cause long-term decreases in the serum creatinine level in the absence of any change in kidney function.

Decreased muscle mass is the most likely cause of this patient's decreased serum creatinine level. She has likely lost significant muscle mass as a consequence of stroke with paralysis, causing immobility and inability to maintain oral protein intake. She has severe protein-calorie malnutrition, as is evidenced by a low BMI and a severely depressed serum albumin level. Because creatinine is derived from the metabolism of creatine, a constituent of skeletal muscle, any condition that results in decreased muscle mass would be expected to cause long-term decreases in the serum creatinine level in the absence of any change in kidney function. Acute, but transient, decreases in creatinine have also been documented in some patients with chronic kidney disease and diabetes mellitus following ischemic stroke.

Diabetic kidney disease is chronically progressive, with rapidity of kidney function decline dependent on type 1 or 2 status, blood pressure and glycemic control, and reduction in proteinuria through use of renin-angiotensin system blockade. There is no known means of reversing diabetic kidney disease, and spontaneous improvement is unlikely.

Chlorthalidone, a thiazide diuretic, likely decreases blood pressure primarily by its effect on endothelial cells but can also result in volume contraction and mild hypovolemia, which generally results in increased, not decreased, serum creatinine.

Lisinopril, an ACE inhibitor, decreases the production of angiotensin II, resulting in decreased arterial blood pressure (systemic effect) and efferent arteriolar dilation (local effect). Both of these processes decrease pressure across the glomerular vascular bed, and thus the glomerular filtration rate. Consequently, serum creatinine is expected to increase by 25% to 30% with appropriate dosing of an ACE inhibitor.

Question 27

A 60-year-old man is evaluated during a routine visit. He has stage G4/A3 chronic kidney disease due to membranous glomerulopathy. He received treatment with cyclosporine and prednisone and received rituximab 2 years ago. Current medications are lisinopril, atorvastatin, furosemide, and calcium carbonate/vitamin D. He received the complete hepatitis B immunization series, pneumococcal polysaccharide, tetanus and diphtheria combined with acellular pertussis, and influenza immunizations 6 months ago.

On physical examination, vital signs are normal. BMI is 27. The remainder of the examination is noncontributory.

Which of the following is an app ropriate approach to pneumococcal vaccination in this patient?

A

Administer the pneumococcal conjugate vaccine now

B

Administer the pneumococcal conjugate vaccine in 6 months

C

Administer the pneumococcal polysaccharide and pneumococcal conjugate vaccines in 6 months

D

Repeat the pneumococcal polysaccharide vaccine now

Choose an Answer Above

Answer & Critique

Correct Answer: B

Educational Objective: Provide appropriate pneumococcal vaccinations for a patient with chronic kidney disease.

Key Point

The Advisory Committee on Immunization Practices recommends pneumococcal vaccination with both the 13-valent pneumococcal conjugate and 23-valent pneumococcal polysaccharide vaccines for all patients with severe chronic kidney disease.

This patient should receive the pneumococcal conjugate vaccine in 6 months. Because infection is a leading cause of death in patients with chronic kidney disease (CKD) and end-stage kidney disease, proper vaccination to prevent infections should improve patient outcomes. The Advisory Committee on Immunization Practices (ACIP) recommends pneumococcal vaccination for all patients with severe CKD. This patient with stage G4/A3 CKD should receive the 13-valent pneumococcal conjugate vaccine (PCV-13) 1 or more years after the 23-valent pneumococcal polysaccharide vaccine (PPSV-23). A second dose of PPSV-23 should be administered 5 or more years after the first dose. Because this patient was immunized with PPSV-23 6 months ago, he should receive PVC-13 in 6 months and PPSV-23 in 4 years and 6 months.

Other immunocompromising conditions that are indications for pneumococcal vaccination are anatomic and functional asplenia, congenital or acquired immunodeficiency (including B- or T-lymphocyte deficiency, complement deficiencies, and phagocytic disorders excluding chronic granulomatous disease), HIV infection, the nephrotic syndrome, leukemia, lymphoma, Hodgkin lymphoma, generalized malignancy, multiple myeloma, solid-organ transplant, and iatrogenic immunosuppression (including long-term systemic glucocorticoids and radiation therapy).

For patients younger than 65 years of age with CKD who have not been previously immunized against invasive pneumococcal disease, the ACIP recommends that PCV-13 be administered first followed by PPSV-23 no sooner than 8 weeks later

Question 28

A 26-year-old woman is evaluated for muscle weakness developing over the past several months. She has no focal symptoms and states that she otherwise feels well. Medical history is unremarkable, and there is no pertinent family history. She takes no medications.

On physical examination, blood pressure is 98/62 mm Hg, pulse rate is 98/min, and respiration rate is 16/min. BMI is 19. There is no lower extremity edema. The remainder of the examination is unremarkable.

Laboratory studies:

Serum electrolytes:	
Sodium	142 mEq/L (142 mmol/L)
Potassium	3.1 mEq/L (3.1 mmol/L)
Chloride	120 mEq/L (120 mmol/L)
Bicarbonate	15 mEq/L (15 mmol/L)
Serum creatinine	1.2 mg/dL (106.1 µmol/L)
Urine electrolytes:	
Sodium	18 mEq/L (18 mmol/L)
Potassium	8.0 mEq/L (8.0 mmol/L)
Chloride	32 mEq/L (32 mmol/L)
Urine pH	5.0
Urine dipstick	No blood or protein

Which of the following is the most likely cause of this patient's acid -base and electrolyte ab normalities?

A
Bulimia nervosa

B
Gitelman syndrome

C
Laxative abuse

D
Surreptitious diuretic use

E
Type 1 (hypokalemic distal) renal tubular acidosis

Answer & Critique

Correct Answer: C

Educational Objective: Identify laxative abuse as a cause of metabolic acidosis.

Key Point

Normal anion gap metabolic acidosis can be caused by gastrointestinal bicarbonate loss induced by laxative abuse.

Laxative abuse is the most likely cause of this patient's acid-base and electrolyte abnormalities. She has a normal anion gap metabolic acidosis in the setting of physical examination findings consistent with low/normal extracellular fluid status and low/normal blood pressure. The etiology of a normal anion gap metabolic acidosis is typically due to either the inability of the kidney to excrete acid (renal tubular acidosis) or loss of bicarbonate, usually through the gastrointestinal tract. Differentiating the cause of a normal anion gap metabolic acidosis may be accomplished by measurement of the urine anion gap, which is calculated as follows: ($U_{Na} + U_{K} - U_{Cl}$). The urine anion gap is a surrogate method of estimating the ability of the kidney to excrete an acid load. The normal physiologic response to systemic acidosis is an increase in urine acid excretion resulting in an increase in urine ammonium, which is difficult to measure clinically. However, because ammonium carries a positive charge, chloride is excreted into the urine in equal amounts with ammonium to maintain electrical neutrality. Therefore, the amount of chloride in the urine reflects the amount of ammonium present, with a positive urine anion gap suggesting a kidney source of acid loss, and a negative urine anion gap is consistent with gastrointestinal bicarbonate loss. The negative urine anion gap in this patient (-6 mEq/L [6 mmol/L]) indicates a gastrointestinal cause of her normal anion gap metabolic acidosis, and laxative abuse is a likely explanation. In addition, hypokalemia combined with low urine potassium indicates appropriate renal compensation to attempt to retain filtered potassium.

The vomiting associated with bulimia nervosa leads to loss of gastric acid with a resulting metabolic alkalosis, not metabolic acidosis.

Active diuretic use leads to kidney potassium wasting and a metabolic alkalosis, as does Gitelman syndrome, a defect that mimics the clinical picture of thiazide diuretic use.

Renal causes of normal anion gap metabolic acidosis are due to specific defects in renal handling of bicarbonate reclamation or in hydrogen ion secretion. Type 1 (hypokalemic distal) renal tubular acidosis is

caused by a defect in hydrogen secretion by the distal tubule and is associated with a positive urine anion gap, a high urine potassium secretion, and hypokalemia.

Question 29

A 65-year-old man is evaluated during a follow-up visit for a preemptive living donor kidney transplant 6 months ago, with a postoperative course complicated by an episode of acute cellular rejection requiring antithymocyte antibody induction. He has done well since then. He has a 10-year history of chronic kidney disease due to diabetic nephropathy and a 35-year history of type 1 diabetes mellitus. Basal cell carcinoma was removed from his nose 2 years ago. Current medications are tacrolimus, mycophenolate mofetil, valganciclovir, and prednisone, 5 mg/d.

On physical examination, temperature is 37.0 °C (98.6 °F), blood pressure is 135/78 mm Hg, pulse rate is 80/min, and respiration rate is 14/min. BMI is 22. There is no lymphadenopathy. Actinic keratoses are present on the forehead. The lungs are clear. The abdomen is nontender without organomegaly. The kidney allograft in the left pelvis is nontender with a well-healed scar. There is no peripheral edema.

Laboratory studies show a serum creatinine level of 1.2 mg/dL (106.1 µmol/L).

In addition to age - and sex-appropriate scr eening, which of the following should this patient be evaluated for?

A

Colon cancer

B Lung cancer

C Prostate cancer

D Skin cancer

E No additional screening

Answer & Critique

Correct Answer: D

Educational Objective: Evaluate for malignancy in a kidney transplant recipient.

Key Point

Kidney transplant patients are at particularly high risk for squamous cell carcinomas of the skin and posttransplant lymphoproliferative disease and should be evaluated for these diseases, in addition to age- and sex-appropriate screening.

In addition to age- and sex-appropriate screening, this kidney transplant recipient should be evaluated for skin cancer. Patients who receive kidney transplants are at increased risk of malignancy compared with the general population, and this risk is attributable, at least in part, to the effects of immunosuppressive medications. Kidney transplant patients are at particularly high risk for squamous cell carcinomas (SCC) of the skin and posttransplant lymphoproliferative disease. Unlike in the general population, SCC is more common than basal cell carcinoma and accounts for approximately 90% of skin cancers in organ recipients. Some studies have shown that transplant recipients have more than a 200-fold increased risk of SCC compared with the general population. Moreover, SCC occurring in a transplant recipient is much more likely to metastasize than in non-transplant patients. Transplant recipients, particularly those with fair skin, should therefore be closely monitored for the development of precancerous or cancerous lesions and promptly treated.

Although kidney transplant recipients are at moderately increased risk for colon and lung cancer, insufficient data support more aggressive screening for these cancers than in the general population. Similarly, male kidney transplant recipients are not at increased of prostate cancer, so risk versus harm of screening should be approached as for the general population.

Question 30

A 68-year-old woman is hospitalized for coronary artery bypass surgery for multi-vessel coronary artery disease. Medical history includes atherosclerotic cardiovascular disease, hypertension, type 2 diabetes mellitus, hyperlipidemia, and chronic kidney disease. Home medications are simvastatin, lisinopril, furosemide, amlodipine, aspirin, and glimepiride.

On physical examination, blood pressure is 150/82 mm Hg, and pulse rate is 76/min. BMI is 25. The remainder of the physical examination is unremarkable.

Laboratory studies are significant for a baseline serum creatinine level of 2.3 mg/dL (203.3 μmol/L), with an estimated glomerular filtration rate (eGFR) of 25 mL/min/1.73 m^2.

Which of the following is considered the strongest predictor of the development of acute kidney injury in the perioperative period for th is patient?

A

Baseline eGFR

B

BMI

C

Hypertension

D

Perioperative lisinopril use

E

Perioperative statin use

Answer & Critique

Correct Answer: A

Educational Objective: Recognize the risk factors for acute kidney injury after cardiac surgery.

Key Point

Preexisting chronic kidney disease is the strongest nonmodifiable predictor of the development of acute kidney injury after cardiac surgery.

This patient's baseline estimated glomerular filtration rate (eGFR) is considered the strongest predictor of the development of acute kidney injury (AKI) in the perioperative period. An elevated preoperative serum creatinine level and the presence of chronic kidney disease (CKD) are the strongest nonmodifiable predictors of the development of AKI after cardiac surgery. This patient has severe kidney disease with an elevated baseline serum creatinine level of 2.3 mg/dL (203.3 µmol/L), with an eGFR of 25 mL/min/1.73 m^2 and stage 4 CKD. Other nonmodifiable risk factors for post–cardiac surgery AKI include advanced age, female gender, reduced left ventricular function or the presence of heart failure, insulin-dependent diabetes mellitus, peripheral vascular disease, and COPD.

Some observational studies have shown a BMI >30 to be a predictor of AKI post–cardiac surgery. However, the strength of the data is weak, and this patient has a BMI of 25.

Hypertension has not been shown to be a strong predictor for the development of AKI post–cardiac surgery.

Lisinopril and simvastatin have not been established as medications that increase the risk of AKI post–cardiac surgery. In fact, some observational studies indicate that they may have renoprotective properties and should be continued in the perioperative setting.

Question 31

A 72-year-old woman is evaluated for a 3-year history of progressively worsening low back pain involving the lumbar spine, sacroiliac joints, and hips. She reports progressive difficulty with rising from a squat and climbing stairs. She also has had several spontaneous fractures over the past year. At the time of presentation, she cannot walk without support. Medical history is also notable for type 2 diabetes mellitus, hypertension, and hyperlipidemia. Medications are glipizide, quinapril, rosiglitazone, atorvastatin, and hydrocodone/acetaminophen.

On physical examination, blood pressure is 147/84 mm Hg, and pulse rate is 82/min. There is a small swelling over the proximal phalanx of the left index finger. There is tenderness upon palpation of the ribs. Examination of the joints and spine is normal. Decreased strength in the proximal muscles of the lower limbs is noted.

Laboratory studies:

Albumin	3.9 g/dL (39 g/L)
Alkaline phosphatase	436 U/L
Calcium	9.0 mg/dL (2.3 mmol/L)
Creatinine	0.9 mg/dL (79.6 µmol/L)
Phosphorus	1.7 mg/dL (0.55 mmol/L)
Intact parathyroid hormone	22 pg/mL (22 ng/L)
1,25-Dihydroxy vitamin D	5.0 pg/mL (12 pmol/L)
25-Hydroxy vitamin D	40 ng/mL (99.8 nmol/L)

24-Hour urine phosphate	1.4 g/24 h (45 mmol/24 h) (normal range, 0.4-1.3 g/24 h [12.9-42 mmol/24 h])

Which of the following is the most likely cause of this patient's hypophosphatemia?

A

Nutritional vitamin D deficiency

B

Oncogenic osteomalacia

C

Primary hyperparathyroidism

D

X-linked hypophosphatemic rickets

Choose an Answer Above

Answer & Critique

Correct Answer: B

Educational Objective: Diagnose oncogenic osteomalacia.

Key Point

Oncogenic osteomalacia is characterized by bone pain and hypophosphatemia with kidney phosphate wasting in the setting of low 1,25-dihydroxy vitamin D and normal 25-hydroxy vitamin D concentrations.

This patient's findings of bone pain and hypophosphatemia with kidney phosphate wasting in the setting of inappropriately low serum concentration of 1,25-dihydroxy vitamin D, normal 25-hydroxy vitamin D concentration, and elevated alkaline phosphatase are consistent with oncogenic osteomalacia. The swelling of the finger is consistent with a mesenchymal tumor. Oncogenic osteomalacia is typically caused by benign mesenchymal tumors of vascular or skeletal origin. Overexpression of fibroblast growth factor–23 by these tumors is associated with decreased resorption of phosphate in the renal tubules with resultant hypophosphatemia and hyperphosphaturia. The tubular defect also impairs calcitriol synthesis. Chronic hypophosphatemia causes abnormal mineralization of bone, increased alkaline phosphatase, and, in the longer term, osteomalacia and associated fractures. Removal of the tumor leads to reversal of the biochemical abnormalities and healing of the bone disease.

Nutritional vitamin D deficiency results in low serum calcium levels and low 25-hydroxy vitamin D concentration, and it does not cause kidney phosphate wasting as seen in this patient.

Primary hyperparathyroidism is defined by an elevated parathyroid hormone level, elevated serum calcium level, and increased 1,25-dihydroxy vitamin D, all of which are absent in this patient.

X-Linked hypophosphatemic rickets can present with the same biochemical markers as noted in this case. However, it usually presents with typical signs of rickets in young children, and clinical expression of this condition in adulthood would not be expected.

Question 32

A 47-year-old man is admitted to the medical ICU with severe sepsis, multi-lobar pneumonia, and acute respiratory distress syndrome. He developed oliguric acute kidney injury on hospital day 3; he has produced only 240 mL of urine over the past 24 hours despite adequate intravenous hydration. He is mechanically ventilated and requires 80% F_{IO_2}. Medical history is unremarkable, and current medications are piperacillin/tazobactam, vancomycin, norepinephrine, vasopressin and propofol infusions, and a proton pump inhibitor.

On physical examination the patient is intubated and sedated. Temperature is 38.5 °C (101.3 °F), blood pressure is 95/60 mm Hg, and pulse rate is 130/min. Estimated central venous pressure is 14 cm H_2O. There is no rash. Generalized anasarca is noted. Examination of the chest reveals coarse breath sounds and inspiratory crackles throughout both lungs.

Laboratory studies:

Blood urea nitrogen	103 mg/dL (36.8 mmol/L)
Creatinine	4.3 mg/dL (380.1 μmol/L)
Electrolytes	
Sodium	137 mEq/L (137 mmol/L)
Potassium	6.0 mEq/L (6.0 mmol/L)
Chloride	97 mEq/L (97 mmol/L))
Bicarbonate	16 mEq/L (16 mmol/L)
Phosphorus	7.2 mg/dL (2.33 mmol/L)
Serum pH	7.2
Urinalysis	3+ blood; 0-2 erythrocytes/hpf; multiple granular casts and tubular epithelial cells

Which of the following is the most appropriate treatment for this patient's kidney failure?

A

Initiate continuous renal replacement therapy

B

Initiate intermittent hemodialysis

C

Initiate slow continuous ultrafiltration

D

Start a furosemide infusion

Choose an Answer Above

Answer & Critique

Correct Answer: A

Educational Objective: Treat acute kidney injury with continuous renal replacement therapy.

Key Point

Continuous renal replacement therapy is preferred for critically ill, unstable patients with acute kidney injury because it provides a slower rate of solute and fluid removal per unit of time, resulting in better hemodynamic tolerance.

Continuous renal replacement therapy (CRRT) is the most appropriate treatment for this patient who has hemodynamic instability and oliguric acute kidney injury (AKI) with laboratory and urinary findings consistent with acute tubular necrosis (ATN). CRRT is indicated for treatment of electrolyte abnormalities (hyperkalemia, hyperphosphatemia), metabolic acidosis, and volume overload as seen in this patient. CRRT represents a spectrum of dialysis modalities specifically developed for the management of critically ill patients with AKI who cannot tolerate traditional intermittent hemodialysis due to hemodynamic instability, or in whom intermittent hemodialysis cannot control volume or metabolic derangement. CRRT is performed continuously (24 hours/day) through a venovenous access. Venous access is obtained by placing a large double-lumen catheter into either the internal jugular, femoral, or subclavian vein, as would be done for hemodialysis. There are several variations of CRRT that may involve diffusion-based solute removal (dialysis) or convection-based solute and water removal (filtration).

The major advantage of CRRT over intermittent hemodialysis is its slower rate of solute and fluid removal per unit of time, resulting in better hemodynamic tolerance. Therefore, CRRT is the preferred method of renal replacement therapy for critically ill unstable patients such as the patient in this case. Furthermore, the continuous nature of the therapy allows for better control of volume, acid-base, electrolytes, and azotemia.

Slow continuous ultrafiltration is a type of extracorporeal therapy by which plasma water is removed continuously. Although this therapy will help with fluid overload, it will not correct the azotemia or electrolyte and acid-base abnormalities in this patient.

Starting a furosemide infusion in this patient will not correct the electrolyte or acid-base abnormalities. Furthermore, in the setting of ATN with oliguria, furosemide is unlikely to be effective in volume removal.

Question 33

A 50-year-old man is hospitalized with acute onset of shortness of breath and fatigue. In the emergency department, he coughed up a large quantity of blood followed by hypoxic respiratory failure, for which he was intubated.

On physical examination, the patient is well developed. He is afebrile; blood pressure is 140/90 mm Hg, and heart rate is 98/min. There is no jugular venous distension. Coarse crackles are heard in the lung fields. There is trace lower extremity edema. The remainder of the physical examination is normal.

Laboratory studies:

Hemoglobin	9.0 g/dL (90 g/L)
Blood urea nitrogen	38 mg/dL (13.6 mmol/L)
Creatinine	3.2 mg/dL (282.9 μmol/L)
Liver chemistry tests	Normal
Urinalysis	3+ blood; 2+ protein; 20-30 erythrocytes/hpf; 5-10 leukocytes/hpf
Urine protein-creatinine ratio	2200 mg/g

A chest radiograph shows bilateral pulmonary infiltrates.

A kidney biopsy is performed, which shows necrotizing, crescentic glomerulonephritis with linear staining of IgG along the glomerular basement membrane.

Which of the following is the most likely diagnosis?

A Anti–glomerular basement membrane antibody disease

B Cardiorenal syndrome

C Membranous nephropathy

D Microscopic polyangiitis

Answer & Critique

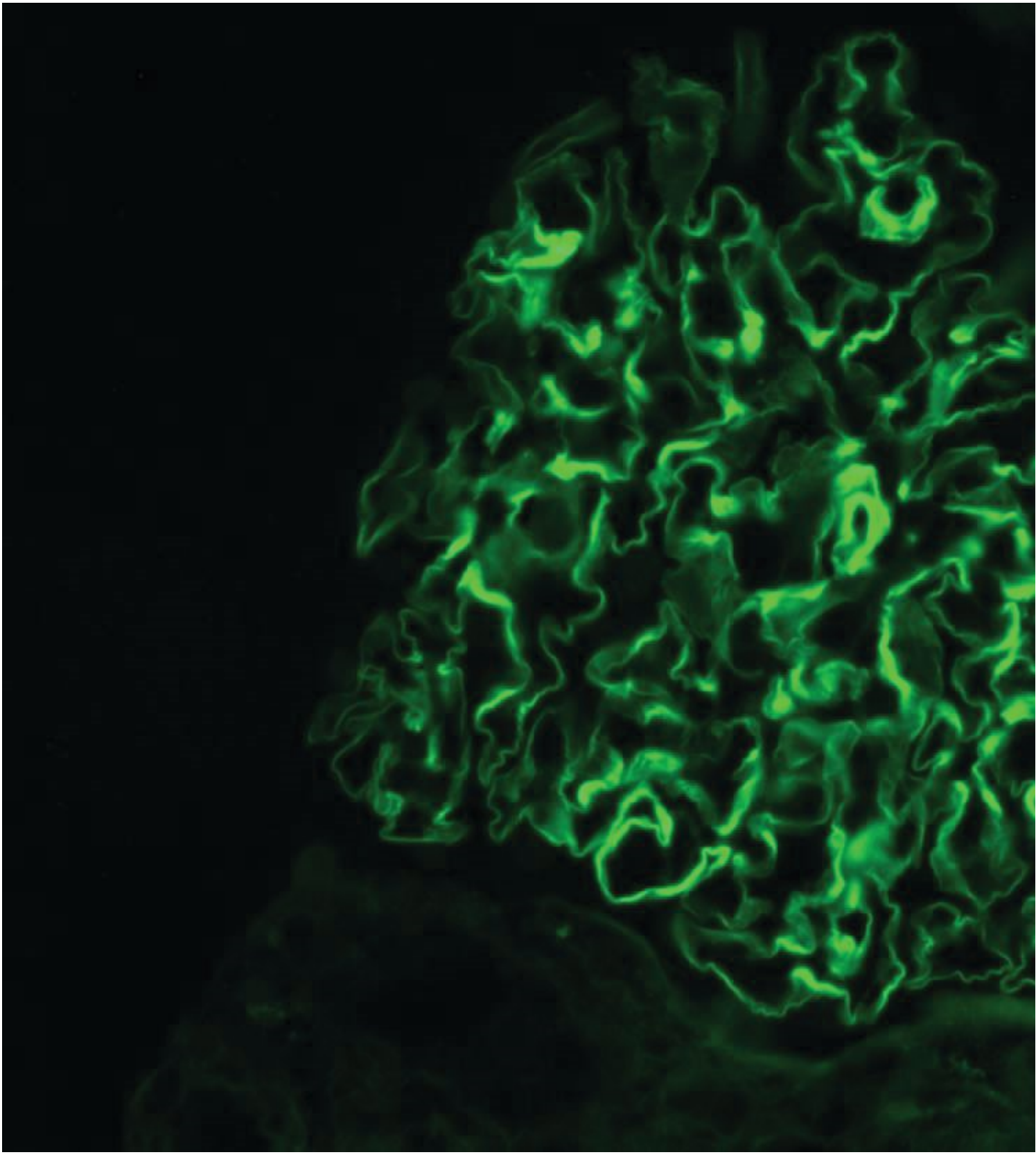
Correct Answer: A

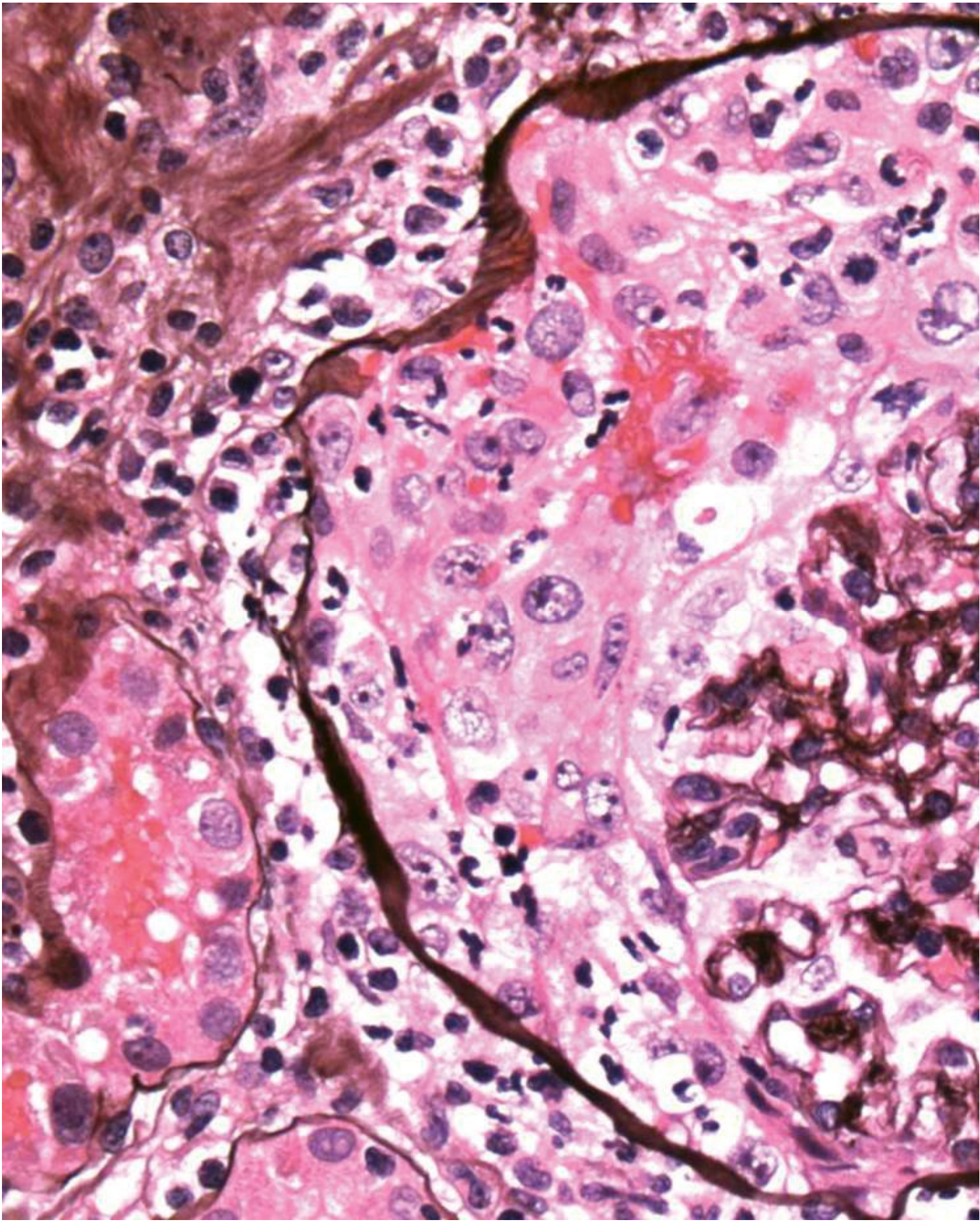
Educational Objective: Diagnose anti–glomerular basement membrane antibody disease.

Key Point

Anti–glomerular basement membrane (GBM) antibody disease is an autoimmune disease caused by antibodies directed against the noncollagenous domain of type IV collagen that bind to the GBM.

The most likely diagnosis is anti–glomerular basement membrane (GBM) antibody disease. This 50-year-old patient has pulmonary-renal syndrome, including hemoptysis followed by hypoxic respiratory failure and kidney failure with an active urine sediment with protein, erythrocytes, and leukocytes, suggesting an underlying glomerulonephritis. The differential diagnosis of pulmonary-renal syndrome includes small-vessel vasculitis (ANCA associated), anti-GBM antibody disease (Goodpasture syndrome), and rarely, other autoimmune diseases such as cryoglobulinemic vasculitis, systemic lupus erythematosus, and IgA vasculitis. Anti-GBM antibody disease is an autoimmune disease caused by antibodies directed against the noncollagenous domain of type IV collagen that bind to the GBM, inciting an inflammatory response resulting in damage to the GBM and the formation of a proliferative and often crescentic glomerulonephritis. The same process occurs with the basement membrane of pulmonary capillaries, leading to pulmonary hemorrhage. Serologies show normal complement levels and elevated levels of anti-GBM antibodies in the serum. On kidney biopsy, there is a proliferative glomerulonephritis, often with many crescents (shown, top panel). There is linear deposition of immunoglobulin along the GBM by immunofluorescence, but no electron-dense deposits on electron microscopy (shown, bottom panel). Treatment is immunosuppressive therapy with cyclophosphamide and glucocorticoids, combined with daily plasmapheresis to remove circulating anti-GBM antibodies.





Although heart failure can be associated with pulmonary edema and hemoptysis with acute kidney injury (cardiorenal syndrome), such patients typically show signs of severe volume overload and normal urine sediment, unlike this patient.

Membranous nephropathy is associated with the nephrotic syndrome with a low serum albumin level, which is not seen in this patient. The nephrotic syndrome alone is not typically associated with pulmonary disease, although it can be complicated with venous thromboembolic manifestations such as pulmonary embolism. However, this patient's pulmonary presentation with significant hemoptysis and infiltrates on chest radiograph is not consistent with pulmonary emboli as the cause of his respiratory failure.

Microscopic polyangiitis is the most common cause of pulmonary-renal syndrome. However, in the absence of a serum ANCA level or evidence of peripheral vasculitic lesions (for example, palpable purpura), it is not possible to clinically differentiate this disease from anti-GBM antibody disease. A kidney biopsy is diagnostic, showing little or no immune deposits in microscopic polyangiitis ("pauci-immune glomerulonephritis"). In this patient, extensive linear deposition of IgG along the GBM is noted, which is classic of anti-GBM antibody disease.

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Question 34

A 54-year-old woman is evaluated during a follow-up visit for chronic osteomyelitis. She has type 2 diabetes mellitus complicated by nephropathy and peripheral neuropathy and was recently diagnosed with osteomyelitis of the left foot associated with a chronic neuropathic ulcer. Bone biopsy and culture demonstrated methicillin-sensitive *Staphylococcus aureus*, and 1 week ago she was started on oral high-dose trimethoprim-sulfamethoxazole and rifampin based on sensitivity data for a planned 6-week course of therapy. Medical history is also significant for hypertension. Medications are trimethoprim-sulfamethoxazole, rifampin, glipizide, and atorvastatin.

On physical examination today, temperature is 37.2 °C (99.0 °F), blood pressure is 126/66 mm Hg, and pulse rate is 78/min. Chest, heart, and abdominal examinations are unremarkable. There is loss of sensation to light touch on the feet bilaterally to the ankles. The ulcer overlying the first metatarsal head on the plantar aspect of the left foot is clean and dry.

Current laboratory studies:

Blood urea nitrogen	28 mg/dL (10 mmol/L) (pretreatment baseline: 26 mg/dL [9.3 mmol/L])
Creatinine	1.8 mg/dL (159.1 µmol/L) (pretreatment baseline: 1.4 mg/dL [123.8 µmol/L])
Potassium	4.7 mEq/L (4.7 mmol/L)

Which of the following is the most appropriate management?

A Discontinue rifampin

B Discontinue trimethoprim-sulfamethoxazole

C Order a urine eosinophil test

D Continue current therapy

Answer & Critique

Correct Answer: D

Educational Objective: Manage elevated serum creatinine due to trimet hoprim.

Key Point

Trimethoprim is known to interfere with creatinine secretion without affecting the glomerular filtration rate and can cause increases in serum creatinine of up to 0.5 mg/dL (44.2 µmol/L); this rise therefore does not reflect a drop in actual kidney function.

Continuing this patient's current antibiotic therapy is the most appropriate management. Creatinine is normally filtered by the kidney from the serum, although a smaller amount is also secreted by the proximal tubule. In patients with more advanced chronic kidney disease (CKD), such as this patient, up to 50% of urine creatinine may be secreted instead of being filtered through the glomerulus. Trimethoprim is known to interfere with creatinine secretion without affecting the glomerular filtration rate (GFR) and can cause increases in serum creatinine of up to 0.5 mg/dL (44.2 µmol/L); this rise in serum creatinine therefore does not reflect a drop in actual kidney function. This effect is reversible upon discontinuation of the medication. Trimethoprim also inhibits the epithelial sodium channel in the collecting tubule, effectively acting as a potassium-sparing diuretic and potentially increasing the serum potassium level. The risk of hyperkalemia is therefore increased when using trimethoprim-containing antibiotics, particularly in patients who are on high-dose trimethoprim, who have underlying CKD that may predispose to hyperkalemia, or who are taking a medication with a potassium-sparing effect (such as an ACE inhibitor or angiotensin receptor blocker). Because of this, trimethoprim should be used with caution and with close monitoring in patients with any of these underlying risk factors who require its use for treating infection. This patient's potassium level is within the normal range, and continued close monitoring during her antibiotic therapy is indicated.

Rifampin may cause red or orange discoloration of the urine but is not associated with a decreased GFR, an increase in serum creatinine, or hyperkalemia.

Urine eosinophil testing by means of special stains has been used classically to diagnose acute interstitial nephritis, which is a diagnostic consideration in a patient taking sulfa drugs. However, testing for urine eosinophils is neither sensitive nor specific for this diagnosis, which recent literature suggests may only be definitively made on the basis of kidney biopsy.

Question 35

A 57-year-old man is evaluated in the emergency department for a 3-day history of left inguinal pain and gross hematuria. He reports no history of kidney stones or kidney disease. Medical history is notable for hypertension and dyslipidemia. Medications are amlodipine and atorvastatin.

