

1. An 18-year-old white man presents to your office after developing gross hematuria. Your physical examination reveals some papules on his face and neck. They are 1–3 mm in size and are nontender. BP is normal, and serum creatinine is 1.2. Urinalysis reveals a pattern of uniformly shaped red blood cells in greater than 100 cells per high power field. The patient has completed high school, but he was known as a very slow learner and a poor student. Imaging of his kidneys reveals some cystic change in both kidneys and a solid-looking vascular mass in the right kidney.

What is the MOST likely diagnosis?

- A. Renal cell carcinoma
- B. ADPKD
- C. Autosomal recessive PKD
- D. Tuberous sclerosis
- E. Von Hippel-Lindau syndrome

Answer: D

Explanation:

The patient described has the skin lesions and renal findings of tuberous sclerosis. The renal lesions are typically angiomyolipomas and can bleed. Although mental retardation is common in this autosomal dominant disorder, it is not inevitable. Von Hippel-Lindau syndrome is a possibility based on the renal finding, but this would not explain the skin lesions. ADPKD is unlikely with this imaging picture and again would not explain the skin lesions. A renal cell carcinoma is possible but at his age is unlikely and is unaccompanied by some genetic syndrome with skin lesions.

2. **On ultrasound images, the normal kidney should have which characteristic?**

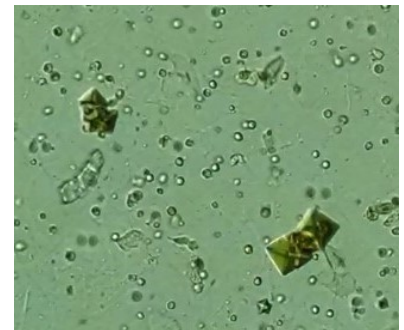
- A. Larger than 14 cm in length
- B. Have wedge-shaped areas of low blood flow in the cortex on Power Doppler
- C. Be equal or less echogenic than the liver
- D. Have symmetric bilateral effacement of the renal sinus echo-complex with dilated calyces

Answer: C

Explanation:

The echogenicity of normal kidneys is less than that of pancreas and equal or less than that of liver and spleen. Increased renal echogenicity indicates renal disease. Normal kidneys measure 9–13 cm on ultrasound exams; A is incorrect. Normal kidneys have no low flow areas on Doppler exams, and wedge-shaped deficiencies are indicative of infarcts; B is incorrect. Dilated calyces should not be present in normal kidneys, and these suggest obstruction or ectasia from prior disease; D is incorrect.

3. A 49-year-old morbidly obese man with a history of hypertension (HTN), metabolic syndrome, osteoarthritis, and gout undergoes a Roux-en-Y bypass procedure. Medications include lisinopril, furosemide, ibuprofen, and glyburide. The patient presents 4.5 weeks later with weakness and fatigue. Labs reveal a serum creatinine of 3.7 mg/dL. Urine sediment demonstrates 1–3 RBCs/HPF, 0–1 WBCs/HPF, 2–5 renal tubular cells/HPF, and the crystals seen in the figure.



Which BEST describes the crystals?

- A. Calcium phosphate crystals
- B. Uric acid crystals
- C. Cystine crystals
- D. Calcium oxalate crystals
- E. Sulfonamide crystals

Answer: D

Explanation:

The patient developed kidney injury after the gastric bypass procedure. The urine microscopy reveals calcium oxalate crystals, which reflect the enteric hyperoxaluria that has developed following the malabsorption induced by the weight loss procedure. With fat malabsorption, calcium is saponified by the fat, allowing free oxalate to be reabsorbed. This leads to increased serum oxalate with subsequent hyperoxaluria and acute oxalate nephropathy. The other crystals are incorrect.

4. Which statement is TRUE about women who donate a kidney before becoming pregnant?

- A. They are at increased risk for progression of kidney disease postpartum.
- B. They are at increased risk for adverse outcomes during pregnancy including preeclampsia.
- C. They are NOT at increased risk for adverse outcomes during or after pregnancy if their kidney function is normal and they have no proteinuria.
- D. They are at increased risk for progression of kidney disease but not adverse outcomes during pregnancy.

Answer: B

Explanation:

Kidney donation is associated with increased risk for adverse outcomes DURING pregnancy. The other answers are incorrect and not observed in the described scenarios.

References:

Garg AX, Nevis IF, McArthur E, Sontrop JM, Koval JJ, Lam NN, Hildebrand AM, Reese PP, Storsley L, Gill JS, Segev DL, Habbous S, Bugeja A, Knoll GA, Dipchand C, Monroy-Cuadros M, Lentine KL; DONOR Network. Gestational hypertension and preeclampsia in living kidney donors. *N Engl J Med* 372:124–133,2015.

5. Which statement is TRUE about the use of ACE inhibitors during pregnancy?

- A. Contraindicated, but only in the second and third trimesters.
- B. Contraindicated, but only in the first trimester.
- C. Contraindicated, but they can be used during breastfeeding postpartum.
- D. Contraindicated, they are contraindicated during pregnancy and during breastfeeding.

Answer: C

Explanation:

ACE inhibitors are contraindicated during pregnancy but can be used in the postpartum period during infant breastfeeding.

References:

Cooper WO, Hernandez-Diaz S, Arbogast PG, Dudley JA, Dyer S, Gideon PS, Hall K, Ray WA. Major congenital malformations after first-trimester exposure to ACE inhibitors. *N Engl J Med* 2006;354:2443–2451.

6. A 50-year-old man was admitted to the hospital with abdominal pain and AKI. A subsequent workup demonstrated the presence of acute pancreatitis, and an abdominal computerized tomography (CT) scan showed multiple renal mass lesions. A kidney biopsy revealed an extensive plasma cell infiltrate.



Laboratory results

C3: 65 (nl >80 IU)	Anti-nuclear antibody (ANA): positive 1:40
C4: 15 (nl >20 IU)	WBC: 8500 with 10% eosinophilia

Based on this patient’s clinical presentation, what is the MOST likely diagnosis?

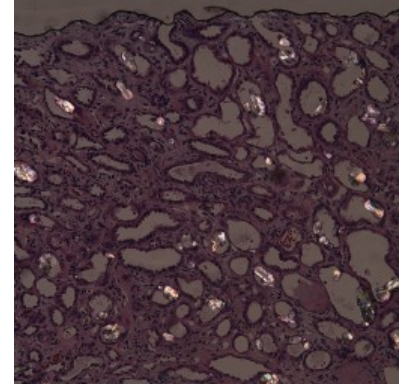
- A. Sarcoidosis with multiple renal granuloma
- B. Myeloma with renal plasmacytomas
- C. IgG4-related systemic disease
- D. Systemic lupus erythematosus (SLE) with systemic vasculitis
- E. Undocumented drug ingestion causing acute allergic interstitial nephritis

Answer: C

Explanation:

This patient presents with IgG4-related systemic disease. It is characterized by a marked plasma cell infiltrate (typically described in a “storiform” cartwheel pattern) that produces expansile destructive lesions. Autoimmune pancreatitis is frequently seen in conjunction with renal disease, but all major organs may demonstrate variable involvement. IgG4 is uniquely deposited in the tubules. The classical complement pathway may be activated with a resultant low C3 and C4, and there may eosinophilia and low-grade ANA titers. A tubulointerstitial nephritis and/or membranous nephropathy is typically seen in the kidney, but obstruction can also occur from the large plasma cell aggregates. Sarcoid and myeloma do not activate complement, nor does acute interstitial nephritis (AIN). None of the other choices are associated with the systemic and laboratory presentation of IgG4-related systemic disease.

7. A 38-year-old morbidly obese woman with a history of CKD, hypertension, osteoarthritis, metabolic syndrome, and gout is started on orlistat 120 mg bid and increased to 120 mg tid (after 1 month) for enhanced weight loss. Medications include enalapril, orlistat, hydrochlorothiazide (HCTZ), naproxen, and glyburide. The patient presents 5.5 weeks later with anorexia, nausea, weakness, and fatigue. She describes 9 days of an exquisitely tender left foot and ankle that are swollen and erythematous. At the time of presentation, she is finishing a 7-day course of trimethoprim-sulfamethoxazole for a urinary tract infection (UTI). Serum creatinine is 3.7 mg/dL (baseline, 1.6 mg/dL). Urine sediment demonstrates red blood cells, white blood cells, renal tubular cells, and a few crystals. A kidney biopsy is performed, and the image is shown under polarization.



Which crystal is seen within the renal tubular lumens on renal biopsy?

- A. Calcium phosphate crystals
- B. Uric acid crystals
- C. Calcium oxalate crystals
- D. Sulfonamide crystals

Answer: C

Explanation:

The patient developed renal failure in the setting of fat malabsorption induced by the weight loss drug orlistat. The urine microscopy reveals calcium oxalate crystals, which reflect the enteric hyperoxaluria that has developed following the malabsorption induced by orlistat. With fat malabsorption, calcium is saponified by the malabsorbed fat, allowing free oxalate to be reabsorbed; this leads to increased serum oxalate with subsequent hyperoxaluria and acute oxalate nephropathy. In the kidney biopsy, calcium oxalate crystals, which polarize positively, are seen within the tubular lumens and are the cause of the AKI. Orlistat is the cause by its mechanism to induce malabsorption. The other options are incorrect as they do not cause acute oxalate nephropathy.

8. A 50-year-old white man has been working in a foundry as a welder for many years. He now presents with an elevated creatinine of 2.3 mg/dL and a urine protein/creatinine ratio of 1.2. There are no old records except for the following information:
- Medical history is positive for hypertension and gout. Smoking history is negative.
 - Renal ultrasound: slightly echogenic but normal size kidneys bilaterally/no stones.
 - EKG: Minimal voltage criteria for left ventricular hypertrophy (LVH).

Urinalysis

Specific gravity: 1.010
 Blood: 0–2 per high power field
 WBC: 0–2 per high power field
 Protein: 1+

What is your assessment?

- A. Patient has unrecognized hypertensive nephropathy
- B. Patient has beryllium nephropathy
- C. Patient has cadmium nephropathy
- D. Patient has lead nephropathy
- E. Patient has mercury nephropathy

Answer: D

Explanation:

Working in a foundry, exposure to heavy metals is a strong consideration (option B or D). The patient could have hypertension nephrosclerosis; but he is Caucasian, and the EKG shows minimal evidence for LVH which would be unlikely in hypertension-induced nephrosclerosis. Cadmium exposure is more likely in a battery plant and has other associations such as bone disease and stones. Cadmium is a well-known cause of hypertension and CKD and gives a picture of chronic tubulointerstitial nephritis with non-nephritic proteinuria and bland urine sediment similar to lead nephropathy but is not associated with gout. Chronic lead toxicity classically has been associated with the triad of gout, hypertension, and CKD, which this patient has. The history for mercury and beryllium toxicity is the wrong environmental exposure.

9. A Chinese patient presented with advanced CKD. No kidney biopsy was performed, but by history, the patient routinely used a variety of Chinese herbs for health and weight loss. He underwent a successful one-haplotype pre-emptive living related transplant from his sister using induction therapy with an IL-2 blocker. Tacrolimus and mycophenolate were used as maintenance immunosuppression with a steroid-free protocol. After 12 months, he now presents with painless gross hematuria but otherwise is afebrile and feeling well.

Labs

Creatinine: 1.2 mg/dL
 Hemoglobin: 12.3 g/dL
 Platelet count: 175,000/mm³
 Urinalysis: 4+ blood, 2+ albumin

Too numerous to count (TNTC) red blood cells (isomorphic)

What is the MOST likely etiology in your differential diagnosis?

- A. Acute humoral-mediated rejection
- B. Renal cell carcinoma of the native kidneys as a consequence of acquired cystic kidney disease and chronic calcineurin exposure
- C. Recurrent IgA nephropathy
- D. Acute BK nephropathy with hemorrhagic cystitis
- E. Transitional cell carcinoma of the native urogenital tract

Answer: E

Explanation:

Patients ingesting Chinese herbs have a high chance of being exposed to *Aristolochia* species plant products. The derivative of these plants, aristolochic acid, is nephrotoxic and leads to a chronic interstitial nephritis. Most importantly is the lifelong risk in these patients of transitional cell carcinoma especially after transplantation, where it may occur in >30% of patients (option E). It has been recommended that a bilateral nephrectomy be considered prior to transplant in patients with aristolochic acid nephropathy. The normal creatinine level and gross hematuria are inconsistent with acute humoral rejection, and the presence of a living donor kidney also makes this less likely. The patient's ethnicity and clinical presentation suggest recurrent IgA nephropathy in the allograft, but RBCs associated with glomerulonephritis should be dysmorphic. The isomorphic RBCs in this case suggest that this is a urologic lesion. BK viremia is an important cause of hemorrhagic cystitis but the risk factors for BK are not present. This patient never had a recently described rejection episode requiring an increase in immunosuppression. In addition, BK nephropathy should be associated with allograft dysfunction. Renal cell carcinoma does occur in transplant patients, but this was a pre-emptive transplant, and acquired cystic disease of the native kidneys is unlikely in the absence of long-term dialysis therapy. This patient most likely has developed a transitional cell cancer of the native urogenital tract from chronic aristolochic acid exposure (option E).

10. A 45-year-old Asian woman has been ordering a variety of alternative medicine compounds over the internet for weight loss. You are very concerned about the fact she takes these unknown supplements and obtain the following tests: BP, 140/90 mm Hg; pulse, 70 beats/min; temperature, 36.5°C.

Labs

Na:	140 mEq/L	Urinalysis:	
K:	3.0 mEq/L	Albumin:	negative
Cl:	95 mEq/L	Blood:	negative
HCO ₃ :	35 mEq/L	WBC:	negative
BUN:	15 mg/dL	Casts:	negative
Cr:	1.0 mg/dL	RBC:	negative

Based on the history and test results, which is MOST likely?

- A. A kidney biopsy is going to show acute interstitial nephritis
- B. The patient is taking star fruit
- C. The patient is taking ephedra-containing compounds
- D. The patient is ingesting products that contain glycyrrhizic acid
- E. The patient is taking high doses of Noni juice

Answer: D

Explanation:

This patient has normal kidney function and a normal urinalysis, so acute interstitial nephritis is not likely. Star fruit is associated with oxalate nephropathy, especially in patients with pre-existing CKD, which is not present in this patient. There are no crystals described in the urinalysis. Ephedra causes hypertension (HTN) and stones and, although this patient has HTN, there is also the presence of hypokalemia. Therefore, when combining hypokalemia, HTN, and alkalosis together, this patient has an excess mineralocorticoid-like syndrome. Although it could be an adrenal adenoma, we know that a similar condition may be present from herbal products that use glycyrrhizic acid as a sweetener (option D). This syndrome is called "apparent" mineralocorticoid excess (AME) to differentiate it from primary hyperaldosteronism. Noni juice can cause hyperkalemia and is not relevant to this patient presentation.

11. Which statement about heavy metal and nonsteroidal anti-inflammatory drug (NSAID) nephrotoxicity is TRUE?

- A. Lead affects the proximal tubule due to the presence of organic anion transporters in this segment
- B. Cadmium affects the distal tubule, leading to type I renal tubular acidosis (RTA)
- C. Gold therapy may result in nephrotic syndrome due to the development of minimal change disease
- D. NSAIDs may cause nephrotic syndrome due to minimal change disease
- E. Platinum-containing chemotherapy agents may cause AKI most commonly from acute interstitial nephritis

Answer: D

Explanation:

NSAIDs cause a unique type of nephrotoxicity characterized by nephrotic range proteinuria with or without AKI from AIN; but when AIN is also present, it is usually without typical AIN coexistent findings of eosinophilia, rash, or fever. The glomerular histology is that of minimal change disease that resolves within weeks of stopping the medication (option D). Lead is a cation, and the organic cation transport (OCT) system (not the organic anion transporter) in the proximal tubule is vital for its absorption and toxicity. Cadmium affects the proximal tubule, and gold causes nephrotic syndrome from membranous disease and not minimal change lesions. Platinum compounds cause acute tubular necrosis (ATN) through both apoptosis and necrosis, especially of the proximal tubule, and do not cause interstitial nephritis.

12. A 28-year-old retired army captain who is otherwise healthy presents with right-sided renal colic. He passed a stone spontaneously but failed to retrieve it. The rest of the history was negative, including family history. He is very active in body building, with daily visits to the gym. Physical examination showed a very muscular young white man with no abnormal findings. A computed tomography (CT) scan that was performed after his renal colic showed a radio-opaque 3-mm stone in the left renal pelvis. Plasma chemistry was entirely normal.

A 24-hour urine analysis showed the following:

Volume:	1.7 L/day	K:	30 mEq/day
Ca:	300 mg/day	P:	1120 mg/day
Oxalate:	25 mg/day	Mg:	65 mg/day
Uric acid:	760 mg/day	SO ₄ :	40 mmol/day
Citrate:	82 mg/day	NH ₄ :	72 mEq/day
pH:	5.6	Creatinine:	2000 mg
Na:	240 mEq/day		

Parameter	Desired value to reduce relative stone risk
Ca	<250 mg/day
Ox	<45 mg/day
Uric acid	<700 mg/day
Citrate	>320 mg/day
pH	5.5–7.0
TV	>2 L/day
Na	<200 mEq/day
K	>50 mEq/day
SO ₄	<30 mmol/day
P	<1100 mg/day
Mg	>60 mg/day
Cl	<200 mEq/day
NH ₄	<45 mEq/day

Which is NOT correct about this patient?

- A. Both the hypercalciuria and hypocitraturia are conferring increased risk for kidney stones
- B. The hyperuricemia and hyperphosphaturia are minor contributors to the stone risk
- C. The hypocitraturia is most likely physiologic in response to acid loading
- D. The high sulfate and low urine pH are promoting calcium oxalate precipitation
- E. There is likely a dietary component to the hypercalciuria

Answer: D

Explanation:

Options A, B, C, and E are correct statements and therefore NOT the correct answer. The stone risk is increased by either and compounded by both hypercalciuria and hypocitraturia. Although hyperuricosuria can increase the risk of calcium oxalate stones and hyperphosphaturia can increase the risk of calcium phosphate stones, they are very mild in this case and contribute relatively very little. Citrate is a major base in the urine and will decrease in response to acid intake. The hypercalciuria is most likely

secondary to high dietary sodium and acid intake. Option D is not correct and therefore the answer is the high sulfate and low urine pH are markers for high acid intake and by themselves do not promote calcium oxalate precipitation.

13. You are asked to evaluate a 45-year-old white woman who has a history of recurrent renal colic. Multiple stones are visible on sonogram, but the plain abdominal x-ray is completely negative. There are no stone analyses on record, but ample uric acid crystals were noted on urinalysis. History is positive for primary hypertension controlled on an ACE inhibitor, hypercholesterolemia treated with simvastatin, and type 2 diabetes treated with metformin and a sulfonylurea. Physical exam reviews an obese female with a body mass index of 35 kg/m². There is no evidence of tophi. The rest of the exam is noncontributory other than obesity. Routine chemistry is within normal limits except for a fasting glucose of 115 mg/dL. Her hemoglobin A_{1c} is 6.7%. Total cholesterol is 180 mg/dL, with LDL of 105 mg/dL.

A 24-hour urine analysis showed the following:

Volume:	2.2 L/day	K:	72 mEq/day
Ca:	143 mg/day	P:	970 mg/day
Oxalate:	20 mg/day	Mg:	70 mg/day
Uric acid:	690 mg/day	SO ₄ :	10 mmol/day
Citrate:	310 mg/day	NH ₄ :	32 mEq/day
pH:	5.0	Net acid:	80 mEq/day
Na:	135 mEq/day	Creatinine:	880 mg/day

Parameter	Desired value to reduce relative stone risk
Ca	<250 mg/day
Ox	<45 mg/day
Uric acid	<700 mg/day
Citrate	>320 mg/day
pH	5.5–7.0
TV	>2 L/day
Na	<200 mEq/day
K	>50 mEq/day
SO ₄	<30 mmol/day
P	<1100 mg/day
Mg	>60 mg/day
Cl	<200 mEq/day
NH ₄	<45 mEq/day

Beware that there are really no true normal values for 24-hour urine. In zero balance state, addition to the body equals output, so the “normal” excretion is what was added to the organism.

Which is MOST correct about this patient?

- She likely has a uric acid stone from high uric acid excretion due to high purine ingestion
- Uric acid crystals are diagnostic of uric acid stones
- The singular most important pathogenic factor is low urine pH
- A major pathogenic factor is high dietary acid intake
- Urolithiasis is occurring as an incidental finding that is not related to her metabolic syndrome

Answer: C

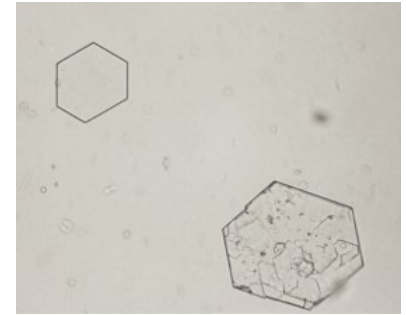
Explanation:

Her 24-hour uric acid excretion is not very high, and even if it is, it is difficult to infer high dietary purine intake on the basis of hyperuricosuria alone (choice A not correct). Uric acid crystal can precipitate in the urine when the urine is concentrated or acidic; however, uric acid crystalluria per se is not diagnostic of uric acid stones (choice B not correct). High dietary acid intake can lower urine pH and is often seen in uric acid stone formers, but her sulfate excretion, which is the best marker for dietary acid intake, in fact is not high (choice D not correct). The low urine pH stems from complex systemic pathophysiologic disturbances including high acid generation and inability of the urine to buffer free H⁺. This is very commonly seen in the metabolic syndrome (choice E not correct). The low urine pH converts urate to the insoluble uric acid, which promotes precipitation and is therefore the most correct statement (choice C is correct).

14. A 19-year-old woman is one of two siblings whose parents immigrated from a small village in a Middle Eastern country. She first presented with renal colic when she was 14 and had suffered from recurrent episodes of renal colic and hematuria. A recent plain x-ray showed two radio-opaque stones in the left kidney and one in the right kidney. Her parents are both healthy, and her older 21-year-old brother is also completely healthy. History is otherwise unremarkable other than the stones. Examination showed a slim 55-kg woman with no abnormal findings. Serum chemistry on several occasions is within normal limits.

A 24-hour urine collection was done. Routine urinalysis showed occasional crystals.

Volume:	1.0 L/day	K:	32 mEq/day
Ca:	110 mg/day	P:	570 mg/day
Oxalate:	18 mg/day	Mg:	57 mg/day
Uric acid:	590 mg/day	SO ₄ :	12 mmol/day
Citrate:	375 mg/day	NH ₄ :	20 mEq/day
pH:	6.1	Creatinine:	705 mg/day
Na:	99 mEq/day		



Parameter	Desired value to reduce relative stone risk
Ca	<250 mg/day
Ox	<45 mg/day
Uric acid	<700 mg/day
Citrate	>320 mg/day
pH	5.5–7.0
TV	>2 L/day
Na	<200 mEq/day
K	>50 mEq/day
SO ₄	<30 mmol/day
P	<1100 mg/day
Mg	>60 mg/day
Cl	<200 mEq/day
NH ₄	<45 mEq/day

Beware that there are really no true normal values for 24-hour urine. In zero balance state, addition to the body equals output, so the “normal” excretion is what was added to the organism.

Which is MOST consistent with the diagnosis in this case?

- A. Alcaptonuria
- B. Cystinuria
- C. 2,8-dihydroxyadeninuria
- D. Primary hyperoxaluria
- E. Xanthinuria

Answer: B

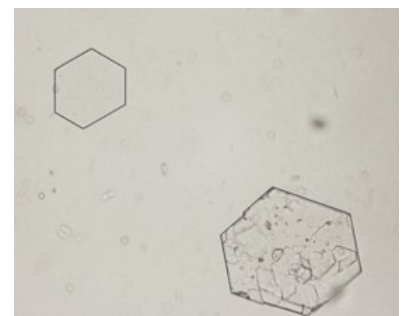
Explanation:

The crystals are diagnostic of cystinuria; no other urinary crystal has this hexagonal appearance.

15. A 19-year-old woman is one of two siblings whose parents immigrated from a small village in a Middle Eastern country. She first presented with renal colic when she was 14 and had suffered from recurrent episodes of renal colic and hematuria. A recent plain x-ray showed two radio-opaque stones in the left kidney and one in the right kidney. Her parents are both healthy, and her older 21-year-old brother is also completely healthy. History is otherwise unremarkable other than the stones. Examination showed a slim 55-kg woman with no abnormal findings. Serum chemistry on several occasions is within normal limits.

A 24-hour urine collection was done. Routine urinalysis showed occasional crystals.

Volume:	1.0 L/day	K:	32 mEq/day
Ca:	110 mg/day	P:	570 mg/day
Oxalate:	18 mg/day	Mg:	57 mg/day
Uric acid:	590 mg/day	SO ₄ :	12 mmol/day
Citrate:	375 mg/day	NH ₄ :	20 mEq/day
pH:	6.1	Creatinine:	705 mg/day
Na:	99 mEq/day		



Parameter	Desired value to reduce relative stone risk
Ca	<250 mg/day
Ox	<45 mg/day
Uric acid	<700 mg/day
Citrate	>320 mg/day
pH	5.5–7.0
TV	>2 L/day
Na	<200 mEq/day
K	>50 mEq/day
SO ₄	<30 mmol/day
P	<1100 mg/day
Mg	>60 mg/day
Cl	<200 mEq/day
NH ₄	<45 mEq/day

What is included in proper management of this condition?

- A. Dietary protein restriction aimed to elevated urine citrate
- B. Lowering the urine pH to 5.0
- C. Allopurinol therapy
- D. Oral α -mercaptopyrionylglycine
- E. Genetic counseling of the family
- F. D and E

Answer: F

Explanation:

A higher urine pH (UpH) will help dissolve the cysteine. Dietary protein restriction may help elevate UpH. However, the urinary citrate is a little low, but this is not a risk for stone formation in this case. Also, the dietary protein intake is not particularly high. Both fluid intake and higher urine pH will help dissolve cysteine. Quantitation of urine cysteine will confirm the diagnosis of cystinuria, and the urinary level is useful in following the patient's response to treatment. Remember that this is not part of the routine stone risk profile. α -Mercaptopyrionylglycine improves solubilization of cysteine. This is an autosomal recessive disease, and the family needs to be educated.

16. A 56-year-old man with morbid obesity, type 2 diabetes, hypertension, and osteoarthritis underwent Roux-en-Y gastric bypass and successfully reduced his body mass index (BMI) from 37 to 28 kg/m². His glycemic control is much improved, antihypertensive dosage reduced, and his osteoarthritis of the knee is virtually gone. While basking in this successful outcome, the clinical progress was disenchanted by a painful episode of renal colic. The patient is otherwise asymptomatic, and physical examination was negative. After spontaneous passage, a computed tomography (CT) scan of the kidney did not reveal any more stones. No stone analysis is available. Laboratory tests in the serum were all normal.

A 24-hour urine showed the following:

Volume:	1.4 L/day	K:	47 mEq/day
Ca:	90 mg/day	P:	1070 mg/day
Oxalate:	49 mg/day	Mg:	56 mg/day
Uric acid:	690 mg/day	SO ₄ :	15 mmol/day
Citrate:	395 mg/day	NH ₄ :	32 mEq/day
pH:	6.0	Creatinine:	1195 mg/day
Na:	123 mEq/day		

Parameter	Desired value to reduce relative stone risk
Ca	<250 mg/day
Ox	<45 mg/day
Uric acid	<700 mg/day
Citrate	>320 mg/day
pH	5.5–7.0
TV	>2 L/day
Na	<200 mEq/day
K	>50 mEq/day
SO ₄	<30 mmol/day
P	<1100 mg/day
Mg	>60 mg/day
Cl	<200 mEq/day
NH ₄	<45 mEq/day

Beware that there are really no true normal values for 24-hour urine. In zero balance state, addition to the body equals output, so the “normal” excretion is what was added to the organism.

Which is MOST important for the increased stone risk in this patient?

- A. Volume depletion from intestinal Na malabsorption is a major contributor to the stone risk
- B. Intestinal bicarbonate wasting is driving a subclinical metabolic acidosis
- C. The metabolic syndrome, although improved, is still putting the patient at risk for uric acid stones
- D. Enteric hyperoxaluria from reduced secretion and increased absorption of oxalate in the intestine is increasing the stone risk
- E. Magnesium malabsorption in the gut is increasing the stone risk

Answer: D

Explanation:

Enteric hyperoxaluria from reduced secretion and increased absorption of oxalate in the intestine is increasing the stone risk and is the most likely reason for increased stone risk (choice D is correct) There is usually not excessive amounts of fluid loss with gastric bypass. This patient’s urine volume is not very low (choice A not correct). Intestinal bicarbonate loss is not a prominent feature of gastric bypass. This patient clearly does not have low urine sodium and citrate, which are hallmarks of intestinal alkali loss (choice B not correct). A metabolic syndrome is perhaps a possibility but the urinary chemistry, particularly the urine pH, is not characteristic of uric acid urolithiasis. The other feature against this model is that the patient did not form stones before the bypass (choice C not correct) when his metabolic syndrome would have put him at a much higher risk. There is occasionally some degree of magnesium malabsorption with this surgical procedure, and low magnesium in the urine can confer some risk in stone formation, but this is not the most important stone risk in this patient (choice E not correct).

17. A previously healthy person has been prescribed a penicillin-containing antibiotic for an upper respiratory tract infection by their internist. After 10 days, the patient presents with clinical findings of an allergic interstitial nephritis.

Which BEST describes what you would find in this patient?

Choice	Kidney size	Skin rash	Eosinophilia	Nephrotic syndrome	Kidney biopsy
A	Small	Absent	Present	Absent	Interstitial B cells and neutrophils
B	Large	Present	Present	Absent	Interstitial T cells
C	Large	Absent	Present	Absent	Interstitial B cells
D	Large	Present	Present	Present	Interstitial T cells
E	Normal	Present	Absent	Absent	Interstitial T cells neutrophils

Answer: B

Explanation:

The classic presentation of a penicillin- or antibiotic-induced interstitial nephritis is the triad of a fever, rash, and eosinophilia. The kidneys are infiltrated by an extensive T-cell population indicating a type IV hypersensitivity etiology for the lesion. The T cells are predominantly CD8 in origin. In addition, there are scattered eosinophils, macrophages, and very rarely B cells. The typical patient has non-nephrotic range proteinuria unless the interstitial nephritis is due to nonsteroidal anti-inflammatory drugs (NSAIDs), when nephrotic syndrome may occur.

18. **Which syndrome is NOT associated with granulomatous interstitial nephritis?**

- A. Tubulointerstitial nephritis and uveitis (TINU)
- B. Sarcoid
- C. Wegener’s
- D. Crohn’s disease
- E. Drug-induced acute interstitial nephritis
- F. All of the above are associated with granulomatous interstitial nephritis

Answer: F

Explanation:

All of the listed diseases can be associated with granulomatous interstitial nephritis. In addition, tuberculosis (TB), Behcet’s, and most drugs that result in classic acute interstitial nephritis (AIN) can be associated with granulomas. The TINU syndrome is very important as a cause of simultaneous ocular and renal involvement.

19. Which statement is TRUE about acute interstitial nephritis (AIN)?

- A. To differentiate AIN from acute tubular necrosis (ATN), a gallium scan can be ordered; the gallium scan will be positive in ATN but negative in AIN
- B. Steroid therapy is ineffective in altering the course of AIN
- C. The presence of WBC casts in the urinalysis excludes drug-induced AIN and is pathognomonic of pyelonephritis
- D. A positive trichrome stain indicates significant fibrosis of the interstitium and predicts the development of CKD
- E. Eosinophiluria is considered diagnostic of AIN

Answer: D

Explanation:

A positive gallium scan indicates the presence of AIN and not ATN. Initiation of steroid therapy, especially within 2 weeks of the diagnosis of AIN, leads to accelerated recovery of renal function and an improved long-term renal function. However, complete recovery of renal function only occurs in 50% of AIN cases, with the remaining cases developing CKD. A trichrome stain indicates the presence of collagen, and therefore, a positive stain will be indicative of a patient with interstitial fibrosis and CKD. The Hansel stain is interpreted as positive once urine eosinophils represent >1% of urine WBCs. Many other causes of urine eosinophils are present other than AIN, including cystitis, prostatitis, and atheroembolic disease; therefore, it is not considered to be a very sensitive or specific test.

20. Which drug is MOST commonly associated with nephrolithiasis?

- A. Acyclovir
- B. Atazanavir
- C. Emtricitabine
- D. Tenofovir
- E. Famcyclovir

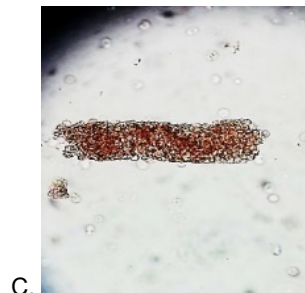
Answer: B

Explanation:

The medication most likely to cause a stone as described is atazanavir. Nephrolithiasis occurs based on the poor solubility of this drug in human urine. It is most soluble in acid urine (pH <4.5) and requires large urine volumes to enhance solubility and prevent precipitation. Acyclovir also is associated with urinary crystals but has not been associated with nephrolithiasis. Emtricitabine and tenofovir do not form urinary crystals. Tenofovir causes proximal tubular injury with AKI and Fanconi syndrome, but Fanconi syndrome could manifest as a proximal RTA which does not lead to stone formation. Famcyclovir is not nephrotoxic.

21. A 58-year-old man with vascular disease, previous MI, hypertension, coronary artery disease, and osteoarthritis developed a rising serum creatinine. He was well until 2 weeks ago when he developed an upper respiratory infection. He was initially treated with azithromycin followed by levofloxacin when symptoms persisted. He now presents with nausea/vomiting, fatigue, and weakness. Vital signs are within normal limits. The exam is unremarkable with no edema, rash, petechiae, or purpura. Labs reveal serum creatinine of 3.3 mg/dL, and urinalysis demonstrates pH 6.0; specific gravity, 1.020; protein 1+; blood 1+; leukocyte esterase 1+; and nitrite negative. You examine the sediment under light microscopy.

Which urine sediment finding in this patient is MOST specific for drug-induced acute interstitial nephritis (AIN) in the patient?



Answer: A

Explanation:

The clinical scenario along with the urine microscopy is vital in identifying various forms of kidney disease – in this case separating AIN from acute tubular necrosis (ATN), glomerulonephritis (GN), and prerenal azotemia. In this case, the finding of a WBC cast strongly suggests AIN from levofloxacin.

22. Which **MOST** closely reflects the overall prevalence of biopsy-proven acute interstitial nephritis (AIN) in biopsies obtained for any clinical indication?

- A. 2–5%
- B. 5–10%
- C. 10–15%
- D. 15–20%
- E. >20%

Answer: A

Explanation:

When examining the kidney biopsy registries of multiple institutions, the prevalence of AIN in these biopsies, obtained for any possible reason, is fairly consistent. The prevalence numbers generally fall between 2% and 5%, with a slight trend for more AIN in recent years.

23. Which **MOST** closely reflects the prevalence of biopsy-proven acute interstitial nephritis (AIN) in patients with AKI?

- A. 5–10%
- B. 10–15%
- C. 15–20%
- D. 20–30%
- E. >30%

Answer: B

Explanation:

In contrast to kidney biopsies obtained for any reason, the prevalence of AIN in biopsies obtained in the setting of AKI is higher. In this setting, AIN is seen in 10–15% of biopsies.

24. Which is the **MOST** common cause of acute interstitial nephritis (AIN) in the United States?

- A. Sarcoidosis
- B. Tubulointerstitial nephritis with uveitis (TINU)
- C. Medications
- D. Viral infections
- E. Sjogren syndrome
- F. IgG4 disease

Answer: C

Explanation:

In the United States and Europe, medications are far and away the most common cause of AIN. Greater than 70% of AIN in developed countries is due to drugs. In contrast, in developing countries, 50% is due to drugs, and 50% is due to infection. The other listed causes make up only a small percentage of the prevalence.

25. In the published literature, which drugs are **MOST** commonly associated with acute interstitial nephritis (AIN)?

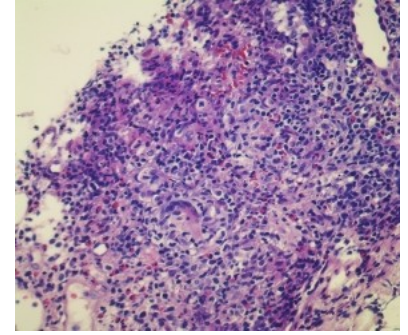
- A. Nonsteroidal anti-inflammatory drugs (NSAIDs)
- B. Antimicrobials
- C. Anticonvulsants
- D. H2 antagonists
- E. Chemotherapeutic agents

Answer: B

Explanation:

Although PPIs are likely the overall leading cause of drug-induced AIN based on their massive worldwide use, the drugs most often noted in the published literature as causing AIN are antimicrobial agents.

26. A 59-year-old woman presents with fever, weight loss, and fatigue for a several-week duration despite broad-spectrum antibiotics. Exam reveals diffuse rash and palpable adenopathy. Severe eosinophilia and AKI are noted. U/A has 2+ proteinuria, 1+ LE. Urine microscopy reveals 6–10 WBCs and 1–5 RBCs/HPF and 2–3 WBC casts/LPF. She undergoes a positron emission tomography (PET) scan for concerns over malignancy when multiple lymph nodes, kidneys, and spleen light up. A kidney biopsy is performed and is shown.



What is the likely cause of this clinical presentation and kidney lesion?

- A. Sarcoidosis with severe granulomatous interstitial nephritis
- B. Severe toxic kidney injury with cortical necrosis
- C. Drug rash, eosinophilia, systemic symptoms (DRESS) syndrome with granulomatous acute interstitial nephritis (AIN)
- D. Lymphomatous infiltration of the kidney
- E. Eosinophilic leukemia with renal infiltration

Answer: C

Explanation:

The clinical scenario is confusing with multiple possibilities; however, the kidney biopsy is diagnostic, showing an inflammatory infiltrate with numerous eosinophils, lymphocytes, and macrophages, as well as granuloma. The diagnosis is eosinophilic AIN in the setting of DRESS. Sarcoidosis can have this renal histopathology, but the presence of fever, eosinophilia, and diffuse skin rash makes it less likely. This is not cortical necrosis on biopsy histopathology. Neither lymphoma nor leukemia cells are seen on biopsy.

27. A 71-year-old woman with hypertension, chronic obstructive pulmonary disease (COPD), coronary artery disease (CAD), ischemic cardiomyopathy, anemia, and stage 3a CKD (Cr, 1.2 mg/dL) was admitted with left lower extremity cellulitis. Intravenous fluids and intravenous piperacillin/tazobactam were administered. On day 8, the patient develops a rising serum creatinine.

In this clinical setting, which will be the MOST diagnostic of drug-induced acute interstitial nephritis (AIN) in this patient?

- A. Clinical history with morbilliform rash and fever
- B. Sterile leukocyturia and WBC casts
- C. Urine eosinophils >5%
- D. Large echogenic kidneys on renal ultrasound
- E. Gallium scan positive at 48–72 hours
- F. Kidney biopsy showing an inflammatory interstitial infiltrate

Answer: F

Explanation:

Clinical history, laboratory findings (including urine microscopy and possibly urine eosinophils), and imaging modalities are all nonspecific and insensitive for the diagnosis of drug-induced AIN. Thus, kidney biopsy demonstrating characteristic histopathology is required to definitively diagnose AIN.

28. A 62-year-old man with coronary artery disease (CAD), hypertension, and type 2 diabetes mellitus (T2 DM) is hospitalized for methicillin-resistant *Staphylococcus aureus* (MRSA) cellulitis of the left leg. Intravenous piperacillin/tazobactam is administered. On day 12 of antibiotics, serum creatinine is noted to increase to 1.9 mg/dL (baseline, 1.1 mg/dL). Kidney function continues to decline over the next 3 days, with serum creatinine increasing to 3.9 mg/dL. Urine microscopy reveals 5–10 RBCs/HPF and 15–20 WBCs/HPF. Urine protein/Cr is 0.74. Renal U/S: bilateral 11-cm echogenic kidneys without hydronephrosis. Kidney biopsy reveals patchy interstitial infiltrate consisting of lymphocytes, plasma cells, and eosinophils, as well as tubulitis, consistent with acute interstitial nephritis (AIN).

In this patient, which is associated with an increased likelihood that kidney function will improve following a course of steroid therapy?

- A. Peak serum creatinine concentration <6 mg/dL
- B. Patchy versus diffuse interstitial infiltrate on kidney biopsy
- C. Steroid therapy initiated within 1 week of diagnosis
- D. Preserved kidney size on ultrasonography
- E. Baseline GFR >60 mL/min/1.73 m²
- F. Proteinuria <1 g/day

Answer: C

Explanation:

None of the laboratory, imaging, or histopathological findings are associated with or predictive of increased renal recovery. Only steroid therapy administered early (within 1 week optimally) appears to increase the likelihood of renal recovery.

29. Steroids are administered to a patient with biopsy-proven acute interstitial nephritis (AIN) due to piperacillin/tazobactam. Serum creatinine (Cr) peaked at 3.9 mg/dL. Serum Cr decreases to 1.9 mg/dL after 10 days. On discharge after 21 days of steroids, serum Cr remains at 1.9 mg/dL.

Which statement about acute interstitial nephritis is TRUE?

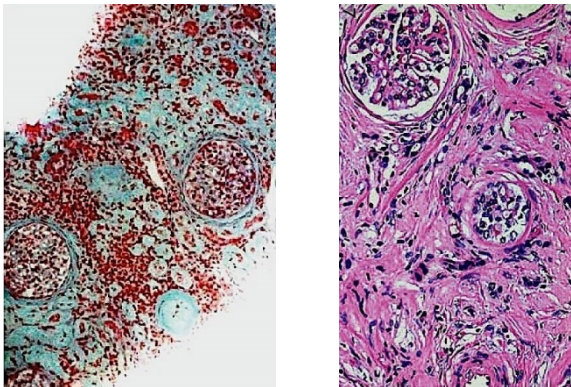
- A. At least 5% of patients with AIN will develop a need for dialysis
- B. Few patients with AIN will develop CKD after drug removal and steroid therapy
- C. Steroids will prevent the development of CKD and ESKD
- D. Those with AIN who develop a need for dialysis are unlikely to recover

Answer: A

Explanation:

Both CKD and ESKD are noted complications of drug-induced AIN, with most published series showing that >5% of patients will require dialysis and as many as 50% develop CKD. Steroids may affect this, but it is unclear at this time.

30. A 49-year-old obese woman with hypertension (HTN), OA, and type 2 diabetes mellitus (T2 DM) presents feeling poorly over the last 4–6 weeks and is noted to have a serum creatinine of 3.2 mg/dL. Medications include glipizide, losartan/hydrochlorothiazide (HCTZ), naproxen, and a health store weight loss regimen (last 2 years). The exam is unremarkable. U/A: 1+ protein, 1+ glucose, trace LE, and trace blood. Urine microscopy: 2–5 WBCs and 1–3 RBCs/HPF, 1–2 waxy casts/LPF. Biopsy is obtained.

**Which is the MOST likely diagnosis?**

- A. Weight loss regimen nephropathy
- B. Obesity-related nephropathy
- C. Nonsteroidal anti-inflammatory drug (NSAID)-induced acute interstitial nephritis
- D. Diabetic nephropathy
- E. HCTZ-induced acute interstitial nephritis

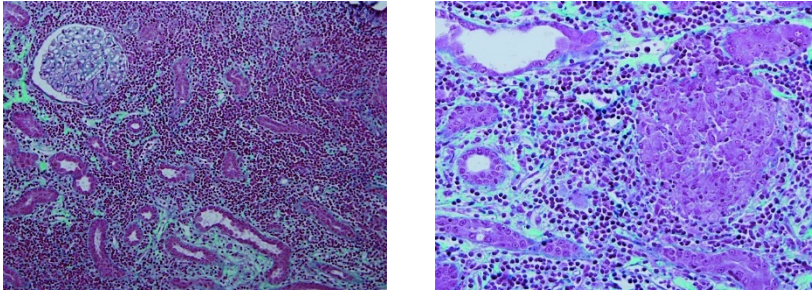
Answer: A

Explanation:

The cause of this renal lesion is aristolochic acid (AA), which is found in contaminated Chinese herbal slimming regimens. AA has also been identified as the environmental agent underlying Balkan-endemic nephropathy. The clinical course is marked by a rapid loss of kidney function and shrunken kidneys with extensive acellular fibrosis on renal histopathology. AA DNA adducts are detected in the kidneys. Patients often develop ESKD and uroepithelial malignancies. The other options do not have this histopathological appearance.

31. A 41-year-old woman presents to her primary care physician with slowly worsening dry cough, polyuria, and generalized fatigue. She describes dry eyes, a rash on her shins, and joint pain, for which she takes ibuprofen. The exam is notable for dry bibasilar lung crackles, tender hepatomegaly, and erythematous shin rash.

Labs: Na, 142 mEq/L; K, 5.3 mEq/L; HCO₃, 18 mEq/L; BUN, 56 mg/dL; sCr, 5.5 mg/dL. Urinalysis: specific gravity, 1004; 1+ pro; 1+ LE; and 1+ blood. Urine microscopy: 5–10 WBCs and 3–5 RBCs/HPF, 1–3 granular casts, and 0–1 WBC casts/LPF. A kidney biopsy is obtained.



What is the MOST likely diagnosis in this clinical setting?

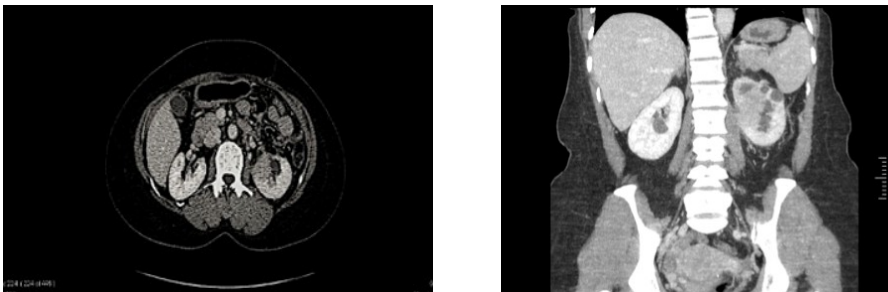
- A. Sjögren’s syndrome with acute interstitial nephritis (AIN)
- B. Sarcoidosis with AIN
- C. Tubulointerstitial nephritis and uveitis (TINU)
- D. Viral syndrome with associated AIN
- E. Nonsteroidal anti-inflammatory drug (NSAID)-associated systemic reaction with associated AIN

Answer: B

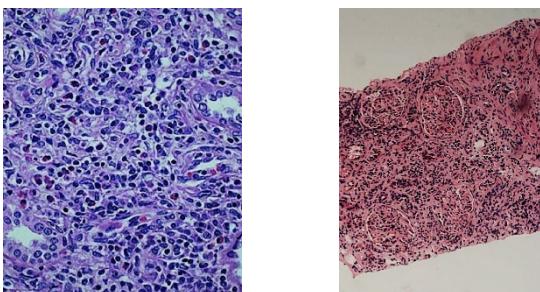
Explanation:

The clinical scenario with pulmonary, eye, skin, and renal involvement, along with the renal biopsy findings of a cellular infiltrate and granuloma, make sarcoidosis the most likely diagnosis. Sjögren’s syndrome usually has eye and kidney involvement (without granuloma) but lacks some of the other signs and symptoms seen in this patient. TINU also has eye and skin involvement, but the eye finding is uveitis. There are no skin or pulmonary findings. Drugs and viruses are also not likely to cause this extensive of a clinical picture.

32. A 61-year-old woman is evaluated for persistent dry cough (despite two different courses of oral antibiotics), malaise, fatigue, low-grade fever, and abdominal pain. Labs reveal the following: WBC, 11.3; Hb, 10.1; Cr, 1.5; and 5–10 WBCs/HPF on urine microscopy. A computed tomography (CT) scan of the chest is performed and shows a left upper lobe infiltrate/mass. A CT scan of the abdomen, performed for abdominal pain, is shown.



The lung mass was biopsied and read as “lymphoplasmacytic infiltrate with reactive changes.” No evidence for cancer with numerous lymphocytes (T and B cells) and plasma cells. A kidney biopsy was obtained to make a definitive diagnosis.



What is the MOST likely diagnosis in this patient?

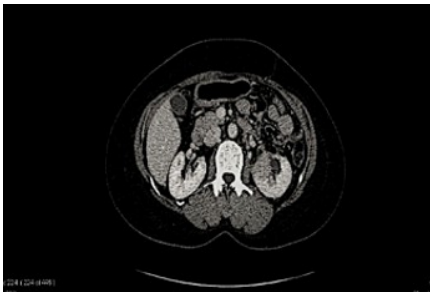
- A. T-cell lymphoma
- B. IgG4 related disease
- C. Sarcoidosis
- D. Castleman’s disease
- E. Eosinophilic granulomatosis with polyangiitis

Answer: B

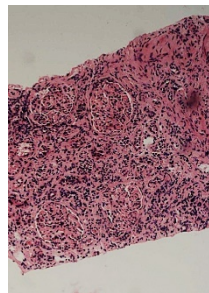
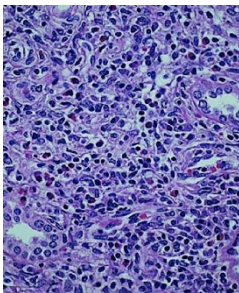
Explanation:

The clinical scenario of malaise, fatigue, low-grade fever, and pulmonary and renal masses noted on imaging and the lymphoplasmacytic infiltrate in lung and kidney tissue makes the diagnosis of IgG4 related disease highly likely. The other diagnoses have different histopathology.

33. A 61-year-old woman is evaluated for persistent dry cough (despite two different courses of oral antibiotics), malaise, fatigue, low-grade fever, and abdominal pain. Labs reveal the following: WBC, 11.3; Hb, 10.1; Cr, 1.5; and 5–10 WBCs/HPF on urine microscopy. A computed tomography (CT) scan of the chest is performed and shows a left upper lobe infiltrate/mass. A CT scan of the abdomen, performed for abdominal pain, is shown.



The lung mass was biopsied and read as “lymphoplasmacytic infiltrate with reactive changes.” No evidence for cancer with numerous lymphocytes (T and B cells) and plasma cells. A kidney biopsy was obtained to make a definitive diagnosis.



What is the MOST appropriate treatment for this patient?

- A. Methotrexate and dexamethasone
- B. Cyclophosphamide and corticosteroids
- C. Corticosteroids alone
- D. Mycophenolic acid and corticosteroids
- E. No therapy is required at this time

Answer: C

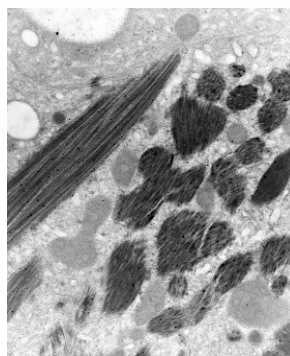
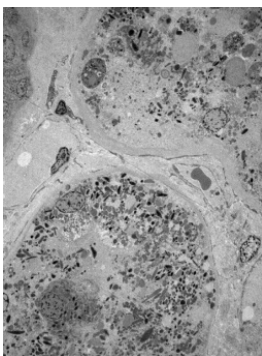
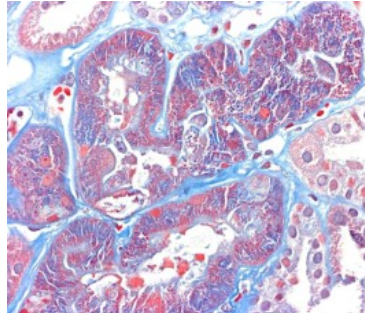
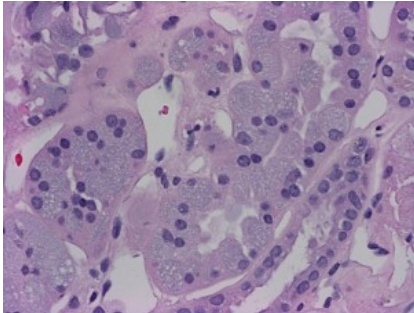
Explanation:

IgG4 is highly responsive to steroids alone. At times, the disease will relapse as steroids are tapered or withdrawn, requiring another course of therapy. Rituximab can be very useful for recurrent disease.

34. A 55-year-old woman with Chronic Obstructive Pulmonary Disease (COPD), hypertension, congestive heart failure (CHF), osteoarthritis, and type 2 diabetes mellitus (T2 DM) presents with progressively worsening weakness. She describes having difficulty getting from the seated to standing position. Medications include inhalers, losartan/hydrochlorothiazide (HCTZ), metformin, carvedilol, naproxen, and aspirin. Vital signs are within normal range. Exam is pertinent for basilar lung crackles, S4 gallop, 1+ ankle edema, and 4/5 muscle weakness.

Labs

Na, 129 mEq/L; K, 2.0 mEq/L; Cl, 105 mEq/L; HCO₃, 14 mEq/L; BUN, 44 mg/dL; serum creatinine, 2.6 mg/dL; glu, 101 mg/dL; Ca, 8.2 mg/dL; and uric acid, 12 mg/dL. Hb, 8.1 g/dL; WBC, 10600/mm³; and Platelets, 100,000/mm³. Total protein is 8.4 grams per 24 hours, and albumin is 3.1 g/dL. U/A: 1+ proteinuria and 2+ glucose. Spot Pro/Cr ratio, 6.1. Urine microscopy: 2–5 granular casts/LPF and 1–3 RBCs/HPF. A kidney biopsy with light microscopy and electron microscopy (EM) is shown.



What is the diagnosis of this renal lesion?

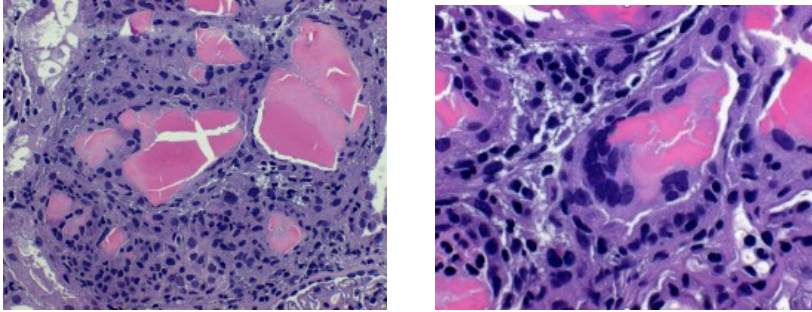
- A. Uric acid crystalline tubulopathy
- B. Naproxen-induced acute tubular injury
- C. Leukemia associated lysozyme-induced tubular injury
- D. Immunotactoid acute tubulopathy
- E. Light chain-induced acute tubular injury

Answer: E

Explanation:

The urinalysis with only 1+ proteinuria but a spot protein creatinine ratio of 6.1 g/g is the key to this case and suggests an overflow proteinuria syndrome as seen most commonly with a monoclonal light chain paraproteinemia. Light chain (LC)-induced acute tubular injury is the correct answer as suggested by the presence of Fanconi syndrome, AKI, and proximal tubules with LC crystals (stain light blue on H&E and dark blue on Masson's trichrome). Significant crystalline inclusions with tubular damage are also seen. On EM, LC crystals appear needle shaped, rectangular, rod-like, and are electron dense. Uric acid crystalline tubulopathy, suggested in this case because the uric acid was elevated, has a different clinical presentation lacking Fanconi syndrome. Although exposure to NSAIDs certainly could exacerbate kidney injury, the clinical presentation and renal histology are not consistent. Although hypokalemia and AKI are consistent with lysozyme-induced tubular injury (the other major overflow proteinuria), the clinical presentation and renal histology (vacuoles) are not. Immunotactoid is a glomerulopathy with large, organized fibrils in the glomerular basement membrane.

35. A 67-year-old man with hypertension, benign prostatic hypertrophy (BPH), and glucose intolerance presents to his primary care provider with back pain for 3 weeks (after vigorous yard work) for which he has been taking ibuprofen. He also takes furosemide, amlodipine, flomax, and baby aspirin. Exam reveals normal VS, mild low lumbar spine discomfort, and trace ankle edema. Labs are drawn and reveal serum creatinine, 4.5 mg/dL; K, 3.2 mEq/L; non-anion gap metabolic acidosis (HCO₃, 15 mEq/L); BUN, 46 mg/dL; sCr, 2.7 mg/dL; serum alb, 3.5 g/dL; uric acid, 10.4 mg/dL; calcium, 11.3 mg/dL; and phosphate, 8.5 mg/dL. Renal ultrasound demonstrated bilateral echogenic kidneys (R, 14 cm; L, 13.8 cm) without hydronephrosis. A kidney biopsy is undertaken, and the light microscopy is shown.



What is the diagnosis of this renal lesion?

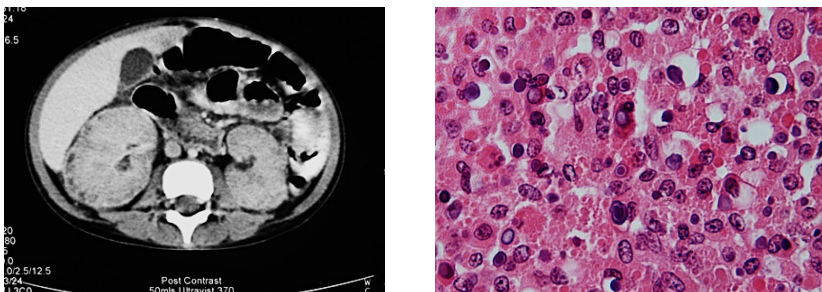
- A. Light chain cast nephropathy
- B. Acute uric acid nephropathy
- C. Acute nephrocalcinosis (calcium-phosphate deposition)
- D. Acute granulomatous interstitial nephritis
- E. Acute infiltrative interstitial nephritis

Answer: A

Explanation:

Light chain cast nephropathy associated with multiple myeloma is correct. The clinical presentation and histology with fractured, glassy casts with associated interstitial reaction/giant cell formation (engulfing casts) are diagnostic of cast nephropathy. Acute uric acid nephropathy from tumor lysis syndrome is incorrect as the clinical presentation and renal histology are not consistent. Acute nephrocalcinosis from calcium-phosphate deposition is possible from the high Ca-Phos product, but the histology is not consistent. Acute granulomatous interstitial nephritis from ibuprofen is possible, but the clinical presentation and lack of granuloma on histology are not consistent with drug-induced acute interstitial nephritis (AIN). Acute infiltrative interstitial nephritis occurs with lymphoma. However, although the kidneys are slightly enlarged, the renal histology does not demonstrate infiltration of the renal interstitium by lymphoma cells.

36. A 57-year-old man is admitted with high fever, fatigue, and R>L flank pain. An exam reveals flank tenderness. AKI is noted with a sCr of 3.1 mg/dL. Urinalysis: specific gravity, 1.015; pH 6.0; 2+ protein; 2–4 RBCs/HPF; 5–10 WBCs/HPF, and 2–3 macrophages/HPF. Urine culture grew Escherichia coli. Renal U/S is abnormal, prompting a magnetic resonance image (MRI). Nephrectomy is undertaken by urology after consultation with radiology and other medical services. The kidney histopathology is shown.



What is the diagnosis in this patient?

- A. Xanthogranulomatous pyelonephritis (XGP)
- B. Emphysematous pyelonephritis
- C. Renal malacoplakia
- D. Renal cell cancer
- E. Chronic bacterial pyelonephritis
- F. Renal tuberculosis

Answer: C

Explanation:

The clinical scenario of renal infection along with the MRI imaging findings and renal histopathology (foam cells with Michelis-Guttman bodies) are diagnostic of renal malacoplakia. Emphysematous pyelonephritis occurs from gas-forming organisms infecting the kidney and is associated with air in renal tissue on imaging and does not have the histopathologic findings noted in

this case. Renal cell cancer is not seen here on histopathology. Renal tuberculosis would have caseating granulomas in the renal parenchyma. XGP often has struvite stones with obstruction and lipid foam cells.

37. In the dialysis unit, a 56-year-old woman who has been receiving dialysis for 3 years from diabetic nephropathy requests attention for a “rash” on her lower abdomen. The rash began as a series of purple nodules, which have now ulcerated and are quite tender.

What is the MOST likely underlying pathology that would be noted on skin biopsy?

- A. Septal panniculitis
- B. Postcapillary venule neutrophilic infiltration
- C. Immune-complex deposition in the dermo-epidermal junction
- D. Proliferation of dermal fibroblasts, thickened collagen bundles, mucin deposition, and increased elastic fibers

Answer: A

Explanation:

The skin lesion described is that of calcific uremic arteriolopathy. Its hallmark on skin biopsy is septal panniculitis.

38. A 46-year-old African-American woman is referred because of detection of dipstick positive proteinuria. She is obese and has had a diagnosis of diabetes mellitus for the last 7 years. She also has moderately controlled hypertension and osteoarthritis. She smokes one pack of cigarettes per day but does not use other drugs or alcohol. Of note, her mother and one of her three siblings also have diabetes mellitus.

Which is TRUE concerning this patient?

