A 65-year-old hospitalized man is evaluated for decreased urine output and increased serum creatinine. The patient was admitted for 3-vessel coronary artery disease and underwent coronary artery bypass grafting surgery yesterday. Other medical conditions include type 2 diabetes mellitus and hypertension. He received a dose of intravenous vancomycin prior to the surgery for prophylaxis of surgical infection. The patient has also been receiving 100 mL/hour of intravenous normal saline for the past 24 hours. He is afebrile. Blood pressure is 130/80 mm Hg and pulse is 80/min. Examination shows bibasilar crackles. The abdomen is soft. Urine output over the past 6 hours is 100 mL. Laboratory results are as follows:

	Day of admission	Today
Blood urea nitrogen	20 mg/dL	35 mg/dL
Serum creatinine	1.3 mg/dL	2.5 mg/dL

Urine sediment microscopy is shown in the **exhibit**. Which of the following is the most likely cause of this patient's current condition?

A. Crystal obstruction in tubules
B. Drug toxicity to renal tubules
C. Glomerulonephritis
D. Interstitial inflammation
E. Ischemic tubular necrosis
F. Prerenal azotemia

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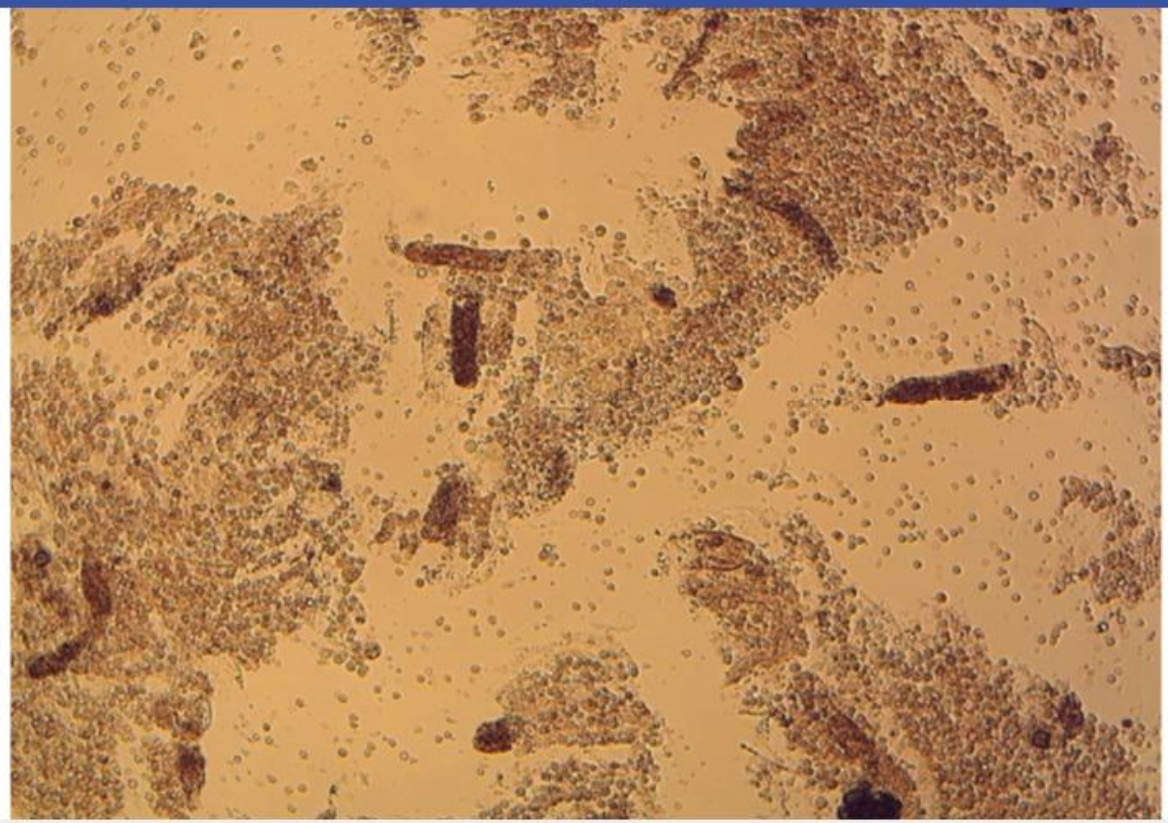

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A 65-year-old hospitalized man is evaluated for decreased urine output and increased serum creatinine. The patient was admitted for 3-vessel coronary artery disease and underwent coronary artery bypass grafting surgery yesterday. Other medical conditions include type 2 diabetes mellitus and hypertension. He received a dose of intravenous vancomycin prior to the surgery for prophylaxis of surgical infection. The patient has also been receiving 100 mL/hour of intravenous normal saline for the past 24 hours. He is afebrile. Blood pressure is 130/80 mm Hg and pulse is 80/min. Examination shows bibasilar crackles. The abdomen is soft. Urine output over the past 6 hours is 100 mL. Laboratory results are as follows:

	Day of admission	Today
Blood urea nitrogen	20 mg/dL	35 mg/dL
Serum creatinine	1.3 mg/dL	2.5 mg/dL

Urine sediment microscopy is shown in the **exhibit**. Which of the following is the most likely cause of this patient's current condition?

- A. Crystal obstruction in tubules [2%]
- B. Drug toxicity to renal tubules [40%]
- C. Glomerulonephritis [1%]
- D. Interstitial inflammation [3%]
- ✔ E. Ischemic tubular necrosis [48%]
- F. Prerenal azotemia [4%]

Omitted
Correct answer

48%

15 Seconds

01/29/2019

Explanation

Urinary casts	Composition	Associated conditions
Hyaline	Tamm-Horsfall protein	Nonspecific, concentrated urine
Fatty	Lipid droplets	Nephrotic syndrome
Waxy	Degenerated hyaline cast	Chronic kidney disease
Granular (muddy brown)	Sloughed tubular epithelial cells with pigmented granules	Acute tubular necrosis
WBC	White blood cells	Pyelonephritis, interstitial nephritis
RBC	Red blood cells	Glomerulonephritis

This patient with **acute kidney injury** has muddy brown casts on urine microscopy; in the setting of recent major surgery this presentation suggests **acute tubular necrosis** (ATN) due to **intraoperative renal ischemia**. Surgeries complicated by significant blood loss or those requiring the use of cardiopulmonary bypass (eg, coronary artery bypass grafting) or aortic clamping can cause renal hypoperfusion. The risk is increased in the elderly and those with a history of chronic kidney disease, diabetes, or congestive heart failure.

ATN is characterized by the presence of **muddy brown granular casts** composed of sloughed renal tubular epithelial cells. Patients have increased serum creatinine, **blood urea nitrogen/ creatinine ratio <20:1** (indicating intrinsic renal pathology), and oliguria (low urine output).

This patient with **acute kidney injury** has muddy brown casts on urine microscopy; in the setting of recent major surgery this presentation suggests **acute tubular necrosis** (ATN) due to **intraoperative renal ischemia**. Surgeries complicated by significant blood loss or those requiring the use of cardiopulmonary bypass (eg, coronary artery bypass grafting) or aortic clamping can cause renal hypoperfusion. The risk is increased in the elderly and those with a history of chronic kidney disease, diabetes, or congestive heart failure.

ATN is characterized by the presence of **muddy brown granular casts** composed of sloughed renal tubular epithelial cells. Patients have increased serum creatinine, **blood urea nitrogen/ creatinine ratio <20:1** (indicating intrinsic renal pathology), and oliguria (low urine output). Histologically, flattened tubular epithelial cells with cellular necrosis and loss of the brush border are seen.

(Choice A) Crystalline-induced kidney injury most commonly occurs from acyclovir or sulfonamide (eg, sulfadiazine) usage. Urinalysis demonstrates needle or rosette-shaped crystals. Vancomycin is not associated with crystal formation.

(Choice B) Vancomycin can cause ATN, but this typically occurs after a prolonged course (days). It is highly unlikely that a single dose would cause ATN.

(Choice C) Glomerulonephritis can cause acute kidney injury, but hematuria and red blood cell casts are expected on urinalysis. In addition, patients are typically hypertensive.

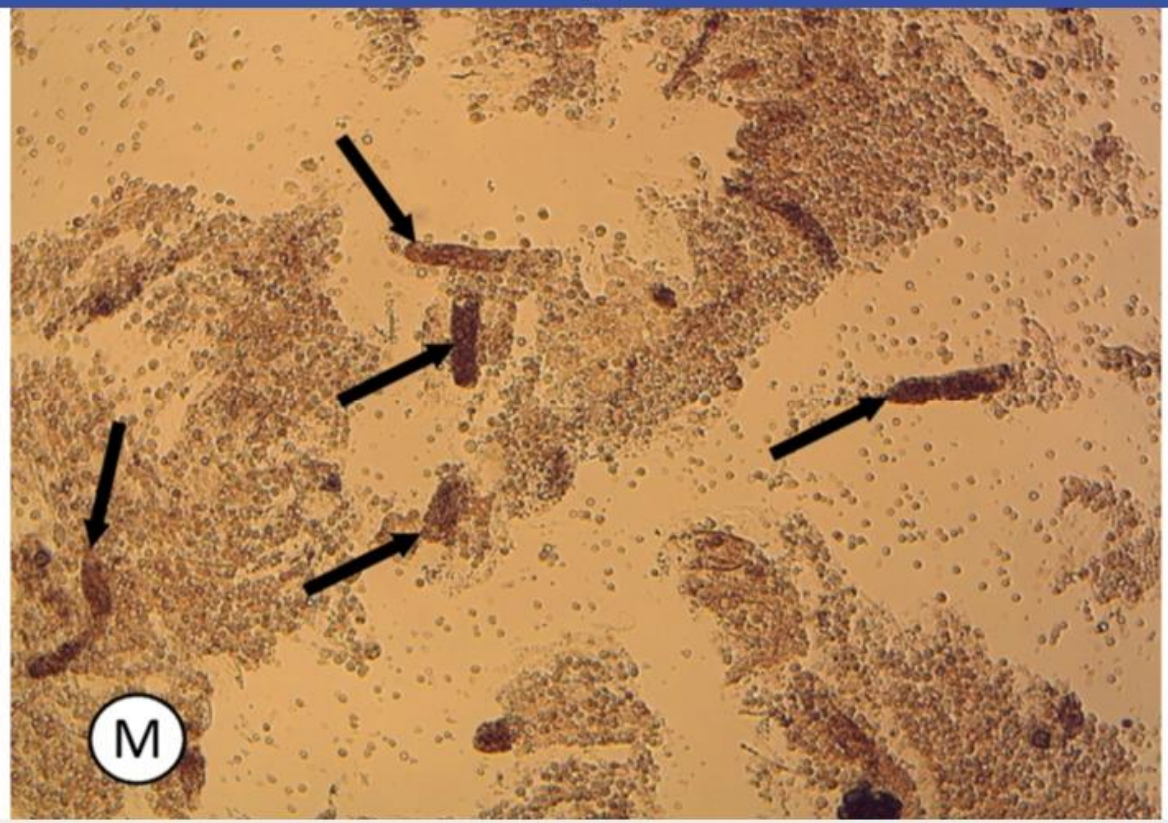
(Choice D) Acute interstitial nephritis can occur after exposure to new drugs, particularly antibiotics and diuretics. However, white blood cells and white cell casts are expected on urinalysis, and patients often have fever and rash.

(Choice F) Prerenal azotemia occurs from less significant renal hypoperfusion without renal ischemia (eg, dehydration). Urinalysis reveals hyaline casts (reflecting concentrated urine) and the blood urea nitrogen/creatinine ratio is elevated (>20:1).

Educational objective:
Surgeries complicated by significant blood loss or those requiring the use of cardiopulmonary bypass or clamping of the aorta can cause sustained renal hypoperfusion and result in acute tubular necrosis (ATN). ATN presents with oliguria, increased serum creatinine, and blood urea nitrogen/creatinine ratio <20:1. Urinalysis is characterized by muddy brown granular casts composed of sloughed renal tubular epithelial cells.

This patient with **acute kidney injury** has muddy brown casts on urine microscopy; in the setting of recent major surgery this presentation

Exhibit Display

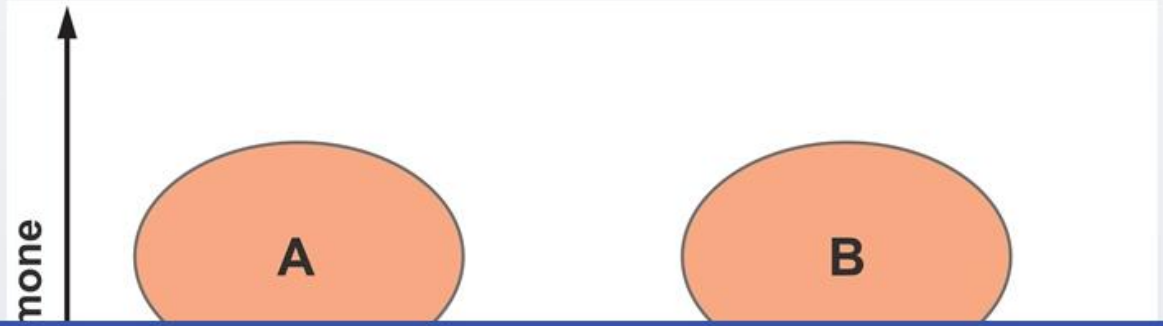


Zoom In | Zoom Out | Reset | Add To Flash Card

A 64-year-old man comes to the office with fatigue. He has hypertension and poorly controlled diabetes complicated by nephropathy and peripheral neuropathy. His renal function has declined steadily over the last few years. On examination, his conjunctivae are pale and he has bilateral 1+ peripheral edema. Laboratory results are as follows:

Serum chemistry	
Sodium	133 mEq/L
Potassium	4.4 mEq/L
Chloride	98 mEq/L
Bicarbonate	22 mEq/L
Blood urea nitrogen	76 mg/dL
Creatinine	5.8 mg/dL

On the graph below, area "C" shows the normal relationship between serum concentrations of free calcium and parathyroid hormone. Which of the following areas most likely represents this patient's current metabolic state?