On physical examination, temperature is 37.2 °C (98.9 °F), blood pressure is 129/78 mm Hg, pulse rate is 96/min, and respiration rate is 12/min. BMI is 24. There is no left costovertebral angle tenderness.

Laboratory studies show normal complete blood count, serum electrolytes, blood urea nitrogen, and serum creatinine. Dipstick urinalysis reveals 3+ blood, trace protein, and negative leukocyte esterase and nitrites. Urine microscopy shows 1-2 leukocytes/hpf, too numerous to count erythrocytes, and no casts.

A kidney ultrasound shows normal-appearing kidneys, no hydronephrosis, and no nephrolithiasis.

Which of the follow ing is the most appropriate diagnostic test to perform next?

A

Doppler ultrasonography of the renal veins

B

Kidney biopsy

C

Noncontrast helical abdominal CT

D

Urine culture

Choose an Answer Above

Answer & Critique

Correct Answer: C

Educational Objective: Evaluate a patient with suspected nephrolithiasis using noncontrast helical abdominal CT.

Key Point

Ultrasonography and noncontrast helical CT of the abdomen are testing options for evaluation of suspected nephrolithiasis; CT is indicated if initial ultrasound testing is negative in a patient with a high clinical suspicion for kidney stones.

Noncontrast helical abdominal CT is the most appropriate diagnostic test to perform next in this patient with a clinical presentation consistent with nephrolithiasis. The findings of unilateral pain combined with hematuria without inflammation on urinalysis suggest nephrolithiasis, and the location of the pain in the inguinal region suggests that the stone may be in the distal ureter. Ultrasonography is increasingly used as an initial study for evaluation of suspected nephrolithiasis because of increased availability, lack of radiation exposure, and lower cost than CT; it is also the study of choice in pregnant patients. However, ultrasonography is less sensitive than CT for detecting kidney stones in the distal ureter or for evaluating other potential nonurologic conditions that may be responsible for the pain. Given this patient's clinical picture that is consistent with nephrolithiasis but with a negative ultrasound for kidney stones, further imaging with noncontrast helical abdominal CT is indicated. Additionally, the absence of hydronephrosis on ultrasound does not rule out nephrolithiasis.

Although renal vein thrombosis can cause hematuria, this diagnosis is less likely given the location of this patient's pain, normal kidney function, and lack of proteinuria. Therefore, Doppler ultrasonography of the renal veins is inappropriate.

Kidney biopsy may be appropriate for patients with suspected glomerulonephritis. Glomerulonephritis typically presents with evidence of decreased kidney function with inflammation and glomerular damage seen as variable proteinuria, hematuria, and possibly dysmorphic erythrocytes and erythrocyte casts on urinalysis. However, this patient's clinical history and laboratory findings are not consistent with glomerulonephritis, and kidney biopsy is not indicated.

Urine cultures are appropriate to diagnose a urinary tract infection or pyelonephritis. However, a urinary tract infection is unlikely in this patient given the absence of dysuria and a urinalysis negative for significant leukocytes, leukocyte esterase, or nitrites.

Question 36

A 72-year-old man is admitted to the ICU with a 3-day history of worsening shortness of breath and edema. He is found to have pulmonary edema with severe hypoxia requiring intubation and mechanical ventilation. Medical history is significant for ischemic cardiomyopathy, coronary artery disease, myocardial infarction, hypertension, hyperlipidemia, and benign prostatic hyperplasia. Medications on admission are aspirin, lisinopril, carvedilol, atorvastatin, and as-needed furosemide.

On physical examination, the patient is afebrile, blood pressure is 92/60 mm Hg, and pulse rate is 112/min. Estimated central venous pressure is 14 cm H_2O. Diffuse crackles are heard throughout both lung fields. Cardiovascular examination reveals an S_3 gallop. There is lower extremity edema to the knees.

A dobutamine infusion is started. A urinary catheter is inserted, and he is given intravenous furosemide with a urine output of 230 mL over the next 4 hours.

Laboratory studies:	
Blood urea nitrogen	76 mg/dL (27.1 mmol/L)
Serum creatinine	3.0 mg/dL (265.2 µmol/L) (baseline: 1.9 mg/dL [168 µmol/L])
Serum electrolytes	Normal
Urine sodium	64 mEq/L (64 mmol/L)
Fractional excretion of sodium	1.9%
Fractional excretion of urea	8.8%
Urinalysis	Specific gravity 1.018; pH 5.5; 1+ protein; 1-2 erythrocytes/hpf; 2-4 leukocytes/hpf; moderate hyaline and fine granular casts

Which of the following is the most likely diagnosis?

A Acute interstitial nephritis
B Acute tubular necrosis
C Obstructive uropathy
D Prerenal acute kidney injury

Answer & Critique

Correct Answer: D

Educational Objective: Diagnose prerenal acute kidney injury in a patient taking diuretics.

Key Point

Because urea is less sensitive to the effects of diuretics, the fractional excretion of urea may be more useful in this setting to identify the cause of acute kidney injury.

The most likely diagnosis is prerenal acute kidney injury (AKI). AKI occurs most commonly in the setting of true volume depletion or decreased effective blood volume as seen in this patient with decreased cardiac output. In patients with AKI and oliguria, the fractional excretion of sodium (FE_{Na}) may be helpful in differentiating between prerenal AKI and AKI from renal tubular cell damage or acute tubular necrosis (ATN). The FE_{Na} measures the percent of filtered sodium excreted in the urine and is calculated as $(U_{Sodium} \times P_{Cr})/(U_{Cr} \times P_{Sodium}) \times 100$. It is considered a more accurate measurement of kidney sodium avidity in prerenal states than the urine sodium concentration because these individuals are both sodium and water avid, which may cause an elevated urine sodium concentration despite kidney sodium retention. However, the FE_{Na} is less reliable when diuretics are being used because the urine sodium may not accurately reflect attempts by the kidney to retain sodium. Because urea is less sensitive to the effects of diuretics, the fractional excretion of urea (FE_{Urea}) may be more useful in this setting. The FE_{Urea} is calculated as $(U_{Urea} \times P_{Cr})/(U_{Cr} \times P_{Urea}) \times 100$, with values <35% suggesting a prerenal state. In this patient, the FE_{Na} is higher than expected in a prerenal state at 1.9%, but the FE_{Urea} is only 8.8%, suggesting an underlying prerenal state.

The urine sediment of a patient with acute interstitial nephritis will typically reflect inflammation with leukocytes, erythrocytes, or leukocyte casts, none of which is seen in this patient's urine sediment.

The urine sediment in patients with ATN will usually show evidence of tubular damage with sloughed tubular epithelial cells or coarse granular casts. These are not present in this patient, making ATN less likely.

Although this patient has a history of benign prostatic hyperplasia, postrenal obstruction is unlikely due to the presence of an indwelling urinary catheter.

Question 37

A 24-year-old woman is evaluated for fever, lower extremity edema, and worsening malar rash. She was diagnosed with systemic lupus erythematosus 2 years ago. Her initial evaluation showed normal kidney function, trace proteinuria, and an otherwise normal urinalysis; periodic monitoring of her kidney function and urinalysis has been unchanged. She has been treated with hydroxychloroquine and prednisone, 5 mg/d, since the time of her diagnosis with good control of her symptoms. Medical history is otherwise unremarkable, and she takes no additional medications.

On physical examination, blood pressure is 140/92 mm Hg. A malar rash is present. Mild erythema and effusion in the left knee and bilateral wrist joints are noted. The remainder of the examination is unremarkable.

Laboratory studies:

Hemoglobin	9.2 g/dL (92 g/L)
C3	Low
C4	Low
Creatinine	1.0 mg/dL (88.4 µmol/L)
Liver chemistry tests	Normal
Anti–double-stranded DNA antibodies	Elevated
Urinalysis	3+ blood; 2+ protein; 20-30 erythrocytes/hpf; 5-10 leukocytes/hpf
Urine protein-creatinine ratio	2200 mg/g

A kidney biopsy shows a diffuse proliferative glomerulonephritis with immunofluorescence microscopy showing granular deposits in the subendothelial, mesangial, and subepithelial areas (IgG, IgM, IgA, C3, and C1q), which are confirmed by electron microscopy, and is classified as class IV lupus nephritis.

Which of the following is the most appropriate treatment?

A

Increase prednisone

B

Increase prednisone and add mycophenolate mofetil

C

Increase prednisone and perform plasmapheresis

D

Continue current therapy and rebiopsy in 3 months

Choose an Answer Above

Answer & Critique

Correct Answer: B

Educational Objective: Treat lupus nephritis with combination immunosuppressive therapy.

Key Point

Most patients with class III lupus nephritis and all patients with class IV lupus nephritis benefit from aggressive combination immunosuppressive therapy.

Increasing prednisone and adding mycophenolate mofetil are indicated for this patient with class IV lupus nephritis (LN). LN occurs in up to 70% of patients with systemic lupus erythematosus (SLE), with the presence of anti–double-stranded DNA antibodies being a marker for risk. All patients with SLE should be evaluated for possible nephritis at the time of diagnosis, with individualized surveillance based on the presence and degree of kidney abnormalities on laboratory studies. Patients who develop LN typically present with extrarenal symptoms of SLE at the time of diagnosis of LN. Glomerular disorders associated with SLE are classified into six different patterns based upon kidney biopsy histopathology, although there may be some overlap between classes in an individual patient, and some patients may evolve from one class to another. Patients with class I or II LN may have minimal or no kidney findings, and those with classes III and IV present with varying degrees of the nephritic syndrome. Patients with class V LN present predominantly with proteinuria. Class VI is the end stage of long-standing LN. This patient is experiencing a major lupus flare with arthritis, rash, fevers, and class IV LN on kidney biopsy. Class IV LN represents diffuse glomerular involvement and is the most common and severe form of nephritis associated with lupus. It is also associated with elevated anti–double stranded DNA antibody levels and hypocomplementemia, particularly during periods of active disease. Most patients with class III and all patients with class IV LN benefit from aggressive combination immunosuppressive therapy. The optimal initial therapy is to increase glucocorticoid doses (typically an intravenous pulse followed by a tapering oral dose), which is accompanied by either intravenous cyclophosphamide or mycophenolate mofetil.

The use of glucocorticoids alone has been associated with an inferior outcome compared with alkylating agents or antimetabolites in combination with glucocorticoids for patients with LN requiring treatment.

The addition of plasmapheresis to immunosuppressive therapy has not been shown to improve outcomes in patients with LN.

The patient has a high probability of worsening kidney function if not aggressively treated in view of the class IV LN, and any delay engenders the risk of irreversible kidney failure.

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Question 38

A 70-year-old woman is evaluated during a new-patient visit. She is asymptomatic. Medical history is significant for osteoporosis and borderline blood pressure elevations; she was advised by her previous physician to periodically check her blood pressures at home. She reports that over the past year these readings have been consistently between 140 and 150 mm Hg systolic and 82 and 86 mm Hg diastolic. She follows a low salt diet and exercises regularly three times a week. Family history is notable for both parents who were diagnosed with hypertension after the age of 65 years. Medications are alendronate and calcium with vitamin D.

On physical examination, temperature is 36.9 °C (98.4 °F), pulse rate is 68/min, and respiration rate is 14/min. Blood pressure is 146/86 mm Hg, with a repeat measurement of 148/86 mm Hg; there are no orthostatic changes.

Laboratory studies show a serum creatinine level of 0.7 mg/dL (61.9 µmol/L) and a serum potassium level of 4.0 mEq/L (4.0 mmol/L); urinalysis is normal.

Electrocardiogram is normal.

Which of the following is the most appropriate next step in management?

A

Begin hydrochlorothiazide

B

Begin lisinopril

C

Obtain echocardiography

D

Continue clinical observation

Choose an Answer Above

Answer & Critique

Correct Answer: D

Educational Objective: Manage elevated blood pressure in an older patient.

Key Point

The eighth report of the Joint National Committee recommends a treatment goal of <150/90 mm Hg for patients with hypertension who are ≥60 years.

Continued clinical observation is appropriate for this older patient with elevated blood pressure measurements. The eighth report of the Joint National Committee (JNC 8) recommends that pharmacologic treatment be initiated to lower blood pressure in patients aged ≥60 years who have systolic blood pressure persistently ≥150 mm Hg or diastolic blood pressure ≥90 mm Hg, and treat to a goal of systolic <150 mm Hg and diastolic <90 mm Hg. This recommendation is based on good-quality evidence that a blood pressure goal of <150/90 mm Hg reduces the risk of cardiovascular events, but there appears to be no added benefit with lower targets (140-149 mm Hg). Therefore, in this 70-year-old patient in whom multiple readings have not shown blood pressure above this threshold for treatment, continued clinical observation with periodic blood pressure determinations and evaluation for potential end-organ damage associated with hypertension is recommended.

Pharmacologic treatment, such as a thiazide diuretic or an ACE inhibitor, is not indicated at this time.

Although echocardiography is more sensitive for detecting left ventricular hypertrophy than electrocardiography, it is not indicated for evaluation of possible hypertension or as an initial study in patients with documented hypertension in the absence of another indication (such as clinical evidence of heart failure).

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Question 39

A 25-year-old man is evaluated for dark-colored urine for 2 days, swelling of the face and hands for 1 day, and severe headaches this morning. He reports having an upper respiratory tract infection 1 week ago with fever, sore throat, and swollen glands, but had otherwise felt well. Medical history is otherwise unremarkable, and he takes no medications.

On physical examination, temperature is 37.2 °C (99.0 °F), blood pressure is 180/90 mm Hg, pulse rate is 88/min, and respiration rate is 14/min. Cardiopulmonary and abdominal examinations are normal. No skin rash or arthritis is present. There is bilateral lower extremity edema to the mid shins.

Laboratory studies:

Albumin	3.3 g/dL (33 g/L)
C3	Low
C4	Normal
Creatinine	1.4 mg/dL (124 µmol/L)
Antistreptolysin O antibodies	Elevated
Urinalysis	3+ blood; 2+ protein; too numerous to count erythrocytes/hpf; 10-15 leukocytes/hpf; numerous erythrocyte casts
Urine protein-creatinine ratio	1900 mg/g
Rapid streptococcal antigen test	Positive

Which of the following is the most likely diagnosis?

A

IgA nephropathy

B

Infection-related glomerulonephritis

C

Lupus nephritis

D

Small-vessel vasculitis

Choose an Answer Above

Answer & Critique

Correct Answer: B

Educational Objective: Diagnose infection-related glomerulonephritis.

Key Point

Infection-related glomerulonephritis is characterized by preceding symptoms of an upper respiratory tract infection suggestive of streptococci, followed by the nephritic syndrome and low C3 levels with normal C4 levels.

This patient likely has infection-related glomerulonephritis (IRGN) following a streptococcal infection. Supportive evidence includes preceding symptoms of an upper respiratory tract infection suggestive of streptococci (rapid streptococcal antigen test is positive and antistreptolysin O antibodies are elevated), followed by the nephritic syndrome in 1 week, and low C3 levels with normal C4 levels (suggesting an alternative pathway of complement activation, which is typical of IRGN). Most patients will show spontaneous resolution of nephritis with conservative management (antibiotics, blood pressure management, and diuretics).

IgA nephropathy (IgAN) is the most common form of glomerulonephritis. Asymptomatic microscopic hematuria with or without proteinuria is the most common presentation of IgAN, and episodic gross hematuria following an upper respiratory tract infection is a classic presentation. Kidney manifestations usually occur concomitantly with the respiratory infection in IgAN ("synpharyngitic" nephritis), as opposed to the typical 7- to 10-day latent period with IRGN. Moreover, complement levels are typically normal in IgAN, whereas C3 is typically low and C4 is normal in IRGN.

Lupus nephritis may occasionally be precipitated by infections. Patients with lupus typically experience systemic manifestations such as rash and arthritis, although kidney-limited disease is sometimes seen. Both C3 and C4 complement levels are depressed in this condition due to the classical pathway of complement being activated. In IRGN, C3 is typically depleted, with normal levels of C4 due to activation of the alternative pathway of complement.

Small-vessel vasculitis is also associated with glomerulonephritis. However, there are frequently other clinical findings of vasculitis present, and complement levels are typically normal.

Question 40

A 54-year-old woman is hospitalized for management of acute kidney injury. Medical history is significant for obesity but is otherwise unremarkable. She reports that she was seen in a weight loss clinic 1 month ago and was prescribed an unknown weight reduction drug, which she has been taking since that time. She takes no other medications.

On physical examination, blood pressure is 140/70 mm Hg, and pulse rate is 72/min. BMI is 40. Estimated central venous pressure is 10 cm H_2O. There are crackles at the lung bases. Heart examination is unremarkable. There is lower extremity edema to the mid-calf bilaterally. The remainder of the examination is unremarkable.

Laboratory studies show a serum creatinine level of 5.1 mg/dL (450.8 μmol/L). Urinalysis is dipstick positive for trace protein, and urine sediment is notable for 0-2 erythrocytes/hpf, 0-5 leukocytes/hpf, and numerous calcium oxalate crystals.

Kidney ultrasound demonstrates normal-sized kidneys with slightly increased echogenicity and no hydronephrosis. Kidney biopsy demonstrates deposition of calcium oxalate crystals within the tubules and the interstitium.

Which of the following is the most likely cause of this patient's acute kidney injury?

A

Aristolochic acid

B

Ephedrine

C

Orlistat

D

Phentermine

Answer & Critique

Correct Answer: C

Educational Objective: Identify orlistat as a cause of acute kidney injury.

Key Point

Orlistat may be a cause of acute kidney injury by triggering acute oxalate nephropathy, particularly in patients with volume depletion or chronic kidney disease.

This patient has acute oxalate nephropathy most likely caused by orlistat. Orlistat is thought to cause acute kidney injury (AKI) through enteric hyperoxaluria. Orlistat blocks fat uptake and results in the production of calcium soaps from unabsorbed fat in the small bowel. Calcium soaps reduce the availability of free enteric calcium, preventing binding of oxalate in the gut by calcium, and allowing for increased intestinal uptake of oxalate and subsequent renal oxalate excretion. Excessive renal oxalate excretion predisposes to development of oxalate crystals within the tubules and interstitium as seen in this patient, causing intratubular obstruction and acute kidney injury. Volume depletion and preexisting kidney disease appear to increase the risk of developing orlistat-associated nephropathy.

Aristolochic acid is present in some herbal preparations and weight loss supplements and can cause nephropathy. This condition is characterized by extensive, primarily interstitial, fibrosis with tubular loss, which is not seen on this patient's kidney biopsy. Patients with this condition are also at increased risk for urothelial malignancies.

Ephedrine is associated with nephrolithiasis, and analysis of the stones reveals the presence of ephedrine, norephedrine, and pseudoephedrine. Patients may also have rhabdomyolysis. These findings are not found in this patient, making this an unlikely cause of her AKI.

Phentermine is not known to cause AKI or other kidney disorders.

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Question 41

A 35-year-old man is evaluated in the emergency department for dyspnea of 24 hours' duration. He also reports progressive lower extremity edema for 1 month. He has no other pertinent personal or family medical history, and he takes no medications.

On physical examination, the patient is afebrile, blood pressure is 120/78 mm Hg, pulse rate is 100/min, and respiration rate is 22/min. Oxygen saturation on ambient air is 88%. BMI is 25. The chest is clear. Examination of the heart is unremarkable. There is bilateral lower extremity pitting edema to the knees. The remainder of the examination is normal.

Laboratory studies:

Albumin	1.8 g/dL (18 g/L)
Creatinine	1.1 mg/dL (97.2 µmol/L)
Urinalysis	Negative for blood; 3+ protein; no cells
Urine protein-creatinine ratio	5500 mg/g

Chest radiograph is normal. CT angiogram of the chest shows a right pulmonary artery embolism.

The patient is started on supplemental oxygen and heparin.

Which of the following is the most likely underlying diagnosis?

A Acute interstitial nephritis

B Membranous glomerulopathy

C Poststreptococcal glomerulonephritis

D Thrombotic microangiopathy

Answer & Critique

Correct Answer: B

Educational Objective: Diagnose membranous glomerulopathy.

Key Point

Although the clinical presentation of membranous glomerulopathy is indistinguishable from other causes of the nephrotic syndrome, the propensity for thromboembolic events is much higher.

The most likely diagnosis is membranous glomerulopathy (MG). This patient has evidence of the nephrotic syndrome, with significant protein loss in the urine, hypoalbuminemia, and edema. He also has a pulmonary embolism, a common complication of the nephrotic syndrome. The clinical presentation of MG is indistinguishable from other causes of the nephrotic syndrome, although the propensity for venous thromboembolism, and particularly renal vein thrombosis, is much higher in MG than other disorders associated with the nephrotic syndrome, such as focal segmental glomerulosclerosis or minimal change glomerulopathy. The pathophysiology of hypercoagulability in the nephrotic syndrome is not well understood, nor has the mechanism underlying the higher propensity for thromboembolism in MG been well defined. The risk appears to be inversely related to the serum albumin level in MG, and prophylactic anticoagulation is frequently given to patients with MG with a serum albumin level of ≤2.8 g/dL (28 g/L). MG is the most common cause of idiopathic nephrotic syndrome in adult white persons but may also be associated with infections, systemic lupus erythematosus, medications, and certain malignancies. Definitive diagnosis is by kidney biopsy.

The hypercoagulable state is associated with the nephrotic syndrome only, not other kidney syndromes such as acute interstitial nephritis or poststreptococcal glomerulonephritis. Additionally, these disorders typically present with evidence of inflammation on urinalysis and kidney failure, neither of which is present in this patient.

The site of thrombosis in thrombotic microangiopathy is the microvasculature, leading to clinical manifestations such as microangiopathic hemolytic anemia, thrombocytopenia, and organ dysfunction (including kidney failure). Large-vessel thrombosis does not occur as is present in this case.

Question 42

A 32-year-old man is evaluated during a follow-up visit for high blood pressure. During a recent insurance examination, his blood pressure was 180/80 mm Hg. He rechecked his blood pressure in a pharmacy, and it was 138/80 mm Hg. Medical history is unremarkable. Family history is notable for both parents who have hypertension; his father experienced a stroke at age 60 years. The patient takes no medications. He has a 10-pack-year history of smoking but stopped smoking 5 years ago. He is asymptomatic, exercises regularly, and follows a heart-healthy, low salt diet.

On physical examination, temperature is 36.8 °C (98.3 °F), blood pressure is 190/90 mm Hg, pulse rate is 90/min, and respiration rate is 14/min. BMI is 28. Blood pressure taken 5 minutes later is 160/80 mm Hg. The blood pressure readings are symmetric in all four limbs, with no postural drop. Retinal examination is normal. Cardiovascular examination is normal.

Laboratory studies show normal serum creatinine and electrolyte levels, and a urinalysis is unremarkable.

Electrocardiogram is normal.

Ambulatory blood pressure monitoring results:

Average blood pressure	121/81 mm Hg
Systolic blood pressure readings >140 mm Hg	15%
Diastolic blood pressure readings >90 mm Hg	20%
Awake/sleep blood pressure decrease	16%/12%

Which of the following is the most appropriate next step in management?

A Order echocardiography

B Order a plasma aldosterone-plasma renin ratio

C Start amlodipine

D Continue clinical follow-up

Answer & Critique

Correct Answer: D

Educational Objective: Manage white coat hypertension.

Key Point

In patients with white coat hypertension, close observation for the emergence of sustained hypertension or end-organ damage is recommended; drug therapy is not usually required.

Continued clinical follow-up is appropriate for this patient with white coat hypertension. He has high blood pressure readings in the clinic; however, his ambulatory blood pressure monitor (ABPM) readings do not meet the definition of hypertension. The diagnosis of white coat hypertension is applied to patients with average blood pressure readings ?140/90 mm Hg in the office and average readings <135/85 mm Hg as determined by ABPM. Daytime (awake) average above 140/90 mm Hg and nighttime (asleep) average above 125/75 mm Hg are also used to diagnose hypertension on ABPM. Analysis of nocturnal readings compared to daytime reading is also helpful. Compared with daytime readings, nocturnal readings are approximately 15% lower ("dipping"). A non-dipping status (failure to drop nocturnal blood pressure by <10%) is associated with more cardiovascular events compared with dipping. This patient dips appropriately at night. Patients with white coat hypertension may have an elevated cardiovascular risk compared with normotensive patients. Moreover, such patients are also at a higher risk for sustained hypertension. Therefore, close observation for sustained hypertension and end-organ damage is recommended in patients with white coat hypertension.

Echocardiography is more sensitive than electrocardiography in detecting evidence of left ventricular hypertrophy. However, it is not used for the diagnosis of hypertension unless there is evidence of end-organ damage or if the information would help guide subsequent treatment. In this patient with a normal ABPM study without evidence of cardiac disease, echocardiography is not indicated.

Evaluation for secondary causes of hypertension such as primary hyperaldosteronism is not indicated in this patient without evidence of sustained hypertension and a normal serum potassium level.

Drug therapy is not recommended unless sustained hypertension or evidence of end-organ damage is present.

Question 43

A 72-year-old man was diagnosed with colon cancer 12 months ago, and surgical resection was performed. He presented with metastatic lesions to the liver 2 months ago, for which he was started on a chemotherapy regimen that includes oxaliplatin with 5-fluorouracil and leucovorin with bevacizumab. He has been experiencing progressive headaches and lower extremity swelling over the past 3 weeks. He reports no diarrhea, mental status changes, or shortness of breath.

On physical examination, temperature is 36.8 °C (98.2 °F), blood pressure is 180/120 mm Hg, pulse rate is 80/min, and respiration rate is 16/min. BMI is 32. There is 2+ pedal edema.

Laboratory studies show a hemoglobin level of 7.5 g/dL (75 g/L), a platelet count of 90,000/μL (90 × 10^9/L), and a serum creatinine level of 2.2 mg/dL (194 μmol/L); a peripheral blood smear shows numerous schistocytes.

Which of the following is the most likely cause of this patient's clinical picture?

A
5-Fluorouracil

B
Bevacizumab

C
Leucovorin

D
Oxaliplatin

Answer & Critique

Correct Answer: B

Educational Objective: Diagnose thrombotic microangiopathy caused by chemotherapy.

Key Point

Two anti-vascular endothelial growth factor inhibitors, bevacizumab and sunitinib, have been linked to thrombotic microangiopathy, which typically subsides after stopping the drug.

Bevacizumab is the most likely cause of this patient's clinical picture. This patient presents with classic features of thrombotic microangiopathy (TMA), including microangiopathic hemolytic anemia, a low platelet count, and kidney dysfunction. Chemotherapeutic agents known to be associated with TMA include mitomycin C, gemcitabine, tyrosine kinase inhibitors, mammalian target of rapamycin (mTOR) inhibitors (sirolimus, everolimus), and anti-vascular endothelial growth factor (VEGF) inhibitors. VEGF inhibitors are an important class of drugs used in treating metastatic cancer, and they are able to induce a form of microangiopathy very similar to preeclampsia/eclampsia that is associated with severe hypertension and kidney failure. VEGF inhibition by endogenous factors is thought to play a key role in development of preeclampsia/eclampsia, and two VEGF inhibitors, bevacizumab and sunitinib, have been linked to TMA, which typically subsides after stopping the drug. Patients typically present with an insidious onset of kidney failure and hypertension (new or exacerbated). There tends to be a variable amount of proteinuria and a relatively bland urine sediment. The cancer is not typically overt (to differentiate from cancer-associated TMA, in which there are widely metastatic lesions at the time of diagnosis of TMA). Plasmapheresis is not usually effective for treatment of VEGF inhibitor–associated TMA and is not indicated.

The other chemotherapeutic agents (5-fluorouracil, leucovorin, oxaliplatin) being administered are not associated with TMA.

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Question 44

A 54-year-old woman is evaluated during a follow-up visit for stage G4/A3 chronic kidney disease due to diabetic nephropathy. She is asymptomatic except for mild fatigue and peripheral edema and reports a good appetite. Medications are ramipril, furosemide, and calcium acetate.

On physical examination, temperature is 37.0 °C (98.6 °F), blood pressure is 128/73 mm Hg, pulse rate is 80/min, and respiration rate is 14/min. BMI is 29. Pallor and pale mucous membranes are noted. There is no jugular venous distention. There is no pericardial friction rub. The lungs are clear. There is no asterixis. Neurologic examination is normal.

Laboratory studies are significant for a serum creatinine level of 2.6 mg/dL (229.8 μmol/L) and an estimated glomerular filtration rate of 19 mL/min/1.73 m^2 (1 year ago: 30 mL/min/1.73 m^2).

After discussing the goals of care, the patient wishes to explore renal replacement options and kidney transplantation.

Which of the following is the most appropriate management?

A

Nephrologist referral now

B

Nephrologist referral in 6 months

C

Repeat creatinine measurement in 2 weeks

D

Continue current management

Answer & Critique

Correct Answer: A

Educational Objective: Appropriately time the referral of a patient with chronic kidney disease to a nephrologist.

Key Point

All patients with stage G4 or G5 chronic kidney disease should be referred to a nephrologist for management, and referral for transplant evaluation is indicated once the estimated glomerular filtration rate is below 20 mL/min/1.73 m^2.

Nephrologist referral and kidney transplant evaluation should occur now. This patient has severe chronic kidney disease (CKD) and will likely require dialysis within the next 1 to 2 years. All patients with stage G4 or G5 CKD should be referred to a nephrologist for evaluation and optimization of metabolic parameters and preparation for dialysis. Because proper preparation for dialysis can take many months, especially if an arteriovenous fistula must be created for hemodialysis, timely referral is important. Hemodialysis and peritoneal dialysis have similar clinical outcomes; choice of modality should be guided by patient preference, willingness, and ability to participate in self-care. All patients who are willing to consider kidney transplant and do not have absolute medical contraindications should be referred for transplant evaluation once their estimated glomerular filtration rate is below 20 mL/min/1.73 m^2 because they are then eligible to be placed on a waiting list for a transplant. This is especially important because the waiting list is several years long in most parts of the United States, and early listing maximizes the chances of surviving until transplant. Also, if a living donor is identified, it is possible that the patient may receive a preemptive transplant before requiring dialysis. It is important to refer patients with CKD to a nephrologist early in the course of the disease for evaluation because late referral is associated with increased mortality.

Waiting to refer to a nephrologist for 6 months will delay proper preparation for dialysis therapy, dialysis access placement, and transplant evaluation.

Rechecking serum creatinine in 2 weeks is not indicated because this patient has long-standing CKD that is unlikely to be significantly improved after 2 weeks, and this approach will unnecessarily delay referral to a nephrologist.

Continuing current management is incorrect because the patient requires timely preparation for renal replacement therapy and transplant referral, and delays in nephrology referral for patients with severe CKD are associated with increased risk of mortality.

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Question 45

A 54-year-old woman is evaluated during a follow-up examination. She has a 22-year history of type 2 diabetes mellitus complicated by sensory neuropathy and proliferative retinopathy, for which she has received laser photocoagulation. She also has hypertension and hyperlipidemia. Medications are metformin, glipizide, atorvastatin, and lisinopril, 20 mg/d.

On physical examination, temperature is normal, blood pressure is 132/78 mm Hg, pulse rate is 72/min, and respiration rate is 12/min. BMI is 29. Cardiopulmonary and abdominal examinations are normal. There is no lower extremity edema. There is decreased sensation to monofilament testing in the feet.

Laboratory studies:

Hemoglobin A_{1c}	6.8%
Creatinine	1.2 mg/dL (106.1 µmol/L) (2 years ago: 0.8 mg/dL [70.7 µmol/L])
Electrolytes	Normal
Urine albumin-creatinine ratio	460 mg/g (5 years ago: <30 mg/g)

Which of the following is the most appropriate management of this patient's hypertension?

A

Add amlodipine

B

Add losartan

C

Reduce lisinopril dose

D

Continue current therapy

Answer & Critique

Correct Answer: D

Educational Objective: Manage diabetic nephropathy.

Key Point

Adequate blood pressure control and use of an ACE inhibitor or angiotensin receptor blocker has been shown to slow the progression of diabetic nephropathy.

Continuing this patient's current therapy is the most appropriate management. This patient has long-standing type 2 diabetes mellitus complicated by proliferative retinopathy and neuropathy. She has worsening proteinuria accompanied by a slow decline in kidney function over several years. Her blood pressure is within the desired range, and she is receiving an ACE inhibitor. Continued management is therefore appropriate. With adequate blood pressure control and use of an ACE inhibitor (or angiotensin receptor blocker [ARB]), progression of diabetic nephropathy is slowed but not eliminated. A maximally tolerated dose of an ACE inhibitor or ARB should be tried in an attempt to lower proteinuria as much as possible.

Calcium channel blockers are effective antihypertensive medications in patients with diabetic nephropathy and hypertension, although they do not have the same degree of renoprotection as either ACE inhibitors or ARBs. Because this patient's blood pressure is well controlled and she is already on an ACE inhibitor, there is no indication for the addition of amlodipine.

Adding an ARB (such as losartan) to an ACE inhibitor has not been shown to improve kidney outcomes, and dual angiotensin system inhibition increases the risk of hyperkalemia and acute kidney injury. It is therefore not recommended, even in patients with significant proteinuria on monotherapy with an ACE inhibitor or ARB.

Both ACE inhibitors and ARBs exert their renoprotective effect by decreasing glomerular hyperfiltration by reducing the glomerular filtration rate (GFR). In most patients with normal to moderately impaired kidney function, this medication-induced decrease in GFR is well tolerated, although this may result in a slight increase in the serum creatinine. Given this patient's mild increase in serum creatinine and normal serum electrolytes, there is no indication for reducing the dose of her ACE inhibitor lisinopril, which is beneficial in treating her hypertension and proteinuria.

Question 46

A 54-year-old man is hospitalized for necrotizing pancreatitis. His course has been complicated by acute respiratory distress syndrome requiring ventilator support. He is hemodynamically unstable and requires an intravenous norepinephrine infusion to maintain a mean arterial blood pressure of 65 mm Hg. On the third hospital day, he develops increasing norepinephrine and oxygen requirements and increasing ventilator airway pressures, and he becomes oliguric. Medications are propofol and fentanyl.

On physical examination, blood pressure is 80/60 mm Hg, pulse rate is 92/min, and respiration rate is 12/min. Estimated central venous pressure is 12 cm H_2O. Heart sounds are normal. There are diffuse pulmonary crackles. The abdomen is modestly distended and tense. Bilateral lower extremity and flank edema are present.

Laboratory studies:

Hemoglobin	9.0 g/dL (90 g/L)
INR	2.0
Creatinine	2.1 mg/dL (185.6 µmol/L) (on admission, 0.9 mg/dL [79.6 µmol/L])
Urine sodium	<10 mEq/L (10 mmol/L)
Urinalysis	Specific gravity 1.022; pH 6.0; 0-1 erythrocytes/hpf; 0-2 leukocytes/hpf; occasional hyaline casts

Kidney ultrasound reveals normal-sized kidneys and no hydronephrosis.

Which of the following is the most appropriate next step in management?