- A. Because she has only been diagnosed with diabetes mellitus for 7 years, her proteinuria is probably not due to diabetic nephropathy
- B. African-American women are the group at greatest risk for development of diabetic nephropathy
- C. Type 1 but not type 2 diabetic nephropathy demonstrates Mendelian inheritance
- D. Presence of two high-risk APOL1 alleles increases the risk of developing diabetic nephropathy
- E. Smoking and hypertension are both associated with an increased risk for progression of diabetic nephropathy

Answer: E

Explanation:

Option A is false. Although patients with type 1 diabetes mellitus usually do not develop diabetic nephropathy (DN) until at least 10 years of disease, the time course in type 2 diabetics is more variable because the time of onset of disease may not be known, and even at initial presentation, a minority of patients with type II diabetes actually have overt nephropathy. **Option B is false.** African-American men have the greatest risk for development of DN. **Option C is false.** Although there is evidence for genetic predisposition, strict Mendelian inheritance has not been shown for either type 1 or type 2 DN. **Option D is false.** Although high-risk APOL1 alleles increase the risk of FSGS, hypertensive nephrosclerosis, and sickle nephropathy, it is not a risk factor for DN. **Option E is true.** Hypertension is well documented to increase progression of DN, and most studies have indicated an association of smoking to an increased progression of DN.

References:

Gall MA, Rossing P, Skott P, Damsbo P, Vaaq A, Bech K, Dejgaard A, Lauritzen M, Lauritzen E, Lougaard P, et al. Prevalence of micro- and macroalbuminuria, arterial hypertension, retinopathy and large vessel disease in European type 2 (non-insulin-dependent) diabetic patients. *Diabetologia* 1991;34(9):655–661.

Pollak MR, Genovese G, Friedman DJ. APOL1 and kidney disease. *Curr Opin Nephrol Hypertens* 2012;21(2):179–182.

Yacoub R, Habib H, Lahdo A, Al Ali R, Varjabedian L, Atalla G, Kassis Aki N, Aldakheel S, Alahdab S, Albitar S. Association between smoking and chronic kidney disease: A case control study. *BMC Public Health* 2010;10:731.

39. A 16-year-old European-American man presents with nephrotic syndrome and normal kidney function. His physical exam is normal except for trace ankle edema. Idiopathic FSGS (lesion, not otherwise specified) is present on kidney biopsy. Despite a 6-month course of oral high-dose steroids (with a statin and ACE inhibitor), proteinuria gradually increases from 4 to 8 g/day. Kidney function remains normal. The patient denies a family history of kidney disease, and there have not been consanguineous marriages in the family.

Which genetic screening test is likely to detect a mutation in more than 5% of sporadic FSGS in adolescents?

- A. Mutations in the *WT1* (Wilm’s Tumor 1) gene
- B. Mutations in the *INF2* (inverted formin-2) gene
- C. Mutations in the *NPHS2* (podocin) gene, including p.R229Q variant
- D. Mutations in the *APOL1* (apolipoprotein L1) gene

Answer: C

Explanation:

Adolescents of European ancestry with sporadic (nonfamilial) forms of steroid-resistant nephrotic syndrome (SRNS) are most likely to have causative mutations in the *NPHS2* gene, present in approximately 6% of such cases. Screen first for the p.R229Q variant, followed by analysis of the whole gene if this variant is present. Although *INF2* mutations can produce SRNS, this is only relevant in autosomal dominant forms of disease, and the patient lacks a family history of nephropathy. *APOL1* mutations are a common cause of idiopathic FSGS in individuals of African ancestry. *WT1* mutations are more often associated with syndromic forms of SRNS (e.g., Denys-Drash and Frasier syndromes).

References:

Santin S, et al. Clinical utility of genetic testing in children and adults with steroid-resistant nephrotic syndrome. *Clin J Am Soc Nephrol* 2013;6:1139–1148.

40. A 58-year-old man presents with the nephrotic syndrome, normal BP, and a serum creatinine of 1.5 mg/dL, with a benign urinary sediment. A serum protein electrophoresis is normal. The kappa-lambda light chain ratio is 0.09 (normal, 0.26–1.65); other serologies including serum complement are normal. An echocardiogram shows thickening of the septal wall with preserved ejection fraction.

Which diagnosis is compatible with this clinical picture?

- A. Amyloidosis
- B. Light chain deposition disease (LCCD)
- C. Both
- D. Neither

Answer: C

Explanation:

The very low kappa-lambda free light chain ratio indicates a lambda gammopathy. This is the typical finding in amyloidosis, while kappa gammopathy is more common in LCCD. However, the inverse relationship can exist too, so the type of light serum light chain restriction, while suggestive of the kidney diagnosis, is not definitive. Therefore, since both LCCD and amyloidosis have been associated with cardiac and kidney involvement, the light chain pattern and cardiac presentation are consistent with both diagnoses.

41. A 49-year-old female patient has been given a clinical diagnosis of multiple myeloma nephropathy after she presented with progressive renal failure, lytic bone lesions, and thrombocytopenia. Her protein electrophoresis showed high levels of IgG-kappa.

Which finding may be present in the kidney biopsy?

- A. Fractured tubular casts
- B. Congo red–positive glomerular and tubular deposits
- C. Acute tubular injury/necrosis
- D. Plasma cell infiltrates
- E. All of the above

Answer: E

Explanation:

Although cast nephropathy is the most common finding in myeloma with kidney failure, any of the following entities can occur either alone or in combination: amyloidosis, light, and heavy chain deposition disease, fibrillary/immunotactoid glomerulonephritis (GN), Fanconi syndrome/renal tubular acidosis (RTA) from light chain proximal tubulopathy, membranoproliferative glomerulonephritis (MPGN), infiltration with plasma cells, acute tubular necrosis (ATN), and uric acid nephropathy.

42. During the workup of a patient with proteinuria and mild renal insufficiency, all serologies are negative except for a small IgG-lambda spike on immunofixation. A kidney biopsy is eventually done, and the pathological report is summarized as follows: mesangial deposits that do not stain for Congo red, mild mesangial proliferation, and immunofluorescence shows IgG with kappa and lambda light chains staining with equal intensity. Electron microscopy shows fibrils measuring 25 nm in diameter.

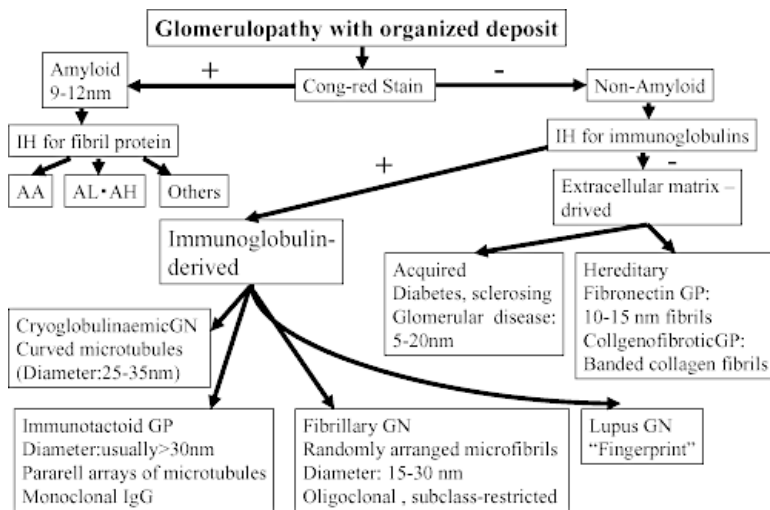
The MOST likely diagnosis is:

- A. Atypical amyloidosis
- B. Fibrillary glomerulopathy
- C. Immunotactoid glomerulopathy
- D. Cryoglobulinemia
- E. Heavy chain deposition disease

Answer: B

Explanation:

When the pathologist finds glomerular deposits, further diagnosis depends on three findings that help define the disease: Congo red staining, immune staining patterns, and the diameter of fibrils, if present, as in the diagram below. A more recent discovery is that a major component of the fibrils is DNA-J heat-shock protein family member B9 (DNAJB9); immunohistochemical staining for DNAJB9 now makes it possible to diagnose FGN in the absence of ultrastructural evaluation.



References:

Joh K. Pathology of glomerular deposition diseases. *Pathol Int* 2007;57(9):551–565.

43. An 18-year-old college student returns from vacation in South America and is admitted with severe bloody diarrhea and fever needing IV fluid resuscitation. On hospital day 5, he is afebrile, and diarrhea has subsided, but he is noted to be increasingly somnolent, and this is followed by a generalized tonic-clonic seizure. Serum chemistries that were normal on admission now show a serum creatinine of 6 mg/dL, and the patient is now oliguric. Stool studies reveal *Shigella dysenteriae*. His platelet count is 20,000/ μ L.

Which is NOT an appropriate treatment for his condition?

- A. Transfusion if Hb <6 g/dL
- B. Antiplatelet therapy with clopidogrel
- C. Hemodialysis
- D. Platelet transfusion prior to placing a dialysis catheter
- E. Eculizumab

Answer: B

Explanation:

In a patient with diarrhea-associated hemolytic uremic syndrome, supportive care including the judicious use of red cell and platelet transfusions, dialysis, and fluid and electrolyte balance is usually adequate until the patient recovers. In the patient with severe neurological manifestations, the use of eculizumab has been proposed even though this is not a primary complement deficiency disorder. Antibiotics, antimotility agents, and antiplatelet agents are not recommended because they are either not useful or associated with harm. In addition, clopidogrel itself is independently associated with developing thrombotic microangiopathy.

44. A 40-year-old white woman presents with sudden onset of facial and lower extremity edema. She had been in excellent health on no prescription or over-the-counter medications. A review of systems was unremarkable for rashes, arthralgias, or oral ulcers. On physical exam, her BP was 110/60 mm Hg, and she had facial swelling and pitting edema extending to the thighs and involving the sacrum. Laboratory data demonstrated a serum creatinine of 1.5 mg/dL, serum albumin of 1.4 g/dL, and serum cholesterol of 600 mg/dL. The complete blood count (CBC) was normal. A urinalysis had 4+ protein with no abnormal sediment, and a 24-hour urine had 20 g of protein. A renal biopsy demonstrated minimal change disease with acute tubular necrosis.

At this point, what is the BEST therapeutic option?

- A. Manage conservatively: sodium and fluid restriction, furosemide, statins, and ACE inhibitors (as tolerated), and wait for spontaneous remission for 6 weeks before treating
- B. In addition to A, begin oral cyclophosphamide and high-dose prednisone daily
- C. In addition to A, begin cyclosporine with high-dose prednisone daily
- D. In addition to A, begin rituximab with high-dose prednisone
- E. In addition to A, begin high-dose prednisone daily or on alternate days

Answer: E

Explanation:

This patient most likely has idiopathic minimal change disease (iMCD). Adult patients with iMCD have an excellent response rate (>90%) to high-dose prednisone (given daily or on alternate days) and conservative treatment (choice E). This response rate is similar to that of children, but the time to response is slower in adults resulting in the need for a more prolonged course of treatment. The use of cyclophosphamide, cyclosporine, rituximab, and even mycophenolate mofetil has been beneficial in iMCD as steroid-sparing agents and thus are used in patients where high-dose steroids alone may be contraindicated such as diabetics or morbidly obese patients. These agents may also be used in iMCD patients with frequently relapsing or steroid-dependent nephrotic syndrome. Although nephrotic patients with minimal change disease can spontaneously remit, this may take years to occur and thus puts patients at increased risk of complications from ongoing nephrotic syndrome. Given the excellent and comparatively rapid response to steroid therapy, a conservative approach alone (choice A) is generally not advocated. A 40-year-old with MCD may warrant a workup for lymphoma and a good history for NSAIA use to determine if it is idiopathic or not.

References:

KDIGO Glomerulonephritis Working Group. KDIGO Clinical Practice Guideline for Glomerulonephritis. *Kidney Int Suppl* 2012;2:139–274.

45. **Which comment regarding adults with the nephrotic syndrome due to idiopathic minimal change disease (MCD) is NOT correct?**

- A. Progression to ESKD is uncommon
- B. It is the most common cause of nephrotic syndrome in children
- C. Spontaneous remission of the nephrotic syndrome does not occur
- D. AKI at presentation is more common in older patients with severe nephrosis and vascular disease on biopsy
- E. The response to steroids may take up to 16 weeks

Answer: C

Explanation:

In untreated adult patients with idiopathic MCD, spontaneous remissions do occur, with similar outcomes as in patients treated with steroids, but may take up to 2 years or more. Given the high remission rate and relatively rapid response to steroid therapy in adults with MCD, most nephrologists would opt to treat patients early on rather than to subject their patients to the significant comorbidities associated with persistence of the nephrotic syndrome (i.e., hyperlipidemia with accelerated atherosclerosis, infections, severe edema, AKI, risk of thromboembolic events).

References:

Hogan J, Radhakrishnan J. The treatment of minimal change disease in adults. *J Am Soc Nephrol* 2013;24:702–711.

46. A 32-year-old black man presented with sudden onset of lower extremity edema. His serum creatinine was 1.8 mg/dL, serum albumin was 2.0 g/dL, and a urinalysis had 4+ protein with 5–10 red blood cells per high power field. A 24-hour urine had 10 g of protein. There is no family history of kidney disease, and he was not morbidly obese. On physical exam, his BP was 160/100 mm Hg and he had 3+ pretibial edema. A serologic workup for secondary causes of the nephrotic syndrome included complement levels, antinuclear antibody titers, hepatitis B surface antigen and antibody, hepatitis C antibody, and HIV antibody, and all were normal or negative. Kidney biopsy demonstrated focal segmental glomerulosclerosis [not otherwise specified (NOS) lesion] and, of the 10 glomeruli in the biopsy, 3 had segmental scars, and there was 15% tubulointerstitial fibrosis; the immunofluorescence was negative, and on electron microscopy, there was diffuse foot process effacement with no evidence of tubuloreticular structures.

The patient was placed on furosemide and ACE inhibitors with some improvement of his BP and lower extremity edema. Additionally, he was placed on high-dose prednisone but continued to have proteinuria of 8 g/d despite being on high-dose prednisone for 16 weeks.

At this point, what is the BEST therapeutic option?

- A. Continue high-dose prednisone for another 1–2 months
- B. Begin cyclophosphamide and taper off prednisone
- C. Begin cyclosporine A in combination with low-dose prednisone
- D. Begin mycophenolate mofetil and taper off prednisone
- E. Begin rituximab and taper off prednisone

Answer: C

Explanation:

Prospective studies support the use of cyclosporine A (often in combination with low-dose prednisone) in the treatment of steroid-resistant FSGS. Although the use of cyclophosphamide, mycophenolate mofetil, and rituximab has been shown to be beneficial as steroid-sparing agents in patients with frequently relapsing/steroid-dependent nephrotic syndrome, these agents have not been as beneficial in the initial induction treatment of steroid-resistant FSGS. The use of continued high-dose prednisone after failing to have any response by 16 weeks would not be advised, as there is little likelihood any further response would occur with another 1–2 months of treatment.

References:

Meyrier A. An update on the treatment options for focal segmental glomerulosclerosis. *Expert Opin Pharmacother* 2009;10:615–628.

KDIGO Glomerulonephritis Working Group. KDIGO Clinical Practice Guideline for Glomerulonephritis. *Kidney Int Suppl* 2012;2:139–274.

47. In nephrotic patients with FSGS, which lesion is associated with highest response rate to treatment with steroids and has the BEST prognosis?

- A. FSGS—not otherwise specified lesion (NOS)
- B. Perihilar lesion
- C. Collapsing lesion
- D. Cellular lesion
- E. Tip lesion

Answer: E

Explanation:

In nephrotic patients with FSGS, the Tip lesion has the greatest response to steroids and the best prognosis, whereas patients with the collapsing lesion are less likely to respond to treatment and have the poorest prognosis. The perihilar lesion is more suggestive of a secondary FSGS etiology.

References:

Korbet SM. Treatment of primary FSGS in adults. *J Am Soc Nephrol* 2012;23:1769–1776.

48. A 65-year-old white man presented with nephrotic syndrome 6 months ago. At that time, he had a normal BP with 4+ pretibial edema. His serum creatinine was 1.0 mg/dL, serum albumin was 2 g/dL, and a 24-hour urine collection had 10 g of protein. The patient had been in good health with no weight loss, night sweats, or fevers and an otherwise negative review of systems. He was on no medications associated with nephrotic syndrome. A serologic workup for secondary causes of the nephrotic syndrome included complement levels, antinuclear antibody (ANA) titers, hepatitis B surface antigen and antibody, hepatitis C antibody, and a rapid plasma reagin (RPR), all of which were normal or negative. His hemoglobin was 14 g/dL, with a normal mean corpuscular volume (MCV). The physical exam was remarkable for a normal BP and significant pretibial edema extending to his thighs but was otherwise negative. A serum anti-PLA2R antibody levels by ELISA were elevated at 200.

Kidney biopsy demonstrated membranous glomerulonephritis. There were no segmental lesions, and the immunofluorescence demonstrated IgG and C3 involving the capillary loops but not the mesangium. Electron microscopy demonstrated widespread subepithelial deposits but no evidence of mesangial deposits or tubuloreticular structures. PLA2R staining was not done on the biopsy specimen. The patient was placed on furosemide, a low sodium diet, and fluid restriction. Additionally, he was placed on ACE inhibitors. Over the course of the next 6 months, although there was improvement in his edema, he continued to have 8 g of proteinuria and edema. He otherwise felt well.

At this point, which is NOT a therapeutic option?

- A. Prednisone alone
- B. Tacrolimus with low-dose prednisone
- C. Prednisone alternating with cyclophosphamide (modified Ponticelli protocol)
- D. Rituximab

Answer: A

Explanation:

The PLA2R level supports the histopathologic diagnosis of idiopathic (primary) membranous glomerulonephritis (MGN). This patient has not gotten better with 6 months of conservative treatment, and therefore a trial of immunosuppression is indicated. Prednisone alone has not been shown to be an effective treatment in numerous prospective controlled trials in patients with idiopathic membranous glomerulonephritis (iMGN), while the other therapeutic options have been shown to be beneficial in iMGN in prospective studies. The recently released MENTOR trial found that rituximab was found to be noninferior to a CNI (cyclosporine) in inducing remission, but remissions lasted significantly longer with rituximab than the CNI. Spontaneous remissions are more likely to occur with lower PLA2R levels.

References:

Cattran D. Management of membranous nephropathy: When and what for treatment. *J Am Soc Nephrol* 2005;16:1188–1194.
 KDIGO Glomerulonephritis Working Group. KDIGO Clinical Practice Guideline for Glomerulonephritis. *Kidney Int Suppl* 2012;2:139–274.

49. You are asked to see a 25-year-old woman at 22 weeks of gestation because her obstetrician detected 1+ proteinuria on routine office dipstick. This is her first pregnancy, and she is unaware of a history of kidney disease and family history is negative. She has noticed some “puffiness” of her ankles. Her BP in the first trimester was 130/84 mm Hg. Her current BP is 122/80 mm Hg. There is 1+ peripheral edema, and a gravid uterus.

Labs

Sodium:	136 mEq/L	Creatinine:	1.2 mEq/L
Potassium:	3.8 mEq/L	Urinalysis:	RBC 25–50/hpf
Chloride:	98 mEq/L		WBC 2–4/hpf
Bicarbonate:	23 mEq/L	Albumin/creatinine ratio:	0.275 mg/g
BUN:	16 mEq/L		

What is the MOST likely diagnosis?

- A. Preeclampsia
- B. ADPKD
- C. Kidney stone
- D. Urinary tract infection
- E. IgA nephropathy

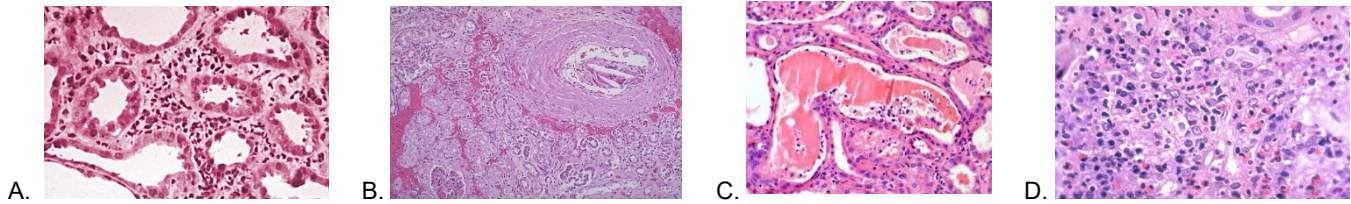
Answer: E

Explanation:

During pregnancy, GFR increases by approximately 50%; thus, a serum creatinine of 1.2 mg/dL represents moderate kidney dysfunction. The differential diagnosis of abnormal renal function at mid-pregnancy includes preeclampsia, preexisting renal disease, and urinary tract infection. In the absence of significant hypertension and proteinuria, it is unlikely that the patient has preeclampsia. Negative family history makes ADPKD unlikely. Moreover, even a sporadic case of ADPKD is likely to have been detected on the 20-week detailed ultrasound. Elevated creatinine is often associated with pyelonephritis during pregnancy, but the absence of fever makes this diagnosis unlikely. There are no suggestive symptoms of renal colic. IgA nephropathy is a common cause of mildly decreased renal function and hematuria, with minimal hypertension and proteinuria.

50. A 67-year-old man with a history of chronic hepatitis C virus infection without cirrhosis and hypertension is admitted to the hospital with 1 week of nonproductive cough and increasing exertional dyspnea. He reports intermittent fevers, for which he has taken over-the-counter ibuprofen. On physical examination, his BP is 114/72 mm Hg, his heart rate is 98 beats/min, and he has bibasilar rales on auscultation of his lungs. His serum creatinine is 5.6 mg/dL, with a sodium of 131 mmol/L, potassium of 4.9 mmol/L, chloride of 112 mmol/L, total carbon dioxide of 18 mmol/L, and calcium of 10.6 mg/dL. His hemoglobin is 10.4 g/dL. On urinalysis he has trace proteinuria by dipstick with many hyaline casts on microscopy. Urine chemistries reveal a sodium of 12 mmol/L, creatinine of 146 mg/dL, and protein of 154 mg/dL.

Which histopathologic finding would MOST likely be present if he were to undergo kidney biopsy?



Answer: C

Explanation:

This patient is presenting with multiple myeloma with acute cast nephropathy (choice C is correct). Clues suggesting the diagnosis include the presence of a very low anion gap (1 mmol/L), hypercalcemia, anemia, and the presence of trace urine protein by dipstick but an elevated urine protein (1.05 mg/mg creatinine) on direct measurement, suggesting the presence of non-albumin protein in the urine. On protein electrophoresis, he was found to have an IgG kappa paraprotein. Choice C shows the classic finding of fractured proteinaceous tubular casts that are characteristic of acute myeloma (cast) nephropathy. Choice A is a biopsy from a patient with acute tubular necrosis, choice B is from a patient with atheroembolic disease, and choice D is from a patient with acute interstitial nephritis.

51. Your new patient with known HIV and relatively stable renal function presents for management of recent onset hypertension and an elevated serum creatinine. His laboratory studies showed the following:

Creatinine 2.0 mg/dl, Urine protein/creatinine ratio 3.4 g/g, Urinalysis 4+ protein and numerous dysmorphic RBCs and RBC casts. His C3 and C4 are low at 55 (nl >80) and 12 (nl >20). His ANA and ANCA are negative. His HIV viral count is 75,000, and his CD4 count is 150.

What does this patient MOST likely have?

- A. HIV-associated nephropathy (HIVAN)
- B. HIV immune complex disease of the kidney (HIVICK)
- C. Unsuspected hepatitis B coinfection
- D. Highly active antiretroviral therapy (HAART) nephrotoxicity
- E. Unsuspected hepatitis C coinfection

Answer: E

Explanation:

This patient has known active HIV and stable kidney function. Historically, HIV was associated with the pathognomonic renal lesion of collapsing FSGS, which is classified as HIV-associated nephropathy (HIVAN). These patients experienced a rapid rate of deterioration and had severe nephrotic syndrome. Patients with HIVAN rarely have hypertension and have normal serum complement levels (therefore, choice A is not likely). HIV immune complex disease of the kidney (HIVICK), showing either predominant IgA nephropathy or diffuse proliferative glomerulonephritis (DPGN) including a lupus-like pattern, has been described, but hypocomplementemia is not associated with this condition either. Hepatitis B is associated with membranous glomerulonephritis (GN) and polyarteritis nodosa but not typically associated with low complement levels (therefore, choice C is not likely). HAART nephrotoxicity is typically a tubulointerstitial disease and does not have a nephritic presentation. Co-infection with hepatitis C may be present in 30%–40% or more patients with HIV depending on demographics and is associated with membranoproliferative glomerulonephritis (MPGN) with or without cryoglobulinemia. The low serum complement levels are characteristic of the presence of immune complexes such as cryoglobulinemia. In cases like this, rheumatoid factor is likely markedly elevated.

52. Match the virus and its associated renal lesion:

Choice	Hepatitis A	HIV	Hepatitis C	Hepatitis B
A	Collapsing FSGS	Acute interstitial nephritis	IgA nephropathy	Acute interstitial nephritis
B	Membranoproliferative glomerulonephritis (MPGN)	Polyarteritis nodosa	Acute interstitial nephritis	Collapsing FSGS
C	Membranous GN	IgA nephropathy	Acute tubular necrosis	MPGN
D	Postinfectious GN	Collapsing FSGS	MPGN	Membranous GN
E	Acute interstitial nephritis	MPGN	Postinfectious GN	IgA nephropathy

Answer: D

Explanation:

Hepatitis A does not result in a chronic carrier state and therefore only (rarely) leads to GN appearing after infection (diffuse proliferative GN). HIV is typically associated with collapsing FSGS, but many other renal lesions are seen, especially HIV immune complex disease of the kidney (HIVICK): often an IgA nephropathy or a diffuse proliferative immune complex GN pattern. Hepatitis C is associated with cryoglobulinemia, membranoproliferative glomerulonephritis (MPGN), and occasionally membranous GN, whereas hepatitis B can be associated with membranous GN, IgA nephropathy, or polyarteritis nodosa. If HIV is most commonly associated with collapsing FSGS, then the only correct choice is D.

53. A patient has been diagnosed with classic HIV-associated nephropathy (HIVAN). He has severe nephrotic syndrome and a recent rise of his serum creatinine from a baseline level of 1.0 to 2.1 mg/dL.

Which treatment may lead to an improvement of his kidney function and nephrotic syndrome?

- A. HAART (highly active antiretroviral) therapy
- B. ACE inhibitors or ARB treatment
- C. Steroid therapy
- D. All of the above
- E. Once established, there is no effective therapy for reversing HIVAN

Answer: D

Explanation:

HIVAN or collapsing FSGS is due to active viral replication in the podocyte and responds with both histologic and functional improvement to HAART therapy and control of viremia. Anti-proteinuric therapies such as ACE inhibitors or ARB have been clearly shown to reduce proteinuria and delay the onset of ESRD. In addition, short-term steroid therapy for patients with severe nephrotic syndrome has been demonstrated to improve renal function and reduce proteinuria. Patients that benefit the most from steroids often have a significant component of interstitial nephritis. Ultimately, patients with HIV that end up on dialysis are candidates for renal transplantation if they have a CD4 count >200 and an undetectable viral load on HAART therapy.

54. **Which statement about HIV-associated collapsing FSGS is NOT true?**

- A. Predominantly diagnosed in patients of black race
- B. Men affected more commonly than women
- C. Primarily seen in cases of advanced HIV infection/AIDS
- D. Radiographic evaluation shows echogenic/occasionally large-sized kidney
- E. Commonly associated with severe hypertension

Answer: E

Explanation:

Typical demographics for a patient with HIV-associated nephropathy (HIVAN) include black males with advanced HIV disease and low CD4 counts. The kidneys may be enlarged due to microcystic dilation, and the parenchyma is usually echogenic. An unusual finding for FSGS is that more than two-thirds of the patients with HIVAN is normotension even in the setting of significant renal disease thought due to a renal sodium tubular leak and cytokine-induced vasodilation. It has also been reported that these patients do not develop edema even in the presence of severe nephrotic syndrome also due to the renal sodium leak and the presence of significant hypergammaglobulinemia offsetting the loss of oncotic pressure from hypoalbuminemia.

55. A patient with hepatitis C has the new onset of uncontrolled hypertension, leukocytoclastic vasculitis of the lower extremity, and AKI. Kidney biopsy shows crescentic membranoproliferative glomerulonephritis (MPGN) secondary to cryoglobulinemia with no evidence of chronicity.

What treatment option is recommended for this situation?

- A. Initiation of Hepatitis C antiviral therapy
- B. Plasmapheresis
- C. Corticosteroids with cyclophosphamide
- D. Rituximab
- E. All the above are options for this patient

Answer: E

Explanation:

The development of cryoglobulins is directly related to active viral replication, which must be controlled using anti-hepatitis C virus therapy. However, additional treatment may be needed because of the presence of acute glomerulonephritis and peripheral vasculitis. Acute removal of the cryoglobulins with plasmapheresis, reducing their production using B cell-depleting therapy with rituximab or cyclophosphamide, and steroids all have been proven to be effective in severe cases of renal cryoglobulinemia. The choice may depend on the acuity of the presentation. If the patient presents with rapidly progressive GN, initial treatment may be plasmapheresis followed by either cyclophosphamide or rituximab. Hepatitis C therapy alone may be appropriate for a more indolent presentation.

56. A 66-year-old Caucasian man has severe degenerative arthritis of the hips and lumbar spine. He has tried Tylenol without successful alleviation of his pain, which is constant and disabling. His rheumatologist now places him on a nonsteroidal anti-inflammatory drug (NSAID) on a daily basis. The pain is controlled, and the patient is much more mobile. After taking the NSAID daily for the last 3 months, new symptoms have developed that include lower extremity swelling and worsening BP.

Laboratory studies reveal the following:

Na: 140 mEq/L	Urinalysis:
K: 5.6 mEq/L	Protein: 4+
Cl: 110 mEq/L	RBC: 1–3/hpf
HCO ₃ : 20 mEq/L	WBC: 1–3/hpf
BUN: 35 mg/dL	
Cr: 2.0 mg/dL	

Physical examination

BP, 160/100 mm Hg; pulse, 80 beats/min
 3+ edema of the lower extremities to the thighs
 Edema of the hands
 Lungs: clear
 Heart: normal rhythm
 Abdomen: normal

What is the MOST likely diagnosis?

- Interstitial nephritis and FSGS
- Interstitial nephritis and minimal change disease
- Interstitial nephritis alone
- Interstitial nephritis and mesangial proliferative GN
- Interstitial nephritis and membranoproliferative GN (MPGN)

Answer: B

Explanation:

This patient has evidence of AKI with nephrotic syndrome. He has been taking NSAIDs, and there is a well-described association of NSAIDs with minimal change disease and acute interstitial nephritis with predominantly lymphocytes. Most patients with this syndrome due to NSAIDs do not develop the triad of fever, rash, and eosinophilia. There would be no reason to suspect de novo FSGS in this patient, and NSAIDs do not result in this lesion. Myeloma kidney is a distinct syndrome of predominant kappa light chain injury with cast precipitation in the distal nephron. The patient would have AKI with non-nephrotic range proteinuria. NSAIDs also have been mildly causally associated with membranous nephropathy and interstitial nephritis, but not MPGN. The hyperkalemia is likely due to RAAS inhibition from NSAID use.

57. A 32-year-old man presents with leukocytoclastic skin lesions on the legs and ears. He has otherwise been in excellent health. He has no history of smoking but does admit to cocaine use. His exam is otherwise normal.

On urinalysis, there are 10–15 dysmorphic red blood cells per high power field, and scattered red cell casts are present. The serum creatinine level is 2.1 mg/dL. Serum complement levels are normal. Anti-nuclear antibody (ANA), proteinase 3-ANCA (PR3-ANCA), and myeloperoxidase-ANCA (MPO-ANCA) are all positive at very high titers.

Kidney biopsy shows a necrotizing and proliferative glomerulonephritis with 2+ staining in the mesangium for IgG.

Which is the MOST likely diagnosis?

- Lupus nephritis
- Autoimmune microscopic polyangiitis
- Cryoglobulinemia
- Drug-induced small vessel vasculitis
- Eosinophilic granulomatosis with polyangiitis

Answer: D

Explanation:

This patient has the classic skin and kidney picture of a small-vessel vasculitis, likely drug induced (choice D). The finding of multiple autoimmune antibodies to both myeloperoxidase (MPO) and proteinase 3 (PR3) and ANA, and at very high levels, suggests a drug-induced vasculitis. It is likely cocaine-induced small-vessel vasculitis associated with levamisole, which is often

used to cut cocaine. Facial necrosis is the classic skin presentation of that entity. It is not unusual for drug-induced vasculitis to have neutropenia on presentation, but granulocyte cell stimulating factor (GCSF) should be avoided because it has been shown to make the vasculitis worse by stimulating production of the pathogenic ANCA antibody. The other more common vasculitis-causing drugs are hydralazine and allopurinol.

References:

McGrath MM, Isakova T, Rennke HG, Mottola AM, Laliberte KA, Niles JL. Contaminated cocaine and antineutrophil cytoplasmic antibody-associated disease. *Clin J Am Soc Nephrol* 2011;6:2799–2805.

58. A 59-year-old man presents with a leukocytoclastic skin rash. Urinalysis reveals numerous dysmorphic red cells per high-power field and red blood cell casts.

Serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase are elevated. Anti-nuclear antibody (ANA), ANCA, and hepatitis serologies are negative. Serum complement studies reveal an undetectable C4 and a low normal C3.

Which is the MOST likely diagnosis?

- A. Lupus nephritis
- B. Myeloperoxidase (MPO)-ANCA small vessel vasculitis
- C. IgA vasculitis (Henoch-Schönlein purpura)
- D. Cryoglobulinemia

Answer: D

Explanation:

Cryoglobulinemia classically presents with a leukocytoclastic rash, often with nephritis and abnormal liver function tests. The hallmark of this disease process is the effect of the cryoglobulins on C4, decreasing it to undetectable levels (often felt to be an in vitro phenomenon), whereas C3 levels are low normal.

59. An 18-year-old man is found to have membranoproliferative glomerulonephritis on kidney biopsy. He has not responded to glucocorticoids. C3 has been persistently depressed. All other serological tests are normal.

Which component of the complement system is MOST likely to be decreased in the serum of this patient?

- A. C1q
- B. C3a
- C. Factor H
- D. C5
- E. Properdin

Answer: C

Explanation:

The abnormalities of factor H, the normal inhibitor of the alternative pathway of complement, have proven to be the most important factor for patients who have membranoproliferative glomerulonephritis, especially those who may be classified with C3 glomerulopathy. Therefore, inhibitors of complement activation (e.g., eculizumab) are being used in the treatment of these patients.

60. A 42-year-old African-American woman presents with a malar rash, alopecia, and nasal ulcers. The serum creatinine level is 2.4 mg/dL. Urinalysis shows one to three red cells per high power field. Urine protein-creatinine ratio is 0.9. C3 and C4 are both depressed. Kidney biopsy demonstrates a thrombotic microangiopathy with only moderate amounts of capillary wall thickening.

Which test would be MOST useful?

- A. Anti-Smith antibody
- B. Anti-double-stranded DNA antibody
- C. Anti-phospholipid antibodies
- D. Anti-myeloperoxidase antibody
- E. Cryoglobulins

Answer: C

Explanation:

In a patient who has many of the features of systemic lupus erythematosus, it is always important to ask the question of whether there is a concurrent anti-phospholipid antibody that may drive a thrombotic microangiopathy, which was found in this case. The relatively bland urine and the finding of thrombotic microangiopathy without major changes of the glomerular capillary wall on kidney biopsy also speak to the presence of an anti-phospholipid antibody.

61. A 52-year-old white woman presents with nephrotic range proteinuria, 4.2 g/24 hr, microscopic hematuria, and serum creatinine of 1.8 mg/dL. Kidney biopsy shows a membranoproliferative appearance with IgG, kappa, and lambda staining, with deposits by electron microscope (EM) in the mesangial and subendothelial areas. These are comprised of randomly arranged nonbranching fibrils.

What is the MOST likely diagnosis?

- A. Amyloidosis
- B. Diabetic fibrillosis
- C. Fibrillary glomerulonephritis
- D. Cryoglobulinemic glomerulonephritis
- E. Immunotactoid glomerulopathy

Answer: C

Explanation:

Amyloid does not show Ig staining and is acellular. Cryoglobulin is typically IgM dominant and shows a short vague substructure or is microtubular. Immunotactoid glomerulopathy (ITG) typically has microtubular (tactoids) substructure. Fibrillary glomerulonephritis (GN) typically is polyclonal with proliferation and shows randomly arranged fibrils (correct answer is choice C).

References:

Herrera GA, Turbat-Herrera EA. Renal diseases with organized deposits: An algorithmic approach to classification and clinicopathologic diagnosis. *Arch Pathol Lab Med* 2010;134(4):512–531.

62. A 73-year-old white man has had a several-month history of sinusitis and intermittent otitis media. He has lost 9 lbs of weight but is afebrile. He has had occasional monoarticular arthritis, migrating from joint to joint. On physical examination, he has crusting in his right nares with an opaque right tympanic membrane. He has mild bilaterally maxillary sinus tenderness. His lung exam is marked by occasional rhonchi. Cardiac exam reveals a grade II/VI systolic ejection murmur at the left sternal border. The abdomen is soft and nontender with no masses. Extremities have 2+ edema.

Laboratory studies

Sodium, serum	139 mmol/L (ref. 135–145 mmol/L)
Potassium, serum	4.2 mmol/L (ref. 3.5–5.0 mmol/L)
Chloride, serum	102 mmol/L (ref. 98–107 mmol/L)
CO ₂	25 mmol/L (ref. 22–30 mmol/L)
BUN	27 mg/dL (ref. 7–21 mg/dL)
Creatinine, serum	1.6 mL/dL (ref. 0.8–1.4 mg/dL)
Hemoglobin	11.5 g/dL (ref. 12.0–16.0 g/dL)
Hematocrit	37% (ref. 36.0–46.0%)
WBC	10,800
Platelet count	340,000
Albumin, serum	3.8 g/dL (ref. 3.5–5.0 g/dL)
Complement C3, serum	105 mg/dL (ref. 88–171 mg/dL)
Complement C4, serum	34 mg/dL (ref. 15–48 mg/dL)
Urinalysis	18 dysmorphic red blood cells, 1 red blood cell cast

Chest x-ray reveals a nodule in the right upper lobe and a hazy density in the left lower lobe.

Which serologic test would MOST likely support the diagnosis?

- A. Anti-nuclear antibody
- B. Anti-glomerular basement membrane antibody
- C. Myeloperoxidase anti-neutrophil cytoplasmic antibody
- D. Proteinase 3 anti-neutrophil cytoplasmic antibody
- E. Anti-double-stranded DNA antibody

Answer: D

Explanation:

This patient most likely has granulomatosis polyangiitis (GPA) and proteinase 3–positive anti–neutrophil cytoplasmic autoantibody. Many of the hallmarks of this disease process are identified, including older age, sinusitis, and intermittent otitis media, suggesting the presence of ear, nose, and throat disease further confounded by crusting in his right nose. A chest x-ray reveals a nodule in the right upper lobe indicative of pulmonary disease and glomerulonephritis manifest by dysmorphic red cells, abnormal renal function, and the presence of peripheral edema. His complement levels are normal; thus, it would be highly unlikely that this patient has lupus nephritis by virtue of his age and sex and because of the normal serum complement levels and the presence of upper and lower respiratory tract disease. The presence of an anti–nuclear antibody or an anti–double-stranded DNA antibody would be unlikely. Most patients with anti–glomerular basement membrane disease are young males, although older females may also develop this disease. Upper and lower respiratory tract disease would be unlikely. The presence of normal serum complement levels further excludes the possibility of systemic lupus erythematosus. This patient could have either a myeloperoxidase or a proteinase 3 ANCA, but it is more likely in the setting of the diagnosis of GPA that he would have a proteinase 3 ANCA, and that is the most reasonable diagnosis.

63. Which form of nephropathy is LEAST strongly associated with autosomal recessive mutations in the apolipoprotein L1 gene (*APOL1*) in individuals of African ancestry?
- Type 2 diabetic kidney disease
 - FSGS
 - HIV-associated nephropathy (HIVAN)
 - Collapsing glomerulosclerosis associated with systemic lupus erythematosus
 - Sickle cell disease–associated nephropathy

Answer: A

Explanation:

APOL1 high-risk alleles are strongly associated with nondiabetic kidney diseases in the spectrum of idiopathic FSGS. These diseases include FSGS, collapsing variant (as in HIV infection and systemic lupus erythematosus), sickle cell nephropathy, and focal global glomerulosclerosis with low-level proteinuria (previously attributed to hypertension). In contrast, *APOL1* is not strongly associated with diabetic forms of nephropathy. Genotyping for *APOL1* has been used to enrich for cases of nondiabetic nephropathy in studies of individuals with African ancestry who have coincident diabetes mellitus and proteinuria.

References:

Freedman BI, Langefeld CD. The new era of *APOL1*-associated glomerulosclerosis. *Nephrol Dial Transplant* 2012;27(4):1288–1291.

64. A 56-year-old man enters the hospital for evaluation of rapidly progressive renal failure. His serum creatinine has risen to 4.5 mg/dL over the last 6 months from a baseline of 1.0 mg/dL. Physical examination is unremarkable. Urinary protein excretion is 4.6 g/24 hours. Urinalysis: 2+ protein and trace blood. Urine microscopy: 1–3 finely granular casts/LPF, 2–5 RBCs/HPF, and 1–3 WBCs/HPF. C3 and C4 were normal. Other serological tests, including ANCA and anti–glomerular basement membrane (GBM), were negative. Concern is raised for an immunoglobulin-related process.

Which laboratory test would produce the highest yield in determining the role of immunoglobulins in this patient's disorder?

- Nephelometric assay for serum free light chains
- Serum protein electrophoresis
- Serum immunofixation electrophoresis
- Urine protein/immunofixation electrophoresis
- The clinical condition is inconsistent with an Ig-mediated process, so only kidney biopsy should be performed

Answer: A

Explanation:

The nephelometric assay for serum free light chains is the best test with highest sensitivity and specificity for a monoclonal gammopathy and thus is preferred over serum or urine immunofixation. Serum protein electrophoresis will miss cases due to its significantly lower sensitivity for monoclonal gammopathies. A kidney biopsy may provide the diagnosis, but it is preferable to confirm the possibility of a paraproteinemia before undertaking the kidney biopsy.

65. In patients with proteinuric stage 4 CKD with increased free serum light chains (LCs) but the absence of bony destruction on evaluation and equivocal bone marrow biopsy results, which statement is correct?
- Elevation of serum free LCs indicates a plasma cell dyscrasia
 - Elevation of serum free LCs is most likely the result of reduced GFR
 - The patient should undergo a kidney biopsy
 - The patient should undergo a positron emission tomography (PET) computed tomography (CT) scan to evaluate for the possibility of malignancy

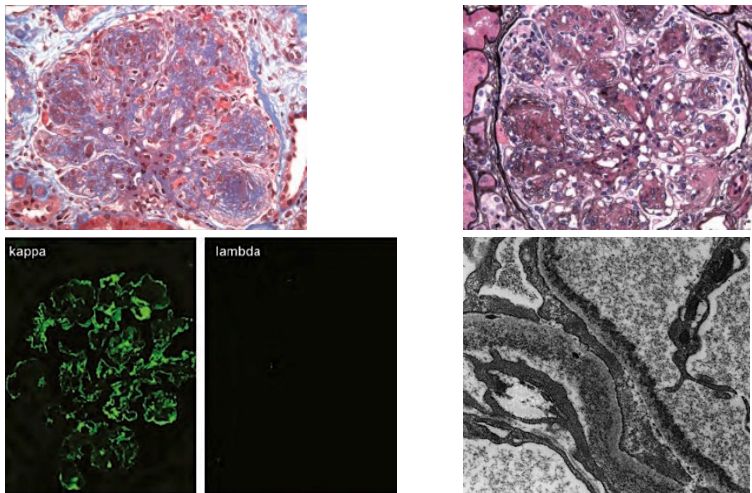
Answer: B

Explanation:

Light chains (LCs) are renally excreted, but their levels will increase in the setting of a decrease in GFR. When this occurs both lambda and kappa will be elevated. A plasma cell dyscrasia is suspected when the kappa/lambda ratio is significantly abnormal. Kappa LC clearance is affected slightly more than lambda in renal failure, and a mild increase in the kappa/lambda ratio can be seen normally with CKD, and this alone does not indicate monoclonality.

Choice B is correct because LCs are filtered at the glomerulus and a reduced GFR will increase in both kappa and lambda LCs. Finding elevated monoclonal LCs and evidence of kidney disease would then be an indication for biopsy. The patient should not undergo a PET CT scan to evaluate for the possibility of malignancy as this is not an appropriate test at this point of clinical evaluation.

66. A 62-year-old man with type 2 diabetes mellitus (T2 DM), hypertension, coronary artery disease (CAD), and hepatitis C virus presents with weakness and fatigue. He is anemic, with an increased serum creatinine from 1.1 to 3.3 mg/dL over 6 months. Exam reveals pale conjunctiva and 2+ LE edema. Electrolytes: Na, 131 mEq/dL; K, 5.2 mEq/dL; Cl, 105 mEq/dL; HCO₃, 20 mEq/dL. U/A has 2+ proteinuria and 1+ blood, and spot Pro/Cr ratio is 6.1. Urine microscopy demonstrates 1–3 waxy casts/LPF and 5–10 RBCs/HPF. The patient undergoes kidney biopsy to establish diagnosis. The first two images are light microscopy followed by immunofluorescence (IF) and electron microscopy (EM).



Which is the MOST likely cause of this patient's rapid decline in kidney function?

- Collapsing FSGS
- Pauci immune glomerulonephritis (GN)
- Light chain deposition disease
- Amyloidosis
- Diabetic nephropathy

Answer: C

Explanation:

The clinical, laboratory, and histopathology data support a diagnosis of light chain deposition disease (LCDD). Kappa restricted light chain staining on IF, nephrotic proteinuria, nodular glomerulus, and granular deposition along basement membranes on EM are diagnostic of LCDD. Amyloid has fibrils on EM. Diabetes is nodular GN but does not have the monoclonal restriction on IF and granular deposits on EM. Pauci immune GN, the lesion typical for a vasculitis, is incorrect as the histopathology should have little to no ("pauci" means few) IF staining or immune deposits on EM.

67. A 67-year-old woman with ovarian cancer recently developed hypertension. Her treatment regimen consisted of debulking surgery followed by six cycles of carboplatin and paclitaxel. Over the last 6 months, she has received therapy with bevacizumab (anti-VEGF), a tyrosine kinase inhibitor, and is benefitting from tumor regression. Her BP was normal when therapy commenced but is now 165/104 mm Hg, rising over the last 3 weeks. Physical examination is unremarkable except for hypertension. Laboratory studies demonstrate normal serum electrolytes, serum creatinine of 1.2 mg/dL, and 3+ proteinuria with a urine protein/creatinine ratio of 1.2 g/g.

At this point, which therapy should be instituted for her hypertension?

- A. No therapy is required at this time
- B. Spironolactone
- C. A dihydropyridine calcium channel blocker (CCB)
- D. Furosemide
- E. Discontinue bevacizumab

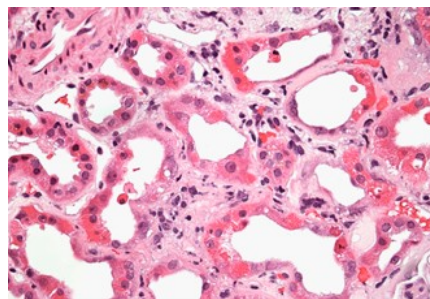
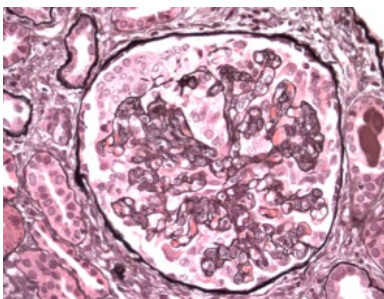
Answer: C

Explanation:

Proteinuria with hypertension is a common adverse effect of anti-VEGF agents. The glomerular lesion is typically a thrombotic microangiopathy, although minimal change disease and FSGS have been described when patients have nephrotic syndrome. The decision to stop the drug is based on the severity of the presentation. When proteinuria is less than 2 g, the general rule is to treat the hypertension and watch, especially when an antitumor effect is present. When proteinuria is about 2 g, the drug is typically stopped until proteinuria improves, and then it may be restarted at a lower dose or a longer interval between treatments. If nephrotic syndrome occurs, then the drug is usually not restarted. Because the proteinuria is "only" 1.2 g, the drug does not have to be stopped, but the hypertension must be treated.

Dihydropyridine CCBs (e.g., nifedipine and amlodipine) are the best choice for treating the hypertension for a few reasons: (1) they target vasoconstriction, (2) they are not associated with GFR reduction, and (3) they do not have any drug-drug interactions with bevacizumab. Non-dihydropyridine CCBs affect P450 metabolism and alter TKI levels and should be avoided. Not starting any therapy is obviously not the correct answer. BP has been increasing over 3 weeks and is currently at 160/100 mm Hg. Spironolactone appears to be a reasonable choice, but it has been shown that anti-VEGF hypertension is associated with low renin-aldosterone levels, making this less optimal. Furosemide is not a first choice for hypertension therapy in a patient with reasonably good kidney function and no evidence to support hypervolemia.

68. A 69-year-old woman with metastatic breast cancer who has been undergoing treatment presents to her primary care physician with complaints of new onset lower extremity edema. Medications include calcium/vitamin D, baby aspirin, amlodipine, naproxen, gemcitabine, paclitaxel, and pamidronate. Exam reveals a BP of 158/92 mm Hg, clear lungs, normal heart sounds, benign abdomen, and 3+ pitting edema to mid-calf. Labs: Na, 134 mEq/L; K, 5.8 mEq/L; Cl, 105 mEq/L; HCO₃, 20 mEq/L; BUN, 62 mg/dL; sCr, 3.8 mg/dL; alb, 2.6 g/dL; Ca, 9.1 mg/dL; phosphate, 5.7 mg/dL; and uric acid, 7.8 mg/dL. U/A: 4+ pro, 1+ blood, trace LE. Urine pro/Cr ratio: 8.5. Urine microscopy: 2–5 granular casts and 0–1 RBC casts/LPF, 5–10 RBCs/HPF (including acanthocytes), 1–3 oval fat bodies/HPF, and amorphous crystals. A kidney biopsy is obtained, and light microcopy is shown below.



What is the cause of kidney disease in this patient?

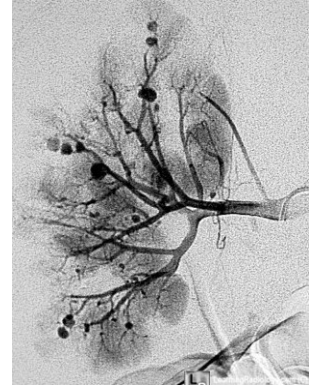
- A. Naproxen
- B. Breast cancer
- C. Pamidronate
- D. Gemcitabine
- E. Paclitaxel

Answer: C

Explanation:

Collapsing FSGS and acute tubular injury are due to pamidronate nephrotoxicity. Based on the pathologic findings, pamidronate toxicity appears to target podocytes and possibly tubular epithelium. Naproxen causes minimal change as well as acute interstitial nephritis (AIN). Gemcitabine has been associated with thrombotic microangiopathy. Breast cancer will cause a membranous lesion, whereas paclitaxel is not associated with glomerular pathology.

69. A 31-year-old woman presented to the Emergency Department with severe headache and visual changes. She also described fatigue, a 7-lb weight loss, and low-grade fever for the last month. BP is 219/112 mm Hg in both arms and legs. Blurred optic disc margins and retinal hemorrhages are observed on eye exam. No abdominal bruits were noted. Labs: hemoglobin, 10.7 g/dL; platelet count, 225 × 1000/μl, and peripheral smear without schistocytes. Serum electrolytes: Na, 135 mEq/L; K, 3.1 mEq/L; and HCO₃, 26 mEq/L. Blood urea nitrogen level was 45 mg/dL, and serum creatinine was 1.7 mg/dL. Urinalysis: specific gravity, 1.012; pH 6.0, trace protein. Urine microscopy: 2–5 granular casts/LPF and 2–5 RTE cells/HPF. A renal arteriogram was performed (see figure).



What is the diagnosis in this patient?

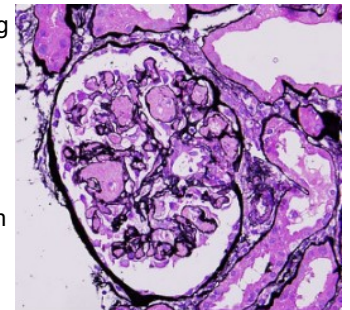
- A. Fibromuscular dysplasia
- B. p-ANCA renal vasculitis (polyangiitis)
- C. Classical polyarteritis nodosa (PAN)
- D. Takayasu’s arteritis
- E. Giant cell arteritis

Answer: C

Explanation:

The clinical scenario and renal arteriogram are diagnostic of classical PAN. Arteriogram demonstrates multiple aneurysms and irregular constrictions in the larger vessels with occlusion of smaller penetrating arteries in the kidneys consistent with PAN. Fibromuscular dysplasia has alternating stenoses and dilatations in the large renal arteries and other end-organ vessels. Takayasu’s arteritis causes stenosis in the aorta and its major branches. Giant cell arteritis involves large- and medium-sized arteries causing stenosis, but primarily involving the extracranial carotid artery. PAN can be idiopathic but often accompanies chronic hepatitis B.

70. A 51-year-old woman presents to the Emergency Department feeling poorly for 2 weeks associated with the new onset of pedal edema and lower extremity rash. Her medical history is significant for chronic low back pain, mild hypertension, pancreatic cancer, atrial fibrillation, obesity, heavy cigarette smoking, and hyperlipidemia. Outpatient medications include naproxen, tramadol, hydrochlorothiazide, sertraline, aspirin, atorvastatin, warfarin, and occasional acetaminophen. She has received three courses of chemotherapy with cisplatin and gemcitabine over the last 8 months. BP is 180/100 mm Hg, with a pulse of 78 beats/min. Physical examination reveals elevated jugular venous pulsations, basilar lung crackles, normal heart sounds with an S4 gallop, benign abdomen, 2+ pitting pedal edema, and a livedo-like rash over the left ankle with an erythematous ulcer. Serum creatinine concentration on admission is 3.2 mg/dL (baseline, 1.1 mg/dL). Electrolytes are normal except for a serum bicarbonate concentration of 18 mEq/L. CBC reveals the following: hemoglobin, 10.2 g/dL; hematocrit, 32%; and platelet count, 155,000. Creatine phosphokinase (CPK) is 1250 U/L, and lactate dehydrogenase (LDH) is 430 U/L. The international normalized ratio (INR) is 2.0. Urinalysis reveals the following: specific gravity, 1.020; pH 5.5; 2+ protein; and 1+ blood. Urine sediment exam under a high-power field reveals 5 renal tubular epithelial cells, 20–30 isomorphic RBCs, and 2–5 dysmorphic RBCs/HPF, 2–5 WBCs/HPF, and 2 granular casts/LPF. Serum creatinine increases over the next 3 days despite discontinuing all medications (5.3 mg/dL). A kidney biopsy is shown.



What is the lesion noted on kidney biopsy?

- A. Membranoproliferative glomerulonephritis (GN)
- B. Thrombotic microangiopathy
- C. Light chain deposition disease
- D. Idiopathic nodular glomerulosclerosis
- E. Focal and segmental necrotizing GN

Answer: B

Explanation:

The clinical scenario and kidney biopsy are consistent with thrombotic microangiopathy from gemcitabine. Naproxen can cause minimal change. The biopsy shows intraglomerular thrombi. The clinical scenario and kidney biopsy are consistent with thrombotic microangiopathy from gemcitabine (correct answer B). Naproxen can cause minimal change. Warfarin can be associated with

heavy glomerular bleeding when the INR gets very high (this patient's INR is therapeutic). This is referred to as "Warfarin nephropathy" (although it can be seen with other anti-thrombotic agents as well). On biopsy, the only finding is RBC casts. Heavy cigarette smoking is associated with idiopathic nodular glomerulosclerosis. Atorvastatin may cause rhabdomyolysis and AKI from myoglobinuric tubular injury. Heavy cigarette smoking is associated with idiopathic nodular glomerulosclerosis. Atorvastatin may cause rhabdomyolysis and AKI from myoglobinuric tubular injury.

71. A 73-year-old woman with a history of hypertension for 10 years and osteoarthritis presents with complaints of new onset lower back pain and progressively worsening fatigue. Examination reveals a BP of 160/94 mm Hg, pale conjunctivae, clear lungs, and normal heart sounds. The lower lumbar spine is tender to palpation, and the ankles have 3+ pitting edema.

Laboratory data reveal an Hb of 7.2 g/dL and serum creatinine of 3.9 mg/dL. Urinalysis: 3+ proteinuria. Bone marrow biopsy: consistent with multiple myeloma. 24-hour urine collection: 8.5 g of albumin and 1.7 g of monoclonal kappa light chain. Renal biopsy using light microscopy demonstrates nodular lesions in the glomerulus. On electron microscopy (EM), granular deposits are noted along the glomerular and tubular basement membranes and in the glomerular nodules.

Which is the MOST likely diagnosis?

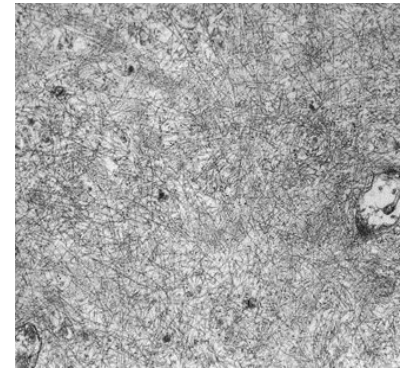
- A. AL amyloidosis of the kidneys
- B. Myeloma cast nephropathy
- C. Immunotactoid glomerulonephritis (GN)
- D. Light chain deposition disease (LCDD)
- E. Fibrillary GN

Answer: D

Explanation:

The clinical, laboratory, and histopathology data support a diagnosis of LCDD. Kappa light chains, nephrotic proteinuria, nodular glomerulus, and granular deposition (along basement membranes and on tubular basement membranes) on EM are diagnostic of LCDD. Amyloid and fibrillary GN have fibrils on EM. Immunotactoid has larger organized deposits on EM. Cast nephropathy is a lesion of the tubules and not the glomerulus.

72. A 65-year-old man presents with bone pain, edema, and progressive weakness. Examination reveals BP of 130/84 mm Hg, pale conjunctivae, clear lungs, and normal heart sounds. The lower lumbosacral spine is tender to palpation, and the ankles have 3+ pitting edema. Laboratory data reveal the following: Hb, 7.7 g/dL; serum creatinine, 4.4 mg/dL; and 3+ proteinuria on urinalysis. Bone marrow biopsy reveals findings consistent with multiple myeloma, and a 24-hour urine collection reveals 6.5 g of albumin and 2.7 g of monoclonal lambda light chain. Renal biopsy using light microscopy demonstrates nodular lesions in the glomerulus. Electron microscopy (EM) of one of the nodules is shown.



Which is the MOST likely diagnosis?

- A. AL amyloidosis of the kidneys
- B. Myeloma cast nephropathy
- C. Immunotactoid glomerulonephritis (GN)
- D. Light chain deposition disease (LCDD)

Answer: A

Explanation:

The clinical, laboratory, and histopathology data support a diagnosis of renal amyloidosis. Lambda light chains, nephrotic proteinuria, nodular glomerulus, and especially the random "haystack" fibrillar deposition in the nodule on EM are diagnostic of renal amyloidosis. LCDD has granular deposits along basement membranes and within nodules. Immunotactoid has larger organized deposits on EM. Cast nephropathy is a lesion of the tubules and not the glomerulus.

73. A 55-year-old African American man with a remote history of intravenous drug use presents with painful red skin lesions and lower extremity edema. He has known diabetes while taking glyburide and hypertension while taking lisinopril. His initial laboratory workup shows a serum creatinine level of 2.1 mg/dL (eGFR 23 mL/min/1.73 m²). Urine shows 3+ protein and 40–50 red blood cells per high power field, 10–20 white blood cells per high power field, and protein/creatinine ratio 5 g/g. Serological workup shows a positive rheumatoid factor, low complement C4 level, normal C3 level, and antinuclear antibody positive at 1:80. ANCA titers are negative.

Which is MOST likely to be shown in a kidney biopsy?

- A. Membranous nephropathy
- B. Membranoproliferative glomerulonephritis with immunoglobulin deposits
- C. Membranoproliferative glomerulonephritis with only C3 deposits
- D. Diabetic nodular sclerosis without any proliferation
- E. Focal segmental glomerulosclerosis

Answer: B

Explanation:

This patient with a vasculitis skin rash, renal insufficiency, nephrotic range proteinuria, and low C4 complement is likely carrying a diagnosis of membranoproliferative glomerulonephritis with immune deposits probably related to hepatitis C infection. Testing for hepatitis C and cryoglobulinemia should be the next step. The positive rheumatoid factor suggests underlying cryoglobulinemia in this patient.

Membranous nephropathy, diabetic glomerulosclerosis, and FSGS are not typically associated with low complement and significant hematuria. Membranoproliferative glomerulonephritis with C3 deposits (C3 glomerulopathy) is associated with low C3 (not low C4).

References:

Cacoub P, Comarmond C, Domont F, Savey L, Saadoun D. Cryoglobulinemia vasculitis. *Am J Med* 2015;128:950–955.

74. A 29-year-old European American man presents with sudden onset of nephrotic syndrome and hypertension. He has preserved kidney function and no reported family history of kidney disease. Physical examination reveals a BP of 149/94 mmHg and has otherwise unremarkable findings except for 1+ bilateral pitting ankle edema. He receives a statin and ACE inhibitor. Kidney biopsy reveals FSGS, lesion not otherwise specified.