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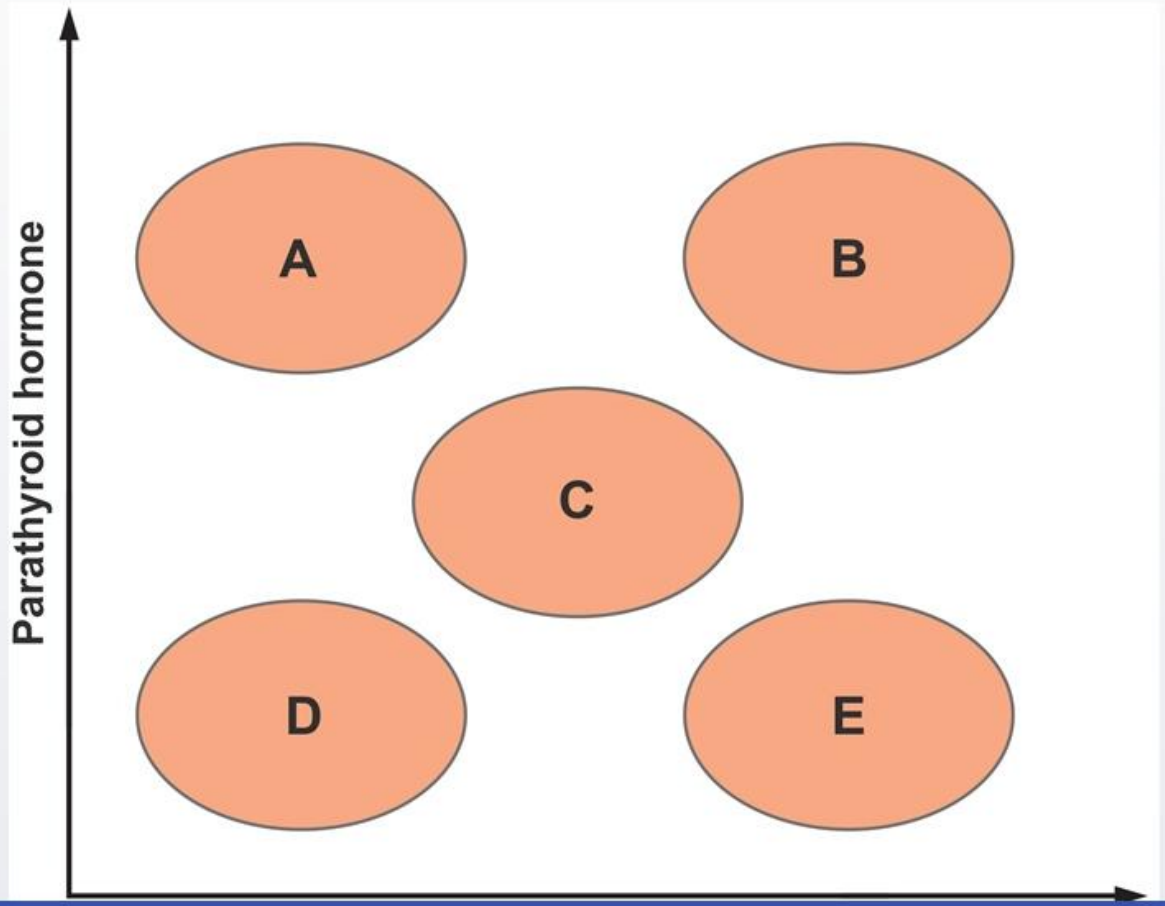

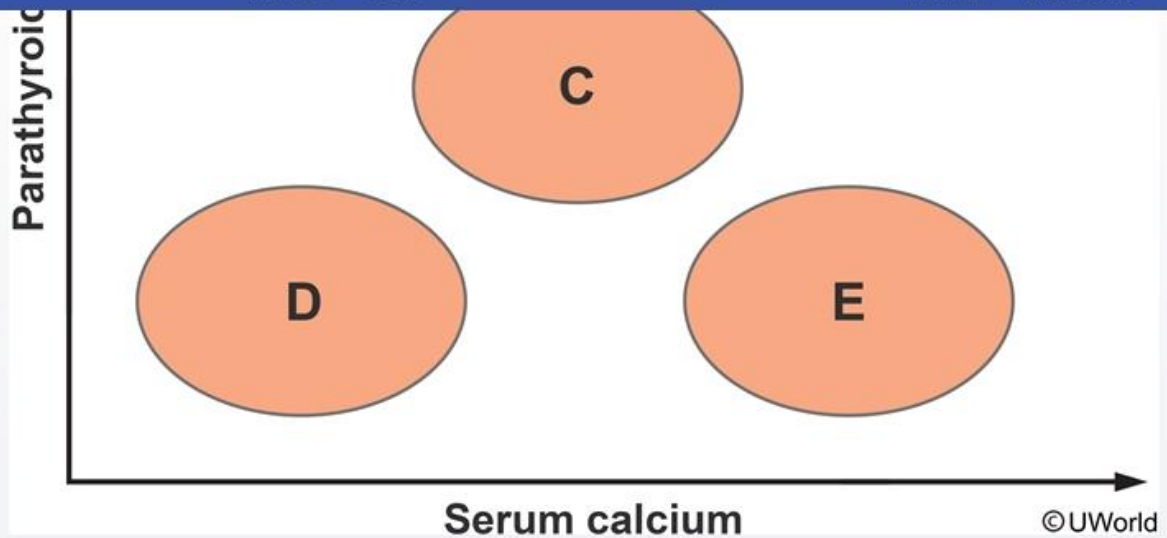

- A. A
- B. B
- C. C
- D. D
- E. E

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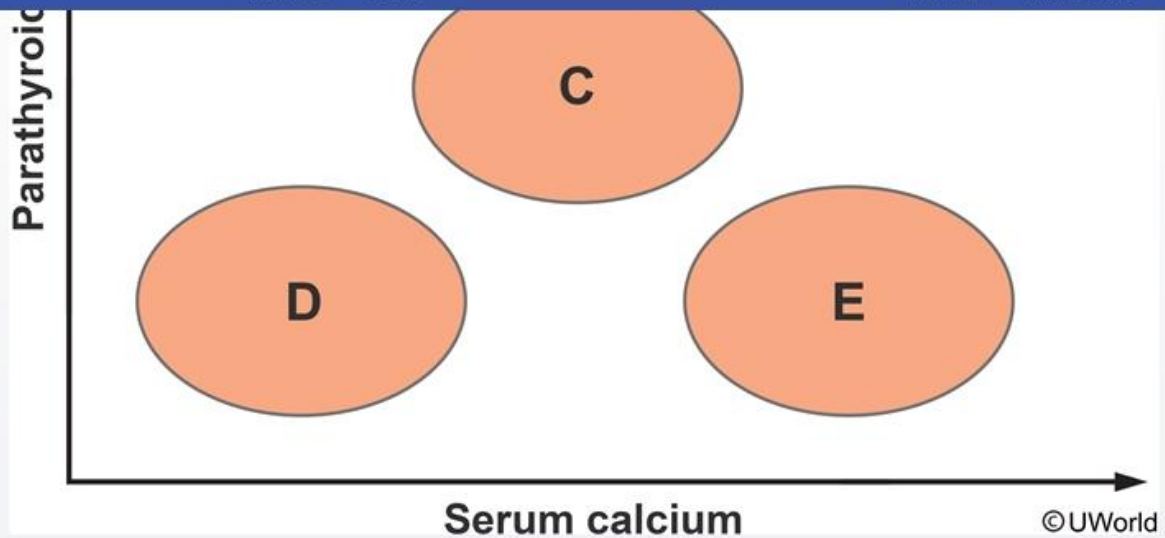


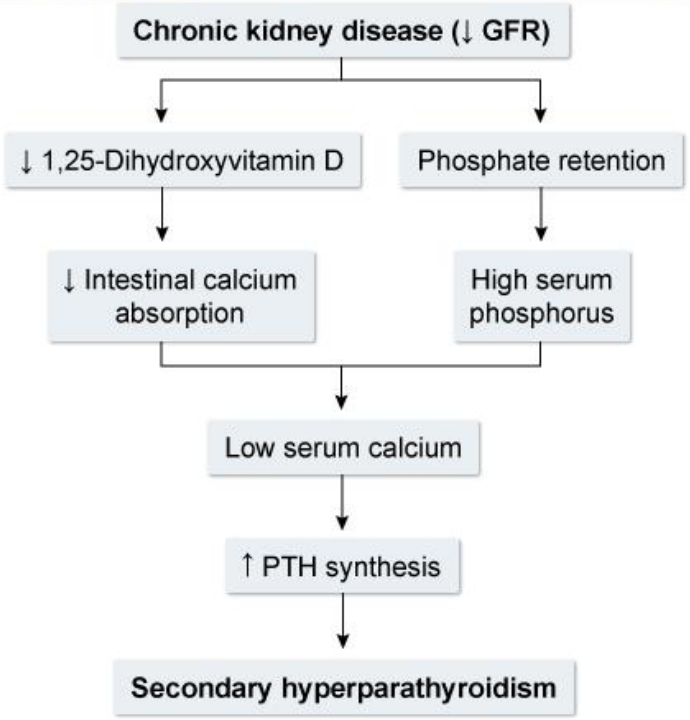
- A. A [77%]
- B. B [8%]
- C. C [3%]
- D. D [5%]
- E. E [5%]

Omitted
Correct answer

77%
Answered correctly

15 Seconds
Time Spent

12/18/2018
Last Updated



GFR = glomerular filtration rate; **PTH** = parathyroid hormone.

In the physiologic state, parathyroid hormone (PTH) causes an overall increase in serum calcium (Ca^{2+}) and a decrease serum phosphate (PO_4) via the following effects:

- Increasing osteoclastic bone resorption, releasing Ca^{2+} and PO_4 into serum
- Increasing renal calcium reabsorption and reducing phosphate reabsorption

In the physiologic state, parathyroid hormone (PTH) causes an overall increase in serum calcium (Ca^{2+}) and a decrease serum phosphate (PO_4) via the following effects:

- Increasing osteoclastic bone resorption, releasing Ca^{2+} and PO_4 into serum
- Increasing renal calcium reabsorption and reducing phosphate reabsorption
- Increasing formation of 1,25-dihydroxycholecalciferol (by upregulating renal 1-alpha-hydroxylase), which increases intestinal Ca^{2+} and PO_4 absorption

PTH production is very sensitive to small changes in serum free Ca^{2+} and is regulated by a negative feedback mechanism: increased Ca^{2+} will suppress PTH, but decreased Ca^{2+} will increase PTH.

In **chronic kidney disease** (CKD), PO_4 clearance declines due to the fall in GFR. The **increased PO_4** binds free serum Ca^{2+}, resulting in **hypocalcemia**. Loss of normal renal parenchyma reduces 1,25-dihydroxyvitamin D synthesis, resulting in a significant decline in intestinal Ca^{2+} absorption and Ca^{2+} release from bone. This further exacerbates the hypocalcemia, which along with hyperphosphatemia and low calcitriol, stimulates PTH production (**secondary hyperparathyroidism**).

(Choice B) In primary hyperparathyroidism, serum Ca^{2+} is elevated but does not suppress PTH due to autonomous gland function. In longstanding CKD, PTH release may become independent of Ca^{2+} levels due to chronic parathyroid cell stimulation; PTH remains elevated despite 1,25-dihydroxyvitamin D and Ca^{2+} supplementation (**tertiary hyperparathyroidism**). However, this is less common than secondary hyperparathyroidism and is usually seen in patients with end-stage renal disease (ie, on dialysis).

(Choice C) Calcitriol and Ca^{2+} supplementation in patients with CKD often returns PTH and Ca^{2+} levels to normal.

(Choice D) Low PTH with hypocalcemia and hyperphosphatemia is seen in hypoparathyroidism.

(Choice E) High serum Ca^{2+} with low PTH is seen in patients with PTH-independent causes of hypercalcemia, which include hypercalcemia of malignancy, vitamin D toxicity, excessive Ca^{2+} ingestion, thyrotoxicosis, and immobilization (Ca^{2+} resorbed from inactive bones).

Educational objective:
Chronic kidney disease usually causes hyperphosphatemia (binds serum Ca^{2+}) and low 1,25-dihydroxyvitamin D (decreases intestinal Ca^{2+}

In **chronic kidney disease** (CKD), PO_4 clearance declines due to the fall in GFR. The **increased PO_4** binds free serum Ca^{2+}, resulting in **hypocalcemia**. Loss of normal renal parenchyma reduces 1,25-dihydroxyvitamin D synthesis, resulting in a significant decline in intestinal Ca^{2+} absorption and Ca^{2+} release from bone. This further exacerbates the hypocalcemia, which along with hyperphosphatemia and low calcitriol, stimulates PTH production (**secondary hyperparathyroidism**).

(Choice B) In primary hyperparathyroidism, serum Ca^{2+} is elevated but does not suppress PTH due to autonomous gland function. In longstanding CKD, PTH release may become independent of Ca^{2+} levels due to chronic parathyroid cell stimulation; PTH remains elevated despite 1,25-dihydroxyvitamin D and Ca^{2+} supplementation (**tertiary hyperparathyroidism**). However, this is less common than secondary hyperparathyroidism and is usually seen in patients with end-stage renal disease (ie, on dialysis).

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Educational objective:
Chronic kidney disease usually causes hyperphosphatemia (binds serum Ca^{2+}) and low 1,25-dihydroxyvitamin D (decreases intestinal Ca^{2+} absorption and Ca^{2+} release from bone). The resulting hypocalcemia stimulates release of parathyroid hormone, causing secondary hyperparathyroidism.

References

- Hyperparathyroidism in chronic kidney disease patients: an update on current pharmacotherapy.
- Secondary and tertiary hyperparathyroidism.

A 24-year-old woman comes to the office for the evaluation of joint pain, fatigue, edema, and weight gain for the past four weeks. She has no previous medical conditions except for recurrent oral ulcers. The patient takes no medications and does not use tobacco, alcohol, or illicit drugs. Blood pressure is 130/80 mm Hg and pulse is 80/min. Examination shows oral mucosal ulcers, facial puffiness, and 3+ peripheral edema. Swelling, erythema, and tenderness are noted over the bilateral metacarpophalangeal and proximal interphalangeal joints. Cardiopulmonary examination reveals no abnormalities. Twenty-four-hour urine protein excretion is 4.5 g. Serum antinuclear antibodies are present. Kidney biopsy shows glomerular capillary wall thickening with no increase in cellularity. When the sample is stained with methenamine silver, irregular spikes protruding from the glomerular basement membrane are seen. This patient most likely has which of the following conditions?