A Bladder pressure measurement

B Erythrocyte transfusion to a target hemoglobin of 11 g/dL (110 g/L)

C Isotonic saline bolus, 500 mL

D Pulmonary artery catheter placement

Answer & Critique

Correct Answer: A

Educational Objective: Diagnose abdominal compartment syndrome.

Key Point

Abdominal compartment syndrome should be suspected in patients with oliguria or increasing serum creatinine levels who have had abdominal surgery, who have received massive fluid resuscitation, who have a tense abdomen, or who have liver or pancreatic disease with ascites.

Bladder pressure measurement is the most appropriate next step in management. Abdominal compartment syndrome (ACS) should be suspected in patients with oliguria or increasing serum creatinine levels who have had abdominal surgery, who have received massive fluid resuscitation, who have a tense abdomen, or who have liver or pancreatic disease with ascites. ACS is typically defined as new organ dysfunction with an intra-abdominal pressure >20 mm Hg. This patient is developing ACS manifested by increased hemodynamic instability, worsening respiratory failure with increased airway pressures and increasing difficulty with oxygenation, a tense abdomen on examination, and oliguric kidney failure. Diagnosis of intra-abdominal hypertension and ACS is accomplished by transduction of bladder pressure. Although medical treatment (diuresis, dialysis, management of ascites) can be tried, surgical decompression of the abdomen is often necessary to definitively treat ACS.

There are no data to support that transfusing patients with severe sepsis to a hemoglobin level above 10 g/dL (100 g/L) improves outcomes. The current Surviving Sepsis Guidelines recommend that, once tissue hypoperfusion has resolved and in the absence of serious comorbidities, erythrocytes should only be transfused when hemoglobin decreases to <7.0 g/dL (70 g/L).

Although this patient's urine sodium is <10 mEq/L (10 mmol/L), clinically he is not intravascularly volume depleted. Therefore, further volume resuscitation is not indicated because it may contribute to worsening organ dysfunction by increasing intra-abdominal pressure.

There is no evidence that hemodynamic monitoring with a pulmonary artery catheter improves clinical outcomes in patients with acute respiratory distress syndrome, and it may be associated with harm.

Question 47

A 68-year-old woman is evaluated for myalgia and generalized weakness. Medical history is significant for hypertension, hyperlipidemia, hypothyroidism, and chronic kidney disease. One week ago, she was hospitalized with symptoms of a transient ischemic attack. Carotid ultrasound revealed 50% stenosis of her left internal carotid. Her serum creatinine level during hospitalization was 1.5 mg/dL (132.6 µmol/L), and her thyroid-stimulating hormone level was 18 µU/mL (18 mU/L). She states that she had not been regularly adherent with her medications prior to admission, but that since discharge she has been taking her medications as prescribed. Current medications are aspirin, high-dose atorvastatin, lisinopril, hydrochlorothiazide, and levothyroxine.

On physical examination, blood pressure is 152/78 mm Hg, and pulse rate is 82/min. She is not orthostatic. Skin turgor is normal. The lung fields are clear. Cardiovascular examination reveals a left carotid bruit and a fourth heart sound. There is diffuse tenderness to palpation of the major muscle groups. Trace lower extremity edema is present.

Laboratory studies:

Complete blood count	Normal
Creatinine	3.0 mg/dL (265.2 µmol/L)
Electrolytes:	
Sodium	132 mEq/L (132 mmol/L)
Potassium	5.6 mEq/L (5.6 mmol/L)
Chloride	100 mEq/L (100 mmol/L)
Bicarbonate	22 mEq/L (22 mmol/L)
Phosphorus	6.0 mg/dL (1.9 mmol/L)
Urinalysis	4+ blood; 0-1 erythrocytes/hpf; 0-2 leukocytes/hpf; numerous granular casts

Which of the followi ng medications is the most likely cause of this patient's acute kidney injury?

A

Atorvastatin

B

Hydrochlorothiazide

C

Levothyroxine

D

Lisinopril

Choose an Answer Above

Answer & Critique

Correct Answer: A

Educational Objective: Diagnose statin-induced rhabdomyolysis.

Key Point

Risk factors for the development of statin-induced rhabdomyolysis include advanced age, female gender, preexisting chronic kidney disease, diabetes mellitus, hypothyroidism, high-dose statin therapy, and use of medications metabolized through cytochrome P450 3A4.

The most likely diagnosis is statin-induced rhabdomyolysis associated with atorvastatin therapy as a cause of this patient's acute kidney injury (AKI). This is supported by her symptoms of muscle weakness, physical examination findings, AKI, and urinalysis with blood but no erythrocytes. Myoglobin released from damaged muscle cause renal tubular obstruction, direct nephrotoxicity, intrarenal vasoconstriction, and AKI. Statin-induced rhabdomyolysis is a rare occurrence, and routine testing of muscle enzymes following initiation of statin therapy is not recommended. However, further evaluation is indicated in patients presenting with suggestive symptoms and clinical findings, as in this patient. Risk factors for development of statin-induced myositis include advanced age, female gender, preexisting chronic kidney disease (CKD), diabetes mellitus, hypothyroidism, high-dose statin therapy, and use of medications metabolized through cytochrome P450 3A4, which may increase serum levels of statins (lovastatin, simvastatin, atorvastatin) metabolized through this pathway. Treatment includes discontinuation of the statin, hydration, and management of any associated electrolyte abnormalities.

Hydrochlorothiazide can cause symptoms of weakness from volume depletion, hyponatremia, or hypokalemia. This patient has no evidence of volume depletion on examination, and her serum potassium level is elevated. Although she has hyponatremia, it is mild and does not explain her symptoms or urinalysis findings.

Although hypothyroidism may be associated with myalgia and elevations of serum muscle enzymes, rhabdomyolysis is rare, and initiation of levothyroxine therapy is not associated with worsening muscle symptoms. This patient's lack of myalgia at the time of hospitalization and mild degree of hypothyroidism make hypothyroid myopathy an unlikely diagnosis.

ACE inhibitors such as lisinopril can cause AKI in certain settings such as hypovolemia or renal artery stenosis. However, this patient's clinical presentation and laboratory findings are not consistent with AKI associated with ACE inhibitor therapy.

Question 48

A 42-year-old man is evaluated during a follow-up visit for chronic kidney disease due to vesicoureteral reflux that progressed to end-stage kidney disease 10 years ago; he has been receiving hemodialysis for 5 years. He is anuric but feels well and reports no other symptoms. Medical history is otherwise unremarkable.

On physical examination, temperature is 37.0 °C (98.6 °F), blood pressure is 145/95 mm Hg, pulse rate is 85/min, and respiration rate is 14/min. BMI is 26. The lungs are clear. The abdominal examination is normal, and there is no costovertebral angle tenderness. The remainder of the examination is normal.

An abdominal ultrasound was recently performed to evaluate a complaint of abdominal discomfort, which has since resolved. This study was remarkable for bilateral small echogenic kidneys with innumerable cysts and a 4-cm mass in the right renal parenchyma.

Which of the following is the most likely diagnosis?

A

Hemorrhagic kidney cyst

B

Renal angiomyolipoma

C

Renal cell carcinoma

D

Transitional cell carcinoma

Choose an Answer Above

Answer & Critique

Correct Answer: C

Educational Objective: Diagnose acquired cystic kidney disease and renal cell carcinoma in a patient with end-stage kidney disease.

Key Point

Acquired cystic kidney disease is associated with a large number of small bilateral kidney cysts, reduced kidney size, and a markedly increased risk for developing renal cell carcinoma.

The most likely diagnosis is renal cell carcinoma. The patient has acquired cystic kidney disease (ACKD), which becomes more common and progresses during the course of end-stage kidney disease (ESKD); the incidence of ACKD rises dramatically as time on dialysis increases. Patients with ACKD typically have a large number of small bilateral kidney cysts and reduced kidney size. For unclear reasons, patients with ACKD have an approximately 30-fold increased risk for developing renal cell carcinoma; despite this, routine screening for this malignancy is not recommended. However, clinicians should have a high level of suspicion for renal cell carcinoma in patients with ESKD who have flank pain or hematuria that may be suggestive of the diagnosis. Despite the relatively high prevalence of renal cell carcinoma in patients with ACKD, it is an uncommon cause of death in patients with ESKD.

The hallmark of autosomal dominant polycystic kidney disease (ADPKD) is large kidneys with multiple kidney cysts, usually originating in the renal collecting duct. Most patients with ADPKD have a positive family history for cystic kidney disease and/or chronic kidney disease. Diagnosis may be complicated by the fact that a hemorrhagic kidney cyst is usually indistinguishable from a solid renal mass on ultrasound. However, in this patient without a family history, small kidneys on ultrasound, and cysts scattered throughout the renal parenchyma, ADPKD with a hemorrhagic renal cyst is unlikely.

Renal angiomyolipomas and bilateral renal cysts are associated with tuberous sclerosis complex (TSC). However, because this is an autosomal dominant disease, there is almost always a positive family history. Additionally, TSC is a systemic disorder with lesions typically present in various organs and tissues and would be a far less common cause of kidney tumors in a patient with ESKD.

Transitional cell or urothelial carcinomas arise from the mucosal surfaces of the urethra, bladder, and ureters and may also occur in the renal pelvis and calyces; in the upper urinary tract, transitional cell carcinomas also tend to be multifocal and only uncommonly form mass lesions within the kidney. This patient's mass is located in the renal parenchyma, and there is not an increased risk of transitional cell carcinoma with ACKD, making this a less likely diagnosis.

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Question 49

A 45-year-old man is evaluated during an annual routine health maintenance visit. History is notable for type 2 diabetes mellitus (diet controlled) diagnosed 3 months ago. Family history is significant for his father who developed end-stage kidney disease due to diabetes at age 68 years. He reports no symptoms and takes no medications.

On physical examination, temperature is 37.0 °C (98.6 °F), blood pressure is 135/78 mm Hg, pulse rate is 70/min, and respiration rate is 12/min. BMI is 31. Cardiac examination reveals no murmur or gallop. The lungs are clear. There is 1+ peripheral edema.

Laboratory studies show a serum creatinine level of 1.0 mg/dL (88.4 µmol/L).

Which of the following is the most appropriate n ext step in management?

A

Measure urine albumin excretion

B

Order kidney ultrasonography

C

Perform dipstick urinalysis

D

Start an angiotensin receptor blocker

Choose an Answer Above

Answer & Critique

Correct Answer: A

Educational Objective: Screen a patient with risk factors for chronic kidney disease.

Key Point

Patients with risk factors for chronic kidney disease should be screened using laboratory studies, most commonly determining the estimated glomerular filtration rate and urine testing for protein or albumin.

Urine albumin excretion measurement is appropriate for this patient with risk factors for chronic kidney disease (CKD). Patients with diabetes mellitus are at a markedly increased risk of CKD, and treatment of patients with diabetes and moderately increased albuminuria (formerly known as microalbuminuria) using ACE inhibitors or angiotensin receptor blockers (ARBs) can reduce the risk of progression to overt nephropathy. Moreover, determining the level of albuminuria and estimated glomerular filtration rate is important for detecting the presence of CKD and accurately staging CKD if present. CKD staging has important implications with regard to clinical prognosis. Guidelines differ among several medical organizations regarding the optimal approach to CKD screening. Whereas the American College of Physicians guidelines state that there is insufficient evidence to support or discourage screening for CKD in persons with CKD risk factors such as diabetes, the National Kidney Foundation and the American Diabetes Association support screening for kidney disease in all patients with diabetes.

There is no evidence to support the value of kidney ultrasonography in persons who have no clinical evidence of kidney disease and no family history of genetic kidney disease such as autosomal dominant polycystic kidney disease.

Dipstick urinalysis is not sufficiently sensitive to detect the presence of moderately increased albuminuria; the results are semiquantitative, and estimations of proteinuria can be significantly affected by urine concentration.

Although ARBs have been demonstrated to reduce the risk of progression from moderately increased albuminuria to overt diabetic nephropathy, no studies have demonstrated a beneficial effect of these medications in patients who do not have increased urine albumin excretion or existing hypertension. It remains unknown whether ARBs or ACE inhibitors are protective in patients with moderately increased albuminuria due to etiologies other than diabetic nephropathy.

Question 50

A 65-year-old man is evaluated for a slowly rising serum creatinine level from 0.8 mg/dL (70.7 µmol/L) to 1.4 mg/dL (124 µmol/L) noted on laboratory testing over the past 8 months. Medical history is significant for benign prostatic hyperplasia and gastroesophageal reflux disease. He feels well and has no current symptoms. Medications are tamsulosin and omeprazole.

On physical examination, temperature is 37.1 °C (98.7 °F), blood pressure is 134/84 mm Hg, pulse rate is 76/min, and respiration rate is 12/min. BMI is 26. There is no rash. The remainder of the examination is unremarkable.

Laboratory studies:

Complete blood count with differential	Normal
Blood urea nitrogen	38 mg/dL (13.6 mmol/L)
Creatinine	1.4 mg/dL (124 µmol/L)
Electrolytes	Normal
Urinalysis	Positive for protein; no blood, glucose, leukocyte esterase, or nitrites; <3 erythrocytes/hpf; 3-5 leukocytes/hpf; no casts or crystals
Urine protein-creatinine ratio	470 mg/g

Kidney ultrasound shows normal-sized kidneys without hydronephrosis or calculi.

Which of the following is the most appropriate next step in management?

A

Discontinue omeprazole

B

Discontinue tamsulosin

C

Order a 24-hour urine collection for creatinine clearance and proteinuria

D

Perform duplex ultrasonography

Choose an Answer Above

Answer & Critique

Correct Answer: A

Educational Objective: Treat interstitial nephritis by discontinuing a me dication.

Key Point

Proton pump inhibitors are a potentially treatable cause of chronic tubulointerstitial disease.

Discontinuing omeprazole is appropriate in this patient who may have interstitial nephritis as a cause of chronic tubulointerstitial disease. In contrast to acute kidney injury, chronic tubulointerstitial disease develops over months to years and is a cause of slowly declining kidney function. Chronic tubulointerstitial disease most commonly results from previous injury due to an episode of acute interstitial nephritis, but it can also result from ongoing, subacute interstitial nephritis and other glomerular, vascular, or obstructive diseases that may cause irreversible injury to the tubules and interstitium, even with treatment or resolution of the initial disease process. Symptoms and physical examination findings in patients with chronic tubulointerstitial disease can be minimal or absent unless an active associated disease is present; therefore, the diagnosis is often discovered by abnormalities detected on laboratory testing done for other purposes. This patient was noted to have progressively worsening kidney function, with the only abnormality being mild leukocytosis on urinalysis and subnephrotic-range proteinuria. Evaluation of chronic tubulointerstitial disease is focused on identification of potentially treatable causes. Because proton pump inhibitors are associated with interstitial nephritis, discontinuation of omeprazole is appropriate in this patient.

Although any drug may cause interstitial nephritis, there are no case reports of tamsulosin-induced interstitial nephritis. Stopping tamsulosin may exacerbate the benign prostatic hyperplasia, which could lead to postrenal acute kidney injury.

A 24-hour urine collection may be useful for measuring kidney function and quantifying proteinuria but would not be helpful in establishing the cause of this patient's declining kidney function.

Duplex ultrasonography can be useful for diagnosing renal artery stenosis, but this patient's clinical features of pyuria, mild proteinuria, normal blood pressure, and symmetric kidney size are not consistent with renal artery disease, making this study unnecessary.

Question 51

A 56-year-old woman is hospitalized for acute decompensated heart failure. Medical history is significant for ischemic cardiomyopathy, coronary artery disease, hypertension, and hyperlipidemia. Medications on admission are aspirin, lisinopril, carvedilol, spironolactone, rosuvastatin, and as-needed furosemide.

Baseline medications are continued, and intravenous diuretics are started resulting in a 2.0-kg negative fluid balance over the initial 36 hours with improvement of her symptoms. However, her serum creatinine level increased to 1.5 mg/dL (132.6 μmol/L) from her baseline of 1.2 mg/dL (106.1 μmol/L).

On physical examination, the patient is afebrile, blood pressure is 112/82 mm Hg, pulse rate is 68/min, and respiration rate is 16/min. Oxygen saturation is 92% on 2 L oxygen by nasal cannula. Estimated central venous pressure is 12 cm H_2O. Examination of the lungs reveals bibasilar crackles, improved from admission. Cardiac examination reveals an S_3 gallop. There is lower extremity edema to the mid-calf.

In addition to continuing her baseline medications, which of the following is the most appropriate next step in management?

A

Add nesiritide and continue intravenous diuretics

B

Continue intravenous diuretics

C

Discontinue intravenous diuretics and begin ultrafiltration

D

Hold intravenous diuretics for 24 hours

Answer & Critique

Correct Answer: B

Educational Objective: Treat a patient with cardiorenal syndrome.

Key Point

In patients with heart failure–related cardiorenal syndrome, treatment is directed toward improving cardiac function and fluid balance, which may optimize kidney function.

Continuing intravenous diuretic therapy is the most appropriate next step in management. In acute decompensated heart failure, elevated renal venous pressure can cause distended renal venules with increased tubular fluid pressure and backleak, leading to venous congestion and cardiorenal syndrome (CRS). This patient has CRS, defined as a change in function of either the heart or kidneys that may influence the function of the other organ system. CRS is categorized into five types: 1) acute heart failure leading to acute kidney injury (AKI) (CRS1), 2) chronic heart failure leading to chronic kidney disease (CKD), 3) AKI leading to acute heart failure, 4) CKD leading to cardiac dysfunction (heart failure, coronary artery disease, arrhythmias), and 5) systemic conditions leading to simultaneous heart and kidney dysfunction (such as sepsis). Management of CRS may be challenging because treatment of one organ system may cause worsening of the other. In patients with heart failure–related CRS, treatment is directed toward improving cardiac function and fluid balance, which may optimize kidney function. However, it is common to see mild to moderate worsening of kidney function associated with treatment of volume overload until fluid balance is achieved. In general, diuresis in heart failure should be maintained until fluid retention (as seen by elevated central venous pressure and peripheral edema) is resolved, even if this results in asymptomatic mild to moderate decreases in kidney function that are followed closely.

Nesiritide, a recombinant human B-type natriuretic peptide that acts as a vasodilator, is available for treatment of selected patients with acute decompensated heart failure. However, there is no evidence that nesiritide improves kidney function when used in this setting and is therefore an inappropriate addition to therapy for this purpose.

Ultrafiltration, or the removal of plasma water through an extracorporeal circuit, has been used in patients unresponsive to diuretics; however, this patient has responded to diuretic therapy, and ultrafiltration is not indicated at present.

Excessive concern about precipitating kidney failure can lead to underutilization of diuretics and persistent volume overload, which may reduce the efficacy of ACE inhibitors and increase the risk of carvedilol-induced decompensated heart failure.

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Question 52

A 32-year-old woman is evaluated during a follow-up visit. She is at 12 weeks' gestation of her first pregnancy. Her pregnancy has been uncomplicated except for persistently elevated blood pressures measured at her obstetric visits. She otherwise feels well. She has no urinary symptoms such as dysuria, hematuria, or foamy urine. She did not receive routine medical care prior to her pregnancy. Family history is notable for hypertension in her parents and one older sibling. Her only medication is a prenatal vitamin.

On physical examination, temperature is 37.1 °C (98.8 °F), blood pressure is 154/93 mm Hg, pulse rate is 87/min, and respiration rate is 16/min. BMI is 24. Funduscopic and neurologic examinations are normal. Chest and cardiac examinations are normal. Abdominal examination is unremarkable. There is trace lower extremity edema.

Laboratory studies show normal liver chemistries and kidney function. A complete blood count is normal except for a hemoglobin level of 10.9 g/dL (109 g/L). Urinalysis is normal.

Which of the following is the most likely diagnosis?

A

Chronic hypertension

B

Gestational hypertension

C

Normal pregnancy

D

Preeclampsia

Choose an Answer Above

Answer & Critique

Correct Answer: A

Educational Objective: Diagnose chronic hypertension in a pregnant patient.

Key Point

Hypertension prior to the 20th week of gestation is most consistent with previously undiagnosed chronic hypertension, which may go undetected in healthy women because of a minimal need for medical evaluation prior to pregnancy.

Chronic hypertension is the most likely diagnosis. Hypertension prior to the 20th week of gestation is most consistent with previously undiagnosed chronic hypertension, which may go undetected in healthy women because of a minimal need for medical evaluation prior to pregnancy. As in nonpregnant patients, chronic hypertension may be primary (formerly known as essential) or secondary. This patient presents at the 12th week of gestation with persistently elevated blood pressures since her pregnancy was discovered, suggesting that her hypertension predated her pregnancy, and is likely primary because she has no other clinical features or laboratory study results to suggest a different cause. The 2013 American College of Obstetricians and Gynecologists (ACOG) guidelines recommend treating persistent blood pressure elevations of >160/105 mm Hg in women with chronic hypertension, with a goal blood pressure with medical therapy in these patients being 120-160/80-105 mm Hg.

The diagnosis of gestational hypertension requires consistent hypertension after the 20th week of gestation without preexisting hypertension or features of preeclampsia and must resolve within 12 weeks of delivery. Because this patient is persistently hypertensive early in her pregnancy, gestational hypertension is not likely

Question 53

Normal physiologic changes associated with pregnancy include increased cardiac output and decreased systemic vascular resistance and blood pressure. Blood pressure elevations to the level seen in this patient are not normally seen in pregnancy, when blood pressures are usually much lower.

Preeclampsia requires the combination of new-onset hypertension after 20 weeks of pregnancy and end-organ damage such as proteinuria, kidney dysfunction, thrombocytopenia, abnormal liver chemistry tests, pulmonary edema, and cerebral or visual symptoms

A 65-year-old man is evaluated in the emergency department for polyuria, polydipsia, and nocturia. Medical history is notable for diabetes mellitus, for which he takes metformin. He has a 45-pack-year history of smoking and does not drink alcohol.

On physical examination, the patient is alert and oriented. Blood pressure is 110/70 mm Hg supine and 100/65 mm Hg standing, pulse rate is 88/min supine and 95/min standing, and respiration rate is 20/min. BMI is 20. Occasional expiratory wheezing is noted in the right posterior lung field.

Laboratory studies:	
Blood urea nitrogen	30 mg/dL (10.7 mmol/L)
Total cholesterol	250 mg/dL (6.48 mmol/L)
Electrolytes:	
Sodium	130 mEq/L (130 mmol/L)
Potassium	4.5 mEq/L (4.5 mmol/L)
Chloride	92 mEq/L (92 mmol/L)
Bicarbonate	24 mEq/L (24 mmol/L)
Glucose	800 mg/dL (44.4 mmol/L)
Plasma osmolality	319 mOsm/kg H2O

Chest radiograph shows a 2-cm cavitary mass in the right upper lobe.

Which of the following conditions is the most likely cause of thi s patient's hyponatremia?

A Adrenal insufficiency

B Hyperglycemia

C Hyperlipidemia

D Reset osmostat

E Syndrome of inappropriate antidiuretic hormone secretion

Answer & Critique

Correct Answer: B

Educational Objective: Diagnose hyperosmolar hyponatremia.

Key Point

Hyperglycemia causes the osmotic translocation of water from the intracellular to the extracellular fluid compartment, which results in a decrease in the serum sodium level by approximately 1.6 mEq/L (1.6 mmol/L) for every 100 mg/dL (5.6 mmol/L) increase in the plasma glucose above 100 mg/dL (5.6 mmol/L).

The most likely diagnosis is hyperosmolar hyponatremia, caused by this patient's significantly elevated plasma glucose level. The patient's elevated plasma osmolality indicates the presence of a hyperosmolar state. Hyperglycemia causes the osmotic translocation of water from the intracellular to the extracellular fluid compartment, which results in a decrease in the serum sodium level by approximately 1.6 mEq/L (1.6 mmol/L) for every 100 mg/dL (5.6 mmol/L) increase in the plasma glucose above 100 mg/dL (5.6 mmol/L). Hyperosmolar hyponatremia can also be the result of exogenously administered solutes such as mannitol or sucrose.

Pseudohyponatremia is caused by significant hyperlipidemia or the presence of paraproteins in the serum. In these situations, the laboratory measurement of plasma glucose is erroneously low, and the plasma osmolality is normal. This patient has a high plasma osmolality, which is not seen in pseudohyponatremia.

Hypothyroidism, adrenal insufficiency, and the syndrome of inappropriate antidiuretic hormone secretion (SIADH) are associated with hypo-osmolar hyponatremia caused by a decrease in the excretion of free water and are not compatible with the patient's hyperosmolality. Although lung cancer is a common cause of SIADH and may be present in this patient with a lung mass, his laboratory studies are not consistent with this being the cause of his hyponatremia.

Reset osmostat refers to a downward setting of the level at which sensors of plasma osmolality trigger the release of antidiuretic hormone and is associated with quadriplegia, tuberculosis, advanced age, pregnancy, psychiatric disorders, and chronic malnutrition. This lowered setpoint leads to stable, mild hypo-osmolar hyponatremia, which is inconsistent with this patient's findings.

Question 54

A 76-year-old woman is evaluated in the emergency department for altered sensorium. Medical records indicate a history of osteoarthritis. Listed medications are acetaminophen, naproxen, aspirin, and tramadol.

On physical examination, the patient is not communicative. Temperature is 36.5 °C (97.7 °F), blood pressure is 108/62 mm Hg, pulse rate is 104/min, and respiration rate is 12/min. BMI is 24. Lung examination revealsno crackles or wheezing. Neurologic examination is remarkable for somnolence but with appropriate responsiveness to noxious stimuli.

Laboratory studies:	
Creatinine	1.2 mg/dL (106.1 µmol/L)
Electrolytes:	
Sodium	139 mEq/L (139 mmol/L)
Potassium	3.9 mEq/L (3.9 mmol/L)
Chloride	102 mEq/L (102 (mmol/L)
Bicarbonate	26 mEq/L (26 mmol/L)
Arterial blood gas studies:	
pH	7.30
PCO2	55 mm Hg (7.3 kPa)
PO2	65 mm Hg (8.6 kPa)

Overdose of which of the following is the most likely cause of this patient's findings?

A Acetaminophen

B Aspirin

C Naproxen

D Tramadol

Answer & Critique

Correct Answer: D

Educational Objective: Identify tramadol overdose as a cause of respiratory acidosis.

Key Point

Primary respiratory acidosis is due to decreased effective ventilation, often noted with opioid overdose, leading to hypercapnia and retention of hydrogen ions.

Tramadol, a weak opioid agonist, is the most likely cause of this patient's respiratory findings. She has primary respiratory acidosis characterized by an elevation in P_{CO_2}, a decrease in pH, and a slight increase in bicarbonate. This patient has laboratory findings that suggest an acute onset. For each 10 mm Hg (1.3 kPa) increase in P_{CO_2}, serum bicarbonate increases acutely by 1.0 to 2.0 mEq/L (1.0-2.0 mmol/L) due to the extracellular-to-intracellular shift of hydrogen ions as an immediate compensatory mechanism. Later, renal compensation leads to increased bicarbonate generation, and, after 24 to 48 hours, leads to an increase in serum bicarbonate of 3.0 to 4.0 mEq/L (3.0-4.0 mmol/L) for every 10 mm Hg (1.3 kPa) increase in P_{CO_2}. Primary respiratory acidosis is due to decreased effective ventilation, often noted with opioid overdose, leading to hypercapnia and retention of hydrogen ions. Respiratory acidosis can also result from intrinsic lung pathology or from processes that impede ventilation.

The early phase of acetaminophen overdose is often not associated with any acid-base abnormality. After 72 to 96 hours, patients will often develop an increased anion gap metabolic acidosis related to lactic acidosis. This patient's anion gap is only 11 with no evidence of a metabolic acidosis, making acetaminophen overdose an unlikely cause of her acid-base disorder.

Although decreased respiratory drive can occur in the setting of salicylate intoxication in the later stages, it is more commonly associated with a mixed acid-base abnormality, including an increased anion gap acidosis and respiratory alkalosis, making this an unlikely diagnosis for this patient.

NSAID overdose typically presents with azotemia and hyperkalemia in addition to an increased anion gap metabolic acidosis (primarily a lactic acidosis), making this diagnosis unlikely in this patient.

Question 55

A 65-year-old woman is hospitalized for pneumonia and sepsis. She has no pertinent personal or family medical history and takes no medications.

On physical examination, the patient is intubated and mechanically ventilated. Temperature is 39.0 °C (102.2 °F), blood pressure is 90/60 mm Hg, pulse rate is 100/min, and respiration rate is 24/min. Estimated central venous pressure is 6 cm H_2O. Central venous oxygen saturation is 60%.

Intravenous fluid resuscitation is to be initiated.

Which of the following resuscitation therapies is contraindicated in thi s patient?

A

Albumin

B

Hydroxyethyl starch

C

Isotonic crystalloids

D

Lactated Ringer solution

Choose an Answer Above

Answer & Critique

Correct Answer: B

Educational Objective: Identify hydroxyethyl starch as a cause of acute kidney injury and increased mortality.

Key Point

Hydroxyethyl starch is associated with an increased risk of acute kidney injury, increased requirement of renal replacement therapy, a trend toward increased blood product transfusion, and increased mortality and is not recommended in patients with severe sepsis.

Resuscitation therapy with hydroxyethyl starch (HES) is most likely to lead to the development of acute kidney injury (AKI). This patient has septic shock and requires fluid resuscitation to prevent or limit multi-organ failure and reduce mortality. Repetitive fluid challenges are performed by giving a 500- to 1000-mL bolus of crystalloid over short intervals while assessing response to target central venous pressure. Most patients need 4 to 6 L of fluid in the first 6 hours, and a frequent error is underestimating the intravascular volume deficit and the amount of fluid required. The fluid input is typically greater than output owing to vasodilation and capillary leak. HES is a synthetic colloid that is associated with an increased risk of AKI, increased requirement of renal replacement therapy, a trend toward increased blood product transfusion, and increased mortality. HES accumulates in the proximal renal tubular epithelial cell, resulting in vacuolization and swelling of the proximal renal tubular cell, tubular obstruction and injury, and an osmotic nephrosis. As a result, the 2013 Surviving Sepsis Campaign recommends against using any HES in patients with severe sepsis.

Volume resuscitation can be achieved with either crystalloid or colloid solutions. The crystalloid solutions are lactated Ringer solution and 0.9% sodium chloride; the colloid solutions include albumin. Evidence from randomized trials and meta-analyses have found no convincing difference between using crystalloid solutions such as normal saline and lactated Ringer and albumin solutions in the treatment of severe sepsis

or septic shock; however, colloid is far more expensive

Question 56

A 76-year-old woman is diagnosed with non–ST-elevation myocardial infarction and is scheduled for urgent coronary angiography. History is significant for type 2 diabetes mellitus, hypertension, and chronic kidney disease. Medications are lisinopril, atorvastatin, furosemide, amlodipine, metoprolol, insulin, aspirin, and heparin.

On physical examination, blood pressure is 152/84 mm Hg, pulse rate is 82/min, and respiration rate is 14/min. There is no jugular venous distention. Cardiac examination reveals regular rhythm with an S_4but no murmurs. The lungs are clear. There is mild lower extremity edema at the ankles.

Laboratory studies are significant for a serum creatinine level of 2.0 mg/dL (176.8 µmol/L) and an estimated glomerular filtration rate of 30 mL/min/1.73 m^2; urinalysis reveals 2+ protein.

In addition to discontinuing diuretic therapy, which of the following is the most appropriate periprocedural management of this patient?

A

Begin intravenous isotonic saline

B

Begin oral *N*-acetylcysteine

C

Begin prophylactic hemodialysis within 2 hours after procedure

D

Discontinue lisinopril for at least 24 hours before procedure

Choose an Answer Above

Answer & Critique

Correct Answer: A

Educational Objective: Manage a patient at risk for co ntrast-induced nephropathy.

Key Point

Administration of intravenous isotonic saline is appropriate for patients at risk for contrast-induced nephropathy.

In addition to discontinuing diuretic therapy, the most appropriate periprocedural management for this patient is to begin intravenous isotonic saline. She is at risk for contrast-induced nephropathy (CIN), and administration of intravenous isotonic saline (1-1.5 mL/kg/h) 3 to 12 hours before the procedure and continued for 6 to 24 hours afterward has been shown to decrease the incidence of CIN in high-risk patients. Risk factors include age older than 75 years, diabetes mellitus, chronic kidney disease, conditions of decreased renal perfusion, and concurrent use of nephrotoxic drugs. Therefore, this patient is at high risk for CIN. In addition to intravenous isotonic saline, other strategies to minimize the risk for CIN include discontinuation of potentially nephrotoxic medications, minimization of contrast volume, and use of low- or iso-osmolal contrast media. The benefit of hydration regimens utilizing isotonic sodium bicarbonate is comparable to isotonic sodium chloride and is not considered to be of significant benefit relative to normal saline.

The benefit of *N*-acetylcysteine in patients at risk for CIN remains controversial, and results from trials are inconsistent. It is therefore not recommended as routine treatment to prevent CIN.

Prophylactic hemodialysis has not been shown to provide benefit compared with medical therapy alone for patients at risk for CIN.

Discontinuation of ACE inhibitors or angiotensin receptor blockers has not been clearly shown to decrease the risk of CIN. Although ACE inhibitors should be discontinued in most cases of acute kidney injury, they can be continued in patients with stable kidney function.

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Question 57

A 57-year-old man is evaluated for a diagnosis of acute kidney injury. He was diagnosed with gastroesophageal reflux disease 3 weeks ago and was prescribed omeprazole. Several days ago he noticed lower extremity swelling and decreased frequency of urination. Laboratory evaluation showed a serum creatinine level of 2.2 mg/dL (194.5 µmol/L). Medical history is otherwise unremarkable, and he takes no other medications. He reports no allergies.

On physical examination, the patient is afebrile, blood pressure is 135/77 mm Hg, pulse rate is 88/min, and respiration rate is 12/min. There is no rash. Cardiac examination and estimated central venous pressure are normal. The lungs are clear. Lower extremity edema to the ankles is present bilaterally.

Dipstick urinalysis reveals blood and trace protein, and urine sediment is notable for 5-10 erythrocytes/hpf, 10-20 leukocytes/hpf, and 1 leukocyte cast.

In addition to discontinuing omeprazole, which of the following is the most appro priate next step in management?

A

Kidney biopsy

B

Oral glucocorticoids

C

Repeat kidney function testing in 5 to 7 days

D

Urine eosinophil testing

Choose an Answer Above

Answer & Critique

Correct Answer: C

Educational Objective: Evaluate kidney function in a patient with acute interstitial nephritis.

Key Point

Discontinuation of the offending agent is the mainstay of therapy for drug-induced acute interstitial nephritis.