Which is MOST appropriate?

- A. Consider immunosuppressive therapy because screening for mutations in adults with sporadic FSGS is not indicated.
- B. Test for mutations in the *INF2* (inverted formin-2) gene.
- C. Test for mutations in the *NPHS2* (podocin) gene, especially the p.R229Q variant.
- D. Test for mutations in the *APOL1* (apolipoprotein L1) gene.
- E. Test for mutations in the *TRPC6* (transient receptor potential cation channel, subfamily 6) gene.

Answer: A

Explanation:

European American adults with sporadic (nonfamilial) forms of FSGS are highly unlikely to have causative mutations detected. Although screening for the p.R229Q variant in the *NPHS2* (podocin) gene can be considered for family planning purposes, few such mutations will be detected in settings such as this one. Podocin mutations are common causes of childhood steroid-resistant nephrotic syndrome with autosomal recessive inheritance (the *NPHS2* p.R229Q variant is permissive, allowing disease with one *NPHS2* disease-causing variant). Although mutations in *INF2* and *TRPC6* cause adult FSGS, this is relevant in autosomal dominant forms of disease: this patient lacks a family history of nephropathy. *APOL1* mutations are common causes of idiopathic FSGS in individuals of African ancestry. The sudden onset and severe nature of this presentation suggest that this is a primary FSGS lesion.

References:

Santin S, Bullich G, Tazon-Vega B, Garcia-Maset R, Gimenez I, Silva I, Ruiz P, Ballarin J, Torra R, Ars E. Clinical utility of genetic testing in children and adults with steroid-resistant nephrotic syndrome. *Clin J Am Soc Nephrol* 2013;6:1139–1148.

75. A 23-year-old woman is referred for hypertension and hypokalemia. BP is 150/90 mm Hg and K⁺ is 2.9 mEq/L despite therapy with amlodipine, carvedilol, and potassium supplements. She has a positive family history of hypertension in her mother (discovered in the first trimester of the first pregnancy) and brother who died suddenly of a hemorrhagic cerebrovascular accident (CVA) last month. Exam: BP, 148/98 mm Hg with a body mass index (BMI) of 30 kg/m².

Evaluation: 138 | 100 / 9 Plasma renin activity 0.9 (nl), plasma aldosterone 46 (↑)
 2.9 | 28 \ 0.7 Glucose, thyroid stimulating hormone (TSH), and serum cortisol normal

24-hour urine (after oral salt loading) = Na⁺ 272 mEq/day, K⁺ 103 mEq/day, creatinine 1.1 g/day, aldosterone excretion rate (AER) 29 (<14 normal), ↑ 18-OH cortisol

What is the MOST appropriate therapy for this patient?

- A. ACE inhibitors
- B. Amiloride
- C. Spironolactone (SPLT)
- D. SPLT and dexamethasone
- E. Triamterene hydrochlorothiazide

Answer: D

Explanation:

This is a classical presentation of glucocorticoid remediable aldosteronism (GRA) in a young lady with hypertension and hypokalemia with a family history of early onset hypertension and hemorrhagic stroke. Biochemical evaluation confirms urinary potassium wasting with increased urinary excretion of aldosterone and 18-OH cortisol during salt loading. In patients with this aldosterone synthase genetic mutation, the zona fasciculata of the adrenal gland produces aldosterone and cortisol induced by adrenocorticotropic hormone (ACTH). Appropriate therapy is dexamethasone to suppress ACTH and an aldosterone antagonist to reduce urinary K⁺ losses.

The positive familial hypercholesterolemia and early-age hypertension with hypokalemia point toward GRA and Liddle syndrome. However, in Liddle syndrome, aldosterone is suppressed, as it is in other syndromes of "apparent mineralocorticoid excess," such as excess licorice ingestion and ACTH-producing tumors. Clinically, it looks like primary hyperaldosteronism, but aldosterone and renin are suppressed.

Amiloride blocks the ENa⁺C channel of Liddle's syndrome; and while SPLT blocks aldosterone's effect on the principal cell, you still need to suppress ACTH with a glucocorticoid in GRA. Treatments with ACE or triamterene hydrochlorothiazide (HCTZ) are nonspecific therapies.

References:

McMahon GT, Dluhy RG. Glucocorticoid-remediable aldosteronism. *Cardiol Rev* 2004;12:44.

Stowasser M, Bachmann AW, Huggard PR, et al. Treatment of familial hyperaldosteronism type I: Only partial suppression of adrenocorticotropic required to correct hypertension. *J Clin Endocrinol Metab* 2000;85:3313.

76. A 22-year-old woman is being evaluated for resistant hypertension and hypokalemia despite therapy with amlodipine, labetalol, losartan, and spironolactone. Within the last 4 years, she has experienced three episodes of pregnancy-associated severe hypertension and hypokalemia in her late third trimester requiring a caesarean section. There were no other features of eclampsia or renal disease. Her younger sister had experienced a similarly complicated pregnancy last month.

Labs: 139 | 98 / 9 PRA, 1.1 (normal <4)
3.1 | 28 \ 0.6 Plasma aldosterone, -3.1 (normal 4–15); urinalysis normal

What is the MOST appropriate diagnosis and management for her current resistant hypertension and hypokalemia?

- A. Diagnosis of primary aldosteronism exacerbated by pregnancy requiring increased spironolactone therapy
- B. Diagnosis of renal artery stenosis due to fibromuscular dysplasia exacerbated by pregnancy requiring percutaneous renal angioplasty
- C. Diagnosis of glucocorticoid remediable aldosteronism (GRA) exacerbated by pregnancy requiring the addition of dexamethasone to her spironolactone
- D. Diagnosis of mineralocorticoid receptor mutation (Geller's syndrome) exacerbated by pregnancy requiring discontinuation of spironolactone

Answer: D

Explanation:

The mineralocorticoid receptor mutation (Geller's syndrome) is a rare disorder that presents as severe hypertension with metabolic alkalosis and hypokalemia in young women during the second and third trimester of pregnancy when progesterone levels are highest. The mutation is transmitted by an autosomal dominant inheritance, and the MR 810 mutation is activated by progesterone (which blocks the normal aldosterone receptor but has the opposite effect in Geller syndrome), and thus the pregnant woman with this mutation will present like other causes of "apparent mineralocorticoid excess": hypertension, hypokalemic metabolic alkalosis with suppressed renin, and aldosterone. Spironolactone (also normally an aldosterone receptor blocker) acts like progesterone in this condition in that it normally is also an aldosterone antagonist that becomes an agonist, thereby worsening hypertension and hypokalemia when administered. Urgent management during the third trimester of pregnancy often requires delivery, and subsequent management includes avoidance of spironolactone. The low PRA and primary aldosteronism exclude the other diagnoses listed including primary aldosteronism, GRA, and renal artery stenosis (RAS).

References:

Geller DS, Farhi A, Pinkerton N. Activating mineralocorticoid receptor mutation in hypertension exacerbated by pregnancy. *Science* 2000;289:119–123.

77. A 30-year-old man with a history of alcohol abuse is brought to the emergency department after being “found down” in a local park. He is confused; not answering any questions; and, at times, is combative. On examination, he is afebrile, BP is 90/40 mm Hg, pulse is 110 beats/min, and respiratory rate is 30 breaths/min. He is disheveled with dilated pupils and hyperemic optic discs. A noncontrast head computed tomography (CT) scan reveals diffuse cerebral edema and ill-defined densities in the putamen.

Laboratory studies

Serum sodium: 149 mEq/L	Serum creatinine: 1.1 mg/dL
Serum potassium: 4.8 mEq/L	Serum glucose: 168 mg/dL
Serum chloride: 111 mEq/L	Serum lactic acid: 1.8 mmol/L
Serum bicarbonate: <5 mEq/L	Posm: 444

What is the MOST likely toxic ingestion?

- A. Isopropyl alcohol
- B. Ethanol
- C. Methanol
- D. Ethylene glycol
- E. Propylene glycol

Answer: C

Explanation:

The patient presents with an anion-gap acidosis associated with a large osmolal gap suggesting toxic alcohol ingestion. The findings of hyperemic optic disks and putamen swelling are suggestive of methanol intoxication.

The clinical findings in methanol intoxication often develop in a characteristic manner. Changes in mentation as a result of methanol are present within the first 6–24 hours but can be the only abnormality for as long as 72–96 hours if patients have also ingested ethanol. The absence of more prominent signs or symptoms at this stage can delay recognition of this disorder. As methanol is metabolized to formic acid, visual and more severe neurologic abnormalities become prominent.

Isopropyl alcohol ingestion would lead to an osmolal gap without a concomitant anion gap, as isopropyl alcohol gets metabolized to acetone which is a weak acid, and thus you see ketosis without acidosis. Ethylene glycol ingestion can lead to a similar laboratory picture as methanol ingestion. However, putamen swelling is not found with ethylene glycol ingestion. Ethanol ingestion may be associated with ketoacidosis, typically after a patient stops drinking, and the osmolal gap is usually small at this point. Propylene glycol is the carrier (solvent) that is used to administer intravenous lorazepam or diazepam. Infusion of either drug usually in the ICU setting may be complicated by propylene glycol toxicity. Propylene glycol toxicity is characterized by hyperosmolarity (osmolal gap) and an anion gap metabolic acidosis, which is often accompanied by AKI and can progress to multisystem organ failure, if severe. It can occur with normal doses and renal function, but it is usually associated with dosages above the recommended range of 0.1 mg/kg/hour and/or renal impairment. The clue to this case is the high anion gap high osmolal gap metabolic acidosis with references to the problems with the eye or vision.

78. A 28-year-old man is referred for evaluation of hypertension. He believes that his hypertension was first diagnosed at age 16 but he was never told what the etiology may be. Of note, his father died at age 42 with a stroke, and he has a brother age 23 with hypertension. On physical examination, he is normal appearing with a BP of 170/100 mm Hg, and his fundoscopic examination reveals mild arteriolar narrowing. There are no abdominal bruits.

Laboratory studies

Serum sodium: 144 mEq/L	Serum creatinine: 1.1 mg/dL
Serum potassium: 3.1 mEq/L	Urine potassium: 89 mEq/24 hr
Serum chloride: 107 mEq/L	Plasma aldosterone: 6 ng/dL
Serum bicarbonate: 29 mEq/L	Plasma renin activity: 0.5

Which would be the MOST likely cause of his hypertension and associated laboratory findings?

- A. Gordon’s syndrome
- B. Liddle’s syndrome
- C. Glucocorticoid remediable hypertension
- D. Gitelman’s syndrome
- E. Primary hyperaldosteronism

Answer: B

Explanation:

Gordon's syndrome (pseudohypoaldosteronism type II) is typified by hyperkalemia and metabolic acidosis and would not fit this presentation. Gitelman's syndrome is notable for the absence of hypertension.

The differential diagnosis for a patient with hypertension and renal potassium wasting (as in this case) includes primary aldosteronism (high aldosterone, low renin), glucocorticoid remediable aldosteronism (high aldosterone, low renin), malignant hypertension (high renin, high aldosterone), as well as other syndromes of apparent mineralocorticoid excess (Licorice, Cushing's syndrome, and Liddle's syndrome – all with low renin, low aldosterone as this patient has). The positive family history suggesting autosomal dominant suggests Liddle's syndrome or glucocorticoid remediable hypertension, but the latter has a high aldosterone level not present in this case. The finding of a plasma aldosterone level of 6 excludes primary aldosteronism. Thus, Liddle's syndrome is the most likely etiology.

79. A 32-year-old man is brought to the emergency department because he is agitated and combative. His friend states that he is into "alcohol and all sorts of other inhalants and intravenous drugs" but cannot specify any substances that the patient may have used today. The patient is uncooperative and tachypneic but appears to be in generally good health.

Laboratory studies

BUN:	10 mg/dL	Arterial blood studies:	
Serum creatinine:	1.0 mg/dL	PO ₂ :	82 mm Hg
Plasma glucose:	175 mg/dL	PCO ₂ :	21 mm Hg
Serum electrolytes:		Bicarbonate:	20 mEq/L
Sodium:	140 mEq/L	pH:	7.55
Potassium:	3.1 mEq/L	Serum ketones:	Positive in 1:64 dilution
Chloride:	111 mEq/L	Urine ketones:	3+
Bicarbonate:	21 mEq/L	Urine glucose:	1+

Which is the MOST likely cause of this clinical syndrome?

- A. Diabetic ketoacidosis
- B. Alcoholic ketoacidosis
- C. Isopropyl alcohol ingestion
- D. Methanol ingestion
- E. Toluene inhalation

Answer: C

Explanation:

This patient has a primary respiratory alkalosis with a pH of 7.55 and a PCO₂ of 21. In terms of acute compensation, the expected decrease in serum bicarbonate is 0.2 mEq/L per 1 mm Hg, or $0.2 \times 19 = 3.8$ mEq/L, so the bicarbonate of 20 mEq/L seems appropriate. The patient has a normal anion gap, so there is no evidence of an anion gap metabolic acidosis, which makes diabetic ketoacidosis, alcoholic ketoacidosis, and methanol ingestion incorrect answers.

The patient has marked ketonemia and ketonuria, which are classic for isopropyl alcohol ingestion because isopropyl alcohol is metabolized to acetone. Remember that acetone, while a ketone, is a very weak acid, so ingestion of acetone results in ketosis without acidosis.

Isopropanol intoxication results from its accidental ingestion or its use in suicide attempts or when used in lieu of ethanol. The most common laboratory abnormality is an increase in the serum osmolality. Metabolic acidosis is usually absent, unless hypotension is sufficient to produce lactic acidosis. Because one of the major metabolites of isopropanol is acetone, the nitroprusside reaction will be positive. The triad of normal acid–base parameters, hyperosmolality, and a positive nitroprusside (urine ketones) reaction of urine and/or blood should suggest this diagnosis. Supportive measures are often sufficient if the patient is not comatose and/or hypotensive. If hypotension is present along with coma, then initiation of hemodialysis has been recommended. Given the effectiveness of dialysis in removing isopropanol and the safety of this procedure, it seems reasonable to initiate hemodialysis in the presence of severe coma, hypotension, or serum isopropanol levels >200 mg/dL. Since acetone (the primary metabolite) is less toxic than isopropyl alcohol (the parent alcohol), there is no indication for alcohol dehydrogenase inhibition with fomepizole or ethanol following isopropyl alcohol exposure.

Toluene (glue sniffing) results in a severe non-anion gap metabolic acidosis (not present here) that may appear to be distal RTA because the urinary anion gap is also positive. But this finding is not from a lack of urinary NH₄⁺, which is the hallmark of D-RTA; the urinary anion gap is positive, even though there is adequate NH₄⁺ excretion, because of anion metabolites (benzoate and hippurate) that are easily excreted by the kidney. Distinguish toluene from D-RTA by determining the urinary osmolal gap; if it is above 150 mOsm/kg in metabolic acidosis, NH₄⁺ production is adequate.

References:

Kraut JA, Kurtz I. Toxic alcohol ingestions: Clinical features, diagnosis and management. *Clin J Am Soc Nephrol* 2008;3:208–225.

80. A 58-year-old woman with CKD stage 4 is admitted to the hospital with protracted vomiting. The following laboratory data are obtained:

Na = 145, K = 4, Cl = 100, HCO₃ = 25 mEq/L
 BUN = 75, Cr = 5, Alb = 3.8
 pH = 7.4, PCO₂ = 40, HCO₃ = 25

Which is TRUE regarding this patient's acid–base status?

- A. Simple metabolic alkalosis
- B. Simple metabolic acidosis
- C. Mixed metabolic acidosis–metabolic alkalosis
- D. Normal acid–base status

Answer: C

Explanation:

Although this patient has a normal pH, the presence of a markedly elevated anion gap (AG = 20) indicates an acid-base problem. In this case, the patient has both metabolic acidosis and alkalosis that essentially cancel each other out. They are both hidden. The clinical history of vomiting and CKD should also be an important clinical clue. Diabetic ketoacidosis with vomiting or CKD with severe volume depletion can be explanations in this case as well. As you take the exam, always calculate the AG even if the HCO₃ is not low.

81. A stuporous 22-year-old man is admitted with a history of behaving strangely. His friends indicated he had problems with a girlfriend and had threatened suicide. He had a history of alcohol abuse.

Laboratory

Na = 140 mEq/L, K = 5 mEq/L, Cl = 95 mEq/L, HCO₃ = 10 mEq/L, glucose 125 mg/dL, BUN 15 mg/dL, Posm = 335 mOsm/kg, pH 7.22, PCO₂ 25 mm, HCO₃ = 10 mEq/L
 Ethanol not detected

Which regarding these findings is TRUE?

- A. The osmolal gap is elevated
- B. The anion gap is normal
- C. Empiric treatment with Fomepizole is indicated
- D. A and C
- E. All of the above

Answer: D

Explanation:

In this case, toxic alcohol ingestion should be suspected. The patient's calculated serum osmolality is approximately 289, and thus a large osmolal gap is present along with an anion gap acidosis. This finding should prompt thinking about a toxic alcohol ingestion such as methanol or ethylene glycol. Although definitive toxic alcohol identification is pending, it would be reasonable to start fomepizole to inhibit alcohol dehydrogenase and the metabolism of an agent such as methanol or ethylene glycol to toxic intermediates. The most common cause of an elevation of osmolal gap is ethanol, and thus every patient suspected of a toxic ingestion should have an ethanol level determined. Ethanol can be considered an alcohol dehydrogenase inhibitor because it ties up the enzyme. When ethylene glycol or methanol is ingested with ethanol, it may be somewhat protective. In fact, before fomepizole was available, the treatment of methanol and ethylene glycol ingestion was an ethanol drip. However, this co-ingestion of toxic alcohol and ethanol when found should not limit or prevent the administration of fomepizole because fomepizole is a much stronger inhibitor of alcohol dehydrogenase.

82. A 47-year-old woman is admitted with acute cholecystitis, which is treated by nasogastric suction and replacement of fluid losses with hypotonic saline (0.45% normal saline) containing 10 mEq KCl/L. The EKG is normal. The following laboratory data are obtained:

Na = 138, K = 2.8, Cl = 85, and HCO₃ = 42 mEq/L
 pH = 7.55, PCO₂ = 56, PO₂ = 92 mm Hg
 Urine Na = 42, Urine K = 45, and Urine Cl = 6 mEq/L
 Urine pH = 6.9

Which description of this acid–base disorder is TRUE?

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

Answer: D

Explanation:

Due to the large amount of nasogastric suctioning and loss of H⁺ ions, the patient has developed a significant metabolic alkalosis, and this is persistent due to the concomitant potassium losses and volume/chloride depletion (note the low urine chloride, which is more accurate than the urine sodium, which tends to be persistently elevated due to urinary losses of bicarbonate). High aldosterone levels contribute to these findings. Respiratory compensation is appropriate as possible. Correction of the metabolic alkalosis will require both volume (containing chloride) and potassium repletion as hypokalemia will help perpetuate the metabolic alkalosis.

83. A medical student asks for your help on an acid–base disturbance that he recently encountered during his medicine rotation. The following labs are presented to you, and the student does not remember the history of the patient.

Laboratory data:

Na = 140 mEq/L, K = 2.0 mEq/L, Cl = 115 mEq/L, HCO₃ = 15 mEq/L, pH = 7.32, PaCO₂ = 30 mm Hg, PaO₂ = 84 mm Hg

Which description of the acid–base disturbance in this case is TRUE?

- A. High anion gap metabolic acidosis
- B. Respiratory alkalosis and metabolic alkalosis
- C. Non–anion gap metabolic acidosis
- D. A and C
- E. All of the above

Answer: C

Explanation:

This patient presents with an acidemia (by Winter's formula, the expected PCO₂ for metabolic acidosis is $1.5 \times [\text{HCO}_3] + 8 = 1.5 \times 15 + 8 = 30.5$). Thus, answer C is correct, and either the patient has a renal tubular acidosis or gastrointestinal losses of bicarbonate. Additionally, a medication such as a carbonic anhydrase inhibitor or the drug topiramate (which has carbonic anhydrase properties) can lead to these findings.

84. A 52-year-old man with end-stage liver disease is intubated for altered mental status due to hepatic encephalopathy. On exam, he is somnolent and minimally arousable to painful stimuli. Pulse rate is 80 beats/min, BP is 92/60 mm Hg, and respiration is 26 breaths/min.

Laboratory studies

BUN: 22 mg/dL
 Serum creatinine: 1.1 mg/dL
 Plasma glucose: 118 mg/dL
 Serum electrolytes:
 Sodium: 132 mEq/L
 Potassium: 4.2 mEq/L
 Chloride: 102 mEq/L
 Bicarbonate: 20 mEq/L

Arterial blood studies

PO₂: 89 mm Hg
 PCO₂: 30 mm Hg
 Bicarbonate: 20 mEq/L
 pH: 7.44

Which acid–base disturbance is MOST likely present?

- A. Respiratory alkalosis
- B. Metabolic alkalosis
- C. Metabolic acidosis/respiratory alkalosis
- D. Metabolic alkalosis/respiratory acidosis
- E. Metabolic acidosis/metabolic alkalosis/respiratory alkalosis

Answer: A

Explanation:

The patient's pH is 7.44, which alone does not help us make a clear determination of the disorders present. The patient has a PCO_2 of 30, suggesting the patient has a respiratory alkalosis. With chronic compensation for a respiratory alkalosis, we would expect a decrease in serum bicarbonate of 0.4 mEq/L per 1 mm Hg change in PCO_2 , e.g., $0.4 \times 10 = 4$ mEq/L, or an expected serum bicarbonate of approximately 20 mEq/L. Therefore, the correct answer is choice A, because this patient has a respiratory alkalosis with chronic compensation resulting in the low serum bicarbonate; and because the anion gap was normal, there is no additional metabolic acidosis present. In general, a pH in the normal range usually indicates a mixed acid-base disorder; however, the compensatory responses to mild–moderate respiratory acidosis and alkalosis may return the pH to the lower and upper end of the normal range, respectively.

85. A 63-year-old man is admitted for refractory hypokalemia and metabolic alkalosis. The patient had a 1-year history of small cell lung carcinoma (SCLC) that was treated with paclitaxel, carboplatin, and gemcitabine. Two weeks before admission, he noticed increasing weakness. On physical examination, his BP was 182/95 mm Hg, and he had 2+ ankle edema.

Cardiovascular and chest examination were unremarkable. Abdominal examination showed no central obesity or striae. Neurologic examination showed proximal muscle weakness. His laboratory values were as follows: BUN, 12 mg/dL; creatinine, 1.1 mg/dL; sodium, 137 mEq/L; K, 2.8 mEq/L; Cl, 85 mEq/L; and HCO_3 , 35 mEq/L. Glucose was 165 mg/dL.

At this point, which laboratory test would provide the cause of his metabolic abnormalities?

- A. Plasma aldosterone
- B. Plasma cortisol
- C. Plasma adrenocorticotropic hormone (ACTH)
- D. Plasma thyroid stimulating hormone
- E. Plasma glucagon

Answer: C

Explanation:

Increased ACTH production by lung cancer (more common with SCLC) increases adrenal production of cortisol and the subsequent rapid and severe metabolic abnormalities characterized by refractory hypokalemia, metabolic alkalosis, and hyperglycemia. In this case, the very high levels of cortisol can activate the mineralocorticoid receptor. Therapy is directed at the tumor, steroid synthesis inhibitors (ketoconazole, metyrapone, and octreotide), and mineralocorticoid receptor blockers/ epithelial sodium channel (eNaC) blockers. Primary hyperaldosteronism gives a metabolic picture exactly like this. However, the patient is not likely to have suddenly sprouted an adrenal adenoma 2 weeks ago. The marked electrolyte abnormalities point towards an ectopic source of ACTH. Thyrotoxicosis may be associated with a K^+ cell shift but not metabolic alkalosis. Plasma glucagon measurement is incorrect.

86. A 61-year-old woman with stage 4 cancer of the cervix developed resistant hypokalemia and hypophosphatemia after her last round of chemotherapy (paclitaxel, carboplatin, and ifosfamide). She denied taking any other medications. She had received potassium supplements over the last 2 weeks but her serum K^+ has remained <3 mEq/L during that time. She does note some muscle wasting, and she is generally weak and complains of polyuria and nocturia.

On physical examination, she is a mildly cachectic appearing woman in no acute distress. BP is 125/80 mm Hg supine without orthostatic change. Chest, heart, and abdominal examinations are unremarkable.

Laboratory results show the following: Na, 144 mEq/L; K, 2.8 mEq/L; Cl, 114 mEq/L; HCO_3 , 18 mEq/L; BUN, 14 mg/dL; creatinine, 1.1 mg/dL; Ca, 8.7 mg/dL; and PO_4 , 2.1 mg/dL. Urine K was 67 mEq/24 hr, and urine PO_4 was 1.2 g/24 hr.

Which is the MOST likely cause of her electrolyte disorder?

- A. Paclitaxel toxicity
- B. Secondary hyperaldosteronism
- C. Tumor production of fibroblast growth factor-23 (FGF-23)
- D. Ifosfamide toxicity
- E. Obstructive uropathy

Answer: D

Explanation:

Ifosfamide-induced Fanconi syndrome, with any combination of proximal renal tubular acidosis, glycosuria, potassium, and phosphate wasting, nephrogenic diabetes insipidus, and AKI following ifosfamide occurs in children and adults. Renal tubular dysfunction can develop months after completing chemotherapy and may never resolve. Paclitaxel is not associated with any significant renal toxicity. Secondary hyperaldosteronism is not supported by any evidence in this case. The patient is not volume

depleted (normal BP without orthostasis) and does not have congestive heart failure, cirrhosis, or nephrotic syndrome. Secondary hyperaldosteronism is usually not associated with hypokalemia and metabolic alkalosis unless diuretics are given. Tumor-produced FGF-23 would produce phosphate wasting and hypophosphatemia but not metabolic acidosis. When electrolyte disturbances develop in the setting of obstructive uropathy, it is most often hyperkalemia with metabolic acidosis. Her borderline hyponatremia and polyuria suggest a concentrating defect (proving it would require a urine osmolality value during a water deprivation test), but these results likely represent a nephrogenic diabetes insipidus from ifosfamide as well. Obstructive uropathy can bring about a transient nephrogenic diabetes insipidus, but not these other findings.

87. A 44-year-old obese man sees his primary care physician for a routine physical examination. The examination is unremarkable, and BP is normal. Serum electrolytes: Na, 139 mEq/L; K, 3.0 mEq/L; HCO₃, 16 mEq/L; Cl, 113 mEq/L; BUN, 14 mg/dL; and serum creatinine, 0.9 mg/dL. Urinalysis: specific gravity, 1.013; pH, 5.3; negative blood, protein, and LE. Urine microscopy is bland. Arterial pH 7.3.

Which medication is associated with the acid-base disorder seen in this patient?

- A. Topiramate
- B. Triamterene
- C. Orlistat
- D. Tiopronin
- E. Atazanavir

Answer: A

Explanation:

Topiramate inhibits carbonic anhydrase. As a result, it is associated with a proximal renal tubular acidosis (RTA) (and distal RTA) often with calcium phosphate stone formation from the latter. Tiopronin has no adverse renal effects. Atazanavir is associated with urinary crystals and nephrolithiasis. Triamterene is associated with urinary crystals but not stones. It is also associated with hyperkalemia from blocking the sodium channels. Orlistat is associated with enteric hyperoxaluria and urinary calcium oxalate crystals.

88. In an HIV-infected patient with pneumocystis pneumonia that undergoes therapy with intravenous pentamidine, which BEST describes the mechanism of hyperkalemia noted with this drug?

- A. Reduced aldosterone action
- B. Reduced renin
- C. Epithelial sodium channel blockade
- D. Apical membrane potassium channel blockade
- E. Reduced insulin secretion

Answer: C

Explanation:

Pentamidine, like amiloride, triamterene, and trimethoprim, is associated with hyperkalemia by blocking the epithelial sodium channel in the principal cell in the cortical collecting duct.

89. Which drug has been associated with the development of lactic acidosis with chronic therapy?

- A. Linezolid
- B. Daptomycin
- C. Neomycin
- D. Tigecycline
- E. Aztreonam

Answer: A

Explanation:

Chronic linezolid therapy is associated with lactic acidosis by disrupting mitochondrial function. The other drugs do not cause lactic acidosis. Remember that propofol and metformin use as well as thiamine deficiency are also associated with lactic acidosis.

90. In an alcoholic with poor nutrition, which medication may be associated with the development of oxoproline acidosis?

- A. Linezolid
- B. Ketorolac
- C. Demeclocycline
- D. Acetaminophen
- E. Tramadol

Answer: D

Explanation:

Acetaminophen can be associated with oxoproline (also known as pyroglutamic acid) acidosis in alcoholics and other patients with poor nutrition (typically elderly females) due to the underlying glutathione and deficiencies these patients maintain. The other drugs are not associated with this form of acidosis. Linezolid is associated with lactic acidosis. Ketorolac can be associated with hyporeninemic hypoaldosteronism and a type 4 renal tubular acidosis (RTA).

91. A 43-year-old woman with a history of primary Sjögren syndrome presents with weakness. On physical examination, there is moderate flaccidity of the extremities, and the deep tendon reflexes are 0–1+ and equal. The medical history is compatible with classical features of sicca syndrome. The initial laboratory findings are concerning.

Sodium	140 mEq/L
Potassium	2.0 mEq/L
Chloride	115 mEq/L
Bicarbonate	15 mEq/L
Blood urea nitrogen	15 mg/dL
Creatinine	0.95 mg/dL
Glucose	102 mg/dL
Arterial blood gases	
pH	7.32
PaCO ₂	30 mmHg
PaO ₂	84 mmHg
Bicarbonate	15 mEq/L

Which is the correct diagnosis of the acid-base disturbance in this case?

- A. High anion gap metabolic acidosis
- B. Respiratory alkalosis and metabolic alkalosis
- C. Non-anion gap metabolic acidosis
- D. Respiratory alkalosis

Answer: C

Explanation:

The arterial pH of 7.32 indicates an acidemia. The HCO₃ of 15 indicates that this is a metabolic acidosis, and the anion gap is only 10. The measured PCO₂ of 30 corresponds to the predicted appropriate response by Winter's formula; and thus, this qualifies as a simple non-anion gap metabolic acidosis. The differential diagnosis for a nongap metabolic acidosis with hypokalemia should be considered. The examination should include a thorough review of systems, medical history, and drug history. For example, identifying prior episodes of weakness, recent and chronic diarrhea, and a history of a ureterosigmoidostomy or immunosuppression by calcineurin inhibitors would be helpful in defining the etiology. Nevertheless, because renal tubular acidosis must be ruled out with the described presentation, testing urine electrolytes will be necessary to distinguish between renal and extrarenal causes of a nongap acidosis. Sjögren syndrome means distal renal tubular acidosis on the boards, but be careful and still look at the serum anion gap, urine pH, and the urinary anion gap to confirm (they are not available in this case). Bad cases of distal renal tubular acidosis may have severe enough hypokalemia to also have muscular weakness and concomitant respiratory acidosis.

92. A 43-year-old woman with a history of primary Sjögren syndrome presents with weakness. On physical examination, there is moderate flaccidity of the extremities, and the deep tendon reflexes are 0–1+ and equal. The medical history is compatible with classical features of sicca syndrome. The initial laboratory findings are concerning.

Sodium	140 mEq/L
Potassium	2.0 mEq/L
Chloride	115 mEq/L
Bicarbonate	15 mEq/L
Blood urea nitrogen	15 mg/dL
Creatinine	0.95 mg/dL
Glucose	102 mg/dL
Arterial blood gases	
pH	7.32
PaCO ₂	30 mmHg
PaO ₂	84 mmHg
Bicarbonate	15 mEq/L

Which response would be MOST compatible with the diagnosis of classical distal renal tubular acidosis in this patient?

- A. Negative urine anion gap and a urine pH >5.5
- B. Positive urine anion gap
- C. Negative urine anion gap and elevated urine osmolality
- D. Calculated urine osmolal gap of >150 mOsm/kg of water

Answer: B

Explanation:

The expected response to a metabolic acidosis is to increase NH₄⁺ excretion in the urine. Since NH₄⁺ is not measured, you will have a urinary cation gap or a urinary negative anion gap. Therefore, a positive urine anion gap in the setting of nongap metabolic acidosis indicates impaired NH₄⁺ excretion as seen in a distal renal tubular acidosis. Although a relatively alkaline urine pH (>5.5) in the setting of a metabolic acidosis is the hallmark of a distal acidification defect, high urine ammonium concentration, as may be seen with extrarenal causes (diarrhea, etc.), can add additional buffer to the urine and cause a similar alkaline urine pH. Thus, an inappropriately high urine pH by itself does not always indicate an acidification defect. Therefore, the urinary anion gap becomes a better estimate of renal NH₄⁺ production. A urine osmolal gap of >150 mOsm/kg predicts a urine ammonium of >75, indicating an appropriate renal response to metabolic acidosis. Low values for the urine osmolal gap (<150 mOsm/kg) denote a renal tubular cause of the normal anion gap acidosis.

93. A 64-year-old obese woman with type 2 diabetes for 26 years, a urine protein/creatinine ratio of 3.5, and Stage 3b CKD assumed to be secondary to diabetic nephropathy is admitted with progressive edema and shortness of breath. Medications include ramipril, 2.5 mg/d, and spironolactone, 12.5 mg/d. On physical examination, the jugular venous pulse is elevated, bilateral rales are present at both bases, and dullness at the right base, as well as 4+ bilateral pedal edema, is noted. The initial laboratory data prompt a nephrology consult.

Sodium	138 mEq/L
Potassium	6.2 mEq/L
Chloride	115 mEq/L
Bicarbonate	13 mEq/L
Glucose	235 mg/dL
Blood urea nitrogen	50 mg/dL
Creatinine	3.4 mg/dL
eGFR	22 mL/min/1.73 m ² (from baseline of 33 mL/min/1.73 m ²)
Arterial blood gases	
pH	7.25
PCO ₂	31 mmHg
Bicarbonate	15 mEq/L

Chest x-ray shows a right pleural effusion and redistribution of pulmonary vasculature with apical prominence. Findings are compatible with moderate pulmonary edema. Plasma renin and aldosterone levels are both low.

Which is the MOST likely etiology of this patient’s findings?

- A. Diabetic ketoacidosis
- B. Respiratory alkalosis associated with moderate pulmonary edema
- C. Drug-induced hyperkalemia
- D. Hyporeninemic hypoaldosteronism and Type 4 renal tubular acidosis

Answer: D

Explanation:

This patient’s presentation is typical for hyporeninemic hypoaldosteronism: presumed diabetic nephropathy, a recent decline in eGFR, evidence of volume overload, hyperkalemia, and a nongap metabolic acidosis. It is likely that the ACE inhibitor and spironolactone are contributing to the hyperkalemia, but these agents alone are insufficient to explain the constellation of findings. Often, mineralocorticoid receptor blockers or ACE or ARB therapy may cause patients with type 2 diabetes and progressive CKD to manifest hyperkalemia often without a nongap acidosis, but the constellation of findings here indicates secondary hypoaldosteronism and hyperkalemia in a patient with progressive decline in eGFR. The hyperkalemia and acidosis are the result of factors that include decreased delivery of sodium and tubule fluid to the distal nephron and the cortical collecting duct principal cell. A reduction in flow is associated with a decrease in potassium secretion via BK channels in the cortical collecting tubule, and the hypoaldosteronism reduces secretion by the hydrogen and hydrogen potassium ATPases. Furthermore, the hyperkalemia per se reduces renal ammonium production and excretion because hyperkalemia directly suppresses ammoniogenesis and inhibits several transporters that require ammonium to substitute for potassium in the thick ascending loop of Henle and the medullary collecting tubule. Therefore, ammonium transport and medullary recycling of ammonium are both suppressed. Therapy for this patient would include cessation of the two potassium-retaining agents, careful diuresis, and administration of a polymer to reduce potassium absorption in the gastrointestinal track, e.g., patiomer or sodium zirconium cyclosilicate when available. The use of sodium polystyrene sulfonate is discouraged, but if used, it should be administered without sorbitol.

References:

Weir MR, Bakris GL, Bushinsky DA, Mayo MR, Garza D, Stasiv Y, Wittes J, Christ-Schmidt H, Berman L, Pitt B; OPAL-HK Investigators. Patiomer in patients with kidney disease and hyperkalemia receiving RAAS inhibitors. *N Engl J Med* 2015;372:211–221.

DuBose TD, Good DW. Chronic hyperkalemia impairs ammonium transport and accumulation in the inner medulla of the rat. *J Clin Invest* 1992;90:1443–1449.

DuBose TD, Caffish CR. Effects of selective aldosterone deficiency on acidification in nephron segments of the rat inner medulla. *J Clin Invest* 1988;82:1624–1632.

94. A 44-year-old woman with a history of multiple abdominal operations for adhesions requiring bowel resection with subsequent “short bowel syndrome” was admitted with severe muscle weakness and orthostatic dizziness. Her recumbent BP was 100/55 mmHg.

Sodium	140 mEq/L
Potassium	2.5 mEq/L
Chloride	125 mEq/L
Bicarbonate	5 mEq/L
pH	7.11
PCO ₂	16 mmHg
PO ₂	100 mmHg
Albumin	4.1 g/dL
Urine pH	6.0
Urine electrolytes	
Na ⁺	20 mEq/L
K ⁺	10 mEq/L
Cl ⁻	65 mEq/L

Which is the BEST acid-base diagnosis?

- A. Anion gap metabolic acidosis
- B. Mixed metabolic acidosis–metabolic alkalosis
- C. Non–anion gap metabolic acidosis
- D. Mixed metabolic acid–respiratory alkalosis

Answer: C

Explanation:

This patient has a severe nongap metabolic acidosis with hypokalemia. The serum albumin level is normal, so the computed anion gap of 10 (i.e., within the normal range) is reliable. The history suggests a nonrenal source for loss of bicarbonate or alkali, and the negative urine anion gap estimates that the urinary ammonium concentration is elevated, not low, indicating a normal renal response to the metabolic acidosis. Thus, the etiology of the non-anion gap acidosis is not renal tubular acidosis but is extrarenal (gastrointestinal) in origin. The Winter equation is the most precise means of predicting the expected value for arterial PCO₂ in a patient with metabolic acidosis. For bicarbonate of 5 mEq/L, the anticipated PCO₂ should be equal to $(1.5 \times 5) + 8$, or 15.5. This patient has a PCO₂ of 16. Neither option A or B are possible because the anion gap is not elevated.

References:

DuBose TD. Disorders of acid-base balance. In: *Brenner and Rector's The Kidney*, 9th Ed., edited by Taal M, Chertow G, Marsden P, Skorecki K, Yu A, Brenner B, Philadelphia, Elsevier, 2015, ch 16.

95. Two patients present with identical plasma potassium levels of 2.5 mmol/L. The first patient is a 35-year-old Asian woman with an onset of severe symmetrical weakness of all extremities approximately 3 hours after ingesting a large serving of ice cream. She has noted a 10-lb weight loss over the last 6 weeks. The physical examination is noteworthy for a BP of 140/70 mmHg and pulse rate of 110/min. A mild tremor is noted. The other patient is a 26-year-old white man who also experiences symmetrical weakness. He admits to chronic inhalation of paint thinner, more excessively over the prior 24 hours.

Which statement regarding the effects of hypokalemia in these patients is TRUE?

- The first patient is more likely to be symptomatic than the second patient because of a higher intracellular potassium concentration.
- The second patient is more likely to be symptomatic than the first patient because of coexistent metabolic acidosis.
- The first patient is more likely to be symptomatic than the second patient because of a coexistent sodium channel mutations.
- Both are equally likely to be symptomatic.
- Metabolic acidosis is more likely to be present in the first patient.

Answer: A

Explanation:

The female patient is more likely to be symptomatic because of a higher intracellular potassium concentration. The female patient presents with features consistent with the acquired form of hypokalemic periodic paralysis occurring in association with hyperthyroidism. This association is more commonly seen in patients of Asian or Mexican descent. During an acute attack, there is a sudden shift of potassium from the extracellular fluid space into the intracellular compartment. Total body potassium content is normal. The large transcellular potassium gradient leads to hyperpolarization of the cell, precipitating weakness. The male patient has hypokalemia with total body potassium depletion due to renal potassium wasting. Because both intracellular and extracellular potassium are decreased, the transcellular potassium gradient is less steep, and cell hyperpolarization is less severe as compared with the patient with periodic paralysis. As a result, the patient inhaling paint thinner is less likely to be symptomatic. Renal potassium wasting due to inhalation of paint thinner is the result of toluene-induced type 1 distal renal tubular acidosis. In addition to direct renal effects that impair distal hydrogen ion secretion, toluene is metabolized to hippuric acid. The subsequent excretion of the sodium salt (sodium hippurate) acts as a nonreabsorbable anion leading to increased distal sodium delivery. These patients are likely to be mildly volume contracted such that this increase in distal sodium delivery will be coupled to increased aldosterone, resulting in renal potassium wasting. Metabolic acidosis leads to a shift of potassium out of cells and can mask the severity of the total body potassium deficit. The potassium deficit should be corrected prior to or along with treatment of the metabolic acidosis. Correcting the acidosis without potassium supplementation can precipitate symptomatic hypokalemia. Patients with the inherited form of hypokalemic periodic paralysis most commonly have a defect in the skeletal muscle calcium channel.

References:

Carlisle EJ, Donnelly SM, Vasuvattakul S, Kamel KS, Tobe S, Halperin ML. Glue-sniffing and distal renal tubular acidosis: Sticking to the facts. *J Am Soc Nephrol* 1991;1:1019–1027.

Groeneveld J, Sijpkens Y, Lin S, Davids M, Halperin M. Approach to the patient with severe hypokalemia: The potassium quiz. *Q J Med* 2005;98:305–316. Lin S. Thyrotoxic periodic paralysis. *Mayo Clin Proc* 2005;80:99–105.

96. A 26-year-old Hispanic woman presents with a several-week history of polyuria and polydipsia. She has lost 10 lbs over this period. Nausea and vomiting started 2 days ago. An evaluation in the emergency room reveals the following laboratory findings:

Sodium	128 mEq/L
Potassium	4 mEq/L
Chloride	90 mEq/L
Bicarbonate	8 mEq/L
Blood glucose	980 mg/dL

Serum and urinary ketones are strongly positive.

Which statement about this patient’s potassium stores is TRUE?

- A. They are normal.
- B. They are increased due to volume contraction and oliguria.
- C. They are reduced due to an osmotic diuresis but not reduced enough to cause hypokalemia.
- D. They are reduced due to an osmotic diuresis, but serum levels remain normal because potassium shifts out of cells in response to the metabolic acidosis.
- E. They are reduced due to an osmotic diuresis, but serum levels remain normal because potassium shifts out of cells in response to insulin deficiency and increased osmolality.

Answer: E

Explanation:

They are reduced due to an osmotic diuresis, but serum levels remain normal because potassium shifts out of cells in response to insulin deficiency and increased osmolality. The patient presents with a diagnosis of diabetic ketoacidosis. Such patients are total body potassium depleted despite typically having increased plasma potassium concentrations on admission. The normal plasma potassium concentration in this patient suggests a severe decrease in total body potassium content. Total body potassium depletion in diabetic ketoacidosis is due to renal potassium wasting resulting from increased distal sodium delivery coupled with increased circulating aldosterone. Distal sodium delivery is increased because of the osmotic diuretic effect of the glucose and excretion of sodium-ketoacid salts. Volume depletion mediates the increase in aldosterone. Despite the total body potassium depletion, serum potassium concentration is often increased or, in this case, normal because of insulin deficiency. In addition, increased extracellular glucose concentration leads to water movement from the intracellular space to the extracellular space, resulting in concentration of intracellular potassium. The increased intracellular-to-extracellular potassium gradient favors the outward movement of potassium. Potassium shifts are not due to metabolic acidosis because diabetic ketoacidosis is an organic acidosis. Only mineral acidosis causes potassium to shift out of cells.

References:

Milionis HJ, Dimos G, Elisaf MS. Severe hyperkalaemia in association with diabetic ketoacidosis in a patient presenting with severe generalized muscle weakness. *Nephrol Dial Transplant* 2003;18:198–200.
 Davids MR, Segal AS, Brunengraber H, Halperin ML. An unusual cause for ketoacidosis. *Q J Med* 2004;97:365–376. Perez G, Oster J, Vaamonde C. Serum potassium concentration in acidemic states. *Nephron* 1981;27:233–243.

97. A 55-year-old African American man presents to the emergency room after ingesting a large amount of aspirin in a suicide attempt. The laboratory test results follow:

Sodium	138 mEq/L
Potassium	3.2 mEq/L
Chloride	102 mEq/L
Bicarbonate	18 mEq/L
Arterial pH	7.48
PCO ₂	21 mmHg
Urine chemistries	
Na	38 mEq/L
K	45 mEq/L
Cl	<10 mEq/L

Which statement is TRUE regarding this patient?

- A. The cause of the hypokalemia is a shift of potassium into cells.
- B. The serum uric acid levels are likely to be low.
- C. The high urine sodium, relative to the urine chloride, is due to proximal tubular dysfunction.
- D. Lactic acid levels are likely to be normal.
- E. Similar acid-base findings would likely be present in a 5-year-old child who ingested a similar amount of aspirin.

Answer: B

Explanation:

The serum uric acid levels are likely to be low. With high-dose aspirin therapy or in the setting of an aspirin overdose, the renal excretion of uric acid is increased, and hypouricemia may be present. In this setting, the hepatic glucuronidation of salicylic acid is saturated, and large quantities of free salicylate are filtered into the tubule. Free salicylate interferes in the reabsorption of uric acid by the proximal tubule accounting for the uricosuric effect. Aspirin overdose is associated with a variety of acid-base and electrolyte disturbances. Salicylates have a direct stimulatory effect on the respiratory center such that respiratory alkalosis is a prominent feature in the overdose setting. An anion gap metabolic acidosis is also present primarily because of increased production and accumulation of ketoacids and lactic acid. Salicylic acid accumulation accounts for only a minor component of the increase in anion

gap. Lactic acid production is increased because of the uncoupling effect of aspirin on oxidative phosphorylation in the mitochondria. Adult patients with aspirin overdose usually present with a mixture of respiratory alkalosis and anion gap metabolic acidosis. A pure metabolic acidosis is unusual in adults. By contrast, children with aspirin overdose may present with an anion gap metabolic acidosis alone, particularly soon after ingestion. Hypokalemia is the result of increased renal potassium excretion. Increased distal delivery of sodium (due to the excretion of sodium salicylate) in combination with increased circulating aldosterone (secondary to volume depletion) accounts for the renal potassium wasting.

References:

Yu T, Gutman A. A study of the paradoxical effects of salicylate in low, intermediate, and high dosage on the renal mechanism for excretion of urate in man. *J Clin Invest* 1959;38:1298–1315.
 Temple A: Pathophysiology of aspirin overdosage toxicity, with implications for management. *Pediatrics* 1978;62:873–876.
 Gabow P, Anderson R, Potts D, Schrier R: Acid-base disturbances in the salicylate intoxicated adult. *Arch Int Med* 1978;138:1481–1484.

98. A 58-year-old woman with Stage 3b CKD secondary to glomerulonephritis is managed conservatively in the clinic for an established baseline serum creatinine of 3 mg/dL and eGFR 20 mL/min/1.73 m². However, the patient is admitted to the hospital with a history of protracted vomiting over the last 3 days.

On examination, orthostasis and dry mucous membranes with reduced skin turgor are documented. The patient's weight has decreased 6 lbs (2.7 kg) below the last recorded value. The following laboratory data are obtained, and nephrology consultation was requested:

Sodium	140 mEq/L
Potassium	3.3 mEq/L
Chloride	85 mEq/L
Bicarbonate	25 mEq/L
Blood urea nitrogen	78 mg/dL
Creatinine	8.0 mg/dL
Albumin	3.9 g/dL
Arterial blood gases	
pH	7.4
PCO ₂	40 mmHg
PaO ₂	92 mmHg
Bicarbonate	25 mEq/L

Which is the MOST accurate diagnosis of the acid-base disturbance in this patient?

- A. Metabolic alkalosis
- B. High anion gap metabolic acidosis
- C. Mixed metabolic acidosis–metabolic alkalosis
- D. Mixed metabolic acidosis–respiratory acidosis
- E. No acid-base disturbance is present

Answer: C

Explanation:

This patient has a normal serum albumin concentration and a calculated anion gap (AG) of 30, clearly establishing the presence of a high AG (HAG) acidosis. The HAG is most likely due to the acute on chronic kidney failure as evidenced by the documented increase in blood urea nitrogen and creatinine levels.

However, the Δ AG (20), markedly exceeds the Δ HCO₃ of 0. This mismatch in Δ values establishes the co-occurrence of metabolic alkalosis and thus explains the resultant “normal” values for arterial pH and HCO₃. Note that the measured and calculated values for HCO₃ are equal (compare the electrolyte panel and arterial blood HCO₃). Options A and B are correct but are insufficient to explain the constellation of findings in this patient. Mixed disorders are common and very important to recognize, and a normal systemic pH in the setting of any acid-base disorder always indicates two primary acid base disorders. Obviously, in this patient, therapy for the acid-base disorder per se is not indicated as the pH is normal. However, because of the volume depletion and associated acute on chronic renal failure, it would be important to give isotonic saline while avoiding volume overload by carefully monitoring hemodynamics and the physician examination.

This case is an example of a hidden metabolic acidosis and a hidden metabolic alkalosis, evident because the metabolic acidosis has an anion gap. A simultaneous non-anion gap acidosis (e.g., diarrhea) and equal metabolic alkalosis (vomiting) effectively “cancel out” each other. It is possible to also have a hidden metabolic acidosis and alkalosis that would not be evident without an anion gap.

Option D is incorrect because the PCO₂ is normal.

References:

DuBose TD. Disorders of acid-base balance. In: *Brenner and Rector's The Kidney*, 9th Ed., edited by Taal M, Chertow G, Marsden P, Skorecki K, Yu A, Brenner B, Philadelphia, Elsevier, 2015, 511–558.
 DuBose TD. Metabolic alkalosis: In: *National Kidney Foundation Primer on Kidney Diseases*, 6th Ed., edited by Gilbert S, Weiner DE, Philadelphia, Elsevier, 2014, 134–143.

99. A 23-year-old woman with type 1 diabetes and history of gastroparesis is admitted to the intensive care unit via the emergency department with a history of recent abdominal pain, nausea, and vomiting.

Sodium	128 mEq/L
Potassium	3.3 mEq/L
Chloride	70 mEq/L
Bicarbonate	37 mEq/L
Blood urea nitrogen	32 mg/dL
Creatinine	3.1 mg/dL
Glucose	639 mg/dL
Albumin	2.5 g/dL
Lactate	1.4 mEq/L
Arterial blood gases	
pH	7.53
PCO ₂	46 mmHg
PaO ₂	91 mmHg
Bicarbonate	37 mEq/L

Serum ketones were 4+ at a dilution of 1:16.

What is the BEST description of the acid-base disorder in this patient?

- A. Metabolic alkalosis
- B. High anion gap metabolic acidosis
- C. Respiratory acidosis
- D. Mixed high gap metabolic acidosis–metabolic alkalosis

Answer: D

Explanation:

This patient has a mixed high anion gap (AG) acidosis and metabolic alkalosis. The metabolic acidosis (DKA) is hidden by the overwhelming metabolic alkalosis (vomiting). Assessing the high AG requires correcting the AG because the serum albumin level is only 2.5 g/dL (or 1.5 g/dL below the normal value of 4.0). The uncorrected AG is 21. The corrected AG is 25 ($2.5 \times 1.5 = 3.75$ or approximately 4; therefore, $21 + 4 = 25$). The AG can be ascribed to ketoacidosis (ketones positive and lactate not significantly elevated). To assess the co-occurrence of metabolic alkalosis, it is important to compare the Δ values. The Δ AG is $25 - 10 = 15$. However, the Δ HCO₃ is 12 mEq/L above the normal value of 25, indicating a large disparity. The large difference in Δ AG and Δ HCO₃ indicates a mixed high AG acidosis and metabolic alkalosis. The most likely etiology in this patient is vomiting. This patient responded to volume re-expansion with isotonic saline and small doses of regular insulin with precautions. The acute on chronic renal failure also resolved.

References:

DuBose TD, Goode AK. Renal acid-base transport. In: *Schrier's Diseases of the Kidney*, 9th Ed., edited by Coffman TM, Falk RJ, Molitoris BA, Neilson EG, Schrier RW, Philadelphia, Lippincott, Williams & Wilkins, 2013.
 DuBose TD. Acidosis and alkalosis. In: *Harrison's Principles of Internal Medicine*, 19th Ed., edited by Kasper DL, Fauci AS, Hauser S, Longo D, Jameson JL, Loscalzo J, New York, McGraw-Hill, ch 66, 2015.

100. **Which statement is TRUE regarding patients with Alport syndrome?**

- A. Most affected males have mutations in the type 4 collagen α -5 chain gene (*COL4A5*) on the Y chromosome.
- B. Heterozygous females with *COL4A5* gene mutations infrequently develop advanced kidney disease.
- C. Patients with autosomal recessive forms have a single mutation in either the α -3 chain of type 4 collagen (*COL4A3*) or the α -4 chain of type 4 collagen gene (*COL4A4*).
- D. More than 50% of cases lack a family history of hematuria or kidney disease (presumed de novo mutations).

Answer: B

Explanation:

All statements are incorrect except answer B. Females with one X-linked mutation in the *COL4A5* gene are carriers; they typically develop mild disease because they possess another (normal) X chromosome. *COL4A5* mutations causing Alport syndrome are located on X chromosomes. Patients with autosomal recessive forms of Alport syndrome must have two mutations to manifest clinical kidney disease. A single mutation in either the *COL4A3* or *COL4A5* gene would cause thin basement nephropathy with hematuria and preserved kidney function.

References:

Haas M. Alport syndrome and thin glomerular basement membrane nephropathy: A practical approach to diagnosis. *Arch Pathol Lab Med* 2009;132:224–232.

101. A 45-year-old man with no prior medical history is involved in a severe motor vehicle accident. On arrival to the emergency department, he is hypotensive with a BP of 82/40 mm Hg and a pulse of 120 beats/min. Intravenous access is obtained, and he receives a bolus of 2 L of 0.9% normal saline.

How much of the 2 L of 0.9% saline will contribute to increasing the volume of the intravascular space?

- A. 2000 mL
- B. 1000 mL
- C. 500 mL
- D. 250 mL

Answer: C

Explanation:

Because the capillary endothelium is highly permeable to sodium, chloride, and water, the infused solution is quickly distributed not only throughout the plasma but also into the interstitial fluid. However, the intracellular compartment is excluded since the normal saline is isosmotic and all the osmolality is from Na which is excluded from the cells. Because the intravascular component makes up 25% of the extracellular compartment, 25% of the 2 L will remain in the intravascular compartment.

102. A 19-year-old woman is brought to the Emergency Department (ED) after she suffered a tonic-clonic seizure outside of a fraternity party. She has no significant medical history and takes no medications. Students who also attended the party reported that “recreational” drugs were at the party, but they are not sure what specifically may have been taken. On arrival to the ED, her vital signs were notable for a temperature of 38.9°C, pulse of 95 beats/min, and BP of 148/70 mm Hg. Her examination was notable for some confusion and lethargy. Otherwise, her physical examination was within normal limits.

Laboratory studies

Serum sodium: 122 mEq/L
 Serum potassium: 4.1 mEq/L
 Serum bicarbonate: 21 mEq/L
 Serum chloride: 91 mEq/L
 Urine osmolality: 455 mOsm/kg

Which is the MOST likely etiology of this patient’s presenting symptoms and laboratory findings?

- A. Psychogenic polydipsia
- B. Synthetic marijuana
- C. “Bath Salt” intoxication
- D. “Ecstasy” intoxication
- E. Cocaine intoxication

Answer: D

Explanation:

Ecstasy [3,4-methylenedioxymethamphetamine (MDMA)] is commonly used by college-aged individuals. Ecstasy leads to feelings of euphoria, emotional empathy, and increased energy. These effects come at a significant risk for complications. Ecstasy has been associated with AKI that is most commonly secondary to nontraumatic rhabdomyolysis but also has been reported in the setting of drug-induced liver failure and drug-induced vasculitis. More common, ecstasy has led to serious hyponatremia and hyponatremia-associated deaths. Hyponatremia in these cases is due to a “perfect storm” of ecstasy-induced effects on water balance. Ecstasy leads to non-osmotic, non-volume mediated secretion of arginine vasopressin and also causes polydipsia as a result of its effects on the serotonergic nervous pathways. Compounding these effects are the ready availability of fluids and the recommendation to drink copiously at rave parties where ecstasy is commonly used.

103. A 49-year-old man with bipolar disorder treated with lithium is brought to the emergency department by his caregiver secondary to altered mental status. He has a history of stage 2 CKD thought to be secondary to diabetes mellitus type 2 and hypertension. On examination, his vital signs are normal, but his neurological examination reveals agitation, ataxia, and nystagmus.

Laboratory studies

Serum sodium: 149 mEq/L

Serum potassium: 4.6 mEq/L

Serum chloride: 114 mEq/L

Serum bicarbonate: 24 mEq/L

Serum creatinine: 1.6 mg/dL

ECG: slightly prolonged QT interval

Serum lithium: 4.3 mmol/L

Which would be your next step in the treatment of this patient?

- A. Intravenous saline with serial lithium levels
- B. Gastric lavage to remove any unabsorbed lithium tablets
- C. Hemodialysis for 4 hours
- D. Hemodialysis for 2 hours
- E. Continuous renal replacement therapy until lithium level is <1.0 mmol/L

Answer: C

Explanation:

This patient presents with acute lithium intoxication. Hemodialysis (HD) is the most efficient and effective means of removing lithium. HD is recommended for asymptomatic patients when the lithium level is >5 or >4 with renal insufficiency. However, his mental status changes and prolonged QT interval make HD the clear choice independent of his level. A 2-hour session would not give enough lithium clearance and risks a rebound in the levels once the session is stopped. Continuous modalities are not as effective in rapidly reducing the lithium level. Given the neurological symptoms and high lithium level, IV saline and gastric lavage could only be considered ancillary therapies but would still require hemodialysis therapy to rapidly reduce the level.

104. A 75-year-old man with small cell lung cancer metastatic to the brain is treated with high-dose dexamethasone. Because of inadequate nutrition, tube feedings are begun. One week later, he becomes lethargic, and laboratory data are obtained. These show the following:

Serum Na, 150; K, 4; Cl, 115; CO₂, 25; BUN, 60 mg/dL; Creat, 1.0 mg/dL

Urine osmolality, 600 mOsm/kg; urine Na, 20 mEq/L; urine K, 15 mEq/L; urine output, 180 mL/hr (3.8 liters a day)

Which is MOST accurate?

- A. The concentrated urine is diagnostic of syndrome of inappropriate antidiuretic hormone secretion (SIADH)
- B. The less than maximally concentrated urine is diagnostic of incomplete diabetes insipidus
- C. The high BUN/creat ratio and low urine sodium are diagnostic of prerenal azotemia due to hypovolemia
- D. The high urine to plasma osmolality ratio indicates that the serum sodium will fall unless salt is added to the tube feedings
- E. The low urine to plasma electrolyte ratio indicates that the serum sodium will rise unless water is added to the tube feedings

Answer: E

Explanation:

The patient has an osmotic diuresis ($600 \text{ mOsm/kg} \times 3.8 \text{ L/d} = 2280 \text{ mOsm/d}$, normal 6-800 mOsm/d) from high rates of urea excretion, which is causing water depletion (hypernatremia), not hyponatremia as seen with water retention in SIADH, making choice A incorrect. Although a urine osmolality of 600 mOsm/kg is less than maximally concentrated, which occurs during a solute diuresis, it is still very concentrated, ruling out diabetes insipidus. The high urine-to-plasma osmolality ratio gives the misleading impression that free water clearance is negative, and the patient is therefore in positive water balance. However, this is true only of the "osmotic free water clearance," and what needs to be considered is the "electrolyte free water clearance." The patient is actually losing electrolyte free water (electrolyte free water clearance is positive) as reflected by the low urine-to-plasma electrolyte ratio (urine Na + urine K is < PNa). Water should be added to the tube feedings to avoid worsening hypernatremia. Although the urine sodium is low and there is a high BUN-to-creatinine ratio, these are not diagnostic signs of hypovolemia; the high BUN may be caused by the urea high appearance rate due to steroids and high protein feedings. The patient's 24-hour urine Na excretion is not low at 76 mEq/d.

105. A previously healthy 60-year-old woman presents to the emergency department with pruritis, dark urine, and light stools. She is alert and oriented, her BP is 130/70 mm Hg, her heart rate is 80 beats/min, and she is afebrile. The skin is jaundiced and excoriated. The liver is enlarged, but there are no ascites or edema. Her serum is as follows: Na, 120 mmol/L; potassium, 4

mmol/L; Cl, 90 mmol/L; HCO₃, 24 mmol/L; BUN, 6 mg/dL; creatinine, 0.8 mg/dL; glucose, 100 mg/dL; plasma osmolality, 290 mOsm/kg; total bilirubin, 12 mg/dL; aspartate aminotransferase, 150 IU; alanine aminotransferase, 200 IU; alkaline phosphatase, 1800 IU; total serum protein, 4.9 g/dL. Triglycerides are normal, and blood alcohol level is negative. Her urine osmolality is 440 mOsm/kg, and her urine Na is 60 mmol/L.