- A. Antiglomerular basement membrane disease
- B. Antineutrophil cytoplasmic antibody–associated glomerulonephritis
- C. Diffuse proliferative nephritis
- D. Focal segmental glomerulosclerosis
- E. Membranoproliferative glomerulonephritis
- F. Membranous glomerulopathy
- G. Postinfectious glomerulonephritis

Submit

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- A. Antiglomerular basement membrane disease [2%]
- B. Antineutrophil cytoplasmic antibody–associated glomerulonephritis [8%]
- C. Diffuse proliferative nephritis [9%]
- D. Focal segmental glomerulosclerosis [4%]
- E. Membranoproliferative glomerulonephritis [14%]
- ✔ F. Membranous glomerulopathy [58%]
- G. Postinfectious glomerulonephritis [1%]

Omitted
Correct answer
F

58%
Answered correctly

4 Seconds
Time Spent

10/02/2018
Last Updated

Explanation

This patient has **nephrotic syndrome** (ie, generalized edema, marked proteinuria). In conjunction with the characteristic biopsy findings, this presentation suggests **membranous glomerulopathy** (MG). MG is caused by immune-complex deposition in the subepithelial portion of the glomerular capillary wall. Light microscopy shows **diffuse thickening** of the **glomerular basement membrane** (GBM) without an increase in glomerular cellularity. Immunofluorescence reveals **granular deposits** of IgG and C3 along the GBM. Electron microscopy demonstrates irregular, electron-dense **immune deposits** located between the GBM and epithelial cells. Protrusion of the GBM through the deposits resemble **spikes and domes** when stained with a silver stain.

MG is a common cause of nephrotic syndrome in adults. Most cases are idiopathic, with the remainder due to chronic infection (eg, viral hepatitis, syphilis), solid tumors (eg, lung, colon), or **systemic lupus erythematosus** (SLE). This patient with inflammatory arthritis, oral ulcers, and antinuclear antibodies likely has MG secondary to SLE (which leads to renal disease from anti–double-stranded DNA immune-complex formation).

(Choices A and B) Anti-GBM disease (ie, Goodpasture disease) and antineutrophil cytoplasmic antibody–associated glomerulonephritis (eg, granulomatosis with polyangiitis) cause rapidly progressive **crescentic disease**, characterized by glomerular hypercellularity with crescent formation (composed of fibrin and proliferating cells). These diseases cause nephritic syndrome (eg, hematuria, red blood cell casts), not isolated proteinuria.

(Choice C) Diffuse proliferative nephritis, another common renal manifestation of SLE, is characterized by proliferation of lymphocytes and endothelial cells within the capillary loops. Diffuse "wire-loop" deposits are often seen.

(Choice D) **Focal segmental glomerulosclerosis** also causes nephrotic syndrome but is characterized by sclerosis in some (but not all) glomeruli (focal) and some portions of the glomerulus. It is commonly associated with drug use (eg, heroin) and viruses (eg, HIV).

(Choice E) **Membranoproliferative glomerulonephritis** is often associated with hepatitis B or C. It is characterized by thickening of the GBM, but, unlike MG, large hypercellular glomeruli are also seen.

(Choice G) Postinfectious glomerulonephritis occurs more commonly in children and causes a nephritic (not nephrotic) syndrome, typically two to four weeks after a group A streptococcal infection. Light microscopy demonstrates enlarged, diffusely hypercellular glomeruli.

Educational objective:

syphilis), solid tumors (eg, lung, colon), or **systemic lupus erythematosus** (SLE). This patient with inflammatory arthritis, oral ulcers, and antinuclear antibodies likely has MG secondary to SLE (which leads to renal disease from anti–double-stranded DNA immune-complex formation).

(Choices A and B) Anti-GBM disease (ie, Goodpasture disease) and antineutrophil cytoplasmic antibody–associated glomerulonephritis (eg, granulomatosis with polyangiitis) cause rapidly progressive **crescentic disease**, characterized by glomerular hypercellularity with crescent formation (composed of fibrin and proliferating cells). These diseases cause nephritic syndrome (eg, hematuria, red blood cell casts), not isolated proteinuria.

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(Choice G) Postinfectious glomerulonephritis occurs more commonly in children and causes a nephritic (not nephrotic) syndrome, typically two to four weeks after a group A streptococcal infection. Light microscopy demonstrates enlarged, diffusely hypercellular glomeruli.

Educational objective:
Membranous glomerulopathy is a common cause of nephrotic syndrome in adults and can occur in association with solid malignancy, viral hepatitis, and systemic lupus erythematosus. Immune-complex deposition in the subepithelial portion of the glomerular capillary wall causes diffuse thickening of the glomerular basement membrane (without increased cellularity); these deposits have a "spike and dome" appearance when stained with silver stains.

References

- The incidence of primary glomerulonephritis worldwide: a systematic review of the literature.

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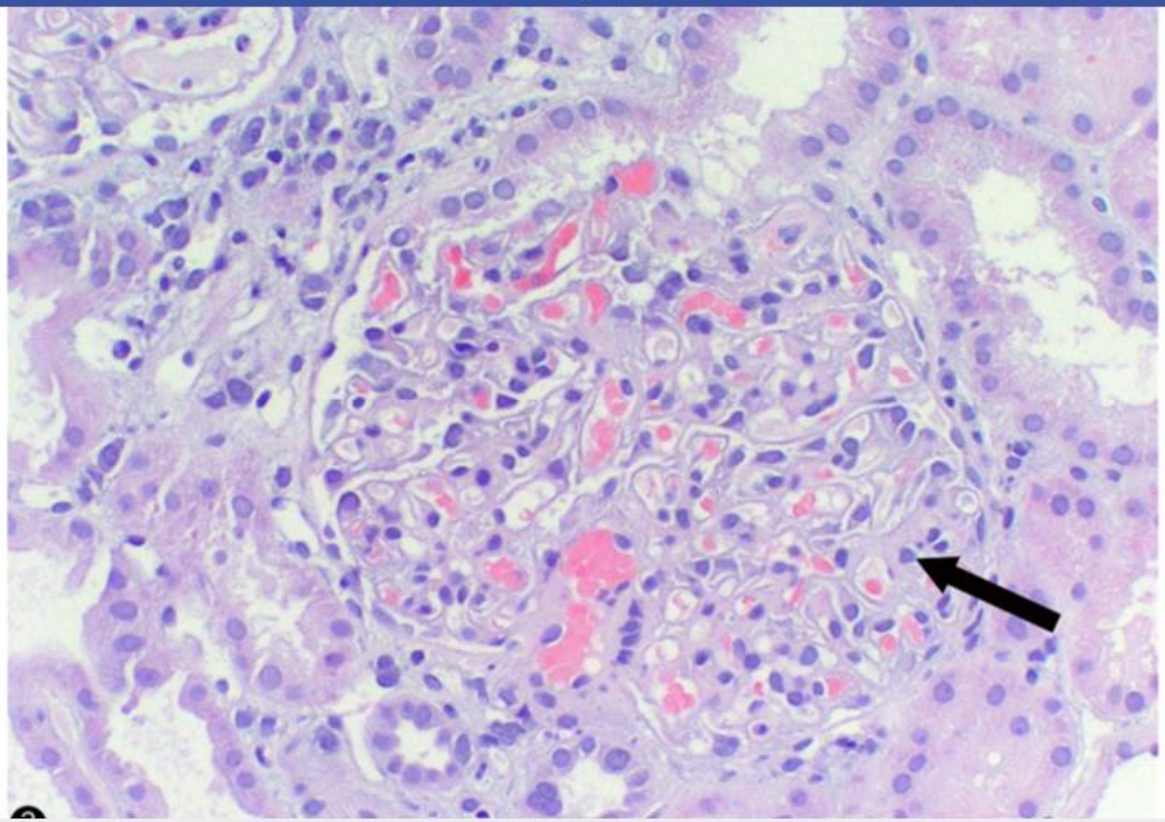

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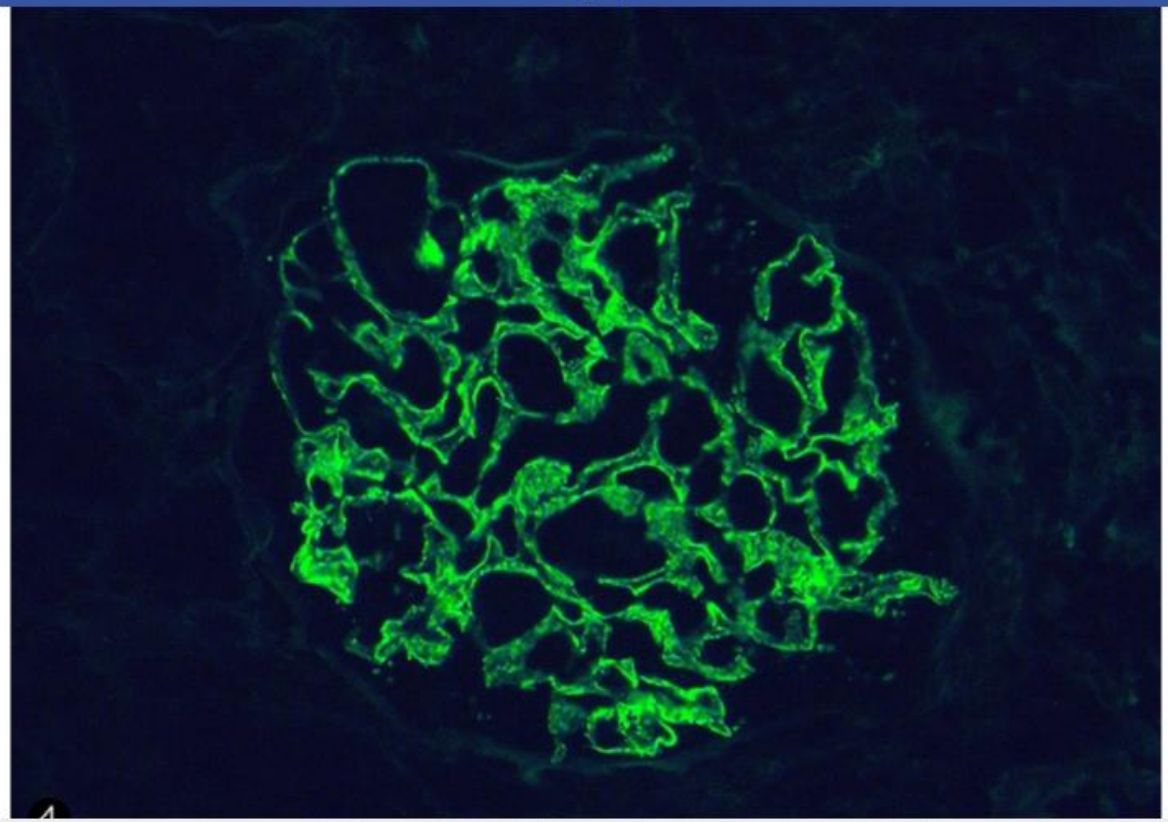

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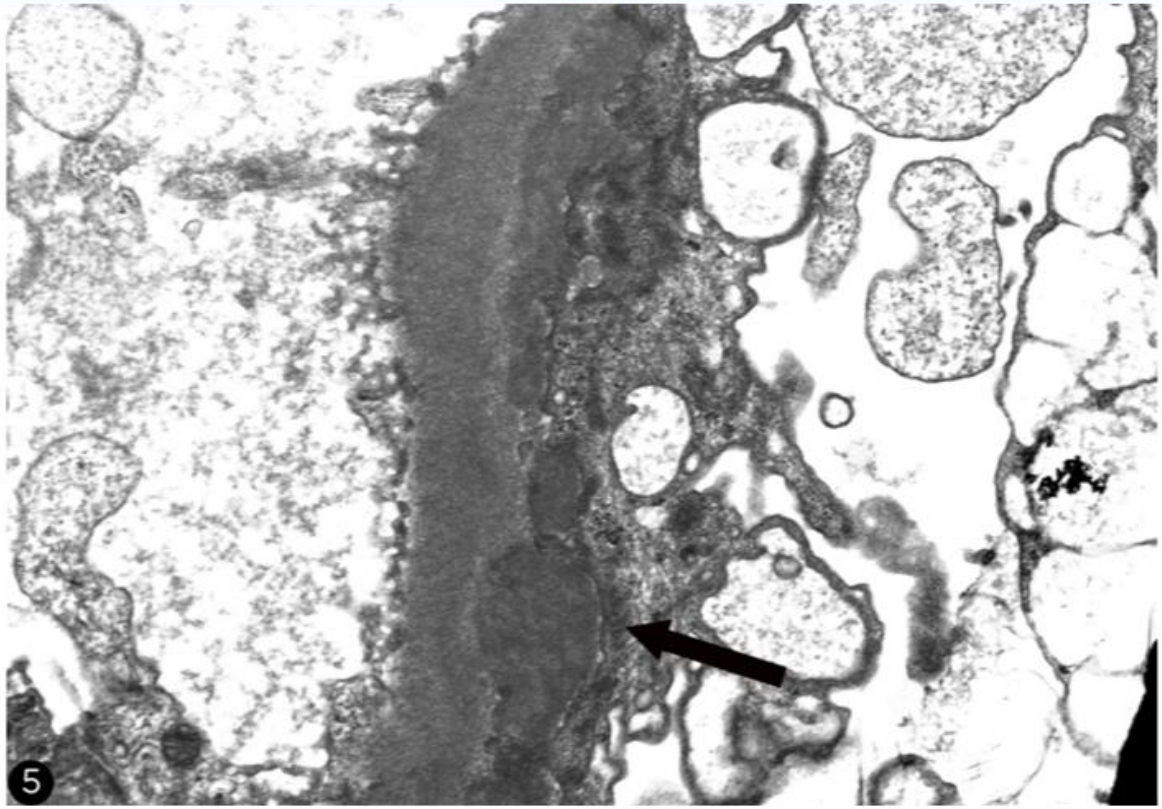

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A 21-year-old man comes to the emergency department due to 1 day of left flank pain and gross hematuria. He reports passage of small blood clots in urine but has had no dysuria or similar symptoms in the past. The patient has no other medical problems and does not take any medications. He does not use tobacco, alcohol, or illicit drugs. His younger sister has sickle cell disease. His temperature is 36.7 C (98 F), blood pressure is 126/70 mm Hg, and pulse is 100/min. Abdominal and genitourinary examination is unremarkable. There is no costovertebral angle tenderness. Which of the following is the most likely cause of this patient's hematuria?