In addition to discontinuing omeprazole, repeat kidney function testing in 5 to 7 days is the most appropriate management for this patient with acute interstitial nephritis (AIN). AIN is a condition in which kidney dysfunction results from infiltration of inflammatory cells into the kidney interstitium. It may be associated with drugs, infection, autoimmune diseases, and malignancy, with drug-induced AIN being the most common. Many patients with AIN may be asymptomatic or present with mild, nonspecific symptoms; only 10% to 30% have the classic triad of fever, rash, and eosinophilia. Urinalysis may reveal mild proteinuria, leukocytes, erythrocytes, and leukocyte casts. Drug-induced AIN should be considered in any patient exposed to a potentially offending drug who presents with unexplained acute kidney injury (AKI). Drug-induced AIN is characterized by a slowly increasing serum creatinine 7 to 10 days after exposure; however, it can occur within 1 day of exposure if the patient has been exposed previously. Drug-induced AIN can also occur months after exposure, often with NSAIDs and proton pump inhibitors (PPIs). This patient has a clinical picture consistent with AIN based on clinical and laboratory evidence of kidney injury and urinalysis showing erythrocytes, leukocytes, and leukocyte casts after recently being started on the PPI omeprazole. Discontinuation of the offending agent is the mainstay of therapy. In patients with mild elevations of serum creatinine and minimal clinical findings, stopping the causative drug with close follow-up is usually adequate therapy.

Kidney biopsy is usually not necessary to diagnose AIN, particularly in patients with a consistent clinical and laboratory picture, as seen in this patient. However, kidney biopsy may be indicated in situations where there are inconsistent clinical and laboratory findings, or if kidney function does not improve immediately upon stopping the offending agent.

The role of glucocorticoids in AIN is controversial, with conflicting evidence of benefit in clinical studies. Glucocorticoids are therefore generally reserved for patients who have not responded to discontinuation of the offending agent.

The presence of urine eosinophils detected by Hansel staining of the urine sediment has been classically associated with the diagnosis of AIN but is not specific because they may be associated with other causes of AKI (such as glomerulonephritis), and the absence of urine eosinophils does not exclude AIN. Therefore, this testing is not clinically useful in this patient.

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Question 58

A 53-year-old woman is evaluated during a follow-up visit for recurrent urinary tract infections. She has been treated for three episodes of urinary tract infection with *Klebsiella* over the past 4 months. Despite an initial response to antibiotics, her urinary tract symptoms return once the antibiotics are stopped. She has no systemic symptoms, including fever or chills. Medical history is otherwise unremarkable. She currently takes no medications.

On physical examination, temperature is 37.1 °C (98.8 °F), blood pressure is 124/74 mm Hg, pulse rate is 72/min, and respiration rate is 12/min. BMI is 22. There is no costovertebral angle tenderness to palpation. The remainder of the examination is unremarkable.

Urine dipstick reveals a pH of 9.0 and is positive for leukocyte esterase and nitrites; urine microscopy shows 8-10 leukocytes/hpf and many coffin-lid–shaped crystals consistent with struvite.

Kidney ultrasound shows a 1.2-cm irregularly shaped stone in the left renal pelvis.

Which of the following is the most appropriate next step in management?

A

Chronic antibiotic therapy

B

Low phosphate diet

C

Stone removal

D

Urine acidification

Choose an Answer Above

Answer & Critique

Correct Answer: C

Educational Objective: Treat a patient with struvite nephrolithiasis by removing the stone.

Key Point

In most patients with known struvite stones, removal of the stones is indicated.

The most appropriate next step in management is to remove the struvite stone in the left renal pelvis. Struvite stones are composed of magnesium ammonium phosphate and occur only when ammonium production is increased, which elevates the urine pH and decreases the solubility of phosphate. This is most commonly a consequence of chronic upper urinary tract infection (UTI) with a urease-producing organism, such as *Proteus* or *Klebsiella*. Struvite stones can grow rapidly and become large, filling the entire renal pelvis and taking on a characteristic "staghorn" shape. Although struvite stones affect less than 10% of patients with kidney stones, they occur more commonly in women and in patients predisposed to chronic or recurrent UTI, including those with urologic diversions or neurogenic bladder.

Although treatment of the initial upper UTI is important to prevent struvite stone development, once struvite stones are formed, they are difficult to treat medically, including with chronic antibiotics. Antibiotics may not penetrate the stone, and colonizing bacteria may create an alkaline environment within the stone that promotes continued or recurrent UTI, stone growth, and chronic inflammatory damage to the kidney. Because of this, stone removal is indicated in most cases, and kidney outcomes have been shown to be improved when struvite stones are removed compared with medical therapy. Removal is commonly by percutaneous nephrolithotomy, shock wave lithotripsy, or a combination of both procedures.

Dietary phosphate reduction and urine acidification would be expected to discourage struvite stone formation but are of minimal effectivene ss once struvite stones have developed.

Question 59

A 28-year-old man is evaluated for a 2-month history of progressive lower extremity edema, weight loss, and fatigue. Medical history is significant for recreational use of inhaled cocaine; he denies injection drug use. He has no other known medical issues and takes no medications.

On physical examination, temperature is 37.2 °C (99.0 °F), blood pressure is 130/90 mm Hg, pulse rate is 90/min, and respiration rate is 20/min. BMI is 28. Temporal wasting is present. The lungs are clear. Cardiac examination is normal, and no pericardial rub is detected. There is no hepatosplenomegaly or evidence of ascites on abdominal examination. The lower extremities show edema to the knees bilaterally. Skin and joint examinations are normal. Mild asterixis is noted.

Laboratory studies:

Albumin	2.5 g/dL (25 g/L)
Liver chemistry studies	Normal
Blood urea nitrogen	98 mg/dL (35 mmol/L)
Creatinine	6.8 mg/dL (601.1 µmol/L)
Urinalysis	1+ blood; 3+ protein; 5 erythrocytes/hpf; 0-2 leukocytes/hpf
Urine protein-creatinine ratio	3700 mg/g

Kidney ultrasound shows mildly enlarged and echogenic kidneys without obstruction.

Kidney biopsy results are indicative of the collapsing variant of focal segmental glomerulosclerosis (FSGS).

Which of the following tests is most likely to establish the cause of this patient's FSGS?

A Hepatitis B and C serologies

B HIV antibody test

C Serum and urine electrophoresis

D Treponemal antibody test

Answer & Critique

Correct Answer: B

Educational Objective: Evaluate for HIV infection in a patient with focal segmental glomerulosclerosis.

Key Point

HIV infection is typically associated with the collapsing form of focal segmental glomerulosclerosis; in the early stages, antiretroviral therapy and angiotensin system blockers may halt disease progression.

The most appropriate test to perform is an HIV antibody test in this patient with focal segmental glomerulosclerosis (FSGS). FSGS is the cause of idiopathic nephrotic syndrome in 25% of cases. FSGS may also be secondary to another process, including hyperfiltration injury to the glomerulus as may occur in chronic hypertension, diabetes mellitus, and conditions in which kidney mass is reduced (progressive kidney disease, obesity, sickle cell disease, reflux nephropathy, or after nephrectomy). Direct injury to podocytes may also cause FSGS as seen with certain drugs (pamidronate, interferon) and infections, including HIV. This patient's kidney biopsy results are indicative of the collapsing variant of FSGS, which is classic for HIV-associated glomerulopathy. Therefore, evaluation for HIV infection as a cause of this patient's FSGS is the most appropriate next diagnostic step. In the early stages of HIV-associated glomerulopathy, antiretroviral therapy and angiotensin system blockers may halt disease progression, thus an early diagnosis is important.

Hepatitis B is typically associated with membranous glomerulopathy, and hepatitis C with cryoglobulinemic glomerulonephritis. Serum and urine electrophoresis can be used to test for monoclonal gammopathies. The treponemal antibody test is used to test for syphilis, which is typically associated with membranous nephropathy. None of these disorders is associated with the collapsing glomerulopathy seen on this patient's kidney biopsy.

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Question 60

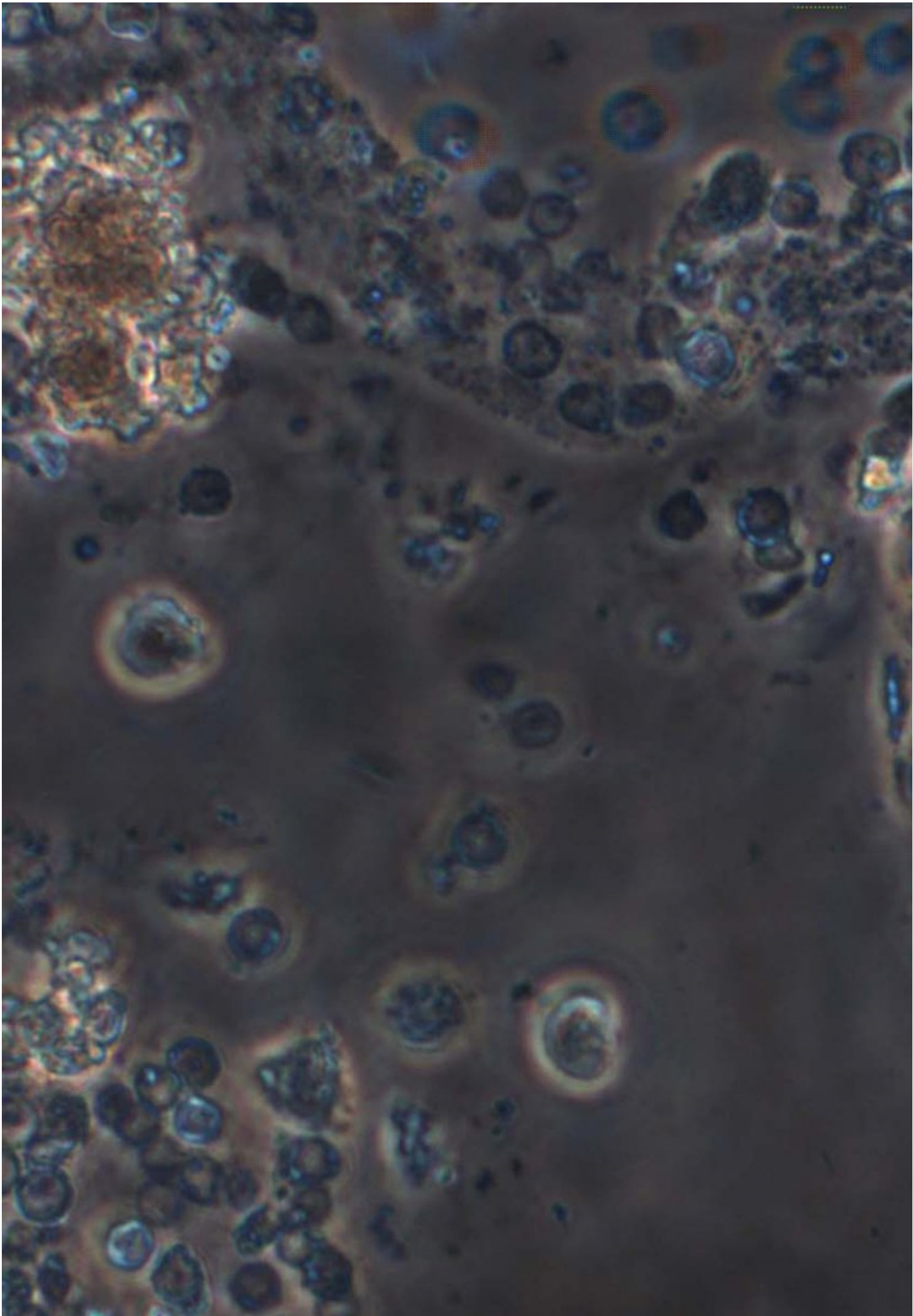
A 60-year-old woman is evaluated for a 3-week history of fever, fatigue, and arthralgia. She also notes intermittent low back pain and weight loss of 4.5 kg (10 lb) during the past 2 months. She reports no dysuria or night sweats. Medical history is significant for urinary tract infections once every 1 to 2 years and osteoarthritis. She has a 25-pack-year smoking history but stopped 15 years ago. Her only medication is as-needed ibuprofen.

On physical examination, temperature is 38.2 °C (100.8 °F), blood pressure is 152/94 mm Hg, pulse rate is 92/min, and respiration rate is 16/min. BMI is 26. Lung, heart, and abdominal examinations are normal. There is no costovertebral angle tenderness. Skin examination reveals nonblanching erythematous palpable papules and macules on the lower legs.

Laboratory studies:

Creatinine	1.8 mg/dL (159.1 µmol/L) (baseline: 0.9 mg/dL [79.6 µmol/L])
Urinalysis	2+ blood; 2+ protein; positive for leukocyte esterase; 20-30 erythrocytes/hpf; 5-10 leukocytes/hpf; no crystals

Urine microscopy results are shown.



Which of the following is the most appropriate next step in management?

A

Antibiotics

B

Cystoscopy

C

Kidney biopsy

D

Kidney ultrasonography

Choose an Answer Above

Answer & Critique

Correct Answer: C

Educational Objective: Diagnose glomerulonephritis.

Key Point

Urgent serologic evaluation and kidney biopsy are indicated to diagnose the cause of glomerulonephritis and guide management.

Kidney biopsy is the most appropriate next step in management. This patient has worsening kidney function and new hypertension associated with significant abnormalities on urinalysis, including proteinuria, leukocytes indicating inflammation, hematuria with dysmorphic erythrocytes (acanthocytes), and erythrocyte casts on microscopy. These findings strongly suggest glomerulonephritis. Constitutional symptoms such as fever and arthralgia, as well as nonblanching rash (palpable purpura) and weight loss, further suggest vasculitis as the most likely etiology. Urgent serologic evaluation and kidney biopsy are indicated to diagnose the cause of glomerulonephritis and guide management.

Although this patient has a history of urinary tract infection (UTI), reports fever, and has leukocytes on her urinalysis, her specific lack of symptoms of UTI or other findings consistent with this diagnosis (no costovertebral angle tenderness or bacteria on microscopic urinalysis) make this a less likely diagnosis. UTI would also not be expected to lead to development of hypertension or kidney failure. Therefore, antibiotics are not indicated.

Cystoscopy is typically used to evaluate for hematuria due to a bladder source, such as bladder cancer. The hematuria associated with a bladder source of bleeding is usually structurally normal compared with the dysmorphic erythrocytes seen in this patient; acanthocytes suggest a glomerular source of bleeding. Also, a bladder source of bleeding, such as a malignancy, would not explain the other findings seen on her urinalysis (significant proteinuria, leukocytosis) or her new hypertension and kidney failure, making cystoscopy an inappropriate next step in management.

Kidney ultrasonography can identify structural abnormalities, including nephrolithiasis. However, in this patient with a clinical picture consistent with acute glomerulonephritis, kidney imaging would not be of high diagnostic yield.

Question 61

A 52-year-old woman is evaluated in the hospital following admission for gastroenteritis and hyponatremia. She reports a 5-day history of diarrhea, nausea, and vomiting, and had been drinking water to maintain hydration. On evaluation in the emergency department earlier today, she was noted to be mildly volume contracted with an initial serum sodium level of 114 mEq/L (114 mmol/L) with normal plasma glucose and minimally elevated blood urea nitrogen levels. Her mental status was normal. She was given 2 liters of normal saline and admitted to the hospital. Medical history is unremarkable, and she takes no medications.

On physical examination, the patient feels better. Temperature is normal, blood pressure is 120/70 mm Hg, pulse rate is 84/min, and respiration rate is 16/min. BMI is 22. Estimated central venous pressure is 6 cm H_2O. Cardiopulmonary examination is unremarkable, and the abdomen is mildly tender to palpation diffusely. The neurologic examination is normal.

Current laboratory studies:

Blood urea nitrogen	14 mg/dL (5 mmol/L)
Creatinine	1.0 mg/dL (88.4 µmol/L)
Electrolytes:	
Sodium	128 mEq/L (128 mmol/L)
Potassium	4.0 mEq/L (4.0 mmol/L)
Chloride	94 mEq/L (94 mmol/L)
Bicarbonate	24 mEq/L (24 mmol/L)
Glucose	90 mg/dL (5 mmol/L)

Which of the following is the most appropriate management of this patient's hyponatremia?

A

Desmopressin intravenously

B

Desmopressin intravenously with 5% dextrose

C

Fluid restriction of 800 mL/d

D

Fluid restriction of 800 mL/d and salt tablets

E

No additional intervention

Choose an Answer Above

Answer & Critique

Correct Answer: B

Educational Objective: Manage overcorrection of sodium in a patient with severe asymptomatic hyponatremia at risk for osmotic demyelination syndrome.

Key Point

Overcorrection of chronic asymptomatic hyponatremia is associated with the development of osmotic demyelination syndrome and should be reversed using desmopressin with 5% dextrose.

Desmopressin intravenously with 5% dextrose is the most appropriate treatment. The patient presented with a 5-day history of gastroenteritis symptoms and severe hyponatremia with a normal neurologic examination. She has chronic asymptomatic hyponatremia that was likely from volume depletion, causing an appropriate elevation in antidiuretic hormone (ADH) secretion, which caused the hyponatremia by retaining the free water she was drinking to maintain hydration. Volume repletion in the hospital led to suppression of ADH production with a subsequent water diuresis, leading to rapid correction. Rapid correction in chronic asymptomatic hyponatremia increases the risk for osmotic demyelination syndrome (ODS), especially in women, which may be delayed for a few days after overcorrection. Overcorrection is considered to be an increase of >8.0 mEq/L (8.0 mmol/L) of the serum sodium within the first 24 hours or >16 mEq/L (16 mmol/L) within the first 48 hours. Desmopressin will terminate the water diuresis, and if given alone will maintain the serum sodium around the current level of 128 mEq/L (128 mmol/L), which still represents overcorrection. Desmopressin intravenously with 5% dextrose will stop the water diuresis and further lower the serum sodium. The 5% dextrose should be given in sufficient volume to reverse the serum sodium level to 120 mEq/L (120 mmol/L) over the first 24 hours and then allowing slow correction.

Fluid restriction alone is inappropriate because the serum sodium will continue correction toward normal and increase the risk of ODS, as will fluid restriction with salt tablets, which will increase the rate of correction.

Providing no further intervention would not reverse the overcorrection, and the patient's serum sodium would likely continue to return to normal, further increasing her risk for ODS.

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Question 62

A 40-year-old woman is evaluated during a follow-up visit for a diagnosis of autosomal dominant polycystic kidney disease (ADPKD). She is asymptomatic but is questioning whether she should be screened for a brain aneurysm. Medical history is otherwise significant for hypertension treated with enalapril. Family history is notable for her father who has ADPKD and is on hemodialysis and her paternal grandmother who died of chronic kidney disease, although she does not know the type. She is not aware of any family history of stroke or other neurologic abnormalities. She works as an administrator in an office.

On physical examination, temperature is 37.0 °C (98.6 °F), blood pressure is 140/90 mm Hg, pulse rate is 80/min, and respiration rate is 15/min. BMI is 22. Cardiovascular, pulmonary, and neurologic examinations are normal. On abdominal examination, nontender masses are palpable bilaterally.

Which of the following is the most appropriate screening regimen for this patient?

A

One-time MR angiography now

B

One-time MR angiography at age 50 years

C

MR angiography now and every 5 years

D

No screening

Choose an Answer Above

Answer & Critique

Correct Answer: D

Educational Objective: Manage intracranial cerebral aneurysm screening in a patient with autosomal dominant polycystic kidney disease.

Key Point

For patients with autosomal dominant polycystic kidney disease, screening for intracranial cerebral aneurysms using MR angiography is only recommended for those with a family history of aneurysm or subarachnoid hemorrhage, those with a previous rupture, or those with high-risk occupations in which a rupture would affect the lives of others.

No screening is necessary for this asymptomatic patient with autosomal dominant polycystic kidney disease (ADPKD). Intracranial cerebral aneurysms (ICAs) can be detected in 10% to 12% of patients with ADPKD, and a ruptured ICA resulting in a subarachnoid or intracerebral hemorrhage is the most serious extrarenal complication of ADPKD. The prevalence of ICA is higher in patients with ADPKD who have a family history of known ICA or hemorrhagic stroke. Therefore, screening using MR angiography is currently only recommended for patients with ADPKD thought to be at high risk, including those with a family history of aneurysm or subarachnoid hemorrhage or those with a previous rupture. In addition, patients with ADPKD who have high-risk occupations in which a rupture would affect the lives of others (such as driving a school bus) should be screened. There are no differences in screening recommendations based on age. Therefore, there is no indication for screening for ICA in this patient with no symptoms suggestive of possible ICA, no family history of known ICA or hemorrhage, and a low-risk occupation.

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Question 63

A 65-year-old woman is evaluated in the emergency department for dysuria, urgency, and polyuria occurring for 4 days. She has no neurologic symptoms. Medical history is significant for depression. Her only medication is fluoxetine, which was started 8 weeks ago.

On physical examination, temperature is 38.0 °C (100.4 °F), blood pressure is 140/90 mm Hg, pulse rate is 85/min, and respiration rate is 15/min. BMI is 30. Cardiovascular, pulmonary, and neurologic examinations are normal. Mild tenderness to palpation of the mid lower abdomen is noted. There is no costovertebral angle tenderness.

Laboratory studies:

Blood urea nitrogen	10 mg/dL (3.6 mmol/L)
Creatinine	1.0 mg/dL (88.4 µmol/L)
Electrolytes:	
Sodium	123 mEq/L (123 mmol/L)
Potassium	4.0 mEq/L (4.0 mmol/L)
Chloride	91 mEq/L (91 mmol/L)
Bicarbonate	24 mEq/L (24 mmol/L)
Glucose	120 mg/dL (6.7 mmol/L)
Plasma osmolality	260 mOsm/kg/H_2O
Urine sodium	40 mEq/L (40 mmol/L)
Urine osmolality	600 mOsm/kg/H_2O
Urinalysis	Too numerous to count leukocytes/hpf

Antibiotics for a urinary tract infection are started.

In addition to discontinuing fluoxetine, which of the following is the mo st appropriate management of this patient's hyponatremia?

A

Fluid restriction

B

Hypertonic saline infusion

C

Isotonic saline infusion

D

Oral demeclocycline

E

Tolvaptan

Choose an Answer Above

Answer & Critique

Correct Answer: A

Educational Objective: Treat chronic hyponatremia.

Key Point

The initial treatment of asymptomatic patients with syndrome of inappropriate antidiuretic hormone secretion includes management of the underlying cause if possible and fluid restriction without limiting sodium intake.

In addition to discontinuing fluoxetine, fluid restriction is the appropriate treatment for this patient. She is euvolemic and has hyponatremia with a decreased plasma osmolality and an inappropriately increased urine osmolality. This clinical and laboratory presentation is highly suggestive of the syndrome of inappropriate antidiuretic hormone secretion (SIADH). SIADH has many causes, including various drugs such as selective serotonin reuptake inhibitors like fluoxetine. The initial treatment of asymptomatic patients with SIADH includes management of the underlying cause if possible and free water restriction (in practical terms, fluid restriction) without limiting sodium intake. Discontinuation of fluoxetine should result in resolution of the SIADH with normalization of the serum sodium. In the interim, fluid restriction with a decrease in intake less than urine output will result in a gradual increase in the serum sodium.

Although the serum sodium is significantly decreased, she has no specific neurologic symptoms, which suggests that the hyponatremia is chronic. Rapid normalization of this patient's serum sodium with hypertonic saline would place her at risk for osmotic demyelination syndrome, which may result in severe neurologic symptoms such as paraplegia, dysarthria, dysphagia, diplopia, and locked-in syndrome. Because of this risk, treatment with hypertonic saline is usually limited to patients with severely symptomatic hyponatremia (such as mental status changes or seizures) to rapidly increase the serum sodium.

Treatment with isotonic saline may correct hyponatremia if it is secondary to hypovolemia, but this patient is euvolemic and most likely has SIADH. In this patient, isotonic saline alone, without concomitant fluid restriction, results in volume expansion but may not correct and may possibly worsen the hyponatremia because of inappropriate retention of the water associated with the infusion.

Oral demeclocycline results in renal resistance to antidiuretic hormone and can be effective in treating patients with SIADH. However, it has been associated with acute kidney injury and is generally reserved for

patients who have failed other therapies. It should be used with caution in patients with preexisting kidney or liver disease.

Tolvaptan, a vasopressin receptor antagonist, results in the excretion of electrolyte free water and is effective in raising the serum sodium in patients with SIADH. It should be used with caution in the treatment of severe, symptomatic hyponatremia, which is not seen in this patient, and as a last resort when other treatments have failed. Because severe liver injury has been reported with its use, the FDA recommends that it not be used in patients with liver disease and that it be used for no more than 30 days.

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Question 64

A 76-year-old woman is evaluated during a follow-up visit for hypertension. She notes fluctuating home blood pressure measurements, with systolic blood pressure measurements in the range of 140 to 150 mm Hg. History is notable for osteoporosis, hip fracture and subsequent hip replacement, and vertebral fracture. Medications are amlodipine, alendronate, calcium, and vitamin D.

On physical examination, the patient appears frail; she has difficulty climbing onto the examination table and requires assistance. Average blood pressure is 152/76 mm Hg based on two measurements, which is consistent with home measurements taken over the past few weeks. Pulse rate is 64/min. BMI is 19. It takes her 20 seconds to walk 6 meters. The remainder of the examination is unremarkable.

Laboratory studies show a normal chemistry panel; a urine dipstick demonstrates no protein.

Which of the fo llowing is the most appropriate next step in management?

A

Add chlorthalidone

B

Add lisinopril

C

Obtain 24-hour ambulatory blood pressure monitoring

D

Continue current regimen

Choose an Answ

Answer & Critique

Correct Answer: D

Educational Objective: Manage stage 1 hypertension in an older, frail patient.

Key Point

The risk of complications, morbidity, and mortality related to lower blood pressure in frail individuals may supersede the potential benefit of lower blood pressure goals.

Continuing the current treatment regimen with the calcium channel blocker amlodipine is appropriate. This 76-year-old patient has stage 1 hypertension and systolic blood pressure measurements in the range of 140 to 150 mm Hg. The treatment goal recommended in the eighth report of the Joint National Committee (JNC 8) for patients with hypertension who are ≥60 years is <150/90 mm Hg. Although she is near this goal, the benefits of further blood pressure reduction must be balanced with the potential risks of increasing a dose, changing the antihypertensive agent, or adding additional antihypertensive agents. Importantly, a recent study defining frailty as the inability to walk 6 meters in less than 8 seconds demonstrated no association with hypertension and mortality, and, in those who were unable to complete the walk test, a reduction in mortality was noted with increased blood pressure. This suggests that the risk of complications, morbidity, and mortality related to lower blood pressure in frail individuals may supersede the potential benefit of lower blood pressure goals.

Although 24-hour ambulatory blood pressure monitoring may be more accurate in defining this patient's blood pressure, home blood pressure monitoring is a reasonable alternative because it is less expensive. Furthermore, additional information is not likely to influence therapy.

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Question 65

A 45-year-old woman was hospitalized 2 days ago after attempting suicide with an overdose of a benzodiazepine. She is now asymptomatic. Medical history is significant for bipolar disorder, treated with lithium for the past 15 years. She has a 45-pack-year history of smoking and drinks 3 to 4 beers daily.

On physical examination, blood pressure is 142/74 mm Hg supine and 140/80 mm Hg standing, pulse rate is 82/min, and respiration rate is 15/min. BMI is 25. Examination of the heart, lungs, and abdomen is normal. There is no peripheral edema.

Laboratory studies:

Electrolytes:	
Sodium	125 mEq/L (125 mmol/L)
Potassium	3.5 mEq/L (3.5 mmol/L)
Chloride	85 mEq/L (85 mmol/L)
Bicarbonate	27 mEq/L (27 mmol/L)
Plasma osmolality	263 mOsm/kg H_2O
Urine sodium	42 mEq/L (42 mmol/L)
Urine osmolality	600 mOsm/kg H_2O

Which of the following is the most likely diagnosis?

A

Beer potomania

B

Lithium-induced renal toxicity

C

Primary polydipsia

D

Syndrome of inappropriate antidiuretic hormone secretion

Answer & Critique

Correct Answer: D

Educational Objective: Diagnose the syndrome of inappropriate antidiuretic hormone secretion.

Key Point

The syndrome of inappropriate antidiuretic hormone secretion is associated with clinical euvolemia, hypo-osmolar hyponatremia, and urine osmolality inappropriately greater than plasma osmolality.

This patient's history and clinical presentation are most consistent with the syndrome of inappropriate antidiuretic hormone secretion (SIADH). On physical examination, she is clinically euvolemic. The appropriate physiologic response to hypo-osmolality in a euvolemic patient is suppression of antidiuretic hormone (ADH) with resultant increase in free water clearance, with urine osmolality less than plasma osmolality. In contrast, this patient demonstrates evidence for increased ADH with hyponatremia and urine osmolality significantly and inappropriately greater than plasma osmolality in spite of her euvolemic status and no apparent stimulus for ADH release.

Because water excretion is, in part, solute dependent, severe limitations in solute intake decrease free water excretion, and hyponatremia may develop in this setting with only modest increases in fluid intake. This syndrome is termed *beer potomania* when observed in patients with chronic alcohol abuse and low solute intake. This patient's relatively high urine osmolality makes beer potomania an unlikely diagnosis.

The most common renal consequence of chronic lithium ingestion is nephrogenic diabetes insipidus; this disorder presents with polyuria and hypernatremia, which are not seen in this patient.

Primary polydipsia should always be considered in the differential diagnosis of patients with mental illness and hyponatremia, particularly those with schizophrenia who are taking psychotropic drugs. Primary polydipsia presents with hyponatremia, decreased plasma osmolality, and decreased urine osmolality, reflecting suppressed ADH levels in response to water overload. Patients with primary polydipsia may also present with abnormalities of ADH regulation such as transient stimulation of ADH release during psychotic episodes and increased renal response to

ADH so that at the same levels of ADH, patients who are psychotic may have higher urine osmolalities and a downward resetting of the osmostat that regulates ADH release. Thus, the urine of patients who are psychotic and have primary polydipsia may not be as dilute as would be expected. The significant elevation in urine osmolality makes SIADH the more likely diagnosis in this patient.

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Question 66

A 34-year-old woman is evaluated for laboratory abnormalities discovered as part of an evaluation for joint pain. She describes the pain as being diffuse and associated with chronically dry eyes and mouth. She also notes recent-onset mild nocturia. Medical history is otherwise negative, and she takes acetaminophen daily for her joint pain.

On physical examination, vital signs are normal. BMI is 23. Mucous membranes and conjunctivae are dry, and mild parotid enlargement is present. There is no evidence of joint inflammation. The remainder of the examination is unremarkable.

Laboratory studies:

Creatinine	0.9 mg/dL (79.6 µmol/L)
Electrolytes:	
Sodium	138 mEq/L (138 mmol/L)
Potassium	3.1 mEq/L (3.1 mmol/L)
Chloride	118 mEq/L (118 mmol/L)
Bicarbonate	12 mEq/L (12 mmol/L)
Glucose	74 mg/dL (4.1 mmol/L)
Urinalysis	pH 7.0; no blood, glucose, protein, erythrocytes, or leukocytes

Which of the following is the most likely cause of this patient's laboratory findings?

A

Acetaminophen

B

Type 1 (hypokalemic distal) renal tubular acidosis

C

Type 2 (proximal) renal tubular acidosis

D

Type 4 (hyperkalemic distal) renal tubular acidosis

Answer & Critique

Correct Answer: B

Educational Objective: Diagnose type 1 (hypokalemic distal) renal tubular acidosis.

Key Point

Type 1 (hypokalemic distal) renal tubular acidosis results from a defect in urine acidification in the distal tubule with impaired excretion of hydrogen ions.

The most likely diagnosis is type 1 (hypokalemic distal) renal tubular acidosis (RTA), which results from a defect in urine acidification in the distal tubule with impaired excretion of hydrogen ions, most commonly caused by decreased activity of the proton pump in distal tubular cells. Because of the inability to excrete hydrogen ions, patients develop a metabolic acidosis with compensatory hyperchloremia, resulting in a normal anion gap (8 mEq/L [8 mmol/L] in this patient) and the inability to acidify urine below a pH of 6.0, even after an acid load. The urine pH is therefore almost always inappropriately elevated for the degree of acidemia, and there is a positive urine anion gap. The same defects also cause potassium wasting, and the increased proximal resorption of citrate that occurs with metabolic acidosis leads to hypocitraturia and increased risk of calcium phosphate kidney stones and nephrocalcinosis. Type 1 (hypokalemic distal) RTA is associated with genetic causes, autoimmune disorders, nephrocalcinosis/hypercalciuria, dysproteinemias, drugs/toxins, and tubulointerstitial disease; this patient likely has sicca complex secondary to Sjögren syndrome and kidney involvement with interstitial nephritis.

Acetaminophen is associated with pyroglutamic acidosis (also known as 5-oxoprolinuria), which causes an increased anion gap metabolic acidosis and is less likely to cause a pure normal anion gap metabolic acidosis.

Type 2 (proximal) RTA involves a defect in regenerating bicarbonate in the proximal tubule and is characterized by a normal anion gap metabolic acidosis, hypokalemia, glycosuria (without hyperglycemia), low-molecular-weight proteinuria, and renal phosphate wasting. However, distal urine acidification mechanisms are intact, and the urine pH is usually less than 5.5 without alkali therapy. This patient's high urine pH, absence of glycosuria, and normal urinalysis are inconsistent with type 2 (proximal) RTA.

Type 4 (hyperkalemic distal) RTA is associated with a urine pH <5.5 and hyperkalemia as a result of hypoaldosteronism, neither of which is seen in this patient.

Question 67

A 65-year-old woman is evaluated during a follow-up visit. She has end-stage kidney disease due to IgA nephropathy; she started peritoneal dialysis 3 months ago. She also has a 10-year history of hypertension. She has done well since starting dialysis, is without current complaints, and has recently resumed exercising regularly. She has three adult children who are encouraging her to explore kidney transplantation and are willing to be evaluated as kidney donors; however, the patient feels that she is "too old." Medications are amlodipine, ramipril, calcitriol, epoetin alfa, and calcium acetate.

On physical examination, temperature is 37.0 °C (98.6 °F), blood pressure is 135/75 mm Hg, pulse rate is 72/min, and respiration rate is 14/min. BMI is 27. The peritoneal dialysis catheter site is nontender without induration or exudate. Cardiac examination reveals normal heart sounds. The lungs are clear. The abdomen is nontender. There is no peripheral edema.

Which of the following kidney replacement strategies is most likely to provide this patient with the best long -term survival?

A

Change from peritoneal dialysis to hemodialysis

B

Continue peritoneal dialysis

C

Continue peritoneal dialysis and evaluate for transplant in 2 to 3 years

D

Refer for transplant evaluation now

Choose an Answer Above

Answer & Critique

Correct Answer: D

Educational Objective: Understand the risks and benefits of kidney transplantation.

Key Point

Kidney transplantation decreases long-term mortality and improves quality of life compared with dialysis.

Kidney transplantation would be the most likely strategy to provide this patient with the best long-term survival. Although there is an increase in short-term morbidity and mortality following transplantation, there is strong evidence that kidney transplantation decreases mortality and improves quality of life over the long term. Even though increased recipient age is also associated with reduced patient and allograft survival than younger patients after transplant, carefully selected older patients also benefit from kidney transplantation, and many centers therefore do not have an absolute age cutoff for transplant recipients. Moreover, this patient has family members who are willing to be evaluated as living kidney donors, and kidneys from living donors have superior outcomes compared with kidneys from deceased donors. Therefore, referral for possible kidney transplant in this otherwise healthy patient would be most likely to improve her long-term survival.