Which diagnosis fits BEST with these findings?

- A. Pseudohyponatremia
- B. Syndrome of inappropriate antidiuretic hormone secretion (SIADH)
- C. Hyponatremia from liver failure
- D. Hyponatremia from cerebral salt wasting
- E. Toxic alcohol ingestion

Answer: A

Explanation:

Although the patient has hyponatremia and the calculated plasma osmolality is low (250 mOsm/kg), the measured plasma osmolality is normal (290 mOsm/kg). Such an osmolal gap can be caused by toxic alcohols, but these do not cause hyponatremia, and there are no other features to suggest that diagnosis. Choices B, C, and D are causes of true hypotonic hyponatremia (no osmolal gap), which the patient does not have, as shown by the normal plasma osmolality. Hypercholesterolemia with lipoprotein X associated with cholestatic or obstructive jaundice is a cause of pseudohyponatremia and is the most likely explanation for the laboratory findings. This could be confirmed by using a direct ion selective measurement, which is not affected by lipid or protein levels in the blood.

106. A 50-year-old man with a history of heavy beer drinking is started on a thiazide diuretic for hypertension. A week later, he develops intractable nausea and vomiting, followed the next day by confusion and frequent falls. After 3 days of these symptoms, his family brings him to the hospital. He is able to communicate, but his speech is slow, and he is confused. His BP is 95/50 mm Hg, his heart rate is 100 beats/min, and he is afebrile. Scleral icterus is present. The heart and lungs are normal, the liver is enlarged and tender, and there is no edema and no focal neurologic signs. His serum results are as follows:

Na, 105 mmol/L; potassium, 1.8 mmol/L; Cl, 64 mmol/L; HCO₃, 35 mmol/L; osmolality, 220 mOsm/kg; BUN, 24 mg/dL; creatinine, 1 mg/dL; glucose, 90 mg/dL. Amylase and lipase are moderately elevated. His urine osmolality is 320 mOsm/kg, urine sodium is 15 mmol/L, urine Cl is 1 mmol/L, and urine potassium is 9 mmol/L. The thiazide diuretic is discontinued, and he is treated with potassium replacement and 0.9% saline at 500 mL/hr. Four hours after admission, his serum sodium is 113 mmol/L and serum potassium is 2.9 mmol/L. The urine output has increased to 400 mL/hr, and a repeat urine osmolality is now 100 mOsm/kg.

Which is the BEST treatment?

- A. Continue 0.9% saline at the current rate
- B. Increase 0.9% saline to match urine output
- C. Stop 0.9% saline and observe
- D. Give tolvaptan
- E. Stop 0.9% saline and give desmopressin (DDAVP)

Answer: E

Explanation:

The patient has chronic hyponatremia caused by thiazide diuretic, large fluid intake, and hypovolemia. He is at high risk for osmotic demyelination syndrome (ODS) because of alcoholism, serum ≤ 105 mEq/L, liver disease, and malnutrition. After stopping the thiazide and volume resuscitation, he is diluting his urine appropriately, and the serum sodium can be expected to correct spontaneously by approximately 2 mEq/L/hr. Because his serum sodium has already increased by 8 mmol/L in less than 24 hours, a further increase will likely cause ODS. Fluid restriction alone will not prevent this, and infusion of 0.9% will increase the rate of correction. Tolvaptan, a vasopressin antagonist, was contraindicated because of liver disease and is inappropriate at this point because the goal now is to stop a water diuresis and not start one. The goal is to stop the water diuresis, and a "DDAVP clamp" is the best way to achieve this goal by forcing urine concentration and preventing further water loss.

107. A 58-year-old man was hospitalized following loss of consciousness and seizures while working in his garden. He had been well but reported muscle cramps for several weeks. History included esophagitis, pneumothorax, hypertension, hypercholesterolemia, a hip fracture, and a similar episode of seizures 1 year earlier. Current medications include omeprazole for 8 years because of epigastric pain and captopril and simvastatin each for 6 years. There was no history of alcohol abuse.

The physical exam was within normal limits except for a positive Trousseau's sign.

Laboratory studies revealed the following:

Hgb: 12.4; Ht: 14; WBC: 5400

BUN: 13 mg/dL; Cr 1.1 mg/dL

Na: 142 mEq/L; Cl 106 mEq/L; K: 2.7 mEq/L; HCO₃: 24 mEq/L

Ca²⁺: 6.7 mg/dL; PO₄: 3.6 mg/dL; Mg²⁺: 0.72 mg/dL; alb: 3.9 g/L

24-hour urine revealed Cr: 1200 mg, Na⁺: 123 mEq, Ca²⁺: 54 mg; Mg²⁺: 10 mg.

What is the likely cause of the hypocalcemia and hypomagnesemia?

- A. Paracellin 1 gene mutation: familial hypomagnesemia with hypercalciuria and nephrocalcinosis (FHHNC)
- B. Hypoparathyroidism
- C. Omeprazole
- D. Gitelman's syndrome

Answer: C

Explanation:

Hypocalcemia (and low parathyroid hormone) is a known complication of hypomagnesemia. The low urinary magnesium excretion indicates that renal handling of magnesium is intact and that the cause of the hypomagnesemia is impaired gastrointestinal absorption of magnesium. Of the potential causes listed above, only omeprazole (and all PPIs) is associated with impairment in gastrointestinal magnesium absorption. FHHNC and Gitelman's syndrome are causes of urinary magnesium wasting; hypoparathyroidism and hypocalcemia do not cause hypomagnesemia.

References:

Epstein M, McGrath S, Law F. Proton-pump inhibitors and hypomagnesemic hypoparathyroidism. *N Engl J Med* 2006;355:1834–1836.

Broeren MA, Geerdink EA, Vader HL, van den Wall Bake AW. Hypomagnesemia induced by several proton-pump inhibitors. *Ann Intern Med* 2009;151:755–756. Cundy T, Dissanayake A. Severe hypomagnesaemia in long-term users of proton-pump inhibitors. *Clin Endocrinol (Oxf)* 2008;69:338–341.

108. A 39-year-old woman is referred to you with a history of hypercalcemia, recently discovered. She is asymptomatic except for unexplained weight loss of 13 lbs over the last 2 months. She takes no prescribed medications or over-the-counter medications. Physical exam reveals a somewhat anxious but healthy appearing woman. BP is 143/60 mm Hg, and pulse is 116 beats/min. She is afebrile. On examination, she has hand tremor and sweaty palms. There is a grade 2/6 apical systolic murmur, but the remainder of the exam is WNL.

Pertinent laboratory studies are as follows:

Hgb: 12.4; Ht: 14; WBC: 5400

BUN: 11 mg/dL; Cr: 0.9 mg/dL

Na: 142 mEq/L; Cl 106 mEq/L; K: 3.7 mEq/L; HCO₃: 24 mEq/L

Ca²⁺: 12.0 mg/dL; PO₄: 3.9 mg/dL; alb: 3.9 g/L

Parathyroid hormone (PTH): 5 ng/L 25 (OH)D: 30 nmol/L (nl)

1,25 (OH)₂D: 9 pg/mL (low)

Which laboratory test could establish the diagnosis?

- A. Serum magnesium
- B. 24-hour urine for creatinine and calcium
- C. Free thyroxine
- D. Alkaline phosphatase

Answer: C

Explanation:

The differential diagnosis in hypercalcemia with low PTH, normal 25(OH)D, and low 1,25(OH)₂D includes hyperthyroidism, malignancy, immobilization, Paget's disease, and milk-alkali syndrome. This patient has signs and symptoms of hyperthyroidism, and an elevated free thyroxine would establish the diagnosis.

References:

Iqbal AA, Burgess EH, Gallina DL, Nanes MS, Cook CB. Hypercalcemia in hyperthyroidism: Patterns of serum calcium, parathyroid hormone, and 1,25-dihydroxyvitamin D₃ levels during management of thyrotoxicosis. *Endocr Pract* 2003;9:517–521.

109. You are asked to consult on a 54-year-old woman with breast cancer and serum calcium of 14.0 mg/dL. Review of systems reveals lethargy, weakness, anorexia, constipation, and bone pain. In addition, she complains of polyuria and polydipsia of several weeks duration.

The laboratory data are as follows:

Hgb: 11.4; Ht: 34; WBC: 5400

BUN: 17 mg/dL; Cr: 1.2 mg/dL

Na: 145 mEq/L; Cl 109 mEq/L; K: 3.7 mEq/L; CO₂: 24 mEq/L

Ca²⁺: 14.0 mg/dL; PO₄: 3.9 mg/dL; alb: 3.5 g/L; parathyroid hormone (PTH): 5 ng/L; 25(OH)D: 30 nmol/L; 1,25(OH)₂D: 29 pg/mL

You decide that she is clearly symptomatic and needs therapy.

Which is NOT recommended as part of the initial therapy of moderate to severe hypercalcemia?

- A. ECF expansion
- B. ECF expansion plus furosemide
- C. Bisphosphonates
- D. Calcitonin

Answer: B

Explanation:

Initial therapy of moderate to severe hypercalcemia includes the administration of saline, calcitonin, and a bisphosphonate. Isotonic saline corrects possible volume depletion due to hypercalcemia-induced urinary salt wasting and, in some cases, vomiting. Hypovolemia exacerbates hypercalcemia by impairing the renal clearance of calcium. Saline therapy rarely normalizes the serum calcium concentration in patients with more than mild hypercalcemia. In the past, administration of a loop diuretic was initiated routinely once fluid repletion had been achieved to further increase urinary calcium excretion. However, this practice was based on an approach that involved intensive administration of furosemide with aggressive fluid hydration.

Saline therapy beyond that necessary to restore euvoolemia has fallen out of favor for several reasons:

- The availability of drugs such as the bisphosphonates and calcitonin that inhibit bone resorption, which is primarily responsible for the hypercalcemia.
- The requirement for careful monitoring because of the potential fluid and electrolyte complications resulting diuresis such as hypokalemia, hypomagnesemia, and volume depletion if the diuretic-induced losses are not replaced.
- Lack of evidence that this regimen effectively lowers serum calcium significantly more than ECF expansion alone.

References:

LeGrand SB, Leskuski D, Zama I. Narrative review: Furosemide for hypercalcemia: An unproven yet common practice. *Ann Intern Med* 2008;149:259–263.

110. A 50-year-old woman undergoes surgery for a craniopharyngioma. Postoperatively, her urine output is noted to be high for 2 days, and she is given two doses of desmopressin. Replacement doses of hydrocortisone are prescribed, and she is discharged from the hospital. Three days later, she is readmitted with obtundation and a serum sodium of 116 mEq/L.

Which is the MOST likely cause of her hyponatremia?

- A. Mineralocorticoid deficiency
- B. Persistent effect of desmopressin
- C. Adrenocorticotropic hormone (ACTH) deficiency
- D. Degenerating hypothalamic neurons

Answer: D

Explanation:

Pituitary disease does not cause mineralocorticoid deficiency, and hypoaldosteronism without cortisol deficiency does not cause severe hyponatremia. ACTH deficiency can cause hyponatremia, but the patient is receiving hydrocortisone. Desmopressin should no longer be working after 3 days. The patient's course is suggestive of the first two phases of the classic triphasic response following injury or transection of the pituitary stalk. Initially diabetes insipidus occurs because with interruption of nerve impulses vasopressin cannot be released from nerve terminals. The second phase syndrome of inappropriate antidiuretic hormone secretion (SIADH) results from unregulated release of stored vasopressin from degenerating neurons. Once vasopressin stores are depleted, permanent diabetes insipidus may ensue.

111. An 8-year-old boy with a family history of central diabetes insipidus (DI) affecting his father and older brother starts wetting the bed. His plasma osmolality in a morning fasting specimen is 298 mOsm/kg, and a concurrent urine osmolality is 320 mOsm/kg. A magnetic resonance image (MRI) of the brain shows a bright spot in the posterior pituitary.

Which BEST describes the likelihood of diabetes insipidus in this patient?

- A. DI is excluded because the urine osmolality is higher than plasma osmolality
- B. The presence of a pituitary bright spot excludes the possibility of DI
- C. The presence of a pituitary bright spot is diagnostic of central DI
- D. Central diabetes is most likely but primary polydipsia is also possible

Answer: D

Explanation:

Despite a high plasma osmolality, the urine is not maximally concentrated. This finding is consistent with either primary polydipsia, which “washes out” the concentration gradient in the renal medulla, or partial DI. The patient’s family history suggests a diagnosis of autosomal dominant hereditary DI. In this progressive disorder, vasopressin-secreting neurons degenerate because of the accumulation of misfolded arginine vasopressin precursors in the neuron’s endoplasmic reticulum, a so-called toxic gain-of-function mutation. Affected patients do not develop clinical signs of DI until several months or years after birth. The pituitary bright spot seen on MRI, which is found in people with a normally functioning hypothalamo-pituitary axis, may be preserved initially but is eventually lost as the disease progresses over time.

112. A 30-year-old woman with von Willebrand’s disease undergoes a hysterectomy for chronic menorrhagia. Postoperatively, she is treated with desmopressin every 8 hours. Two days after surgery, she complains of nausea and vomiting, she is not oriented to time or place, and laboratory data show serum sodium of 106 mEq/L and Uosm of 600 mOsm/kg.

Which is the BEST therapeutic strategy for the first 24 hours?

- A. 0.9% saline and discontinue desmopressin
- B. Tolvaptan and discontinue desmopressin
- C. Tolvaptan and continue desmopressin
- D. 3% saline and continue desmopressin

Answer: D

Explanation:

The patient has symptomatic hyponatremia, mandating a prompt increase in serum sodium concentration, but her electrolyte disturbance has developed gradually enough to put her at risk of osmotic demyelination if the increase is excessive. Discontinuing desmopressin will not increase the serum sodium concentration fast enough because the drug has a long half-life; once its effect has abated, a brisk water diuresis will develop that can return the serum sodium concentration to normal within 24 hours (overcorrection). Giving 0.9% saline while desmopressin is still working (choice A) risks lowering the serum sodium concentration further because of desalination. Giving tolvaptan alone (choice B) will antagonize the desmopressin and also risk over-rapid correction. Giving tolvaptan with desmopressin (choice C) is akin to doing nothing; she needs her plasma sodium concentration (PNa) to increase because she is symptomatic. Initiating therapy with a bolus of 3% saline while continuing desmopressin (choice D) as a “DDAVP clamp” will achieve the desired PNa and CNS goal and is the best way to control the rate of increase in PNa.

113. A 60-year-old man with bipolar disorder managed for 30 years with lithium carbonate is admitted for acute cholecystitis. Postoperatively, his urine output is replaced milliliter for milliliter with 0.9% saline. The next day, he is obtunded, and his serum sodium concentration is found to be 168 mEq/L.

Which about his condition is TRUE?

- A. Rapid correction should be avoided because it could cause cerebral edema
- B. Mortality is higher in this condition if correction is faster than 0.25 mEq/L/hour
- C. Severe hyponatremia indicates that his extracellular fluid volume is reduced, so treatment should begin with a 1-L bolus of 0.9% saline
- D. His serum sodium should be lowered rapidly to avoid central pontine myelinolysis

Answer: D

Explanation:

Although rapid correction of hyponatremia causes cerebral edema in infants, it has not been reported in adults. Moreover, the duration of hyponatremia is insufficient to allow accumulation of excess brain organic osmolytes. Hyponatremia does not necessarily mean that the ECF volume is contracted. In this case, the postoperative administration of saline to replace water losses would result in excess total body sodium and expansion of the ECF volume despite intracellular fluid volume contraction. A rapid increase in serum sodium concentration, even when starting with a normal serum sodium, has been reported to cause central pontine and extrapontine myelinolysis, similar to what occurs after rapid correction of chronic hyponatremia. Rapid relowering of the serum sodium has been shown to be protective of this complication in patients with hyponatremia, and it is indicated in this case as there is no risk of causing cerebral edema.

114. A 40-year-old man with a history of alcoholic liver disease and withdrawal seizures is started on hydrochlorothiazide for hypertension and a selective serotonin reuptake inhibitor (SSRI) for depression. Two weeks later, he is admitted with a seizure. Serum sodium is 101 mEq/L and serum potassium is 2 mEq/L. He is given 2 L of 0.9% saline in the Emergency Department and several runs of KCl. Six hours later, he is transferred to the intensive care unit and treated with 3% saline, increasing his serum sodium to 122 mEq/L. His mental status initially improves, and the 3% saline is discontinued, but on the third hospital day, he is noted to be obtunded. His serum sodium is now 120 mEq/L, and his serum potassium is 3 mEq/L.

Which treatment is the BEST choice?

- A. Resume 3% saline aiming for correction by 0.5 mEq/L per hour
- B. Resume 3% saline aiming for correction by 6 mEq/L per day
- C. Replace KCl using a solution containing 20 mEq potassium in 50 mL water
- D. Administer desmopressin and D5W with 40 mEq KCl/L

Answer: D

Explanation:

The patient has several risk factors (alcoholism, liver disease, serum Na <105 mEq/L, and hypokalemia) that make him more susceptible to osmotic demyelination syndrome (ODS) from rapid correction of hyponatremia. Obtundation developing after initial improvement of hyponatremic encephalopathy is a characteristic feature of this disorder. Therefore, further increase in the serum sodium should be avoided. Administering a concentrated KCl solution will further increase his serum sodium through the Edelman equation: $PNa = (\text{total body Na} + \text{total body K}) / \text{total body water}$. Relowering the serum sodium with D5W and desmopressin has been reported to abort early ODS. KCl should be administered along with D5W because the patient is potassium depleted, and the administered glucose will stimulate insulin release, which will worsen hypokalemia. In addition, it may replete potassium lost from the brain during the adaptation to hyponatremia.

115. A 68-year-old woman develops neurological symptoms after treatment for thiazide-induced hyponatremia. A magnetic resonance image (MRI) shows findings consistent with central pontine myelinolysis (CPM). She becomes progressively obtunded and is now tetraplegic and aspirating. She is placed on a ventilator. The family indicates that the patient never wanted to be kept alive on a ventilator and asks about withdrawal of care.

Which is the BEST description of her prognosis?

- A. Survival from this condition is extremely rare
- B. Although survival is possible, the patient is likely to remain in a persistent vegetative state
- C. The prognosis correlates best with how extensive the lesions are on MRI
- D. Complete recovery of neurological function can occur in up to one-third of cases with this severity of illness

Answer: D

Explanation:

Once thought to be a fatal disease (as was true when cases were identified at autopsy), CPM diagnosed by MRI imaging is rarely fatal unless care is inappropriately withdrawn. Complete recovery can occur, even in patients who are ventilator dependent. Full recovery may take months.

116. You are asked to see a 24-year-old woman who is being treated for pre-eclampsia and is noted to have a serum calcium of 7.6 mg/dL and a serum phosphate of 5.1 mg/dL, with a serum albumin of 4.0 g/L. She has a BUN of 18 and a creatinine of 1.8 mg/dL.

Which is the likely cause of the hypocalcemia?

- A. Renal failure
- B. Hyperphosphatemia
- C. Hypermagnesemia
- D. Hyperkalemia

Answer: C

Explanation:

Hypermagnesemia associated with magnesium infusion for treatment of pre-eclampsia can cause hypocalcemia by binding to the calcium-sensing receptor and reducing levels of parathyroid hormone. Hyperphosphatemia can lower serum calcium but does not cause significant hypocalcemia at this level. Hyperkalemia has no effect on the serum calcium concentration.

References:

Cholst IN, Steinberg SF, Tropper PJ, Fox HE, Segre GV, Bilezikian JP. The influence of hypermagnesemia on serum calcium and parathyroid hormone levels in human subjects. *N Engl J Med* 1984;310:1221–1225.

Suzuki K, Nonaka K, Kono N, Ichihara K, Fukumoto Y, Inui Y, Miyagawa J, Onishi T, Hayashi C, Tarui S. Effects of the intravenous administration of magnesium sulfate on corrected serum calcium level and nephrogenous cyclic AMP in normal human subjects. *Calcif Tissue Int* 1986;39:304–309.

Monif GR, Savory J. Iatrogenic maternal hypocalcemia following magnesium sulfate therapy. *JAMA* 1972;219:1469–1470.

117. You are asked to see a 43-year-old man with the following laboratory values:

Hgb: 12.9; WBC: 5600

BUN: 13 mg/dL; Cr: 1.3 mg/dL

Na: 135 mEq/L; K: 2.9 mEq/L; Cl: 100 mEq/L; CO₂: 30 mEq/L

Ca: 9.0 mg/dL; Mg: 0.9 mEq/L; albumin: 3.9 g/L 24-hour urine: Cr: 1.5 g; Ca: 280 mg; Mg: 60 mg

You point out to the medical student that hypomagnesemia with 24-hour urine excretion greater than 10–20 mg is not due to gastrointestinal loss and is primarily due to reduced reabsorption of magnesium in the ascending limb of Henle's loop and/or the distal tubule. You also note that the increased calcium excretion suggests that the impaired magnesium transport is caused by a defect in loop transport.

Which is NOT associated with impaired magnesium reabsorption in the loop of Henle?

- A. Cetuximab
- B. Familial hypomagnesemia with hypercalciuria and nephrocalcinosis
- C. Bartter's syndrome
- D. Calcineurin inhibitors

Answer: A

Explanation:

Mutations in the *claudin-16* gene (formerly known as *paracellin-1* gene) have been shown to be responsible for the rare inherited disorder known as familial hypomagnesemia with hypercalciuria and nephrocalcinosis (FHHNC), which impairs reabsorption of calcium and magnesium in the loop of Henle. Calcineurin inhibitors primarily reduce expression of claudin 16 in the ascending limb of Henle's loop. Bartter's syndrome is often linked to mild hypomagnesaemia owing to the dissipation of the lumen-positive transepithelial voltage that is the driving force for paracellular calcium and Mg²⁺ transport in the loop of Henle. Monoclonal antibodies targeting the epithelial growth factor (cetuximab, panitumumab, and matuzumab) are associated with the progressive development of hypomagnesemia due to renal magnesium wasting in the distal tubule.

References:

Tejpar S, Piessevaux H, Claes K, Piront P, Hoenderop JG, Verslype C, Van Cutsem E. Magnesium wasting associated with epidermal-growth-factor receptor-targeting antibodies in colorectal cancer: A prospective study. *Lancet Oncol* 2007;8:387–394.

de Baaij JHF, Hoenderop JGJ, Bindels RJM. Regulation of magnesium balance: Lessons learned from human genetic disease. *Clin Kidney J* 2012;5(Suppl 1):i15.

118. A patient with multiple myeloma is found to have a low serum sodium concentration.

Which test would BEST demonstrate that this is a case of pseudohyponatremia?

- A. Indirect potentiometry
- B. Flame photometry
- C. Measurement of plasma osmolality
- D. Plasma rather than serum sodium concentration (heparinized tube)

Answer: C

Explanation:

In pseudohyponatremia, the serum sodium concentration is artifactually low because of an increase in the nonaqueous component of a serum or plasma sample. Osmolality is a property of the aqueous component of the sample so that the plasma osmolality remains normal, and there is a "gap" between the osmolality calculated from the serum sodium concentration, BUN, and blood glucose and the measured value.

Measurement of the serum or plasma sodium concentration with an ion-specific electrode without dilution of the sample (direct potentiometry) would show that the sodium concentration is really normal. However, measuring the sodium concentration with indirect potentiometry (used in most automated devices) requires a dilution step that will yield an artificially low value. Diluting the sample requires that an aliquot of serum or plasma be obtained; that aliquot will contain a lower-than-normal amount of plasma water. The plasma and serum sodium concentrations will not be different in pseudohyponatremia (as they are in

pseudohypokalemia). The plasma osmolality value (choice C) will be normal in pseudohyponatremia and confirm that diagnosis if direct potentiometry is not available. In this case, multiple myeloma has a high paraprotein level that increases the solid component of the blood (also with severe hyperlipidemia) that is responsible for pseudohyponatremia.

References:

Weissberg LS. Pseudohyponatremia: A reappraisal. *Am J Med* 1989;86(3):315–318.

Vaswani SK. Pseudohyponatremia in multiple myeloma. *South Med J* 1993;86(2):251–252. Turchin A. Clinical problem-solving. Mind the gap. *N Engl J Med* 2003;349(15):1465–1469.

119. A previously healthy 33-year-old woman presents with an axillary mass. Workup reveals Burkitt's lymphoma. The medical history was unremarkable except for an episode of acute anemia that was mentioned. She was told that it was related to an antibiotic administered many years ago, and she was instructed to avoid sulfonamide antibiotics. Initial laboratory data show the following levels: serum creatinine, 1.1 mg/dL; PO₄, 7.5 mg/dL; and uric acid, 13.6 mg/dL.

Which is the MOST appropriate therapy for hyperuricemia prior to initiating tumor-specific chemotherapy?

- A. Rasburicase
- B. Alkalinization of the urine
- C. Allopurinol
- D. Oral phosphate binder

Answer: C

Explanation:

Allopurinol, which blocks xanthine oxidase and prevents the conversion of hypoxanthine/xanthine to uric acid, is the correct choice. Although it does not lower previously formed uric acid, it is the best choice in this case due to the contraindication to rasburicase. Urinary alkalinization increases the solubility of uric acid in the urine thereby decreasing intratubular uric acid crystal deposition and preventing/reducing acute urate nephropathy. However, there is a cost: calcium-phosphate deposition in the kidneys can occur (it is less soluble in an alkaline urine), as well as systemic complications from alkali infusion (symptomatic hypocalcemia). An oral phosphate binder will not significantly lower serum PO₄ levels in the setting of tumor lysis syndrome. Rasburicase metabolizes uric acid to allantoin, which is very soluble and is excreted by the kidneys. The drug is degraded in the circulation, does not require liver or renal dosing, and is generally safe. The only major contraindication is use in patients with G6PD deficiency. In this situation and in this case, the drug can cause anemia and methemoglobinemia. Thus, the drug is contraindicated in this patient.

120. A 67-year-old man with acute myelogenous leukemia presents with fatigue and weakness. Exam reveals normal vital signs and relatively unremarkable findings. Labs reveal white blood cell count of 130,000/mL, serum uric acid of 8.7 mg/dL, serum calcium of 7.4 mg/dL, and a phosphate of 8.1 mg/dL. Serum creatinine is 1.4 mg/dL. There is concern for tumor lysis syndrome.

Which therapy is contraindicated in this patient?

- A. Urinary alkalinization
- B. Intravenous saline
- C. Rasburicase
- D. Allopurinol

Answer: A

Explanation:

Urinary alkalinization is no longer recommended for tumor lysis syndrome (TLS). Increasing urinary pH (alkalinization) decreases uric acid precipitation (increases solubility), but it also enhances calcium-phosphate (CaPO₄) crystal deposition (risking acute phosphate nephropathy) within renal tubules. So, while alkalinization is good for uric acid, it is bad for CaPO₄.

Intravenous saline is harmless and potentially helpful in setting of volume depletion by increasing urinary flow rates. Rasburicase is a fairly safe drug that is potentially helpful by lowering serum uric acid level and preventing acute urate nephropathy. It is harmful if patient has *G6PD* deficiency, as this will cause hemolytic anemia and methemoglobinemia and is contraindicated in patients with *G6PD* deficiency. Allopurinol is a fairly safe drug if dosed appropriately for level of kidney function. It will help reduce further uric acid production but will not correct hyperuricemia. Hypoxanthine and xanthine levels are increased when allopurinol is used and there is a high cellular turnover as seen in TLS. These two compounds can precipitate in renal tubules at a high pH urine and is another potential reason urine alkalinization should be avoided in TLS where allopurinol is often used.

121. A 47-year-old man with squamous cell cancer of the larynx was treated with radiotherapy and chemotherapy including cisplatin, bleomycin, and paclitaxel. He returns to the clinic, and hyponatremia is observed. The patient complains of frequent episodes of dizziness, and he is found to be orthostatic. He is taking no other medications and denies pain. He does feel as though he might faint on occasion. There is no edema in his extremities, and the rest of the examination is unremarkable. His laboratory results show the following: BUN, 20 mg/dL; creatinine, 1.5 mg/dL (1.1 mg/dL 2 months ago); sodium, 123 mEq/L; K, 3.7 mEq/L; Cl, 90

mEq/L; and HCO_3^- , 24 mEq/L. The rest of the laboratory results, including Ca, PO_4 , and Mg, were normal. Urine sodium is 110 mEq/L, and urine osmolality is 410 mOsm/L.

Which is the MOST likely cause of this patient's clinical condition?

- A. Cisplatin-induced renal salt wasting
- B. Syndrome of inappropriate antidiuretic hormone secretion
- C. Bleomycin-induced renal salt wasting
- D. Paclitaxel-induced autonomic neuropathy

Answer: A

Explanation:

A high urine sodium in the setting of obvious signs of volume depletion is an inappropriate renal response and indicates "salt wasting." Cisplatin is the only drug in this list known to cause this. Ifosfamide has been reported to have this effect as well.

Cisplatin causes kidney injury with various manifestations, including AKI (acute tubular necrosis), tubulopathies (proximal tubulopathy/Fanconi syndrome, salt wasting, Mg^{2+} wasting, nephrogenic diabetes insipidus), and CKD. The syndrome of inappropriate antidiuretic hormone secretion (SIADH) from malignancy is not consistent with the hallmark of SIADH: euolemia.

Bleomycin does not cause renal salt wasting. Paclitaxel can produce autonomic neuropathy and orthostatic hypotension but not renal salt wasting.

122. A 61-year-old retired male postal worker with a history of hypertension, anemia, osteoporosis, and gastritis begins treatment with 5-fluorouracil, leucovorin, and cetuximab for metastatic colon cancer. Other medications include pantoprazole, iron sulfate, quarterly intravenous ibandronate, and amlodipine. After 14 weeks of therapy, the patient presents with weakness and peri-oral numbness and tingling. A physical exam reveals positive Trousseau's phenomenon and positive Chvostek's sign. Laboratory data reveal the following: K^+ , 3.0 mEq/L; Ca^{2+} , 6.5 mg/dL; Mg^{2+} , 0.7 mg/dL; albumin, 3.3 g/dL; BUN, 18 mg/dL; and serum creatinine, 1.4 mg/dL. Aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase are normal. Urine studies show a fractional excretion of Mg of 10%.

Which is the MOST likely cause of the clinical presentation and laboratory abnormalities?

- A. Cetuximab
- B. Pantoprazole
- C. Ibandronate
- D. Leucovorin
- E. 5-Fluorouracil

Answer: A

Explanation:

The patient developed hypomagnesemia from renal Mg wasting as indicated by the fractional excretion of Mg of 10%.

Hypomagnesemia was associated with hypokalemia and hypocalcemia. Cetuximab is a monoclonal antibody against epidermal growth factor receptor (EGFR). Binding of EGF to its receptor is associated with movement of the magnesium channel (TRPM6) to the apical membrane to allow for reabsorption of magnesium in the distal collecting tubule. Cetuximab competes for the receptor and, by doing so, disrupts movement of TRPM6 to the apical membrane, resulting in Mg wasting and hypomagnesemia. Proton pump inhibitors (choice B) can cause hypomagnesemia; but by inhibiting gastrointestinal absorption, the urine fractional excretion of Mg would be expected to be very low (<3%).

123. A 22-year-old woman is dancing in the mosh pit with her friends. She is drinking plenty of Powerade to "keep hydrated." After a few hours, she begins to develop irritability and confusion. She suddenly develops a seizure and is emergently transported to the local hospital emergency department. She is unresponsive but has a BP of 105/60 mm Hg. The exam is otherwise unremarkable. Laboratory data: serum Na, 114 mEq/L; serum K, 5.2 mEq/L; HCO_3^- , 14 mEq/L (anion gap of 24); and serum creatinine, 1.3 mg/dL. Hematocrit is 43%, and platelets are 345. Creatine phosphokinase (CPK) is 1575 U/L.

What is the MOST appropriate treatment?

- A. 3% saline at 50 mL/hr
- B. Normal saline at 250 mL/hr
- C. 3% saline at 50 mL/hr with a DDAVP clamp
- D. 3% saline by bolus 100-150 mL therapy every 15 minutes until alert

Answer: D

Explanation:

This is likely a case of ecstasy-induced hyponatremia. The mechanism is not completely known but likely is a combination of syndrome of inappropriate antidiuretic hormone secretion (SIADH) and excessive hypotonic fluid ingestion. The seizure induced by hyponatremia is the cause of the elevated anion gap (lactic) acidosis. AKI is most commonly reported from ecstasy after it causes rhabdomyolysis, which is also noted in this patient. Premenopausal women are at much greater risk of developing hyponatremia and the effects of hyponatremia than men.

The patient has symptomatic hyponatremia and should have her serum Na immediately increased. Giving 3% by infusion (50 mL/h) may not be fast enough; the preferred therapy is rapid Na increase using 3% saline bolus therapy. Ecstasy-induced hyponatremia is one of the few causes of severe symptomatic hyponatremia that is acute (marathon-induced hyponatremia is another). Given that her hyponatremia is clearly acute, the rate of correction causing central pontine myelinolysis is not a concern, and DDAVP is not necessary. Giving normal saline by itself is never a good idea for SIADH because the kidneys can desalinate the IVF and further lower the serum Na.

124. A patient receiving intravenous immunoglobulin (IVIG) is found to have a serum sodium of 128 mEq/L. The BUN and blood glucose are normal. The calculated plasma osmolality is 266 mOsm/kg, and the measured plasma osmolality is 290 mOsm/kg. Measuring the serum sodium with a direct ion selective electrode confirmed a value of 128 mEq/L.

What is the mechanism of the hyponatremia?

- A. Pseudohyponatremia due to the carrier (sucrose or maltose)
- B. Pseudohyponatremia due to the immunoglobulin
- C. True hyponatremia from renal salt wasting
- D. True hyponatremia from syndrome of inappropriate antidiuretic hormone secretion (SIADH)

Answer: A

Explanation:

IVIG can cause hyponatremia through two different mechanisms. Because IVIG significantly increases the total protein content of blood, pseudohyponatremia can occur as the solid component of blood increases (the same situation can occur with severe hyperlipidemia). The typical laboratory method of measuring serum sodium (indirect ion selective) will produce a low result. However, the plasma osmolality measurement will be normal (an osmolar gap will be present), and the serum sodium value will be normal if measured by a direct ion selective method.

The other mechanism is related to the vehicle or carrier for the IVIG: sucrose or maltose. These sugars can accumulate in the blood (especially if renal failure is present). Because they do not enter cells, the result can be osmotic disequilibrium between the cellular and the extracellular compartments, pulling water out of cells and diluting the sodium concentration in the extracellular compartment. This is similar to what happens with hyperglycemia, but without an osmolal gap because glucose can be measured and included in the calculated serum osmolality. For this patient, neither sucrose nor maltose is measured, so you will have an osmolal gap, but when measured by direct ion selective methods, the serum sodium will still be low because of the water movement. The osmolal gap in this patient is from the retained sucrose, but the serum sodium is actually low when studied with direct ion selective electrodes. In effect, this is not true pseudohyponatremia at all; that term should be reserved for situations in which the serum sodium is low with indirect ion selective methods but normal with direct ion selective methods.

True hyponatremia from salt wasting and SIADH should not have an osmolal gap.

125. A postoperative ultrasound is obtained 6 weeks after fistula creation.

Which measurement is associated with the MOST likelihood that the fistula will be used successfully for dialysis?

- A. Diameter 4.6 mm, access flow 625 mL/min
- B. Diameter 3.2 mm, access flow 550 mL/min
- C. Diameter 5.1 mm, access flow 380 mL/min
- D. Diameter 3.5 mm, access flow 420 mL/min

Answer: A

Explanation:

Both the diameter and blood flow of the fistula measured 4–6 weeks postoperatively are predictive of successful use of the fistula for dialysis. The combination of a diameter >4 mm AND access flow >500 mL/min predicts a 95% success rate. A combination of fistula diameter <4 mm AND access flow <500 mL/min predicts a 33% likelihood of fistula success.

References:

Robbin ML, Chamberlain NE, Lockhart ME, et al. Hemodialysis arteriovenous fistula maturity: US evaluation. *Radiology* 2002;225:59–64.

126. You treat a patient with dialysis catheter–related bacteremia with systemic antibiotics and an antibiotic lock.

Which is TRUE?

- A. A cure is most likely with *Staph epidermidis* infections
- B. A cure is most likely with *Staph aureus* infections
- C. A cure is most likely with gram-negative bacterial infections
- D. A cure is equally likely with all bacterial organisms

Answer: C

Explanation:

Published studies have consistently shown that treatment of dialysis catheter–related bacteremia with an antibiotic lock is most successful (~90%) with gram-negative infections, somewhat less successful with *Staph epidermidis* infections (~75%), and least successful with *Staph aureus* infections (~40%).

References:

Allon M. Treatment guidelines for dialysis catheter-related bacteremia: An update. *Am J Kidney Dis* 2009;54:13–17.

127. A 23-year-old man with ESKD secondary to focal segmental glomerulosclerosis is being dialyzed three times a week through a tunneled dialysis catheter. Yesterday, he was admitted to the hospital with a 1-day history of fever and chills. His catheter exit site was non-tender and non-erythematous. Blood cultures are growing gram-positive cocci.

Which would be the MOST appropriate next step in the therapy of this patient?

- A. Intravenous vancomycin and gentamicin
- B. Intravenous vancomycin, gentamicin, and guidewire exchange of the infected catheter
- C. Intravenous vancomycin
- D. Intravenous vancomycin and guidewire exchange of the infected catheter
- E. Intravenous nafcillin and instillation of an antibiotic lock in the catheter lumens

Answer: D

Explanation:

The bacterial biofilm coating the inner lumen of the catheter is the major source of catheter-related bacteremia in patients with tunneled hemodialysis catheters. Thus, treatment requires removal or exchange of the infected catheter. Alternatively, an antibiotic lock can be used in conjunction with systemic antibiotics to kill the bacteria in the biofilm, while attempting to salvage the catheter. Systemic antibiotics alone may temporarily treat the bacteremia. However, the infection recurs in ~75% of patients once the antibiotic course has been completed. There is no role for the addition of an aminoglycoside in the treatment of gram-positive infections. Nafcillin would be appropriate only after antimicrobial sensitivities return.

References:

Allon M. Dialysis catheter-related bacteremia: Treatment and prophylaxis. *Am J Kidney Dis* 2004;44:779–791.

128. A 58-year-old man with stage 4 CKD from diabetes mellitus (DM) and hypertension (HTN) is seen for cardiovascular risk management. He has no history of coronary artery disease (CAD), cerebrovascular accident (CVA), or congestive heart failure (CHF). His DM and HTN are optimally treated.

Lipid panel

Cholesterol: 235 mg/dL, LDL: 112 mg/dL, Triglycerides: 207 mg/dL

Which will be accomplished by effective LDL-lowering therapy with simvastatin and ezetimibe?

- A. Reduce major atherosclerotic events
- B. Reduce patient mortality
- C. Slow the progression of CKD
- D. Reduce the incidence of ESKD

Answer: A

Explanation:

The correct answer is A. In the randomized, controlled SHARP (Study of Heart and Renal Protection) trial, CKD and ESKD patients given LDL-lowering therapy with simvastatin and ezetimibe had a significant 17% reduction in major atherosclerotic events over 5 years of study. Active therapy did not result in a reduction in patient mortality or incidence of ESKD, nor did it slow the progression of CKD. Active therapy was well tolerated and did not result in excessive risk of myopathy, hepatitis, or cancer.

129. A 52-year-old African-American man is seen at follow-up for CKD stage 4 with an eGFR of 26 mL/min per 1.73 m² attributable to diabetic nephropathy. BP is well controlled on ACE inhibitor therapy, but he has metabolic acidosis with a serum bicarbonate level of 18 mEq/L. You prescribe Na+HCO₃ therapy with the intent to treat his metabolic acidosis, reduce metabolic bone disease, and slow the progression of his CKD.

What is the MOST likely explanation for how alkali therapy slows the progression of CKD?

- A. Increased systemic BP with increased renal blood flow
- B. Improved glomerular hemodynamics with efferent arteriolar vasodilatation
- C. Reduced tubular-interstitial damage by limiting inflammatory urinary biomarkers such as endothelin (ET) and transforming growth factor (TGF)- β
- D. Improved ultrafiltration coefficient (Kf) of glomerular hemodynamics

Answer: C

Explanation:

The correct answer is C. Observational studies and two randomized controlled trials (RCTs) demonstrated that correction of metabolic acidosis resulted in slower progression of CKD. The recent RCT of Phisitkul et al. examined potential mechanisms of this slower loss of eGFR. Alkali therapy reduced the urinary excretion of ET, *N*-acetyl-glucosamine (NAG), TGF- β , and albumin, suggesting an attenuation of tubular injury and damage consistent with prior experimental observations in the 5/6 nephrectomy model of CKD. It is hypothesized that up-regulated urinary NH₄ excretion per nephron may up-regulate renal complement and ET production as potential second messengers of tubular-interstitial damage.

References:

de Brito-Ashurst I, Varagunam M, Rafferty MJ, Yaqoob MM. Bicarbonate supplementation slows progression of CKD and improves nutritional status. *J Am Soc Nephrol* 2009;20:2075–2084.

Phisitkul S, Khanna A, Simoni J, Broglio K, Sheather S, Rajab MH, Wesson DE. Amelioration of metabolic acidosis in patients with low GFR reduced kidney endothelin production and kidney injury, and better preserved GFR. *Kidney Int* 2010;77:617–623.

Simon EE, Hamm LL. A basic approach to CKD. *Kidney Int* 2010;77:567–569.

130. A 66-year-old man with moderately controlled type 2 diabetes, hypertension, and stage 4 CKD with nephrotic range proteinuria and serum creatinine of 2.5 mg/dL is admitted to the hospital because he has suffered a cerebrovascular accident.

Which is the BEST answer concerning this patient?

- A. Type 2 diabetic patients with CKD always have increased albuminuria
- B. Intensive glycemic control of type 2 diabetes does not decrease incidence of nephropathy and cardiovascular mortality
- C. In type 2 diabetes, proteinuria correlates with increased incidence of coronary heart disease but not with stroke
- D. In both type 1 and type 2 diabetes, hypertension usually indicates evidence of diabetic nephropathy

Answer: B

Explanation:

Option A is false. The DEMAND (Developing Education on Microalbuminuria for Awareness of reNal and cardiovascular risk in Diabetes) study indicated that 17% of patients with type 2 diabetes and CKD stages 3–5 had normoalbuminuria.

Option B is true. The ACCORD trial indicated an increased risk of overall mortality with intensive glucose lowering in this population. Recent meta-analyses have indicated a decrease in cardiovascular disease outcomes, specifically nonfatal myocardial infarctions and risk of progression of nephropathy but could not confirm that there was any decrease in nephropathy incidence or cardiovascular mortality.

Option C is false. Increasing proteinuria also correlates with increasing incidence of strokes in patients with type 2 diabetes.

Option D is false. Unlike type 1 diabetes, because patients presenting with type 2 diabetes are older, they often develop hypertension prior to onset of diabetic kidney injury.

References:

- Dwyer JP, Parving HH, Hunsicker LG, Ravid M, Remuzzi G, Lewis JB. Renal dysfunction in the presence of normoalbuminuria in type 2 diabetes: Results from the DEMAND Study *Cardiorenal Med* 2012;2(1):1–10.
- Kelly TN, Bazzano LA, Fopnseca VA, Thethi TK, Reynolds K, He J. Systematic review: Glucose control and cardiovascular disease in type 2 diabetes. *Ann Int Med* 2009;151(6):394–403.
- Hemmingsen B1, Lund SS, Gluud C, Vaag A, Almdal T, Hemmingsen C, Wetterslev J. Intensive glycaemic control for patients with type 2 diabetes: systematic review with meta-analysis and trial sequential analysis of randomised clinical trials. *BMJ* 2011;343:6898.
- Buehler AM, Cavalcanti AB, Berwanger O, Figueiro M, Laranjeira LN, Zazula AD, Kioshi B, Bugano DG, Santucci E, Sbruzzi G, Guimaraes HP, Carvalho VO, Bordin SA. Effect of tight blood glucose control versus conventional control in patients with type 2 diabetes mellitus: a systematic review with meta-analysis of randomized controlled trials. *Cardiovascular Therapeutics* 2013;31(3):147-60.
- Miettinen H, Haffner SM, Lehto S, Ronnema T, Pyorala K, Laakso M. Proteinuria predicts stroke and other atherosclerotic vascular disease events in nondiabetic and non-insulin-dependent diabetic subjects. *Stroke* 1996;27(11):2033–2039.

131. A 33-year-old woman with known primary aldosteronism due to an adrenal adenoma has well controlled hypertension on spironolactone and hydrochlorothiazide. She is now referred to you by the Obstetric clinic since she has been recently found to be 10 weeks pregnant.

She is complaining of light headedness and low home BP measurements. The patient discontinued her hydrochlorothiazide 4 weeks ago and has now held her spironolactone therapy for the last 2 weeks.

Examination: Patient appears well. BP is 96/62 mm Hg seated. Examination is normal other than trace pedal edema.

Labs: 136 | 100 / 9 PRA, 1.2; thyroid stimulating hormone (TSH), normal
 3.6 | 26 \ 0.6 Plasma aldosterone, 48 (normal 5–14); urinalysis, normal

What is the MOST likely explanation for normalization of her BP and potassium off therapy?

- A. Infarction of her adrenal adenoma as a complication of her pregnancy
- B. Increase in peripheral vasodilatation as a function of placental relaxin production
- C. Pregnancy induced increase in progesterone levels antagonizing the effects of aldosterone
- D. Spontaneous remission of her adenoma primary aldosteronism seen in approximately 20% of cases

Answer: C

Explanation:

The pregnancy-induced rise in progesterone levels attenuated the effects of the high aldosterone levels associated with the patient's primary aldosteronism state resulting in normalization of BP and serum potassium. Early investigators had observed this salutary effect of pregnancy in primary aldosteronism and also reported the return of hypertension and metabolic alkalosis with hypokalemia postpartum. Adrenal infarction and/or spontaneous remission of primary aldosteronism is possible, yet very unlikely. Peripheral vasodilation in pregnancy is physiological and often mediated *via* prostaglandins and other vasodilatory modulators. Relaxin is associated with placental implantation and growth early in pregnancy and later with relaxation of the symphysis pubis and cervix for delivery.

References:

Biglieri EG, Slaton PE. Pregnancy and primary aldosteronism. *J Clin Endocr* 1967;27(11):1628–1632.

132. **Which statement is TRUE regarding hypertensive patients of African ancestry who lack diabetes and have subnephrotic proteinuria, for instance, for participants in the African American Study of Kidney Disease and Hypertension (AASK) Trial?**

- A. Kidney biopsies typically reveal membranous nephropathy, with interstitial fibrosis and arteriolar hyalinosis
- B. Aggressive treatment of hypertension to approximately 135/85 mm Hg using ACE inhibitors reliably halts progression of nephropathy
- C. Progression of kidney disease strongly relates to the presence of two risk variants in the apolipoprotein L1 gene (*APOL1*), with an autosomal recessive pattern of inheritance
- D. Combination therapy with angiotensin receptor blockers and angiotensin converting enzyme inhibitors shows synergistic benefit in slowing progression of the kidney disease

Answer: C

Explanation:

Kidney biopsies in hypertensive, nondiabetic African-American patients with low level proteinuria, typical of those enrolled in the NIH-sponsored AASK Trial, revealed focal global glomerulosclerosis with interstitial fibrosis and small intrarenal vascular changes that did not correlate with systemic BP (FSGS may also be present). AASK cohort results revealed that nearly 60% of subjects treated with ACE inhibitors to the low BP target still reached the composite end point (either ESKD, doubling of serum creatinine concentration, or death) after 10-year follow-up. In contrast to BP target or class of antihypertensive medication, two *APOL1* risk variants was the only predictor of progressive kidney failure. This demonstrates that this kidney disease is not likely caused by high BP but resides in the spectrum of *APOL1*-associated nephropathy, as for idiopathic FSGS and HIV-associated collapsing glomerulopathy in individuals of African ancestry.

References:

Lipkowitz MS, Freedman BI, Langefeld CD, Comeau ME, Bowden DW, Kao WH, Astor BC, Bottinger EP, Iyengar SK, Klotman PE, Freedman RG, Zhang W, Parekh RS, Choi MJ, Nelson GW, Winkler CA, Kopp JB, and the AASK investigators. Apolipoprotein L1 gene variants associate with hypertension-attributed nephropathy and rate of kidney function decline in African Americans. *Kidney Int* 2013;83(1)114–120.

133. You are prescribing medications for a 72-year-old man with chronic glomerulonephritis. His serum creatinine has been stable at 2 mg/dL for approximately 8 months. He now develops an upper respiratory illness characterized by fever, chest pain, cough, and hemoptysis, and his chest x-ray shows a left lower lobe infiltrate. He is allergic to penicillin but has tolerated cephalosporin antibiotics in the past. Your examination reveals an acutely ill male with obvious discomfort in breathing. Temperature is 102.6°F, pulse is 106 beats/min and regular, and he has a BP of 142/60 mm Hg. He is 6'1" tall and weighs 205 lbs.

What is the BEST choice of antibiotic therapy for this patient?

- A. Dose his cephalosporin as if he had normal kidney function
- B. Calculate his estimated GFR and cut his cephalosporin dose proportionate to his GFR decline but give at the usual dose intervals
- C. Calculate his estimated GFR and increase the interval between maintenance cephalosporin doses depending on the percent reduction of his GFR
- D. Treat him with a penicillin despite his drug allergy because of his acute illness
- E. After a loading cephalosporin dose, give him 75% of the usual maintenance dose at regular intervals

Answer: E

Explanation:

The patient is acutely ill, and cephalosporin antibiotics have a very wide therapeutic margin. It is important to get antibiotics on board as soon as possible considering the fact that he may have a life-threatening bacterial pneumonia. Cephalosporin drug accumulation does not usually occur until GFR is less than 30 mL/min/1.73 m². It therefore is inappropriate to cut his dose proportionate to his GFR decline or to extend the dose interval between maintenance doses. Either of these strategies has the risk of underdosing him. However, answer A is incorrect because he has severely impaired renal function and could accumulate cephalosporins rapidly. It would be very risky to treat him with penicillin despite his drug allergy in the face of other less hazardous alternatives. Thus, it is best to get the antibiotic on board quickly with a loading dose and then reduce his maintenance dose slightly keeping the antibiotic level high.

134. A 46-year-old woman has CKD due to type 2 diabetes mellitus. She is obese and has frequent lower urinary tract infections. Usually, these clear with short-term antibiotics. Each time, the organism in her urine is sensitive to a number of commonly used drugs. Her baseline serum creatinine is 3.2 mg/dL. She is 5'1" tall and presents now with a fever of 103°F and a shaking chill, and urine microscopy reveals copious bacteria and white cells. In addition, two to three white cell casts are observed per high power field in her urinalysis.

What is the BEST course of treatment for her after drawing the appropriate urine and blood cultures?

- A. Antibiotics adjusted on the basis of her kidney function
- B. Antibiotics given in usual amounts
- C. Renally adjusted aminoglycoside therapy
- D. Continuous antibiotic infusion

Answer: B

Explanation:

The patient probably has an acute pyelonephritis with renal dysfunction. This is difficult to treat unless adequate antibiotic is present in the urine. Thus, if you simply adjust her antibiotics based on her kidney function, she may achieve only subtherapeutic urine levels. Antibiotics given in the usual amounts probably will be the best therapy.

Aminoglycosides have the risk of toxicity and enter the urine primarily through glomerular filtration, which is not a good choice in this individual. Continuous antibiotic infusions are usually not as effective as intermittent therapy because the bacterial killing is usually related to the peak blood level of antibiotics.

135. What can favorably influence progression to ESKD in the course of late stage (CKD stage 3–4) ADPKD?

- A. ACE inhibition
- B. Calcium channel blockers
- C. Dietary protein restriction
- D. Avoidance of caffeine
- E. None of the above

Answer: E

Explanation:

None of the abovementioned modalities to change progression to ESKD in ADPKD have been shown to be efficacious; thus, E is the correct answer. The HALT-PKD trial did suggest some benefit from combination ACE inhibitor/ARB therapy in early-stage ADPKD. However, the most recent trial data shows that in early ADPKD, the combination of lisinopril and telmisartan did not significantly alter the rate of increase in total kidney volume. Compared with standard BP control, rigorous BP control was associated with a slower increase in total kidney volume, no overall change in the estimated GFR, a greater decline in the left ventricular mass index, and greater reduction in urinary albumin excretion.

References:

Schrier RW, Abebe KZ, Perrone RD, Torres VE, Braun WE, Steinman TI, Winklhofer FT, Brosnahan G, Czarnecki PG, Hogan MC, Miskulin DC, Rahbari-Oskoui FF, Grantham JJ, Harris PC, Flessner MF, Bae KT, Moore CG, Chapman AB; HALT-PKD Trial Investigators. Blood pressure in early autosomal dominant polycystic kidney disease. *N Engl J Med* 2014;371:2255–2266.

136. What BEST manages resistant upper urinary tract infections in patients with PKD and CKD stage V?

- A. Fluoroquinolones
- B. High-dose cephalosporins
- C. Gentamicin/meropenem
- D. Trimethoprim/sulfamethoxazole adjusted to the level of renal function
- E. Bilateral nephrectomy

Answer: A

Explanation:

Certain antibiotics are known to penetrate cysts and renal parenchyma in patients with ADPKD. Among these are the fluoroquinolones and trimethoprim/sulfamethoxazole. However, in contrast to fluoroquinolones where minimal dose adjustment is needed, adjusting the trimethoprim/sulfamethoxazole to the level of renal function will result in low urinary concentrations and low cyst concentrations. If the drug is used, the doses should be normal. Gentamicin and cephalosporins do not penetrate cysts well, and bilateral nephrectomies are too radical of a therapy unless there is abscess formation and failure of antibiotic treatment.

137. Which statement about cerebral aneurysms in ADPKD is TRUE?

- A. Cerebral aneurysms affect 20% of all patients with ADPKD
- B. Cerebral aneurysms cluster within families
- C. Screening for cerebral aneurysms should be carried out in all patients with ADPKD
- D. Cerebral aneurysms more than 5 mm in size are associated with a 50% chance of rupture
- E. New cerebral aneurysms arise frequently, and patients should be screened every year for their occurrence

Answer: B

Explanation:

Patients with ADPKD have an increase incidence of cerebral aneurysms. With a family history of aneurysms, the incidence is approximately 20%. In all patients with PKD, the incidence is closer to 2–5%. Therefore, screening for cerebral aneurysms is not recommended for all patients. If aneurysms are detected more than 5 mm in size but less than 10 mm, they should be followed since the risk of rupture is low; in those greater than 10 mm, the chance of rupture increases. Aneurysms do arise in previously screened patients, and most experts believe that patients with known aneurysms should be rescreened every 2–3 years to monitor for occurrence and to monitor the growth of aneurysms already present.

138. In patients with the phenotype of ADPKD, which secondary complication is MOST common?

- A. Polycystic liver disease
- B. Cerebral artery aneurysms
- C. Mitral valve prolapse
- D. Renal stones
- E. Diverticulosis

Answer: A

Explanation:

Secondary complications are common in ADPKD. With modern imaging techniques, polycystic liver disease is virtually universal. This complication appears earlier and is more severe in women than men, but men develop this complication almost inevitably if they live long enough. Diverticulosis is common but the percentage is estimated to be only slightly greater than that of the general population. Cerebral aneurysms are present in approximately 5% of patients. Mitral valve prolapse when looked for is present in 10–15% of patients, and renal stones are noted in approximately 20% of patients.

139. A 52-year-old man has a BP of 132/88 mm Hg on his yearly physical exam, which was confirmed on three subsequent visits. He is a nonsmoker, his body mass index (BMI) is 29 kg/m², his LDL is 110 mg/dL, and HDL is 35 mg/dL. His fasting glucose is 85 mg/dL.

Which treatment is the MOST appropriate?

- A. Low-dose diuretic
- B. Low-dose angiotensin receptor blocker
- C. Healthy lifestyle changes
- D. Ambulatory BP monitoring

Answer: C

Explanation:

This patient has “prehypertension,” defined as BP 120–139/80–89 mm Hg. Although JNC 7 (Seventh Joint National Committee) guidelines from the National High Blood Pressure Education Program consider BP in this range as prehypertension, other professional guidelines (British Hypertension Society, International Society of Hypertension/World Health Organization) label this category as “high normal.” The US guidelines have chosen the term prehypertension to emphasize the fact that the relationship between BP and cardiovascular morbidity and mortality is linear, beginning at BP of 115/75 mm Hg. Although this level of BP is considered high normal, or prehypertension, the available data from clinical trials do not support pharmacologic treatment in persons without other major risk factors (e.g., diabetes, renal disease, evidence of target organ damage); therefore, choices A and B are incorrect. Rather, lifestyle modifications (maintaining ideal body weight, exercise, DASH diet, and moderate alcohol intake) are recommended, and regular follow-up of BP is recommended, because there is also an increased risk of developing hypertension. Choice D, ambulatory BP monitoring, is not recommended because the major indication for this test is to diagnose white coat hypertension, which is defined as hypertension (140/90 mm Hg) in the office and normal BP everywhere else. This patient does not have hypertension in the office, and there is no reason to suspect white coat hypertension.

140. A 55-year-old woman with ESKD has been undergoing treatment with peritoneal dialysis for the last 3 years. She is 5'6" tall and weighs 180 lbs (body surface area, 1.91 m²; BMI, 29 kg/m²). She has been using a cyclor overnight with the following prescription: 2.5 L × 4 exchanges overnight with 2.5-L last bag fill with dextrose-based solution. Over the last 12 months, her urine volume has gradually diminished, and by the time of her last assessment of dialysis adequacy, she had become anuric. The weekly Kt/V_{urea} on this last 24-hour dialysate collection, completed last week, was 1.53.

Which is the MOST effective initial approach to increase the small solute clearances in this patient?

- A. Transfer to hemodialysis
- B. Add a 2.5-L day-exchange following the last bag fill
- C. Change the last bag fill from dextrose-based solution to icodextrin
- D. Increase the number of night-time exchanges to seven

Answer: B

Explanation:

Increasing the 24-hour peritoneal dialysate drain volume will result in an increase in peritoneal urea clearances. It is possible to modify the current peritoneal dialysis prescription to maximize urea clearances, and hence, transfer to hemodialysis is not necessary (incorrect option A). Each one of the remaining three options will result in higher 24-hour peritoneal dialysate drain volumes; of these, adding a day exchange will result in the greatest increase in drain volume, and hence, the greatest increase in small solute clearances (option B, correct answer). Even though substituting glucose with icodextrin will result in higher

ultrafiltration volume, the gain in drain volume (300–500 mL) will be considerably lower than with the addition of a day exchange (incorrect option C). Similarly, the gain in ultrafiltration volume with an increase in frequency of night-time cycling will be considerably smaller (incorrect option D). Moreover, increasing the frequency of night-time cycling runs the risk of removal of water without commensurate removal of sodium secondary to sodium sieving. Hence, increasing the frequency of night-time cycling is not recommended.

141. A 63-year-old man has ESKD secondary to hypertensive nephrosclerosis and has been undergoing treatment with continuous ambulatory peritoneal dialysis (CAPD). His peritoneal dialysis prescription consists of four exchanges of 2.5 L and he is currently anuric. At the time of his most recent assessment of peritoneal dialysis adequacy, the following parameters were obtained:
- Serum urea nitrogen: 77 mg/dL
 - Dialysate urea nitrogen: 72 mg/dL
 - Total ultrafiltration volume: 1000 mL
 - Volume of distribution of urea: 40 L

Which represent the CLOSEST approximation of the weekly Kt/Vurea?

- A. 1.4
- B. 1.6
- C. 1.8
- D. 2.0
- E. 2.2

Answer: C

Explanation:

To calculate weekly Kt/V, it is necessary to know K, t, and V. K is urea clearance = $[(D \times V)/P]$, where D is the dialysate concentration of urea nitrogen (mg/dL), V is the dialysate drain volume per unit time, and P is the serum concentration of urea nitrogen (mg/dL).

The 24-hour peritoneal dialysate drain volume = Volume instilled + Ultrafiltration volume 2500×4 each + 1000 = 11,000 mL
 $K, \text{ mL/min} = (72/77) \times (11,000/1440) = 7.14 \text{ mL/min}$
 $K, \text{ L/week} = 7.14 \times 10.04 = 71.7 \text{ L/wk}$
 $t = 1 \text{ (wk)}$
 $V = \text{volume of distribution of urea} = 40 \text{ L}$
 $Kt/V = (71.7 \times 1)/40 = 1.79$

Hence, the correct answer is C.

142. A 45-year-old woman has ESKD secondary to ADPKD and has been undergoing peritoneal dialysis for the last 6 months using a night-time cyler. Her current prescription is four exchanges of 2.0 L overnight with a 2-L last bag fill, which she carries through the day. At the time of her last assessment of dialysis adequacy, the total weekly Kt/V urea was 1.76; her renal Kt/Vurea was estimated to be 0.15. Over the last few weeks, she has recently noticed a protuberance at her umbilicus. The physical examination is consistent with the protuberance being an umbilical hernia. You discuss the case with the surgeon and decide on a tension-free hernioplasty using a polypropylene mesh to repair the hernia.

Which represents the BEST approach to the management of the dialysis therapy around the time of hernia repair?