- A. Acute pyelonephritis
- B. Amyloidosis
- C. Fanconi syndrome
- D. Hemolytic-uremic syndrome
- E. Hypersensitivity interstitial nephritis
- F. Ischemic tubular necrosis
- G. Lead nephropathy
- H. Papillary necrosis
- I. Renal artery stenosis
- J. Urate nephropathy

Submit

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- A. Acute pyelonephritis [5%]
- B. Amyloidosis [1%]
- C. Fanconi syndrome [4%]
- D. Hemolytic-uremic syndrome [9%]
- E. Hypersensitivity interstitial nephritis [4%]
- F. Ischemic tubular necrosis [17%]
- G. Lead nephropathy [0%]
- ✔ H. Papillary necrosis [49%]
- I. Renal artery stenosis [1%]
- J. Urate nephropathy [7%]

Omitted
Correct answer
H

49%
Answered correctly

4 Seconds
Time Spent

11/11/2018
Last Updated

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Explanation

Abrupt-onset gross hematuria in an otherwise healthy patient with a family history of sickle cell disease suggests **renal papillary necrosis (RPN)** due to underlying sickle cell trait. Conditions associated with RPN include:

- **Sickle cell** disease or trait: Sickled cells cause obstruction of small kidney vessels, predisposing to ischemia.
- **Analgesic nephropathy**: Many nonsteroidal anti-inflammatory drugs inhibit renal blood flow by decreasing prostaglandin synthesis and vasoconstricting the afferent arterioles. Certain analgesics can cause ischemia in patients predisposed to renal hypoperfusion.
- Diabetes mellitus: Diabetic metabolic abnormalities (eg, nonenzymatic glycosylation) cause changes in vascular walls, leading to renal vasculopathy and subsequent hypoperfusion.
- Pyelonephritis and urinary tract obstruction: The edematous interstitium of the pyelonephritic kidney compresses the medullary vasculature, leading to ischemia. In this patient, acute pyelonephritis is unlikely in the absence of fever or costovertebral angle tenderness **(Choice A)**.

Gray-white or yellow necrosis of the distal two-thirds of the renal pyramids is seen macroscopically and corresponds microscopically to **coagulation necrosis** with preserved tubule outlines; cortical surface scars can develop subsequently as inflammatory foci are replaced by fibrous depressions. Symptoms are due to sloughed papillae (sometimes visible in urine as tissue flecks) and include dark or **bloody urine** and colicky **flank pain** (due to ureteral obstruction).

(Choices B and J) Amyloidosis and uric acid nephropathy rarely cause hematuria. Amyloidosis occurs most frequently in the elderly and uric acid nephropathy typically occurs in patients with malignancy (leukemia) or gout.

(Choices C, E, F, G, and I) Fanconi syndrome (polyuria, acidosis, hypophosphatemia), lead nephropathy (Fanconi-like syndrome), hypersensitivity interstitial nephritis (fever, rash, and renal dysfunction due to drug reaction), renal artery stenosis (hypertension in older patients), and acute tubular necrosis (acute kidney injury due to ischemia or nephrotoxins) are not typically characterized by gross hematuria.

(Choice D) Hemolytic-uremic syndrome (microangiopathic hemolytic anemia, thrombocytopenia, acute renal failure) generally occurs 1-2 weeks after a diarrheal illness (classically due to *Escherichia coli* O157:H7).

Educational objective:

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vasoconstricting the afferent arterioles. Certain analgesics can cause ischemia in patients predisposed to renal hypoperfusion.

- Diabetes mellitus: Diabetic metabolic abnormalities (eg, nonenzymatic glycosylation) cause changes in vascular walls, leading to renal vasculopathy and subsequent hypoperfusion.
- Pyelonephritis and urinary tract obstruction: The edematous interstitium of the pyelonephritic kidney compresses the medullary vasculature, leading to ischemia. In this patient, acute pyelonephritis is unlikely in the absence of fever or costovertebral angle tenderness **(Choice A)**.

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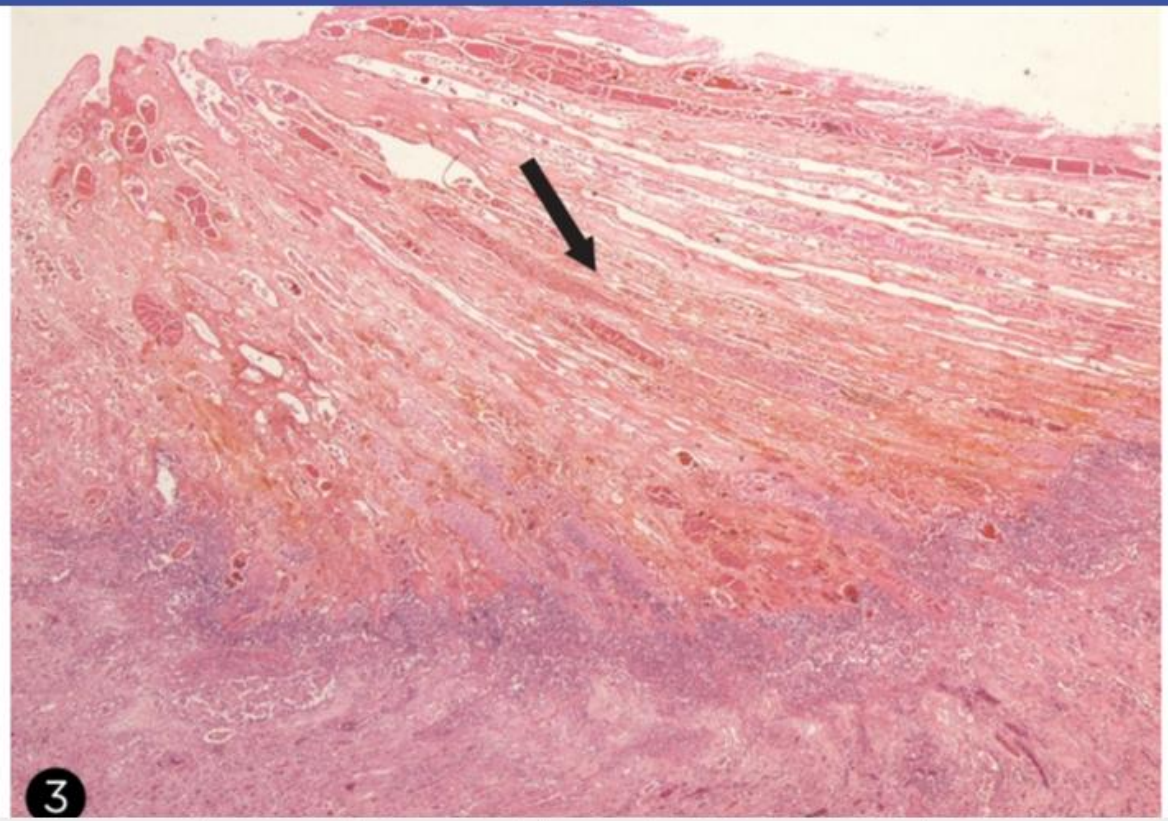
Educational objective:
Renal papillary necrosis classically presents with gross hematuria, acute flank pain, and passage of tissue fragments in urine. It is most commonly seen in patients with sickle cell disease or trait, diabetes mellitus, analgesic nephropathy, or severe obstructive pyelonephritis.

References

- Sickle cell trait and renal papillary necrosis.

vasoconstricting the afferent arterioles. Certain analgesics can cause ischemia in patients predisposed to renal hypoperfusion.

Exhibit Display



Zoom In | Zoom Out | Reset | Add To Flash Card

A 32-year-old woman comes to the emergency department with sudden-onset left flank pain and nausea. The pain radiates to the left groin and she is unable to find a comfortable position on the examination table. The pain is intermittent and waxes and wanes in severity. Temperature is 36.7 C (98 F), blood pressure is 140/90 mm Hg, and pulse is 92/min. She has mild tenderness to percussion over the left flank. Bowel sounds are hypoactive. Which of the following recommendations would most likely prevent a recurrence of this patient's condition?

- A. Avoid alcohol use
- B. Complete a course of antibiotics
- C. Drink plenty of water daily
- D. Follow a high-fiber diet
- E. Follow a high-sodium diet
- F. Follow a low-calcium diet
- G. Follow safe sexual practices

Submit

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- A. Avoid alcohol use [1%]
- B. Complete a course of antibiotics [2%]
- ✔ C. Drink plenty of water daily [82%]
- D. Follow a high-fiber diet [6%]
- E. Follow a high-sodium diet [0%]
- F. Follow a low-calcium diet [5%]
- G. Follow safe sexual practices [2%]

Omitted
Correct answer
C

82%
Answered correctly

4 Seconds
Time Spent

11/30/2018
Last Updated

Explanation

Risk & prevention of kidney stones

Explanation

Risk & prevention of kidney stones		
Stone type	**Risk factors**	**Prevention**
Calcium stones (oxalate, phosphate)	• Hypercalciuria (eg, hyperparathyroidism) • Hyperoxaluria (eg, malabsorption, low-calcium diet) • Hypocitraturia (eg, distal RTA) • Diet: ↑ sodium, ↑ protein, ↑ oxalate, ↓ calcium	• Reduce sodium, animal protein, oxalate intake • Increase potassium intake; moderate calcium intake • Thiazide diuretics
Uric acid	• Gout • Myeloproliferative disorders	• Urine alkalinization • Allopurinol
Magnesium ammonium phosphate (struvite)	• Recurrent upper urinary infection (eg, *Klebsiella*, *Proteus*)	• Stone removal • Suppressive antibiotics
All types	• Dehydration	• Increase fluid intake

RTA = renal tubular acidosis.

This patient has acute flank pain and tenderness consistent with **nephrolithiasis**. The pain associated with nephrolithiasis (renal colic) is often severe and, although it may wax and wane, is generally not positional. The pain commonly radiates to the groin, especially as the stone passes down the ureter to the ureterovesical junction. Nausea and vomiting are common, and bowel sounds are often diminished due to an associated ileus. Hematuria is usually present but may not be grossly visible.

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This patient has acute flank pain and tenderness consistent with **nephrolithiasis**. The pain associated with nephrolithiasis (renal colic) is often severe and, although it may wax and wane, is generally not positional. The pain commonly radiates to the groin, especially as the stone passes down the ureter to the ureterovesical junction. Nausea and vomiting are common, and bowel sounds are often diminished due to an associated ileus. Hematuria is usually present but may not be grossly visible.

Most kidney stones are calcium-based (calcium oxalate, calcium phosphate). But regardless of chemical composition, low fluid intake can lead to **supersaturation** of urine with crystalline material and promote stone formation. **Increasing fluid intake** can reduce the risk of all types of stones.

(Choice A) Excessive alcohol intake can trigger acute pancreatitis. The pain associated with pancreatitis is typically located in the epigastric area rather than the flank and radiates to the back rather than the groin.

(Choice B) Recurrent infections of the upper urinary tract with urease-producing organisms (eg, *Klebsiella*, *Proteus*) can lead to formation of magnesium ammonium phosphate (struvite) stones. These stones are often large and may fill the renal pelvis. Although patients may have mild flank pain due to recurrent infection, acute renal colic is uncommon as these large stones do not travel down the ureter.

(Choice D) A high-fiber diet is associated with a decreased risk of diverticulitis. This condition typically presents over a few days (not suddenly, as in this patient) with lower abdominal pain and tenderness in the left lower quadrant.

(Choice E) Calcium passively follows the reabsorption of sodium and water in the renal tubules. Increased dietary sodium intake leads to reduced sodium reabsorption in the proximal tubule and lowers calcium reabsorption (leading to hypercalciuria).

(Choice F) Dietary calcium binds oxalate in the gut to form unabsorbable calcium oxalate. Low-calcium diets lead to increased absorption of free oxalate, which is then excreted in the urine; the resulting hyperoxaluria promotes the formation of calcium oxalate stones. Low-calcium diets are therefore paradoxically associated with increased risk of stone formation.

(Choice G) Untreated infection with chlamydia or gonorrhea can lead to pelvic inflammatory disease, presenting with lower abdominal pain and fever. Examination findings include mucopurulent cervical discharge and cervical motion tenderness.

Educational objective:

(Choice A) Excessive alcohol intake can trigger acute pancreatitis. The pain associated with pancreatitis is typically located in the epigastric area rather than the flank and radiates to the back rather than the groin.

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Educational objective:
Urine supersaturation is the main mechanism underlying all types of renal stones. Low fluid intake increases the concentration of stone-forming agents, thereby promoting stone formation. All patients with nephrolithiasis should be advised to maintain adequate fluid intake.

References

- Treatment and prevention of kidney stones: an update.

A 67-year-old man comes to the office due to generalized weakness, easy fatigability, anorexia, and intermittent nausea for the past several months. He also says that he is "itching and scratching a lot." Physical examination shows bilateral lower extremity pitting edema and skin excoriations. Laboratory results show a serum creatinine level of 3.4 mg/dL and a blood urea nitrogen level of 48 mg/dL. A renal biopsy is performed. Light microscopy of the tissue sample shows widespread narrowing of the renal arterioles with deposition of homogeneous, glassy material in the subendothelial space that stains pink with periodic acid-Schiff (PAS) stain. This patient most likely has which of the following underlying conditions?

A. Atheroembolic renal disease
B. Diabetes mellitus
C. Malignant hypertension
D. Multiple myeloma
E. Rapidly progressive glomerulonephritis

Submit

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- A. Atheroembolic renal disease [4%]
- ✔ B. Diabetes mellitus [52%]
- C. Malignant hypertension [12%]
- D. Multiple myeloma [16%]
- E. Rapidly progressive glomerulonephritis [13%]

Omitted
Correct answer
B

52%
Answered correctly

3 Seconds
Time Spent

12/08/2018
Last Updated

Explanation

This patient's symptoms (eg, fatigue, weakness, itching) are most likely due to accumulation of uremia toxins secondary to progressive **chronic kidney disease**. His renal biopsy shows deposition of eosinophilic hyaline material in the intima and media of small arteries and arterioles, which is characteristic of **hyaline arteriolosclerosis**. It is typically seen in patients with untreated or poorly controlled **hypertension** (HTN) or **diabetes**

Explanation

This patient's symptoms (eg, fatigue, weakness, itching) are most likely due to accumulation of uremia toxins secondary to progressive **chronic kidney disease**. His renal biopsy shows deposition of eosinophilic hyaline material in the intima and media of small arteries and arterioles, which is characteristic of **hyaline arteriolosclerosis**. It is typically seen in patients with untreated or poorly controlled **hypertension** (HTN) or **diabetes mellitus**. Chronic/repetitive endothelial injury caused by hemodynamic stress (in HTN) or hyperglycemia causes leakage of plasma constituents across the vascular endothelium and stimulates smooth muscle cell (SMC) proliferation and excessive extracellular matrix production. In diabetics, development of hyaline arteriolosclerosis is related not only to the duration of the disease but also to the degree of any concomitant hypertension.