There is no clinical indication for this patient to change from peritoneal dialysis to hemodialysis, and clinical outcomes, including mortality and quality of life, are approximately equivalent between these modalities. The choice between peritoneal dialysis and hemodialysis should therefore be driven by patient-specific factors and patient preference if dialysis is pursued.

There is evidence that risk of graft loss and overall mortality are increased in patients who have been treated with dialysis prior to transplant, and that this risk of graft loss and overall mortality increase with the length of dialysis prior to transplant. Therefore, continuing dialysis and reevaluating for possible transplant in 2 to 3 years would not be an optimal management strategy in this otherwise good candidate for transplantation.

Question 68

A 49-year-old woman is evaluated during a follow-up visit for a 5-year history of stage G3b/A2 chronic kidney disease (CKD) and a 15-year history of hypertension. Medical history is otherwise unremarkable. She is a never-smoker. Family history is notable for her mother who developed end-stage kidney disease due to hypertension at age 60 years. Medications are lisinopril, amlodipine, and hydrochlorothiazide.

On physical examination, temperature is 37.0 °C (98.6 °F), blood pressure is 134/85 mm Hg, pulse rate is 73/min, and respiration rate is 12/min. BMI is 24. There is no jugular venous distention. An S_4 gallop is heard. The lungs are clear. There is no peripheral edema. The remainder of the examination is unremarkable.

Laboratory studies are notable for a serum creatinine level of 2.1 mg/dL (185.6 µmol/L), an estimated glomerular filtration rate of 31 mL/min/1.73 m^2, and a urine albumin-creatinine ratio of 20 mg/g.

Which of the following is the most appropriate management?

A

Begin a low protein diet

B

Lower blood pressure to <130/80 mm Hg

C

Switch hydrochlorothiazide to furosemide

D

No changes to current therapy

Answer & Critique

Correct Answer: D

Educational Objective: Manage blood pressure and diet to slow progression of chronic kidney disease.

Key Point

The eighth report from the Joint National Committee recommends a target blood pressure of <140/90 mm Hg and ACE inhibitors or angiotensin receptor blockers as first-line agents for treatment of hypertension in patients with chronic kidney disease.

Maintaining the current antihypertensive regimen and a standard protein diet is appropriate in this patient to help slow progression of her chronic kidney disease (CKD).

Although earlier, small studies suggested that low protein diets may slow CKD progression, the landmark Modification of Diet in Renal Disease study did not detect a significant protective effect of protein-restricted diets in preventing progression of kidney disease. However, low protein diets may delay onset of symptomatic uremia in patients with late-stage CKD (stage G4/G5).

The eighth report from the Joint National Committee (JNC 8) recommends a target blood pressure of <140/90 mm Hg with ACE inhibitors or angiotensin receptor blockers as first-line agents for treatment of hypertension in patients with CKD. This patient currently meets this recommended goal with an ACE inhibitor as part of her regimen. Although previously recommended by several organizations, there are currently insufficient data to support targeting blood pressures lower than 140/90 mm Hg to prevent progression of kidney disease with the possible exception of patients with severe proteinuria (stage A3 or an albumin-creatinine ratio >300 mg/g), in which some randomized controlled trials have suggested the benefit of a lower blood pressure goal of <130/80 mm Hg.

Volume expansion may contribute to hypertension in CKD; therefore, maintaining normal volume status is important for long-term blood pressure control. Although the diuretic effect of thiazides becomes less effective as the glomerular filtration rate drops, often requiring a switch to a loop diuretic, this patient is clinically euvolemic and with adequate blood pressure control. Additionally, diuretics themselves do not alter progression of proteinuria or CKD. Therefore, there is no indication for switching diuretic therapy in this patient.

Question 69

A 65-year-old man is evaluated during a follow-up visit for stage G3b/A3 chronic kidney disease due to diabetic nephropathy. He reports doing well with good baseline exercise tolerance and no shortness of breath. Medical history is also significant for type 2 diabetes mellitus and hypertension. Medications are basal bolus insulin and lisinopril.

On physical examination, temperature is normal, blood pressure is 145/75 mm Hg, pulse rate is 82/min, and respiration rate is 16/min. BMI is 28. There is no jugular venous distention. The lungs are clear.

Laboratory studies:

Bicarbonate	Normal
Creatinine	1.9 mg/dL (168 μmol/L)
Potassium	4.0 mEq/L (4.0 mmol/L)
Estimated glomerular filtration rate	42 mL/min/1.73 m^2
Urine protein-creatinine ratio	3900 mg/g

Kidney ultrasound shows mildly echogenic kidneys that are of normal size with no obstruction.

Which of the following is the most appropriate treatment?

A

Add an angiotensin receptor blocker

B

Increase lisinopril dose

C

Replace lisinopril with amlodipine

D

No change in current medications

Answer & Critique

Correct Answer: B

Educational Objective: Treat a patient who has chronic kidney disease and proteinuria.

Key Point

Blood pressure control using an ACE inhibitor or angiotensin receptor blocker is the therapy of choice in patients with chronic kidney disease.

The most appropriate treatment for this patient is to increase the dose of the ACE inhibitor lisinopril. He has chronic kidney disease (CKD) with nephrotic-range proteinuria (urine protein-creatinine ratio >3500 mg/g or a urine protein excretion >3500 mg/24 h) and inadequately controlled hypertension. Increasing lisinopril should decrease his blood pressure and result in some decrease in proteinuria. Although many clinicians are hesitant to escalate the dose of an ACE inhibitor or angiotensin receptor blocker (ARB) in patients with significant CKD, careful upward titration is generally well tolerated with close clinical follow-up. The eighth report from the Joint National Committee (JNC 8) recommends lowering blood pressure to <140/90 mm Hg, although some experts recommend a lower blood pressure goal of <130/80 mm Hg in patients with heavy proteinuria.

Recent studies have demonstrated that although adding an ARB to an ACE inhibitor usually decreases proteinuria, combination therapy does not improve clinical outcomes and increases the risk of acute kidney injury and hyperkalemia.

Most patients with CKD, and those with CKD and proteinuria in particular, should be treated with an ACE inhibitor or ARB as preferred initial medications due to their demonstrated ability to slow CKD progression. Therefore, replacing lisinopril with the calcium channel blocker amlodipine is not appropriate in this case.

Continuing this patient's current therapy would not improve blood pressure control or decrease proteinuria.

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Question 70

A 43-year-old man is evaluated in the emergency department for abdominal pain. He has a history of alcohol abuse, with repeated episodes of acute intoxication requiring medical therapy. He also has a history of several episodes of acute pancreatitis, but no history of seizure disorder. He takes no medications.

On physical examination, temperature is 37.4 °C (99.3 °F), blood pressure is 112/66 mm Hg, and pulse rate is 76/min. BMI is 20. There is no evidence of trauma or head injury. There is no evidence of ascites. The abdomen is tender to palpation. Neurologic examination reveals normal pupillary and corneal reflexes, normal muscle tone, and a downgoing plantar reflex.

Laboratory studies:

Blood urea nitrogen	28 mg/dL (10 mmol/L)
Calcium	8.6 mg/dL (2.2 mmol/L)
Creatinine	1.2 mg/dL (106.1 µmol/L) (baseline, 0.8 mg/dL [70.7 µmol/L])
Electrolytes:	
Sodium	135 mEq/L (135 mmol/L)
Potassium	4.9 mEq/L (4.9 mmol/L)
Chloride	96 mEq/L (96 mmol/L)
Bicarbonate	12 mEq/L (12 mmol/L)
Ethanol	62 mg/dL (0.062 g/dL)
Glucose	72 mg/dL (4 mmol/L)
Lactate	0.8 mEq/L (0.8 mmol/L)
Plasma osmolality	293 mOsm/kg H_2O
Phosphorus	3.7 mg/dL (1.2 mmol/L)

Urinalysis	pH 5.5; specific gravity 1.020; no blood, ketones, or cells

Which of the following is the most likely cause of this patient's acidosis?

A

Acute kidney injury

B

Alcoholic ketoacidosis

C

D-Lactic acidosis

D

Rhabdomyolysis

Choose an Answer Above

Answer & Critique

Correct Answer: B

Educational Objective: Diagnose alcoholic ketoacidosis.

Key Point

Alcoholic ketoacidosis occurs in patients with chronic ethanol abuse, frequently with associated liver disease, and develops following an episode of acute intoxication.

The most likely diagnosis is alcoholic ketoacidosis. This patient has an increased anion gap metabolic acidosis of 27, and ketoacidosis due to acute ethanol intoxication is the most likely cause. Alcoholic ketoacidosis occurs in patients with chronic ethanol abuse and liver disease and develops following an episode of acute intoxication, at which time the ingested ethanol may have already been extensively metabolized, leading to low or normal serum ethanol levels. Ethanol is oxidized to acetaldehyde and then to acetic acid, during which process the electron-carrier coenzyme nicotinamide adenine dinucleotide (NAD^+) is reduced to NADH in increasing amounts. Simultaneously, rising catecholamine levels cause lipolysis with subsequent generation of free fatty acids and ketone bodies, such as acetoacetate. The high ratio of NADH to NAD^+ leads to increased reduction of acetoacetate to β-hydroxybutyrate. Because the nitroprusside reagent in the serum and urine ketone assays detects only acetoacetate, these tests may be falsely negative due to decreased acetoacetate levels despite the presence of increased levels of the ketone β-hydroxybutyrate, as in this case. Definitive diagnosis may require direct measurement of β-hydroxybutyrate levels in the serum, which is available in some laboratories.

Acute kidney injury can lead to an increased anion gap metabolic acidosis due to the accumulation of acidic metabolic by-products and phosphates and sulfates. However, this degree of anion gap would not be expected in this patient who is mildly prerenal with a normal serum phosphorus level.

D-Lactic acidosis is an uncommon cause of increased anion gap metabolic acidosis that is typically identified in patients with small-bowel bacterial overgrowth. Bacterial production of D-lactic acid is undetectable by the serum lactate assay, which recognizes only the L enantiomer. However, this disorder is not associated with chronic alcohol use and would not be a likely diagnostic consideration in this patient.

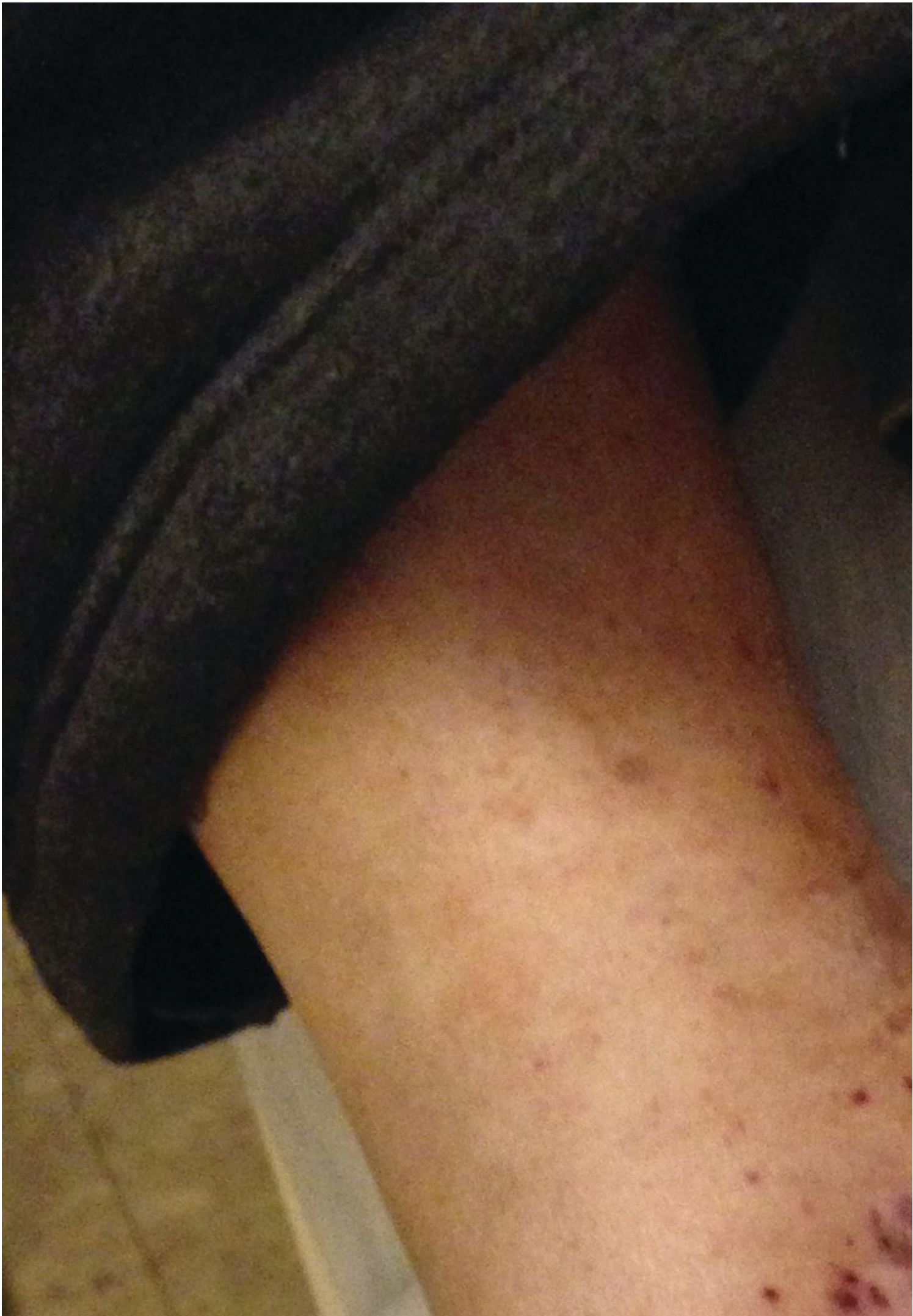
Rhabdomyolysis is a diagnostic consideration in a patient with a history of alcohol abuse and an anion gap metabolic acidosis, but this condition is frequently associated with hyperkalemia, hyperphosphatemia, hypocalcemia, and a urinalysis positive for blood with no erythrocytes visible on urine microscopy.

Question 71

A 50-year-old man is evaluated in the hospital for fatigue, joint pain, and skin lesions. His symptoms started 2 weeks ago with fever and sore throat, which subsided in 2 days. Fatigue and joint pain were noted 1 day after the onset of sore throat, which worsened over the subsequent days. Four days after the onset of symptoms, he noted dark red spots on his ankles and shins, which spread to involve his legs, thighs, and buttocks; the skin lesions were not painful or itchy. He also notes intermittent central abdominal pain, crampy in nature and not related to food. He has hypertension that was previously well controlled with lisinopril and hydrochlorothiazide.

On physical examination, temperature is 37.8 °C (100.0 °F), blood pressure is 170/84 mm Hg, pulse rate is 78/min, and respiration rate is 14/min. BMI is 28. Examination of the joints shows tenderness and increased warmth in the knees, ankles, and elbows without effusions. Cardiac and lung examinations are normal. There is mild guarding around the periumbilical area on abdominal examination.

The appearance of the skin is shown.



Laboratory studies:

Albumin	3.1 g/dL (31 g/L)
Complements (C3 and C4)	Normal
Creatinine	1.8 mg/dL (159 µmol/L)
Hepatitis B antibody profile	Negative
Hepatitis C antibody profile	Negative
Urinalysis	3+ blood; 2+ protein; 50-100 erythrocytes/hpf; 10-15 leukocytes/hpf; few erythrocyte casts
Urine protein-creatinine ratio	2200 mg/g

Lupus serologies, antistreptolysin O antibodies, ANCA, and anti–glomerular basement membrane antibodies are pending. Blood cultures are pending. Stool occult blood test is positive.

Which of the following is the most likely diagnosis?

A

Cryoglobulinemic vasculitis

B

Endocarditis

C

IgA vasculitis

D

Systemic lupus erythematosus

Choose an Answer Above

Answer & Critique

Correct Answer: C

Educational Objective: Diagnose IgA vasculitis.

Key Point

IgA vasculitis is associated with abdominal pain, palpable purpura, arthralgia, and glomerulonephritis, with normal complement levels.

The most likely diagnosis is IgA vasculitis (Henoch-Schönlein purpura). This patient presents with fatigue, joint pain, abdominal pain, petechial/purpural skin lesions, and glomerulonephritis following an upper respiratory tract infection. The differential diagnosis of vasculitis with glomerulonephritis includes infection-related vasculitis (such as endocarditis), cryoglobulinemia, systemic lupus erythematosus, ANCA-associated vasculitis, and IgA vasculitis. Although serologic tests and blood cultures are pending, the patient most likely has IgA vasculitis based on the presence of the tetrad of palpable purpura, arthralgia, abdominal pain, and glomerulonephritis. Although no diagnostic serologic tests for this condition exist, normal complement levels support this diagnosis. Diagnosis is confirmed with biopsy of the affected organ.

Infection-related glomerulonephritis such as endocarditis activates the alternative pathway of complement with low C3 and normal C4 levels. The classical pathway of complement is activated with cryoglobulinemic vasculitis (C4, and sometimes C3, is depressed) and systemic lupus erythematosus (both C3 and C4 are low). In this patient, complement levels are normal, making these diseases less likely. Additionally, cryoglobulinemic vasculitis is associated with hepatitis C virus infection, which is not present in this patient.

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Question 72

A 23-year-old woman is evaluated in the emergency department for generalized weakness and lightheadedness of 4 hours' duration. She has had no previous contact with the health care system and takes no medications.

On physical examination, blood pressure is 120/80 mm Hg supine and 105/70 mm Hg sitting, and pulse rate is 95/min supine and increases to 108/min upon standing. BMI is 26. Skin turgor is poor. Multiple dental caries are present. There is no jugular venous distention. Cardiac examination reveals a regular rhythm with no murmurs. The lungs are clear. Bowel sounds are hyperactive. The abdomen is soft, nontender, and nondistended.

Laboratory studies:

Electrolytes:

Sodium	138 mEq/L (138 mmol/L)
Potassium	2.8 mEq/L (2.8 mmol/L)
Chloride	90 mEq/L (90 mmol/L)
Bicarbonate	36 mEq/L (36 mmol/L)
Urine studies:	
Sodium	45 mEq/L (45 mmol/L)
Potassium	42 mEq/L (42 mmol/L)
Chloride	5.0 mEq/L (5.0 mmol/L)
pH	7.0

Which of the following is the most likely cause of this patient's hypokalemia?

A

Bartter syndrome

B

Hypokalemic periodic paralysis

C

Sjögren syndrome

D

Vomiting

Answer & Critique

Correct Answer: D

Educational Objective: Identify vomiting as a cause of hypokalemia.

Key Point

Hypokalemia due to vomiting is associated with metabolic alkalosis, increased urine potassium excretion, and decreased urine chloride excretion.

Vomiting is the most likely cause of this patient's hypokalemia. She presents with hypokalemic metabolic alkalosis with extracellular volume depletion. Hypokalemia, defined as a serum potassium concentration <3.5 mEq/L (3.5 mmol/L), can be life-threatening when severe. Patients usually have minimal symptoms unless serum potassium levels are <3.0 mEq/L (3.0 mmol/L); symptoms correlate with the rapidity of the decrease, ranging from generalized weakness and malaise to paralysis, depending on the serum potassium level. This patient's history (generalized weakness and lightheadedness), physical examination findings (volume contraction and dental caries), and urine electrolyte levels are most consistent with vomiting from bulimia nervosa. Vomiting results in loss of hydrogen chloride and fluid from gastric secretions, and, if persistent, results in volume contraction. Hypovolemia activates the renin-angiotensin system with an increase in sodium-hydrogen exchange and increased bicarbonate reabsorption in the proximal tubule due to increased luminal hydrogen ion, and exacerbated by decreased chloride available for reabsorption with sodium. Increased aldosterone secretion stimulates sodium-potassium exchange in the distal tubule. The urine electrolytes in this patient reflect these physiologic changes. With volume depletion, the urine sodium concentration is generally low (<20 mEq/L [20 mmol/L]) due to the kidney's conservation of sodium. However, in this case, excess filtered bicarbonate associated with the alkalosis is excreted through the renal tubule, and sodium is lost in the urine as an obligatory cation with bicarbonate necessary to maintain electroneutrality; this results in increased urine sodium excretion. Because of this, the urine chloride is a more accurate determination of volume status than the urine sodium in metabolic alkalosis. The urine chloride concentration is low (<20 mEq/L [20 mmol/L]), reflecting gastrointestinal losses and prolonged volume contraction that leads to avid reabsorption of chloride with sodium. The urine potassium concentration in this patient is elevated (>40 mEq/L [40 mmol/L]) due to increased aldosterone production and distal nephron bicarbonate delivery that promote potassium loss through the kidney. Treatment of these abnormalities is to treat the vomiting and provide volume expansion

with normal saline and potassium replacement, which will reverse these changes and correct the acid-base and electrolyte abnormalities.

Bartter syndrome mimics the effect of a loop diuretic and is accompanied by increased urine sodium (>40 mEq/L [40 mmol/L]), urine potassium (>40 mEq/L [40 mmol/L]), and chloride excretion (>40 mEq/L [40 mmol/L]).

Hypokalemic periodic paralysis is due to a shift of potassium into cells and is not associated with a metabolic alkalosis; furthermore, urine potassium would be low (<20 mEq/L [20 mmol/L]) and not increased.

Hypokalemia from Sjögren syndrome occurs in the setting of renal tubular acidosis, and a hyperchloremic metabolic acidosis would occur, which is not seen in this patient.

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Question 73

A 35-year-old woman is evaluated in the emergency department for new-onset lower extremity edema. She notes a 1-week history of progressive shortness of breath and fatigue. She attended a picnic 10 days ago and subsequently developed bloody diarrhea, which has largely subsided. Medical history is otherwise unremarkable, and she takes no medications.

On physical examination, temperature is 37.8 °C (100.0 °F), blood pressure is 190/90 mm Hg, pulse rate is 100/min, and respiration rate is 20/min. BMI is 27. There is no skin rash. Cardiopulmonary examination is normal. The abdomen is diffusely tender but without rebound. Bilateral lower extremity edema is noted to the level of the mid calves. On neurologic examination, mental status is normal, and there are no other focal findings.

Laboratory studies:

Hemoglobin	7.0 g/dL (70 g/L)
Platelet count	50,000/μL (50×10^9/L)
Creatinine	7.2 mg/dL (636.5 μmol/L)
Urinalysis	2+ blood; 1+ protein; 0-2 erythrocytes/hpf; 0-2 leukocytes/hpf

Which of the following is the most appropriate next step in diagnosis?

A
ADAMTS13 activity level

B
Kidney biopsy

C
Peripheral blood smear

D
Urine protein electrophoresis

Answer & Critique

Correct Answer: C

Educational Objective: Diagnose thrombotic microangiopathy.

Key Point

Shiga toxin–associated hemolytic uremic syndrome is a diarrhea-associated syndrome of microangiopathic hemolytic anemia, thrombocytopenia, and kidney failure caused by Shiga toxin–producing *Escherichia coli*.

The next step in diagnosis is a peripheral blood smear. This patient has findings suggestive of Shiga toxin–associated hemolytic uremic syndrome (HUS). This is a diarrhea-associated syndrome of microangiopathic hemolytic anemia, thrombocytopenia, and kidney failure caused by Shiga toxin–producing *Escherichia coli*, typically with serotypes O157:H7, O104:H4, and, less commonly,*Shigella dysenteriae*. Shiga toxin binds to endothelial cells, triggering thrombosis and resulting in a thrombotic microangiopathy. It also binds to renal mesangial cells, podocytes, and renal tubular cells, causing direct damage. These actions lead to acute kidney injury (AKI). Although this patient has a consistent clinical history, a peripheral blood smear is essential to determine whether the anemia is caused by a microangiopathic hemolytic process as indicated by the presence of schistocytes. Stool cultures may reveal the offending organism. Treatment is primarily supportive, and many patients require dialysis.

ADAMTS13 is a metalloprotease enzyme that cleaves von Willebrand factor; low activity levels are supportive of a diagnosis of thrombotic thrombocytopenic purpura (TTP). Although this would be a reasonable study in this patient if a likely diagnosis of Shiga toxin–associated HUS were less clear to assess for the possibility of TTP, confirmation of true thrombocytopenia and microangiopathic hemolytic anemia would be an initial diagnostic step before additional testing.

Kidney biopsy would show evidence of capillary thrombosis as well as glomerular and tubular damage, but it is not necessary to establish the diagnosis of Shiga toxin–associated HUS.

Urine protein electrophoresis may be useful in evaluating AKI due to monoclonal urine immunoglobulin light chains (Bence Jones proteins). Although a plasma cell disorder may cause

anemia and AKI due to precipitation of light chains in the renal tubule (myeloma kidney), it is not a cause of microangiopathic hemolytic anemia or thrombocytopenia as seen in this patient.

Question 74

A 28-year-old woman is evaluated in the emergency department for right flank pain of several days' duration and an episode of gross hematuria. She is in her 24th week of pregnancy, which has been uncomplicated, and she has had regular obstetric care. She reports no fevers or chills, abdominal pain, changes in bowel habits, dysuria, or urinary frequency. Family history is notable for her mother with kidney stones. Her only medication is a prenatal vitamin.

On physical examination, the patient is in moderately painful distress localized to the right flank area. Temperature is 37.0 °C (98.6 °F), blood pressure is 118/68 mm Hg, pulse rate is 78/min, and respiration rate is 12/min. BMI is 28. She has a gravid uterus, and the abdominal examination is otherwise unremarkable. There is no costovertebral angle or suprapubic tenderness. The remainder of the examination is normal.

Urinalysis shows large blood and >50,000 erythrocytes/hpf but is otherwise normal.

Which of the following is the most appro priate diagnostic test to perform next?

A
Abdominal MRI

B
Bilateral kidney ultrasonography

C
Low-dose noncontrast helical CT

D
Plain abdominal radiography

E
Transvaginal ultrasonography

Answer & Critique

Correct Answer: B

Educational Objective: Evaluate a pregnant patient for suspected nephrolithiasis using ultrasonography.

Key Point

Ultrasonography is the preferred diagnostic imaging modality for pregnant patients with suspected nephrolithiasis because it does not expose patients to radiation.

Bilateral kidney ultrasonography is the most appropriate diagnostic study for this pregnant patient with suspected nephrolithiasis. Although noncontrast helical CT has traditionally been the most commonly used imaging technique for suspected nephrolithiasis because it detects most stones, provides helpful anatomic information, visualizes the entire urinary tract, and may potentially provide alternative diagnoses if nephrolithiasis is not detected, it is associated with significant radiation exposure and is therefore contraindicated in pregnant women. Kidney ultrasonography is increasingly being used as an initial diagnostic study for nonpregnant patients with suspected nephrolithiasis, particularly younger patients, to avoid significant radiation exposure, and it is the study of choice for pregnant women with possible kidney stones. Although it is less sensitive than CT for kidney stones, particularly for small stones or those in the distal urinary tract, a positive study for nephrolithiasis can exclude complications such as hydronephrosis and remove the need for more extensive additional testing.

Abdominal MRI can be used during pregnancy, but it is not optimal for imaging kidney stones. Ultrasonography is preferred, although MRI may be a diagnostic option if additional imaging is required for diagnosis.

Low-dose CT is both sensitive and specific for detecting kidney stones but is also associated with significant radiation exposure, similar to conventional stone protocol CT. Low-dose CT is absolutely contraindicated in the first trimester of pregnancy and is used only in specific situations in pregnant women in the second or third trimesters. It is not an appropriate study for this patient.

Plain abdominal radiography has limited utility for suspected nephrolithiasis due to its inability to detect radiolucent stones and the limited anatomic information it provides. It also involves radiation exposure and is not an appropriate next test in this patient.

Transvaginal ultrasonography may be used to detect distal ureteral stones in pregnant women with suspected nephrolithiasis and an unrevealing kidney ultrasound. However, it is not an appropriate next test for this patient.

Question 75

A 28-year-old man is evaluated for recurrent nephrolithiasis. Medical history is significant for Crohn disease complicated by multiple small bowel strictures requiring resection. He began developing kidney stones 3 years ago following his last bowel surgery. Analysis of the stones has consistently shown calcium oxalate, and he has been adherent to a low oxalate diet, oral hydration to maintain urine output of at least 2 L/d, and intake of 2 g of calcium carbonate with each meal. However, he has continued to have periodic episodes of kidney stones. Medical history is otherwise unremarkable. Medications are infliximab and calcium carbonate.

On physical examination, temperature is 37.1 °C (98.8 °F), blood pressure is 131/78 mm Hg, pulse rate is 84/min, and respiration rate is 12/min. BMI is 22. The abdominal examination shows healed surgical incisions and is otherwise unremarkable. The remainder of the examination is normal.

Laboratory studies, including complete blood count, electrolytes, and kidney function, are normal. Urinalysis is normal; 24-hour urine chemical analysis shows normal levels of calcium, citrate, and uric acid, but elevated oxalate.

Plain abdominal radiographs show multiple small stones in both kidneys.

Which of the following is the most appr opriate additional treatment for this patient?

A

Cholestyramine

B

Hydrochlorothiazide

C

Potassium citrate

D

Pyridoxine

Choose an Answer Above

Answer & Critique

Correct Answer: A

Educational Objective: Treat calcium oxalate nephrolithiasis with bile salt binders in a patient with enteric hyperoxaluria.

Key Point

Patients with enteric hyperoxaluria and calcium oxalate nephrolithiasis may benefit from treatment with bile salt binders to decrease intestinal oxalate absorption.

Treatment with cholestyramine is an appropriate additional therapy for this patient with enteric hyperoxaluria. Hyperoxaluria predisposes to calcium oxalate stone formation. Excessive oxalate in the urine may result from excessive intake (from foods such as chocolate, spinach, rhubarb, or green and black tea) or in situations in which there is significant restriction in dietary calcium intake, which decreases binding of calcium to dietary oxalate in the gut and increases oxalate absorption. Enteric hyperoxaluria results from malabsorption when excessive free fatty acids in the gastrointestinal lumen bind calcium, increasing free oxalate absorption in the colon as may be seen in patients with small bowel disease or bowel resection. In addition to maintaining an adequate urine output of at least 2 L/d and ensuring adequate dietary calcium intake, patients with enteric hyperoxaluria may benefit from the bile salt binder cholestyramine, which also binds oxalate in the gut. This therapy is indicated in this patient with recurrent calcium oxalate nephrolithiasis following small bowel resection unresponsive to other treatments.

Thiazide diuretics, such as hydrochlorothiazide, are used in patients with idiopathic hypercalciuria to reduce calcium excretion in the urine by inducing mild hypovolemia that results in increased sodium reabsorption and passive calcium reabsorption in the proximal tubule. However, this patient does not have evidence of hypercalciuria, and thiazide therapy would not decrease the excessive oxalate in the urine.

Urine citrate inhibits stone formation by binding calcium in the tubular lumen, preventing it from precipitating with oxalate. Citrate excretion can be enhanced in patients with low urine citrate levels by alkalinizing the serum with potassium citrate, which decreases uptake of filtered citrate from the tubular lumen. However, this patient does not have evidence of hypocitraturia and would not be expected to benefit from additional urine citrate.

Pyridoxine is indicated in some patients with primary hyperoxaluria to improve glyoxylate metabolism and reduce overproduction of oxalate. However, this would not be effective in this patient with enteric hyperoxaluria.

Question 76

An 80-year-old woman is evaluated in the emergency department for tinnitus, confusion, and unsteady gait. She also has had dry heaves and vomiting for the past few days. Her family notes progressive decline in her overall functional status over the preceding 2 weeks. Medical history is notable for hypertension and osteoarthritis. Medications are lisinopril, hydrochlorothiazide, and aspirin.

On physical examination, temperature is 37.1 °C (98.8 °F), blood pressure is 140/68 mm Hg, pulse rate is 96/min, and respiration rate is 24/min. Estimated central venous pressure is 4.0 cm H_2O. Abdominal examination is unremarkable.

Laboratory studies:	
Electrolytes:	
Sodium	142 mEq/L (142 mmol/L)
Potassium	3.2 mEq/L (3.2 mmol/L)
Chloride	100 mEq/L (100 mmol/L)
Bicarbonate	20 mEq/L (20 mmol/L)
Arterial blood gases:	
Ph	7.56
P_{CO_2}	22 mm Hg (2.9 kPa)

Chest radiograph is normal.

Which of the following is the most likely diagnosis?

A

Respiratory alkalosis with chronic compensation

B

Respiratory alkalosis and increased anion gap metabolic acidosis

C

Respiratory alkalosis and metabolic alkalosis

D

Respiratory alkalosis, increased anion gap metabolic acidosis, and metabolic alkalosis

Choose an Answer Above

Answer & Critique

Correct Answer: D

Educational Objective: Diagnose a complex mixed acid-base disorder.

Key Point

Analysis of acid-base disorders requires the identification of the likely dominant acid-base disorder, followed by an assessment of the secondary, compensatory response; when measured values fall outside the range of the predicted secondary response, a mixed acid-base disorder is present.

The most likely diagnosis is a complex mixed acid-base disorder consisting of respiratory alkalosis, increased anion gap metabolic acidosis, and metabolic alkalosis. Analysis of acid-base disorders requires the identification of the likely dominant acid-base disorder, followed by an assessment of the secondary, compensatory response. When measured values fall outside the range of the predicted secondary response, a mixed acid-base disorder is present; multiple acid-base disturbances may coexist in a single patient. This patient's dominant acid-base disorder is alkalosis, as indicated by the blood pH of 7.56. The low P_{CO_2} indicates a respiratory component to the alkalosis. The expected compensation for chronic respiratory alkalosis is a decrease in the serum bicarbonate of 4 to 5 mEq/L (4-5 mmol/L) for each 10 mm Hg (1.3 kPa) decrease in the P_{CO_2}. The expected serum bicarbonate concentration in this patient is calculated to be 14 to 16 mEq/L (14-16 mmol/L), and the measured serum bicarbonate of 20 mEq/L (20 mmol/L) suggests coexistence of a metabolic alkalosis. This patient also has an elevated anion gap indicating the presence of an increased anion gap metabolic acidosis. The change of the anion gap from normal is 10 mEq/L (10 mmol/L). Calculating the ratio of the change in the anion gap (Δ anion gap) to the change in bicarbonate level (Δ bicarbonate), or the "Δ-Δ ratio," can help confirm if there is a coexisting acid-base disturbance. A ratio of <1 may reflect the presence of concurrent normal anion gap metabolic acidosis, whereas a ratio of >2 may indicate the presence of metabolic alkalosis. This patient's Δ-Δ ratio is 2.5, confirming the coexistence of a metabolic alkalosis. The clinical scenario most likely responsible for this complex acid-base disorder is salicylate toxicity with central hyperventilation from the salicylate, anion gap metabolic acidosis from the salicylate, and metabolic alkalosis from gastritis and vomiting.