- A. Observe for 4 weeks without any peritoneal or hemodialysis treatment
- B. Hemodialysis *via* a central venous catheter
- C. Low-volume supine peritoneal dialysis for 4–6 weeks
- D. No change in peritoneal dialysis prescription is needed around the time of hernia surgery

Answer: C

Explanation:

In the postoperative period following hernia repair, it is important to minimize intraperitoneal pressure to reduce the probability of hernia recurrence and occurrence of leaks. Thus, continuing the usual fill volumes, including when patient is upright, is clearly inappropriate (incorrect option D). In patients with significant residual renal function, the simplest thing to do would be to observe patients closely without any dialysis therapy. However, this patient does not have sufficient residual renal function at the time of hernia surgery and hence will require continued dialysis support (incorrect option A). There is considerable published experience that demonstrates the safety of performing peritoneal dialysis with low intraperitoneal fill volumes only when the patient is supine (option C, correct option). Hence, this reflects the preferred approach and has considerably less morbidity for the patient compared with placing a central venous catheter for performing hemodialysis temporarily (incorrect option B).

143. A 23-year-old woman has ESKD secondary to chronic glomerulonephritis and has been undergoing peritoneal dialysis (PD) for the last 3 months. She started her menstrual periods yesterday, and last night, when she connected her to the cyclor, she noted that the dialysate in the initial drain was pink in color. She reports to the dialysis unit the next day. The PD nurse does several in-and-out exchanges, but the fluid remains pinkish-red. The initial sample is sent for cell count, and only 30 white blood cells (WBCs), in addition to 800 red blood cells, were noted.

Which represents the BEST plan of action in this patient?

- A. Intravaginal ultrasound to evaluate for ectopic pregnancy
- B. Intraperitoneal heparin for the period of hemoperitoneum
- C. Empiric treatment with antibiotics for presumed peritonitis
- D. Peritoneal fluid cytology to exclude peritoneal carcinomatosis

Answer: B

Explanation:

Occurrence of hemoperitoneum is not uncommon in young, menstruating women at the time of menstrual flow. This is thought to reflect retrograde movement of blood through the fallopian tubes into the peritoneal cavity. This is a benign and self-limited process and, in the absence of any other clinical manifestations, requires no further investigation (incorrect options A and D). Furthermore, in this patient, the peritoneal white blood cell count is considerably less than the threshold of 100 WBCs/mm³ required for the diagnosis of PD-related peritonitis (incorrect option C). The greatest risk in patients with hemoperitoneum is that the blood will clot in the lumen of the peritoneal dialysis catheter and lead to catheter dysfunction. Thus, if the peritoneal dialysis fluid fails to clear after in-and-out exchanges, it is prudent to add heparin to the dialysate to prevent the blood from clotting (option B, correct option).

144. A 53-year-old woman has been undergoing treatment with peritoneal dialysis (PD) for the last 2 years. She woke up this morning with abdominal pain, and when she drained the dialysate, she noted it was cloudy. She called the dialysis facility, and she was asked by the nurse to come to the clinic. Other than abdominal pain, she denied any additional symptoms. On examination, her abdomen was diffusely tender. Examination of the peritoneal catheter exit site and tunnel was unremarkable. The nurse confirmed that the dialysis fluid appeared cloudy, and a presumptive diagnosis of PD-associated peritonitis was made. She sent a sample of the peritoneal dialysis effluent for cell count, gram stain, and culture.

Which represents the BEST approach for the empiric management of PD-related peritonitis?

- A. Combination therapy with cefazolin and ceftazidime
- B. Monotherapy with vancomycin
- C. Combination therapy with cefazolin and rifampin
- D. Monotherapy with ciprofloxacin

Answer: A

Explanation:

Empiric therapy for PD-related peritonitis initially requires adequate coverage for both gram-positive organisms and for gram-negative organisms. This most often requires the use of two medications. Combination therapy with cefazolin and ceftazidime meets this requirement (correct option A). Monotherapy with vancomycin or combination therapy with cefazolin and rifampin provides gram-positive coverage but not coverage for gram-negative organisms. Hence, neither of these options is appropriate (incorrect options B and C). Although ciprofloxacin provides coverage for some gram-positive and gram-negative organisms, its use leads to rapid emergence of resistance, and it is not recommended for use as monotherapy (incorrect option D).

145. A 45-year-old man with ESKD secondary to IgA nephropathy is planning on starting treatment with peritoneal dialysis (PD). He plans on doing continuous ambulatory PD, and your program uses a twin bag disconnect system. He lives alone and has no pets at home. He wants to know what he can do to minimize the risk for PD-related peritonitis.

Which has been demonstrated to be consistently effective in reducing risk of PD-related peritonitis?

- A. Use of icodextrin for the long overnight dwell
- B. Daily application of an antibiotic cream at the peritoneal dialysis catheter exit site
- C. Insertion of a pre-sternal peritoneal dialysis catheter
- D. Use of sterile gloves for performing peritoneal dialysis exchanges

Answer: B

Explanation:

In randomized controlled trials, daily application of either mupirocin or gentamicin has been shown to be effective in reducing peritonitis rates in patients treated with peritoneal dialysis (correct option B). There is no evidence that use of icodextrin or use of

pre-sternal catheter in lieu of an abdominal exit site has any effect on peritonitis rates (incorrect options A and C). Hand hygiene is critical in reducing infectious risk related to the performance of a PD exchange. However, it is not necessary to use sterile gloves (incorrect option D).

146. You are rounding at the dialysis unit and visit a 45-year-old man with ESKD due to diabetes and hypertension. You note he has high interdialytic weight gain (between 5 and 8 kg), and he reports thirst between dialysis. BP during the visit was 149/83 mm Hg. Previous BP was as follows: predialysis BP, 166/87, 152/82, and 147/89 mm Hg; postdialysis BP, 120/71, 116/72, and 128/75 mm Hg.

Exam

Obese in no acute distress, no jugular venous distension (JVD), heart is regular without a murmur; lungs are clear, abd obese, extr without edema, and left arm arterio-venous fistula (AVF) with intact thrill and bruit.

Labs

Sodium: 135 mEq/L
Potassium: 4.8 mEq/L
Chloride: 97 mEq/L
Bicarbonate: 25 mEq/L
Creatinine: 9.7 mg/dL

Phosphorus: 6.0 mg/dL
Calcium: 9.2 mg/dL
Parathyroid hormone: 273 pg/mL
Albumin: 4.0 mg/dL
spKt/V: 1

Medications

Carvedilol: 25 mg bid
Lisinopril: 40 mg qd
Amlodipine: 10 mg qd

Dialysis prescription

Na: 140 mEq/L; 2.0 K/2.5 Ca; HCO₃, 40
Qb 500, Qd 800
Treatment time, 4 hours

What is the appropriate management of this patient's high interdialytic weight gain and high BP?

- Tell him to watch how much fluid he drinks (<1 L/day)
- Tell him to limit his sodium intake (<2 g/day)
- Tell him to limit his sodium intake (<2 g/day) and lower his dialysate sodium
- Add a new antihypertensive medication

Answer: C

Explanation:

This patient has a low predialysis serum sodium (135 mg/dL), which is his sodium set point. When he undergoes dialysis against a dialysate sodium of 140 mg/dL, this results in an elevated dialysate-to-plasma sodium gradient, which favors sodium diffusion from dialysate to plasma. As a consequence, his plasma sodium will increase during dialysis. This will stimulate thirst to reduce his plasma sodium (and osmolality) back to his set point. High dietary sodium intake will also increase his plasma sodium and osmolality. When osmolality of extracellular fluid increases, osmoreceptors in the hypothalamus shrink and stimulate thirst. Thus, lowering the dietary sodium and lowering his dialysate sodium will both help reduce thirst and minimize interdialytic weight gain. Reducing his free water intake is not correct because the stimulus for thirst is the increase in osmolality. Adding a new antihypertensive medication is not appropriate at this time as it is possible that reducing his interdialytic weight gain may help improve his high predialysis BP.

References:

Flanigan MJ. Role of sodium in hemodialysis. *Kidney Int Suppl* 2000;76:S72–S78.

147. **Which is TRUE regarding sodium balance in hemodialysis patients?**

- A standard dialysate sodium of 140 mEq/L is appropriate for all dialysis patients
- Because 6% of plasma is colloidal, a dialysate sodium set 5–10 mEq/L higher than the patients serum sodium is adequate for isotonic dialysis
- Gibbs-Donnan effect predicts that isotonic dialysis will only occur if the dialysate sodium is set less than the patients plasma sodium activity
- Because most patients ultrafiltrate 3–6 lbs of fluid (with convective Na loss) during a typical hemodialysis treatment, it is nearly always possible to achieve adequate sodium removal purely by convective sodium loss

Answer: C

Explanation:

The distribution of predialysis serum sodium is such that nearly 75% of patients have a predialysis sodium of <140 mEq/L. Although most of sodium flux during hemodialysis is due to convection, it is also partially due to diffusion. Prediction of the diffusion of sodium depends on the dialysate to patient sodium gradient, which is dependent on the activity of sodium (activity coefficient of Na × the concentration of Na) and the difference between the activity of Na in the blood versus activity of Na in the dialysate.

Serum sodium fails to take into consideration that about 6% of plasma is colloidal, so true plasma sodium is likely higher (i.e., 140 mEq/L serum measurement in 0.94 L of water = plasma sodium of 149 mEq/L). However, the Gibbs-Donna effect is such that protein-induced asymmetry will result in isotonic flow across the dialysis membrane. Proteins are large osmotically active particles that are negatively charged anions that influence the distribution of other ions so that electrochemical equilibrium is maintained. With the osmotic force of proteins in plasma, the effective gradient favors the movement of sodium from dialysate to plasma even though the difference would be anticipated to favor movement to the dialysate. Thus, answer A is not correct in that a dialysate Na of 140 mEq/L is not appropriate for all patients, particularly those patients who have a very low predialysis sodium. Answer B is incorrect as it fails to take into consideration the Gibbs-Donnan effect, and thus, a dialysate sodium 5–10 mEq/L higher than serum will not result in isonatric dialysis. Answer D is incorrect because it fails to account for diffusive differences in sodium removal related to the dialysate-to-plasma sodium gradient, which can influence an additional 100 mEq/L of Na removal. Although ultrafiltration will result in a net sodium loss, the lack of diffusive loss of sodium (and the possible addition of diffusion of sodium into the patient) may result in inability to adequately remove the sodium gained in the interdialytic period.

References:

Peixoto AJ, Gowda N, Parikh CR, Santos SF. Long-term stability of serum sodium in hemodialysis patients. *Blood Purif* 2010;29(3):264–267.

148. A 65-year-old man with ESKD has been on dialysis for 3 years. He has diabetes and hypertension but no history of cardiac disease or congestive heart failure. He has a close relationship with other patients at the hemodialysis (HD) unit, and one of his friends recently died at home from presumed sudden cardiac arrest. The patient is increasingly concerned that his BP is now too high and may be putting him at high risk for death.

On review of his BP trends during his last few treatments, you note the following:

- Predialysis: 130/70 mm Hg; postdialysis: 148/78 mm Hg
- Predialysis 145/77 mm Hg; postdialysis: 158/84 mm Hg
- Predialysis 139/82 mm Hg; postdialysis: 149/82 mm Hg

Which is TRUE regarding this patient's BP?

- A. The increase in his BP during dialysis is an independent risk factor for increased hospitalizations and death
- B. Randomized controlled trials in hemodialysis patients have demonstrated that targeting a lower BP will lower his risk for adverse cardiovascular outcomes
- C. A 44-hour ambulatory systolic BP of 135–145 mm Hg is associated with the best survival in HD patients
- D. None of the above

Answer: A

Explanation:

No randomized controlled trials to date have tested the hypothesis that lower BP improves cardiovascular morbidity or mortality in HD patients; thus, answer B is incorrect. Recent studies have demonstrated that hypertension during hemodialysis (intradialytic hypertension) is associated with increased hospitalization rates and higher death rates up to 2 years. Although routine hemodialysis unit BP measurements (which are often inaccurate) do not exhibit a normal linear relationship with adverse outcomes, elevated 44-hour ambulatory BP has been shown to be associated with higher mortality. In this study, an ambulatory BP above ~120 mm Hg was associated with higher 6-year mortality. In a previous study, Alborzi et al. demonstrated that the ambulatory systolic BP with the lowest association with mortality in hemodialysis patients was between 115 and 125 mm Hg.

References:

Inrig JK, Oddone EZ, Hasselblad V, Gillespie B, Patel UD, Reddan D, Toto R, Himmelfarb J, Winchester JF, Stivelman J, Lindsay RM, Szczech LA. Association of intradialytic blood pressure changes with hospitalization and mortality rates in prevalent ESRD patients. *Kidney Int* 2007;71:454–461.

Inrig JK, Patel UD, Toto RD, Szczech LA. Association of blood pressure increases during hemodialysis with 2-year mortality in incident hemodialysis patients: A secondary analysis of the Dialysis Morbidity and Mortality Wave 2 Study. *Am J Kidney Dis* 2009;54:881–890.

Agarwal R, Satyan S, Alborzi P, Light RP, Tegegne GG, Mazengia HS, Yigazu PM. Home blood pressure measurements for managing hypertension in hemodialysis patients. *Am J Nephrol* 2009;30(2):126–134.

Alborzi P, Patel N, Agarwal R. Home blood pressures are of greater prognostic value than hemodialysis unit recordings. *Clin J Am Soc Nephrol* 2007;6:1228–1234.

149. Patient SS is a 79-year-old woman with ESKD due to diabetes mellitus (DM) and hypertension. The patient has frequent episodes of intradialytic hypotension requiring normal saline and cessation of ultrafiltration.

Which is LEAST effective at managing this patient's hypotension during hemodialysis?

- A. Midodrine before dialysis
- B. Sequential ultrafiltration (isolated ultrafiltration followed by hemodialysis)
- C. Sodium modeling
- D. High sodium dialysis
- E. Cool dialysate

Answer: B

Explanation:

In a single-blinded cross-over study of 10 hemodialysis patient with intradialytic hypertension, each patient underwent 1 week of standard dialysis (dialysate Na of 138 mEq/L), followed by 1 week of each of the following: high sodium dialysate, in which the patient was dialyzed using a dialysate sodium of 144 mEq/L; sodium modeling, during which the dialysate sodium decreased from 152 to 140 mEq/L in the last half hour of dialysis; 1 hour of isolated ultrafiltration followed by 3 hours of isovolemic dialysis; and cool temperature dialysis in which the dialysate was cooled to 35°C. There were significantly fewer hypotensive episodes per treatment in the sodium modeling, high sodium, and cool temperature protocols compared with the standard protocol ($P < 0.05$). Ultrafiltration followed by dialysis was associated with a significantly greater number of hypotensive episodes per treatment than any of the three test protocols ($P < 0.05$). Prior small studies have also demonstrated midodrine improves BP stability during hemodialysis among patients with intradialytic hypotension.

References:

Dheenan S, Henrich WL. Preventing dialysis hypotension: A comparison of usual protective maneuvers. *Kidney Int* 2001;59:1175–1181.

Lin YF, Wang JY, Deng JC, Lin SH. Midodrine improves chronic hypotension in hemodialysis patients. *Am J Med Sci* 2003;325(5):256–261.

Cruz DM, Mahnensmith RL, Perazella MA. Intradialytic hypotension: Is midodrine beneficial in symptomatic hemodialysis patients? *Am J Kidney Dis* 1997;30:772–779.

150. Ms. R is a 65-year-old woman with ESKD due to diabetes and hypertension. On review during her weekly rounds, her dry weight is 62 kg, with an interdialytic weight gain of 2–3 kg; her dialysis prescription is 4-hour Monday, Wednesday, and Friday, dialysate Na 140 mEq/L, blood flow (Qb) 500, dialysate flow (Qd) 800 via arterio-venous fistula (AVF).

Exam

BP: 150/90 mm Hg predialysis, 145/85 mm Hg postdialysis without intradialytic hypotension

Exam unremarkable except for left upper arm AVF and no leg edema

Medications: sevelamer 800 mg three times per day (TID) with meals, Toprol XL 50 mg daily, lisinopril 40 mg daily, amlodipine 10 mg daily, nephro-vite tablet daily, doxercalciferol 1 µg IV with each dialysis treatment, epogen 2200 units IV with each dialysis treatment.

Labs

Sodium: 139 mEq/L

Potassium: 4.2 mEq/L

Chloride: 105 mEq/L

Bicarbonate: 25 mEq/L

Creatinine: 9.2 mg/dL

Phosphorus: 4.8 mg/dL

Calcium: 9.2 mg/dL

Parathyroid hormone: 155 pg/mL

Albumin: 4.0 mg/dL

spKt/V: 1.62

Hemoglobin: 11.0 g/dL

Which is TRUE regarding treating this patient's BP?

- A. Challenging dry weight is only effective at lowering BP in dialysis patients who have signs of volume overload
- B. Observational data suggest that antihypertensive treatment may decrease survival
- C. There is a 50% increased risk of intradialytic hypotension with targeting postdialysis BP <130/80 mm Hg
- D. Daily hemodialysis has been shown to lower systolic BP and to reduce left ventricular mass and death

Answer: D

Explanation:

In the dry weight reduction intervention trial (DRIP), challenging dry weight (0.1/kg per treatment) resulted in a 7 mm Hg lower ambulatory BP at 8 weeks compared with usual care. These patients did not have signs of volume overload on exam, and thus answer A is incorrect. Two recent meta-analyses have shown an association between antihypertensive treatment and better survival. In a retrospective study, Davenport et al. demonstrated that the greater the number of patients who were at the Kidney

Disease Outcomes Quality Initiative (KDOQI) guidelines BP target of <130/80 mm Hg with individual dialysis units, the greater the incidence of intradialytic hypotension within that unit. However, this did not answer the question of whether targeting to lower BP increases the risk of intradialytic hypotension. In the frequent hemodialysis network trial, patients randomized to six times per week dialysis versus three times per week dialysis had a 10 mm Hg lower predialysis systolic BP and lower LV mass and mortality.

References:

Agarwal R, Alborzi P, Satyan S, Light RP. Dry-weight reduction in hypertensive hemodialysis patients (DRIP): A randomized, controlled trial. *Hypertension* 2009;53:500–507.

Heerspink HJ, Ninomiya T, Zoungas S, de Zeeuw D, Grobbee DE, Jardine MJ, Gallagher M, Roberts MA, Cass A, Neal B, Perkovic V. Effect of lowering blood pressure on cardiovascular events and mortality in patients on dialysis: A systematic review and meta-analysis of randomised controlled trials. *Lancet* 2009;373:1009–1015.

Agarwal R, Sinha AD. Cardiovascular protection with antihypertensive drugs in dialysis patients: Systematic review and meta-analysis. *Hypertension* 2009;53:860–866.

Davenport A, Cox C, Thuraisingham R. Achieving blood pressure targets during dialysis improves control but increases intradialytic hypotension. *Kidney Int* 2008;73:759–764.

FHN Trial Group, Chertow GM, Levin NW, Beck GJ, Depner TA, Eggers PW, Gassman JJ, Gorodetskaya I, Greene T, James S, Larive B, Lindsay RM, Mehta RL, Miller B, Ornt DB, Rajagopalan S, Rastogi A, Rocco MV, Schiller B, Sergeeva O, Schulman G, Ting GO, Unruh ML, Star RA, Klinger AS. In-center hemodialysis six times per week versus three times per week. *New Engl J Med* 2010;363:2287–2300.

151. Which has been demonstrated in randomized controlled trials in hemodialysis patients to improve survival?

- A. Normalizing hemoglobin with erythropoiesis-stimulating agents (ESAs)
- B. Lowering LDL with a statin
- C. Lowering BP
- D. Preventing intradialytic hypotension
- E. None of the above

Answer: E

Explanation:

Normalizing hemoglobin among patients on hemodialysis did not improve survival. Neither the Deutsch Diabetics on Dialysis Study (4D) nor A study to evaluate the Use of Rosuvastatin in subjects On Regular Hemodialysis (AURORA) study demonstrated improved survival among diabetic ESKD patients with the use of statins. The Study for Heart and Renal Protection (SHARP) trial (which included both CKD and ESKD) showed a decreased risk of atherosclerotic events with statin + ezetimibe but no improvement in overall survival. No trials have tested the hypothesis that lowering BP or preventing IDH can improve survival in hemodialysis patients.

References:

Besarab A, Bolton WK, Browne JK, Egrie JC, Nissenson AR, Okamoto DM, Schwab SJ, Goodkin DA. The effects of normal as compared with low hematocrit values in patients with cardiac disease who are receiving hemodialysis and epoetin. *New Engl J Med* 1998;339:584–590.

Wanner C, Krane V, Marz W, Olschewski M, Mann JF, Ruf G, Ritz E; German Diabetes and Dialysis Study Investigators. Atorvastatin in patients with type 2 diabetes mellitus undergoing hemodialysis. *New Engl J Med* 2005;353:238–248.

Fellstrom BC, Jardine AG, Schmieder RE, Holdaas H, Bannister K, Beutler J, Chae DW, Chevaile A, Cobbe SM, Gronhagen-Riska C, De Lima JJ, Lins R, Mayer G, McMahon AW, Parving HH, Remuzzi G, Samuelsson O, Sonkodi S, Sci D, S'leymanlar G, Tsakiris D, Tesar V, Todorov V, Wiecek A, W'hrich RP, Gottlow M, Johnsson E, Zannad F; AURORA Study Group. Rosuvastatin and cardiovascular events in patients undergoing hemodialysis. *New Engl J Med* 2009;360:1395–1407.

Baigent C, Landray MJ, Reith C, Emberson J, Wheeler DC, Tomson C, Wanner C, Krane V, Cass A, Craig J, Neal B, Jiang L, Hooi LS, Levin A, Agodoa L, Gaziano M, Kasiske B, Walker R, Massy ZA, Feldt-Rasmussen B, Krairitichai U, Ophascharoensuk V, Fellstrom B, Holdaas H, Tesar V, Wiecek A, Grobbee D, de Zeeuw D, Gronhagen-Riska C, Dasgupta T, Lewis D, Herrington W, Mafham M, Majoni W, Wallendszus K, Grimm R, Pedersen T, Tobert J, Armitage J, Baxter A, Bray C, Chen Y, Chen Z, Hill M, Knott C, Parish S, Simpson D, Sleight P, Young A, Collins R; SHARP Investigators. The effects of lowering LDL cholesterol with simvastatin plus ezetimibe in patients with chronic kidney disease (Study of Heart and Renal Protection): A randomized placebo-controlled trial. *Lancet* 2011;377:2181–2192.

152. You are rounding at the dialysis unit and visit a 42-year-old man with ESKD due to diabetes and hypertension. He has moderate interdialytic weight gain (5–7 kg) and reports that he has gained some weight. He also complains of somnolence and fatigue.

Exam

BP: 148/83 mm Hg predialysis; weight: 118 kg; patient is obese, no jugular venous distension (JVD), heart is regular without a murmur, lungs are clear, abdomen is obese, extremities without edema, and right arm arteriovenous fistula (AVF) with intact thrill and bruit.

Labs

Sodium: 140 mEq/L
 Potassium: 4.2 mEq/L
 Chloride: 103 mEq/L
 Bicarbonate: 28 mEq/L
 Creatinine: 8.9 mg/dL
 Phosphorus: 5.5 mg/dL

Calcium: 9.4 mg/dL
 Hemoglobin: 10.4 mg/dL
 Parathyroid hormone: 422 pg/mL
 Albumin: 4.0 mg/dL
 spKt/V: 1.55

Medications

Carvedilol: 25 mg bid Lisinopril: 40 mg qd Amlodipine: 10 mg qd Epopen: 2200 units tiw

Dialysis prescription

Na: 140 mEq/L; 2.0 K/2.5 Ca, HCO₃, 40
 Blood flow (Qb) 500, dialysate flow (Qd) 800 Treatment time: 4 hours

What is the appropriate management of this patient at this time?

- A. Order a sleep study
- B. Start a new antihypertensive medication
- C. Increase his treatment time
- D. Increase his erythropoiesis-stimulating agent dose

Answer: A

Explanation:

This patient is on conventional hemodialysis, he is obese, and he has large interdialytic weight gain. All of these place him at risk for volume overload, which increases his risk for sleep apnea and for elevated BP. The patient also complained of somnolence, which may be the result of obstructive sleep apnea. A sleep study is warranted in this patient to evaluate this. His antihypertensive medications should not be adjusted yet because treatment of sleep apnea, if present, can help control his BP. Increasing his treatment time may help with control of volume, which in turn can help reduce symptoms of sleep apnea, if diagnosed. However, this is not warranted yet. Although anemia can result in increased fatigue, this patient's hemoglobin is within target range, and increasing his ESA is not indicated.

153. **What laboratory variable is the MOST closely associated with an increased probability of death in ESKD patients?**

- A. High calcium
- B. Low albumin
- C. High phosphorus
- D. Low hemoglobin

Answer: B

Explanation:

In numerous observational studies, low serum albumin is a potent mortality predictor. The relationship between high calcium and adverse mortality is uncertain, as some studies have shown a relationship and others have not. Similarly, high phosphorus does not always demonstrate a normal relationship with mortality as it is partly confounded by nutritional intake, and the relationship is altered by comorbid conditions. Low hemoglobin, although associated with increased mortality, is less predictive of adverse outcomes than low albumin.

154. Ms. F is a 72-year-old woman with diabetes, hypertension, and ESKD, which developed following coronary artery bypass surgery a few months earlier. Her hospital course was prolonged, and she has been in rehabilitation since discharge. She reports a lack of motivation to continue with physical therapy and decreased interest in social interactions.

On review during her weekly rounds, her dry weight is 62 kg with interdialytic weight gains (IDWG) of 2–3 kg, her dialysis prescription is as follows: 4-hour Monday, Wednesday and Friday (MWF), dialysate Na 140 mEq/L, blood flow (Qb) 500, dialysate flow (Qd) 800 *via* arterio-venous fistula (AVF).

Exam

BP: 122/68 mm Hg predialysis; exam unremarkable except for right chest permcath and no left edema.

Medications

sevelamer 800 mg TID with meals, Toprol XL 25 mg daily, lisinopril 40 mg daily, nephro-vite tablet daily, doxercalciferol 1 µg IV with each dialysis treatment, erythropoietin 4400 units IV with each dialysis treatment.

Labs

Sodium: 138 mEq/L	Calcium: 8.8 mg/dL
Potassium: 4.1 mEq/L	Parathyroid hormone: 248 pg/mL
Chloride: 105 mEq/L	Albumin: 3.8 mg/dL
Bicarbonate: 25 mEq/L	spKt/V: 1.64
Creatinine: 4.4 mg/dL	Hemoglobin: 10.4 g/dL
Phosphorus: 4.7 mg/dL	spKt/V: 1.82

Which is TRUE regarding treating this patient's mood disorder?

- A. Patients on hemodialysis (HD) are less likely to be hospitalized for a psychiatric disorder than those on peritoneal dialysis (PD)
- B. ESKD patients have similar rates of psychiatric conditions as patients with other chronic medical conditions
- C. Treatment of depression in ESKD patients is different than the general population
- D. Depression is associated with increased mortality in ESKD patients

Answer: D

Explanation:

Patients on hemodialysis are more likely to be hospitalized for a psychiatric condition than those on PD; thus, answer A is incorrect. The etiology is uncertain but may be related to patient selection and that patients with psychiatric conditions are more likely to be deemed unsuitable for PD. ESKD patients have a much higher rate of psychiatric conditions than patients with other chronic medical conditions; thus, answer B is incorrect. Although no randomized controlled trials of depression treatment have been performed in ESKD patients, observational data suggest that the best therapy is medications + counseling, which is similar to that in the general population. The presence of depression has been associated with higher mortality in ESKD patients; thus, answer D is correct.

155. A 46-year-old man with ESKD due to diabetes begins to report unpleasant sensations in his legs associated with an urgent desire to move. He reports that the feeling is worse at night and during hemodialysis. He states that it is difficult to stay on dialysis due to the need to move. Additionally, his wife reports that the patient has frequent limb movement during sleep and that the patient often kicks her in the middle of the night.

Which has NOT been shown to improve restless leg syndrome symptoms in hemodialysis patients?

- A. Iron therapy
- B. Erythropoiesis-stimulating agents (ESAs)
- C. Kidney transplantation
- D. Short daily dialysis

Answer: B

Explanation:

Restless leg syndrome (RLS) and periodic limb movement disorder are common among hemodialysis patients. RLS has been shown to affect 14–57% of hemodialysis patients compared with 5–15% of the general population. Periodic limb movement (PLM) occurs in greater than 50% of hemodialysis patients. Although the pathogenesis of RLS and PLM is not fully understood, various factors have been associated with sleep disorders including anemia, iron deficiency, elevated serum calcium, and central and peripheral nervous system disorders. Similar to the general population, pharmacologic treatment options include the use of renally dosed dopaminergic agonists. Small randomized controlled trials and observational cohort studies have demonstrated iron therapy, short daily dialysis, and kidney transplantation to be associated with improved RLS symptoms. Although iron therapy improved RLS in a small randomized controlled trial of hemodialysis patients, ESAs have not been demonstrated to improve RLS.

156. **Which can cause dementia, osteomalacia, and anemia in ESKD patients?**

- A. Aluminum excess
- B. Lanthanum carbonate
- C. Temazepam
- D. Sertraline

Answer: A

Explanation:

Aluminum toxicity was previously more common than seen today due to declining use of aluminum-containing binders, improved water purification, and the use of high flux dialyzers. However, sporadic outbreaks due to contamination of the local water supply still occur. Slow accumulation of aluminum over many years can cause osteomalacia, bone and muscle pain, iron-resistant microcytic anemia, hypercalcemia, and neurologic abnormalities. Acute aluminum neurologic toxicity can be fatal. Evaluation of

presumed aluminum toxicity includes obtaining serum aluminum concentrations. The Kidney Disease Outcomes Quality Initiative (KDOQI) work group also recommends a low-dose deferoxamine test be administered among a patient suspected of having aluminum overload or toxicity. If there is an increase in serum aluminum of $>50 \mu\text{g/L}$ 2 days after infusion, this confirms the presence of aluminum overload. Removal of aluminum excess among symptomatic patients with aluminum overload includes using deferoxamine; however, side effects such as mucormycosis and neurotoxicity have been associated with its use.

157. **Which medication is associated with mental status changes when dosed excessively in a patient with advanced renal insufficiency?**
- A. Ranitidine
 - B. Omeprazole
 - C. Loperamide
 - D. Bismuth (pepto bismol)
 - E. Ondansetron

Answer: A

Explanation:

The only drug on that list that needs to be dose adjusted in the setting of CKD or AKI is ranitidine. This drug is associated with changes in mental status when not appropriately dosed for level of kidney function.

158. **In a patient with advanced CKD, which medication is associated with neurotoxicity when not dosed appropriately for level of kidney function?**
- A. Gancyclovir
 - B. Acyclovir
 - C. Voriconazole
 - D. Flucytosine
 - E. Valgancyclovir

Answer: B

Explanation:

Acyclovir is an antiviral agent that needs to be dose adjusted in the setting of reduced GFR. In addition to causing crystal-induced AKI, the drug is associated with neurotoxicity when not appropriately dosed for the level of GFR. Dialysis effectively removes the drug and should be considered for those with severe neurotoxicity and advanced CKD or severe AKI. The other drugs are not associated with this same issue.

159. **In an ESKD patient treated with high-dose intravenous immunoglobulin (IVIG) for desensitization, which complication has been described?**
- A. Hemolytic anemia
 - B. Thrombocytopenia
 - C. Hyperviscosity
 - D. Transfusion-related acute lung injury
 - E. Pure red cell aplasia

Answer: A

Explanation:

High-dose IVIG has been associated with significant hemolytic anemia in ESKD patients receiving this therapy for desensitization and treatment of antibody-mediated rejection. Hemolysis occurs due to passive acquisition of A/B isohemagglutinins from the IVIG product. RBCs are coated with antibody and eventually undergo erythrophagocytosis.

160. A 79-year-old man with hypertension, coronary artery disease, ischemic cardiomyopathy with ejection fraction (EF) 40%, and stage 4 CKD (eGFR = $26 \text{ mL/min per } 1.73 \text{ m}^2$) presented to the Emergency Department with weakness. He had 3–4/5 muscle strength in both of his arms and legs. Labs returned showing the following: K, 6.1 mEq/L ; and digoxin, 2.5 ng/mL (normal range, $0.8\text{--}2.0 \text{ ng/mL}$).

In this patient with hyperkalemia and digoxin toxicity, which therapy should be used?

- A. Digoxin-specific Fab fragments
- B. Plasmapheresis
- C. Continuous veno-venous hemodialysis
- D. Albumin-based dialysis
- E. High flux hemodialysis

Answer: A

Explanation:

Digoxin toxicity in a patient with underlying kidney disease and hyperkalemia is best treated with digoxin-specific Fab fragments. The Fab fragments bind digoxin, making it no longer available to bind the subunit of the Na⁺, K⁺ ATPase pump. This allows the Na⁺, K⁺ ATPase pump to move K into cells, correcting hyperkalemia (within 1–4 hours). None of the other modalities will significantly remove digoxin.

161. In a patient with ESKD on chronic maintenance hemodialysis, which anticoagulant does NOT require dose adjustment?

- A. Danaparoid
- B. Argatroban
- C. Fondaparinux
- D. Enoxaparin
- E. Lefirudin

Answer: B

Explanation:

Compared with the other anticoagulants, argatroban is metabolized and cleared by the liver, whereas the rest of the options are cleared by the kidneys and require dose adjustment.

162. An increase in which is MOST likely to cause an erythropoiesis-stimulating agent (ESA)-hypo-responsive anemia by reducing iron availability for erythropoiesis in CKD and ESKD patients?

- A. Heparin
- B. Transferrin
- C. Ferroportin
- D. Hypoxia-inducible factor
- E. Divalent metal ion transporter

Answer: A

Explanation:

Heparin, which is produced by the liver, is a peptide that modulates iron movement in the body through its effect on ferroportin expression in cell membranes. Anemia, hypoxia, and inflammation (interleukin-6) increase hepatic production of heparin, which causes ferroportin to be removed from cell membranes and limits release of iron from reticuloendothelial cells for RBC production. This causes an ESA-hypo-responsive state (functional iron deficiency).

163. For a patient receiving dialysis, which statement about dietary phosphorus is TRUE?

- A. Milk has a low phosphorus-to-gram-of-protein ratio.
- B. Dietary estimates generally overestimate dietary phosphorus intake.
- C. The US Department of Agriculture requires that the phosphorus content of enhanced meats be included on the food label.
- D. Medications contribute significantly to dietary phosphorus intake.

Answer: D

Explanation:

Medications can make up a significant component of dietary phosphorus intake. Dairy products have a high dietary phosphorus-per-gram-of-protein ratio. Dietary estimates commonly underestimate phosphorus intake. The US Department of Agriculture does not currently require that the phosphorus content of enhanced meats be included on the food label.

164. A 66-year-old man with alcoholic cirrhosis is admitted to the intensive care unit with a large variceal bleed, aspiration pneumonia, and hypotension. He develops AKI and is started on postdilution continuous veno-venous hemofiltration (CVVH) with the following parameters:

Blood flow rate: 200 mL/min
 Post-filter replacement fluid rate: 3000 mL/hr
 Fluid removal rate: 100 mL/hr
 Anticoagulation: None

On exam, he is mechanically ventilated. He weighs 100 kg. He has a double lumen 13-Fr dialysis catheter in his right internal jugular vein for CVVH. His hematocrit is 30%, platelet count is 73,000, and international normalized ratio (INR) is 1.9. Within the last 24 hours, his hemofilter has clotted three times.

Which is the MOST appropriate next step for improving hemofilter patency?

- Add heparin anticoagulation
- Decrease blood flow rate to 100 mL/min
- Change postfilter replacement fluid to prefilter replacement fluid
- Decrease postfilter replacement fluid rate to 1000 mL/hr
- Add dialysate at rate of 1000 mL/hr

Answer: C

Explanation:

Clotting of the CVVH circuit is most likely potentiated by the high filtration fraction. The filtration fraction is equal to the ultrafiltration rate divided by the plasma flow rate. For this patient, the ultrafiltration rate is 3100 mL/hr (postfilter replacement fluid rate plus fluid removal rate). Plasma flow rate is $200 \text{ mL/min} \times 60 \text{ min/hr} \times (1 - \text{hematocrit}) = 12,000 \text{ mL/hr} \times 0.7$. Thus, the filtration fraction is equal to 3100 mL/hr divided by 8400 mL/hr, which equals 0.37 or 37%. A filtration fraction of more than 25–30% is thought to be associated with increased clotting.

Option A is contraindicated given his current variceal bleed and high risk for further hemorrhage. Option B is incorrect because decreasing the blood flow rate will increase the filtration fraction (300 mL/hr divided by 4200 mL/hr gives a filtration fraction of 7%). Option C is the correct answer because changing the postfilter replacement fluid to prefilter dilutes the hematocrit and decreases the filtration fraction to an acceptable range: $3100 \text{ mL/hr} / [(200 \text{ mL/min} \times 60 \text{ min} \times 0.7) + 3000 \text{ mL/hr}] = 0.27$ or 27%. Although option D will decrease the filtration fraction (1200 mL/hr divided by 8400 gives a filtration fraction of 13%), it reduces the effluent rate (or total ultrafiltration rate) to 1100 mL/hr, giving a dose of 11 mL/kg/hr (1100 mL/hr divided by 100 kg). Based on the ATN (Acute Renal Failure Trial Network) and RENAL (Randomized Evaluation of Normal versus Augmented Level Replacement Therapy) trials, the minimal accepted dose of CRRT is 20–25 mL/kg/hr. Option E is not correct because adding a dialysate will increase the dose of CRRT but will not affect the high filtration fraction because the postfilter replacement fluid remains unchanged.

References:

Joannidis M, Oudemans-van Straaten H. Clinical review: Patency of the circuit in continuous renal replacement therapy. *Critical Care* 2007;11:218.
 Uchino S, Fealy N, Baldwin I, Morimatsu H, Bellomo R. Pre-dilution vs. post-dilution during continuous veno-venous hemofiltration: Impact on filter life and azotemic control. *Nephron Clin Pract* 2003;94:c94–c98.
 Van der Voort PH, Gerritsen RT, Kuiper MA, Egbers PH, Kingma WP, Boerma EC. Filter run time in CVVH: Pre- versus postdilution and nadroparin versus regional heparin-protamine anticoagulation. *Blood Purif* 2005;23:175–180.

165. A 62-year-old woman presents for a consultation because her primary care physician noted that her creatinine value had increased to 1.1 mg/dL, equivalent to an eGFR of 59 mL/min/1.73 m² by the MDRD equation. The patient reports no recent illnesses, no lightheadedness, normal oral intake, no symptoms of dysuria or change in urination, and no medication changes over the last few years. Urine analysis shows a specific gravity of 1.010 and no protein or hematuria. The patient's medications include lisinopril, 5 mg daily, and aspirin, 81 mg daily. Because of her creatinine level, the patient is concerned about CKD and her risk of needing dialysis in the future.

Which is an accurate assessment of this patient?

- The patient has CKD, and risk factor reduction should be investigated.
- Repeat testing that also includes cystatin C level or creatinine clearance should be considered.
- The patient has CKD, and at her current stage, her risk of needing dialysis is double her risk of developing ESKD.
- Taking lisinopril caused the change in her renal function, and no further workup is necessary.

Answer: B

Explanation:

The patient has one laboratory result with a creatinine level of 1.1 mg/dL. The MDRD equation is most accurate with the population used for its development: patients with stage 3 CKD. Underestimation can be ≤29% in healthy people. Further investigation with creatinine clearance, checking cystatin C, or using a different equation that better estimates GFR at higher renal function would be more appropriate. Because she does not qualify for a diagnosis of CKD, answers A and C are not correct. Although taking lisinopril can cause an increase in creatinine through its mechanism of action, this medication is not described as new to the patient and therefore is less likely to be the cause.

References:

Rule A, Larson TS, Bergstralh EJ, Slezak JM, Jacobsen SJ, Cosio FG. Using serum creatinine to estimate glomerular filtration rate: Accuracy in good health and in chronic kidney disease. *Ann Intern Med* 2004;141:929–937.
 KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Available at: http://www.kdigo.org/clinical_practice_guidelines/pdf/CKD/KDIGO_2012_CKD_GL.pdf. Accessed April 12, 2018.

166. A 78-year-old woman with a history of stage 3b CKD is seen in follow-up at the nephrology office. Her hemoglobin level was noted to have decreased to 9.1 g/dL. After a workup is performed, CKD is considered the cause of the decrease. An erythropoietin-stimulating agent (ESA) is initiated.

Which outcome can be expected after the use of an ESA?

- A. Regression of left ventricular hypertrophy
- B. Decreased mortality
- C. Fewer cardiac events
- D. Decreased progression of renal disease
- E. Decreased transfusion needs

Answer: E

Explanation:

ESA therapy has been helpful in decreasing transfusion needs (answer E), but the evidence is sparse regarding improvement in factors such as left ventricular hypertrophy, cardiac events, progression of renal disease, and mortality. Other benefits were once thought to include improved quality of life and decreased fatigue, but evidence has not supported those claims.

References:

Palmer SC, Saglimbene V, Mavridis D, Salanti G, Craig JC, Tonelli M, Wiebe N, Strippoli GF. Erythropoiesis-stimulating agents for anemia in adults with chronic kidney disease: A network meta-analysis. *Cochrane Database Syst Rev* 2014;(12):CD010590.
 Covic A, Nistor I, Donciu MD, Dumea R, Bolignano D, Goldsmith D. Erythropoiesis-stimulating agents (ESA) for preventing the progression of chronic kidney disease: A meta-analysis of 19 studies. *Am J Nephrol* 2014;40(3):263–279.
 Wish J. Anemia and other hematologic complications of chronic kidney disease. In: *Primer on Kidney Disease*, edited by Gilbert S, Weiner DE, Philadelphia, Elsevier Saunders, 2014.

167. A 46-year-old man presents to his primary care physician to discuss recently diagnosed BP elevation. In review, the patient reports that he does not take any over-the-counter medications, he has gained 10 pounds over the last year, and he drinks two or three caffeinated beverages daily. He reports a lifelong history of excess sweating and no history of family cancers or endocrine disorders. On examination, his BP is 152/92, heart rate 72/min, and BMI 27. His lungs are clear, his heart is regular, there are no skin lesions, and trace edema is present in his lower extremities. Laboratory evaluation showed the following results, reflecting values that have been stable for many years.

<u>Serum</u>		<u>Urine</u>	
Sodium	140 mEq/L	Qualitative	
Potassium	3.4 mEq/L	Specific gravity	1.020
Chloride	109 mEq/L	Blood	Negative
Bicarbonate	28 mEq/L	Protein	Negative
Urea nitrogen	32 mg/dL	Red blood cells	0–1 per high-power field
Creatinine	2.2 mg/dL	White blood cells	0–3 per high-power field
		Casts	Negative
		Crystals	None

Given these findings, which is MOST likely responsible for his hypertension?

- A. CKD
- B. Primary hyperaldosteronism
- C. Caffeine intake
- D. Weight gain

Answer: A

Explanation:

Although many factors influence BP, patients with CKD have difficulty maintaining sodium and water balance and up-regulation of the RAAS, which leads to hypertension. An increase in BP is less likely to need secondary workup in CKD patients, especially given his age at diagnosis and other factors. Although weight gain, caffeine intake, and aldosterone level could be influential in this case, the most likely cause would be CKD.

References:

Horowitz B, Miskulin D, Zager P. Epidemiology of hypertension in CKD. *Adv Chronic Kidney Dis* 2015;22(2):88–95.

168. A 68-year-old man with a history of diabetic nephropathy is evaluated. Over the last year, his creatinine concentration has increased from 2.0 mg/dL to 3.0 mg/dL due to progressive disease. He is adherent to his medication regimen of allopurinol, 100 mg once daily; metoprolol, 50 mg once daily; amlodipine, 10 mg once daily; atorvastatin, 20 mg once daily; and insulin glargine, 20 units at bedtime.

Because of declining kidney function, which medication likely needs a dose adjustment?

- A. Insulin
- B. Amlodipine
- C. Atorvastatin
- D. Metoprolol
- E. Allopurinol

Answer: A

Explanation:

CKD slows down the metabolism of insulin, resulting in an increase in the incidence of hypoglycemia. Progressive CKD causes increased insulin sensitivity and prolonged duration of action, which decreases the need for insulin; therefore, answer A is correct. Although allopurinol needs its dose adjusted for CKD, this patient is already receiving a low dose, so no further adjustment is needed. No dose adjustments are required for amlodipine, atorvastatin, or metoprolol in progressive CKD.

References:

Thomas SS, Zhang L, Mitch WE. Molecular mechanisms of insulin resistance in CKD. *Kidney Int* 2015;88(6):1233–1239.

169. A 79-year-old woman is diagnosed with a urinary tract infection (UTI) and is prescribed antibiotics. She faithfully takes these medications, and after 4 days starts to develop paresthesia in her hands and feet. She reports this to her primary care physician. A laboratory evaluation shows the following results:

<u>Serum</u>		<u>Urine</u>	
Sodium	140 mEq/L	Qualitative	
Potassium	4.2 mEq/L	Specific gravity	1.020
Chloride	109 mEq/L	Blood	1+
Bicarbonate	26 mEq/L	Protein	Trace
Urea nitrogen	52 mg/dL	Red blood cells	3–5 per high-power field
Creatinine	2.2 mg/dL	White blood cells	>50 per high-power field
eGFR	23 mL/min/1.73 m ²	Casts	Negative
		Crystals	None

Which medication was MOST likely used for treatment of her UTI?

- A. Sulfamethoxazole/trimethoprim
- B. Nitrofurantoin
- C. Fosfomycin
- D. Ampicillin

Answer: B

Nitrofurantoin has been available since 1952 and remains a first-line medication for uncomplicated cystitis. It is effective against *Escherichia coli*, *Klebsiella*, and *Enterobacter* species, which makes it popular for this purpose. However, nitrofurantoin is less effective in patients with decreased renal function because of the limitations to entering the urination system created by decreased eGFR. An additional adverse effect is peripheral nerve toxicity. Ciprofloxacin can cause the same peripheral nerve toxicity, but this is not an adverse effect of the medications listed in answers A, C, and D.

References:

Tan IL, Polydefkis MJ, Ebenezer GJ, Hauer P, McArthur JC. Peripheral nerve toxic effects of nitrofurantoin. *Arch Neurol* 2012;69(2):265–268.

Li R, Leslie S. Cystitis. *Stat Pearls*. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK482435/>. Accessed April 12, 2018.

170. Which values in the same patient would give the highest Kt/V?

Choice	Pre-Hemodialysis Blood Urea Nitrogen	Post-Hemodialysis Blood Urea Nitrogen	Ultrafiltration Amount
A.	100 mg/dL	35 mg/dL	1.0 L
B.	200 mg/dL	80 mg/dL	1.0 L
C.	20 mg/dL	7 mg/dL	2.0 L
D.	100 mg/dL	40 mg/dL	2.0 L

Answer: C

Explanation:

Kt/Vurea depends on the urea reduction ratio (URR) (diffusive urea clearance) and how much fluid containing urea is removed (convective urea clearance) via ultrafiltration during hemodialysis. The URR is calculated as follows: (pre- and post-hemodialysis blood urea nitrogen [BUNpre] – BUNpost) ÷ BUNpre x 100. The URR in answers A and C is 65% and in answers B and D 60%. Of the higher URRs A and C, answer C has a larger ultrafiltration amount, providing greater urea clearance, and thus would give the highest Kt/V. Even though answer B would remove the greatest amount of urea, Kt/V depends not on the amount of urea removed but on the amount of blood cleared. Kt/V is not related to blood urea nitrogen level.

References:

Qunibi WY, Henrich WL. Prescribing and assessing adequate hemodialysis. Available at:

https://www.uptodate.com/contents/prescribing-and-assessing-adequate-hemodialysis?search=KT%2FV%20&source=search_result&selectedTitle=1~51&usage_type=default&display_rank=. Accessed April 12, 2018.

171. Your hemodialysis patient has a monthly Kt/V of 1.5 but is experiencing uremic symptoms, nausea, anorexia, itching, insomnia, and fatigue.

What is a potential explanation?

- A. The dry weight needs adjustment.
- B. The patient is not always adherent to the hemodialysis schedule.
- C. Access recirculation is occurring during hemodialysis.
- D. The post-hemodialysis blood urea nitrogen (BUN) was drawn 30 minutes after the treatment ended.

Answer: B

Explanation:

The dry weight should not affect these symptoms. Access recirculation would explain this, but the Kt/V would be low. If the post-hemodialysis BUN were drawn too late, the BUN would rebound, and the Kt/V would be too low. The monthly Kt/V is a single value, and a patient may be adherent on “Kt/V day” but nonadherent on other days, coming off treatment early or not showing up, and could be uremic with what appears to be an adequate hemodialysis regimen.

References:

Qunibi WY, Henrich WL. Prescribing and assessing adequate hemodialysis. Available at:

https://www.uptodate.com/contents/prescribing-and-assessing-adequate-hemodialysis?search=KT%2FV%20&source=search_result&selectedTitle=1~51&usage_type=default&display_rank=. Accessed April 12, 2018.

Berkoben M, Blankestijn PJ. Arteriovenous fistula recirculation in hemodialysis. Available at:

<https://www.uptodate.com/contents/arteriovenous-fistula-recirculation-in-hemodialysis>. Accessed April 12, 2018.

172. Which pre-hemodialysis potassium level is associated with the lowest mortality?

- A. 3.8–4.6 mEq/L
- B. 5.3–5.7 mEq/L
- C. 4.1–4.6 mEq/L
- D. 4.6–5.3 mEq/L

Answer: D

Explanation:

An increase in mortality can result from either too low or too high a potassium level before dialysis. The reasons are multifactorial and probably reflect dietary adherence, good nutrition, and good dialysis.

References:

Kovesdy CP, Regidor DL, Mehrotra R, Jing J, McAllister CJ, Greenland S, Kopple JD, Kalantar-Zadeh K. Serum and dialysate potassium concentrations and survival in hemodialysis patients. *Clin J Am Soc Nephrol* 2007;2(5):999–1007.

173. Assuming the dialysis blood flow is the same for all access options, which is used for the most efficient dialysis?

- A. An arteriovenous fistula that has a blood flow of 1 L/min with normal venous pressure
- B. An arteriovenous fistula that has a blood flow of 500 mL/min with normal venous pressure
- C. A central venous catheter in a patient with a cardiac output of 6 L/min (assuming no access recirculation occurs)
- D. All of the above options are equivalent in efficiency

Answer: C

Explanation:

Normally an arteriovenous fistula (AVF) or an arteriovenous graft (AVG) provide the most efficient hemodialysis. There is normally little access recirculation with an AVF or AVG unless there is an outflow obstruction as predicted by high venous return pressure. However, cardiopulmonary recirculation can still occur with both AVF and AVG, even if no access recirculation occurs. The most efficient treatment uses a central venous catheter where there is no cardiopulmonary recirculation, as long as no access recirculation occurs.

References:

Schneditz D, Kaufman AM, Polaschegg HD, Levin NW, Daugirdas JT. Cardiopulmonary recirculation during hemodialysis. *Kidney Int* 1992;42(6):1450–1456.

174. What could cause metabolic alkalosis in a hemodialysis patient who is otherwise stable?

- A. Crack cocaine
- B. Large patient size (water volume V)
- C. Diet high in meat protein
- D. Large intradialytic weight gain

Answer: A

Explanation:

Larger patients need more bicarbonate delivered during hemodialysis. The arterial blood plasma of larger patients may be on the more acidic side of the curve, whereas smaller patients could get alkalotic on a “standard” bicarbonate bath. Animal protein produces more acid and thus would decrease the bicarbonate level. Large intradialytic weight gain could cause a dilution acidosis, not contraction alkalosis. Crack cocaine is often cut with sodium bicarbonate and could be an explanation for metabolic alkalosis in a patient with ESKD.

References:

Abramowitz MK. Bicarbonate balance and prescription in ESRD. *J Am Soc Nephrol* 2017;28(3):726–734.

Diskin CJ, Stokes TJ, Dansby LM, Radcliff L, Carter TB. Recurrent metabolic alkalosis and elevated troponins after crack cocaine use in a hemodialysis patient. *Clin Exp Nephrol* 2006;10(2):156–158.

175. A 52-year-old obese white man was referred for hypertension [BP, 150/90 mm Hg] and excessive snoring/insomnia suggestive of obstructive sleep apnea (OSA). A sleep study confirms the diagnosis of OSA with high apnea hypopnea index (AHI) >20. Continuous positive airway pressure (CPAP) therapy is recommended.

What is the likely effect of CPAP after 1 month of therapy on his systolic and diastolic BP?

- A. -15/-10 mm Hg
- B. -10/-6 mm Hg
- C. -3/-2 mm Hg
- D. No effect
- E. +4/+2 mm Hg

Answer: C

Explanation:

The correct answer is C. Observational cohort studies suggest that OSA may result in a moderate increase in BP of 7–15/4–10 mm Hg compared to a matched cohort. However, recent meta-analysis of randomized controlled trials (RCTs) evaluating the impact of 4–8 weeks of CPAP therapy on systolic and diastolic BP demonstrate only a modest reduction in BP of 1–3/0.7–2 mm Hg. Hence, a hypertensive patient with OSA may expect only modest improvement in BP control, and the clinician must remain vigilant for the need for antihypertensive medications. Of note, recent observations suggest that OSA may be highly prevalent in our CKD and ESKD population who carry a high burden of hypertensive diseases.

References:

Calhoun DA. Obstructive sleep apnea and hypertension. *Curr Hypertens Rep* 2010;12:189–195.

Rosas SE. Sleep apnea in individuals with chronic kidney disease: A wake-up call. *Clin J Am Soc Nephrol* 2011;6:954–956.

176. A 58-year-old man is seen in consultation for preoperative evaluation. He had vague right upper quadrant pain with a computed tomography (CT) evaluation noting cholelithiasis, which will require elective laparoscopic cholecystectomy. Of note, he has hypertension and a 2.5-cm left adrenal mass discovered incidentally during evaluation for abdominal pain on the CT scan.

The patient relates a 10-year history of hypertension easily controlled with an ARB. He is asymptomatic currently.

Labs: 138 | 100 / 15
 4.3 | 25 \ 0.9

With an adrenal “incidentaloma” mass, what is the likelihood of identifying an adrenal cancer or hyperfunctioning lesion (pheochromocytoma, primary aldosteronism, Cushing’s)?

- A. <1%
- B. 3–5%
- C. 10–20%
- D. 25%

Answer: C

Explanation:

The correct answer is C. A review of 2005 patients with an “incidentaloma” adrenal mass may have a remarkable chance (10–20%) of clinically relevant disease: Cushing’s syndrome, 7.9%; pheochromocytoma, 5.6%; primary aldosteronism, 1.2%; adrenocortical cancer, 4.7%; and metastatic cancer, 2.5%. Thus, this patient should have a biochemical evaluation to exclude pheochromocytoma before elective surgery. Moreover, nearly half of all recently diagnosed sporadic pheochromocytomas have been initially detected as an “incidentaloma,” and half of these patients lacked classical symptoms of pheochromocytoma.

References:

Kaplan NM. *Kaplan’s Clinical Hypertension*, 10th Ed. Philadelphia: Lippincott Williams & Wilkins; 2010:150.

Young WF. Clinical practice. The incidentally discovered adrenal mass. *N Engl J Med* 2007;356:601–610.

177. A newly referred 45-year-old woman is seen in your office and has a BP of 150/90 mm Hg. She reports that her BP was normal last month at the gynecologist’s office and 3 months ago when she donated blood. Her BMI is 26 kg/m². Echocardiography (ECG) is normal without evidence of left ventricular hypertrophy (LVH).

Which is the BEST management option?

- A. Begin diuretic therapy
- B. Schedule return visit in 1 year
- C. Schedule patient for ambulatory BP monitoring
- D. Schedule echocardiogram

Answer: C

Explanation:

This patient may have white coat hypertension, defined as office BP >140/90 mm Hg on at least three separate clinic/office visits with at least two sets of measurements of less than 140/90 mm Hg in non-clinic settings, plus the absence of target organ damage. Patients with white coat hypertension are at lower risk for cardiovascular events compared with those with sustained hypertension, although they are at greater risk for developing sustained hypertension. Drug treatment of white coat hypertension has not been shown to reduce morbid events. Ambulatory BP monitoring is considered to be the “gold standard” test to diagnose white coat hypertension, as it provides multiple measurements of BP in the non-clinic setting, including during sleep. Choice A is not correct, since there is some uncertainty regarding the diagnosis of hypertension and prescribing a medication with potential adverse effects that might be unnecessary would be inappropriate. Choice B is incorrect. Although there is uncertainty regarding the diagnosis of hypertension, it is still possible that the patient has elevated BP. It is important to clarify this issue, and if hypertension is conclusively diagnosed, she should be treated with lifestyle modifications and antihypertensive medication. Choice D is incorrect. There is no evidence for LVH on either physical examination or ECG. Echocardiography is more sensitive in detecting LVH or diastolic dysfunction and would be a reasonable examination to perform if her BP on ambulatory monitoring is just under the threshold for treatment, e.g., average 24-hour systolic/diastolic of 128/80 mm Hg. In this case, an echocardiogram might help to decide whether to initiate antihypertensive therapy.

178. A 28-year-old woman with type 1 diabetes is referred for management of hypertension in anticipation of pregnancy. She wants to start a family in the next 3 months. She is currently taking Losartan 50 mg daily and hydrochlorothiazide (HCTZ) 12.5 mg daily. Her BP is 110/70 mm Hg.

Which is the BEST approach to treatment?

- A. Discontinue losartan
- B. Discontinue hydrochlorothiazide
- C. Change losartan to aliskiren
- D. Wait until patient becomes pregnant then adjust medications

Answer: A

Explanation:

ARB exposure during the second and third trimesters has been associated with neonatal renal failure and death. First trimester exposure has been associated with cardiac abnormalities. Diuretics may be continued during pregnancy, particularly in women with sodium-sensitive hypertension or edema and when women have been taking them prior to pregnancy. Choice B is incorrect because it would be inappropriate to continue the losartan. Choice C is incorrect because renin inhibitors would be expected to have similar fetal toxicity as ARBs, an effect attributed to the dependence of the fetal kidney on the renin-angiotensin system. Choice D is incorrect because of the recent information regarding fetal problems with first trimester exposure to renin-angiotensin system blockers. Some women do not make appointments to see their physicians until the second trimester of pregnancy; thus, the safest approach would be to discontinue the losartan prior to conception. If BP remains low through the first trimester, it may be possible to further lower the dose of HCTZ, e.g., to every other day.

179. A 68-year-old man has been treated for hypertension for 20 years. He has gained about 15 lbs in the last 20 years. His medications include lisinopril 20 mg daily, amlodipine 10 mg daily, and hydrochlorothiazide 25 mg daily. His BP is 160/95 mm Hg, and his labs are normal, including potassium and renal function. Workup for secondary hypertension is negative.

Which is the BEST treatment?

- A. Add atenolol
- B. Add doxazosin
- C. Add spironolactone
- D. Add clonidine

Answer: C

Explanation:

The correct answer is C: add spironolactone. This patient has resistant hypertension, because he has poorly controlled BP despite three medications. Patient characteristics more likely to be associated with resistant hypertension include older age, BMI >30 kg/m², higher baseline BP, diabetes, and African-American race. Excess dietary salt intake and heavy alcohol intake are also well-recognized contributory factors. A high proportion of patients with resistant hypertension have secondary hypertension due to either primary aldosteronism or renovascular hypertension; therefore, these entities should be ruled out with appropriate testing. Treatment of resistant hypertension should include appropriate lifestyle modifications, withdrawal of interfering medications, and correction of secondary causes. Mineralocorticoid receptor antagonists (spironolactone, amiloride, eplerenone) have also been demonstrated to be particularly effective in resistant hypertension. Choice A, atenolol, is incorrect. Beta blockers are of questionable efficacy in older patients who are more likely to respond to calcium channel blockers or diuretics. Choice B, doxazosin, is incorrect because this agent has not been shown to be as effective as other drugs in reducing cardiovascular endpoints. Choice D is incorrect because, although clonidine may be effective in lowering BP, it is associated with significant side effects and has not been evaluated as rigorously as spironolactone in patients with resistant hypertension.

180. An 85-year-old woman comes for a follow-up evaluation for hypertension. She does not smoke and adheres to a Dietary Approaches to Stop Hypertension (DASH) diet. At an office visit 1 month ago, her BP was 170/70 mm Hg. She was diagnosed with hypertension and chronic stable angina 7 years ago and currently takes metoprolol, sublingual nitroglycerin as needed, and aspirin. On physical examination, her BP is 186/70 mm Hg, pulse rate is 60 beats/min, and respiration rate is 12 breaths/min. BMI is 22 kg/m². Cardiopulmonary examination reveals no jugular venous distention, carotid bruits, murmur, extra cardiac sounds, or pulmonary crackles. The abdomen is soft without masses or bruits. Neurologic examination is normal.

Laboratory studies

Serum electrolytes: Normal
 Blood urea nitrogen: 16 mg/dL
 Serum creatinine: 1.01 mg/dL
 Urinalysis: Normal

An electrocardiogram demonstrates increased voltage in precordial leads. Ultrasound of the kidneys is normal.

In addition to reinforcing lifestyle modifications, which is the MOST appropriate next step in this patient's management?