(Choice A) Atheroembolic renal disease typically occurs after manipulation of the aorta (eg, abdominal aortic aneurysm repair) in adults with widespread atherosclerosis. Atheroemboli with cholesterol clefts are seen within the arterial lumen.

(Choice C) Malignant hypertension (extreme or rapidly developing hypertension) causes fibrinoid necrosis and hyperplastic arteriolosclerosis. Fibrinoid necrosis is characterized by localized destruction of the vascular wall with a circumferential ring of pink, amorphous material surrounding the lumen. Hyperplastic arteriolosclerosis consists of onion-like, concentric thickening of the walls of arterioles due to laminated layers of SMCs with intervening basement membrane reduplication (**onion skinning**). This patient's lack of concentric SMC thickening and absence of vascular necrosis are more suggestive of hyaline arteriolosclerosis.

(Choice D) Nephropathy in multiple myeloma is most often due to excess excretion of free light chains (Bence Jones proteins) that precipitate with Tamm-Horsfall protein to form obstructing tubular casts (cast nephropathy). These casts are seen as amorphous hyaline material in the tubular lumen.

(Choice E) Rapidly progressive glomerulonephritis (RPGN), including the idiopathic variety, may occur in the absence of a systemic vasculitic syndrome. Therefore, a patient with RPGN need not have renal arteriolar lesions.

Educational objective:
Homogeneous deposition of eosinophilic hyaline material in the intima and media of small arteries and arterioles characterizes hyaline arteriolosclerosis. This is typically produced by untreated or poorly controlled hypertension and/or diabetes

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Educational objective:
Homogeneous deposition of eosinophilic hyaline material in the intima and media of small arteries and arterioles characterizes hyaline arteriolosclerosis. This is typically produced by untreated or poorly controlled hypertension and/or diabetes.

A 68-year-old man comes to the emergency department due to lower abdominal pain and nausea. His symptoms started the prior evening, when he began to feel abdominal fullness and discomfort. This progressed to pain over the lower abdomen and constant nausea without vomiting. The patient last urinated >24 hours ago. He has had difficulty initiating urination and a feeling of incomplete voiding for the last year but avoided seeing a physician. Temperature is 36.7 C (98 F), blood pressure is 150/90 mm Hg, and pulse is 95/min. Physical examination shows suprapubic tenderness and fullness without guarding or rebound. Rectal examination reveals an enlarged, smooth prostate. Serum creatinine is 2.6 mg/dL and blood urea nitrogen is 22 mg/dL. A urinary catheter is placed, with immediate collection of 800 mL of urine and relief of the patient's symptoms. The following day, serum creatinine is improved. This patient's condition is associated with increased risk for which of the following?

- A. Bladder transitional cell carcinoma
- B. Glomerulonephritis
- C. Priapism
- D. Prostatic adenocarcinoma
- E. Urinary tract infection

Submit

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- A. Bladder transitional cell carcinoma [4%]
- B. Glomerulonephritis [5%]
- C. Priapism [0%]
- D. Prostatic adenocarcinoma [9%]
- ✔ E. Urinary tract infection [78%]

Omitted
Correct answer
E

78%
Answered correctly

3 Seconds
Time Spent

08/22/2018
Last Updated

Explanation

This patient with progressive lower urinary tract symptoms and an enlarged prostate has **benign prostatic hyperplasia** (BPH). Bladder-outlet obstruction with **acute urinary retention** is a common complication of BPH and can occur with progressive disease or be triggered by

Explanation

This patient with progressive lower urinary tract symptoms and an enlarged prostate has **benign prostatic hyperplasia** (BPH). Bladder-outlet obstruction with **acute urinary retention** is a common complication of BPH and can occur with progressive disease or be triggered by medications that decrease bladder contractility (eg, sympathomimetic or anticholinergic medications).

Enlargement of the prostate (**static obstruction**) and contraction of prostatic smooth muscle (**dynamic obstruction**) compress the prostatic urethra, which increases the hydrostatic pressure required to overcome resistance to flow. As the bladder empties during micturition, urinary pressures diminish; if urinary pressure falls below the prostatic compressive pressure, urine flow stops, leaving a **residual volume** of urine in the bladder. Complete emptying of the bladder is a defense mechanism against urinary tract infection; if the bladder does not empty completely, the residual urine can act as a growth medium for **pathogenic bacteria**. Other complications of BPH include bladder hypertrophy, hydroureter and hydronephrosis, and chronic kidney disease (obstructive uropathy).

(Choice A) Major risk factors for bladder transitional cell carcinoma include smoking and occupational exposure to aromatic amine-containing dyes. The risk is not significantly increased in patients with BPH.

(Choice B) Glomerulonephritis causes primary (intrarenal) azotemia and is not typically associated with BPH. Common causes of glomerulonephritis in adults include IgA nephropathy and membranoproliferative glomerulonephritis.

(Choice C) Priapism is prolonged erection of the penis that is not due to ongoing sexual stimulation. It may occur secondary to conditions that impair venous outflow from the penis (eg, sickle cell) or due to use of certain medications (eg, phosphodiesterase-5 inhibitors, trazodone). BPH does not increase the risk for priapism.

(Choice D) The risk for prostatic adenocarcinoma increases with age and is greatest in black patients and in individuals with a family history of prostate cancer. However, the risk is not appreciably increased in those with BPH or urinary obstruction.

Educational objective:
Benign prostatic hyperplasia can increase resistance to urine flow in the urethra and lead to incomplete bladder emptying during micturition. The residual urine can act as a growth medium for pathogenic bacteria and increase the risk for urinary tract infection.

A 7-year-old boy with a two-day history of colicky abdominal pain now develops bloody stools. His mother states that his urine also appeared red today. Physical examination reveals palpable skin lesions on his buttocks. Which of the following additional findings is most consistent with this patient's condition?

- A. Impetigo
- B. Joint pain
- C. Swollen lymph nodes
- D. Red eyes
- E. Oral ulcers

Submit

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29

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- A. Impetigo [10%]
- ✔ B. Joint pain [64%]
- C. Swollen lymph nodes [10%]
- D. Red eyes [6%]
- E. Oral ulcers [7%]

Omitted
Correct answer
B

64%
Answered correctly

3 Seconds
Time Spent

02/06/2019
Last Updated

Explanation

This patient presents with classic signs of Henoch-Schönlein purpura (HSP), the most common small vessel vasculitis in children. This disease classically affects boys 2-10 years old, and is often preceded by viral or streptococcal upper respiratory infections. Symptoms of HSP generally develop a few weeks after the associated illness resolves. It is hypothesized that antigen from the infection stimulates production of IgA antibodies and that IgA-containing immune complexes then deposit on vessel walls, inducing an inflammatory reaction. HSP is therefore an IgA-mediated leukocytoclastic (hypersensitivity) vasculitis.

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The effects of this vasculitis are seen most prominently in the following organ systems:

1. **Gastrointestinal tract:** Intermittent severe abdominal pain is common in HSP. Vasculitis within the GI tract may result in upper and lower GI bleeding (hematemesis and bloody diarrhea, respectively) as well as bowel wall edema. Patients with HSP also have an increased risk of intussusception.
2. **Kidneys:** Renal involvement in HSP is identical to that seen in IgA nephropathy (Berger disease), a condition characterized by IgA leukocytoclastic vasculitis limited to the kidney. Both diseases cause mesangial proliferation and crescent formation.
3. **Skin:** HSP classically causes "palpable purpura" on the buttocks and lower extremities. These lesions may begin as urticarial papules or plaques and subsequently evolve into purpura. The cutaneous findings in HSP result from leukocytoclasis of cutaneous vessels.
4. **Joints:** Self-limited migratory arthralgias and arthritis are most commonly seen in the large joints of the lower extremities (ankle and knee joints), possibly because of their dependent nature.

(Choice A) Impetigo is a superficial skin infection characterized by a "honey-colored" crust. Streptococcus and Staphylococcus species are generally responsible.

(Choices C and D) Swollen lymph nodes and red eyes are characteristic findings in Kawasaki disease. Other symptoms of Kawasaki disease include high fevers, strawberry tongue, perioral erythema and fissuring, and periungual desquamation.

(Choice E) Oral ulcers can be a component of many illnesses, including pemphigus vulgaris, paraneoplastic pemphigus, Behçet disease and Crohn's disease.

Educational Objective:

mediated leukocytoclastic (hypersensitivity) vasculitis.

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Educational Objective:
Henoch-Schönlein purpura (HSP) generally affects young children and is classically preceded by an upper respiratory infection. This IgA-mediated hypersensitivity (leukocytoclastic) vasculitis commonly causes abdominal pain, joint pain, lower extremity palpable purpura and hematuria.

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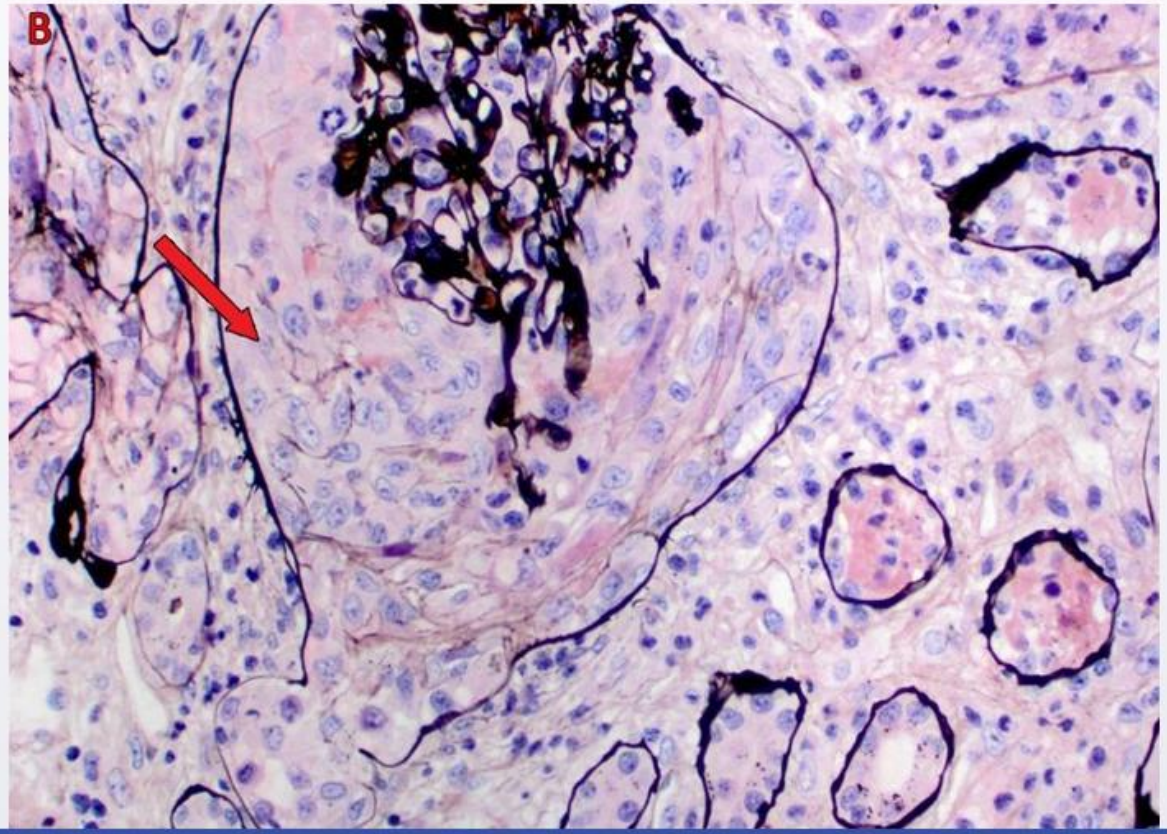
A 34-year-old man is being evaluated for acute hematuria and oliguria. He has no chronic medical conditions and takes no medications on a regular basis. Blood pressure is 170/100 mm Hg. Blood urea nitrogen is 38 mg/dL and serum creatinine is 4.5 mg/dL. The patient undergoes kidney biopsy. The following microscopic changes are seen after silver staining to highlight the glomerular tuft:



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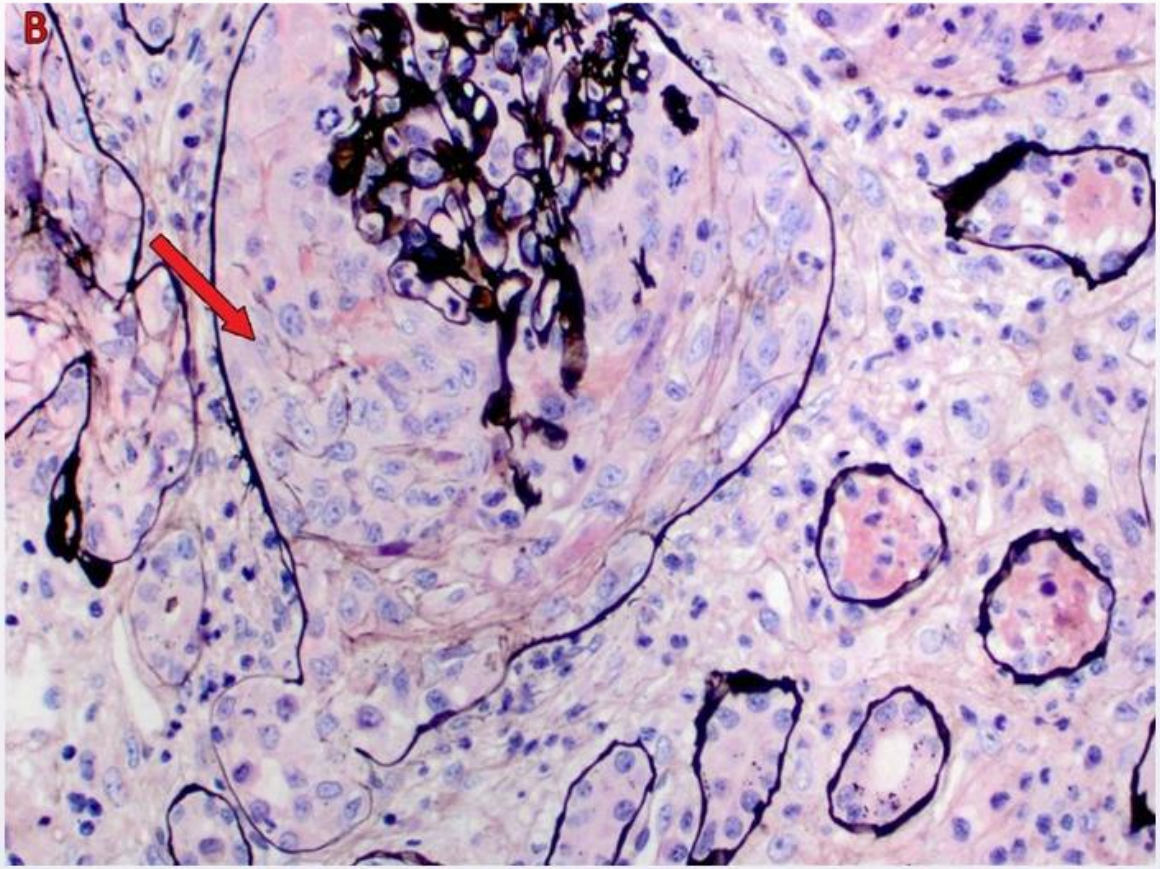
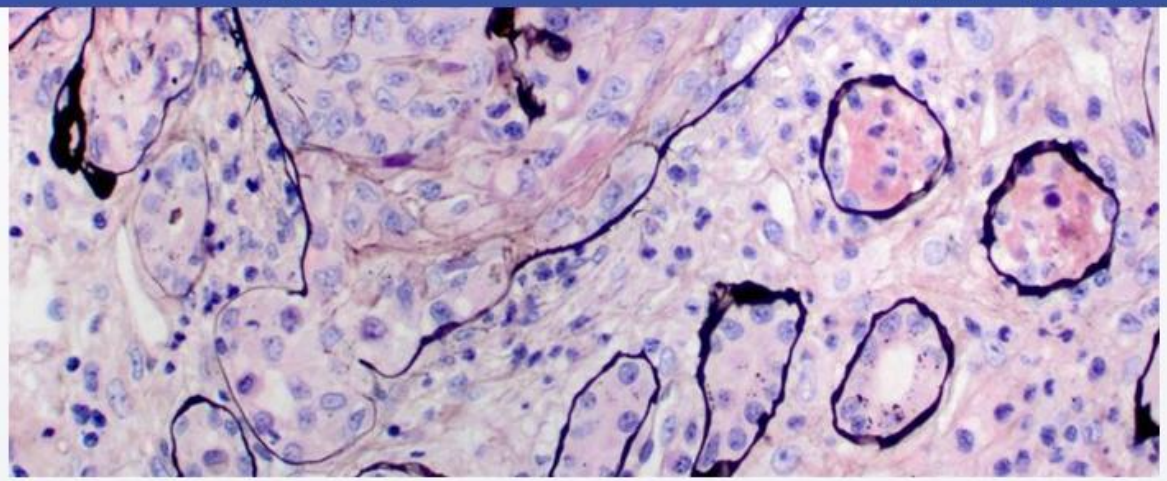


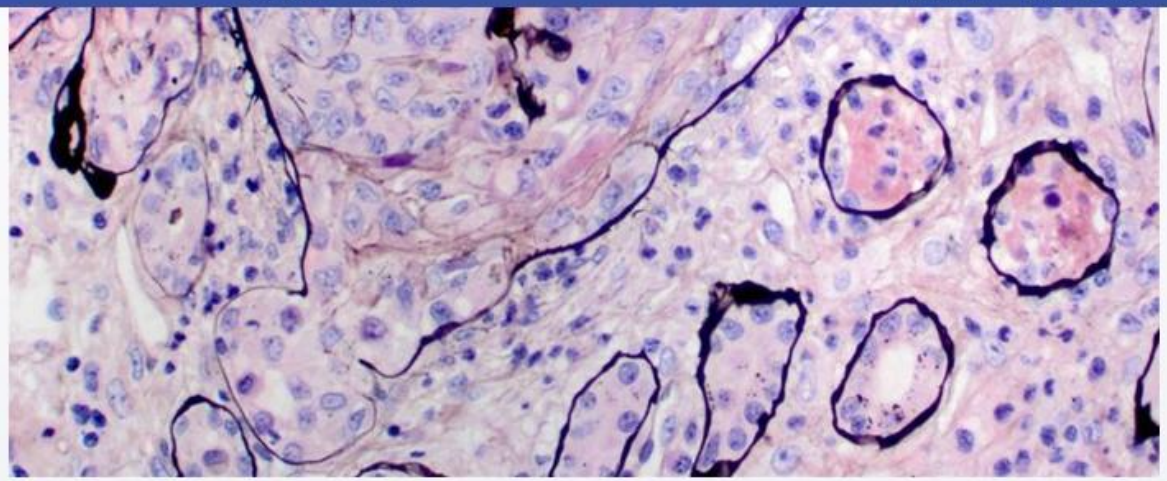
The area marked with an arrow is likely to have abnormal deposition of which of the following substances?



The area marked with an arrow is likely to have abnormal deposition of which of the following substances?

- A. Amyloid
- B. Fibrin
- C. IgE
- D. Lipid
- E. Myoglobin

Submit



The area marked with an arrow is likely to have abnormal deposition of which of the following substances?

- A. Amyloid [22%]
- ✔ B. Fibrin [63%]
- C. IgE [4%]
- D. Lipid [2%]
- E. Myoglobin [6%]

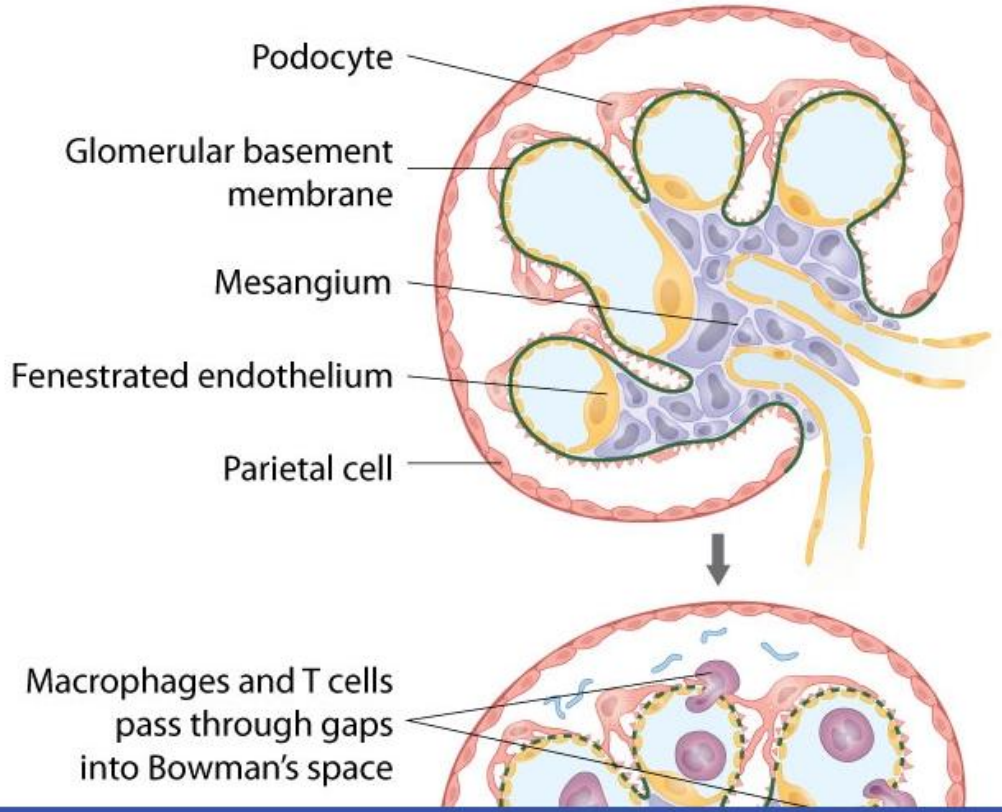
Omitted
Correct answer

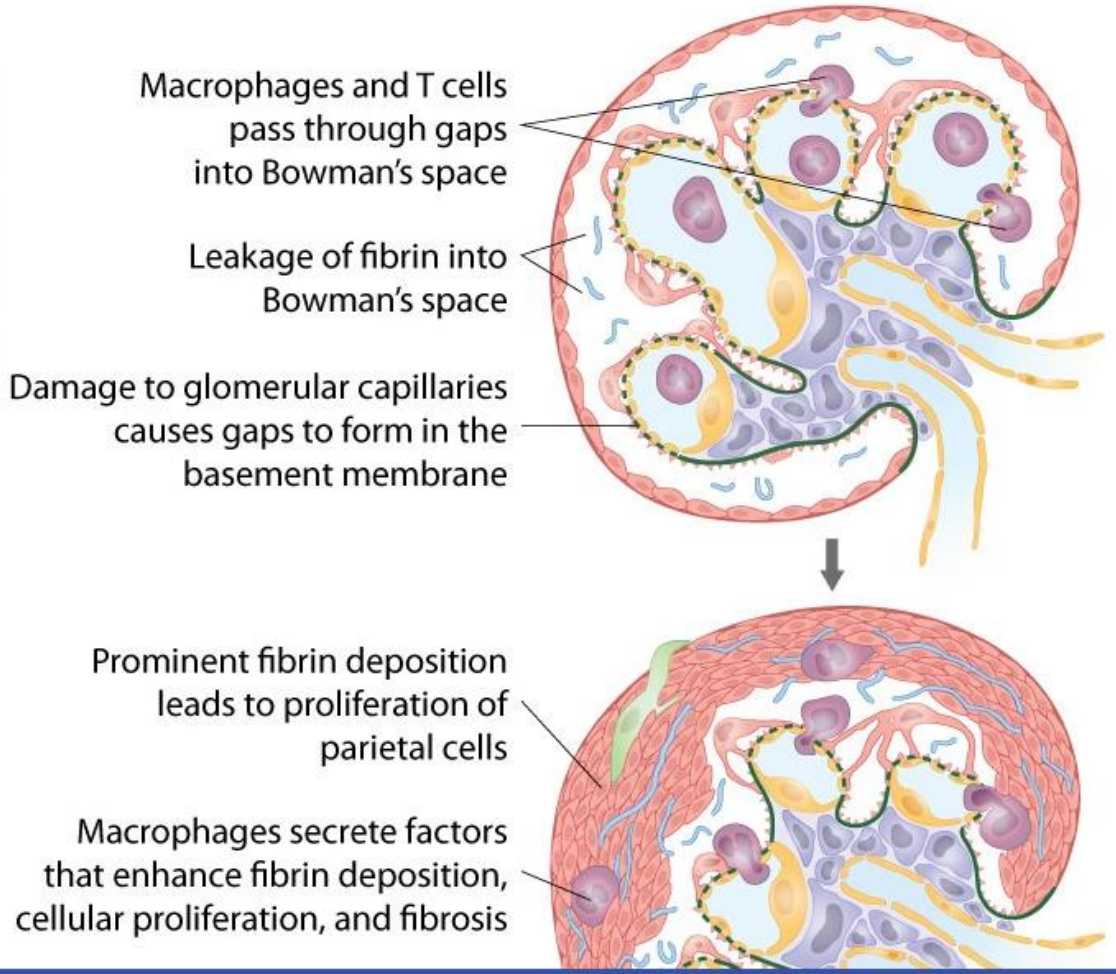
63%
Answered correctly

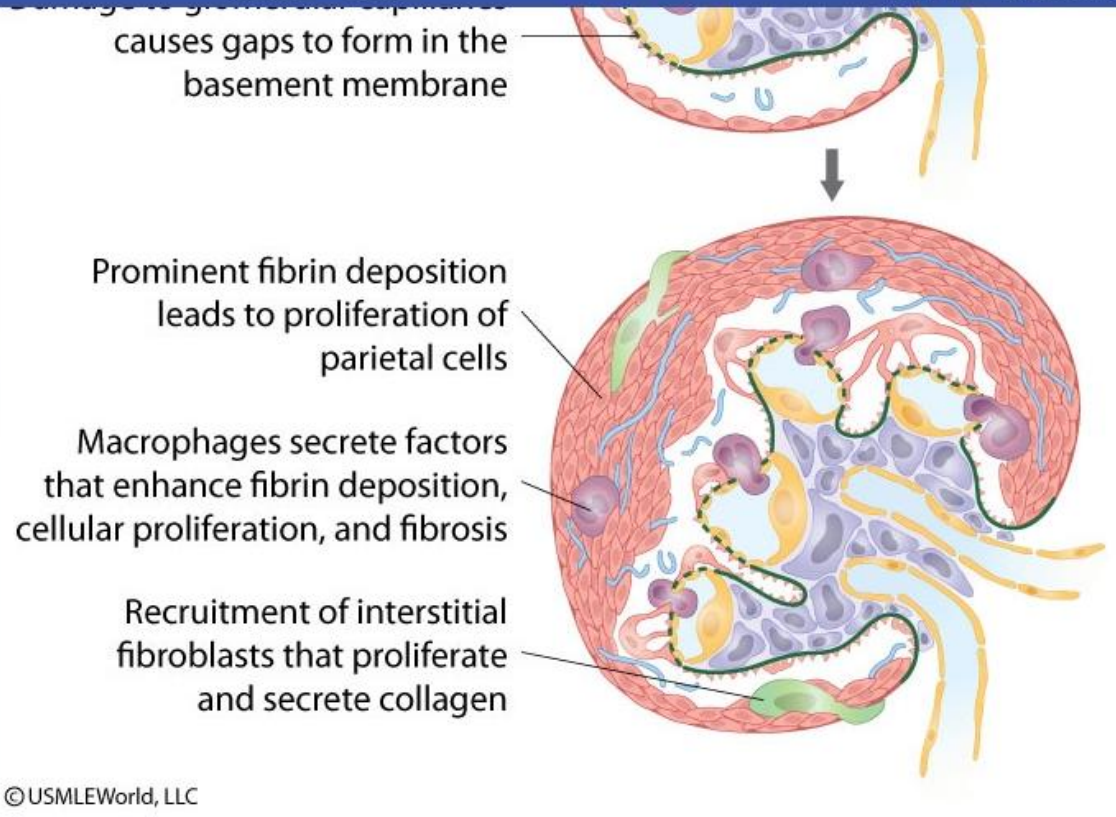
10 Seconds
Time Spent

01/02/2019
Last Updated

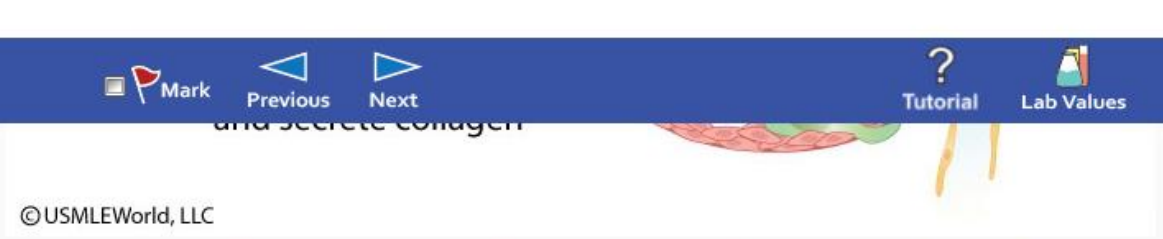
Pathogenesis of crescent formation in rapidly progressive glomerulonephritis







This patient with acute renal failure and hematuria has a glomerular crescent noted on light microscopy. **Glomerular crescents**, defined as >2 layers of **proliferating cells within the Bowman space**, form in response to immune or inflammatory-mediated injury to glomerular capillaries. Disruption of the glomerular basement membrane allows gaps to form within the capillary, resulting in an influx of coagulation factors (eg, tissue factor, fibrinogen) and inflammatory cells (eg, lymphocytes, macrophages) into the Bowman space. Initiation of the coagulation cascade promotes



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Crescent formation is diagnostic of **rapidly progressive glomerulonephritis** (RPGN), a syndrome of severe renal injury that can occur in a number of disease processes (eg, anti-glomerular basement antibody [Goodpasture] disease, granulomatosis with polyangiitis). Like other nephritic syndromes, it typically presents with hematuria, hypertension, and progressive renal failure; however, renal decompensation and progression to end-stage renal disease occur particularly quickly (weeks to months) in RPGN.