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Question 77

A 53-year-old woman is evaluated during a routine follow-up visit. Medical history is significant for hypertension and chronic active hepatitis B infection. Her hepatitis B infection has been treated with tenofovir for the past 5 years with suppression of her serum hepatitis B DNA levels. She currently notes mild generalized weakness but otherwise feels well. Medications are ramipril and tenofovir.

On physical examination, temperature is 37.0 °C (98.6 °F), blood pressure is 136/79 mm Hg, pulse rate is 70/min, and respiration rate is 14/min. BMI is 22. Abdominal examination shows a normal-sized liver and no splenomegaly. The remainder of the examination is normal.

Laboratory studies:

Bicarbonate	21 mEq/L (21 mmol/L)
Creatinine	1.2 mg/dL (106.1 µmol/L) (3 years ago: 0.8 mg/dL [70.7 µmol/L])
Glucose	87 mg/dL (4.8 mmol/L)
Phosphorus	2.2 mg/dL (0.71 mmol/L)
Urinalysis	1+ protein; 2+ glucose; no cells or casts

Which of the following is the most likely cause of thi s patient's kidney findings?

A

Hypertensive nephropathy

B

Membranoproliferative glomerulonephritis

C

Membranous glomerulopathy

D

Tubulointerstitial disease

Answer & Critique

Correct Answer: D

Educational Objective: Diagnose drug-induced tubulointerstitial disease presenting as Fanconi syndrome.

Key Point

Kidney disease with a tubulointerstitial process is characterized by a slowly progressive course without a clear inciting event, subnephrotic proteinuria, bland urine sediment, and a kidney ultrasound showing atrophic kidneys.

This patient has tubulointerstitial disease, likely due to long-standing exposure to tenofovir. Evidence for a tubulointerstitial process includes a slowly progressive course without a clear inciting event, subnephrotic proteinuria, bland urine sediment, and a kidney ultrasound showing atrophic kidneys. History and physical examination should focus on conditions associated with tubulointerstitial disease and a careful review of medications, because numerous medications may induce tubulointerstitial disease. An associated characteristic that may be present with tubulointerstitial disease is abnormal tubular handling of glucose, amino acids, uric acid, phosphate, and bicarbonate (termed *Fanconi syndrome*); renal tubular acidosis is also common. Patients may also have concentrating defects and may present with nocturia and polyuria. With more advanced disease, anemia may be present due to the destruction of erythropoietin-producing cells in the kidney. This patient's findings are consistent with tubulointerstitial disease with Fanconi syndrome, indicated by glucosuria in the context of normoglycemia, trace proteinuria, and hypophosphatemia. Because tenofovir has been associated with tubulointerstitial disease, it is the likely cause in this patient.

Hypertensive nephropathy involves damage to the vascular structures, glomeruli, and tubulointerstitial regions of the kidney. It may cause progressive kidney failure, often with elevated protein excretion (less than 1000 mg/24 h). However, the rapid progression of kidney dysfunction and the presence of tubular dysfunction (Fanconi syndrome) characteristic of tubulointerstitial disease make hypertensive nephropathy less likely in this patient.

Membranoproliferative glomerulonephritis may also be associated with chronic hepatitis B infection and involves immune complex deposition in the glomeruli. It typically presents with hematuria (often with dysmorphic erythrocytes and/or erythrocyte casts), variable degrees of proteinuria, and a reduced glomerular filtration rate. This would not be a consistent finding in this patient with a bland urine sediment.

Membranous glomerulopathy is common in patients with chronic hepatitis B infection and appears to be related to subendothelial and mesangial immune deposits in the glomeruli. Because it primarily affects the glomeruli, it is associated with high levels of proteinuria, usually in the nephrotic range, and would not be expected to present with tubular dysfunction and Fanconi syndrome as seen in this patient.

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Question 78

A 37-year-old man is evaluated in the emergency department for nausea and vomiting of 12 hours' duration. The patient states that he has been drinking large amounts of alcohol for several weeks and has eaten very little for the past week. His last alcoholic drink was more than 24 hours ago. He also reports intermittent diarrhea for the past 2 months. History is notable for chronic alcoholism. He takes no medications.

On physical examination, the patient is cachectic. Blood pressure is 100/65 mm Hg, and pulse rate is 105/min. BMI is 17. Proximal muscle wasting is noted. There is no evidence of jaundice or ascites. The liver is enlarged and mildly tender. There is no asterixis. Neurologic examination is unremarkable.

While awaiting the results of laboratory studies, the patient is given intravenous saline with dextrose and vitamins. His respiration rate becomes markedly diminished, and he requires intubation. His laboratory studies return and show the following:

Laboratory studies:

Albumin	3.0 g/dL (30 g/L)
Calcium	8.0 mg/dL (2.0 mmol/L)
Electrolytes:	
Sodium	132 mEq/L (132 mmol/L)
Potassium	3.4 mEq/L (3.4 mmol/L)
Chloride	90 mEq/L (90 mmol/L)
Bicarbonate	32 mEq/L (32 mmol/L)
Magnesium	1.7 mg/dL (0.7 mmol/L)
Phosphorus	1.5 mg/dL (0.48 mmol/L)

Which of the following is the most likely cause of this patient's respiratory failure?

A

Hypocalcemia

B

Hypokalemia

C

Hypomagnesemia

D

Hyponatremia

E

Hypophosphatemia

Choose an Answer Above

Answer & Critique

Correct Answer: E

Educational Objective: Diagnose hypophosphatemia due to refeeding syndrome.

Key Point

Intravenous dextrose-containing fluids can exacerbate hypophosphatemia by stimulating insulin release, which promotes phosphate uptake by the cells and worsening hypophosphatemia.

The most likely cause of this patient's respiratory failure is hypophosphatemia, which occurs in patients with chronic alcohol use, malnutrition, or critical illness. Symptoms rarely occur unless the serum phosphate concentration is <2.0 mg/dL (0.65 mmol/L); severe symptoms occur with a serum phosphate concentration <1.0 mg/dL (0.32 mmol/L). Symptoms include weakness, myalgia, rhabdomyolysis, arrhythmias, heart failure, respiratory failure, seizures, coma, and hemolysis. This patient has chronic alcoholism with moderate hypophosphatemia on presentation. Factors that contribute to hypophosphatemia in the patient with chronic alcohol use include decreased dietary intake of phosphate and vitamin D, chronic diarrhea, and a direct toxic effect of alcohol on the proximal tubule. Intravenous dextrose-containing fluids can exacerbate the hypophosphatemia by causing a refeeding syndrome. Glucose stimulates insulin release, which promotes phosphate uptake by the cells and worsening hypophosphatemia. Severe hypophosphatemia can cause respiratory failure from impaired diaphragmatic contractility.

In general, total calcium declines by 0.8 mg/dL (0.2 mmol/L) for each 1.0 g/dL (10 g/L) decrement in serum albumin concentration. This patient's calcium correction for hypoalbuminemia is 8.8 mg/dL (2.2 mmol/L), which is not low and does not explain the respiratory failure.

This patient has mild hypokalemia. Although severe hypokalemia can cause profound muscle weakness, it is unlikely that his serum potassium would decrease to such critically low levels to cause paralysis based on his current treatment.

The patient's magnesium level is within the lower limits of normal range and unlikely to be the cause of his respiratory failure.

Although the patient does have hyponatremia, it is not severe and would not result in respiratory failure. Symptoms of acute hyponatremia are caused by cerebral edema and usually do not manifest until the sodium concentration is lower than 125 mEq/L (125 mmol/L).

Question 79

A 57-year-old woman is evaluated during a preoperative physical examination for a total left knee replacement. Medical history is significant for osteoarthritis; her only medication is over-the-counter ibuprofen, which she takes multiple times daily for pain relief.

On physical examination, blood pressure is 152/90 mm Hg, and pulse rate is 64/min. BMI is 34. Severe osteoarthritic changes are noted in the left knee. Trace pitting edema in the ankles is noted. The remainder of the examination is unremarkable.

Laboratory studies show a serum creatinine level of 1.2 mg/dL (106.1 µmol/L) and a serum potassium level of 5.1 mEq/L (5.1 mmol/L); urine dipstick demonstrates no blood or protein.

Which of the following is the most appropriate next step in the management of this patient's blood pressure?

A

Begin a low-dose ACE inhibitor

B

Begin low-dose hydrochlorothiazide

C

Discontinue ibuprofen

D

Obtain a plasma aldosterone-plasma renin ratio

Choose an Answer Above

Answer & Critique

Correct Answer: C

Educational Objective: Identify NSAIDs as a cause of elevated blood pressure.

Key Point

Identification of medications that contribute to blood pressure elevation is necessary in patients with elevated blood pressure not yet defined as hypertension.

Discontinuing ibuprofen is an appropriate next step in managing this patient's blood pressure. She has elevated blood pressure not yet defined as hypertension, a diagnosis that requires a systolic blood pressure ?140 mm Hg and/or a diastolic blood pressure ?90 mm Hg documented during three separate office visits over a period of 1 week or longer. In this case, a review of medications, including over-the-counter and herbal medications, is important because a number of these agents can contribute to elevated blood pressure. This patient is taking an NSAID, ibuprofen, for osteoarthritis. All NSAIDs contribute to hypertension by inhibition of cyclooxygenase-2 in the kidneys, promoting sodium retention and increased intravascular volume. Additional effects of NSAIDs include hyperkalemia, which is mild in this case. NSAIDs lower renal renin secretion and angiotensin II–induced aldosterone release, reducing urine potassium excretion. Therefore, discontinuing the ibuprofen is appropriate for this patient. Reassessing her blood pressure when not taking an NSAID will provide a more accurate measure of her baseline blood pressure status.

Beginning antihypertensive therapy at this point is not indicated; in particular, ACE inhibitor use would be contraindicated because further inhibition of the renin-angiotensin system could exacerbate this patient's hyperkalemia.

Similarly, hydrochlorothiazide is an effective antihypertensive agent, but initiating treatment is not indicated prior to establishing a diagnosis of hypertension.

A plasma aldosterone-plasma renin ratio is used to evaluate patients with hypertension and a high suspicion for hyperaldosteronism (for example, evidence of resistant hypertension and a low serum potassium level). Testing is therefore not indicated in this patient without a clear diagnosis of hypertension and who has hyperkalemia.

Question 80

A 64-year-old man is hospitalized with confusion, nausea, and dizziness. He has not felt well for weeks. Medical history is notable for hypertension, atrial fibrillation, and hyperlipidemia. He had a superior mesenteric artery embolus 2 years ago and had a resection of a large segment of his small bowel. He has chronic diarrhea. Medications are rosuvastatin, metoprolol, warfarin, and enalapril. His wife confirms that he takes no additional medications, including over-the-counter drugs or supplements.

On physical examination, temperature is 37.2 °C (99.0 °F), blood pressure is 108/60 mm Hg, pulse rate is 96/min, and respiration rate is 18/min. BMI is 22. He is confused to place and time and is easily distractible. The remainder of the physical examination is noncontributory.

Laboratory studies:	
Blood urea nitrogen	14 mg/dL (5 mmol/L)
Electrolytes:	
Sodium	140 mEq/L (140 mmol/L)
Potassium	3.8 mEq/L (3.8 mmol/L)
Chloride	106 mEq/L (106 mmol/L)
Bicarbonate	20 mEq/L (20 mmol/L)
Glucose	90 mg/dL (5 mmol/L)
Lactate	Normal
Arterial blood gases:	
Ph	7.37
PCO2	36 mm Hg (4.8 kPa)
Plasma osmolality	296 mOsm/kg H2O

Which of the following is the most likely diagnosis?

A
D-Lactic acidosis

B
Ethylene glycol or methanol poisoning

C
Propylene glycol toxicity

D
Pyroglutamic acidosis

Answer & Critique

Correct Answer: A

Educational Objective: Diagnose D-lactic acidosis.

Key Point

Manifestations of D-lactic acidosis include intermittent confusion, slurred speech, ataxia, and an increased anion gap metabolic acidosis with a normal plasma lactate level.

This patient has an increased anion gap metabolic acidosis, and the most likely cause is D-lactic acidosis. Accumulation of the D-isomer of lactate can occur in patients with short-bowel syndrome following jejunoileal bypass or small-bowel resection. In these patients, excess carbohydrates that reach the colon are metabolized to D-lactate. Symptoms include intermittent confusion, slurred speech, and ataxia. Laboratory studies show increased anion gap metabolic acidosis with normal plasma lactate levels, because the D-isomer is not measured by conventional laboratory assays for lactate. Diagnosis should be considered in patients with an unexplained increased anion gap metabolic acidosis in the appropriate clinical context; it is confirmed by specifically measuring D-lactate.

Ethylene glycol or methanol intoxication should be suspected in patients with an increased anion gap metabolic acidosis associated with a serum bicarbonate level <10 mEq/L (10 mmol/L) and a plasma osmolal gap >10 mOsm/kg H_2O. This patient's serum bicarbonate level is 20 mEq/L (20 mmol/L) and the calculated osmolal gap is 6 mOsm/kg H_2O, making alcohol poisoning a less likely diagnosis.

Propylene glycol is a solvent used as a vehicle for numerous intravenously administered medications. In propylene glycol toxicity, laboratory findings include increased anion gap metabolic acidosis and concomitant increased osmolal gap. The metabolic acidosis is principally due to L-lactic and D-lactic acidosis, the acid metabolites of propylene glycol. This patient's clinical history and osmolal gap are not consistent with propylene glycol toxicity.

Pyroglutamic acidosis is a cause of increased anion gap metabolic acidosis in patients receiving therapeutic doses of acetaminophen on a chronic basis. Clinical manifestations are limited to mental status changes and increased anion gap metabolic acidosis. The syndrome most commonly occurs in patients with critical illness, poor nutrition, liver disease, or chronic kidney disease as well as in persons on a vegetarian diet. Diagnosis can be confirmed by measuring urine levels of pyroglutamic acid. This patient's history is most compatible with D-lactic acidosis and does not support acetaminophen ingestion.

Question 81

A 70-year-old woman is evaluated in the emergency department for acute-onset fever and rigors that began during hemodialysis. She has end-stage kidney disease due to chronic glomerulonephritis. She started hemodialysis 1 month ago via a right internal jugular tunneled cuffed catheter. A left forearm arteriovenous fistula was placed 1 week ago. Medications are labetalol, sevelamer, epoetin alfa, and calcitriol.

On physical examination, temperature is 37.9 °C (100.2 °F), blood pressure is 145/95 mm Hg, pulse rate is 95/min, and respiration rate is 20/min. BMI is 23. Examination of the right internal jugular catheter site reveals no tenderness, induration, or discharge. The left forearm arteriovenous fistula is nontender with a clean, well-healed surgical incision. There is no heart murmur. The lungs are clear. The remainder of the physical examination is unremarkable.

Laboratory studies are notable for a leukocyte count of 13,000/μL (13×10^9/L) and a plasma lactate level of 1.0 mEq/L (1.0 mmol/L). Blood cultures are pending.

A chest radiograph is normal.

Which of the following is the most appropriate next step in management?

A

Begin vancomycin

B

Begin vancomycin and ceftazidime

C

Exchange dialysis catheter over a wire

D

Remove dialysis catheter and observe

Choose an Answer Above

Answer & Critique

Correct Answer: B

Educational Objective: Treat suspected catheter-related bacteremia in a patient with end-stage kidney disease.

Key Point

Immediate empiric broad-spectrum antibiotics must be initiated in patients with end-stage kidney disease who are on dialysis and have suspected catheter-related infection.

The most appropriate next step in management is to begin broad-spectrum antibiotic coverage, such as vancomycin plus ceftazidime. This patient with end-stage kidney disease (ESKD) who is receiving dialysis via a catheter is at high risk for catheter-related bacteremia. Infection is the second most common cause of death in patients with ESKD (after cardiovascular disease), and catheter-related infections are an important cause of morbidity and mortality. It is therefore important to provide immediate empiric broad-spectrum antibiotics in patients dialyzing via a catheter who exhibit evidence of infection unless there is another obvious source of fever. Most dialysis-related bacteremias are caused by gram-positive bacteria, and empiric coverage must include therapy that takes into account the local resistance patterns of *Staphylococcus aureus*. Additionally, gram-negative organisms should also be covered until culture results are known and appropriate, focused antimicrobial therapy is prescribed.

If blood cultures remain negative, empiric antibiotics may be stopped if symptoms have resolved and no other potential source of infection has been identified. If blood cultures return positive, it is usually advisable to remove the catheter because success rates for catheter salvage are low for most organisms. If there is no evidence of infection of the catheter tunnel, dialysis catheters can be safely exchanged over a wire in patients who have been asymptomatic on appropriate antibiotic therapy for at least 48 hours. However, either removing or exchanging the dialysis catheter in the setting of possible infection without antibiotic therapy is not appropriate.

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Question 82

A 66-year-old woman is hospitalized for nausea and vomiting, worsening dyspnea on exertion, and weakness of 4 days' duration. Medical history is notable for heart failure, COPD, and hypertension. Medications are carvedilol, amlodipine, albuterol, and tiotropium inhalers.

On physical examination, blood pressure is 108/65 mm Hg, pulse rate is 98/min, and respiration rate is 20/min. Oxygen saturation is 91% on ambient air. BMI is 36. Cardiovascular examination demonstrates an S_4 and no jugular venous distention. Lung examination demonstrates no wheezing or crackles. There is 1+ pitting edema in the ankles. The remainder of the physical examination is normal.

Laboratory studies:	
Bicarbonate	29 mEq/L (29 mmol/L)
Potassium	3.0 mEq/L (3.0 mmol/L)
Arterial blood gas studies:	
pH	7.47
P_{CO_2}	44 mm Hg (5.9 kPa)
P_{O_2}	70 mm Hg (9.3 kPa)

A chest radiograph shows flattened diaphragms and a narrow cardiac silhouette.

Which of the following is the most appropriate next step in management?

A Administer 0.9% saline intravenously

B Administer furosemide intravenously

C Measure urine chloride level

D Measure urine sodium level

Answer & Critique

Correct Answer: C

Educational Objective: Measure urine chloride levels to determine the cause of metabolic alkalosis.

Key Point

Measurement of urine chloride levels can be useful to determine volume status and saline responsiveness in patients with metabolic alkalosis.

Measurement of this patient's urine chloride level is the most appropriate next step in management. She has a metabolic alkalosis as evidenced by the elevated blood pH and elevated serum bicarbonate level. Metabolic alkalosis is caused by net loss of acid or retention of serum bicarbonate. Metabolic alkalosis can be classified as either occurring with normal extracellular fluid volume, hypovolemia, or decreased effective arterial blood volume and increased extracellular fluid volume (heart failure, cirrhosis, nephrosis), or occurring with increased extracellular fluid volume and hypertension. This patient's clinical volume status is equivocal; blood pressure is slightly low and pulse rate is slightly high, yet there is peripheral edema, which could be explained by either cardiac or noncardiac causes (for example, a side effect of amlodipine), and mild hypoxia, which could be cardiac or pulmonary in etiology, given her medical history. Urine chloride measurement can help determine the cause of metabolic alkalosis, particularly if it is difficult to clinically assess volume status. In such patients, a low (<15 mEq/L [15 mmol/L]) urine chloride suggests reduction in extracellular volume and the presence of saline-responsive metabolic alkalosis. Conditions that are associated with saline-responsive metabolic alkalosis include vomiting, remote use of diuretics, and post-hypercapnic metabolic alkalosis. If the urine chloride is high (>15 mEq/L [15 mmol/L]), the metabolic alkalosis is saline resistant and can be caused by active diuretic use, stimulant laxative abuse, and rare renal tubular disorders such as Gitelman and Bartter syndromes. In this case, the patient's metabolic alkalosis is due to vomiting, and a low urine chloride would direct appropriate management to saline infusion.

Saline infusion without first categorizing the nature of the metabolic alkalosis is inappropriate and potentially dangerous in patients with limited cardiac reserve or hypoxia.

There is no clear evidence of volume overload that requires administration of a loop diuretic such as furosemide. Loop diuretic therapy is likely to worsen metabolic alkalosis by increasing the secretion of aldosterone and distal delivery of sodium, resulting in urine potassium and hydrogen loss.

In patients with metabolic alkalosis, measurement of urine chloride rather than urine sodium is used to determine volume status and saline responsiveness because urine sodium can be artificially high during periods of appropriate compensatory urine bicarbonate excretion (sodium is the primary cation excreted in an obligatory fashion with bicarbonate).

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Question 83

A 42-year-old woman is evaluated in the emergency department for an episode of blood in her urine associated with right-sided abdominal pain. She reports no dysuria, urgency, or frequency. She notes a history of chronic, nonlocalized abdominal discomfort, but has no history of urinary tract infections. She otherwise has been healthy. Family history indicates that her mother and father are both alive without medical problems, as are three brothers and one sister. She is sexually active, and her only medication is an oral contraceptive.

On physical examination, the patient is in mild distress. Temperature is 37.0 °C (98.6 °F), blood pressure is 150/100 mm Hg, pulse rate is 88/min and regular, and respiration rate is 15/min. BMI is 30. Cardiovascular and pulmonary examinations are normal. There is no costovertebral angle tenderness. On abdominal examination, there is diffuse tenderness to moderate palpation without rebound. There are palpable masses in the right and left abdomen, with increased discomfort with palpation on the right.

Laboratory studies:

Hematocrit	42%
Leukocyte count	8500/µL (8.5×10^9/L)
Blood urea nitrogen	25 mg/dL (8.9 mmol/L)
Creatinine	2.0 mg/dL (176.8 µmol/L)
Urinalysis	Too numerous to count erythrocytes/hpf; 3-5 leukocytes/hpf
Human chorionic gonadotropin	Negative

Which of the following is the most likely diagnosis?

A Autosomal dominant polycystic kidney disease

B Renal cell carcinoma

C Renal vein thrombosis

D Urinary tract infection

Answer & Critique

Correct Answer: A

Educational Objective: Diagnose autosomal dominant polycystic kidney disease.

Key Point

A negative family history does not exclude autosomal dominant polycystic kidney disease (ADPKD)—approximately 15% of patients with ADPKD have spontaneous mutations that result in the disease.

The most likely diagnosis is autosomal dominant polycystic kidney disease (ADPKD). The hallmark of ADPKD is large kidneys with multiple kidney cysts, and patients may have resulting chronic, mild abdominal discomfort; in some cases, palpable abdominal masses occur, as in this patient. Patients with ADPKD may also present acutely with severe pain and hematuria resulting from bleeding of a cyst, as seen in this patient. ADPKD is the most common inherited kidney disorder, occurring in 1 of 400 to 1 of 1000 live births. Although transmitted in an autosomal dominant manner, a negative family history does not necessarily exclude ADPKD. Approximately 15% of patients with ADPKD have spontaneous mutations that result in the disease. Alternatively, one of the patient's parents may have a less severe phenotype without clinical manifestations.

Renal cell carcinoma does not occur with greater frequency in patients with ADPKD than in the general population and does not present with bilateral abdominal masses.

Renal vein thrombosis may present with acute-onset flank pain and macroscopic hematuria and may show enlargement of the involved kidney. However, renal vein thrombosis does not result in bilateral abdominal masses and is more commonly seen in hypercoagulable states, such as the nephrotic syndrome or the antiphospholipid antibody syndrome. This patient has no evidence of hypercoagulability.

Gross hematuria often occurs in patients with urinary tract infection. However, this patient has no accompanying urinary symptoms, and the leukocytes in her urine are likely the result of gross bleeding into the urinary tract. Additionally, urinary tract infection would not explain the abdominal masses seen in this patient.

Question 84

A 42-year-old man is hospitalized to begin chemotherapy for recently diagnosed Burkitt-like lymphoma. He is started on aggressive intravenous volume repletion with isotonic sodium chloride and allopurinol. Three days into receiving hyper-CVAD therapy (cyclophosphamide, vincristine, doxorubicin, dexamethasone), he develops decreasing urine output to 0.6 mL/kg/h. His only other medication is as-needed ondansetron.

On physical examination, blood pressure is 130/72 mm Hg. There is lymphadenopathy involving the cervical and submental chains and supraclavicular areas bilaterally, as well as bulky axillary and inguinal lymphadenopathy. Heart rate and rhythm are regular. Lungs are clear. The spleen is palpable approximately 4 cm below the left costal margin. There is no hepatomegaly. There is no edema, cyanosis, or clubbing of the extremities.

Laboratory studies:

Blood urea nitrogen	22 mg/dL (7.9 mmol/L)
Calcium	7.3 mg/dL (1.8 mmol/L) (baseline, 8.7 mg/dL [2.2 mmol/L])
Creatinine	1.3 mg/dL (114.9 µmol/L) (baseline, 0.9 mg/dL [79.6 µmol/L])
Phosphorus	6.5 mg/dL (2.1 mmol/L) (baseline, 3.3 mg/dL [1.1 mmol/L])
Potassium	5.1 mEq/L (5.1 mmol/L) (baseline, 4.3 mEq/L [4.3 mmol/L])
Urate	14 mg/dL (0.83 mmol/L) (pretreatment level, 6.2 mg/dL [0.37 mmol/L])
Urinalysis	pH 5.5; multiple urate crystals

Which of the following is the most appropriate treatment?

A Begin hemodialysis

B Begin urine alkalinization

C Increase allopurinol dose

D Substitute rasburicase for allopurinol

Answer & Critique

Correct Answer: D

Educational Objective: Treat tumor lysis syndrome.

Key Point

Patients with tumor lysis syndrome and evidence of uric acid nephropathy require treatment with rasburicase to reduce serum urate levels.

Rasburicase is appropriate to treat hyperuricemia in this patient with tumor lysis syndrome (TLS). TLS is characterized by the massive release of uric acid, potassium, and phosphate into the blood from rapid lysis of malignant cells. It typically occurs after initiation of cytotoxic therapy for hematologic malignancies with large tumor burden (such as high-grade lymphomas) or high cell counts (such as acute lymphoblastic leukemia), but TLS can also occur spontaneously. Acute kidney injury (AKI) results from intratubular precipitation of urate and calcium phosphate crystals. Clinical features include hyperuricemia, hyperkalemia, hyperphosphatemia, and hypocalcemia. General principles for the management of patients at high or intermediate risk or presenting with TLS are aggressive volume expansion, management of hyperkalemia, and preventive therapy for hyperuricemia. This patient has TLS with evidence of uric acid nephropathy and requires rasburicase to reduce serum urate levels. Rasburicase rapidly converts uric acid to allantoin, which is 5 to 10 times more soluble than uric acid and readily excreted through the kidney. Rasburicase has a much faster action than allopurinol and can decrease serum urate levels within 4 hours of administration.

Indications for dialysis include oliguria or anuria, persistent hyperkalemia, hyperphosphatemia-induced symptomatic hypocalcemia, and a calcium phosphate product $\geq 70\ mg^2/dL^2$ in the setting of AKI. This patient has none of these indications for dialysis.

Urine alkalinization increases the excretion of uric acid by increasing its solubility. However, in the setting of hyperphosphatemia, it can cause precipitation of calcium phosphate crystals in the kidney. Urine alkalinization is not necessary when rasburicase is used, and it role in TLS is controversial.

Allopurinol competitively inhibits xanthine oxidase, blocking the metabolism of hypoxanthine and xanthine to uric acid. Allopurinol effectively decreases the formation of new uric acid and therefore does not affect circulating uric acid. Increasing the dose of allopurinol is therefore not indicated.

Question 85

A 20-year-old woman is seen during a follow-up visit for hematuria. She was evaluated 1 week ago for hematuria of 5 days' duration. She recalled having a sore throat around the time of onset of hematuria, but no fever, dysuria, flank pain, or other symptoms. Urinalysis at that time showed too numerous to count erythrocytes/hpf with a few erythrocyte casts. Laboratory studies at that time showed the following: normal complement levels, a serum creatinine level of 0.7 mg/dL (61.9 µmol/L), negative antinuclear antibodies and ANCA, and a urine protein-creatinine ratio of 1100 mg/g. Kidney ultrasound was normal. She has been healthy, and her only medication is an oral contraceptive pill.

On physical examination, temperature is 37.1 °C (98.7 °F), blood pressure is 130/80 mm Hg, pulse rate is 78/min, and respiration rate is 16/min. BMI is 22. Mild pharyngeal congestion is noted. There is no edema. The remainder of the physical examination, including skin, joints, and nasal and oral mucosa, is normal.

Current laboratory studies show a urinalysis with 5-10 erythrocytes/hpf without casts, a serum creatinine level of 0.6 mg/dL (53 µmol/L), and a urine protein-creatinine ratio of 100 mg/g.

Which of the following is the most appropriate next step in management?

A

ACE inhibitor therapy

B

Kidney biopsy

C

Oral glucocorticoids

D

Continued observation

Choose an Answer Above

Answer & Critique

Correct Answer: D

Educational Objective: Manage IgA nephropathy.

Key Point

Observation with serial blood pressure measurements, urine studies, and serum creatinine levels is appropriate for patients with IgA nephropathy with low-risk features for progression.

Continued observation is the appropriate next step in management in this patient with likely IgA nephropathy (IgAN). IgAN is the most frequent cause of chronic glomerulonephritis, occurs more commonly in men, and most frequently occurs in the second to third decades of life. IgAN involves formation of autoantibodies against structurally abnormal IgA leading to immune complex formation; these immune complexes are deposited in the glomeruli in IgAN or in multiple extrarenal sites in IgA vasculitis (Henoch Schönlein purpura). This young patient has asymptomatic gross hematuria with a nephritic urine sediment without the full nephritic syndrome (hypertension and azotemia are absent). The presence of nephritis with normal or negative serologies (particularly normal complement levels) and improving kidney function and proteinuria suggests IgAN as the most likely diagnosis. IgAN tends to be a chronic condition with a good prognosis in most patients. Factors associated with a worse outcome include hypertension, kidney dysfunction, persistent proteinuria >1000 mg/g, and mesangial and endothelial proliferation with tubulointerstitial damage on kidney biopsy. However, continued observation with serial blood pressure measurements, serum creatinine levels, and urine studies is appropriate in this patient without high-risk features and an improving clinical course.

Treatment with inhibitors of the renin-angiotensin system (such as an ACE inhibitor) slow the rate of progression of most proteinuric chronic kidney diseases and are often used in patients with IgAN with significant proteinuria and high-risk features. However, low-risk patients with minimal proteinuria are usually not actively treated and are followed with continued observation.

Kidney biopsy is usually reserved for patients with high risk for poor outcome. It is not indicated in this patient with no high-risk features of progressive IgAN, such as a urine protein-creatinine ratio >1000 mg/g or a low glomerular filtration rate.

Glucocorticoids are used to treat patients with high-risk disease.

Question 86

A 35-year-old woman is evaluated during a follow-up visit. She is at 37 weeks' gestation of her first pregnancy. Preeclampsia was diagnosed at 32 weeks when she was found to be hypertensive with mild proteinuria; she was previously normotensive. Her subsequent prenatal obstetric and laboratory monitoring has remained stable, and she is without symptoms. Medical history is otherwise unremarkable, and her only medication is a prenatal vitamin.

On physical examination, temperature is 36.9 °C (98.4 °F), blood pressure is 148/85 mm Hg, pulse rate is 87/min, and respiration rate is 12/min. BMI is 27. Examination of the lungs and heart is normal. The abdomen shows expected changes of pregnancy but is otherwise normal. There is trace bipedal edema. The remainder of the examination is unremarkable.

Laboratory studies are significant for a normal platelet count, blood urea nitrogen, serum creatinine, electrolyte panel, and liver chemistry studies.

Which of the followin g is the most appropriate next step in management?

A
Antihypertensive therapy

B
Aspirin therapy

C
Delivery of the baby

D
Glucocorticoids

E
Continued monitoring until term

Answer & Critique

Correct Answer: C

Educational Objective: Manage preeclampsia.

Key Point

Definitive therapy for preeclampsia is delivery of the baby.

The most appropriate next step in management is delivery of the baby in this woman with preeclampsia without features of severe disease. Preeclampsia is classically defined as new-onset hypertension after 20 weeks of pregnancy with proteinuria (≥300 mg/24 h or a urine protein-creatinine ratio ≥300 mg/g). Delivery of the baby is the definitive treatment for preeclampsia. In patients with preeclampsia and severe disease, generally defined as severe hypertension (systolic blood pressure ≥160 mm Hg or diastolic blood pressure ≥110 mm Hg), thrombocytopenia (platelet count <100,000/μL [100 × 10^9/L]), kidney dysfunction (serum creatinine concentration >1.1 mg/dL [97.2 μmol/L] or doubling of the serum creatinine concentration in the absence of other kidney disease), impaired liver function (elevated blood concentrations of liver aminotransferases to twice the normal concentration), pulmonary edema, or cerebral or visual symptoms, management decisions are usually made based on the balance of fetal and maternal risk with the implications of preterm delivery. In women with preeclampsia without severe features, delivery at 37 weeks has been shown to optimize both maternal and neonatal outcomes (such as fetal growth restriction, abruption placentae, hemorrhage due to thrombocytopenia, seizures, cerebral hemorrhage, pulmonary edema, and kidney injury) and is the most appropriate next step in managing this patient.

Treatment of mild hypertension in preeclampsia has not been shown to alter the course of disease or improve fetal outcomes. Therefore, antihypertensive treatment is generally reserved for patients with preeclampsia with severe hypertension, which is not present in this patient.

There is evidence that low-dose aspirin therapy may be beneficial in reducing the occurrence of preeclampsia in moderate- to high-risk women. However, it does not have a role in treating preeclampsia or eclampsia.

Glucocorticoids are used to accelerate fetal lung maturation if delivery is contemplated before the 34th week of pregnancy but do not directly affect outcomes in preeclampsia. Therefore, their use is not indicated in this patient.

Because of the benefit of delivery at 37 weeks' gestation in women with preeclampsia, continued monitoring beyond this time is not optimal.

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Question 87

A 40-year-old man is seen in follow-up for evaluation of proteinuria detected on urinalysis as part of an insurance physical examination. He is otherwise asymptomatic. Medical history is significant for obesity but is otherwise unremarkable with no prior kidney disease. He takes no medications.

On physical examination, patient is afebrile, blood pressure is 155/105 mm Hg, pulse rate is 74/min, and respiration rate is 14/min. BMI is 38. Cardiopulmonary and abdominal examinations are unremarkable. There is no arthritis, rash, or lower extremity edema.

Laboratory studies:

Albumin	4.2 g/dL (42 g/L)
Complements (C3 and C4)	Normal
Creatinine	1.0 mg/dL (88.4 μmol/L)
Antinuclear antibodies	Negative
Hepatitis B surface antigen	Negative
Hepatitis C antibodies	Negative
HIV antibodies	Negative
Urinalysis	3+ protein; no blood or cells
Urine protein-creatinine ratio	2000 mg/g

Kidney biopsy shows enlarged glomeruli with focal segmental sclerosis; immunofluorescence is nonspecific, and electron microscopy shows mild foot process effacement.

In addition to starting an ACE inhibitor, which of the following is the most appropriate additional next step in management?