- A. Follow-up in 3–6 months
- B. Hydrochlorothiazide
- C. Lisinopril
- D. Losartan

Answer: B

Explanation:

The most appropriate next step in this patient's management is low-dose hydrochlorothiazide and follow-up in 1 week. Antihypertensive therapy has been shown to benefit patients between 60 and 80 years of age, and a trial published in 2008 demonstrated that antihypertensive therapy in patients greater than 80 years of age is associated with a decrease in stroke and cardiovascular mortality. Most guidelines recommend lowering systolic BP in patients older than 60 years of age to less than 160 mm Hg and, if possible, to 140 mm Hg or lower if tolerated. Because older patients with hypertension are more likely to be salt sensitive and responsive to a diuretic, low-dose hydrochlorothiazide would be appropriate for this patient. Follow-up evaluation in 1 week also is indicated to assess for electrolyte abnormalities (e.g., hyponatremia or hypokalemia) or increased serum creatinine. Follow-up in 3–6 months without further treatment would not be appropriate due to significantly elevated BP. Patients with stage 2 hypertension (systolic BP \geq 160 mm Hg or diastolic pressure \geq 100 mm Hg) usually require treatment with multiple drugs to achieve target BP levels. Adding an ACE inhibitor or an ARB would be less likely to be beneficial in an elderly patient than a diuretic.

181. A 23-year-old woman with a history of type 1 diabetes for 15 years comes to you for counseling regarding pregnancy. She has been told that she has albumin in her urine, and she has had laser treatment for retinopathy. She is taking lisinopril and multiple insulin injections daily.

Her BP is 110/70 mm Hg.

Labs

A_{1C}: 8%
 Serum creatinine: 0.9 mg/dL
 Urine albumin/creatinine: 100 mg/g

In addition to advising discontinuation of ACE inhibition, what is the MOST important aspect of preconception management?

- A. Evaluation of urinary protein excretion after discontinuation of lisinopril
- B. Switching to an alternative antihypertensive agent
- C. Referral to endocrinologist for better glycemic control
- D. Cardiac stress test
- E. Ophthalmologic exam

Answer: C

Explanation:

In women with diabetes, poor glycemic control in the first trimester of pregnancy is associated with a high incidence of fetal malformations, and strict glycemic control is of the utmost importance in women with pregestational diabetes. It is likely that urinary protein excretion will increase after discontinuation of lisinopril, and although it may be useful to document the level of proteinuria prior to pregnancy, this will not necessarily have an impact on the outcome. Switching to an alternative antihypertensive agent can be done at any time prior to conception, but, given the low BP on lisinopril and the expected decrease in BP during pregnancy, it may not be necessary to prescribe antihypertensive medication during pregnancy. Cardiac stress testing and ophthalmologic

exams, although useful, are not as important as achieving strict glycemic control as early in pregnancy as possible. If the woman has any cardiac symptoms or history, then stress testing would be more urgent, but in a 23-year-old, this is not likely.

182. A 78-year-old woman with long-standing hypertension, hyperlipidemia, stage 3 CKD (eGFR 38 mL/min/1.73 m²), and CAD is admitted with acute retrosternal chest pain. A non-ST segment elevation myocardial infarction is diagnosed based on troponin elevation and electrocardiographic criteria and she is scheduled for urgent coronary angiography. Her usual outpatient medications include lovastatin, losartan, and furosemide.

Which intervention will have the greatest impact on reducing her risk of contrast-associated AKI?

- A. Discontinuation furosemide
- B. Discontinuation of losartan
- C. Infusion of isotonic saline
- D. Administration of oral *N*-acetylcysteine

Answer: C

Explanation:

The intervention associated with the greatest reduction in the risk for contrast-induced nephropathy is the administration of isotonic crystalloids prior to and following the angiographic procedure (choice C is correct). Data regarding the benefit of isotonic sodium bicarbonate relative to isotonic saline are conflicting. Although acute administration of furosemide is associated with increased risk of contrast-induced nephropathy, the added benefit of discontinuation of chronic diuretic therapy is not established and appears to be less than the benefit of volume administration (choice A is incorrect). Similarly, there are inadequate data regarding the benefit of discontinuation of angiotensin receptor blockers or angiotensin converting enzyme inhibitors (choice B is incorrect). The benefit associated with *N*-acetylcysteine administration is also controversial; when used, it should only be administered in conjunction with and not in lieu of administration of intravenous isotonic crystalloids (choice D is incorrect).

183. You are called to see a 40-year-old woman, who is 3 days postpartum, because of elevated BP. The obstetrician is ready to send her home and wants to make sure she has outpatient follow-up for her BP. She was not aware of having hypertension prior to pregnancy, had mild preeclampsia at term, and was delivered *via* Caesarean section. Her BPs for the first 2 postpartum days ranged from 130 to 160/80 to 90 mm Hg.

What is your recommendation to the obstetrician?

- A. Stop nonsteroidal anti-inflammatory drugs (NSAIDs) and begin labetalol 100 mg twice per day (BID)
- B. Start lisinopril 10 mg daily
- C. Start hydrochlorothiazide 12.5 mg daily
- D. Discharge patient because BP is likely to normalize in the next few days
- E. Start nifedipine extended release 30 mg and arrange follow-up at 6 weeks postpartum

Answer: A

Explanation:

NSAIDs are currently the default order for peripartum analgesia; all women are automatically started on ibuprofen 800 mg three times a day (TID) at most hospitals in the United States, and most obstetricians are unaware that NSAIDs can cause elevated BP. Therefore, the consulting physician should assume women are being treated with NSAIDs and confirm with the hospital staff. Risk factors for postpartum exacerbation of hypertension include antepartum hypertension, older age, and NSAID use. In fact, in most women, BP is highest in the first 1–2 weeks postpartum, so most likely this patient's BP will increase in the next few days rather than decrease. Therefore, NSAIDs should be discontinued, and labetalol, which can be taken while breastfeeding, should be started. Although captopril gets into breast milk in very small amounts, little information is available regarding the safety of lisinopril during breast feeding, so this medication should be avoided.

Hydrochlorothiazide (HCTZ) does not get into breast milk in clinically significant amounts and is considered safe; however, it may be associated with decreased milk production. It would not be prudent to discharge the patient without some treatment strategy, especially if she is still taking NSAIDs, because her BP is likely to increase rather than decrease in the next few days. Although nifedipine XL is an acceptable medication for pregnancy and lactation, the patient should be followed more closely to assess response to treatment. Recent literature has documented that most pregnancy-related intracerebral hemorrhages and strokes occur in the postpartum period rather than antepartum. NSAIDs should also be discontinued in any women with postpartum hypertension.

184. A 68-year-old man is identified with elevated BPs of approximately 180/90 mm Hg during a routine examination. Previous examinations were associated with no such elevations. He is a long-term smoker and is overweight (BMI, 31 kg/m²). He takes no regular medications. Labs are normal with the exception of a serum creatinine of 1.3 mg/dL. A renal artery ultrasound demonstrates a single artery to the right kidney (9.6 cm) with a peak systolic velocity of 310 cm/sec and one to the left kidney (10.8 cm) with peak velocity of 140 cm/sec.

What does the MOST appropriate next step in his evaluation and management include?

- A. Initiation of antihypertensive drug therapy with lisinopril
- B. Functional renal scanning with a captopril renogram
- C. Renal angiography and endovascular stenting
- D. Renal denervation

Answer: A

Explanation:

For an individual with unilateral renovascular disease, much of the decision about further evaluation depends on response to drug therapy, specifically ACE inhibition. If BP is controlled and renal function is stable, current data indicate that little is to be gained by further maneuvers. Scanning with captopril renography is less commonly done and would not be the first step. The merit of angiography and stent therapy would depend in part on the response to ACE inhibition (as above), so would normally be undertaken after such a trial. Renal denervation until now has been contraindicated in the presence of renovascular disease and cannot be recommended at this time.

185. A 37-year-old woman undergoing routine gynecological evaluation is identified with elevated BP (170/110 mm Hg). She had been a smoker and has been having occasional morning headaches. She is otherwise well but takes propranolol for headaches. A single pregnancy was associated with severe hypertension in the last month, but this resolved after delivery.

Examination

BP, 165/105 mm Hg; grade II retinopathy with arteriovenous nicking. A soft systolic murmur is present over the left sternal border, and a bruit is detected over the umbilicus. CBC, BUN, creatinine, glucose, and electrolytes are normal, as is the urinalysis.

Which examination is MOST likely to yield useful information regarding the rise in BP?

- A. Serum human chorionic gonadotrophin (HCG)
- B. Plasma renin activity
- C. Computed tomography (CT) angiography of the abdominal vessels
- D. Renal vein renin levels
- E. Gadolinium-enhanced magnetic resonance angiography (MRA)

Answer: C

Explanation:

The single most probable cause of secondary hypertension is fibromuscular dysplasia, which commonly develops in mid- to distal renal artery segments and is most likely to be identified on CT angiography. HCG testing may be appropriate for several reasons but would not explain hypertension in any event. Peripheral plasma renin and renal vein renin levels have been useful when positive in the past but are infrequently performed. They are especially susceptible to suppression by beta blockade, such as the propranolol in this subject. MRA may be considered but has generally been less reliable for distal vessels in the kidney.

186. A 38-year-old woman is noted to develop headaches and a rise in BP 3 weeks after a motor vehicle accident in which her car had been destroyed. Emergency room evaluation demonstrated bruises over her back and torso, and her arm had been broken. Laboratory values and vital signs had been normal. She takes no regular medications.

Today: She is wearing a cast over her right upper arm. BP, 185/110 mm Hg; pulse, 94 beats/min. No bruits are audible. Laboratory evaluation: CBC: Hgb: 11.0 g/dL; WBC: 8100; platelets: 120,000; Creatinine, 1.1 mg/dL; Na⁺, 128 mEq/L; K⁺, 3.4 mEq/L.

In this setting, on what should the selection of the MOST effective antihypertensive drug therapy be based?

- A. Mineralocorticoid receptor blockade
- B. Sympathetic inhibition
- C. Angiotensin receptor blockade
- D. Blockade of diluting site sodium reabsorption
- E. Vasopressin receptor blockade

Answer: C

Explanation:

This is likely a sequel to renal trauma, with localized kidney ischemia and/or infarction from dissection/contusion of the kidney. Page kidney is the term to describe renal trauma with a perinephric hematoma compressing the renal parenchyma, causing renal ischemia and RAAS activation. Such a sequence commonly induces activation of the renin-angiotensin system (most often unilateral) that responds to blockade of that system. Mineralocorticoid receptor blockade might address hypokalemia but not likely lower BP if angiotensin dependent. Sympatholytic drugs and/or diuretics might lower BP but likely would aggravate electrolyte disorders and would not be the first choice. Blockade of the vasopressin receptor has little role in this context.

187. A 38-year-old woman is noted to develop headaches and a rise in BP 3 weeks after a motor vehicle accident in which her car had been destroyed. Emergency room evaluation demonstrated bruises over her back and torso, and her arm had been broken. Laboratory values and vital signs had been normal. She takes no regular medications.

Today: She is wearing a cast over her right upper arm. BP, 185/110 mm Hg; pulse, 94 beats/min. No bruits are audible. Laboratory evaluation: CBC: Hgb: 11.0 g/dL; WBC: 8100; platelets: 120,000; Creatinine, 1.1 mg/dL; Na⁺, 128 mEq/L; K⁺, 3.4 mEq/L.

In this setting, what is the MOST likely cause of hypertension?

- A. Pain with central sympathetic outflow
- B. Page kidney
- C. Renal artery thrombosis
- D. Illicit drug use
- E. Excessive dietary salt intake

Answer: B

Explanation:

This is likely a sequel to renal trauma, with localized kidney ischemia and/or infarction from dissection/contusion of the kidney. Page kidney is the term to describe renal trauma with a perinephric hematoma compressing the renal parenchyma, causing renal ischemia and RAAS activation. Such a sequence commonly induces activation of the renin-angiotensin system (most often unilateral) that responds to blockade of that system. Mineralocorticoid receptor blockade might address hypokalemia but not likely lower BP if angiotensin dependent. Sympatholytic drugs and/or diuretics might lower BP but likely would aggravate electrolyte disorders and would not be the first choice. Blockade of the vasopressin receptor has little role in this context.

188. A 76-year-old man has been treated for hypertension for 20 years. Over the last 2 years, his medical regimen has been increased in the face of rising pressures and development of symptomatic angina, for which he underwent coronary stenting. Medications now include aspirin, simvastatin, clopidogrel, metoprolol, lisinopril, and amlodipine and isosorbide. Activities are limited by lower extremity claudication. You are asked to see him because serum creatinine has risen from 1.7 mg/dL a year ago to 2.6 mg/dL. CBC, electrolytes, and urinalysis are unremarkable. BP, 175/80 mm Hg; pulse, 65 beats/min. Bruits are audible in the neck, abdomen, and groin.

A renal artery ultrasound identifies a right kidney of 9.2 cm length, cortical thinning, and peak systolic velocities greater than 370 cm/s. The left kidney is 11.6 cm and appears normal. Peak systolic velocities could not be determined, but a “parvus tardus” waveform in the segmental branches is identified. Resistive index is 0.71.

As you review his options, what does the MOST probable outcome of renal revascularization include?

- A. Renal artery atheroembolism
- B. Recurrent renal artery stenosis within the stent
- C. Recovery of kidney function in the left kidney
- D. Unchanged GFR
- E. Discontinuation of antihypertensive drug therapy

Answer: D

Explanation:

Most (52%) patients with longstanding atherosclerotic renovascular disease, as present in this patient, have “stabilization” of creatinine—without much change. Some recover GFR (answer C; 27%). Although atheroembolism can occur (<5% in current series), as can recurrent stenosis (<15%), these are relatively infrequent. BP may be easier to control, but removal of BP drugs in longstanding hypertension almost never occurs.

189. A 76-year-old man has been treated for hypertension for 20 years. Over the last 2 years, his medical regimen has been increased in the face of rising pressures and development of symptomatic angina, for which he underwent coronary stenting. Medications now include aspirin, simvastatin, clopidogrel, metoprolol, lisinopril, and amlodipine and isosorbide. Activities are limited by lower extremity claudication. You are asked to see him because serum creatinine has risen from 1.7 mg/dL a year ago to 2.6 mg/dL.

CBC, electrolytes, and urinalysis are unremarkable. BP, 175/80 mm Hg; pulse, 65 beats/min. Bruits are audible in the neck, abdomen, and groin.

A renal artery ultrasound identifies a right kidney of 9.2 cm length, cortical thinning, and peak systolic velocities greater than 370 cm/s. The left kidney is 11.6 cm and appears normal. Peak systolic velocities could not be determined, but a “parvus tardus” waveform in the segmental branches is identified. Resistive index is 0.71.

As you review his situation, of what would the MOST useful data regarding the ability to salvage his kidney function with renal revascularization consist?

- A. Serum creatinine less than 3.0 mg/dL
- B. Previous treatment with statins
- C. Tolerance to ACE inhibitor therapy
- D. Cortical thinning by ultrasound
- E. Resistive index in the left kidney

Answer: E

Explanation:

Although reliability varies between laboratories, finding a low resistive index has been associated with improved functional outcomes more commonly than elevated levels, which suggest poor microvascular blood flow during diastole. The actual level of creatinine does not reliably predict the outcome for a specific patient, nor does the previous treatment with statins or ACE inhibitor therapy. Cortical thinning on one kidney is considered an adverse sign but does not have the data strength associated with resistive indices.

190. **Which is the MOST likely cause of hypertension and proteinuria observed in pre-eclampsia?**

- A. Increased angiotensin II and aldosterone
- B. Decreased vascular endothelial growth factor (VEGF)
- C. Increased catecholamines
- D. Decreased prostaglandin E
- E. Increased endothelin
- F. None of the above

Answer: B

Explanation:

VEGF, as well as other factors, is produced in normal pregnancy. VEGF is one of the factors that is required for both systemic and glomerular endothelial function. In the setting of pre-eclampsia, circulating VEGF levels are decreased due to binding by soluble flt, which is a VEGF receptor that is excessively produced in this setting. By binding VEGF, soluble flt causes hypertension *via* endothelial dysfunction (decreased nitric oxide and increased endothelin) and AKI with proteinuria by disturbing the glomerular endothelium (inducing endotheliosis).

191. **Which drug is associated with the profile described below?**

<u>Plasma Renin Activity</u>	<u>Renin level</u>	<u>Angiotensin II</u>	<u>Aldosterone</u>
low	high	low	low

- A. Enalapril
- B. Eplerenone
- C. Valsartan
- D. Triamterene
- E. Aliskiren

Answer: E

Explanation:

Aliskiren, which is a renin inhibitor, effects the RAAS hormones differently than other RAAS blockers such as the ACE inhibitors (ACEIs), ARBs, and aldosterone antagonists. ACEIs raise plasma renin activity and renin levels, but lower All and aldosterone. ARBs raise plasma renin activity, renin levels and All levels, but lower aldosterone. Aldosterone antagonists raise the levels of all of the hormones but antagonize the mineral corticoid receptor.

192. A 55-year-old woman is referred for recently identified BP above 175/105 mmHg on several occasions. A gynecological examination 1 year earlier recorded BP levels of 135/80 mmHg. The patient has been developing persistent morning headaches but is otherwise well. She acknowledges occasional use of ibuprofen, 600 mg, and acetaminophen for headaches but takes no other medications regularly.

On examination, her BMI is 28.2 and her truncal weight predominant. She has a heart rate of 72/min and (oscillometric) BP 172/104 mmHg. Pulses are symmetric and present, and no edema is evident. Her complete blood count values are normal; her urinalysis shows trace amounts of protein with normal microscopic findings. Other laboratory tests show the following:

Creatinine	0.8 mg/dL
Sodium	144 mEq/L
Potassium	3.8 mEq/L
Bicarbonate	29 mEq/L
Chloride	104 mEq/L

Regarding the increase in BP observed during this interval, which is MOST correct?

- An increase in BP at this age is expected as part of normal aging.
- Administration of nonsteroidal anti-inflammatory agents accounts for this change.
- This increase represents less than a doubling of cardiovascular risk over the long-term.
- Excess aldosterone effect should be excluded.

Answer: D

Explanation:

Although BP increases with age, it is unlikely that a 40-mmHg increase over 1 year would occur without a secondary element. Although nonsteroidal anti-inflammatory drugs can interfere with antihypertensive drug effects, they rarely induce de novo hypertension. An increase in BP >40/30 mmHg increases long-term cardiovascular risk at least 4-fold over baseline levels. A recently developing increase in these levels accompanied by the mild elevation of serum sodium and bicarbonate is most typical of excess aldosterone effect.

References:

Vasan RS, Beiser A, Seshadri S, Larson MG, Kannel WB, D'Agostino RB, Levy D. Residual lifetime risk for developing hypertension in middle-aged women and men: The Framingham Heart Study. *JAMA* 2002;287:1003–1010.
Lewington S, Clarke R, Qizilbash N, Peto R, Collins R. Prospective Studies Collaboration: Age-specific relevance of usual blood pressure to vascular mortality: A meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet* 2002;360:1903–1913.

193. A 45-year-old woman has BP levels between 150–160/85–95 mmHg, despite administration of daily lisinopril, 10 mg, and amlodipine, 5 mg. She indicates that BP levels are excellent at home, and she wants to base her management on home BP readings rather than office levels.

Which MOST correctly describes the attributes of management of hypertension using home BP measurements?

- Prospective studies based on home readings demonstrate reduced cardiovascular event rates.
- Systematic studies using home BP readings and pharmacologic adjustments improve adherence.
- Home readings increase patient “empowerment” but increase adverse events.
- Increased BP “anxiety” associated with home readings leads to reduced medication adherence.

Answer: B

Explanation:

Home BP readings have been established to lead to improved medication adherence. Although home readings “empower” individuals, no clinical outcome data have been established based on home readings. For some patients, anxiety associated with home readings is problematic but does not lead to less adherence in studies to date.

References:

McManus RJ, Mant J, Bray EP, Holder R, Jones MI, Greenfield S, Kaambwa B, Banting M, Bryan S, Little P, Williams B, Hobbs FD. Telemonitoring and self-management in the control of hypertension (TASMINH2): A randomised controlled trial. *Lancet* 2010;376:163–172.
White WB, Gulati V. Managing hypertension with ambulatory blood pressure monitoring. *Curr Cardiol Rep* 2015;17:2.

194. A 62-year-old woman is referred for treatment-resistant hypertension. Initial BP levels measured more than 5 years earlier were 178/110 mmHg. She wants to be considered for renal denervation based on the failure of her current antihypertensive drug regimen, which includes chlorthalidone, 25 mg/d; carvedilol, 25 mg twice daily; minoxidil, 10 mg twice daily; amlodipine, 10 mg; furosemide, 40 mg; and spironolactone, 50 mg. Office BP readings on three separate visits average 165/90 mmHg. The patient appears well. Retinal findings demonstrate arteriolar nicking, and 1+ lower extremity edema is present. Laboratory tests yield the following values:

Serum creatinine	1.1 mg/dL
Sodium	138 mEq/L
Potassium	4.1 mEq/L
Bicarbonate	25 mEq/L

Urinalysis reveals trace proteinuria and normal microscopic findings. A renal artery duplex ultrasound shows normal findings.

Based on results from prospective trials, which is MOST directly applicable to her request?

- A. Prospective trials in Europe identify a 25–30 mmHg reduction in BP after renal denervation as compared with sham controls.
- B. Toxicology studies in “resistant hypertension” identify complete absence of antihypertensive medications in >50% of patients referred for trials.
- C. Prospective sham-controlled trials in the United States failed to identify a clinically relevant BP reduction with denervation beyond that observed in the control group.
- D. No renal denervation devices or procedures are approved in the United States.

Answer: D

Explanation:

All of the statements regarding renal denervation are at least partially correct, but answer D is absolutely correct as relevant to her management in the United States. Initial trials (in Australia and later in Europe) demonstrated large BP reductions, but follow-up studies overall have been much lower. “Resistant hypertension” has been identified with major degrees of nonadherence—but less than stated here. Answer C is a correct statement but subject to the concerns about trials in general. European trials have demonstrated a meaningful BP reduction with denervation that they believe persists despite similar levels of nonadherence in both treatment groups.

References:

Yoruk A, Tankut SS, Gassler JP, Bisognano JD. Present and future of interventional treatment of resistant hypertension. *Curr Hypertens Rep* 2017;19:4.
 Strauch B, Petrák O, Zelinka T, Rosa J, Somlóová Z, Indra T, Chytil L, Marešová V, Kurcová I, Holaj R, Wichterle D, Widimský J Jr. Precise assessment of noncompliance with the antihypertensive therapy in patients with resistant hypertension using toxicological serum analysis. *J Hypertens* 2013;31:2455–2461.

195. A 62-year-old woman presents with newly detected hypertension at levels of 155/105 mmHg. Previous therapy with metoprolol, 25 mg twice daily, and chlorthalidone, 12.5 mg/d, was associated with BP of 150/100 mmHg after a 3-month trial. The patient has a strong family history of cardiovascular disease, but she is otherwise healthy and takes no other medications. She is a nonsmoker.

Examination reveals a well-appearing woman with a BMI of 26 kg/m² and BP 152/98 mmHg (oscillometric). No bruits are identified, and pulses are symmetric throughout her extremities. From laboratory studies, her complete blood count values and urinalysis results are normal; other values are as follows:

Serum creatinine	0.9 mg/dL
eGFR	69 mL/min/1.73 m ²
Sodium	142 mEq/L
Potassium	4.0 mEq/L
Bicarbonate	30 mEq/L
Plasma renin activity	2.6 ng/mL/h
Plasma aldosterone	21 ng/dL
Lipid profile	
Total cholesterol	239 mg/dL
HDL	32 mg/dL
LDL	175 mg/dL

A renal artery ultrasound examination demonstrates elevated velocities in the proximal right renal artery. Peak systolic velocities are 280 cm/s. The right kidney is 11.0 cm, and the left measures 12.0 cm in length. Resistive indices in segmental vessels range between 0.70 and 0.71.

Based on these findings and results of prospective randomized trials, which is MOST appropriate to optimize antihypertensive drug therapy?

- A. Valsartan, 160 mg at bedtime
- B. Spironolactone, 50 mg/d
- C. Doxazosin, 2 mg at bedtime
- D. Amlodipine, 5 mg once daily
- E. Furosemide, 20 mg

Answer: A

Explanation:

This individual has renovascular disease associated with newly identified hypertension. Based on data from the CORAL and ASTRAL studies, blockade of the renin-angiotensin system is safe and likely to reduce cardiovascular risk equal to revascularization for such an individual, making use of an angiotensin blocker most appropriate. All other antihypertensive agents, including spironolactone, doxazosin, and amlodipine, can be considered but are less appropriate for an individual with renovascular hypertension. Numerous trials indicate that patients with renovascular disease treated with RAAS blockade have reduced morbidity and mortality as compared with treatment with other agents. Furosemide has a short half-life and is less effective as an antihypertensive for patients with relatively preserved GFR.

References:

Cooper CJ, Murphy TP, Cutlip DE, Jamerson K, Henrich W, Reid DM, Cohen DJ, Matsumoto AH, Steffes M, Jaff MR, Prince MR, Lewis EF, Tuttle KR, Shapiro JI, Rundback JH, Massaro JM, D'Agostino RB Sr, Dworkin LD; CORAL Investigators. Stenting and medical therapy for atherosclerotic renal-artery stenosis. *N Engl J Med* 2014;370:13–22.

Chrysochou C, Foley RN, Young JF, Khavandi K, Cheung CM, Kalra PA. Dispelling the myth: The use of renin-angiotensin blockade in atheromatous renovascular disease. *Nephrol Dial Transplant* 2012;27:1403–1409.

Hackam DG, Duong-Hua ML, Mamdani M, Li P, Tobe SW, Spence JD, Garg AX. Angiotensin inhibition in renovascular disease: A population-based cohort study. *Am Heart J* 2008;156:549–555.

196. A 54-year-old athletic man has BP elevation to 180/110 mmHg identified during the introduction to a healthy-living resort program. He has taken no medications previously and is a nonsmoker. Physical examination has otherwise normal findings, and his BMI is 26. Laboratory tests show normal results from the complete blood count, urinalysis, and a lipid panel. His serum creatinine level is 1.5 mg/dL. Antihypertensive therapy with metoprolol, 100 mg/d, and hydrochlorothiazide, 25 mg/d, is initiated. The addition of lisinopril, 10 mg/d, is followed by an increase in creatinine level to 2.6 mg/dL and discontinued. Administering amlodipine, 10 mg/d, is associated with BP levels of 156/94 mmHg. A renal artery ultrasound demonstrates a small right kidney (7.0 cm in length) with no evident blood flow. The left kidney is 13.5 cm in length with a segmental resistive index of 0.67. Peak systolic velocities at the origin of the left renal artery are 420 cm/s. A radionuclide renal scan demonstrates <10% of filtration on the right and 90% on the left.

Which is the MOST appropriate next step in his management?

- A. Laparoscopic nephrectomy of the right “pressor” kidney
- B. Measurement of renal vein renin levels
- C. Endovascular stent placement for the left renal artery
- D. Addition of spironolactone

Answer: C

Explanation:

This relatively young individual presents as renovascular hypertension with a solitary functioning kidney. Although the right kidney is small and appears to have vessel occlusion, the major concern is the status of the left, solitary functioning kidney with high-grade stenosis (as verified by the increase in creatinine level after administration of the ACE inhibitor lisinopril). The important issue is to ensure vascular supply to the left kidney in this young individual, making endovascular stent placement the preferred next step. Removing the small kidney may be considered; it is not the priority here. Renal vein renin levels may add further diagnostic information but are less pressing than protecting the left kidney. Addition of spironolactone as a fourth drug for medical management may be considered but fails to ensure the viability of the left kidney.

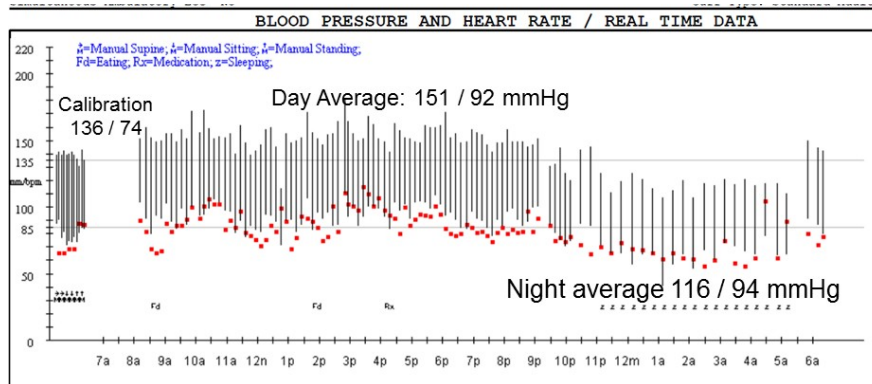
References:

Kane GC, Textor SC, Schirger A, Garovic VD. Revisiting the role of nephrectomy for advanced renovascular disease. *Am J Med* 2003;114:729–735.

197. A 23-year-old man developed headaches and episodes of elevated BP during his final year of university studies. During the first 2 years, he had been given lisdexamfetamine for management of attention-deficit/hyperactivity disorder, but this had been discontinued more than a year previously. Office BP readings with his home physician have ranged 120–130/72–80 mmHg when he is not taking therapy.

He is otherwise healthy and takes no medications, including nonsteroidal anti-inflammatory agents. His physical examination yields normal findings with an office BP of 122/72 mmHg (oscillometric) and 130/80 mmHg by the physician. His BMI is 24.5. He shows mild arteriolar narrowing and no edema. Laboratory test results are normal for the complete blood count, lipid profile, electrolyte values, and urinalysis. His creatinine level is 0.9 mg/dL.

A 24-hour ambulatory BP monitor was undertaken (figure).



Based on the ambulatory BP monitor information, which is MOST appropriate?

- A. Evaluation for obstructive sleep apnea
- B. Imaging diagnostic studies for pheochromocytoma
- C. Management as “masked hypertension”
- D. Reassurance that no further studies are needed

Answer: C

Explanation:

The basis for this question is recognizing patterns of BP elevation only occurring during out-of-office settings, with normal readings both with his home physician and in the current office. The elevation is significant and sustained during awake hours (the definition of masked hypertension). Overnight readings and heart rate appear normal, making obstructive sleep apnea less likely. BP levels and heart rate are stable, not paroxysmal, making pheochromocytoma less likely also. Choosing to do no further studies is incorrect because this individual clearly is developing symptoms and risk associated with elevated pressures that need both definition and treatment. The risks of masked hypertension have been identified as substantial.

References:

White WB, Gulati V. Managing hypertension with ambulatory blood pressure monitoring. *Curr Cardiol Rep* 2015;17:2.

198. A 73-year-old man is admitted with congestive cardiac failure characterized by dyspnea, lower extremity edema, and hypertension (BP 190/105 mmHg on admission). Troponins and serial cardiograms demonstrate no changes over 2 days. He is treated with oxygen and furosemide (40 mg IV daily), in addition to baseline medications: carvedilol, 12.5 mg twice daily; lisinopril, 10 mg daily; and isosorbide mononitrate, 60 mg daily. The patient’s creatinine level increases from 1.4 mg/dl to 2.6 mg/dL during this interval. On day 3, examination shows a BP of 160/98 mmHg, 1+ lower extremity edema, 2+ neck vein distention, and bruits audible over the carotid and femoral regions. The complete blood count has normal results; other laboratory tests yield the following values:

Creatinine	2.6 mg/dL
Sodium	132 mEq/L
Potassium	3.4 mEq/L
Bicarbonate	28 mEq/L
Glucose	118 mg/dL
Urinalysis	3+ protein

An echocardiogram reveals an ejection fraction of 65% with left ventricular thickening posterior wall thickness 12 mm) and mild aortic stenosis.

Which additional laboratory study is MOST appropriate at this time?

- A. 24-hour urine for protein
- B. Urinary sodium excretion
- C. Aldosterone/renin ratio
- D. Renal artery duplex ultrasound
- E. Hemoglobin A1c

Answer: D

Explanation:

This case represents a variant of “cardiorenal” syndrome attributable to renovascular disease (usually bilateral) with increasing creatinine and hypertension associated with circulatory congestion. The renovascular abnormality is most likely to be identified with renal duplex ultrasonography. Although urinary protein and sodium levels may be of interest, they are less directly relevant, as are values for renin and aldosterone. Although glucose levels are modestly elevated, hemoglobin A1c is less directly relevant here.

References:

Messlerli FH, Bangalore S, Makani H, Rimoldi SF, Allemann Y, White CJ, Textor S, Sleight P. Flash pulmonary oedema and bilateral renal artery stenosis: The Pickering syndrome. *Eur Heart J* 2011;32:2231–2235.

199. A 76-year-old man presents with concerns about losing kidney function with newly identified hypertension to levels of 165/100 mmHg. After lisinopril, 10 mg/d, is given, BP levels decrease to 130/74 mmHg. Renal artery duplex ultrasound demonstrates peak systolic velocities in the right renal artery of 280 cm/s. CT angiography demonstrates a reduction in renal size in the right kidney, as depicted in the figure, compared with the contralateral kidney.

On examination, the patient’s BP is 126/76 mmHg; he has a pulsatile aorta and diminished pulses in the lower extremities. Urinalysis yields normal findings, and laboratory values are as follows:

Creatinine	1.2 mg/dL
eGFR	58 mL/min/1.73 m ²
Sodium	141 mEq/L
Potassium	4.8 mEq/L
Plasma renin activity	12 ng/mL/h (normal 0.8–2.0, with normal sodium intake)



Figure: CT angiogram and T2 map: Unilateral Renovascular Disease

Based on these data, which is the MOST correct interpretation of his renal hemodynamics and function?

- A. Renal blood flow and GFR are reduced without affecting oxygenation.
- B. Ischemic nephropathy is developing in the right kidney.
- C. Reduced kidney size reflects decreased fractional sodium reabsorption.
- D. Activation of renin beyond the renal artery stenosis reflects diminished oxygen delivery.

Answer: A

Explanation:

This case represents moderate renal artery stenosis with renin release and loss of blood flow to one kidney beyond a moderate occlusion. Studies of tissue oxygenation in both animals and humans indicate well-preserved tissue oxygenation despite considerable decreases in blood flow, and no ischemia is present in this patient. Biopsy data and serial follow-up of kidney function indicate that most such individuals do not lose function despite these changes during follow-up for more than 5 years. Poststenotic

kidneys become sodium “avid” as a result of enhanced sodium reabsorption (the basis of functional tests for renovascular hypertension in years past). Elevated renin levels represent a loss of perfusion pressure to the juxtaglomerular apparatus, not a decrease in oxygen levels in this instance

References:

Juillard L, Lerman LO, Kruger DG, Haas JA, Rucker BC, Polzin JA, Riederer SJ, Romero JC. Blood oxygen level-dependent measurement of acute intra-renal ischemia. *Kidney Int* 2004;65:944–950.

Warner L, Gomez SI, Bolterman R, Haas JA, Bentley MD, Lerman LO, Romero JC. Regional decrease in renal oxygenation during graded acute renal arterial stenosis: A case for renal ischemia. *Am J Physiol Regul Integr Comp Physiol* 2009;296:R67–R71.

Gloviczki ML, Glockner JF, Lerman LO, McKusick MA, Misra S, Grande JP, Textor SC. Preserved oxygenation despite reduced blood flow in poststenotic kidneys in human atherosclerotic renal artery stenosis. *Hypertension* 2010;55:961–966.

ASTRAL Investigators; Wheatley K, Ives N, Gray R, Kalra PA, Moss JG, Baigent C, Carr S, Chalmers N, Eadington D, Hamilton G, Lipkin G, Nicholson A, Scoble J. Revascularization versus medical therapy for renal-artery stenosis. *N Engl J Med* 2009;361:1953–1962.

200. A 36-year-old woman developed an increase in BP to 152/96 mmHg during the second trimester of her third pregnancy. Her serum creatinine level was 0.8 mg/dL, and proteinuria was negative. Antihypertensive therapy included labetalol with stable BP levels through delivery. Six months after delivery, BP remained elevated with normal urinalysis and protein test results. Renal artery duplex scanning indicated elevated systolic velocities to 230 cm/s in the mid-portion of the right renal artery.

Which measure is MOST appropriate for this individual?

- A. Transition to ACE inhibitor therapy
- B. Renal angiography and percutaneous transluminal renal angioplasty (PTRA)
- C. Magnetic resonance angiography
- D. Transition to amlodipine therapy

Answer: B

Explanation:

This is a prototypical case of fibromuscular dysplasia (FMD) causing hypertension in a relatively young woman, leading to persistent hypertension that was first evident during pregnancy. Although medical therapy may be considered, they are less desirable, particularly during a period when breastfeeding is often in progress. Particularly when hypertension from FMD develops at this age, it responds well to PTRA and may spare or lower the requirement for lifelong BP medication. Magnetic resonance angiography is less likely to demonstrate FMD than other modalities and is unnecessary here.

References:

Olin JW, Sealove BA. Diagnosis, management, and future developments of fibromuscular dysplasia. *J Vasc Surg* 2001;53:826–836.

201. **Which statement is TRUE regarding kidney disease among nondiabetic African American people with hypertension and low-level (<1 g/d) proteinuria?**
- A. The most common lesion on kidney biopsy is FSGS, collapsing variant.
 - B. Aggressive treatment of hypertension to <120/80 mmHg using ACE inhibitors reliably halts nephropathy progression.
 - C. Progression of kidney disease strongly relates to the presence of two risk variants in the apolipoprotein L1 gene (*APOL1*) with autosomal recessive inheritance.
 - D. Arteriolar changes including narrowing and hyalinosis are infrequently present.

Answer: C

Explanation:

Kidney biopsies among hypertensive, nondiabetic African American patients with low-level proteinuria, typical of those enrolled in the NIH-sponsored African American Study of Kidney Disease and Hypertension (AASK), reveal focal global glomerulosclerosis with interstitial fibrosis and small vessel arteriolar changes (vascular lesions do not correlate with systemic BP). Subnephrotic forms of FSGS may also be observed, but collapsing lesions are uncommon. AASK results revealed that nearly 60% of participants treated with ACE inhibitors to the low BP target reached the composite end point of ESKD, doubling of serum creatinine concentration, or death after 10-year follow-up. In contrast to BP target or class of antihypertensive medication, presence of two *APOL1* renal-risk variants was the only predictor of progressive kidney failure. This demonstrates that this kidney disease is not likely caused by high BP but resides in the spectrum of *APOL1*-associated nephropathy, as for idiopathic FSGS and HIV-associated collapsing glomerulopathy in individuals of African ancestry.

References:

Lipkowitz MS, Freedman BI, Langefeld CD, Comeau ME, Bowden DW, Kao WH, Astor BC, Bottinger EP, Iyengar SK, Klotman PE, Freedman RG, Zhang W, Parekh RS, Choi MJ, Nelson GW, Winkler CA, Kopp JB; AASK investigators. Apolipoprotein L1 gene variants associate with hypertension-attributed nephropathy and rate of kidney function decline in African Americans. *Kidney* 013;83:114–120.

202. A 36-year-old man with hypertension develops severe rhabdomyolysis after a type B aortic dissection. You are asked to see him on hospital day 4 for management of AKI. His admission weight was 72 kg, and he is now 84 kg. His BP is currently 102/60 mm Hg with a central venous pressure of 17 cm. He is mechanically ventilated with FIO₂ of 50%. He is on dopamine 2.5 µg/kg/min and no other vasopressors. His urine output was 400 mL over the last 24 hours. The intensivist caring for the patient requests that he be started on CRRT for volume management. His labs are:
- BUN 66 mg/dL
 - Creatinine 4.4 mg/dL (baseline creatinine 0.9 mg/dL with normal urinalysis)
 - Potassium 5.5 mEq/L
 - Bicarbonate 19 mEq/L
 - Phosphorous 8.5 mg/dL
 - Creatine kinase (CK) 80,000 U/L

Which is correct?

- A. Continuous veno-venous hemofiltration is preferable to continuous veno-venous hemodialysis in this patient to shorten the course of myoglobinuric AKI
- B. The patient's degree of fluid overload is associated with an increased risk of death
- C. Initiating RRT when the BUN is less than 60 mg/dL is associated with decreased mortality
- D. Sustained low efficiency dialysis is preferable to CRRT for phosphate removal in this patient
- E. The patient's degree of renal failure indicates that he is less likely to recover renal function and will be dialysis dependent

Answer: B

Explanation:

In observational studies in pediatric and adult patients, fluid overload at the time of dialysis initiation has been associated with increased risk of death. Option A is incorrect. CRRT with conventional high flux membranes may remove some myoglobin, but the sieving coefficients remain low. Isolated case reports demonstrate higher myoglobin clearances with super high flux (SHF) membranes. However, no RRT modality has shown that removal of myoglobin can shorten or prevent the course of AKI from rhabdomyolysis. Option C is incorrect. There is insufficient evidence to support any management approaches for the timing of RRT as associated with a decreased mortality risk. There are insufficient data to support option D. CRRT is effective in removing phosphate, and more than 80% of patients on CRRT develop hypophosphatemia and require phosphate supplementation. Option E is incorrect. Given the patient's normal baseline renal function, young age, and lack of significant comorbidities, he should recover renal function and be dialysis independent.

References:

Bouchard J, Soroko SB, Chertow GM, Himmelfarb J, Ikizler TA, Paganini EP, Mehta RL; Program to Improve Care in Acute Renal Disease (PICARD) Study Group. Fluid accumulation, survival and recovery of kidney function in critically ill patients with acute kidney injury. *Kidney Int* 2009;76:422–427.

Goldstein SL, Somers MJ, Baum MA, Symons JM, Brophy PD, Blowey D, Bunchman TE, Baker C, Mottes T, McAfee N, Barnett J, Morrison G, Rogers K, Fortenberry JD. Pediatric patients with multi-organ dysfunction syndrome receiving continuous renal replacement therapy. *Kidney Int* 2005;67:653–658.

203. A 47-year-old man with alcoholic pancreatitis develops gram-negative sepsis. He is mechanically ventilated and requires 60% FIO₂. BP is 95/60 mm Hg on a norepinephrine infusion. He is febrile, and his heart rate is 130 beats/min. Examination of the chest reveals coarse breath sounds and inspiratory crackles throughout both lungs. He has generalized anasarca. He has made 200 mL of urine over the last 24 hours. His current weight is 90 kg. His admission weight was 78 kg. His medications include piperacillin/tazobactam, gentamicin, and solumedrol.

Laboratory values

Blood urea nitrogen: 103 mg/dL
 Creatinine: 4.3 mg/dL
 Sodium: 137 mEq/L
 Potassium: 5.8 mEq/L
 Chloride: 97 mEq/L
 Bicarbonate: 16 mEq/L
 Serum pH: 7.3

Which is the MOST appropriate next step in this patient's management?

- A. Start an infusion of furosemide at 20 mg/hr
- B. Initiate slow continuous ultrafiltration (SCUF) with a fluid removal of 200 mL/hr
- C. Initiate intermittent hemodialysis (HD) three times a week targeting a daily Kt/V of 0.9
- D. Initiate continuous veno-venous hemodiafiltration (CVVHDF) with an effluent rate of 2000 mL/hr
- E. Initiate continuous veno-venous hemofiltration (CVVH) with an effluent rate of 1500 mL/hr

Answer: D

Explanation:

Although several prior single-center studies have suggested improved outcomes associated with more intensive renal replacement therapy in critically ill patients with AKI, neither the multicenter VA/NIH Acute Renal Failure Trial Network (ATN) Study nor the multicenter ANZICS (Australian and New Zealand Intensive Care Society) Randomized Evaluation of Normal versus Augmented Level (RENAL) Study demonstrated improved outcomes with more intensive therapy. In the ATN Study, there was no difference in mortality when a strategy utilizing 6 days/wk intermittent hemodialysis (IHD) with a target Kt/Vurea of 1.2–1.4/treatment in hemodynamically stable patients and CVVHDF at 35 mL/kg/hr in hemodynamically unstable patients was compared to 3 days/wk IHD with a target Kt/Vurea of 1.2–1.4/treatment in hemodynamically stable patients and CVVHDF at 20 mL/kg/hr in hemodynamically unstable patients. In the RENAL Study, CVVHDF at 40 mL/kg/hr and CVVHDF at 25 mL/kg/hr were also associated with similar mortality rates. Option D provides CVVHDF at a total effluent flow rate of between 20 and 25 mL/kg/hr (correct answer).

Option A is incorrect because a furosemide infusion will not treat the metabolic or acid–base abnormalities of the patient. Similarly, option B is incorrect because SCUF will not provide solute clearance and acid–base control. In option C, IHD is provided on a three times per week schedule using a prescription that delivers an inadequate Kt/Vurea (<1/treatment) and has been associated with increased mortality. Furthermore, the patient is hemodynamically unstable with volume overload, making CRRT the appropriate choice. Option E is incorrect by providing an inadequate dose of CRRT (effluent rate <20 mL/kg/hr).

References:

Palevsky PM, Zhang JH, O'Connor TZ, Chertow GM, Crowley ST, Choudhury D, Finkel K, Kellum JA, Paganini E, Schein RM, Smith MW, Swanson KM, Thompson BT, Vijayan A, Watnick S, Star RA, Peduzzi P; VA/NIH Acute Renal Failure Trial Network. Intensity of renal support in critically ill patients with acute kidney injury. *N Engl J Med* 2008;359:7–20.
RENAL Replacement Therapy Study Investigators. Intensity of continuous renal replacement therapy in critically ill patients. *N Engl J Med* 2009;361:1627–1638.

204. Which regarding renal replacement therapy (RRT) in AKI is TRUE?

- A. Randomized controlled trials demonstrate that early initiation of RRT is associated with improved patient outcomes
- B. The ATN trial (VA/NIH Acute Renal Failure Trial Network) was a “modality” study, which demonstrated that there is no difference in survival between CRRT and intermittent hemodialysis (IHD)
- C. The ATN and the RENAL trials have shown that “high” or “low,” the dose of dialysis is unimportant and is not a determinant of patient survival
- D. CRRT, rather than intermittent RRT, is better for AKI patients with increased intracranial pressure or hemodynamic instability
- E. Randomized controlled trials have demonstrated higher rates of renal recovery among patients treated with CRRT compared with IHD

Answer: D

Explanation:

In a patient with acute brain injury, IHD may worsen neurological status by compromising cerebral perfusion pressure. Both hypotension and disequilibrium can be avoided by the slow progressive removal of fluids and solutes that occurs during CRRT.

Option A is the incorrect answer because no randomized controlled trials have shown earlier initiation of RRT improves survival, only observational studies. Option B is incorrect because the ATN trial was a dose study comparing standard intensity to high intensity RRT; it did not compare one RRT modality to another. Option C is incorrect because both the RENAL and the ATN trial study showed no benefits of increasing CRRT doses in AKI patients above effluent flows of 20–25 mL/kg/hr. Option E is incorrect because insufficient evidence exists regarding the superiority of CRRT over IHD in regard to renal functional recovery. The studies are mainly observational and conflicting.

References:

Davenport A. Continuous renal replacement therapies in patients with acute neurological injury. *Semin Dial* 2009;22:165–168.
Bagshaw SM, Peets AD, Hameed M, et al. Dialysis disequilibrium syndrome: Brain death following hemodialysis for metabolic acidosis and acute renal failure—a case report. *BMC Nephrol* 2004;5:9.
Lin CM, Lin JW, Tsai JT, et al. Intracranial pressure fluctuation during hemodialysis in renal failure patients with intracranial hemorrhage. *Acta Neurochir Suppl* 2008;101:141–144.

205. A 45-year-old man with hepatitis C cirrhosis and hepatorenal syndrome is placed on CRRT with no anticoagulation as a bridge to liver transplantation. He remains on CRRT for 7 days, and his acid–base status is within normal limits prior to transplantation. He develops severe metabolic alkalosis immediately after liver transplantation. He is continued on CRRT intra- and postoperatively for persistent renal failure. The CRRT prescription has not changed from the preoperative period.

Which is MOST likely to be responsible for the acid–base disturbance?

- A. Transfusion of blood products
- B. Increased ureagenesis by the transplanted liver
- C. Increased urinary ammonium excretion
- D. High bicarbonate CRRT solutions
- E. Potassium depletion

Answer: A

Explanation:

Metabolic alkalosis is the most common acid–base disturbance in the immediate postoperative period and is most prominent during the first 24–48 hours after surgery. Precipitating factors include the large citrate load from stored blood and fresh frozen plasma (FFP) that is metabolized to bicarbonate. Therefore, the correct answer is A. Neither option B nor C makes sense in the setting of liver transplant. There is no suggestion of the use of high bicarbonate solutions for CRRT because the patient had normal acid–base parameters prior to transplantation with no change in CRRT prescription after transplantation. Further, the rapid development of severe metabolic alkalosis due to CRRT is unlikely. Therefore, D is an incorrect option. There is no reason to expect hypokalemia from the history, making E an incorrect option.

References:

Driscoll DF, Bistran BR, Jenkins RL, Randall S, Dzik WH, Gerson B, Blackburn GL. Development of metabolic alkalosis after massive transfusion during orthotopic liver transplantation. *Crit Care Med* 1987;15(10):905–908.

206. A mechanically ventilated patient with fulminant hepatic failure and AKI is started on continuous veno-venous hemofiltration (CVVH) for severe metabolic acidosis. Her pH is 7.3, bicarbonate is 10 mmol/L, and lactate is 6.5 mmol/L.

Which buffer is the BEST choice for the CVVH replacement fluid?

- A. Acetate
- B. Lactate
- C. Bicarbonate
- D. Citrate
- E. Insufficient evidence to support a particular buffer

Answer: C

Explanation:

The use of bicarbonate as a buffer in the dialysate or replacement fluid of AKI patients results in better correction of acidosis, lower lactate levels, and improved hemodynamic tolerance in patients with circulatory problems and in those with liver dysfunction. Insufficient lactate conversion due to impaired lactate clearance as in liver failure or increased endogenous lactate production as in circulatory shock will result in worsening acidosis, especially because bicarbonate losses are ongoing in the extracorporeal circuit. Two small, randomized crossover comparisons of bicarbonate- and lactate-buffered solutions in AKI patients treated with CRRT found elevated serum lactate levels with lactate, an effect that was more pronounced in patients with liver dysfunction. An observational trial in 27 patients found a compromised lactate conversion in patients with liver disease, those on inotropic support, and in patients with initial blood lactate measurements of >10 mmol/L and large base deficits.

The use of acetate has been largely abandoned in view of the associated hemodynamic instability. A major contraindication for the use of citrate anticoagulation is severely impaired liver function or shock with muscle hypoperfusion, both representing a risk of citrate accumulation. Markedly reduced citrate clearances and lower ionized calcium levels have been found in patients with acute liver failure or with severe liver cirrhosis.

References:

Barenbrock M, Hausberg M, Matzkies F, et al. Effects of bicarbonate- and lactate-buffered replacement fluids on cardiovascular outcome in CVVH patients. *Kidney Int* 2000;58:1751–1757.

Tan HK, Uchino S, Bellomo R. The acid-base effects of continuous hemofiltration with lactate or bicarbonate buffered replacement fluids. *Int J Artif Organs* 2003;26:477–483.

Zimmerman D, Cotman P, Ting R, et al. Continuous veno-venous haemodialysis with a novel bicarbonate dialysis solution: Prospective cross-over comparison with a lactate buffered solution. *Nephrol Dial Transplant* 1999;14:2387–2391.

Apsner R, Schwarzenhofer M, Derfler K, et al. Impairment of citrate metabolism in acute hepatic failure. *Wien Klin Wochenschr* 1997;109:123–127.
 Kramer L, Bauer E, Joukhadar C, et al. Citrate pharmacokinetics and metabolism in cirrhotic and noncirrhotic critically ill patients. *Crit Care Med* 2003;31:2450–2455.

207. You are prescribing antibiotics for a patient on CRRT. The patient has AKI due to sepsis and shock. He is anuric. You prescribe CRRT at 25 mL/kg/hr.

What is the BEST way to dose antibiotics in this patient?

- A. Measure the effluent ultrafiltration and dialysate and calculate a clearance of creatinine
- B. Know the protein binding of the antibiotic you are prescribing and calculate the unbound fraction that will be cleared
- C. Dose as in any patient with no renal function
- D. Reduce the loading dose of antibiotic because of the renal failure

Answer: A

Explanation:

The best way to prescribe an antibiotic for CRRT is to measure the amount of effluent ultrafiltration and the spent dialysate calculating a creatinine clearance in the fluid. This will give you an idea of the total renal clearance and drug dosing can be based on that information. One of the most common errors in antibiotic dosing in this situation is to underdose; thus, reducing the loading dose of antibiotic is incorrect, but one does need to adjust for renal disease so you cannot dose normally. The protein binding properties of the drug are important, but this alone will not help you dose properly; you still must know the estimated rate of removal (creatinine clearance). Certainly, to avoid drug accumulation and possible toxicity, for many antibiotics, you cannot dose assuming that the patient has normal renal function. Thus, A is the correct answer.

208. A 75-year-old obese (BMI 35 kg/m²) Caucasian man with stage 3 CKD (baseline eGFR of 49 mL/min/1.73 m² and creatinine of 1.4 mg/dL) underwent mitral valve replacement and two-vessel coronary artery bypass grafting. On postoperative day 1, he had a BP of 90/50 mm Hg and heart rate of 101 beats/min. Diagnostic workup showed cardiac tamponade. Urgent contrast study was performed using 150 mL of “low osmolar” contrast (Omnipaque 350). On postoperative day 2, his serum creatinine was found to be 2.9 mg/dL, and his urine output dropped significantly. He was initiated on renal replacement therapy the next day because of continuous decline in renal function and oliguria.

In assessing risk for AKI, which is MOST accurate?

- A. Baseline creatinine of 1.4 mg/dL is essentially normal and does not pose a risk for AKI
- B. The use of iso-osmolar iodinated contrast agent provides substantial protection from AKI compared with low osmolar contrast agents
- C. Obesity independently predicts AKI after cardiac surgery
- D. Reducing the dose of osmolar contrast does not reduce the risk of AKI

Answer: C

Explanation:

(A) This patient had CKD stage 3 with an eGFR of 49 mL/min/1.73 m². CKD is the most important predictor of AKI. (B) The use of iso-osmolar contrast agent is probably not warranted because current data do not substantiate improved efficacy in the prevention of AKI over low osmolar iodinated contrast agents. (C) Obesity is an independent risk factor for AKI. (D) Reducing the dose of contrast agents reduces the risk of AKI.

References:

Billings FT, Pretorius M, Schildcrout JS, Mercaldo ND, Byrne JG, Ikizler TA, Brown NJ. Obesity and oxidative stress predict AKI after cardiac surgery. *J Am Soc Nephrol* 2012;23:1221–1228.
 Weisbord SD, Gallagher M, Kaufman J, Cass A, Parikh Cr, Chertow GM, Shunk KA, McCullough PA, Fine MJ, Mor MK, Lew RA, Hunage GD, Conner TA, Brophy MT, Lee J, Soliva S, Palevsky PM. Prevention of contrast-induced AKI: A review of published trials and the design of the Prevention of Serious Adverse Events Following Angiography (PRESERVE) trial. *Clin J Am Soc Nephrol* 2013;8(9):1618–1631.
 Hsu CY, Ordonez JD, Chertow GM, Fan D, McCulloch CE, Go AS. The risk of acute renal failure in patients with chronic kidney disease. *Kidney Int* 2008;74:101–107.

209. A 56-year-old man with a history of hepatitis C virus (HCV) infection previously treated with pegylated interferon and ribavirin is admitted with increasing confusion and abdominal swelling. Outpatient medications include propranolol, lactulose, and spironolactone. On physical examination, he is grossly jaundiced, his BP is 100/50 mm Hg, his neck veins are visible at the level of the clavicle when lying flat, his abdomen is protuberant with shifting dullness, and he has no peripheral edema. His serum creatinine, which had been 0.8 mg/dL 3 months earlier, is 2.6 mg/dL, with a serum sodium of 128 mmol/L. His urine sodium is 14 mmol/L. Urine microscopy reveals many bile-stained finely granular casts.

Which therapy should be instituted?

- A. Infusion of 500 mL of 5% albumin
- B. Bolus infusion of 500 mL of isotonic saline followed by a continuous infusion at 150 mL/hr
- C. Oral midodrine, subcutaneous octreotide and 0.5 g/kg intravenous 25% albumin
- D. Refer for placement of a transjugular intrahepatic portosystemic shunt (TIPS)

Answer: B

Explanation:

This patient presented with AKI in the setting of decompensated liver disease. Although this may represent the development of hepatorenal syndrome, intravascular volume depletion must be ruled out by evaluating the clinical response to intravenous fluids. Although either crystalloid or colloids can be used for volume resuscitation, only choice B provides sufficient volume administration to correct intravascular volume depletion (choice A is incorrect). Although guidelines for the treatment of hepatorenal syndrome recommend albumin infusion, these recommendations are not evidence-based and an infusion of 0.5 g/kg of 25% albumin would not be sufficient to correct volume depletion. In addition, although vasoconstrictor therapy with either the vasopressin analogue terlipressin or with the combination of midodrine and octreotide, in combination with albumin infusion, has been shown to be effective at reversing hepatorenal syndrome in some patients, this should not be instituted until after an adequate trial of volume resuscitation with crystalloid or colloid (choice C is incorrect). TIPS would not be used as primary therapy of hepatorenal syndrome (choice D is incorrect).

210. A 58-year-old woman is hospitalized with necrotizing pancreatitis. Her course has been complicated by acute respiratory distress syndrome (ARDS) requiring ventilatory support and hemodynamic instability, requiring a continuous infusion of intravenous norepinephrine to maintain a mean arterial BP of 65–70 mm Hg. She is receiving empiric treatment with meropenem. On the third hospital day, her norepinephrine infusion needs to be increase from 0.04 to 0.13 $\mu\text{g}/\text{kg}/\text{min}$ to maintain a mean arterial pressure of 60 mm Hg, she has increased oxygen requirements to maintain a transcapillary oxygen saturation $>92\%$ and is noted to have increased airway pressures on the ventilator, and she has become oliguric. On physical examination, her central venous pressure is 12 mm Hg, her abdomen is modestly distended but tense, and she has bilateral lower extremity and flank edema. Her urine sodium is <10 mmol/L. A Hansel's stain of the urine is positive for eosinophils. Her serum creatinine has increased from 0.9 mg/dL on admission to 2.1 mg/dL.

Which is MOST appropriate for evaluation and management of her AKI?

- A. Bolus administration of 500–1000 mL of isotonic saline
- B. Insertion of a pulmonary artery catheter
- C. Discontinuation of moxifloxacin, begin intravenous steroids
- D. Transduction of bladder pressure

Answer: D

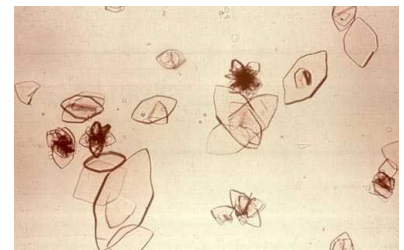
Explanation:

This patient is developing abdominal compartment syndrome manifested by increased hemodynamic instability, worsening respiratory failure with increased airway pressures and increasing difficulty with oxygenation, a tense abdomen on exam, and oliguric kidney failure. Diagnosis of intra-abdominal hypertension and abdominal compartment syndrome is accomplished by transduction of bladder pressure (choice D is correct). Treatment is abdominal decompression. Although her urine sodium is <10 mm Hg, clinically she is not intravascularly volume depleted, and further volume resuscitation is not indicated (choice A is incorrect). There is no evidence that hemodynamic monitoring with a pulmonary artery catheter improves clinical outcomes compared with use of central venous pressure measurement in patients with ARDS and may be associated with harm (choice B is incorrect). Although the presence of eosinophiluria may suggest interstitial nephritis, the positive predictive value for this diagnosis is low. Although discontinuation of moxifloxacin might be considered, treatment with intravenous steroids is not indicated in this setting (choice C is incorrect).

211. You are asked to see a 57-year-old man for AKI. Representative findings from urine microscopy are shown in the figure.

With which etiology of AKI are these urine microscopy findings MOST consistent?

- A. Acyclovir toxicity
- B. Methotrexate toxicity
- C. Tumor lysis syndrome
- D. Ethylene glycol ingestion



Answer: C

Explanation:

Acyclovir, methotrexate, and ethylene glycol toxicity and tumor lysis syndrome can all present with crystalluria. The crystals present on microscopy are uric acid crystals, which would be most consistent with AKI due to tumor lysis syndrome (choice C is correct). Acyclovir crystals are needle shaped (choice A is incorrect), and methotrexate forms amorphous, brown-colored precipitates in the urine (choice B is incorrect). The crystals associated with ethylene glycol toxicity are dumbbell and needle-shaped calcium oxalate monohydrate crystals and envelope-shaped calcium oxalate dihydrate crystals (choice D is incorrect).

212. A 37-year-old woman with no significant medical history is admitted to the hospital with complaints of dysuria, fevers, and flank pain. She had noticed dysuria and hematuria approximately 1 week prior to hospitalization and was seen in an urgent care center. A diagnosis of urinary tract infection was made, and she was treated with oral levofloxacin. Her symptoms initially improved, but over the last 48 hours, she has noticed worsening dysuria, chills, and left-sided flank pain. On evaluation in the Emergency Department, her BP was 118/82 mm Hg, with a heart rate of 102 beats/min, her temperature was 38.7°C, and the remainder of her physical exam was remarkable only for mild tenderness to palpation over her left flank. Her serum creatinine was 2.7 mg/dL, and her white blood cell count was 14,200/mm³ with 78% neutrophils, 14% lymphocytes, and 7% monocytes. Her urine had a pH of 7.0 and was 2+ positive for blood, 1+ positive for protein, and 3+ positive for leukocyte esterase. On urine microscopy, there were 5–10 red blood cells and 20–40 white blood cells per high power field. There were many fine granular casts seen and few white blood cell casts. A Hansel stain of the urine was positive for eosinophils.