(Choice A) Amyloid is visualized as **amorphous mesangial deposits** on light microscopy or, when stained with Congo red, as apple-green, birefringent deposits under polarized light. It is associated with nephrotic syndrome (heavy proteinuria, hyperlipidemia), not with nephritic syndrome as seen in this patient.

(Choice C) Goodpasture disease can cause RPGN and is characterized by antibodies against the glomerular basement membrane. However, these antibodies are usually IgG, or occasionally IgM or IgA. IgE mediates immediate hypersensitivity reactions, and participates in host defenses against some parasites, but it does not participate in the pathogenesis of RPGN.

(Choice D) The **clear cells** seen in renal cell carcinoma (RCC) have a high lipid content, which is responsible for the **yellow tinge** noted on gross histology. RCC can cause hematuria and hypertension but does not cause crescent formation or renal failure.

(Choice E) Myoglobinuria is seen in rhabdomyolysis; urine dipstick is positive for blood, but red blood cells are absent on urinalysis. Myoglobin is toxic to renal tubular cells and induces **acute tubular necrosis**, not glomerular injury and crescent formation.

the deposition of **large quantities of fibrin**, while inflammatory cells proliferate and release growth factors and inflammatory cytokines that recruit fibroblasts and stimulate parietal cell proliferation. This eventually results in progressive glomerular hypercellularity, fibrosis, and irreversible renal injury.

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Educational objective:
Crescent formation on light microscopy is diagnostic for rapidly progressive glomerulonephritis. Crescents consist of glomerular parietal cells, lymphocytes, and macrophages along with abundant fibrin deposition. Crescents eventually become fibrotic, disrupting glomerular function and causing irreversible renal injury.

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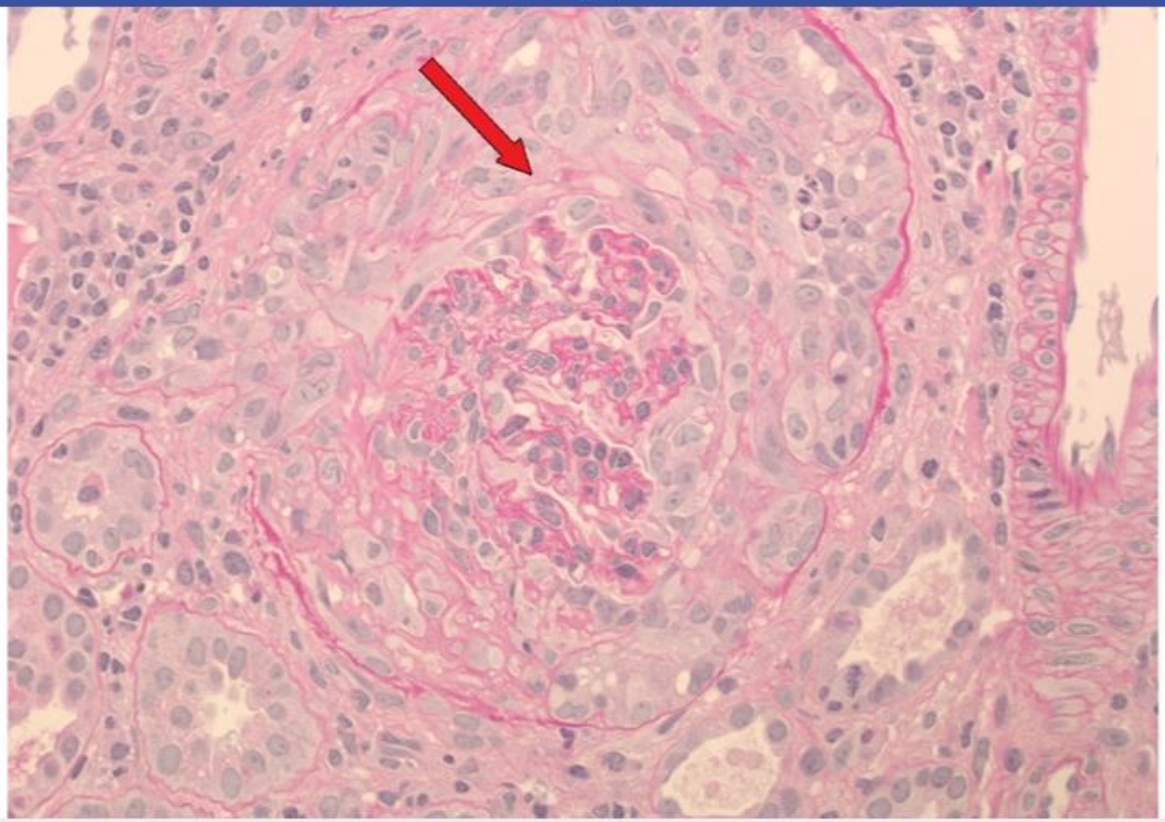

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A 38-year-old man comes to the emergency department because he has been vomiting blood. After appropriate resuscitation measures, he undergoes upper gastrointestinal endoscopy, which reveals a bleeding duodenal ulcer. During hospital day 2, the patient develops decreased urine output. Serum creatinine rises to 3.0 mg/dL from a baseline of 1.2 mg/dL. Renal biopsy shows patchy epithelial necrosis of the tubules, tubulorrhexis, and intratubular casts. On hospital day 8, urine output significantly increases and serum creatinine levels decline. Over the next few days, this patient is at highest risk for which of the following complications?

- A. Hyperphosphatemia
- B. Hypokalemia
- C. Metabolic acidosis
- D. Urinary protein loss
- E. Volume overload

Submit

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- A. Hyperphosphatemia [5%]
- ✔ B. Hypokalemia [64%]
- C. Metabolic acidosis [15%]
- D. Urinary protein loss [11%]
- E. Volume overload [2%]

Omitted
Correct answer
B

64%
Answered correctly

3 Seconds
Time Spent

01/30/2019
Last Updated

Explanation

Stages of acute tubular necrosis	
Initiation stage	• Tubular injury resulting from: - Ischemia (eg, hemorrhage, acute MI, sepsis, shock)

Stages of acute tubular necrosis	
Initiation stage (24-36 hours)	• Tubular injury resulting from: ◦ Ischemia (eg, hemorrhage, acute MI, sepsis, shock) ◦ Cytotoxins (eg, radiologic contrast agents, aminoglycosides, myoglobin)
Maintenance stage (1-3 weeks)	• Oliguric renal failure (↓ GFR, ↓ urine output, fluid overload) • ↑ Creatinine/BUN, ↑ potassium, metabolic acidosis
Recovery phase (months)	• Gradual increase in urine output, leading to high-volume diuresis • Continued impairment of renal tubular function, resulting in electrolyte wasting (↓↓ potassium, magnesium, phosphorus, calcium)
BUN = blood urea nitrogen; **GFR** = glomerular filtration rate; **MI** = myocardial infarction.	

This patient developed acute renal failure after gastrointestinal hemorrhage; renal biopsy showing epithelial necrosis of the tubules, tubulorrhexis, and intratubular casts is consistent with **acute tubular necrosis** (ATN). ATN is characterized by tubular injury due to renal ischemia (eg, shock, hemorrhage) or direct cytotoxicity (eg, radiologic contrast agents, aminoglycosides).

The clinical course of ATN can be broken into 3 stages. The **initiation** stage is marked by the inciting event (eg, hemorrhage, as in this patient) and the onset of tubular injury. If significant tubular damage occurs, the **maintenance** stage (oliguric stage) follows in 24-36 hours. During this stage, **urine output decreases** and patients may develop volume overload. Renal tubular dysfunction results in the characteristic low urinary osmolality (<350 mOsm/kg), high urinary sodium (>30 mEq/L), and high urinary fractional sodium excretion (>1%).

In spite of the seemingly profound damage that occurs to nephrons in ATN, tubular epithelial cells have excellent regenerative capacity. If the patient survives the maintenance stage (by conservative management or dialysis), the **recovery** stage follows in 1-3 weeks. Glomerular filtration rate often improves before renal tubular function is restored, so patients can develop **transient polyuria** (sometimes >3 L/day) with significant **electrolyte wasting** because tubular resorptive capacity remains impaired. During this time, patients are at high risk of developing clinically

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In spite of the seemingly profound damage that occurs to nephrons in ATN, tubular epithelial cells have excellent regenerative capacity. If the patient survives the maintenance stage (by conservative management or dialysis), the **recovery** stage follows in 1-3 weeks. Glomerular filtration rate often improves before renal tubular function is restored, so patients can develop **transient polyuria** (sometimes >3 L/day) with significant **electrolyte wasting** because tubular resorptive capacity remains impaired. During this time, patients are at high risk of developing clinically significant electrolyte imbalances, particularly **hypokalemia**, which can be life-threatening. Serum concentrations of magnesium, phosphorus, and calcium may also be low. Most patients recover completely, depending on the magnitude of the initial injury.

(Choices A, C, and E) Hyperphosphatemia, anion gap metabolic acidosis, and volume overload occur in the maintenance stage of ATN. This patient's spontaneous diuresis and falling creatinine are more consistent with the recovery phase.

(Choice D) Protein-losing nephropathies (eg, nephrotic syndrome) occur due to significant glomerular damage. Because the destruction in ATN is largely tubular, protein loss is unexpected. Patients with nephrotic syndrome typically develop progressive renal dysfunction, which would not be expected to improve after 8 days.

Educational objective:
Acute tubular necrosis is characterized by tubular injury due to renal ischemia or direct cytotoxicity. The course of the disease can be broken into 3 stages: initiation (initial insult), maintenance (oliguric renal failure), and recovery. During the recovery period, glomerular filtration rate improves prior to restoration of renal tubular resorptive capacity, so transient polyuria and electrolyte wasting (eg, hypokalemia) can occur.

A 5-year-old boy is brought to the office by his mother, who notes that her son's eyes and feet have looked puffy over the last several weeks. She is unaware of exactly when this began but says the patient had a mild upper respiratory tract infection several weeks ago. The boy has no pain but mentions that his shoes seem to fit tightly and bother him, especially when he runs outside during recess at school. The mother also remarks that the boy's urine has been excessively foamy recently. On further questioning, the mother states that she has seasonal allergies and asks whether her child also has allergies. Physical examination is remarkable for periorbital edema and lower extremity edema. Urinalysis shows 4+ proteinuria but is otherwise unremarkable. Which of the following secondary changes is most likely in this patient?

A. Decreased liver albumin synthesis
B. Decreased plasma aldosterone level
C. Increased capillary oncotic pressure
D. Increased liver lipoprotein synthesis
E. Increased renal sodium wasting

Submit

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- A. Decreased liver albumin synthesis [8%]
- B. Decreased plasma aldosterone level [4%]
- C. Increased capillary oncotic pressure [12%]
- ✔ D. Increased liver lipoprotein synthesis [65%]
- E. Increased renal sodium wasting [8%]

Omitted
Correct answer
D

65%
Answered correctly

3 Seconds
Time Spent

01/29/2019
Last Updated

Explanation

Overview of nephrotic syndrome

Glomerular injury

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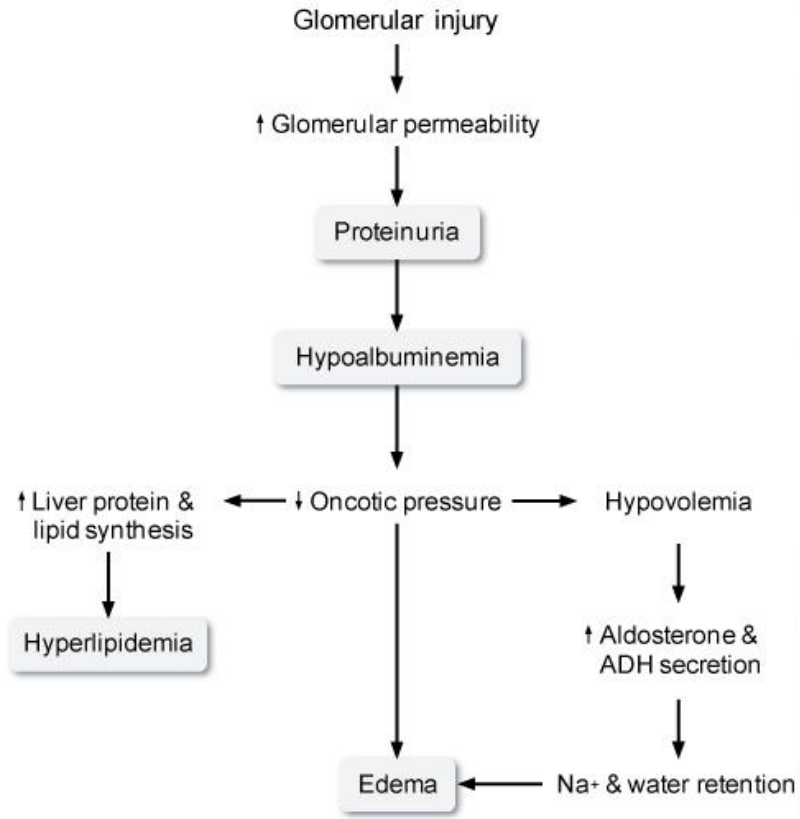
Overview of nephrotic syndrome



ADH = antidiuretic hormone.