A

Prednisone

B

Rapid plasma reagin test

C

Tacrolimus

D

Weight loss

Choose an Answer Above

Answer & Critique

Correct Answer: D

Educational Objective: Manage secondary focal segmental glomerulosclerosis.

Key Point

In obese patients with likely secondary focal segmental glomerulosclerosis, weight loss is sometimes associated with a drop in proteinuria, as is the use of ACE inhibitors or angiotensin receptor blockers, and is the preferred initial therapy.

In addition to starting an ACE inhibitor, weight loss is indicated for this patient with likely secondary focal segmental glomerulosclerosis (FSGS). This patient with obesity, hypertension, and nephrotic-range proteinuria (with normal serum albumin) has FSGS on kidney biopsy. FSGS may be primary (idiopathic) or secondary, and the appropriate therapeutic approach is based on determining the likely cause of the disorder. Primary FSGS involves glomerular injury due to an unclear insult; features suggesting primary FSGS include a low serum albumin level and extensive foot process effacement on kidney biopsy. Patients usually present with hypertension, hypoalbuminemia, and some degree of kidney failure in addition to nephrotic-range proteinuria. Some patients with primary FSGS respond well to immunosuppressive therapy, and this is typically offered to patients with this diagnosis. Secondary FSGS is believed to result from an adaptive response to glomerular hypertrophy or hyperfiltration associated with a number of conditions (including obesity) in which the glomerular filtration rate may be markedly increased; glomeruli on biopsy are often enlarged, reflecting hyperfiltration with only mild foot process effacement. These patients have minimal edema and rarely have the full spectrum of the nephrotic syndrome. In obese patients with likely secondary FSGS, weight loss is sometimes associated with a drop in proteinuria, as is the use of ACE inhibitors or angiotensin receptor blockers, and is the preferred initial therapy.

Immunosuppressive therapy with glucocorticoids or other agents such as the calcineurin inhibitor tacrolimus is not indicated in secondary FSGS.

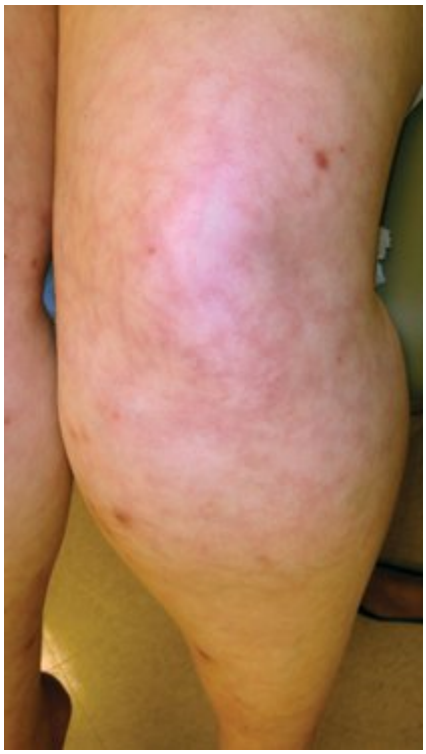
FSGS is not typically associated with syphilis, and testing for this entity using a rapid plasma reagin test is not indicated.

Question 88

A 77-year-old woman was evaluated in the hospital for worsening kidney function. She presented 14 days ago with substernal chest pain and underwent coronary catheterization that showed left anterior descending arterial thrombosis that was treated with balloon angioplasty and stenting. Hospital course was uneventful, and she was discharged 11 days ago. She now presents for a follow-up evaluation. Medical history is significant for hypertension, type 2 diabetes mellitus, and stage 3A chronic kidney disease. She has a 90-pack-year smoking history and continues to smoke. Current medications are aspirin, lisinopril, atorvastatin, clopidogrel, metoprolol, and insulin.

On physical examination, temperature is 37.6 °C (99.7 °F), blood pressure is 140/86 mm Hg sitting and 134/78 mm Hg standing, and pulse rate is 66/min sitting and 70/min standing. BMI is 28. The lungs are clear, and the heart and abdominal examinations are normal. There is no lower extremity edema.

Skin findings of the lower extremities are shown.



Laboratory studies:

Blood urea nitrogen	48 mg/dL (17.1 mmol/L)
Creatinine	3.1 mg/dL (274 µmol/L) (baseline: 1.3 mg/dL [114.9 µmol/L])
Urinalysis	1+ blood; 2+ protein; positive for leukocyte esterase; 5-10 erythrocytes/hpf; 10-15 leukocytes/hpf with eosinophils; no casts or crystals

Which of the following is the most likely diagnosis?

A

Acute interstitial nephritis

B

Atheroembolism

C

Contrast-induced nephropathy

D

Polyarteritis nodosa

Choose an Answer Above

Answer & Critique

Correct Answer: B

Educational Objective: Diagnose atheroembolic kidney disease.

Key Point

Acute kidney injury is a common result of cholesterol embolization, which causes peripheral eosinophilia and hypocomplementemia and shows evidence of inflammation on urinalysis, frequently with eosinophiluria present.

The most likely diagnosis is atheroembolism of cholesterol crystals. Disruption of an atheromatous plaque by instrumentation or anticoagulation during this patient's cardiac catheterization likely caused embolization of cholesterol crystals from the plaque through the arterial circulation distal to the point of disruption. These crystals lodge in capillary beds and cause vascular obstruction but also trigger an inflammatory response. Acute kidney injury (AKI) is a common result of cholesterol embolization, which causes peripheral eosinophilia and hypocomplementemia and shows evidence of inflammation on urinalysis, frequently with eosinophiluria present. Embolization may also lead to digital ischemia or infarction ("blue toe" syndrome) due to digital arterial occlusion or central scotoma due to central retinal artery occlusion. Although not specific for cholesterol atheroembolism, livedo reticularis (areas of lace-like mottled and purplish skin over the legs and thighs) is commonly associated with this disorder. Management is primarily supportive; anti-inflammatory agents (such as glucocorticoids) are not routinely given for treatment of cholesterol atheroembolism.

Acute interstitial nephritis (AIN) should be suspected following the initiation of new medications, although none of the agents this patient is taking has been reported as a cause of AIN. A diffuse rash, but not livedo reticularis, is characteristic of AIN. Eosinophiluria was previously believed to diagnose AIN, but urine eosinophil determination has been shown to be neither sensitive nor specific in the diagnostic evaluation of AIN.

Contrast-induced nephropathy (CIN) is a diagnostic consideration given the dye load associated with cardiac catheterization. However, CIN typically presents as acute tubular necrosis with granular casts, and AKI due to CIN typically peaks at 24 to 72 hours but improves within 5 to 7 days.

Polyarteritis nodosa (PAN) is a necrotizing vasculitis of medium-sized arteries, sometimes associated with hairy cell leukemia or infection with hepatitis B or C. PAN may present with livedo reticularis, as in this patient, but kidney manifestations usually include renal arterial aneurysms with perirenal hematomas and severe hypertension, which findings are missing here. This patient also lacks any of the other neurologic or gastrointestinal manifestations of PAN.

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Question 89

A 57-year-old man is evaluated for treatment of newly diagnosed hypertension. History is notable for hyperlipidemia, which is treated with moderate-dose simvastatin. The patient is black.

On physical examination, blood pressure is 151/94 mm Hg, and pulse rate is 72/min. BMI is 28. The remainder of the examination is unremarkable.

Laboratory studies show a serum creatinine level of 1.0 mg/dL (88.4 µmol/L), a fasting plasma glucose level of 104 mg/dL (5.8 mmol/L), and a serum potassium level of 4.5 mEq/L (4.5 mmol/L); a urine dipstick demonstrates no blood or protein.

In addition to recommending lifestyle modifications, which of the following is the most app ropriate initial antihypertensive therapy for this patient?

A

Amlodipine

B

Diltiazem

C

Hydrochlorothiazide

D

Lisinopril

Choose an Answer Above

Answer & Critique

Correct Answer: C

Educational Objective: Treat stage 1 hypertension in a black patient.

Key Point

The eighth report of the Joint National Committee recommends a thiazide diuretic or a calcium channel blocker alone or in combination as initial therapy for black patients with hypertension.

The thiazide diuretic hydrochlorothiazide is the most appropriate agent for treating hypertension in this 57-year-old patient who is black. He has stage 1 hypertension, defined as a systolic blood pressure of 140-159 mm Hg and/or a diastolic blood pressure of 90-99 mm Hg. Thiazide diuretics (such as hydrochlorothiazide) and calcium channel blockers (such as amlodipine or diltiazem) alone or in combination are effective hypertensive treatment options for black patients and are recommended by the eighth report of the Joint National Committee (JNC 8) as initial therapy in this patient group. However, this patient is already taking a moderate dose of a statin (simvastatin) that undergoes significant metabolism via the cytochrome P450 3A4 (CYP3A4) pathway; lovastatin and, to a lesser extent, amlodipine are also metabolized through this pathway. Several calcium channel blockers inhibit or are metabolized through the CYP3A4 pathway and can increase the risk of statin myopathy in patients taking one of these particular statins. The dihydropyridine agents verapamil and diltiazem and the non-dihydropyridine agent amlodipine have been associated with increased risk with concurrent therapy with these drugs. Thus, hydrochlorothiazide is the most appropriate choice for this patient. The JNC 8 recommends a blood pressure goal of <140/90 mm Hg for black patients (for age ≥60 years, the target is <150/90 mm Hg, regardless of race). Prior recommendations had suggested blood pressure goals of <135/85 mm Hg in black patients given the higher risk of stroke and kidney disease compared with white patients. However, the African American Study of Kidney Disease and Hypertension (AASK) trial (comprised of black patients with hypertension and chronic kidney disease) did not demonstrate any difference in more aggressive (achieved blood pressure of 128/78 mm Hg) or less aggressive (achieved blood pressure of 141/85 mm Hg) blood pressure goals in slowing the rate of glomerular filtration rate decline or other secondary end points. Given his age and race, this patient's blood pressure goal is <140/90 mm Hg, according to JNC 8.

In general, black persons have less blood pressure response to renin-angiotensin system agents than other agents, despite similar plasma renin activity. Therefore, the ACE inhibitor lisinopril is not indicated for this patient.

Question 90

A 24-year-old man is hospitalized following an attempted suicide by overdose.

On physical examination, the patient has trouble staying awake and does not respond to questions. Temperature is 37.0 °C (98.6 °F), blood pressure is 146/96 mm Hg, pulse rate is 112/min, and respiration rate is 22/min. BMI is 28. The general medical examination is normal. On neurologic examination, his pupils react to light and are symmetric. Deep tendon reflexes are slightly diminished but symmetric.

Laboratory studies:	
Blood urea nitrogen	28 mg/dL (10 mmol/L)
Creatinine	2.2 mg/dL (194.5 µmol/L)
Electrolytes:	
Sodium	136 mEq/L (136 mmol/L)
Potassium	4.0 mEq/L (4.0 mmol/L)
Chloride	96 mEq/L (96 mmol/L)
Bicarbonate	12 mEq/L (12 mmol/L)
Glucose	90 mg/dL (5 mmol/L)
Plasma osmolality	314 mOsm/kg H_2O
Serum ethanol	Undetectable
Arterial blood gases:	
pH	7.24
P_{CO_2}	28 mm Hg (3.7 kPa)
P_{O_2}	102 mm Hg (13.6 kPa)

Additional toxicology studies are pending.

Intravenous hydration and fomepizole are administered, and emergent hemodialysis is planned.

Which of the following is the most appropriate additional management intervention in this patient?

A

Activated charcoal gastric decontamination

B

Intravenous ethanol

C

Intravenous sodium bicarbonate

D

No additional therapy

Choose an Answer Above

Answer & Critique

Correct Answer: C

Educational Objective: Treat acute ethylene glycol poisoning with intravenous sodium bicarbonate.

Key Point

Empiric therapy with sodium bicarbonate, fomepizole, and hemodialysis is indicated for patients with suspected ethylene glycol intoxication.

The most appropriate additional management intervention in this patient is intravenous sodium bicarbonate therapy. He has findings typical of ethylene glycol intoxication, with evidence of central nervous system depression presumably due to the alcohol, an increased anion gap metabolic acidosis of 28 mEq/L (28 mmol/L), an osmolal gap of 27 mOsm/kg H_2O, and kidney failure likely resulting from deposition of calcium oxalate crystals in the renal tubules. Because the laboratory confirmation of ethylene glycol intoxication may take days, empiric therapy for patients with likely ethylene glycol intoxication is recommended pending confirmation. Treatment usually consists of intravenous hydration, fomepizole (a competitive inhibitor of alcohol dehydrogenase), and hemodialysis to clear both the parent alcohol as well as the toxic metabolites. Intravenous sodium bicarbonate therapy is also recommended in suspected ethylene glycol or methanol ingestion when the blood pH is below 7.30. This is because the toxic metabolites of ethylene glycol (glycolate, glyoxylate, and oxalate) and methanol (formate) penetrate tissues more effectively when in the neutral state, which is increased by an acidic blood pH. Bicarbonate is given to normalize the blood pH and maximize formation of the ionized forms of the associated toxic metabolites.

Both ethylene glycol and methanol are completely absorbed from the gastrointestinal tract, with peak serum levels occurring within 1 to 2 hours of ingestion. Therefore, gastric decontamination, such as with activated charcoal, is not usually performed unless the timing of a large ingestion is known and decontamination can be performed within 1 hour.

Intravenous ethanol was traditionally used as a competitive inhibitor of alcohol dehydrogenase; it is effective because this enzyme has greater affinity for ethanol than for ethylene glycol or methanol. However, fomepizole has been found to be a superior therapy to ethanol, is easier to administer, and has fewer side effects. Although ethanol is a reasonable second-line therapy, there is no benefit to coadministration of fomepizole and ethanol.

Given the patient's possible ingestion of ethylene glycol with an associated low blood pH, not providing bicarbonate therapy would be inappropriate.

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Question 91

A 61-year-old woman is evaluated during a routine health maintenance visit. She has no symptoms or concerns at this time. She has stage G4/A1 chronic kidney disease due to autosomal dominant polycystic kidney disease and a 22-year history of hypertension. Medications are fosinopril, furosemide, and sodium bicarbonate.

On physical examination, temperature is 37.0 °C (98.6 °F), blood pressure is 129/72 mm Hg, pulse rate is 84/min, and respiration rate is 14/min. BMI is 28. Bilateral flank fullness is noted. The lungs are clear. There is no peripheral edema.

Laboratory studies:

Calcium	9.0 mg/dL (2.3 mmol/L)
Creatinine	2.8 mg/dL (247.5 µmol/L)
Phosphorus	3.5 mg/dL (1.13 mmol/L)
Intact parathyroid hormone	450 pg/mL (450 ng/L)
25-Hydroxy vitamin D	42 ng/mL (104.8 nmol/L)

Which of the following is the most appropriate next step in management?

A

Bisphosphonate therapy

B

Dual-energy x-ray absorptiometry scan

C

Oral calcitriol

D

Parathyroidectomy

Answer & Critique

Correct Answer: C

Educational Objective: Treat secondary hyperparathyroidism in a patient with chronic kidney disease.

Key Point

Patients with chronic kidney disease and normal calcium and phosphorus levels should be treated with active vitamin D analogues to reduce elevated parathyroid hormone levels and prevent renal osteodystrophy.

The most appropriate next step in management is to begin oral calcitriol. This patient has secondary hyperparathyroidism due to severe chronic kidney disease (CKD). The first priority in treating these patients is to attempt to normalize calcium and phosphorus levels and treat vitamin D deficiency, if present. This patient has normal calcium, phosphorus, and 25-hydroxy vitamin D levels. If vitamin D levels are robust and the phosphorus level is normal, but the parathyroid hormone (PTH) level is elevated above target levels, active vitamin D analogues should be initiated. This is because 1-α hydroxylation of 25-hydroxy vitamin D is impaired in most patients with severe CKD, and these patients should begin oral calcitriol (1,25-dihydroxy vitamin D) or a calcitriol analogue (such as paricalcitol or doxercalciferol) to maintain bone health. Calcitriol directly suppresses PTH production by the parathyroid glands, thereby protecting bones from osteitis fibrosa cystica, which can occur as a result of chronic secondary hyperparathyroidism. Vitamin D analogues should be discontinued in the setting of hypercalcemia or hyperphosphatemia.

Bisphosphonates may be used in the treatment of osteoporosis. However, bisphosphonates may actually worsen some types of bone disease observed in the setting of CKD, especially adynamic bone disease.

Current Kidney Disease Improving Global Outcomes (KDIGO) guidelines do not recommend the routine use of dual-energy x-ray absorptiometry (DEXA) scans in patients with CKD because DEXA has poor predictive value for distinguishing histologic subtypes of bone disease in patients with CKD.

This patient does not have primary hyperparathyroidism, which is typically characterized by inappropriately elevated PTH levels in the setting of hypercalcemia. She has secondary hyperparathyroidism, which is driven by multiple factors, including reduced renal production of calcitriol and factors that are often present in patients with CKD such as hyperphosphatemia and hypocalcemia. Parathyroidectomy is reserved for patients with secondary hyperparathyroidism that is refractory to medical therapy (often referred to as tertiary hyperparathyroidism).

Question 92

A 38-year-old man is evaluated in the emergency department for acute abdominal pain. Medical history is significant for excessive alcohol use and recurrent acute pancreatitis. He drinks six beers daily. He takes no medications.

On physical examination, the patient is in acute distress and indicates epigastric pain. Temperature is 38.0 °C (100.4 °F), blood pressure is 160/88 mm Hg, pulse rate is 88/min, and respiration rate is 20/min. BMI is 25. Chest and heart examinations are normal. The abdomen is slightly distended, with tenderness to minimal palpation in the epigastric area. There is no peripheral edema.

Laboratory studies:	
Leukocyte count	10,000/µL (10×10^9/L)
Blood urea nitrogen	15 mg/dL (5.4 mmol/L)
Creatinine	1.2 mg/dL (106.1 µmol/L)
Electrolytes:	
Sodium	128 mEq/L (128 mmol/L)
Potassium	4.0 mEq/L (4.0 mmol/L)
Chloride	99 mEq/L (99 mmol/L)
Bicarbonate	24 mEq/L (24 mmol/L)
Glucose	90 mg/dL (5 mmol/L)
Lipase	620 U/L
Plasma osmolality	290 mOsm/kg H_2O

Urine osmolality	400 mOsm/kg H_2O

Which of the following is the most likely cause of this patient's hyponatremia?

A

Adrenal insufficiency

B

Pseudohyponatremia

C

Psychogenic polydipsia

D

Syndrome of inappropriate antidiuretic hormone secretion

Answer & Critique

Correct Answer: B

Educational Objective: Diagnose pseudohyponatremia.

Key Point

Pseudohyponatremia is caused by a laboratory error in the measurement of serum sodium due to the presence in the serum of elevated serum lipid levels or abnormal paraproteins such as myeloma proteins.

The most likely diagnosis is pseudohyponatremia. Plasma osmolality can be measured using the following equation:

$$\text{Plasma Osmolality (mOsm/kg } H_2O) = 2 \times \text{Serum Sodium (mEq/L)} + \text{Plasma Glucose (mg/dL)}/18 + \text{Blood Urea Nitrogen (mg/dL)}/2.8$$

Using this formula, this patient's calculated plasma osmolality is approximately 266 mOsm/kg H_2O. However, his measured plasma osmolality is in the normal range. In the absence of ingested osmoles such as methanol or ethylene glycol, a normal plasma osmolality in a patient with a low serum sodium level strongly suggests pseudohyponatremia, caused by a laboratory error in the measurement of serum sodium. In normal persons, 93% of plasma is water. Laboratory analysis of serum sodium measures the amount of sodium (and thus the concentration of sodium) dissolved in the plasma water. If a substance is present that decreases the proportion of plasma that is water, such as in laboratories using ion-selective electrodes and indirect potentiometry, the measured serum sodium and concentration will be falsely low, resulting in pseudohyponatremia. There are two usual causes of pseudohyponatremia: elevated serum lipid levels or the presence in the serum of abnormal paraproteins such as myeloma proteins. This patient has a medical history, symptoms, and signs suggestive of acute pancreatitis, which can be caused by significant hypertriglyceridemia and may result in pseudohyponatremia.

Patients with adrenal insufficiency may also have hyponatremia, caused by increased antidiuretic hormone (ADH) secretion in response to hypovolemia from urine salt wasting. However, these patients demonstrate a decrease in plasma osmolality rather than a normal plasma osmolality as seen in this patient.

Psychogenic polydipsia, in which patients ingest massive amounts of water, is characterized by hyponatremia with decreased plasma osmolality and decreased urine osmolality to less than the plasma osmolality, indicating maximum suppression of ADH with maximal urine dilution. These findings are not present in this patient.

Patients with the syndrome of inappropriate antidiuretic hormone secretion have hyponatremia with decreased plasma osmolality, which is not seen in this patient.

Question 93

A 25-year-old woman is evaluated for an acute onset of swelling of the lower extremities and a 9.1-kg (20 lb) weight gain over 10 days. She notes that her urine output has diminished and that her urine appears "frothy." Medical history is significant for an unknown kidney problem as a child that resolved with medical therapy. She currently takes no medications.

On physical examination, temperature is normal, blood pressure is 100/70 mm Hg, pulse rate is 74/min, and respiration rate is 14/min. BMI is 22. Anasarca is present. Decreased breath sounds are noted at both lung bases. Cardiac examination is normal. Abdominal distention with edema of the abdominal wall is present. There is no skin rash or joint swelling.

Laboratory studies:

Albumin	1.2 g/dL (12 g/L)
Creatinine	1.1 mg/dL (97.2 μmol/L)
Urinalysis	3+ protein; 0-2 erythrocytes/hpf; 0-2 leukocytes/hpf
Urine protein-creatinine ratio	10,500 mg/g

Kidney biopsy results reveal normal-appearing glomeruli on light microscopy with immunofluorescence staining showing no immune complex deposition; electron microscopy results are pending.

Which of the following is the most appropriate treatment?

A

Cyclophosphamide

B

Lisinopril

C

Prednisone

D

No pharmacologic treatment

Answer & Critique

Correct Answer: C

Educational Objective: Treat minimal change glomerulopathy with glucocorticoids.

Key Point

Glucocorticoids are recommended as first-line therapy in the treatment of minimal change glomerulopathy unless there are contraindications.

Glucocorticoids are indicated for this patient who most likely has minimal change glomerulopathy (MCG). MCG is the most common cause of idiopathic nephrotic syndrome in children and accounts for approximately 10% of cases in adults. Although the mechanism of MCG is not well understood, it results in fusion and dysfunction of the epithelial foot processes of the glomerulus, causing significant loss of protein and other macromolecules into the urine. Patients with MCG typically present with acute onset of edema and weight gain due to fluid retention. Urine protein levels tend to be significantly elevated (urine protein-creatinine ratio typically 5000-10,000 mg/g). The abrupt onset of the full nephrotic syndrome, a history of kidney disease in childhood that remitted, negative serologic tests, and a kidney biopsy showing normal light microscopic findings and negative immunofluorescence are diagnostic of MCG. Electron microscopy is confirmatory and usually demonstrates the extensive effacement of the podocyte foot processes. Most patients with MCG are symptomatic, and the disease does not remit spontaneously in the weeks or months after presentation. Treatment with immunosuppressive medications is recommended to prevent complications of severe nephrotic syndrome, including severe symptomatic edema, thromboembolic events, and infections. Glucocorticoids such as prednisone are recommended as first-line therapy unless there are contraindications. More than 80% of patients respond within 16 weeks of treatment. Alternative first-line therapy for patients with contraindications to glucocorticoids (for example, obesity, impaired glucose tolerance or diabetes mellitus, or psychiatric conditions) includes calcineurin inhibitors such as cyclosporine.

Alkylating agents such as cyclophosphamide are reserved for frequently relapsing or glucocorticoid-dependent patients with MCG.

ACE inhibitors such as lisinopril or angiotensin receptor blockers (typically used to inhibit the progression of chronic kidney disease) are typically not indicated to treat MCG because the duration of disease is short with glucocorticoid therapy, and patients are not hypertensive.

Although MCG is not a common cause of end-stage kidney disease in adults, and untreated patients may slowly improve, the nephrotic-range proteinuria of MCG is associated with a significantly increased risk for thromboembolism and infection. Therefore, because most patients treated with glucocorticoid therapy recover with a favorable prognosis, not providing treatment is inappropriate.

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Question 94

A 19-year-old man is evaluated in the emergency department for weakness and inability to walk that began shortly after a 5-mile run. In the morning, he had a related episode of weakness of both lower limbs that lasted for 1 hour and resolved spontaneously. He also notes about a 5.0-kg (11-lb) weight loss over the past 7 months, episodes of palpitations, and heat intolerance. He was previously in good health. He takes no medications.

On physical examination, blood pressure is 150/90 mm Hg, pulse rate is 106/min, and respiration rate is 20/min. BMI is 18. The thyroid is enlarged. There is a fine tremor of the outstretched hands. There is symmetric muscle weakness with areflexia in the lower and upper extremities. The remainder of the examination is unremarkable.

Laboratory studies:

Electrolytes:	
Sodium	142 mEq/L (142 mmol/L)
Potassium	2.0 mEq/L (2.0 mmol/L)
Chloride	104 mEq/L (104 mmol/L)
Bicarbonate	24 mEq/L (24 mmol/L)

Which of the following is the most likely diagnosis?

A

Bartter syndrome

B

Hypokalemic periodic paralysis

C

Primary hyperaldosteronism

D

Sjögren syndrome

Answer & Critique

Correct Answer: B

Educational Objective: Diagnose thyrotoxic periodic paralysis.

Key Point

Hypokalemic periodic paralysis secondary to thyrotoxicosis is characterized by generalized flaccid muscle weakness from a sudden intracellular potassium shift precipitated by strenuous exercise or a high carbohydrate meal.

This patient has features of acquired hypokalemic periodic paralysis occurring in association with hyperthyroidism (thyrotoxic periodic paralysis). Hypokalemic periodic paralysis is a rare familial or acquired disorder characterized by generalized flaccid muscle weakness from a sudden intracellular potassium shift precipitated by strenuous exercise or a high carbohydrate meal. Attacks may also occur spontaneously. The acquired form occurs with thyrotoxicosis and is found in men of Asian or Mexican descent. This patient's hyperthyroidism is suggested by the presence of hypertension, tachycardia, palpitations, tremor, heat intolerance, and weight loss. Hypokalemic periodic paralysis resolves with treatment of hyperthyroidism.

Bartter syndrome represents a group of autosomal recessive renal tubular disorders characterized by metabolic alkalosis, hypokalemia, and normal to low blood pressure with mild volume depletion. It is not associated with high blood pressure as seen in this patient.

Primary hyperaldosteronism is associated with hypertension and hypokalemia and is not associated with attacks of sudden weakness or paralysis.

Hypokalemia from Sjögren syndrome occurs in the setting of renal tubular acidosis; in this setting, a hyperchloremic metabolic acidosis with hypokalemia would occur, which is not present in this patient.

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Question 95

A 33-year-old woman seeks preconception counseling. She and her partner plan to conceive a child within the next few months. She stopped taking her oral contraceptive several months ago. She has a 3-year history of hypertension treated successfully with losartan. Her home blood pressure measurements are typically in the range of 110-115/70-75 mm Hg. She feels well and has no specific complaints. Medical history is otherwise normal, and family history is notable for hypertension in her parents. Medications are losartan, 50 mg/d, and a prenatal vitamin.

On physical examination, temperature is 37.1 °C (98.8 °F), blood pressure is 112/71 mm Hg, pulse rate is 87/min, and respiration rate is 16/min. BMI is 23. The remainder of the examination, including neurologic examination, is normal.

Laboratory studies, including complete blood count, liver chemistries, kidney function studies, and urinalysis, are normal.

Which of the following is the most appropriate next step in management?

A

Continue losartan at current dose

B

Decrease losartan dose to 25 mg/d

C

Stop losartan and monitor blood pressure

D

Switch losartan to labetalol

Choose an Answer Above

Answer & Critique

Correct Answer: C

Educational Objective: Manage hypertension during pregnancy.

Key Point

ACE inhibitors, angiotensin receptor blockers, and direct renin inhibitors are associated with adverse fetal and neonatal outcomes; these medications are absolutely contraindicated during pregnancy and should be stopped prior to conception.

The most appropriate next step in management is to stop the angiotensin receptor blocker (ARB) losartan and monitor the blood pressure in this patient with hypertension who is attempting to conceive. ARBs, ACE inhibitors, and direct renin inhibitors are all associated with adverse fetal and neonatal outcomes; these agents are absolutely contraindicated during pregnancy and should be stopped prior to conception. Physiologic changes associated with pregnancy cause the systemic blood pressure to fall during most of gestation, and there is evidence that neither the patient nor the fetus appears to be at risk from mildly elevated blood pressure during pregnancy. The 2013 American College of Obstetricians and Gynecologists (ACOG) guidelines recommend treating persistent blood pressure elevations of >160/105 mm Hg in pregnant women with chronic hypertension, with a goal blood pressure with medical therapy in these patients being 120-160/80-105 mm Hg. Because this patient's current blood pressure is well below the recommended goal of therapy and her blood pressure would be expected to decline once she conceives, monitoring her blood pressure once the losartan is stopped is a reasonable approach. If her blood pressure rises into the recommended treatment range, reinstitution of treatment with a medication likely to be safe in pregnancy may be warranted.

Labetalol, a β-blocker with some α-blocking effect, may help preserve placental blood flow and is considered to be relatively safe during pregnancy. However, all antihypertensive medications cross the placenta, and it would be preferable to avoid treatment with any medication during early pregnancy. Because this patient might be able to be managed without medication should she become pregnant, switching to another agent from her ARB is not preferable. However, if further medical therapy is required, labetalol would be an appropriate option.

Question 96

A 45-year-old man is evaluated for increased urination and thirst of several months' duration. He also notes twice-nightly nocturia during this time period. Medical history is significant for bipolar disorder diagnosed 20 years ago that has been successfully treated with lithium.

On physical examination, blood pressure is 110/70 mm Hg supine and 105/65 mm Hg standing, pulse rate is 88/min supine and 95/min standing, and respiration rate is 20/min. BMI is 25. Examination of the lymph nodes, chest, heart, and abdomen is normal.

Laboratory studies:	
Blood urea nitrogen	24 mg/dL (8.6 mmol/L)
Creatinine	1.5 mg/dL (132.6 µmol/L)
Electrolytes:	
Sodium	144 mEq/L (144 mmol/L)
Potassium	4.5 mEq/L (4.5 mmol/L)
Chloride	115 mEq/L (115 mmol/L)
Bicarbonate	24 mEq/L (24 mmol/L)
Glucose	90 mg/dL (5 mmol/L)
Plasma osmolality	320 mOsm/kg H_2O
Urine osmolality	240 mOsm/kg H_2O

Which of the following is the most appropriate diagnostic test to perform next?

A

Cosyntropin stimulation test

B

Serum thyroid-stimulating hormone measurement

C

Urine sodium measurement

D

Water restriction test

Choose an Answer Above

Answer & Critique

Correct Answer: D

Educational Objective: Diagnose lithium-induced nephrogenic diabetes insipidus using a water restriction test.

Key Point

An inadequate response to water restriction (urine osmolality does not rise despite rising plasma osmolality) suggests either central or nephrogenic diabetes insipidus.

The most appropriate diagnostic test to perform next is a water restriction test to evaluate for diabetes insipidus (DI). DI is caused by either an absence of antidiuretic hormone (ADH) secretion (central DI) or renal resistance to ADH (nephrogenic DI), which results in an inability to appropriately concentrate the urine in response to an increase in plasma osmolality. This patient's symptoms of polyuria and polydipsia, in association with long-standing lithium therapy, are suggestive of nephrogenic DI. Lithium is one of the most common causes of nephrogenic DI in adults. On laboratory testing, serum sodium and plasma osmolality are usually high normal or slightly elevated, whereas urine osmolality is lower than plasma osmolality. Like the patient described, most patients with DI do not usually have frank hypernatremia because increased thirst stimulates oral consumption of fluids, which maintains the serum sodium near the upper normal range as long as access to fluids is not impaired. In a water restriction (or deprivation) test, urine volume, urine osmolality, and plasma sodium concentration are measured hourly after complete water restriction. A normal urine osmolality response (usually defined as an increase in urine osmolality above 600 mOsm/kg H_2O) indicates that ADH release and corresponding renal response to ADH are intact. A failure of the urine osmolality to rise despite rising plasma osmolality suggests either central or nephrogenic DI. Desmopressin is then administered. Patients with central DI will respond with increased urine osmolality, whereas in patients with nephrogenic DI (as is likely in this patient), desmopressin will not result in increased urine osmolality after water restriction, confirming the diagnosis.

The cosyntropin stimulation test is used to diagnose adrenal insufficiency, which is manifested by hyponatremia, decreased plasma osmolality, and increased urine osmolality, none of which is seen in this patient.

Hypothyroidism, which is diagnosed by the finding of a high thyroid-stimulating hormone level, can be associated with hyponatremia. In contrast to this patient with DI, patients with hyponatremia secondary to hypothyroidism present with hyponatremia, decreased plasma osmolality, and increased urine osmolality.

A urine sodium measurement is useful in the evaluation of patients with suspected urinary salt wasting, such as those with adrenal insufficiency. Patients with DI have a deficit of free water rather than urinary salt wasting, and as such, urine sodium measurement is not useful in diagnosing DI.

Question 97

A 45-year-old man is evaluated in the emergency department for proximal muscle weakness worsening over the course of the day. Medical history is significant for non-anuric end-stage kidney disease, hypertension, and hyperlipidemia. Medications are lisinopril, atorvastatin, amlodipine, aspirin, and sevelamer. He missed his regular hemodialysis session yesterday and has not been dialyzed for 3 days.

On physical examination, blood pressure is 170/90 mm Hg, and pulse rate is 77/min. Estimated central venous pressure is 10 cm H_2O. Cardiac examination reveals a regular rhythm with an S_4 but no murmurs. The lungs are clear. There is 2+ edema of the lower extremities.

Laboratory studies are significant for a plasma glucose level of 110 mg/dL (6.1 mmol/L) and a serum potassium level of 8.0 mEq/L (8.0 mmol/L).

An electrocardiogram shows peaked T waves.

Emergent hemodialysis is planned.

In addition to intravenous calcium gluconate, which of the following is the most appropriate next st ep in treatment?

A

Intravenous glucose and insulin

B

Intravenous high-dose bumetanide

C

Intravenous sodium bicarbonate

D

Oral sodium polystyrene sulfonate in sorbitol

Choose an Answer Above

Answer & Critique

Correct Answer: A

Educational Objective: Treat hyperkalemia using intravenous glucose and insulin to rapidly shift potassium intracellularly.

Key Point

To quickly lower serum potassium levels related to hyperkalemia, initial treatment involves intravenous glucose (to counteract hypoglycemia) and insulin to rapidly shift potassium intracellularly.