Based on the presence of urinary eosinophils, approximately what is the probability that her AKI is due to acute interstitial nephritis?

- A. 30%
- B. 50%
- C. 70%
- D. 90%

Answer: A

Explanation:

Urinary eosinophils are a poor diagnostic tool for the diagnosis of acute interstitial nephritis. In a recent study of biopsy proven acute interstitial nephritis, the presence of >5% urine eosinophils had a positive predictive value for the presence of interstitial nephritis of approximately 30% and a negative predictive value of approximately 80–90%. Urine eosinophils may be seen in multiple other conditions including acute tubular necrosis, atheroembolic disease, glomerulonephritis, and pyelonephritis and lower urinary tract infections. Thus, urinary eosinophils are not a useful biomarker for the diagnosis of acute interstitial nephritis.

213. **Which abnormality is associated with nonsteroidal anti-inflammatory drugs (NSAIDs)?**

- A. Hypokalemia
- B. Impaired urinary concentrating mechanism
- C. Activation of the RAAS pathway
- D. Hyponatremia
- E. Enhanced diuretic activity

Answer: D

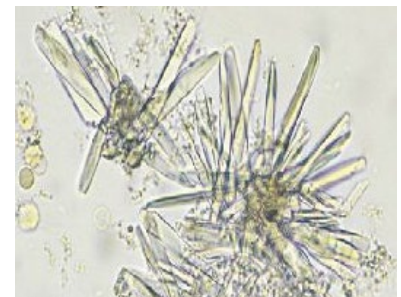
Explanation:

NSAIDs inhibit the RAAS pathway by reducing renin production through inhibition of prostaglandins from the macula densa. Therefore, NSAIDs also lead to a hyporeninemic hypoaldosteronism state and hyperkalemia but not hypokalemia. NSAIDs enhance the urine concentrating ability by reducing prostaglandin E₂ (PGE₂), which normally attenuates the action of ADH. By doing so, NSAIDs counteract the effect of diuretics by reducing renal blood flow, increasing proximal urine sodium reabsorption, and by enhancing urine concentrating ability.

214. A 50-year-old man underwent a colonoscopy 2 weeks ago. He now has noticed swelling of his legs and had a laboratory evaluation done. The following results were obtained:

Creatinine (mg/dL)	BUN (mg/dL)	Urinalysis
2.1	30	Bland Sediment

These crystals were noted in the urine:



Based on these findings, what can you confidently state?

- A. The von Kossa stain (calcium phosphate) in this patient's renal biopsy will be positive
- B. This patient has nephrocalcinosis due to calcium oxalate crystal deposition
- C. In a biopsy, this patient will have intense deposition of uric acid in the tubules
- D. This patient likely will have hypophosphatemia as a result of Fanconi's syndrome from nephrocalcinosis
- E. These are calcium oxalate crystals that have caused AKI as a result of the polyethylene glycol present in the colonoscopy prep

Answer: A

Explanation:

This is a typical example of phosphate nephropathy. There will be intense precipitation of calcium phosphate crystals in the medulla, with much less involvement in the cortex. The serum phosphate levels were likely >7 mg/dL, resulting in phosphaturia. The crystals of calcium oxalate are "envelope"-shaped, whereas the ones pictured here are needle-like, typical of calcium phosphate. Uric acid crystals are various shapes (e.g., rhomboid, barrel) but rarely needle-like. The best stain for calcium phosphate is the von Kossa stain, which will not stain calcium oxalate.

215. Chronic use of lithium may be associated with a variety of renal syndromes.

Which is NOT a part of the spectrum of lithium-induced renal disease?

- A. Nephrogenic diabetes insipidus (DI)
- B. Type II renal tubular acidosis (RTA)
- C. AKI
- D. Minimal change disease
- E. Renal microcysts

Answer: B

Explanation:

Lithium causes a down-regulation of aquaporins and leads to nephrogenic DI. Both AKI and chronic kidney injury are reported with lithium. Nephrotic syndrome due to minimal change disease and FSGS has been associated with lithium. Lithium can also lead to formation of renal microcysts (severely dilated renal tubules). However, lithium causes type I RTA and not type II RTA.

216. A 39-year-old man presents for evaluation of upper abdominal pain. Physical examination revealed fullness in the left upper quadrant and the presence of marked axillary adenopathy. A computed tomography (CT) scan of the abdomen demonstrated an enlarged spleen and multiple enlarged para-aortic lymph nodes. Lymph node biopsy showed a B-cell lineage non-Hodgkin's lymphoma. He is transferred to a tertiary care center where they note an increasing serum creatinine. He had not yet undergone any specific antitumor therapy. Urine output is now 450 mL/24 hr. Laboratory values are as follows: sodium, 133 mEq/L; potassium, 6.0 mEq/L; chloride, 102 mEq/L; bicarbonate, 17 mEq/L; BUN, 58 mg/dL; creatinine, 5.5 mg/dL; calcium, 8.0 mg/dL; phosphorus, 6.9 mg/dL; and uric acid, 12.4 mg/dL. No abnormality was seen on his electrocardiogram.

Prior to initiating chemotherapy, which therapy should be administered?

- A. Hemodialysis
- B. Urine alkalinization
- C. Glucose and insulin infusion
- D. Intravenous calcium
- E. Intravenous fluid challenge

Answer: A

Explanation:

Hemodialysis is the correct answer as the patient has spontaneous clinical tumor lysis syndrome (TLS), large tumor burden, serious electrolyte disturbances, and stage 3 AKI. Hemodialysis +/- CRRT is required. Urinary alkalinization increases solubility of uric acid in the urine but requires good kidney function (adequate GFR) with large urinary volumes to prevent or reduce acute urate nephropathy. Thus, urinary alkalinization will not work and is potentially harmful in this case. Insulin and glucose shifts K^+ into cells and improves hyperkalemia, but otherwise will not help the entire clinical picture.

Intravenous calcium stabilizes neuromuscular tissues in the setting of hyperkalemia but is potentially harmful with high serum PO_4 due to calcium-phosphate precipitation and will not help the entire clinical picture. Intravenous fluids are helpful if the patient is volume depleted, but otherwise will not be helpful and could be harmful if the patient develops hypervolemia.

217. A 51-year-old woman with acute myeloblastic leukemia underwent myeloablative therapy followed by allogenic stem cell transplantation. After 9 days, she complains of right upper quadrant pain and develops jaundice. Urine output decreases over 24 hours to 400 mL.

Physical exam

BP, 120/80 mm Hg; temperature, 99°F. Heart and lung examination are normal. Right upper quadrant is tender and 2+ edema is noted.

Labs

U/A 1+ protein with bland urine sediment. Electrolytes are normal with a BUN of 32 mg/dL and creatinine of 2.8 mg/dL. Liver function tests (LFTs): bilirubin, 4.9 mg/dL; alkaline phosphatase, 670 IU. Right upper quadrant ultrasound demonstrates no biliary stones and reversal of flow in the portal vein.

Which is the MOST likely cause of the clinical presentation in this patient?

- A. Sclerosing cholangitis
- B. Sinusoidal obstruction syndrome
- C. Graft versus host disease
- D. Occult sepsis
- E. Acalculous biliary obstruction

Answer: B

Explanation:

Sinusoidal obstruction syndrome is a known serious complication of stem cell transplantation. Busulfan, cyclophosphamide, and total body irradiation are risk factors for hepatic VOD. It occurs less commonly with less intensity myeloablative transplant. The pathophysiology involves sinusoidal obstruction, portal hypertension, and microvascular intrahepatic portosystemic shunting. The clinical presentation is similar to hepatorenal syndrome with AKI, low BP, and sodium retentive state. The other options do not explain the clinical scenario.

218. A 55-year-old man with renal cell carcinoma underwent left nephrectomy. Additional therapy with bevacizumab is given, and he develops hypertension and proteinuria (1+ protein on dipstick) with urine protein/urine creatinine of 0.92. Salt restriction is implemented, and his medication list is reviewed to ensure no other causes are present.

What is the likely mechanism for proteinuria?

- A. Loss of nephrin from podocytes
- B. Tubular injury
- C. Loss of vascular endothelial growth factor (VEGF)
- D. Podocyte mutation
- E. Intraglomerular hypertension
- F. *In situ* immune complex formation

Answer: C

Explanation:

Reduced VEGF production by podocytes from anti-VEGF drugs is associated with endothelial injury (endotheliosis), with subsequent disruption of the glomerular filtration barrier and the development of proteinuria. Loss of nephrin from podocytes is not the primary mechanism underlying the development of proteinuria with anti-VEGF drugs (although it might contribute). Although ischemic tubular injury may develop from anti-VEGF drugs, the proteinuria that occurs is primarily from glomerular injury (endothelial and epithelial cell damage). Although proteinuria can occur with intraglomerular hypertension, it is not the mechanism underlying proteinuria that occurs with anti-VEGF drugs. A small number of immune complex glomerulonephritis (GN) cases have been described with these drugs.

219. A 45-year-old man with a history of treatment for Hodgkin's disease 3 years ago enters for evaluation of an elevated serum creatinine. He has felt well and has no new complaints. He has been taking naproxen for back and knee pain and describes decreased urine stream and dribbling with voiding. His physical examination is unremarkable. His BP is 140/80 mm Hg. Laboratory studies show a BUN of 31 mg/dL and creatinine of 2.7 mg/dL (previous value 6 months ago was 1.2 mg/dL). Electrolytes, Ca, and PO₄ are all normal. A urinalysis shows 1+ protein, with no casts or formed elements. A renal ultrasound followed by a computed tomography (CT) scan of his abdomen (shown) are undertaken.



Which is the MOST likely cause of the patient's kidney injury?

- A. Obstructive uropathy
- B. Acute interstitial nephritis due to naproxen
- C. Lymphomatous infiltration of the kidneys
- D. Membranous glomerulopathy secondary to neoplasm
- E. Renal vein thrombosis

Answer: C

Explanation:

Lymphomatous infiltration of the kidneys is the correct answer as the patient has known Hodgkin's disease, which has likely relapsed, along with AKI. The CT scan showing massive kidneys is nearly diagnostic of infiltration by lymphoma. Obstructive uropathy is incorrect as there is no hydronephrosis. Acute interstitial nephritis is also not characterized by massive renomegaly (there can be some increase in renal size and echogenicity). Membranous glomerulopathy secondary to neoplasm is not supported with absence of high-grade proteinuria. Renal vein thrombosis is also not a good option as the patient is not nephrotic, and there are no imaging data (ultrasound or CT showing renal vein clot).

220. A 62-year-old man is brought to the Emergency Department 2 hours after ingesting a bottle of sustained release lithium carbonate tablets. He was a bit sluggish but appropriately interactive. BP was 125/72 mm Hg. Examination was unremarkable except for a fine resting and intention tremor. Lithium level was 2.1 mg/dL, whereas serum creatinine was 1.7 mg/dL (baseline 1.5 mg/dL).

In addition to supportive care, which oral treatment will MOST effectively remove lithium from the gastrointestinal (GI) tract in this patient?

- A. Sorbitol
- B. Activated charcoal
- C. Magnesium citrate
- D. Polyethylene glycol (PEG)
- E. Lactulose

Answer: D

Explanation:

This case of lithium overdose asks about the treatment of drug removal from the GI tract in the setting of ingestion of sustained release lithium. In contrast to many intoxications and overdoses, PEG rather than activated charcoal is the appropriate choice for lithium overdose. Because these are sustained release tablets, it is important to remove as much as possible from the GI tract. Sorbitol and lactulose are not as effective as PEG.

221. A 77-year-old man with type 2 diabetes mellitus, gout, hypertension, hyperlipidemia, and stage 3b CKD (eGFR, 40 mL/min/1.73 m²) presents with chest pain and electrocardiographic changes consistent with myocardial ischemia. He undergoes a cardiac catheterization and is pretreated with intravenous fluids to reduce the risk of contrast-associated renal injury. The patient develops transient hypotension during the procedure with BP dropping to 72/48 mm Hg for a few minutes. He receives a total of 100 mL of noniodinated iso-osmolar contrast during the procedure. Over the next days, the patient develops severe hypertension and gastrointestinal (GI) bleeding. His BP is 162/88, his heart rate is 80, and he is afebrile. His mentation is intact, he has jugular vein pressure at 10 cm, his heart is regular without murmur, he has no crackles or wheezing in his lungs, and no lower leg edema is present. He has no abdominal tenderness. His skin is without lesions. The serum creatinine increases to 6.5 mg/dL, and the patient requires hemodialysis for uremia and hyperkalemia. He remains dialysis dependent for 3 weeks before recovering to a new baseline serum creatinine of 4.9 mg/dL.

What is the MOST likely cause of AKI in this patient?

- A. Contrast-induced nephrotoxicity
- B. Cardiorenal syndrome
- C. Acute tubular necrosis
- D. Cholesterol embolization
- E. Acute interstitial nephritis (AIN)

Answer: D

Explanation:

In this case, the combination of AKI with severe hypertension and GI bleeding following an invasive vascular procedure strongly suggests the diagnosis of cholesterol embolization to the kidneys and GI tract. The course is inconsistent with contrast-induced AKI as he developed prolonged severe AKI and ended up with worse CKD after the procedure. Hypotension was transient and unlikely

to have induced severe acute tubular necrosis (ATN). AIN is unlikely in the absence of new drug exposure except contrast. There is nothing to support cardiorenal syndrome in the case stem.

222. A 19-year-old female college student is evaluated for easy bruising, bleeding gums, anorexia, nausea, and weakness. Examination reveals normal vital signs, hypertrophic bleeding gums, diffuse lymphadenopathy, and splenomegaly. Laboratory data are remarkable for normal electrolytes; BUN, 38 mg/dL; serum creatinine, 1.3 mg/dL; WBC count, 280,000; hemoglobin, 7.5 g/dL; platelet count, 95,000; serum calcium, 8.6 mg/dL; serum phosphate, 3.5 mg/dL; and uric acid level, 7.0 mg/dL. Bone marrow biopsy confirms acute myelomonocytic leukemia (AMML) in blast crisis. Intravenous fluids and allopurinol (900 mg initially, followed by 300 mg twice daily) are initiated prior to chemotherapy administration. Seven days later, serum electrolytes reveal the following:

Na, 135 mEq/L; K, 5.3 mEq/L; and HCO₃, 12 mEq/L. BUN is 71 mg/dL, and serum creatinine is 5.3 mg/dL. Other labs: WBC count, 98,000; hemoglobin, 6.9 g/dL; platelet count, 31,000; serum Ca, 8.8 mg/dL; serum phosphate, 6.8 mg/dL; and uric acid, 7.5 mg/dL. Urinalysis: specific gravity, 1.012; pH 7.5; few needle-shaped crystals. Spot urine uric acid:creatinine ratio is 0.8. Renal ultrasound demonstrates 15-cm kidneys bilaterally without hydronephrosis, cysts, or stones.

What is the MOST likely cause of AKI in this patient?

- A. Acute uric acid nephropathy
- B. Leukemic infiltration of renal interstitium
- C. Acute calcium phosphate deposition
- D. Acute interstitial nephritis (AIN)

Answer: B

Explanation:

The clinical scenario, laboratory data, and ultrasound all support leukemic infiltration of the kidney as the cause of AKI in this patient. AMML is a tissue invasive leukemia, and despite chemotherapy, the peripheral count remained elevated. The large kidney on ultrasound also supports the diagnosis of leukemic infiltration. Acute uric acid nephropathy is not likely with the low urine uric acid/Cr ratio and alkaline urine pH, which solubilizes uric acid. The calcium-phosphate product is not high enough to be associated with renal deposition. AIN is unlikely with AKI occurring very rapidly.

223. A 59-year-old man with non-small cell lung cancer, gastric esophageal reflux disease (GERD), and osteoarthritis presents with new onset pedal edema, hypertension, and proteinuria. Medications include pantoprazole, calcium carbonate, indomethacin, cephalexin, and weekly bevacizumab [anti-vascular endothelial growth factor (VEGF) monoclonal antibody]. BP is 180/105 mm Hg. Exam: 2+ pedal edema and no skin rash. Laboratory data: serum creatinine increased from 1.0 to 1.3 mg/dL, urinalysis with 2+ protein (no other abnormalities), and spot urine protein:creatinine ratio of 1.9.

What is the MOST likely cause of the clinical presentation in this patient?

- A. Indomethacin
- B. Pantoprazole
- C. Bevacizumab
- D. Cephalexin

Answer: C

Explanation:

The patient developed hypertension, mild AKI, and proteinuria from bevacizumab. This drug is a monoclonal antibody against VEGF. VEGF is required for both systemic and glomerular endothelial function. By binding VEGF, bevacizumab causes hypertension *via* endothelial dysfunction (decreased nitric oxide and increased endothelin) and AKI with proteinuria by disturbing the glomerular endothelium (inducing and endotheliosis). Ibuprofen may cause AKI through multiple effects [acute interstitial nephritis (AIN), acute tubular necrosis (ATN), etc.] but causes proteinuria from either minimal change or membranous lesion. Pantoprazole causes AKI from drug-induced AIN as does cephalexin. Neither causes severe hypertension.

224. **Which drug causes nephrotoxicity by entering the proximal tubule *via* binding to megalin/cubilin in the apical membrane?**

- A. Tenofovir
- B. Gentamicin
- C. Ifosfamide
- D. Trimethoprim
- E. Cimetidine

Answer: B

Explanation:

Drugs cause toxicity through various mechanisms. Entry into tubular cells is one such mechanism for nephrotoxicity. Gentamicin enters proximal tubular cells *via* the apical membrane megalin/cubilin receptor pathway. Tenofovir enters cells *via* the basolateral organic anion transporter pathway. Ifosfamide, trimethoprim, and cimetidine enter proximal tubular cells *via* the basolateral organic cation transporter pathway.

225. **Through which mechanism does Tenofovir cause proximal tubular injury such as AKI and Fanconi syndrome?**

- A. Mitochondrial dysfunction
- B. Na⁺K⁺ ATPase inhibition
- C. Membrane phospholipid injury
- D. Lysosomal dysfunction
- E. Golgi apparatus dysfunction

Answer: A

Explanation:

Tenofovir is well described to cause AKI and proximal tubular injury *via* mitochondrial toxicity. This has been shown in both animals and humans. Mitochondria are distorted and swollen and often present in a lower number with tenofovir toxicity.

226. **Which drug can cause the combination of AKI, Fanconi syndrome, and nephrogenic diabetes insipidus?**

- A. Tenofovir
- B. Gentamicin
- C. Cisplatin
- D. Amphotericin B
- E. Mitomycin C

Answer: A

Explanation:

Tenofovir is well described to cause proximal tubular injury with associated AKI and Fanconi syndrome, as well as a nephrogenic diabetes insipidus. Gentamicin is associated with AKI, Fanconi syndrome, and a Bartter-like syndrome. Cisplatin causes AKI, Fanconi syndrome, salt wasting, and magnesium wasting. Amphotericin B causes AKI and a distal renal tubular acidosis (RTA). Mitomycin C causes a thrombotic microangiopathy.

References:

Isnard-Bagnis C, Aloy B, Deray G, Tourret J: Tenofovir nephrotoxicity [French]. *Nephrol Ther* 2016; 12(3):179–189
Irizarry-Alvarado JM, Dwyer JP, Brumble LM, Alvarez S, Mendez JC: Proximal tubular dysfunction associated with tenofovir and didanosine causing Fanconi syndrome and diabetes insipidus: A report of 3 cases. *AIDS Read* 2009; 19(3):114–121.

227. A 39-year-old man with HIV disease recently complicated by pneumocystis pneumonia and esophageal candidiasis is admitted with left flank pain and hematuria. A computed tomography (CT) scan of the kidneys shows unilateral hydronephrosis on the left with an obstructing stone. The urologist performs a retrograde stone removal and sends the stone for analysis. The patient's medications at this time include fluconazole, acyclovir, atazanavir, ritonavir, abacavir, trimethoprim-sulfamethoxazole, tramadol, acetaminophen, and oxycodone.

Stone analysis in this patient would reveal constituents from which medication?

- A. Atazanavir
- B. Acyclovir
- C. Trimethoprim-sulfamethoxazole
- D. Abacavir
- E. Ritonavir

Answer: A

Explanation:

The medication most likely to cause a stone in this patient and also described in the literature is atazanavir. Nephrolithiasis occurs based on the poor solubility of this drug in human urine. It is most soluble in acid urine (pH <4.5) and requires large urine volumes to enhance solubility and prevent precipitation. Sulfamethoxazole is associated with urinary crystals but is rarely associated with kidney stone formation. Acyclovir also is associated with urinary crystals but has not been associated with nephrolithiasis. Abacavir and ritonavir are extremely rare causes of urinary crystals.

228. In those who ingest ecstasy, which is the MOST common cause of AKI?

- A. Volume depletion
- B. Direct tubular toxicity
- C. Acute interstitial nephritis (AIN)
- D. Rhabdomyolysis
- E. Hemolysis

Answer: D

Explanation:

Ecstasy causes renal syndromes such as hyponatremia and AKI. AKI is most commonly reported from ecstasy when it has caused rhabdomyolysis. Volume depletion alone is possible, but usually those who ingest ecstasy maintain hydration which is one of the hyponatremia. Polymorphism of CYP2D6 is the reason why some people are more likely to have complications with taking this substance. Hemolysis, direct tubular toxicity, and AIN have not been described with this drug.

References:

Davies O, Batajoo-Shrestha B, Sosa-Popoteur J, Olibrice M: Full recovery after severe serotonin syndrome, severe rhabdomyolysis, multi-organ failure and disseminated intravascular coagulopathy from MDMA. *Heart Lung* 2014; 43(2):117–119

229. An 83-year-old woman with coronary artery disease (CAD), gastric esophageal reflux disease (GERD), and hypertension is admitted to the hospital with fever and confusion. Urinalysis has significant pyuria, and culture rapidly grows *Klebsiella* species. She is begun on intravenous ciprofloxacin (400 mg twice daily) for *Klebsiella* urosepsis. Medications include aspirin, esomeprazole, furosemide, and a multivitamin. BP is 130/65 mm Hg, pulse is 100 beats/min, and temperature is 101.4°F. She has no abnormalities on physical examination. Admission labs: WBC, 23,000; hemoglobin, 11.1 g/dL; serum Na, 128 mEq/L; serum K, 3.6 mEq/L; serum HCO₃, 33 mEq/L; and serum creatinine, 1.5 mg/dL. Urinalysis: specific gravity, 1.023; pH 7.1; 5–10 RBCs/HPF; and 40–50 WBCs/HPF. At 48 hours, urine output abruptly declines, and serum creatinine increases to 2.7 mg/dL. Kidney function worsens despite 2.0 L of lactated Ringers solution. Urine microscopy reveals 25–30 RBCs/HPF; 40–50 WBCs/HPF, and occasional needle-like crystals. On day 5 of hospitalization (serum creatinine is 5.5 mg/dL), a kidney biopsy is obtained for oliguric AKI.

Which is the MOST likely cause of AKI in this patient?

- A. Acute thrombotic microangiopathy
- B. Crystalline-induced nephropathy
- C. Acute interstitial nephritis (AIN)
- D. Acute postinfectious glomerulonephritis (GN)
- E. Acute tubular injury/necrosis (ATN)

Answer: B

Explanation:

The clinical scenario is most consistent with ciprofloxacin-associated crystalline nephropathy as the cause of AKI. In support are the factors that lead to ciprofloxacin crystal precipitation in the renal tubules—excessive dose, alkaline urine, underlying kidney injury, and old age. The timing is rapid, which fits crystalline disease rather than AIN from ciprofloxacin. The clinical picture and urine findings do not fit postinfectious GN. ATN is possible, but the lack of hypotension makes this less likely.

230. In the critically ill septic patient admitted to the intensive care unit (ICU) with sepsis and multiple end organ failure, which fluid management strategy is associated with an increased risk of AKI?

- A. Albumin
- B. Hydroxyethyl starch (HES)
- C. Lactated Ringers
- D. Fresh frozen plasma
- E. Cryoprecipitate

Answer: B

Explanation:

Intravenous HES has been shown to be nephrotoxic in many case reports, observational studies, and prospective trials. AKI, sometimes requiring dialysis, is more common when this drug is used in critically ill patients with sepsis and acute lung injury/acute respiratory distress syndrome (ARDS). The other resuscitative fluids have not been shown to have the same nephrotoxic potential as HES.

231. In a patient with an aggressive lymphoma complicated by tumor lysis syndrome, which is the MOST common adverse effect of rasburicase therapy?
- A. Marrow suppression
 - B. Hepatic toxicity
 - C. Central nervous system (CNS) toxicity
 - D. Hemolytic reaction
 - E. Life-threatening hypouricemia

Answer: D

Explanation:

Rasburicase when used to prevent/treat hyperuricemia in the setting of tumor lysis syndrome has not been associated with any of the noted complications except a hemolytic reaction in patients who have an underlying G6PD deficiency. This happens in G6PD because hydrogen peroxide is one of the major byproducts of the conversion of uric acid to allantoin, and G6PD provides antioxidants.

232. A 47-year-old woman is admitted to the intensive care unit (ICU) in a coma after being found in her basement. Her family states that the patient is diabetic and takes pills for knee pain and depression. Her BP is 92/50 mm Hg, and the pulse is 118 beats/min. On exam, scattered bruises over her trunk and 1+ lower extremity edema are seen. Laboratory values: osmolar gap, 7; HCO₃, 6 mEq/L; and AG, 36. Serum creatinine is 4.2 mg/dL, and serum glucose is 147 mg/dL. Hemoglobin is 8.6 g/dL, and WBC is 18,000. Lactic acid level is 4.7 mg/dL, and serum/urine ketones are negative. Prothrombin time (PT)/international normalized ratio (INR) and partial thromboplastin time (PTT) are normal. Urinalysis demonstrates 1–3 granular casts/LPF, 1–5 RBCs/HPF, and 1–5 WBCs/HPF.

What is the MOST likely cause of the clinical scenario?

- A. Isopropyl alcohol intoxication
- B. Salicylate intoxication
- C. Ethylene glycol (EG) intoxication
- D. Metformin overdose
- E. Propylene glycol (PG) intoxication

Answer: C

Explanation:

This clinical scenario is consistent with EG intoxication. Ingested EG has been fully metabolized to its toxic metabolites including glycolic acid, glyoxalate, and oxalic acid, which cause the anion gap metabolic acidosis and end organ failure. Metformin is unlikely as the overdose because the anion gap far exceeds the lactic acid level, suggesting other organic anions are present. Isopropyl alcohol causes an osmolar gap but rarely causes an anion gap unless there is cardiovascular collapse with severe lactic acidosis. Salicylate overdose is also unlikely in the absence of serum and urine ketones. PG intoxication most often occurs in the hospital in the setting of high-dose infusion of medications that have PG as the vehicle (lorazepam, phenobarbital).

233. Which dosing recommendation is appropriate for rasburicase use in tumor lysis syndrome?
- A. Dose reduction in renal failure
 - B. No dose adjustment
 - C. Dose reduction in liver failure
 - D. Dose reduction with CYP450-3A4 enzyme inhibitor
 - E. Dose escalation in edematous states (large volume of distribution)

Answer: B

Explanation:

Rasburicase has an overall half-life of 18 hours. It is degraded in the circulation *via* peptide hydrolysis. This pathway is independent of renal and hepatic function. Thus, renal or liver failure or the CYP450 enzymes have no effect on drug dosing.

234. A 65-year-old man is admitted to the intensive care unit (ICU) with septic shock. Six liters of intravenous lactated Ringers is administered, but the patient remains in shock. He has AKI, and serum K is 5.7 mEq/L.

In choosing an intravenous vasopressor for this patient, which will raise serum potassium concentration and potentially worsen hyperkalemia?

- A. Dopamine
- B. Epinephrine
- C. Norepinephrine
- D. Vasopressin
- E. Phenylephrine

Answer: E

Explanation:

Phenylephrine is a nonselective α -agonist that may cause hyperkalemia by blocking the cellular uptake of potassium. Although β_2 agonism increases cellular uptake of potassium, α agonism has the opposite effect. Dopamine and vasopressin have no effect on α receptors, whereas norepinephrine and epinephrine have both α and β receptor agonism. These two drugs are more often associated with hypokalemia rather than hyperkalemia.

235. A 28-year-old woman is brought to the Emergency Department after being found confused by her sister. An empty bottle of acetaminophen is noted. BP is 102/60 mm Hg. On exam, the patient is obtunded and has asterixis. Acetaminophen level is 510 $\mu\text{g/mL}$, the serum transaminase levels are >4000 IU/L, and serum creatinine is 5.2 mg/dL. The patient is treated with *N*-acetylcysteine and 4 L of intravenous 0.9% sodium chloride. Despite this, the serum creatinine increases to 5.8 mg/dL, and the serum transaminase levels increase to >5000 IU/L over the next 24 hours. The patient is more lethargic, and BP is 102/58 mm Hg. The patient is cleared for a liver transplant and placed on the emergency waiting list.

Which is the BEST option to treat the patient while awaiting liver transplant?

- A. Hemodialysis
- B. Peritoneal dialysis
- C. Continuous veno-venous hemofiltration (CVVH)
- D. Albumin-based dialysis (MARS)

Answer: C

Explanation:

Continuous dialysis modalities offer unique advantages in patients at risk for increased intracranial pressure (ICP) such as those with acute hepatic failure. The slow removal of solutes does not lead to osmotic disequilibrium and rises in ICP. This makes CVVH the preferred modality for these patients although there are no randomized trials to demonstrate this benefit.

236. A 67-year-old man with hypertension, coronary artery disease (CAD), stage 3b CKD (eGFR, 43 mL/min/1.73 m²), hyperlipidemia, and Chronic Obstructive Pulmonary Disease (COPD) is admitted to the medical intensive care unit (ICU) with multilobar pneumonia associated with acute respiratory failure requiring mechanical ventilation. The patient also develops hypotension requiring intravenous vasopressors despite 5 L of intravenous lactated Ringers solution, resulting in a central venous pressure (CVP) ranging between 12 and 16. He is treated with broad-spectrum antibiotics awaiting culture information. Labs: BUN, 46 mg/dL; serum creatinine, 1.8 mg/dL; and glucose, 225 mg/dL. The intensivist starts an insulin drip to more tightly control the serum glucose level (goal of 80–110 mg/dL).

Which effect of tight glucose control with insulin therapy is MOST likely in this patient?

- A. Reduced risk of AKI
- B. Reduced mortality risk
- C. Increased risk of hypoglycemia
- D. Reduced ICU length of stay
- E. Increased ventilator-free days
- F. None of the above

Answer: C

Explanation:

While early studies suggest benefits of tight glucose control in patients with sepsis, further investigations have not demonstrated mortality benefits, reduced ICU length of stay or mortality. However, there was a much higher risk of hypoglycemia in these patients.

237. A patient is undergoing continuous veno-venous hemofiltration (CVVH) for sepsis complicated by AKI and multiorgan failure. Laboratory testing reveals that the BUN has increased from 64 to 110 mg/dL. The current CVVH prescription is a blood flow rate of 150 mL/min and 1 L/hr prefilter replacement fluid rate.

In this patient on CVVH, which maneuver will MOST effectively increase urea clearance?

- A. Increase replacement fluid rate from 1.0 to 1.5 L/hr
- B. Increase blood flow rate from 150 to 250 mL/min
- C. Increase the filter surface area
- D. Increase the filter pore size

Answer: B

Explanation:

In this patient, the most efficient way to improve solute clearance is to increase the blood flow rate. Prefilter administration of replacement fluid is associated with lower solute clearance than postfilter replacement fluid. While all of these changes would improve clearance, the most clearance will be seen with a change in blood flow rate.

238. A 72-year-old man is admitted with a non-ST segment elevation myocardial infarction. He has a history of morbid obesity but now after gastric bypass has a current weight of 98 kg, and he has hypertension, hyperlipidemia, diabetes mellitus, and Stage G3bA2 CKD. Medications on admission include furosemide, 40 mg twice daily; losartan, 100 mg daily; and atorvastatin, 80 mg daily. On physical examination, his lungs are clear with cough, and he has no peripheral edema. On a transthoracic echocardiogram, he has hypokinesis of the anteroseptal left ventricular wall and has an estimated left ventricular ejection fraction of 35%–40%. He is scheduled for coronary angiography, and you are consulted to advise how to best mitigate the risk of postprocedural AKI.

Which suggestion regarding fluid administration should you make?

- A. Do not give any IV fluids given the reduced ejection fraction.
- B. Give 0.45% saline intravenously at a rate of 100 mL/hour for 6 hours before and 6 hours after the procedure.
- C. Give 0.9% saline intravenously at a rate of 100 mL/hour for 12 hours before and 12 hours after the procedure.
- D. Give isotonic sodium bicarbonate intravenously at a rate of 75 mL/hour for 6 hours before and 6 hours after the procedure.

Answer: C

Explanation:

Of the four choices provided, the administration of isotonic crystalloid at a rate of 1 mL/kg per hour for 6 to 12 hours before and after the procedure is the most appropriate option.

Although there has been recent controversy, administration of IV crystalloid remains the primary strategy for mitigation of the risk of AKI after iodinated contrast administration, even in the setting of reduced ejection fraction.

Isotonic crystalloid has been demonstrated to provide greater benefit than hypotonic crystalloid. There is no additional benefit of sodium bicarbonate as compared with isotonic saline, and the rate provided in this choice is lower than ideal. Studies examined the difference in outcomes between saline and lactated ringers but not between saline and bicarbonate-containing solutions.

239. A 37-year-old man with a history of non-Hodgkin lymphoma is scheduled for surveillance contrast-enhanced CT scan 5 years after completion of chemotherapy. On initial presentation, he had bulky retroperitoneal adenopathy, which resulted in severe hydronephrosis of his right kidney and persistent loss of kidney function on that side. His serum creatinine had been 0.8 mg/dL prior to presenting with his lymphoma but has been stable at 1.0–1.2 mg/dL for the past 5 years. His measured albumin/creatinine ratio in the urine is 7.8 µg/mg.

In addition to ensuring that he is not taking any nonsteroidal anti-inflammatory drugs, which recommendation to prevent contrast-associated AKI is MOST appropriate?

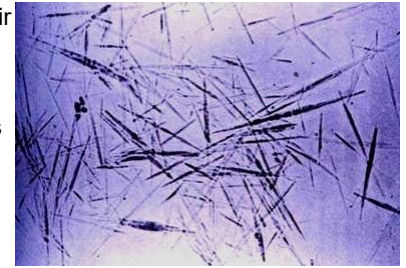
- A. Administer 3 mL/kg 1.26% sodium bicarbonate intravenously prior to contrast administration and 1.5 mL/kg for 4 hours after contrast administration.
- B. Administer 1200 mg oral N-acetylcysteine twice daily beginning 1 hour prior to contrast administration for a total of four doses.
- C. Begin rosuvastatin, 20 mg daily, for 5 days.
- D. Provide reassurance that no specific preventative interventions are required.

Answer: D

Explanation:

Although this patient has stage 2 CKD, he is at relatively low risk (<1%) for development of AKI after IV contrast administration for a contrast-enhanced CT scan. Therefore, no specific interventions for prevention of contrast-associated AKI are indicated.

240. A 43-year-old man with chronic HIV infection treated with abacavir, lamivudine, and atazanavir develops multidermatomal zoster infection over his left thorax and abdomen and is given intravenous acyclovir. Four days after initiation of treatment, he presents with nausea, vomiting, and dizziness. On admission, his BP is 96/64 mmHg with a heart rate of 104/min when lying and 80/52 mmHg with a heart rate of 134/min on standing. His mucous membranes are dry, and he has no edema. His blood urea nitrogen is 67 mg/dL, his creatinine 4.3 mg/dL, and his serum uric acid is noted to be 16.3 mg/dL. His urinalysis has a specific gravity of 1.026, pH 5.0, and 2+ blood by dipstick. Microscopic examination of the urine demonstrates the finding in the figure.



Which is the MOST likely cause of this patient’s AKI?

- A. Atazanavir
- B. Abacavir
- C. Acyclovir
- D. Hyperuricemia

Answer: C

Explanation:

This patient has acyclovir-associated crystalline nephropathy with the classic finding of needle-shaped crystals on urinalysis. Although most commonly associated with IV dosing, crystalline nephropathy can develop with oral administration, particularly if high doses are used or there is underlying renal insufficiency or severe volume depletion, as is the case in this patient. Indinavir may also be associated with crystalline nephropathy; however, the needle-shaped atazanavir crystals are broader than the fine acyclovir crystals and are more commonly arranged in plates or rosettes rather than as individual needles. The solubility of atazanavir increases at lower pH.

Uric acid nephropathy, as seen in tumor lysis syndrome, is associated with hexagonal crystals of uric acid rather than the needle-shaped sodium urate crystals seen in gout. Abacavir is not associated with crystalline nephropathy.

241. A 53-year-old woman with cirrhosis secondary to nonalcoholic steatohepatitis who is awaiting liver transplantation is admitted to the hospital with increased confusion. Her family reports that over the past 3 days, she has refused to take her lactulose because of diarrhea but has continued to take her propranolol, furosemide, and spironolactone. On admission, her BP is 90/60 mmHg and heart rate 84/min. She is oriented only to person and has asterixis on examination. Her skin and sclera are grossly icteric, her neck is obese, her neck veins cannot be visualized, her lungs are clear, her abdomen is obese and distended, and she has no peripheral edema. Admission laboratory tests demonstrate the following:

Blood urea nitrogen	41 mg/dL (baseline 18 mg/dL)
Plasma creatinine	3.1 mg/dL (baseline 1.2 mg/dL)
Sodium	128 mEq/L
Potassium	6.1 mEq/L
Hemoglobin	11.8 g/dL (baseline 12.4 g/dL)
White blood cells	11,300/μl
Platelets	78,000/μl
International normalized ratio	1.9

Her urine specific gravity is 1.012. On urine microscopy, she has many bile-stained granular casts. On bedside ultrasound, she has moderate ascites.

In addition to stopping her furosemide and spironolactone and medically managing her hyperkalemia, which is the MOST appropriate initial management for her AKI?

- A. Administer 1 g/kg of hyperoncotic albumin and begin octreotide and oral midodrine.
- B. Administer IV isotonic crystalloid.
- C. Perform large-volume paracentesis.
- D. Begin continuous venovenous hemofiltration.

Answer: B

Explanation:

The differential diagnosis of this patient includes prerenal azotemia secondary to volume depletion, hepatorenal syndrome, or acute tubular necrosis. The first step in evaluation and management is adequate volume repletion. Although hyperoncotic (20% or 25%) albumin can be used, IV isotonic crystalloid is appropriate as the initial resuscitation fluid for a patient who is clinically volume depleted.

There is no clinical need for performance of a large-volume paracentesis (although a diagnostic paracentesis to rule out spontaneous bacterial peritonitis would be appropriate). Performing a large-volume paracentesis in the setting of clinical volume depletion increases the risk for development of hepatorenal syndrome.

Administration of octreotide and midodrine in combination with IV hyperoncotic albumin would be an appropriate option for vasoconstrictor therapy for treatment of hepatorenal syndrome once that diagnosis is established based on failure to respond to adequate volume resuscitation but is not appropriate as initial therapy.

Similarly, initiation of renal replacement therapy as the initial management of her AKI prior to an adequate trial of volume resuscitation is not appropriate.

242. A 76-year-old man is admitted to the hospital with a history of multiple recent falls. He has a history of hypertension, hyperlipidemia, chronic obstructive lung disease, coronary artery disease that has been medically managed, nephrolithiasis, a 4.3-cm abdominal aortic aneurysm that has been stable in size on serial abdominal ultrasounds, and benign prostatic hypertrophy with a prior episode of urinary retention in the setting of a urinary tract infection 3 years prior to this hospitalization. Medications include fosinopril, carvedilol, rosuvastatin, enteric-coated aspirin, tamsulosin, and a budesonide/formoterol inhaler. On physical examination, his BP is 122/76 mmHg and heart rate 84/min. His oral mucosa is slightly dry, he has multiple ecchymoses from his falls and 4/5 strength in his left leg, but examination findings are otherwise unremarkable. Admission laboratory studies demonstrate the following:

Blood urea nitrogen	46 mg/dL ("normal" 6 mo prior to admission)
Plasma creatinine	2.9 mg/dL ("normal" 6 mo prior to admission)
Sodium	132 mEq/L
Potassium	5.1 mEq/L
Chloride	108 mEq/L
Total CO ₂	20 mEq/L
Glucose	112 mg/dL
Calcium	11.7 mg/dL
Albumin	3.1 g/dL
Total protein	8.4 g/dL
Hemoglobin	10.3 g/dL
Urine studies	
Urine creatinine	100 mg/dL
Urine total protein	360 mg/dL
Protein:creatinine ratio	3.6

Urinalysis showed specific gravity 1.010, pH 6.0, trace protein and 1+ blood by dipstick. A postvoid residual urine volume by ultrasound in the emergency department was reported to be 165 mL.

Which is the MOST likely etiology for his kidney disease?

- A. Amyloidosis
- B. Atheroembolic disease
- C. Light chain cast nephropathy
- D. Obstructive uropathy

Answer: C

Explanation:

This patient is presenting with multiple myeloma with light chain cast nephropathy. The diagnosis should be suggested by several features of the presentation, including anemia, hypercalcemia, a low anion gap (4 mmol/L), and a discrepancy between the urine dipstick, which demonstrated only trace protein, and the measured protein/creatinine ratio in the urine (3.6 g/g), suggesting the presence of nonalbumin protein in the urine. Amyloidosis, which could also be associated with the presence of a paraprotein, would be associated with significant albuminuria and would not be associated with a discrepancy between the protein by urine dipstick and the total protein/creatinine ratio. Although the patient has an abdominal aortic aneurysm, which may be associated with atheroembolic disease, no other signs or symptoms are present suggesting this as an etiology. Although the postvoid residual urine volume is mildly elevated, this is probably insufficient to account for this degree of kidney dysfunction and does not account for the other noted abnormalities.

243. A 45-year-old woman with decompensated hepatitis C cirrhosis presents with worsening renal function. Her baseline serum creatinine had been 1.5 mg/dL as an outpatient. She is sent in from the liver clinic because her serum creatinine level is 2.5 mg/dL. She is afebrile. On examination, her BP is 100/62 mmHg and temperature is 97°F. Her jugular venous pressure is not elevated. Her abdomen is markedly distended with caput and a fluid wave. She has 3+ lower extremity edema. Her laboratory tests reveal the following:

White blood cells	8800/ μ l
Hemoglobin	9.2 g/L
Sodium	128 mEq/L
Potassium	4.9 mEq/L
Blood urea nitrogen	48 mg/dL
Creatinine	2.5 mg/dL
Calcium	8.0 mg/dL
Total bilirubin	5 mg/dL

The patient has a urine sodium level <10 mEq/L; urinalysis reveals trace protein and negative heme; urine sediment reveals 2–5 pigmented granular casts per low power field. Abdominal ascites fluid reveals 20 polymorphonuclear cells per milliliter. The patient is given IV albumin at 1 g/kg for 2 days, and on day 3, her serum creatinine is 3.0 mg/dL.

What is the MOST likely cause of AKI in this patient?

- A. Volume depletion
- B. Acute tubular necrosis
- C. Hepatorenal syndrome
- D. Acute glomerulonephritis

Answer: C

Explanation:

The patient received loading with IV albumin and is not volume depleted. Although there are a few granular casts per low power field, there is little to indicate that the patient has acute tubular necrosis (no obvious stimuli and the urine sodium is extremely low). Although patients with hepatitis C and cirrhosis can have acute GN, there is no evidence to suggest GN (bland sediment). Given the decompensated cirrhosis, the progressively worsening renal function, the BP in the low range, and the low urine sodium, the diagnosis is hepatorenal syndrome by exclusion.

244. A patient with a history of congestive heart failure and known left ventricular ejection fraction of 25% is admitted to the hospital with a 20-lb fluid gain, shortness of breath, and an increased creatinine level (2.9 mg/dL, from a prior value of 1.9 mg/dL). His BP is 134/82 mmHg, his jugular venous pressure 14 cm H₂O, and his lungs have crackles one-half up both lung fields. He has 3+ lower extremity and sacral edema. His outpatient medications include carvedilol, 12.5 mg twice daily; lisinopril, 20 mg daily; furosemide, 80 mg twice daily; metolazone, 5 mg once daily; and atorvastatin, 40 mg daily.

Which is the MOST likely cause of AKI?

- A. Poor cardiac output leading to cardiogenic shock and low renal blood flow
- B. Acute tubular necrosis due to nephrotoxicity of loop diuretics
- C. Venous congestion leading to neurohormonal and hydraulic effects on kidney function
- D. Atorvastatin-induced rhabdomyolysis in the setting of preexisting CKD

Answer: C

Explanation:

Clinicians frequently cite “poor forward flow” as the reason for AKI in patients with cardiac dysfunction, but the evidence suggests that low cardiac output is not associated with renal dysfunction in patients with heart failure. There is little to no correlation between cardiac index and renal function according to several observational studies. Instead, renal function in heart failure is associated with venous congestion and intra-abdominal pressure. Venous congestion itself activates the sympathetic and renin angiotensin aldosterone systems, which contributes to intrarenal vasoconstriction. Loop diuretics are NOT nephrotoxic (another common clinical colloquialism). Diuretics only worsen renal function when the intravascular volume is reduced in too rapid a manner or reduced when volume overload is not present. Furthermore, although statins can occasionally cause rhabdomyolysis, there is no evidence of rhabdomyolysis in this case, and CKD does not itself increase the risk of statin-induced rhabdomyolysis.

References:

Hanberg JS, Sury K, Wilson FP, Brisco MA, Ahmad T, Ter Maaten JM, Broughton JS, Assefa M, Tang WH, Parikh CR, Testani JM. Reduced cardiac index is not the dominant driver of renal dysfunction in heart failure. *J Am Coll Cardiol* 2016;67:2199–2208.

Mullens W, Abrahams Z, Francis GS, Sokos G, Taylor DO, Starling RC, Young JB, Tang WH. Importance of venous congestion for worsening of renal function in advanced decompensated heart failure. *J Am Coll Cardiol* 2009;53:589–596.

Damman K, Navis G, Smilde TD, Voors AA, van der Bij W, van Veldhuisen DJ, Hillege HL. Decreased cardiac output, venous congestion and the association with renal impairment in patients with cardiac dysfunction. *Eur J Heart Fail* 2007;9:872–878.

Testani JM, Khera AV, St John Sutton MG, Keane MG, Wiegers SE, Shannon RP, Kirkpatrick JN. Effect of right ventricular function and venous congestion on cardiorenal interactions during the treatment of decompensated heart failure. *Am J Cardiol* 2010;105:511–516.

245. A 72-year-old man with hypertension presents to the emergency department with slurred speech, headache, and weakness after falling at home. He has a 3-day history of decreased oral intake, dizziness, fever, and yellow sputum production. A CT scan of the head demonstrates moderate edema associated with an intracranial hemorrhage and mass effect. Prior to admission to the intensive care unit (ICU), he develops pulseless electrical activity arrest and undergoes successful CPR. He is transferred to the ICU while receiving a norepinephrine infusion after receiving 6 L of IV fluids. Nephrology is consulted 6 hours later for anuric AKI (serum creatinine 6.1 mg/dL) and volume overload. He is mechanically ventilated with a fraction of inspired oxygen of 70% and continues to receive a norepinephrine infusion. He is febrile with an elevated white blood cell count and mild thrombocytopenia. Chest radiograph is read as pneumonia with superimposed edema. Renal ultrasound has normal findings. The nephrologist decides to start giving the patient CRRT. The intensivist asks the nephrologist the reason for initiating CRRT instead of intermittent hemodialysis (IHD).

Which is the STRONGEST evidence for supporting CRRT?

- A. CRRT results in better renal recovery.
- B. CRRT improves survival in patients who are hemodynamically unstable.
- C. CRRT causes less intracranial pressure shifts in patients with acute brain injury.
- D. CRRT improves patient survival in sepsis-mediated AKI.
- E. CRRT reduces patient ventilator days through more effective volume removal.

Answer: C

Explanation:

Among patients with acute brain injury, IHD may worsen neurological status by compromising cerebral perfusion pressure. For patients with cerebral edema, continuous therapy is recommended to prevent decreased cerebral blood flow. CRRT will also prevent sudden changes in serum osmolality. Both hypotension and disequilibrium can be avoided by the slow progressive removal of fluids and solutes that occurs during CRRT administration.

Insufficient evidence exists regarding the superiority of CRRT over IHD with regards to renal functional recovery. The studies are mainly observational, and no randomized trial has demonstrated that CRRT improves renal recovery when compared with IHD (choice A). In addition, no randomized clinical trials (RCTs) have shown that CRRT improves survival in patients who are hemodynamically unstable when compared with IHD (choice B).

Despite the notion that CRRT with convective therapy can potentially remove cytokines and other inflammatory mediators in septic patients, no RCTs have demonstrated a benefit of convective therapy (CVVH) when compared with diffusive therapy in septic patients with AKI (choice D). In addition, no RCTs comparing high-volume hemofiltration (HVHF) (total effluent or ultrafiltration rates ≥ 50 mL/kg/h) with standard dose CVVH (20–25 mL/kg/h) have demonstrated a survival benefit or improved organ dysfunction. Furthermore, HVHF has been shown to cause excessive loss of electrolytes, nutrients, and antibiotics. Therefore, at this time, HVHF for removal of cytokines or septic mediators is not supported.

No studies have shown that CRRT administration decreases ventilator days (choice E).

References:

Davenport A. Continuous renal replacement therapies in patients with acute neurological injury. *Semin Dial* 2009;22:165-168.

246. A 29-year-old man is evaluated in the emergency department after being found on the floor in his apartment by friends who had not seen him in a few days.

On physical examination, the patient is somnolent and minimally responsive. His temperature is 37.2°C (98.9°F), BP 93/60 mmHg, pulse rate 125/min, and respiration rate 14/min with 99% oxygen saturation on ambient air. His skin is mottled and edematous on the posterior surface of the legs, buttocks, and back. Neurologic examination reveals no focal or lateralizing findings. The remainder of the examination has normal findings.

Blood urea nitrogen	122 mg/dL
Calcium	6.8 mg/dL
Creatine kinase	115,000 U/L
Serum creatinine	5.9 mg/dL
Sodium	149 mEq/L
Potassium	5.7 mEq/L
Chloride	110 mEq/L
Bicarbonate	16 mEq/L
Glucose	94 mg/dL
Phosphorus	8.5 mg/dL
Urinalysis	
Specific gravity	1.015
pH	6.5
	3+ blood
	1+ protein
	0–5 erythrocytes/high power field, 1–3 leukocytes/high power field, dark granular casts
Toxicology screening	Pending

During the 3 hours he has been in the hospital, his total urine output has been 60 mL. He has received minimal fluids. Electrocardiogram reveals sinus tachycardia with no ST- or T-wave changes.

Which is the MOST appropriate treatment for this patient?

- A. Hemodialysis
- B. Rapid infusion of intravenous isotonic sodium bicarbonate in 5% glucose
- C. Intravenous calcium infusion
- D. Rapid infusion of intravenous 0.9% saline

Answer: D

Explanation:

The patient has rhabdomyolysis. Aggressive volume repletion with isotonic saline is the best initial treatment to reduce risk of intratubular cast formation and AKI.

Hemodialysis is reserved for severe AKI or intractable hyperkalemia. This patient has not been challenged with IV fluids and has evidence of hypovolemia by examination (choice A).

The use of fluids with intravenous bicarbonate is controversial. Administering IV bicarbonate to keep urine pH >6.5 may prevent precipitation of the myoglobin and therefore decrease tubular injury. However, it may also further reduce ionized calcium and increase the likelihood of symptomatic hypocalcemia in patients who already have severe hypocalcemia. Bicarbonate can also cause precipitation of calcium phosphate in the tubules in patients with hyperphosphatemia (choice B).

Hypocalcemia in rhabdomyolysis is due to the sequestration of calcium in damaged muscle cells. Rebound calcium can be worsened by administration of calcium and can result in severe hypercalcemia. Calcium should only be given if the patient is asymptomatic or in severe hyperkalemia if electrocardiogram (EKG) changes present. This patient did not have EKG findings of severe calcium (choice C).

References:

Bosch X, Poch E, Grau JM. Rhabdomyolysis and acute kidney injury. *N Engl J Med* 2009;361:62–72.

247. An 18-year-old college student returns from vacation in South America and is admitted after having severe bloody diarrhea and fever for 5 days, followed by oliguria. His diarrhea has subsided. He is afebrile, his BP is 100/60 mmHg, pulse is 98 beats/minute, and physical examination findings are normal. Over the next 4 hours, he is noted to be increasingly somnolent, followed by a generalized tonic-clonic seizure.

Admission laboratory tests are notable for a serum creatinine of 6 mg/dL, hemoglobin 7.5g/dL, platelet count 20,000/μL, and LDH 1542 U/mL. Stool culture is pending. ADAMTS13 levels are normal.

Which is appropriate treatment for his condition?

- A. Intravenous ciprofloxacin
- B. Anti-platelet therapy
- C. Platelet transfusion
- D. Plasmapheresis
- E. Fluid resuscitation

Answer: E

Explanation:

For a patient with likely diarrhea-associated hemolytic uremic syndrome, supportive care including fluid and electrolyte balance and dialysis for uremia is usually adequate until the patient recovers. For the patient with severe neurological manifestations, the use of eculizumab has been proposed but is controversial. Antibiotics, plasmapheresis, antimotility agents, and antiplatelet agents are not recommended because they are either not useful or are associated with harm.

References:

George JN, Nester CM. Syndromes of thrombotic microangiopathy. *N Engl J Med* 2014;371:654–666.

248. You are asked to consult on a patient who has been admitted with septic shock and requires administration of multiple therapeutic agents. His baseline serum creatinine level is 1.0 mg/dL and is now 2.3 mg/dL. He has essentially no urine output despite a normal renal ultrasound and a Foley catheter in place. He is receiving antibiotics, and you are asked to prescribe them in terms of his AKI.

On which should you base your calculations?

- A. Current serum creatinine concentration
- B. Current eGFR
- C. Presumption that his GFR equals 0
- D. On the rate of change of serum creatinine over the next 4–6 hours
- E. On a timed creatinine clearance

Answer: C

Explanation:

When prescribing antibiotics for this patient, the serum creatinine should be interpreted carefully because he is making no urine. His current eGFR likely does not reflect the fact that he has virtually no glomerular filtration. Thus, dosing of drugs should be based on the presumption that his GFR is 0.

249. A 73-year-old woman was referred for evaluation of confusion. She had difficulty keeping her balance during the last few days and complained of headache, dry mouth, and polyuria. Her history reveals a radius fracture 2 months ago. Although a DEXA scan did not suggest osteoporosis, she took an over-the-counter product containing calcium (800 mg/day) and vitamin D (150 IU D3/day). Labs revealed a serum calcium of 16 mg/dL and albumin of 4.0 g/L. Intact parathyroid hormone (PTH) was 5 pg/mL and PTH-related protein (PTHrP) was undetectable. 25(OH)D was 574 ng/mL.

What is the likely diagnosis?

- A. Sarcoidosis
- B. Lymphoma
- C. Vitamin D intoxication
- D. Immobilization

Answer: C

Explanation:

Sarcoidosis and lymphoma can both produce hypercalcemia associated with elevated levels of 1,25(OH)₂D but not 25(OH)D. Elevated levels of 25(OH)D indicate vitamin D intoxication. In this case, the history revealed ingestion of an over-the-counter product labeled as containing only 150 IU vitamin D/day. Actual measurement of the product indicated a concentration providing 150,000 U/day.

References:

Koutkia P, Chen TC, Holick MF. Vitamin D intoxication associated with an over-the-counter supplement. *N Engl J Med* 2001;345:66–67.

Kaptein S, Risselada AJ, Boerma EC, Egbers PH, Nieboer P. Life-threatening complications of vitamin D intoxication due to over-the-counter supplements. *Clin Toxicol* 2010;48:460–462.

Lowe H, Cusano NE, Binkley N, Blaner WS, Bilezikian JP. Vitamin D toxicity due to a commonly available “over the counter” remedy from the Dominican Republic. *J Clin Endocrinol Metab* 2011;96:291–295.

250. A 65-year-old woman presented with a 17-year clinical history of musculoskeletal pain, muscular weakness in the pelvic girdle, spontaneous fractures, and difficulty in walking. Over the ensuing years, the patient suffered other multiple spontaneous fractures, and the muscular pains worsened until she became bedridden. When you were asked to see her, you noted an associated history of hypophosphatemia (1–2 mg/dL) also beginning 17 years prior. Serum calcium levels were consistently normal. You recommended Indium111-octreotide scintigraphy, which visualized an area of pathologic increased signal uptake in the left groin, consistent with a mass containing a high density of somatostatin receptors. After surgery, histologic examination of the resected specimen indicated a hemangiopericytoma.

Which does NOT characterize tumor-induced osteomalacia, typically due to benign small mesenchymal tumors?

- A. Hypophosphatemia and normocalcemia
- B. Elevated fibroblast growth factor (FGF)23 levels
- C. Normal 25(OH)D levels
- D. Elevated calcitriol levels

Answer: D

Explanation:

Tumor-induced osteomalacia is typically caused by benign mesenchymal tumors of vascular or skeletal origin. Overexpression of FGF23 by these tumors is associated with decreased resorption of phosphate in the renal tubules. This phosphate wasting leads to the characteristic findings of hypophosphatemia and hyperphosphaturia. Chronic hypophosphatemia causes abnormal mineralization of bone, increased alkaline phosphatase, and, in the longer term, osteomalacia and associated fractures. Vitamin D metabolism is abnormal in tumor-induced osteomalacia, as it is in X-linked and autosomal dominant hypophosphatemic rickets. Thus, plasma concentrations of calcitriol are reduced, even though elevated levels are to be expected in the presence of hypophosphatemia.

References:

Agus ZS. Oncogenic hypophosphatemic osteomalacia. *Kidney Int* 1983;24:113–123.

Jonsson KB, Zahradnik R, Larsson T, White KE, Sugimoto T, Imanishi Y, Yamamoto T, Hampson G, Koshiyama H, Ljunggren O, Oba K, Yang IM, Miyauchi A, Econs MJ, Lavigne J, Jüppner H. Fibroblast growth factor 23 in oncogenic osteomalacia and X-linked hypophosphatemia. *N Engl J Med* 2003;348:1656–1663.

Westerberg P, Linde T, Vanderschueren D, et al. Oncogenic osteomalacia illustrating the effect of fibroblast growth factor 23 on phosphate homeostasis. *Clin Kidney J* 2012;5:240.

251. A 36-year-old woman with metastatic breast cancer enters the Emergency Department complaining of lethargy and weakness. She has been treated with carboplatin and paclitaxel at her last chemotherapy 3 weeks ago. She is on acetaminophen with codeine for mild bone pain. Her husband notes that she has produced little urine for the last 24 hours. She is barely communicative. Her physical examination shows a chronically ill-appearing woman with a BP of 125/80 mm Hg supine and 120/75 mm Hg standing. Urine output is 10 mL/hr. Cardiac, chest, and abdominal examinations are unrevealing and without edema. Her laboratory results show the following: BUN, 78 mg/dL; serum creatinine, 6.6 mg/dL; sodium, 133 mEq/L; K, 3.7 mEq/L; Cl, 107 mEq/L; HCO₃, 24 mEq/L; calcium, 14.2 mg/dL; PO₄, 8 mg/dL; and ionized calcium, 2.0 mmol/L.

At this point, which treatment would you recommend?

- A. Saline plus furosemide
- B. Zoledronic acid
- C. Calcitonin
- D. Low calcium dialysis

Answer: D

Explanation:

Low calcium bath hemodialysis is the correct therapy to effectively lower severe hypercalcemia in a patient with severe AKI. Rapidly lowering the serum Ca²⁺ level may facilitate kidney recovery. It will also correct hyperphosphatemia and underlying uremia. Saline plus furosemide is useful to lower serum calcium in patients who are volume depleted and suffer primarily from prerenal AKI. In a patient with severe AKI, it will not be effective and risks causing hypervolemia and its associated complications. Zoledronic acid is a bisphosphonate that is effective for moderate to severe hypercalcemia but will not correct hypercalcemia for several days and risks further kidney injury (toxic acute tubular necrosis). Calcitonin is useful for mild to moderate hypercalcemia but will not correct hypercalcemia for several days. This drug by itself is often ineffective.

252. In a patient with sarcoidosis, which is the MOST common renal manifestation?

- A. Granulomatous interstitial nephritis
- B. Nephrolithiasis
- C. Hypercalciuria
- D. Membranous glomerulonephritis
- E. Minimal change nephropathy

Answer: C

Explanation:

Sarcoidosis causes several renal lesions. The most common is isolated hypercalciuria. All of the other listed lesions are described with sarcoidosis but are less common.

253. A 35-year-old obese woman develops acute onset of right flank pain. A computed tomography (CT) scan shows a kidney stone lodged at the ureteropelvic junction associated with mild to moderate hydronephrosis. Urology performs retrograde stenting and removal of the calculus. It is sent for stone analysis, revealing calcium phosphate.

Which drug may be associated with the development of calcium phosphate kidney stones?

- A. Atazanavir
- B. Triamterene
- C. Orlistat
- D. Tiopronin
- E. Topiramate

Answer: E

Explanation:

Topiramate inhibits carbonic anhydrase. As a result, it is associated with a renal tubular acidosis (RTA) – proximal and distal RTA – with calcium phosphate stone formation. Tiopronin does not have adverse renal effects. Atazanavir is associated with urinary crystals and nephrolithiasis. Triamterene is associated with urinary crystals but not stones. It is also associated with hyperkalemia from blocking the sodium channels. Orlistat is associated with enteric hyperoxaluria and urinary calcium oxalate crystals.

254. A 22-year-old man presents with recurrent cramps and is found to have hypomagnesemia with the following laboratory findings: Hgb, 12.4; Ht, 14; WBC, 5400; blood urea nitrogen (BUN); 15 mg/dL; Cr, 1.4 mg/dL; Na, 142 mEq/L; Cl, 107 mEq/L; K, 2.7 mEq/L; CO₂, 24 mEq/L; Ca²⁺, 6.7 mg/dL; PO₄, 3.6 mg/dL; Mg²⁺, 0.72 mg/dL; alb, 3.9 g/L

Twenty-four-hour urine revealed the following: Cr, 1200 mg; Na⁺, 123 mEq; Ca²⁺, 254 mg; Mg²⁺, 29 mg

A defect in magnesium transport in which segment of the renal tubule is MOST compatible with these findings?

- A. The thick ascending limb (TAL) of the loop of Henle
- B. The early distal tubule
- C. The late distal nephron
- D. The proximal tubule
- E. The descending limb of the loop of Henle

Answer: A

Explanation:

This patient has urinary magnesium wasting associated with hypercalciuria. Renal magnesium wasting due to defective transport in the TAL is typically associated with hypercalciuria, whereas defects in the early distal tubule are associated with hypocalciuria and defects in the late distal nephron are associated with normal urinary calcium excretion.

References:

Praga M, Vara J, González-Parra E, Andres A, Alamo C, Araque A, Ortiz A, Rodicio JL. Familial hypomagnesemia with hypercalciuria and nephrocalcinosis. *Kidney Int* 1995;47:1419–1425.

Nicholson JC, Jones CL, Powell HR, Walker RG, McCredie DA. Familial hypomagnesemia—Hypercalciuria leading to end-stage renal failure. *Pediatr Nephrol* 1995;9:74–76.

Benigno V, Canonica CS, Bettinelli A, von Vigier RO, Truttmann AC, Bianchetti MG. Hypomagnesemia-hypercalciuria-nephrocalcinosis: A report of nine cases and a review. *Nephrol Dial Transplant* 2000;15:605–610.

Müller D, Kausalya PJ, Bockenhauer D, Thumfart J, Meij IC, Dillon MJ, van't Hoff W, Hunziker W. Unusual clinical presentation and possible rescue of a novel claudin-16 mutation. *J Clin Endocrinol Metab* 2006;91:3076–3079.

Konrad M, Hou J, Weber S, Dötsch J, Kari JA, Seeman T, Kuwertz-Bröking E, Peco-Antic A, Tasic V, Dittrich K, Alshaya HO, von Vigier RO, Gallati S, Goodenough DA, Schaller A. CLDN16 genotype predicts renal decline in familial hypomagnesemia with hypercalciuria and nephrocalcinosis. *J Am Soc Nephrol* 2008;19:171–181.

255. You are following a 62-year-old man with ESKD on hemodialysis with secondary hyperparathyroidism. Recently, he was started on cinacalcet 30 mg daily. Today, the patient is complaining of some “twitchy muscles” and facial numbness. His other medications include sevelamer 2400 mg tid with meals, calcitriol 0.5 µg IV with each dialysis session, carvedilol 25 mg tid, lisinopril 20 mg daily, erythropoietin 4000 units with each dialysis session, and a multivitamin. His most recent laboratory work 1 week ago was notable for the following: serum calcium, 7.8 mg/dL; serum phosphorus, 9.8 mg/dL; and PTH level, 1265 pg/mL.

Which would be your next step in management of this patient?

- A. Increase the cinacalcet dose to 60 mg daily
- B. Repeat the serum phosphorus and, if >9 mg/dL, add aluminum hydroxide
- C. Change the dialysis bath to a high calcium bath and send an emergent serum calcium and ionized calcium level
- D. Add gabapentin 300 mg at bedtime
- E. Reassure the patient that this sounds like anxiety

Answer: C

Explanation:

Cinacalcet, by lowering PTH levels, can lead to symptomatic hypocalcemia as found in this patient. The patients who are at highest risk are those with relatively low serum calcium at initiation of cinacalcet. Thus, it is important to measure serum calcium approximately 1 week after starting cinacalcet and to be aware of the possibility of hypocalcemia as a potential occurrence. In this case, the easiest and most rapid course of action would be to increase the dialysate calcium and check the serum calcium level. If available, oral calcium (such as calcium carbonate) could also be given.

256. A 36-year-old woman is admitted to the emergency department with lethargy and confusion that has developed and worsened over the last 36 hours. The patient has a history of obsessive-compulsive disorder and most recently has become fixated on her risk for osteoporosis. In response to her concerns, she has been taking the following: 6 servings of yogurt/day, 12 calcium carbonate 500 mg tablets/day, and ergocalciferol 50,000 units daily. She takes no other medications. On arrival to the emergency department, she was lethargic and only oriented to person.

Her vital signs were notable for a BP of 85/40 mm Hg and a pulse of 130 beats/min. Her physical examination was notable for dry mucous membranes and her lethargy and confusion.

Laboratory studies revealed the following:

Sodium: 147 mEq/L	Blood urea nitrogen: 126 mg/dL
Potassium: 3.8 mEq/L	Creatinine: 3.9 mg/dL
Bicarbonate: 35 mEq/L	Calcium: 14.9 mg/dL
Chloride: 100 mEq/L	Phosphorus: 4.3 mg/dL

Which laboratory value would you expect to see in this patient?

- A. Spot urine sodium of 110 mEq/L
- B. Parathyroid hormone level of 4 ng/L
- C. Parathyroid hormone level of 356 ng/L
- D. Parathyroid-related hormone level of 22 pmol/L (normal, <2.0 pmol/L)

Answer: B

Explanation:

This patient likely has milk-alkali syndrome (also called calcium-alkali syndrome to signify that it is a high calcium intake and not necessarily milk only that is a key determinant of this syndrome). Milk-alkali syndrome is caused by the ingestion of large amounts of calcium and absorbable alkali, with resulting hypercalcemia. If unrecognized and untreated, milk-alkali syndrome can lead to metastatic calcification and renal failure. Calcium-alkali syndrome is now more common in postmenopausal women with the use of over-the-counter (OTC) calcium and vitamin D supplements. Calcium- or milk-alkali syndrome is now the third most common cause of hypercalcemia in hospitalized patients.

Calcium absorption is completed within 4 hours of intake. Avid absorption of large doses may lead to suppression of PTH, which then leads to enhanced bicarbonate retention by the kidney. (The data are clear that PTH is suppressed in milk-alkali syndrome.) Continuing ingestion of calcium carbonate and bicarbonate retention leads to alkalosis, which causes increased calcium resorption in the distal collecting system of the kidney. Also, hypercalcemia produces a renal concentrating defect that can be considered a form of nephrogenic diabetes insipidus.

Resultant dehydration and volume depletion (with a resulting low urine sodium) may worsen the hypercalcemia. PTH is further suppressed by hypercalcemia. This cyclic pathophysiology maintains hypercalcemia and alkalosis as long as calcium and alkali are taken in by mouth. A low PTH level impairs gastrointestinal (GI) absorption of phosphate. Therefore, low PTH levels may be part of the mechanism by which phosphate levels either remain normal or rise abnormally high in many patients.

References:

Medarov BI. Milk-alkali syndrome. *Mayo Clin Proc* 2009;84:261–267.

Muldowney WP, Mazbar SA. Roloids-yogurt syndrome: A 1990s version of milk-alkali syndrome. *Am J Kidney Dis* 1996;27:270–272.

257. You are consulted to see a 19-year-old man with a history of hypocalcemia. The patient was noted to have hypocalcemia 2 years ago after suffering a seizure. Serum calcium values typically range from 7.1 to 8.8 mg/dL. Serum magnesium levels are 1.4 mg/dL, and serum PTH levels are 10 ng/L. A spot urine calcium to creatinine ratio was 0.37. Of note, his father was diagnosed with hypocalcemia, which was asymptomatic and has not required therapy. The patient's renal ultrasound is notable for nephrocalcinosis.

Mutations in which protein account for the pathogenesis of this patient's condition?

- A. Vitamin D receptor
- B. Calcium-sensing receptor (CaSR)
- C. Sodium-potassium-chloride cotransporter in the ascending limb of the loop of Henle
- D. Calcitonin receptor

Answer: B

Explanation:

Autosomal dominant hypocalcemia (ADH) is commonly caused by an activating mutation of the CaSR gene. Most reported mutations occur in the extracellular domain of the CaSR, although some occur in the transmembrane domain. Sporadic de novo mutations in the CaSR have also been identified. Such patients are often labeled as having idiopathic hypoparathyroidism, unless their CaSR gene is subjected to mutational analysis.

Clinical manifestations: The majority of ADH patients are asymptomatic and therefore are not diagnosed until adulthood, when hypocalcemia is incidentally noted. A few patients, however, have symptomatic hypocalcemia. Children in particular may become symptomatic with seizures and neuromuscular irritability during periods of stress, such as a febrile illness, and may be mislabeled as having febrile seizures.

The biochemical features are as follows:

- Serum calcium concentration usually in the range of 6–8 mg/dL (1.5–2.0 mmol/L), but as low as 5 mg/dL in occasional families;
- Normal (or only slightly low) serum PTH concentrations;
- High or high normal urinary calcium excretion rather than the expected low excretion;
- Recurrent nephrolithiasis and nephrocalcinosis, particularly during treatment with vitamin D and calcium supplementation;
- No previous normal serum calcium values; and
- Low serum magnesium concentration (in some).

The usual biochemical tests do not reliably discriminate this disorder from other forms of PTH-deficient hypoparathyroidism. In addition to the features listed above, the major clinical clue to this syndrome is its familial nature and the tendency of patients to develop renal complications during treatment with calcium and vitamin D supplementation. The diagnosis can be confirmed by analysis for mutations in the CaSR gene.

References:

Brown EM. Clinical lessons from the calcium-sensing receptor. *Nat Clin Pract Endocrinol Metab* 2007;3:122–133.

258. A 62-year-old man with ESKD, type 2 diabetes mellitus, coronary artery disease, and recent onset of atrial fibrillation complains of painful nodules on his lower abdominal wall that have been present for about 2 months. His current medications include the following: sevelamer 2400 mg tid with meals, lisinopril 40 mg daily, carvedilol 25 mg bid, a renal formulation multivitamin, cinacalcet 30 mg daily, warfarin 4 mg daily, gabapentin 300 mg at bedtime, lantus and Humalog insulin, and omeprazole 20 mg daily. The abdominal wall lesions have the following appearance:

Most recent laboratory work: serum calcium, 9.0 mg/dL; serum phosphorus, 8.9 mg/dL; serum PTH, 1897 ng/L.



Which medication is MOST likely associated with this skin lesion?

- A. Cinacalcet
- B. Omeprazole
- C. Gabapentin
- D. Sevelamer
- E. Warfarin

Answer: E

Explanation:

This patient has features of calciphylaxis. Calciphylaxis is a serious disorder characterized by systemic medial calcification of the arterioles that leads to ischemia and subcutaneous necrosis. Calciphylaxis is one of several types of extraosseous calcification (which also includes intimal, medial, and valvular calcifications) that may occur in patients with ESKD. Hyperparathyroidism, active vitamin D administration, hyperphosphatemia, and an elevated plasma calcium x phosphate product (Ca x P) are implicated in the genesis of calciphylaxis or calcific uremic arteriopathy (CUA).

Several medications have been implicated as significant risk factors for the development of CUA and these include the following: warfarin, calcium-based binders and vitamin D analogs, and systemic glucocorticoids. CUA can develop in the setting of warfarin anticoagulation through inhibition of vitamin K–dependent carboxylation of matrix Gla protein (MGP), a mineral-binding extracellular matrix protein that actively inhibits calcification of arteries and cartilage in an animal model. Thus, warfarin should be immediately discontinued in this patient, and alternative forms of anticoagulation should be considered.

References:

Mazhar AR, Johnson RJ, Gillen D, Stivelman JC, Ryan MJ, Davis CL, Stehman-Breen CO. Risk factors and mortality associated with calciphylaxis in end-stage renal disease. *Kidney Int* 2001; 60:324–332.

259. A patient with ESKD is diagnosed with calciphylaxis. All offending medications are discontinued. However, the skin lesions have worsened and developed a necrotic central area. The patient is prescribed a course of IV sodium thiosulfate in an effort to improve these skin lesions.

Which is a potential side effect of sodium thiosulfate?

- A. Metabolic alkalosis
- B. Non–anion gap metabolic acidosis
- C. Anion gap metabolic acidosis
- D. Hypokalemia
- E. Hyponatremia

Answer: C

Explanation:

Although sodium thiosulfate is almost always well tolerated, an associated increased anion gap metabolic acidosis has been reported and may be severe. The mechanism by which sodium thiosulfate causes acidosis is not known. One hypothesis is that thiosulfate is oxidized to sulfate either by the liver or by intestinal bacteria. Although IV sodium thiosulfate administration is usually excreted quickly and only thus partially metabolized, the excretion of nonmetabolized sodium thiosulfate is diminished among hemodialysis patients, resulting in an increase in metabolism to sulfate. Sodium thiosulfate itself is not an acid, as it does not donate protons. The use of high-bicarbonate dialysate may resolve sodium thiosulfate-induced metabolic acidosis.

References:

Cicone JS, Petronis JB, Embert CD, Spector DA. Successful treatment of calciphylaxis with intravenous sodium thiosulfate. *Am J Kidney Dis* 2004;43:1104–1108.

260. Which activity does fibroblast growth factor-23 (FGF-23) have?

- A. Is secreted by pulmonary fibrocytes
- B. Activates sodium-dependent phosphate reabsorption in the proximal tubule
- C. Activates hepatic production of 25(OH)vitamin D
- D. Inhibits 1- α hydroxylase activity in the proximal tubule
- E. Inhibits PTH production by the parathyroid glands

Answer: D

Explanation:

FGF-23 is a key regulator of phosphate homeostasis, and its production by bone osteocytes is stimulated by rises in serum phosphorus that occur in the setting of CKD. FGF-23 then acts on numerous downstream targets in an attempt to normalize serum phosphorus levels. These targets include 1) increases in PTH secretion from the parathyroid gland; 2) decreases in sodium-dependent phosphate reabsorption by the proximal tubule; and 3) decreases in 1- α hydroxylase activity. FGF-23 excess has also been associated with an increased risk for cardiovascular mortality.

References:

Liu S, Quarles LD. How fibroblast growth factor 23 works. *J Am Soc Nephrol* 2007;18:1637–1647.

261. A 48-year-old woman who underwent deceased donor kidney transplantation 4 years ago comes to the office because of a 2-month history of progressively severe left thigh and groin pain. She states that the pain is more severe when she is walking. There is no history of trauma. Other medical history includes the following: focal segmental glomerulosclerosis, osteoporosis treated with alendronate, and hypertension treated with lisinopril. Current immunosuppression medications include the following: tacrolimus, mycophenolic acid, and prednisone. Physical examination reveals pain with internal rotation and abduction of the left hip. Range of motion is limited slightly due to pain.

Serum laboratory work reveals the following:

Calcium: 10.2 mg/dL

Phosphorus: 2.6 mg/dL

Creatinine: 1.1 mg/dL

Parathyroid hormone (PTH), intact: 105 pg/nL

An MRI of her hip reveals a “double line sign” on T2 images, as well as a decreased marrow signal on the T1 image.

Which medication MOST likely increased her risk for development of this condition?

- A. Tacrolimus
- B. Mycophenolic acid
- C. Alendronate
- D. Prednisone
- E. Lisinopril

Answer: D

Explanation:

Avascular necrosis (AVN), sometimes referred to as osteonecrosis or ischemic necrosis, may occur as the result of several conditions or incidents, trauma being the most common. However, excessive corticosteroid use (cortisone) is also a high-risk factor that can lead to steroid-induced AVN. Unfortunately, when associated with excessive cortisone (steroid) use, AVN often is bilateral (occurring in both hips). It may also present in the hip and knee, complicating both assessment and treatment.

AVN occurs when the blood supply to the bone is disrupted, resulting in ischemia that eventually leads to bone cell death. This can lead to rapid joint destruction and bone collapse.

References:

Chan KL, Mok CC. Glucocorticoid-induced avascular bone necrosis: Diagnosis and management. *Open Ortho J* 2012;6:449–457.

262. **Which is TRUE regarding sevelamer as opposed to calcium-based phosphate binders for the treatment of hyperphosphatemia in CKD patients?**
- A. KDIGO guidelines recommend sevelamer as the first-line phosphate binder in all patients with hyperphosphatemia
 - B. Sevelamer is associated with significantly better control of serum phosphorus levels compared with calcium-based phosphate binders
 - C. Meta-analyses have shown improved mortality with non-calcium-based phosphate binders such as sevelamer
 - D. Calcium acetate and sevelamer both lower LDL cholesterol to similar degrees
 - E. Sevelamer is associated with a significantly lower incidence of gastrointestinal side effects

Answer: C

Explanation:

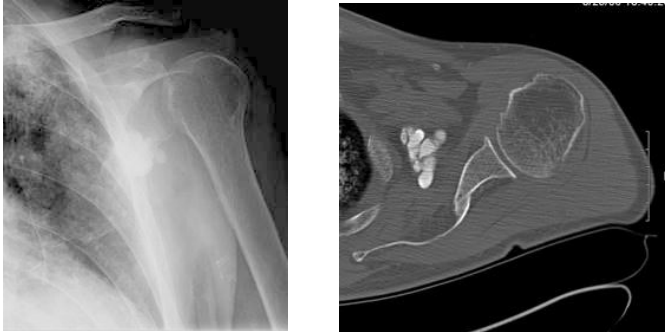
In two separate meta-analyses, sevelamer and non-calcium-containing phosphate binders have shown decreased mortality. Most recently, in a meta-analysis of 25 studies and 4770 participants, there was a 46% reduction in all-cause mortality risk for sevelamer compared with calcium-containing binders. Sevelamer is also associated with a lower serum calcium, higher intact PTH, lower total and LDL cholesterol, reduced risk of hypercalcemia, and increased risk of gastrointestinal side effects. Of note, although

studies differ, this most recent analysis did not find that sevelamer and calcium-containing binders differed greatly in the resulting serum phosphorus levels. KDIGO guidelines recommend restricting calcium-containing binders for patients with known vascular calcification, persistently low PTH, low/dynamic bone turnover, and persistent/recurrent hypercalcemia.

References:

Patel L, Bernard LM, Elder GJ. Sevelamer versus calcium-based binders for treatment of hyperphosphatemia in CKD: A meta-analysis of randomized controlled trials. *Clin J Am Soc Nephrol* 2016;11;232–244.

263. A 57-year-old man on chronic hemodialysis for 16 years with severe secondary hyperparathyroidism, anemia, intradialytic hypotension, idiopathic thrombocytopenic purpura (with bleeding episodes), and chronic back and knee pain developed severe left shoulder pain that worsened despite warm compresses, ibuprofen, and oxycodone. A plain film of the left shoulder is shown. A computed tomography (CT) scan was obtained and is also shown.



What is the diagnosis in this patient?

- A. Metastatic calcification
- B. B2-microglobulin deposition
- C. Brown tumor from severe secondary hyperparathyroidism
- D. Soft tissue bleed with calcific hematoma

Answer: A

Explanation:

The plain radiograph of the shoulder demonstrates tumoral calcification adjacent to the subscapularis muscle. The cause of this calcific lesion is metastatic calcification. The physiologic processes that predispose to metastatic calcification are not entirely known but include the following: 1) chronic metabolic acidosis leaching calcium and phosphate from bones; 2) severe secondary hyperparathyroidism; 3) intermittent metabolic alkalosis that develops during the hemodialysis procedure (predisposing to soft tissue precipitation of calcium salt); and 4) an elevated calcium-phosphate product, in particular hypercalcemia.

References:

Garg S, Sandur S, Buller GK. Dyspnea and left shoulder pain in an end-stage renal disease patient. *Semin Dial* 2007;20:172–173.

264. An ESKD patient on hemodialysis for 8 years develops painful, ulcerating calcific uremic arteriopathy (CUA) of the legs and abdomen. Labs include an intact PTH of 215 pg/mL, calcium of 9.2 mg/dL, and phosphate of 6.1 mg/dL.

In addition to aggressive wound care, which therapy is MOST appropriate for this patient?

- A. Low calcium dialysate, lanthanum with meals, and low-dose intravenous paricalcitol
- B. Urgent subtotal parathyroidectomy
- C. Intravenous sodium thiosulfate, lanthanum with meals, and daily dialysis with low calcium dialysate
- D. Intravenous pamidronate, oral cinacalcet, and lanthanum with meals

Answer: C

Explanation:

The optimal treatment for CUA is not known, but a multi-interventional strategy is likely to be more effective than any single therapy. No significant benefits in outcomes have been shown with any of the five most frequently used strategies for treatment. Further randomized control trials are needed. Aggressive wound care and adequate pain control are very important. Hyperbaric oxygen therapy is implemented, if available. IV sodium thiosulfate administered thrice weekly over the last hour of HD is recommended until there is resolution of the lesions. Correcting calcium and phosphate are also important and should be accomplished with avoidance of calcium-containing phosphate binders and vitamin D. Intact PTH should be lowered to less than 300 pg/mL with cinacalcet or surgical parathyroidectomy. Increased HD with a low calcium dialysate is also recommended to

correct calcium and phosphate to low normal levels. Stopping subcutaneous injections, intravenous iron, and warfarin are also recommended, as these may worsen lesions or cause new ones to form.

References:

Udomkarnjananun S, Kongnatthasate K, Praditpornsilpa K, Eiam-Ong S, Jaber BL, Susantitaphong P: Treatment of calciphylaxis in CKD: A systematic review and meta-analysis. *Kidney Int Rep* 2018; 4(2):231–244.
Baldwin C, Farah M, Leung M, Taylor P, Werb R, Kiaii M, Levin A. Multi-intervention management of calciphylaxis: A report of 7 cases. *Am J Kidney Dis* 2011;58:988–991.

265. Which is TRUE about treatment of secondary hyperparathyroidism in ESKD patients?

- A. Cinacalcet and paricalcitol improve overall mortality in ESKD patients
- B. Surgical parathyroidectomy is associated with improved survival in dialysis patients
- C. Surgical parathyroidectomy is not considered a risk factor for adynamic bone disease
- D. Repeated percutaneous alcohol ablation of parathyroid glands in ESKD patients with secondary hyperparathyroidism is more effective than surgical parathyroidectomy

Answer: B

Explanation:

Despite improved medical treatment of secondary hyperparathyroidism, parathyroidectomy is still necessary for many patients on chronic dialysis. The effect of parathyroidectomy on patient survival was examined. The study demonstrated an adjusted relative risk of death hazard ratio of 0.80 (0.65–0.99) for dialysis patients undergoing parathyroidectomy compared with matched controls, suggesting that parathyroidectomy was associated with improved survival in these patients. Cinacalcet and paricalcitol have not been shown to improve patient survival. Two randomized controlled trials, ADVANCE and EVOLVE, were performed to assess the effects of cinacalcet on cardiovascular calcification and the risk of cardiovascular events and mortality, respectively. The primary analysis of both trials did not find significant effects of cinacalcet on mortality; adynamic bone disease develops in situations with reduced osteoanabolic stimulation caused by oversuppression of PTH and multifactorial skeletal resistance to PTH actions in uremia. Various risk factors have been linked to adynamic bone disease, including calcium loading, aging, diabetes, hypogonadism, parathyroidectomy, peritoneal dialysis, and antiresorptive therapies, among others. Percutaneous ablation of parathyroid hyperplasia has not been shown to be more effective than surgical parathyroidectomy.

References:

Ivarsson KM, Akaberi S, Isaksson E, Reihner E, Rylance R, Prütz KG, Clyne N, Almquist M. The effect of parathyroidectomy on patient survival in secondary hyperparathyroidism. *Nephrol Dial Transplant* 2015;30:2027–2033.
Boyer J. Adynamic bone disease: From bone to vessels in chronic kidney disease. *Semin Nephrol* 2014;34:626–640.
Parfrey PS, Drüeke TB, Block GA, et al: The effects of cinacalcet in older and younger patients on hemodialysis: The Evaluation of Cinacalcet HCl Therapy to Lower Cardiovascular Events (EVOLVE) trial. *Clin J Am Soc Nephrol* 2015; 10(5):791–799

266. A 48-year-old man with ESKD from membranous glomerulonephritis has been receiving dialysis for 25 years. Recently he suffered a fractured humerus from a fall. His PTH is 1576 pg/mL and serum alkaline phosphatase 592 U/L. His PTH level has remained elevated despite receiving phosphate binders, paricalcitol, and cinacalcet. A parathyroidectomy is planned.

Which is MOST likely to occur during the first year after his surgery?

- A. Hypokalemia
- B. Increase in all-cause hospitalization
- C. Reduction in hospitalization for hypocalcemia
- D. Worsening of bone pain, myopathy, and pruritus

Answer: B

Explanation:

All-cause hospitalization increases in the first year after parathyroidectomy largely because of admissions for hypocalcemia. Hyperkalemia, not hypokalemia, can be seen in the immediate postoperative period. Hospitalization for hypocalcemia increases while bone pain, myopathy, and pruritus generally improve after parathyroidectomy.

References:

Ishani A, Liu J, Wetmore JB, et al: Clinical outcomes after parathyroidectomy in a nationwide cohort of patients on hemodialysis. *Clin J Am Soc Nephrol* 2015; 10(1):90–97.

267. A 75-year-old man with ESKD secondary to polycystic kidney disease is seen while receiving hemodialysis. Monthly dialysis laboratory test results return with the following values: PTH 825 pg/ml, calcium 9.7 mg/dL, and phosphorus 5.2 mg/dL. He is receiving high doses of non–calcium-containing phosphate binders and 8 µg of paracalcitol per treatment. You decide to add cinacalcet.

Which statement about cinacalcet is TRUE?

- A. Decreases the serum phosphorus concentration by 25-50%
- B. Decreases PTH concentration even in patients with severe secondary hyperparathyroidism
- C. Reduces the sensitivity of the PTH receptor to calcium
- D. Causes a downregulation of the calcium-sensing and vitamin D receptors in the parathyroid gland

Answer: B

Explanation:

Cinacalcet decreases PTH concentration by an average of 47% even in patients with severe secondary hyperparathyroidism. Serum phosphorus declines on average by 7%. Calcimimetics such as cinacalcet increase the sensitivity of the calcium-sensing receptor for calcium. Cinacalcet upregulates the calcium-sensing and vitamin D receptors in the parathyroid gland.

268. A 74-year-old man is starting dialysis as a result of diabetic nephropathy. Prior to starting dialysis, he had been treated with calcium-containing binders. Laboratory tests yield the following values:

Blood urea nitrogen	97 mg/dL
Serum creatinine	9.7 mg/dL
PTH	35 pg/mL
Serum calcium	10.2 mg/dL
Serum phosphorus	5.5 mg/dL

How would you manage his suspected bone disorder?

- A. Start paracalcitol.
- B. Start cinacalcet.
- C. Switch to non–calcium-containing phosphate binders.
- D. Increase his dialysate calcium concentration.

Answer: C

Explanation:

The patient likely has adynamic bone disease. Of the choices listed, the best would be to switch to non–calcium-containing phosphate binders. The other choices would likely lead to further suppression of PTH.

269. You are counseling a family with ADPKD about possible kidney transplant donation. All potential donors are ABO blood type compatible. The recipient is a 38-year-old man on dialysis who is in excellent health except for his ESKD. He has a 19-year-old son with no known ADPKD. The recipient’s brother is 25 years old and has normal renal function with a single cyst in his right kidney and two 1-cm cysts in his left kidney. He and the potential recipient are human leukocyte antigen (HLA) identical. The potential recipient has another sibling, a sister, who is 52 years old with no cysts and an estimated GFR of 70 mL/min/1.73 m². She is haploidentical. The sister’s son, age 24, is healthy and also has agreed to be a potential donor.

Among the group of potential donors, who would be the BEST donor?

- A. The 19-year-old son
- B. The HLA-identical brother
- C. The 24-year-old nephew
- D. The haploidentical sister
- E. None of the above

Answer: C

Explanation:

PKD is transmitted as an autosomal dominant, and the sister who is 50 years old is free of the disease and has normal function but is 14 years older than the recipient. Because of the autosomal dominant form of transmission, the nephew should not have the disease. He is healthy and much younger than his mother, and therefore, the nephew would be an ideal donor. The HLA identical brother is less than 30 years old and has cysts in both kidneys and thus is likely to carry the abnormal gene for PKD. The 19-year-

old son of the patient is too young to exclude PKD without DNA testing and even then the exclusion would not be foolproof. The haploidentical sister is significantly older than the patient and thus the nephew probably would be the best donor, although the sister is acceptable.

270. A 26-year-old African-American man received a deceased donor renal transplant 6 weeks ago. The donor and recipient were cytomegalovirus (CMV) positive. Immunosuppression has included mycophenolate mofetil 1 g twice per day, cyclosporine 200 mg twice per day, and prednisone 7.5 mg daily. Over the last 2 days, he has developed a fever, cough, and some pleuritic chest pain on the right side. Chest x-ray reveals an infiltrate in the left lower lobe. His temperature is 100°F. You order the appropriate blood and sputum cultures and start him on azithromycin for 3 days. You ask him to come back to the clinic in 1 week. He returns at that time feeling much better. His serum creatinine, however, is increased to 1.7 mg/dL, with a BUN of 27. These are both increased from his baseline values. His volume status appears appropriate on physical examination.

At this point, what would you immediately do?

- A. Biopsy and treat for acute rejection
- B. Draw donor-specific antibodies
- C. Reduce his cyclosporine dose
- D. Observe the patient for a few days and recheck labs
- E. Get a stat ultrasound to exclude ureteral obstruction

Answer: D

Explanation:

Drug interactions are very common with cyclosporine-based immunosuppression. The interaction of macrolides with cyclosporine due to inhibiting cytochrome P450 enzymes is common. Usually, the serum creatinine rises over several days and returns to normal on the same dose of cyclosporine once the antibiotic has left the patient's system. Treating for rejection is logical but probably unnecessary in this case given the circumstances. He is clinically improved, and his only real abnormality is the rise in creatinine, which probably can be attributed to the drug interaction. Drawing donor-specific antibodies at this point would also be unnecessary because there is no evidence of a humoral-mediated process. He is unlikely to have any infection from CMV, with both donor and recipient being positive and this being an early time post-transplant. Ureteral obstruction is possible, but there is no clinical evidence that this is the case.

271. **Which is correct regarding the use of mycophenolate for immunosuppression?**

- A. Routine trough blood level monitoring has been shown to be effective in reducing side effects
- B. Substituting enteric-coated mycophenolate has improved the gastrointestinal safety profile
- C. Mycophenolate is associated with a reduced incidence of BK viremia
- D. Mycophenolate causes more diarrhea in patients treated with tacrolimus than cyclosporine
- E. Mycophenolate is efficacious only in doses greater than 2 g/day

Answer: D

Explanation:

Mycophenolate has been a valuable addition to the therapeutic armamentarium of transplant physicians. Its major side effect is gastrointestinal upset including nausea, vomiting, abdominal cramping, and diarrhea. Because of the inhibition of enterohepatic circulation with cyclosporine, total mycophenolate mofetil (MMF) exposure is greater with MMF/Tacrolimus (Tac). Routine blood levels are not clinically useful, and enteric coating in controlled studies is not efficacious in reducing side effects. BK virus is enhanced in MMF-based regimens.

272. **Which drug class is MOST likely to result in transplant rejection if immunosuppressive drug doses are not adjusted?**

- A. Macrolide antibiotics
- B. Non-dihydropyridine calcium channel blockers
- C. Antifungal drugs
- D. Anticonvulsants
- E. Trimethyl sulfamethoxazole

Answer: D

Explanation:

Macrolide antibiotics, antifungal agents such as fluconazole and ketoconazole, and non-dihydropyridine calcium channel blockers all inhibit metabolism and predispose to toxicity and not rejection. Anticonvulsants induce the cytochrome P4503A4 isoenzyme and thus often result in subtherapeutic drug levels unless doses are adjusted upward. Trimethyl sulfamethoxazole has little effect on cytochrome P450 metabolism.

273. A 46-year-old man is being treated with alemtuzumab induction therapy, 30 mg IV as a single dose followed by tacrolimus monotherapy. High-dose corticosteroids are given at the time of transplant and tapered rapidly over 7 days. This is the patient's first transplant. The donor is a haploidentical sister, and the patient has never received a blood transfusion. Plasma panel reactive antibodies are negative.

When comparing immuno-modulating induction agents, which is TRUE?

- A. Compared with basiliximab, alemtuzumab is associated with fewer early rejection episodes
- B. Alemtuzumab is superior to thymoglobulin in lowly sensitized transplant recipients
- C. Alemtuzumab is inferior to thymoglobulin in highly sensitized patients
- D. Basiliximab has more first dose reaction side effects than alemtuzumab
- E. Post-transplant lymphoproliferative disease is more common with alemtuzumab than thymoglobulin

Answer: A

Explanation:

Alemtuzumab has been used successfully with rapid steroid withdrawal in renal transplant recipients. In low-risk patients, this drug is superior to basiliximab, fewer rejection reactions are seen early, and graft and patient survival is excellent. Alemtuzumab causes more first dose reactions than basiliximab. It has not been shown to be superior to thymoglobulin for high-risk patients, and the relative frequency of post-transplant lymphoproliferative disease (PTLD) after both agents seems to be similar.

References:

Hanaway MJ, Woodle ES, Mulgaonkar S, Peddi VR, Kaufman DB, First MR, Croy R, Holman J; INTAC Study Group. Alemtuzumab induction in renal transplantation. *N Engl J Med* 2011;364:1909–1919.

274. A 25-year-old patient has been diagnosed with relapsing hemolytic uremic syndrome (HUS) and is approaching ESKD. A living-donor transplantation is being considered.

Which gene mutation has the BEST prognosis following renal transplantation?

- A. Factor H
- B. Factor I
- C. CD46 (MCP)
- D. C3

Answer: C

Explanation:

HUS features overactivity of the alternative complement pathway. The most common cause is the loss of function of the complement regulators: Factor H, Factor I, and membrane cofactor. Less often atypical HUS comes from a gain of function mutation of C3 or Factor B. All of the mutations listed above other than CD46 are associated with recurrence of disease after renal transplantation. CD46 is tissue bound, so the new kidney (assuming it is coming from a normal donor) will have normal structure and function of CD46 and hence is not associated with recurrence.

References:

Fremeaux-Bacchi V1, Moulton EA, Kavanagh D, Dragon-Durey MA, Blouin J, Caudy A, Arzouk N, Cleper R, Francois M, Guest G, Pourrat J, Seligman R, Fridman WH, Loirat C, Atkinson JP. Genetic and functional analyses of membrane cofactor protein (CD46) mutations in atypical hemolytic uremic syndrome. *J Am Soc Nephrol* 2006;17:2017–2025.

275. A 50-year-old woman with a history of membranous glomerulopathy as a cause of ESKD received a renal transplant 6 years ago. She has nephrotic range proteinuria and a rise in her serum creatinine from her baseline. Her biopsy shows thickened glomerular capillary loops on Periodic Acid-Schiff (PAS), double contours on silver stain, C4d positivity of intertubular capillaries, and multilayering of capillary basement membrane.

What is the MOST likely diagnosis?

- A. Acute humoral rejection
- B. Recurrent membranous glomerulopathy
- C. Acute T cell-mediated rejection
- D. Transplant glomerulopathy
- E. Chronic active antibody-mediated rejection

Answer: E

Explanation:

The clinical story provided suggests a diagnosis of recurrent membranous glomerulopathy, transplant glomerulopathy, or chronic active antibody-mediated rejection. Recurrent membranous glomerulopathy should show spikes on silver stain and not double contours. Furthermore, deposits should be documented on electron microscopy. Transplant glomerulopathy is likely present, but the finding of both C4d positivity and multilayering of capillary basement membrane defines the more inclusive diagnosis of chronic active antibody-mediated rejection. The C4d positivity supports a diagnosis of acute humoral rejection, but all of the other findings are more consistent with chronic disease. No evidence is described that supports a diagnosis of acute T cell-mediated rejection. This shows interstitial inflammation, endothelialitis, and arteritis at various degrees.

276. A 32-year-old man is evaluated for a kidney transplant after learning that he has kidney failure on routine health evaluation. He admits to a past with multiple unhealthy choices including IV drug use, resulting in HIV and Hepatitis C. He has an offer for a living-related renal transplant, so he can avoid dialysis.

Which condition represents an absolute contraindication to kidney transplantation?

- A. HIV positivity and history of thrush
- B. History of IV drug use 10 years ago
- C. Hepatitis C positive with liver biopsy showing mild inflammation
- D. Renal cell carcinoma (RCC) with extension into the renal vein 2 years ago

Answer: D

Explanation:

Know the relative versus absolute contraindications to kidney transplantation. All of these conditions are not contraindications to transplant except RCC that has possible spread beyond its borders; therefore, a waiting period that is longer than 2 years is recommended. There is no need to delay transplant in a patient that has a small or incidentally discovered RCC that has been removed in its entirety.

References:

Frasca G, Brigante F, Volpe A, Cosmai L, Gallieni M, Porta C: Kidney transplantation in patients with previous renal cancer: A critical appraisal of current evidence and guidelines. *J Nephrol* 2019; 32: 57–64.

Kasiskie BL, Cangro CB, Hariharan S, Hricik DE, Kerman RH, Roth D, Rush DN, Vazquez MA, Weir MR. The evaluation of renal transplant candidates: Clinical practice guidelines. *Am J Transplant* 2001;1(Suppl 2):5–95.

277. **Compared with tacrolimus, a decrease in which is associated with cyclosporine?**

- A. Diabetes mellitus
- B. Hirsutism
- C. Nephrotoxicity
- D. Hypertension

Answer: A

Explanation:

Know the side effect profiles associated with the two available calcineurin inhibitors. Cyclosporin is known to have less diabetes association. It has more hirsutism, while tacrolimus has alopecia. The hypertension may be higher in cyclosporin, but both medications are implicated in this finding. The differences between nephrotoxicity are similar.

References:

Fung JJ. Tacrolimus and transplantation: A decade in review. *Transplantation* 2004;77(Suppl):S41–S43.

Webster AC, Woodroffe RC, Taylor RS, Chapman JR, Craig JC. Tacrolimus vs ciclosporin as primary immunosuppression for kidney transplant recipients: Meta-analysis and meta-regression of randomized trial data. *BMJ* 2005;331:810.

278. A 68-year-old man with ESKD secondary to type 2 diabetes mellitus complains of fatigue 9 months following a living donor transplant from his son. His postoperative course has been unremarkable, and there have been no episodes of rejection. His BP was elevated prior to transplantation and remained elevated after transplant. Medications include tacrolimus, mycophenolate mofetil, amlodipine, lisinopril, sulfamethoxazole-trimethoprim, omeprazole, and insulin. Laboratory studies show the following: BUN, 18 mg/dL; serum creatinine, 0.8 mg/dL; WBC, 5700; Hgb, 9.3 g/dL; Hct, 28.3%.

Which medication is MOST likely contributing to the patient's anemia?

- A. Lisinopril
- B. Omeprazole
- C. Amlodipine
- D. Tacrolimus

Answer: A

Explanation:

Recognize the causes of anemia in kidney transplant recipients. ACE inhibitors are a well-described cause of anemia in this patient population. Amlodipine has no issues associated with anemia. Omeprazole can limit the absorption of magnesium, so this should be monitored. Although tacrolimus can cause marrow suppression, other adverse effects are often seen first. This leaves lisinopril as the most likely cause of anemia, possibly due to its ability to limit angiotensin II, which is a stimulator of erythropoietin, or its ability to increase renal blood flow, therefore limiting hypoxia-inducible factors.

References:

Vanrenterghem Y, Ponticelli C, Morales JM, Abramowicz D, Baboolal K, Eklund B, Kliem V, Legendre C, Morais Sarmiento AK, Vincenti F. Prevalence and management of anemia in renal transplant recipients: A European survey. *Am J Transplant* 2003;3:835–845.

279. Which immunosuppressant has been associated with a decreased incidence of squamous cell carcinoma of the skin in patients at high risk for recurrent cutaneous cancer?

- A. Azathioprine
- B. Sirolimus
- C. Cyclosporine
- D. Tacrolimus

Answer: B

Explanation:

Be familiar with the antineoplastic effects of sirolimus. This medication is often used in patients with a history of skin cancers to help reduce the risk of recurrence. Side effects of sirolimus include edema, hypertriglyceridemia, hypertension, and mouth sores.

References:

Euvard S, Morelon E, Rostaing L, Goffin E, Brocard A, Tromme I, Broeders N, del Marmol V, Chatelet V, Domp Martin A, Kessler M, Serra AL, Hofbauer GF, Pouteil-Noble C, Campistol JM, Kanitakis J, Roux AS, Decullier E, Dantal J; TUMORAPA Study Group. Sirolimus and secondary skin-cancer prevention in kidney transplantation. *N Engl J Med* 2012;367:329–339.

280. Long-term survival of renal allografts tends to be the worst in patients with which combination?

- A. Donor specific antibody (DSA) negative, C4d staining negative
- B. DSA positive, C4d negative
- C. DSA negative, C4d positive
- D. DSA positive, C4d positive

Answer: D

Explanation:

Know the risks for chronic humoral rejection.

References:

Cosio F, Gloor JM, Sethi S, Stegall MD. Transplant glomerulopathy. *Am J Transplant* 2008;8:492–496.

281. Which posttransplant malignancy is often mediated by Epstein-Barr viral infection?

- A. Cancer of the cervix
- B. Basal cell carcinoma of the skin
- C. Kaposi's sarcoma
- D. Lymphoma

Answer: D

Explanation:

Know the most common malignancies that occur after kidney transplantation. Learners should also know which skin cancers are most common after kidney transplantation. Lymphoma, often arising in the CNS, has been well associated with Epstein-Barr infection. Kaposi's sarcoma is also seen post transplant but associated with human herpesvirus 8 (HHV8). Cervical cancer is associated with human papillomavirus (HPV).

References:

Vajdic CM, McDonald SP, McCredie MR, van Leeuwen MT, Stewart JH, Law M, Chapman JR, Webster AC, Kaldor JM, Grulich AE. Cancer incidence before and after kidney transplantation. *JAMA* 2006;296:2823–2831.
Penn I. Primary kidney tumors before and after renal transplantation. *Transplantation* 1995;59:480–485.

282. Kathy is a 48-year-old Asian woman who underwent cadaveric renal transplant 8 months ago. She is cytomegalovirus (CMV) D+/R- and completed 6 months of valganciclovir prophylaxis about 2 months ago. She received alemtuzumab induction and is currently taking cyclosporine 150 mg BID, mycophenolic acid 500 mg BID, and TMP-SMX ss QD. She presents with a week of progressive fatigue, a swollen lymph node under her arm, and new fevers over the last 2 days.

Which infection does she MOST likely have?

- A. Cytomegalovirus
- B. BK virus
- C. Bacteremia from the central line she had in place for the first 4 postoperative days
- D. *Aspergillus* pneumonia
- E. *Pneumocystis jiroveci* pneumonia

Answer: A

Explanation:

Infections typically occur in three time periods: early post-transplant (first 30 days after transplant), peak immunosuppression period (30 days to 6 months after transplant), and late infections (≥ 6 months after transplant). This infection is occurring in the late infection period but is occurring about 2 months after stopping valganciclovir prophylaxis. Six months of valganciclovir prophylaxis is associated with an approximate 16% incidence of CMV, most of it occurring in the first few months after stopping prophylaxis.

References:

Fishman JA. Infections in solid-organ transplantation. *N Eng J Med* 2007;357:2601–2614.
Humar A, Lebranchu Y, Vincenti F, Blumberg EA, Punch JD, Limaye AP, Abramowicz D, Jardine AG, Voulgari AT, Ives J, Hauser IA, Peeters P. The efficacy and safety of 200 days valganciclovir for cytomegalovirus prophylaxis in high-risk kidney transplant recipients. *Am J Transplant* 2010;10:1228–1237.
Razonable RR, Humar A, for the AST ID Community of Practice. Cytomegalovirus infections in solid organ transplantation. *Am J Transplant* 2013;13:s93–s106.

283. Sarah is a 67-year-old Caucasian woman who underwent living donor kidney transplantation 5 years ago. She is establishing care with you.

In reviewing her vaccinations, which do you recommend to the patient?

- A. Never receive an influenza vaccine because of the risk of rejection
- B. Receive the Zostavax because she is older than 65 years of age
- C. She and her close contacts should receive their influenza vaccine every year
- D. She should receive a Bacillus Calmette–Guérin (BCG) vaccine if she plans to travel to India
- E. It is ok for her husband to receive the smallpox vaccine prior to starting a new job in the US military

Answer: C

Explanation:

All transplant recipients and their close contacts should receive their annual influenza vaccine every year. They should maintain routine adult screening, but live vaccines, including the Zostavax and BCG, are generally contraindicated in transplant recipients. Live virus vaccines can usually be safely given to close contacts of transplant recipients with the exception for smallpox vaccine, which is contraindicated in close contacts because of the risk of disseminated vaccinia in the transplant recipient.

References:

Danzinger-Isakov L, Kumar D, for the AST ID Community of Practice. Vaccination in solid organ transplantation. *Am J Transplant* 2013;13:s311–s317.

284. On kidney biopsy, by what is acute humoral rejection characterized?

- A. Mesangial staining for C4d
- B. Interstitial fibrosis
- C. Interstitial nephritis
- D. Neutrophils in peritubular and/or glomerular capillaries
- E. Tubulitis

Answer: D

Explanation:

A classical histological finding in acute humoral rejection is the presence of neutrophils in peritubular and/or glomerular capillaries. Mesangial staining for C4d is present in all biopsies and is used as a positive control. Interstitial fibrosis is a chronic nonspecific alteration. Interstitial nephritis is typical of drug hypersensitivity or infection. Tubulitis is seen in acute cell-mediated rejection and is not a feature of humoral rejection.

285. A 40-year-old man received his renal allograft 1 year ago and was recently treated for acute cellular rejection, type 2. Subsequent to the treatment for acute rejection, his maintenance immunosuppressive regimen was increased. His creatinine had initially improved in response to therapy, but it has risen again 2 months later. A biopsy was performed.

What are the findings MOST likely to show?

- A. Tubulitis
- B. Nuclear inclusions in tubular epithelial cells with chronic inflammation
- C. Nuclear inclusions in tubular epithelial cells with acute necrotizing inflammation
- D. Endothelialitis
- E. Mixed interstitial inflammation with eosinophils

Answer: B

Explanation:

This patient most likely now has a polyoma virus infection. The findings described in choice B are those representing polyoma virus infection, which has increased immunosuppression as the most important risk factor. The findings in A and D represent type 1 and type 2 rejection, respectively, and are less likely to complicate successful treatment of rejection. The findings in C are those of adenovirus, which is a rare infection not usually associated with changes in immunosuppression. The findings in E would be seen in association with drug hypersensitivity. However, they are not associated with immunosuppressive regimens.

286. A transplant patient on the same tacrolimus dose for 5 years started on a health food diet and over-the-counter herbal products. The transplant center noted that his tacrolimus levels have abruptly decreased to unacceptably low levels, putting him at risk for rejection. The nurse coordinator accused him of being noncompliant, but the patient insisted he was taking his medication as prescribed.

What is your assessment?

- A. This patient is noncompliant with medications.
- B. This patient is taking grapefruit extracts.
- C. This patient is taking St. John's Wort.
- D. This patient is taking creatine supplements.
- E. This patient is taking echinacea.

Answer: C

Explanation:

St. John's Wort contains biologically active substances that activate the hepatic P450 system and P-glycoprotein system, enhancing the metabolism of tacrolimus and increasing its secretion, respectively (option C). Grapefruit extracts do the opposite and inhibit the metabolism of calcineurin inhibitors, raising the drug levels. Creatine is nephrologically safe to take and does not affect drug levels of tacrolimus. Echinacea is also devoid of any drug interactions with the P450 system; therefore, it should not alter the drug levels. The cytochrome P450 system, specifically the CYP3A4 pathway, is the one that is affected by St. John's Wort, and many antiarrhythmics, highly active antiretroviral therapy (HAART), thyroid supplements, oral contraceptives, and antiseizure agents may be affected.

287. You are seeing a 54-year-old male engineer with ADPKD who is being evaluated for possible kidney transplantation. His current estimated GFR is 17 mL/min/m². He is interested in learning the various risks and benefits of the different immunosuppressive regimens and recalls reading something about a new trial demonstrating long-term superiority of a newer medication, belatacept.

Which is TRUE about belatacept?

- A. Seven years after transplantation, eGFRs were significantly higher with belatacept than with cyclosporine
- B. Compared with cyclosporine, belatacept is associated with a significantly higher rate of serious infections
- C. Compared with cyclosporine, belatacept is associated with a significantly higher rate of cancer
- D. Belatacept was associated with greater graft and patient survival but only in those patients receiving grafts from extended criteria donors
- E. Patients on belatacept develop donor-specific antibodies at a higher rate than patients receiving cyclosporine

Answer: A

Explanation:

A seminal trial demonstrated that an immunosuppressive regimen based on costimulatory blockade with belatacept led to superior graft and patient survival rates at 7 years after transplant, as well as improved eGFR compared with a cyclosporine-based regimen. Furthermore, rates of serious infections or cancer were similar to the cyclosporine-based regimen. In a prior trial in patients receiving belatacept after transplant with extended criteria donors, patient and graft outcomes were equivalent to those with cyclosporine. Finally, the development of donor-specific antibodies occurs at a similar frequency as patients receiving cyclosporine.

References:

Vincenti F, Rostaing L, Grinyo J, Rice K, Steinberg S, Gaithe L, Moal MC, Mondragon-Ramirez GA, Kothari J, Polinsky MS, Meier-Kriesche HU, Munier S, Larsen CP. Belatacept and long-term outcomes in kidney transplantation. *N Engl J Med* 2016;374:333–343.

288. Cytomegalovirus (CMV) is a common infection after transplant.

Which statement is FALSE regarding preventative strategies?

- A. Universal antiviral prophylaxis is associated with a lower rate of graft failure
- B. Only universal antiviral prophylaxis is protective against CMV after transplant
- C. In high-risk (D+/R-) kidney transplant patients, 6 months of valganciclovir is associated with a lower risk of CMV infection than 3 months
- D. Valacyclovir can be used to prevent CMV among kidney transplant patients
- E. CMV-negative or leuko-reduced blood products should be used in CMV D-/R- patients to prevent CMV infection

Answer: B

Explanation:

Both universal antiviral prophylaxis (medications to all recipients) and preemptive therapy (prophylaxis toward high-risk recipients) are associated with reduced risk of CMV infection and disease. Universal prophylaxis is associated with a lower risk of graft rejection and failure than preemptive therapy. High risk (D+/R-) kidney transplant recipients have a reduced rate of CMV at 1 year, with 6 months of valganciclovir prophylaxis compared with 3 months of valganciclovir prophylaxis (choice C). High-dose valacyclovir has been proven to reduce the frequency of CMV among kidney transplant recipients (choice D). The risk of CMV in D-/R- patients can be minimized by using CMV-negative or leuko-reduced blood (choice E).

References:

Humar A, Lebranchu Y, Vincenti F, Blumberg EA, Punch JD, Limaye AP, Abramowicz D, Jardine AG, Voulgari AT, Ives J, Hauser IA, Peeters P. The efficacy and safety of 200 days valganciclovir for cytomegalovirus prophylaxis in high-risk kidney transplant recipients. *Am J Transplant* 2010;10:1228–1237.

Razonable RR, Humar A; for the AST ID Community of Practice. Cytomegalovirus infections in solid organ transplantation. *Am J Transplant* 2013;13:s93–s106.

289. **Which is TRUE regarding the use of belatacept?**

- A. It is contraindicated in patients with allergies or prior exposure to horse serum
- B. It is contraindicated in patients who are seronegative to Epstein-Barr virus (EBV)
- C. A higher mycophenolate mofetil (MMF) dose may be needed after switching from cyclosporine to belatacept
- D. Belatacept dose adjustment is needed when there is use of drugs metabolized through the cytochrome P450 system

Answer: B

Explanation:

Belatacept, a selective T-cell costimulation blocker, is a soluble fusion protein consisting of the modified extracellular domain of cytotoxic T-lymphocyte-associated protein (CTLA)-4 fused to a portion (hinge-CH2-CH3 domains) of the Fc domain of a human

immunoglobulin G1 antibody. Belatacept is produced by recombinant DNA technology in a mammalian cell expression system, and thus prior exposure to horse or rabbit serum is not a contraindication (choice A). There is an increased risk for developing post-transplant lymphoproliferative disorder (PTLD), predominantly involving the CNS. Recipients without immunity to EBV are at a particularly increased risk; therefore, belatacept should be used in EBV-seropositive patients only (choice B). Do not use belatacept in transplant recipients who are EBV seronegative or with unknown EBV serostatus. As cyclosporine decreases mycophenolic acid (MPA) levels by preventing enterohepatic recirculation of MPA, belatacept does not. A lower MMF dosage may be needed after switching from cyclosporine to belatacept, because this may result in higher MPA concentrations and increase the risk for adverse reactions related to MPA (choice C). No dosage adjustments are needed for drugs metabolized via CYP1A2, CYP2C9, CYP2D6, CYP3A, and CYP2C19 when coadministered with belatacept.

References:

Belatacept drug information (<http://www.fda.gov/downloads/Drugs/DrugSafety/UCM261711.pdf>).

290. Compared with all patients in the national transplant database in the United States, which outcome is expected with HIV-positive kidney transplant patients whose conditions are well controlled with a combined antiretroviral treatment regimen?
- A. Higher rates of allograft survival and lower rejection rates
 - B. Higher patient survival rates
 - C. Lower patient and allograft survival, with higher rejection rates
 - D. Similar rates of infections

Answer: C

Explanation:

Renal transplantation is now being performed in carefully selected patients with undetectable viral load levels and CD4 counts >200/mm³. In a cohort of 150 patients, patient and allograft survival was somewhere between all patients in the US national transplant database and those ≥65 years of age. A higher-than-expected rejection rate was noted at years 1 and 3. HIV infection remained well controlled without any complications from HIV. Infection rates were higher than average.

References:

Stock PG, Barin B, Murphy B, Hanto D, Diego JM, Light J, Davis C, Blumberg E, Simon D, Subramanian A, Millis JM, Lyon GM, Brayman K, Slakey D, Shapiro R, Melancon J, Jacobson JM, Stosor V, Olson JL, Stablein DM, Roland ME. Outcomes of kidney transplantation in HIV-infected recipients. *N Engl J Med* 2010;363:2004–2014.

291. A 45-year-old woman who lost her first transplantation to recurrent FSGS is evaluated for a second transplant. History is notable for 3 childbirths and a motor vehicle accident requiring 3 blood transfusions. Her fiancé, who is a potential kidney donor, fathered one of her children. Her PRA is 65%. On examination, her BMI is 33, her BP 159/90 mmHg, and her heart rate 88/min.

	Blood Type	HLA Typing		
Patient	AB	A2, 3	B3, 9	DR2, 12
Fiancé	O	A2, 4	B7, 9	DR2, 12
First kidney transplantation		A2, 3	B8, 10	DR3, 14

The complement-dependent cytotoxicity crossmatch shows a positive T- and B-cell crossmatch. Luminex testing reveals a donor-specific antibody for A4.

Which is the MOST likely cause of the positive crossmatch?

- A. Anti–blood group antibodies
- B. Her elevated PRA
- C. Antigen exposure during pregnancy
- D. Sensitization during first kidney transplant

Answer: C

Explanation:

The potential donor was the father of one of the recipient’s children. That child received half of his or her HLA antigens from the father (and half from the mother). During pregnancy, the fetus exposed the mother’s immune system to the HLA antigens that the fetus inherited from the father. This exposure may well have led to antibody formation and a positive crossmatch, indicating the potential for later rejections (choice C). Without HLA-testing the child (and checking whether the child carries HLA A4), we do not know with absolute certainty that is how our patient (the potential recipient) developed the antibody to A4. Nonetheless, given the choices provided, this is the most likely explanation.

Because the recipient is AB (a universal recipient), she would not have antibodies to either A or B, and furthermore, the donor is O, a universal donor with no red blood cell surface antigens against which to have any antibody expression (choice A).

The PRA, or panel of reactive antibodies, simply quantifies the antibodies that a recipient has against a group of potential donors. It is not the cause of sensitization; it is a measure of sensitization (choice B).

The kidney of the first donor does not share any unique antigens with the fiancé. In other words, any antigens that the first kidney and the fiancé have (A2) are present in the recipient and thus would not generate an antibody response (choice D).

References:

Mulley WR, Kanellis J. Understanding crossmatch testing in organ transplantation: A case-based guide for the general nephrologist. *Nephrology* 2011;16:125–133.

Kumbala D, Zhang R. Essential concept of transplant immunology for clinical practice. *World J Transplant* 2013;3:113–118.

Susal C, Morath C. Virtual PRA replaces traditional PRA: Small change but significantly more justice for sensitized patients. *Transpl Int* 2015;28:708–709.

292. A 40-year-old woman who is 7.5 years status post-deceased donor kidney transplant for ESKD secondary to IgA is referred for evaluation after her serum creatinine level increases from 1.1 to 1.5 mg/dL. She has not taken her prednisone for 3 years. Current immunosuppression includes mycophenolate mofetil, 1000 mg twice daily, and tacrolimus, 2 mg twice daily. Her tacrolimus trough is 4 ng/mL.

A kidney biopsy is obtained and reveals acute rejection, type IA (Banff '15) with prominent aggregates of interstitial plasma cells and diffuse C4d peritubular capillary deposition with glomerular and peritubular capillaritis.

Which is the MOST appropriate next test to obtain?

- A. Donor-specific antibodies
- B. Flow cytometry
- C. Mycophenolate trough
- D. Panel of reactive antibodies (PRA)

Answer: A

Explanation:

The patient has evidence of a cellular rejection (the Type IA), but the other findings (peritubular capillaritis and C4d deposition) are indicative of an antibody-mediated rejection (AMR). Assessing AMR requires 3 findings: morphologic evidence on biopsy (the peritubular capillaritis), evidence of antibody interacting with endothelium (the C4d staining), and then serologic evidence.

Presence of donor-specific antibodies (DSAs) would be that final criterion or the serologic evidence needed for the diagnosis (choice A). In addition, finding DSAs is important for management, because reducing them would be a goal. Flow cytometry is used before transplant to determine whether there may be anti-T- or B-cell antibodies present in the recipient (choice B).

A mycophenolate trough would not help you with either diagnosis or management. It is a test that is infrequently used clinically and, in this case, would provide little information (choice C).

The PRA is a test done for patients awaiting a transplant to provide a measure of how sensitized the patient is against an array of HLA antigens commonly found in the patient's area. If the patient has a lot of antibodies (and thus is very sensitized), it will be harder to find a kidney that the transplant candidate will be able to receive (choice D).

References:

Garces JC, Giusti S, Staffeld-Coit C, Bohorquez H, Cohen AJ, Loss GE. Antibody-mediated rejection: A review. *Ochsner J* 2017;17:46–55.

293. You are considering changing the therapy for a 19-year-old female college freshman who received a kidney transplant from her sister from a regimen of tacrolimus, mycophenolate mofetil, and prednisone to one of belatacept, mycophenolate mofetil, and prednisone.

Which is an important factor influencing your decision?

- A. The higher incidence of viral infections in tacrolimus-treated patients compared with those taking belatacept
- B. The decreased likelihood of a rejection with a belatacept-based regimen compared with a tacrolimus-based regimen
- C. The increased ability to monitor for and prevent nonadherence in patients receiving belatacept compared with those receiving tacrolimus
- D. The decreased likelihood of post-transplant lymphoproliferative disease with belatacept compared with tacrolimus

Answer: C

Explanation:

Unlike tacrolimus, belatacept is given intravenously in an infusion center or by a visiting nurse at the patient's home. Consequently, you will know if the dose is given. In addition, the effect is long-lasting. One dose lasts a month, and thus the patient is not dependent on taking a medication daily. Even if the patient skips the mycophenolate mofetil and prednisone, they still have belatacept in their system.

Viral infections are as common in belatacept-treated patients as those receiving standard immunosuppression.

Rejections are seen more frequently at the beginning in belatacept-treated patients and no less frequently later on. Nevertheless, kidney function is better.

Post-transplant lymphoproliferative disease has been frequently seen among patients who are Epstein–Barr virus negative and taking belatacept and even more frequently when compared with tacrolimus early on.

References:

Lerch C, Kanzelmeyer NK, Ahlenstiel-Grunow T, Froede K, Kreuzer M, Drube J, Verboom M, Pape L. Belatacept after kidney transplantation in adolescents: A retrospective study. *Transpl Int* 2017;30:494–501.

Masson P, Henderson L, Chapman JR, Craig JC, Webster AC. Belatacept for kidney transplant recipients. *Cochrane Database Syst Rev* 2014;11:CD010699.

Taylor AL, Watson CJ, Bradley JA. Immunosuppressive agents in solid organ transplantation: Mechanisms of action and therapeutic efficacy. *Crit Rev Oncol Hematol* 2005;56:23–46.