The most appropriate treatment for lowering this patient's serum potassium level most quickly is intravenous glucose and insulin. He has end-stage kidney disease (ESKD) and presents with hyperkalemia and peaked T waves on electrocardiogram. Hyperkalemia is defined as a serum potassium level >5.0 mEq/L (5.0 mmol/L). Any level >6.0 mEq/L (6.0 mmol/L) can be life-threatening. Signs and symptoms are related to adverse effects of serum potassium on skeletal and cardiac muscle cell membranes, including muscle weakness and cardiac conduction and rhythm abnormalities. Intravenous calcium gluconate stabilizes the myocardium by lowering the threshold potential and is usually administered acutely to decrease the risk of arrhythmias; however, calcium does not have any effect on serum potassium levels. Major underlying causes of persistent hyperkalemia are disorders in which urine potassium excretion is impaired. The most common cause is chronic kidney disease with a glomerular filtration rate <20 mL/min/1.73 m^2 or acute kidney injury. The appropriate treatment for reducing serum potassium quickly in this patient with ESKD and hyperkalemia is both insulin and glucose given intravenously to rapidly shift potassium intracellularly. Insulin effectively drives potassium into cells by increasing activity of the Na-K-ATPase pump in skeletal muscle. Glucose is given to counteract potential hypoglycemia associated with insulin therapy.

High-dose loop and thiazide diuretics increase kidney potassium loss, particularly when combined with saline hydration, in patients with normal kidney function or mild to moderate kidney failure. However, this effect is not immediate, and bumetanide would be ineffective in this patient with ESKD.

Intravenous sodium bicarbonate raises the serum pH and leads to a shift of potassium into cells as part of the buffering process. However, it has not been shown to be an effective or predictable method for producing a hypokalemic response, especially in patients with ESKD.

Oral sodium polystyrene sulfonate in sorbitol binds potassium in the colon in exchange for sodium. It is not useful for acute control of hyperkalemia because its effect on potassium is delayed for at least 2 hours and peaks at 4 to 6 hours. In addition, its effect on hyperkalemia is modest.

Question 98

A 60-year-old woman is evaluated during a follow-up visit for hypertension. History is also notable for hyperlipidemia. She tolerates her medications well except for minor pedal edema since starting her antihypertensive medication. She is active and plays tennis three times per week. Current medications are amlodipine, 5 mg/d, and rosuvastatin.

On physical examination, the average of two blood pressure measurements is 152/86 mm Hg, which is consistent with measurements she has obtained at home over the past 3 months. Pulse rate is 64/min. BMI is 22. Trace pedal edema is noted. The remainder of the examination is unremarkable.

Laboratory studies show a normal chemistry panel; a urine dipstick demonstrates no protein.

Which of the following is the most appropriate next step in management?

A

Add lisinopril

B

Add metoprolol

C

Increase amlodipine to 10 mg/d

D

Continue current regimen

Answer & Critique

Correct Answer: A

Educational Objective: Manage stage 1 hypertension in an older patient.

Key Point

The eighth report of the Joint National Committee recommends a blood pressure goal of <150/90 mm Hg for patients with hypertension who are ≥60 years.

Addition of the ACE inhibitor lisinopril is appropriate. This 60-year-old patient has stage 1 hypertension. The eighth report of the Joint National Committee (JNC 8) recommends a treatment goal of <150/90 mm Hg for patients with hypertension who are ≥60 years. Given her age and no evidence of cardiovascular or kidney disease and lack of frailty, this patient's treatment goal according to JNC 8 is <150/90 mm Hg. In her circumstance, given a longer expected lifetime than the general population for this age, cautious stepped care for lower blood pressure goals is reasonable. Increasing the dose of one agent is less effective in reducing blood pressure than the addition of a second agent at low dose, which also avoids the risk of side effects more commonly seen at higher doses. In this case, the minor pedal edema may be exacerbated by increasing the amlodipine.

In the absence of any indications for β-blocker therapy (tachycardia, history of angina, or a recent myocardial infarction), metoprolol is not indicated for the initial therapy of hypertension. It can be considered as add-on therapy typically in the setting of vasodilator-induced tachycardia, but given the low resting pulse rate in this patient, an alternative agent should be considered. The Avoiding Cardiovascular Events in Combination Therapy in Patients Living with Systolic Hypertension (ACCOMPLISH) trial demonstrated the benefit of combination therapy with a calcium channel blocker and an ACE inhibitor in reducing cardiovascular events compared with combination therapy using a thiazide diuretic and an ACE inhibitor.

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Question 99

A 54-year-old man is evaluated for elevated blood pressure noted recently at a local health fair. He has no other medical history and takes no medications.

On this visit and on two subsequent nurse visits, the patient's blood pressure measurements are less than 140/90 mm Hg. BMI is 34. Cardiac examination reveals an S_4 gallop. The remainder of the examination is normal.

Laboratory studies show a normal chemistry panel, and a urine dipstick demonstrates no blood or protein.

Electrocardiogram demonstrates evidence of left ventricular hypertrophy.

Which of the following is the most appropriate next step in management?

A

Ambulatory blood pressure monitoring

B

Lisinopril

C

Plasma aldosterone-plasma renin ratio

D

Repeat blood pressure measurement in 6 months

Choose an Answer Above

Answer & Critique

Correct Answer: A

Educational Objective: Diagnose masked hypertension using ambulatory blood pressure monitoring.

Key Point

Ambulatory blood pressure monitoring may be helpful in diagnosing masked hypertension in patients with end-organ manifestations but normal office blood pressure measurements.

Ambulatory blood pressure monitoring (ABPM) is appropriate for this patient who likely has masked hypertension. He has evidence of end-organ manifestations (left ventricular hypertrophy) that is potentially related to hypertension, yet has not presented with blood pressure measurements consistent with hypertension (≥140/90 mm Hg). This raises the possibility of masked hypertension, which is defined as normal office blood pressure measurements but elevated blood pressure (>135/85 mm Hg) in the ambulatory setting. Prior to initiating medical therapy, a more detailed assessment of this patient's blood pressure should be pursued, with ABPM as an appropriate next step. Although ABPM does not carry a formal indication for the diagnosis of masked hypertension, it may be useful in establishing this blood pressure pattern. ABPM-ascertained hypertension is associated with a higher risk of cardiovascular death compared with office or home blood pressure–determined hypertension.

The left ventricular hypertrophy identified by electrocardiogram in this case may be secondary to hypertension but also may be due to other (such as genetic) causes and requires formal echocardiography to further evaluate and guide therapy. Initiating a blood pressure–lowering agent is not appropriate until both blood pressure and the electrocardiogram findings are clarified further with ABPM and echocardiography.

A plasma renin-plasma aldosterone ratio is used to evaluate for hyperaldosteronism as a secondary cause of hypertension and is typically indicated in patients with difficult-to-treat blood pressure elevations and hypokalemia. This patient has not been diagnosed with hypertension and has no electrolyte abnormalities.

Because this patient has evidence of end-organ damage possibly due to hypertension, follow-up assessment of his blood pressures in 6 months might further delay diagnosis and is not appropriate.

Question 100

A 46-year-old woman is evaluated in the emergency department for difficulty catching her breath, generalized weakness, and paresthesias of the hands and feet. Medical history is significant for hypertension and generalized anxiety disorder. Medications are hydrochlorothiazide and paroxetine.

On physical examination, the patient appears anxious and is breathing rapidly. Temperature is 36.5 °C (97.7 °F), blood pressure is 108/62 mm Hg, pulse rate is 104/min, and respiration rate is 24/min. Oxygen saturation on ambient air is 99%. BMI is 24. There is no stridor, crackles, or wheezing on lung examination. The remainder of the physical examination is normal.

Laboratory studies:

Bicarbonate	21 mEq/L (21 mmol/L)
Arterial blood gas studies:	
pH	7.58
P_{CO_2}	22 mm Hg (2.9 kPa)
P_{O_2}	103 mm Hg (13.7 kPa)

Which of the following is the most likely acid -base disorder in this patient?

A

Metabolic alkalosis and acute respiratory compensation

B

Metabolic alkalosis and chronic respiratory compensation

C

Respiratory alkalosis and acute metabolic compensation

D

Respiratory alkalosis and chronic metabolic compensation

Answer & Critique

Correct Answer: C

Educational Objective: Diagnose respiratory alkalosis.

Key Point

Primary acute respiratory alkalosis is characterized by a low P_{CO_2} and an appropriately reduced serum bicarbonate.

The most likely acid-base disorder in this patient is respiratory alkalosis with acute metabolic compensation. This patient has primary acute respiratory alkalosis, likely resulting from a panic attack associated with her anxiety disorder. Acute respiratory alkalosis is evidenced by a low P_{CO_2} and an appropriately reduced serum bicarbonate occurring in response to the lowered P_{CO_2}. For each 10 mm Hg (1.3 kPa) decrease in P_{CO_2}, serum bicarbonate falls acutely by 2.0 mEq/L (2.0 mmol/L) due to intracellular-to-extracellular shift of hydrogen ions as an immediate buffering mechanism. If the respiratory alkalosis is persistent, renal compensation will eventually occur, leading to reduced proximal tubule reabsorption of bicarbonate, and, after 24 to 48 hours, a further decrease in serum bicarbonate totaling 3.0 to 4.0 mEq/L (3.0-4.0 mmol/L) for every 10 mm Hg (1.3 kPa) decrease of P_{CO_2}. The reduction in bicarbonate of 4.0 mEq/L (4.0 mmol/L) for the decrease in P_{CO_2} of 18 mm Hg (2.4 kPa) indicates that renal compensation has not yet occurred. The laboratory studies are not consistent with a primary metabolic alkalosis because the bicarbonate is not elevated.

Question 101

A 58-year-old woman is evaluated during a follow-up visit for a 5-year history of stage G3b/A1 chronic kidney disease caused by analgesic nephropathy. History is also notable for hypertension. She takes amlodipine and no longer uses analgesics.

On physical examination, temperature is 37.0 °C (98.6 °F), blood pressure is 132/78 mm Hg, pulse rate is 82/min, and respiration rate is 14/min. BMI is 26. Cardiac examination reveals no murmur, rub, or gallop. The lungs are clear.

Laboratory studies:	
Creatinine	1.8 mg/dL (159.1 µmol/L)
Electrolytes:	
Sodium	140 mEq/L (140 mmol/L)
Potassium	5.4 mEq/L (5.4 mmol/L)
Chloride	110 mEq/L (110 mmol/L)
Bicarbonate	18 mEq/L (18 mmol/L)
Arterial blood gases:	
pH	7.36
P_{CO_2}	35 mm Hg (4.7 kPa)
Estimated glomerular filtration rate	33 mL/min/1.73 m^2

Which of the following is the most appropriate treatment?

A

Intravenous sodium bicarbonate

B

Oral potassium citrate

C

Oral sodium bicarbonate

D

Continue current therapy

Choose an Answer Above

Answer & Critique

Correct Answer: C

Educational Objective: Treat metabolic acidosis with alkali therapy to slow progression of chronic kidney disease.

Key Point

Oral alkali therapy to maintain serum bicarbonate levels between 23 and 29 mEq/L (23-29 mmol/L) reduces the risk of progression of chronic kidney disease.

Treatment with oral sodium bicarbonate, 0.5 mEq/kg/d, is appropriate. This patient with chronic kidney disease (CKD) has a normal anion gap metabolic acidosis. Normal anion gap metabolic acidosis may be due to failure of the kidneys to excrete the daily fixed acid load, gastrointestinal loss of bicarbonate, diversion of urine through a gastrointestinal conduit, or retention of hydrogen ions derived from organic anions that are excreted in the urine as sodium salts. The cause is often apparent from the history. This patient's history of analgesic nephropathy, normal anion gap metabolic acidosis, and hyperkalemia suggests the presence of distal (type 4) renal tubular acidosis. Studies have demonstrated that administration of oral alkali to maintain serum bicarbonate levels between 23 and 29 mEq/L (23-29 mmol/L) reduces the risk of progression of CKD. Typical starting doses of alkali for metabolic acidosis due to CKD are 0.5 to 1.0 mEq/kg/d.

The patient has a relatively mild and asymptomatic decrease in serum bicarbonate, and there is no indication for acute administration of intravenous sodium bicarbonate.

Although citrate becomes metabolized to bicarbonate and is therefore considered to be a “bicarbonate equivalent,” this patient has hyperkalemia, which is likely due to the decreased ability of the kidneys to excrete potassium in the setting of CKD. Potassium citrate could therefore exacerbate the existing hyperkalemia and should be avoided. Bicarbonate treatment will help correct this patient's hyperkalemia.

Current guidelines suggest treatment with alkali to keep serum bicarbonate levels between 23 and 29 mEq/L (23-29 mmol/L). Therefore, providing no alkali therapy to this patient with a serum bicarbonate level of 18 mEq/L (18 mmol/L) would be inappropriate.

Question 102

A 35-year-old man is evaluated in the hospital for acute kidney injury. He presented with worsening fatigue, decreased urination, and progressive swelling in the ankles occurring over the course of 2 to 3 weeks. Laboratory studies at the time of diagnosis showed a serum creatinine level of 6.7 mg/dL (592.3 µmol/L) (baseline of 0.9 mg/dL [79.6 µmol/L] 1 year ago). Medical history is significant for a 3-year history of inflammatory bowel disease that has been well controlled with daily mesalamine therapy. He does not take any over-the-counter drugs.

On physical examination, temperature is 37.0 °C (98.6 °F), blood pressure is 118/67 mm Hg, pulse rate is 60/min, and respiration rate is 16/min. BMI is 20. Cardiac examination is normal. The lungs show crackles at the bases bilaterally. There is lower extremity edema to the mid calf. The remainder of the examination is normal.

Dipstick urinalysis shows 1+ protein but is otherwise normal. Urine microscopy shows 2-3 erythrocytes/hpf, 5-10 leukocytes/hpf, and leukocyte casts. Urine protein-creatinine ratio is 1060 mg/g. Urine cultures are negative.

Kidney ultrasound shows normal-sized kidneys with mildly increased parenchymal echogenicity, no hydronephrosis, and no renal calculi.

Which of the following is the most likely cause of this patient's acute kidne y injury?

A

Interstitial nephritis

B

Lupus nephritis

C

Membranous glomerulopathy

D

Rapidly progressive glomerulonephritis

Answer & Critique

Correct Answer: A

Educational Objective: Diagnose interstitial nephritis caused by mesa lamine therapy.

Key Point

In patients with interstitial nephritis, the hallmark findings on urinalysis are sterile pyuria and leukocyte casts.

The most likely diagnosis is interstitial nephritis caused by mesalamine therapy. Interstitial nephritis is characterized by an inflammatory infiltrate into the kidney interstitium that can lead to tubular dysfunction and kidney failure. Interstitial nephritis may be associated with autoimmune diseases and infections but is most commonly caused by drugs. Mesalamine-induced interstitial nephritis is a well-described complication that can be either acute or chronic and may occur months to years after exposure, even in patients who have safely tolerated the medication in the past. Sterile pyuria and leukocyte casts are hallmarks of interstitial nephritis, which can present acutely or may progress indolently and present as chronic kidney disease of unclear duration. Mild subnephrotic proteinuria also can be seen with interstitial nephritis.

Kidney disease in systemic lupus erythematosus is relatively common and may have a variable presentation, often with significant hematuria, proteinuria, and cellular casts. However, lupus nephritis is unlikely in this patient because of the absence of extrarenal lupus manifestations, his male gender, and lack of significant proteinuria or hematuria.

Membranous glomerulopathy primarily affects the glomerulus and is therefore associated with heavy proteinuria and the nephrotic syndrome, making this an unlikely diagnosis for this patient.

Rapidly progressive glomerulonephritis is associated with hematuria and erythrocyte casts and variable proteinuria, usually with other clinical manifestations such as hypertension. In some cases, other systemic symptoms or clinical findings associated with an underlying etiology may be present, such as pulmonary hemorrhage or upper and lower respiratory tract involvement. None of these findings is present in this patient, making this diagnosis unlikely.

Question 103

A 41-year-old woman is evaluated during a routine obstetrics visit. She is in the third trimester of her first pregnancy. Her previous visits have been unremarkable, with blood pressures within the normal range for pregnancy. She has noticed mild shortness of breath with exertion and mild peripheral edema in her lower extremities. She reports no urinary changes. Medical history is notable for type 1 diabetes mellitus; she reports well-controlled blood sugars. Family history is notable for her mother who has hypertension. Medications are insulin and prenatal vitamins.

On physical examination, temperature is 37.1 °C (98.8 °F), blood pressure is 162/112 mm Hg, pulse rate is 87/min, and respiration rate is 16/min. BMI is 28. Cardiac examination reveals a grade 2/6 crescendo-decrescendo murmur at the right upper sternal border and an S_3 gallop. Estimated central venous pressure is 14 cm H_2O. Bibasilar crackles are noted at the lung bases bilaterally. The patient has a gravid uterus and an otherwise unremarkable abdominal examination. There is trace lower extremity edema.

Laboratory studies are significant for a platelet count of 75,000 µL (75×10^9/L); a comprehensive metabolic profile with liver chemistry tests, peripheral blood smear, and urinalysis are normal.

Which of the following is the most likel y diagnosis?

A

Chronic hypertension

B

HELLP syndrome

C

Normal changes of pregnancy

D

Preeclampsia

Choose an Answer Above

Answer & Critique

Correct Answer: D

Educational Objective: Diagnose preeclampsia.

Key Point

Preeclampsia is classically defined as new-onset hypertension after 20 weeks of pregnancy with proteinuria but can also be diagnosed in patients without proteinuria if the hypertension is accompanied by other end-organ damage.

The most likely diagnosis is preeclampsia, which is classically defined as new-onset hypertension after 20 weeks of pregnancy with proteinuria (≥300 mg/24 h or a urine protein-creatinine ratio ≥300 mg/g). According to new guidelines, preeclampsia can also be diagnosed in patients without proteinuria if the hypertension is accompanied by one of the following conditions: thrombocytopenia (platelet count <100,000/μL [100 × 10^9/L]), kidney dysfunction (serum creatinine concentration >1.1 mg/dL [97.2 μmol/L] or a doubling of the serum creatinine concentration in the absence of other kidney disease), impaired liver function (elevated blood concentrations of liver aminotransferases to twice the normal concentration), pulmonary edema, or cerebral or visual symptoms. Because this patient meets the criteria for blood pressure elevation and also has thrombocytopenia and possibly mild pulmonary edema, the diagnosis of preeclampsia may be made without the presence of proteinuria. She has several risk factors for preeclampsia, including advanced maternal age and first pregnancy. Other risk factors for preeclampsia include family history, diabetes mellitus, obesity, chronic kidney disease, and twin gestation.

Chronic hypertension is defined as systolic pressure ≥140 mm Hg and/or diastolic pressure ≥90 mm Hg that existed before pregnancy, is present before the 20th week of gestation, or persists longer than 12 weeks postpartum. This patient had normal blood pressures prior to her most recent visit, making chronic hypertension unlikely.

The diagnosis of HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome requires evidence of hemolysis and abnormal liver chemistry tests in addition to thrombocytopenia.

Normal hemodynamic changes occurring during pregnancy include an increase in cardiac output and reduction in both systemic vascular resistance and systemic blood pressure. Therefore, the significant blood pressure elevation seen in this patient who was previously normotensive is not considered to be a normal

change associated with pregnancy. Crackles, an S_3 gallop, and an elevated central venous pressure would not be expected findings during a normal pregnancy and reinforce the diagnosis of preeclampsia.

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Question 104

A 69-year-old woman is evaluated during a follow-up visit for stage G4/A1 chronic kidney disease due to hypertensive nephrosclerosis. History is also significant for peripheral arterial disease with right femoral-popliteal bypass 1 year ago. Medications are metoprolol, atorvastatin, aspirin, and calcium acetate.

On physical examination, temperature is 37.0 °C (98.6 °F), blood pressure is 132/89 mm Hg, pulse rate is 61/min, and respiration rate is 13/min. BMI is 27. There is an audible S_4 gallop and reduced pedal pulses. The lungs are clear. The lower extremities are warm with normal capillary refill. There is no peripheral edema.

Laboratory studies:

Albumin	4.2 g/dL (42 g/L)
Calcium	8.3 mg/dL (2.1 mmol/L)
Creatinine	2.6 mg/dL (229.8 µmol/L)
Phosphorus	6.9 mg/dL (2.23 mmol/L)
Intact parathyroid hormone	95 pg/mL (95 ng/L)
Estimated glomerular filtration rate	22 mL/min/1.73 m^2

Review of a previous chest radiograph is remarkable for a heavily calcified aorta but is otherwise clear.

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In addition to dietary counseling regarding a low phosphate diet, which of the following is the most appropriate treatment?

A

Calcitriol

B

Calcium carbonate

C

Cinacalcet

D

Sevelamer

Choose an Answer Above

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Question 104

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Intact parathyroid hormone	95 pg/mL (95 ng/L)
Estimated glomerular filtration rate	22 mL/min/1.73 m^2

Review of a previous chest radiograph is remarkable for a heavily calcified aorta but is otherwise clear.

In addition to dietary counseling regarding a low phos phate diet, which of the following is the most appropriate treatment?

13%

A Calcitriol

15%

B Calcium carbonate

11%

C Cinacalcet

61%

D Sevelamer

Answer & Critique

Correct Answer: D

Educational Objective: Treat hyperphosphatemia in a patient with chronic kidney disease.

Key Point

Patients with chronic kidney disease and hyperphosphatemia should be counseled regarding a low phosphate diet, and most patients require phosphate binders.

In addition to dietary counseling regarding a low phosphate diet, this patient with stage G4/A1 chronic kidney disease (CKD) who now has hyperphosphatemia should begin taking a phosphate binder such as sevelamer. Elevated serum phosphorus levels, particularly exceeding 6.5 mg/dL (2.09 mmol/L), are closely associated with increased mortality. Most patients with severe CKD require oral phosphate binders to be administered with meals. This patient also has known cardiovascular disease and vascular calcification. The Kidney Disease Improving Global Outcomes (KDIGO) guidelines suggest avoiding the use of calcium-containing phosphate binders in patients with known vascular calcification due to the potential for an increase in calcium absorption and worsening calcification of vessel walls. Therefore, a non-calcium–containing phosphate binder such as sevelamer or lanthanum is the preferred agent for this patient. Ferric citrate, another non-calcium–containing phosphorus binder, was recently approved for use in patients receiving dialysis but is not yet approved for patients with non-dialysis CKD.

Although this patient has secondary hyperparathyroidism, administration of calcitriol will increase intestinal absorption of calcium and phosphorus, which will exacerbate the hyperphosphatemia and potentially worsen vascular calcification.

Although administration of oral calcium carbonate will lead to increased absorption of calcium that may treat this patient's mild hypocalcemia and reduce her parathyroid hormone (PTH) levels, it may exacerbate vascular calcium in the setting of severe hyperphosphatemia.

Administration of the calcimimetic cinacalcet will likely decrease this patient's PTH level toward the normal range; however, it will worsen her hypocalcemia and is not an effective treatment for the hyperphosphatemia.

Question 105

A 72-year-old man is evaluated for a 3-month history of slowly progressive anemia and fatigue. He has a 3-year history of end-stage kidney disease and receives hemodialysis three times weekly. Prior to starting hemodialysis he was able to maintain adequate iron stores with oral iron therapy. Erythropoietin for symptomatic anemia was initiated 3 years ago with the onset of dialysis; he responded well, with an increase in his hemoglobin level to 11 g/dL (110 g/L) and a decrease in symptoms. There have been no changes in his medications, which consist of erythropoietin, three times weekly; oral iron sulfate, 325 mg three times daily; lisinopril; metoprolol; nifedipine; sevelamer; and aspirin.

On physical examination, the patient is afebrile. Blood pressure is 144/94 mm Hg, pulse rate is 76/min, and respiration rate is 16/min. The lungs are clear. There is no edema.

Laboratory studies:

Hemoglobin	9.8 g/dL (98 g/L)
Ferritin	80 ng/mL (80 µg/L)
Transferrin saturation	12%

Which of the following is the most appropriate management?

A

Administer intravenous iron

B

Increase erythropoietin dose

C

Increase oral iron dose

D

Measure erythropoietin level

Choose an Answer Above

Answer & Critique

Correct Answer: A

Educational Objective: Treat chronic kidney disease–related iron deficiency anemia with intravenous iron.

Key Point

Iron deficiency is the most common cause of hyporesponsiveness to erythropoietin, and guidelines recommend intravenous rather than oral iron replacement among hemodialysis patients who require iron.

The most appropriate management of this patient with chronic kidney disease–related iron deficiency anemia is to administer intravenous iron. Iron deficiency is the most common cause of hyporesponsiveness to erythropoietin. It is therefore important to optimize iron stores to maximize the response to erythropoietin. Many patients who receive hemodialysis are unable to maintain adequate iron stores by oral supplementation. The Kidney Disease Improving Global Outcomes (KDIGO) recommendations suggest maintaining transferrin saturation levels of >30% and serum ferritin levels of >500 ng/mL (500 µg/L). In hemodialysis patients, parenteral iron therapy is preferred to oral iron therapy because it is more effective in increasing hemoglobin concentrations and iron stores. Patients treated with intravenous iron are more likely to reduce the dose of erythropoiesis-stimulating agents (ESAs) compared with those taking oral iron. KDIGO guidelines recommend intravenous rather than oral iron replacement among hemodialysis patients who require iron.

As the estimated glomerular filtration rate declines below 30 mL/min/1.73 m^2 (stages G4-G5), anemia can become symptomatic. ESAs are highly effective in raising hemoglobin concentrations and alleviating symptoms, although these medications are associated with risks and are expensive. Once iron stores are replaced, KDIGO guidelines suggest avoiding dosing erythropoietin to achieve a hemoglobin level >11.5 g/dL (115 g/L) unless there are compelling reasons to do so to improve quality of life and the patient agrees to the risks.

There is no role for the routine measurement of erythropoietin levels in the setting of chronic kidney disease because this expensive test does not aid in the diagnosis or guide treatment decisions.

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Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group. KDIGO Clinical Practice Guideline for

Question 106

A 52-year-old man is evaluated for a recent diagnosis of membranous glomerulopathy (MG). He presented with a 1-month history of increasing lower extremity edema and was found to have nephrotic-range proteinuria. Evaluation included normal serum complement levels; negative serologies for antinuclear antibodies, hepatitis B, and hepatitis C; and negative serum protein electrophoresis. Kidney biopsy showed changes consistent with MG; staining for antibodies to the phospholipase A_2 receptor (PLA_2R) was negative. Medical history is otherwise significant for hypertension. He is up-to-date with recommended health maintenance interventions. He has a 25-pack-year smoking history and is a current smoker. His only medication is ramipril.

On physical examination, temperature is 36.7 °C (98.0 °F), blood pressure is 140/80 mm Hg, pulse rate is 68/min, and respiration rate is 14/min. BMI is 31. Pulmonary and abdominal examinations are normal. There is lower extremity edema to the knees bilaterally.

Which of the following is the most appropriate n ext diagnostic step?

A

Chest radiography

B

PET/CT of the chest

C

Whole body CT

D

No additional testing

Choose an Answer Above

Answer & Critique

Correct Answer: A

Educational Objective: Evaluate a patient for secondary causes of membranous glomerulopathy.

Key Point

An extensive evaluation for cancer is not indicated in patients with membranous glomerulopathy beyond age-appropriate cancer screening except for those with symptoms suggestive of a cancer diagnosis or significant risk factors for specific malignancies.

Chest radiography is the most appropriate next diagnostic step. This middle-aged patient presented with the insidious onset of the nephrotic syndrome with membranous glomerulopathy (MG) demonstrated on kidney biopsy. MG may be primary (idiopathic) or secondary to other causes. Primary MG is associated with the antibody to the phospholipase A_2 receptor (PLA_2R) on the podocyte surface in up to 80% of patients, and the presence of the antibody supports this diagnosis. Testing for anti-PLA_2R antibodies may be performed on serum or by staining of kidney biopsy tissue. Secondary causes of MG include malignancies (solid organ cancers, especially lung, colon, and breast), autoimmune diseases (such as lupus or mixed connective tissue disease), infections (hepatitis B and C), and medications (penicillamine, gold, and NSAIDs). Evaluation for potential secondary causes should always be undertaken in patients with MG, especially those who are negative for PLA_2R antibodies. Serologic tests for lupus and hepatitis were negative in this patient, and he has not been exposed to potential offending medications. Although MG may be associated with malignancy, an extensive evaluation for cancer is not indicated in patients with a diagnosis of MG beyond age-appropriate cancer screening except for those with symptoms suggestive of a cancer diagnosis (such as weight loss or blood in the stool) or significant risk factors for specific malignancies. Because of this patient's significant smoking history and his associated increased risk for lung cancer, chest radiography should be obtained as part of his evaluation for secondary MG.

Both PET and PET coupled with CT are useful studies in evaluating selected patients with known malignancy, often for staging purposes. However, neither is indicated to initially evaluate for lung cancer. Similarly, whole body CT is of low yield in searching for malignancy.

Although an extensive evaluation for malignancy is usually not indicated in patients with MG beyond age-appropriate cancer screening, this patient's increased risk for lung cancer warrants further evaluation.

Question 107

A 57-year-old man is hospitalized with *Streptococcus viridans* endocarditis; intravenous ceftriaxone for 6 weeks will be initiated. History is significant for stage G5/A2 chronic kidney disease due to IgA nephropathy and hypertension. Placement of a left forearm arteriovenous fistula occurred 12 days ago. He does not yet require dialysis. Medications are lisinopril, furosemide, and sevelamer.

On physical examination, temperature is 37.0 °C (98.6 °F), blood pressure is 128/84 mm Hg, pulse rate is 77/min, and respiration rate is 17/min. BMI is 25. A grade 3/6 holosystolic murmur is present at the left sternal border. There is no pericardial rub. The arteriovenous fistula has a palpable thrill. The lungs are clear. There is no asterixis. There is no peripheral edema.

Which of the following is the most appropriate vascular access for antibiotic administration?

A

A peripherally inserted central catheter line

B

A single-lumen catheter in the left subclavian vein

C

A single-lumen catheter in the right internal jugular vein

D

The arteriovenous fistula

Choose an Answer Above

Answer & Critique

Correct Answer: C

Educational Objective: Protect sites of current or future vascular access in a patient with severe chronic kidney disease.

Key Point

Protection of the peripheral veins for future vascular access is essential in patients with chronic kidney disease.

Placement of a single-lumen catheter in the right internal jugular vein to allow for 6 weeks of intravenous ceftriaxone is appropriate for this patient with severe chronic kidney disease (CKD). This strategy seeks to protect the integrity of peripheral veins. Protecting peripheral veins is an important consideration for all patients with severe CKD or end-stage kidney disease (ESKD) because adequate veins are a prerequisite for the creation of arteriovenous fistulas, which are associated with lower mortality than other forms of vascular access for hemodialysis. Because most patients will require multiple vascular accesses during the course of ESKD therapy, it is critical to protect peripheral veins even if patients already have a functional dialysis access. Small-bore single-lumen catheters placed into the internal jugular vein are less likely to impair venous drainage from the arm than subclavian catheters.

Peripherally inserted central catheter (PICC) lines have a high risk of causing permanent thrombosis or sclerosis to peripheral veins that might otherwise be useful for the creation of vascular access for hemodialysis. PICC lines should be avoided in patients with severe CKD or ESKD who are expected to require future hemodialysis.

Subclavian catheters have a high risk of causing stenosis of the subclavian veins, which can impede return of blood from the arm with arteriovenous dialysis access due to high blood flows. High venous pressure due to subclavian stenosis can lead to arm edema and failure of the arteriovenous access.

The patient's arteriovenous fistula should not be used to administer daily intravenous antibiotics. Inserting needles into a recently created fistula can damage it because the walls of the vein will not have had adequate time to “arterialize,” which usually requires at least 2 to 3 months. Dialysis vascular access sites should only

be accessed by trained dialysis personnel due to the need to protect against injury and/or infection to the access site. It is also important to avoid inflating blood pressure cuffs on the arm with vascular access to avoid injury or thrombosis.

Bibliography

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Question 108

A 32-year-old woman is evaluated in the emergency department 30 minutes after a motor vehicle accident in which she struck her head on the steering wheel. She is awake and conversant and has no major symptoms aside from a mild headache. She is at 23 weeks' gestation of her second pregnancy. She has been receiving routine prenatal care, and her pregnancy has been uncomplicated. Her only medication is a prenatal vitamin.

On physical examination, the patient is in neck immobilization. Temperature is 37.1 °C (98.7 °F), blood pressure is 111/63 mm Hg, pulse rate is 76/min, and respiration rate is 12/min. BMI is 24. There is a contusion on the upper forehead but no other evidence of trauma. The abdomen shows normal changes of pregnancy but is otherwise normal. The remainder of the physical and neurologic examinations is unremarkable.

Initial laboratory studies show a serum sodium level of 131 mEq/L (131 mmol/L); the remainder of the electrolytes, blood urea nitrogen, and serum creatinine are normal.

Which of the following is the most likely cause of this patient's decrease in her serum sodium level?

A

Cerebral salt wasting

B

Normal physiologic changes of pregnancy

C

Pituitary apoplexy

D

Syndrome of inappropriate antidiuretic hormone secretion

Choose an Answer Above

Answer & Critique

Correct Answer: B

Educational Objective: Identify normal physiologic changes of pregnancy as the cause of decreased serum sodium levels in a pregnant patient.

Key Point

While the plasma volume increases during pregnancy, water retention exceeds the concomitant sodium retention, resulting in mild hypo-osmolality and hyponatremia; these hormonally mediated changes do not need direct therapy and resolve following delivery.

Normal physiologic changes of pregnancy are the most likely cause of this pregnant patient's decrease in her serum sodium level. While the plasma volume increases during pregnancy, water retention exceeds the concomitant sodium retention, resulting in mild hypo-osmolality and hyponatremia. The plasma osmolality typically decreases by 8 to 10 mOsm/kg H_2O, and the serum sodium decreases by 4.0 mEq/L (4.0 mmol/L). These hormonally mediated changes in plasma osmolality and serum sodium do not require therapy and resolve following delivery.

Cerebral salt wasting can be mistaken for the syndrome of inappropriate antidiuretic hormone secretion (SIADH) and can occur in response to central nervous system disease (particularly subarachnoid hemorrhage) and closed head injury. It is associated with an increased loss of sodium by the kidney, resulting in hyponatremia. However, these changes occur over a longer timeframe than seen in this patient with recent head trauma.

Pituitary apoplexy is acute hemorrhage into the pituitary gland and would be a consideration in this patient. If severe, it may cause headache, vision changes due to ocular nerve compression, and hypopituitarism. All pituitary hormonal deficiencies can occur, including adrenocorticotropic hormone (ACTH) deficiency, which may lead to cortisol deficiency and hypotension if it occurs rapidly. Although the resulting cortisol deficiency may result in mild hyponatremia, this would not occur immediately after injury. Additionally, this patient has a normal blood pressure for pregnancy and no other symptoms or clinical findings suggesting this diagnosis.

Neurologic conditions such as a closed head injury from a motor vehicle accident can cause the SIADH, but hyponatremia would not develop acutely upon initial presentation as in this patient.