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This child most likely has minimal change disease, the most common cause of **nephrotic syndrome** in children. It typically presents suddenly after an upper respiratory infection. The classic features of nephrotic syndrome are **heavy proteinuria** (>3.5 g/day in adults and >50 mg/kg/day in children), **hypoalbuminemia** (<3 g/dL), **generalized edema**, and **hyperlipidemia**. Two mechanisms, **underfilling and overfilling**, contribute to the pathogenesis of edema in nephrotic syndrome. The underfilling mechanism is particularly significant in minimal change disease in children and presents as follows:

1. **Increased glomerular capillary permeability** to plasma proteins leads to massive **loss of protein** (predominantly albumin) in the urine.
2. The large decrease in serum albumin causes a **drop in intravascular oncotic pressure**, which results in fluid moving into the interstitial space and edema formation **(Choice C)**.
3. The fluid shift results in intravascular volume depletion (ie, underfilling), which triggers the renin-angiotensin-aldosterone system to increase aldosterone synthesis (secondary hyperaldosteronism) and antidiuretic hormone secretion **(Choice B)**. The result is intravascular **sodium and water retention (Choice E)**. This fluid leaks back out into the interstitial space due to the low oncotic pressure, exacerbating the edema.
4. Low intravascular oncotic pressure stimulates **increased lipoprotein production** in the liver. Impaired lipid catabolism due to decreased lipoprotein lipase and abnormal transport of circulating lipid particles also contributes to hyperlipidemia.

(Choice A) When the serum albumin level decreases due to its massive loss in the urine, the liver responds by increasing albumin synthesis. However, the amount of renal albumin loss exceeds the liver synthetic capacity.

Educational objective:

Minimal change disease is the most common childhood nephrotic syndrome. Increased glomerular capillary permeability causes massive protein (eg, albumin) loss in the urine. Hypoalbuminemia reduces plasma oncotic pressure, which causes a fluid shift into the interstitial space, resulting in edema. Low oncotic pressure also triggers increased lipoprotein production in the liver (ie, hyperlipidemia).

References

ADH = antidiuretic hormone

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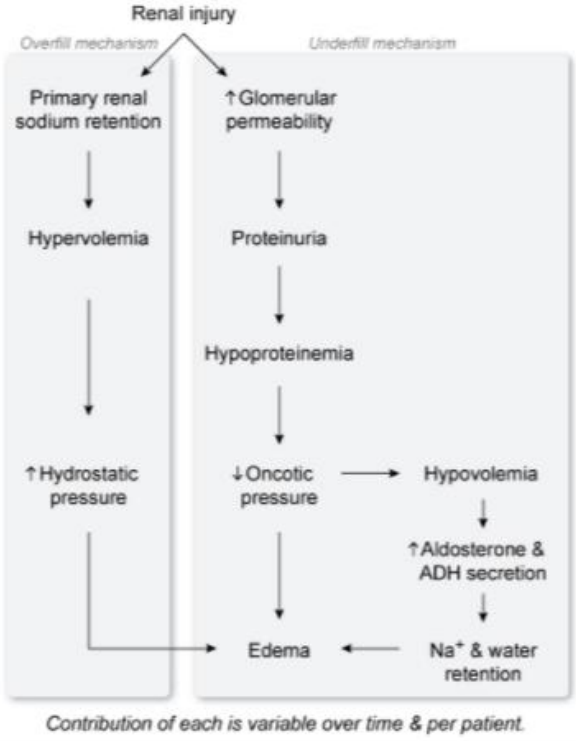
Mechanism of edema formation in nephrotic syndrome



Contribution of each is variable over time & per patient.

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References

A 10-year-old boy is brought to the office due to dark brown urine that he first noticed yesterday after swimming practice. Blood pressure is 130/80 mm Hg. Physical examination is normal with the exception of bilateral periorbital edema. Laboratory results are as follows:

Serum chemistry	
Sodium	140 mEq/L
Potassium	4 mEq/L
Blood urea nitrogen	14 mg/dL
Creatinine	1.4 mg/dL
Creatine kinase	86 U/L
Urinalysis	
Protein	1+
Leukocyte esterase	negative
Nitrites	negative
White blood cells	1-2/hpf
Red blood cells	many/hpf
Casts	RBC casts

Which of the following is the most likely diagnosis?

A. Minimal change disease

Creatine kinase	86 U/L

Urinalysis

Protein	1+
Leukocyte esterase	negative
Nitrites	negative
White blood cells	1-2/hpf
Red blood cells	many/hpf
Casts	RBC casts

Which of the following is the most likely diagnosis?

A. Minimal change disease
B. Nephrolithiasis
C. Postinfectious glomerulonephritis
D. Pyelonephritis
E. Rhabdomyolysis

Submit

Creatine kinase	86 U/L

Urinalysis

Protein	1+
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Nitrites	negative
White blood cells	1-2/hpf
Red blood cells	many/hpf
Casts	RBC casts

Which of the following is the most likely diagnosis?

- A. Minimal change disease [14%]
- B. Nephrolithiasis [1%]
- ✔ C. Postinfectious glomerulonephritis [63%]
- D. Pyelonephritis [1%]
- E. Rhabdomyolysis [18%]

Omitted
Correct answer

63%
Answered correctly

6 Seconds
Time Spent

09/25/2018
Last Updated

Explanation

Acute poststreptococcal glomerulonephritis	

Clinical features	• Can be asymptomatic
	• If symptomatic:
	  ◦ Gross hematuria (tea- or cola-colored urine)
	  ◦ Edema (periorbital, generalized)
	  ◦ Hypertension

Laboratory findings	• Urinalysis: + protein, + blood, ± red blood cell casts
	• Serum:
	  ◦ ↓ C3 & possible ↓ C4
	  ◦ ↑ Serum creatinine
	  ◦ ↑ Anti-DNase B & ↑ AHase
	  ◦ ↑ ASO & ↑ anti-NAD (from preceding pharyngitis)

AHase = antihyaluronidase; **anti-DNase B** = antideoxyribonuclease-B; **ASO** = antistreptolysin O.

This pediatric patient with periorbital edema, hypertension, and hematuria with red blood cell (RBC) casts, as well as mild proteinuria on urinalysis, has **poststreptococcal glomerulonephritis**, a nonsuppurative complication of a pharyngeal or skin (eg, impetigo) infection. Infection with nephritogenic strains of group A *Streptococcus* (eg, *S pyogenes*) can induce formation of antigen-antibody complexes, which are deposited on the glomerular basement membrane. Subsequent activation of complement and inflammation can lead to **nephritic syndrome** 2-4 weeks after the infection; because of this delay, parents may not report the inciting infection.

Urine studies in nephritic syndrome typically reveal RBCs, mild protein, and **RBC casts** (indicating an intrarenal process). Serum studies show elevated creatinine, **antistreptococcal antibodies** (from recent infection), and decreased C3 (glomerular complement deposition). For refractory cases in which biopsies are indicated, histology shows **diffusely enlarged, hypercellular glomeruli**, RBC casts in nephron tubules, and

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(Choice A) Minimal change disease is the most common cause of pediatric nephrotic syndrome. It is characterized by immune-related loss of the normal glomerular anionic charge (which prevents filtration of negatively charged albumin), leading to heavy proteinuria. However, hematuria and hypertension are unexpected.

(Choice B) Nephrolithiasis is a common cause of hematuria; however, the glomeruli are not involved, so RBC casts are unexpected. In addition, nephrolithiasis is rare in children and typically presents with back pain radiating to the groin.

(Choice D) Pyelonephritis is most commonly due to an ascending bacterial infection from the bladder. Microscopic urinalysis findings are similar to those of a urinary tract infection (eg, bacteria, leukocytes, nitrites, leukocyte esterase) with the addition of white blood cell casts.

(Choice E) Rhabdomyolysis can occur after strenuous exercise and results in muscle pain, elevated creatine kinase levels, and myoglobinuria (ie, positive urine dipstick for blood without RBCs on microscopy). This patient's normal creatine kinase level and the presence of many RBCs on urine microscopy are not suggestive of rhabdomyolysis.

Educational objective:
Poststreptococcal glomerulonephritis presents most commonly in children with hematuria, hypertension, and periorbital edema. Red blood cell casts and mild proteinuria may be present on urinalysis, and serum creatinine may be elevated.

References

has **poststreptococcal glomerulonephritis**, a nonsuppurative complication of a pharyngeal or skin (eg, impetigo) infection. Infection with

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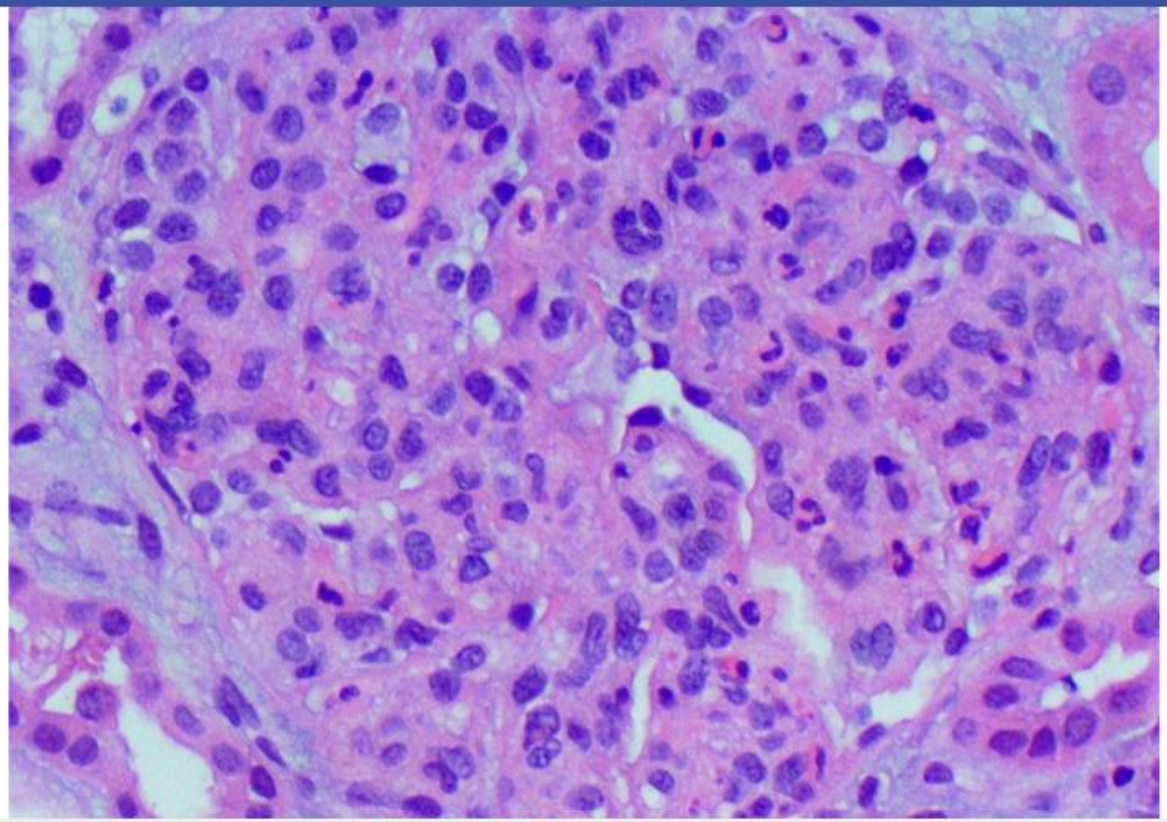

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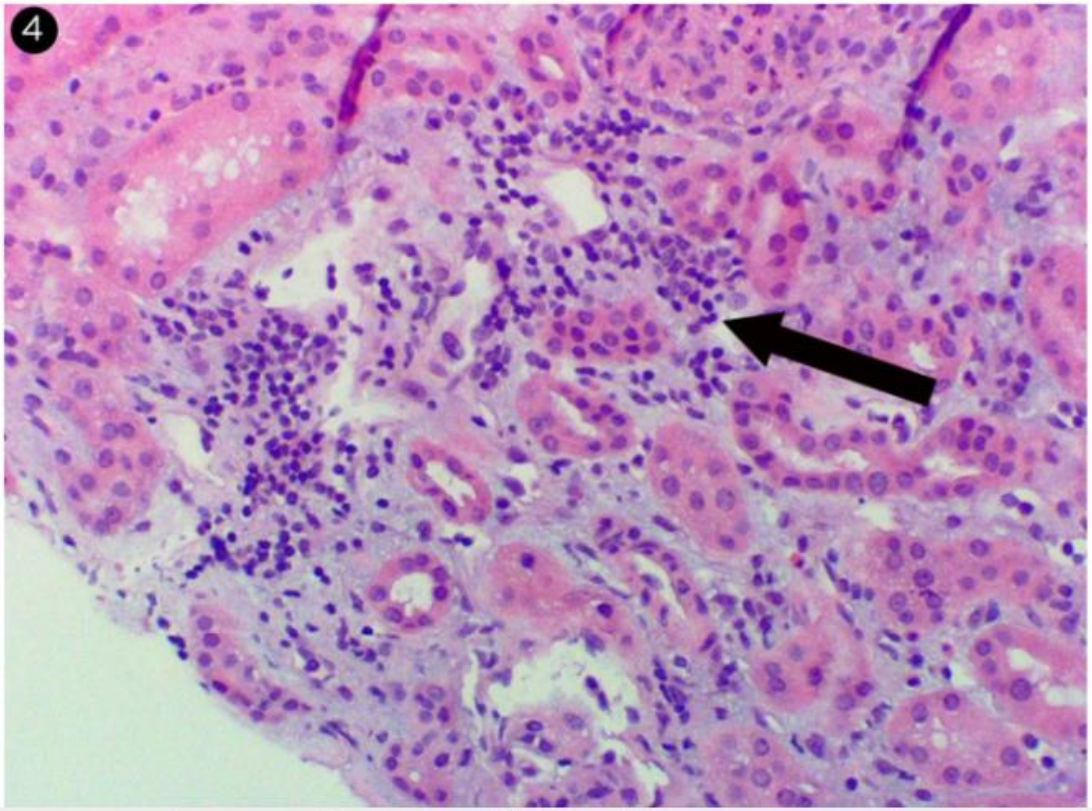

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A 46-year-old woman being evaluated for irregular vaginal bleeding is found to have invasive cervical carcinoma. She undergoes total abdominal hysterectomy and bilateral salpingo-oophorectomy. Pelvic lymphadenectomy was also performed, during which several enlarged nodes around the pelvic vessels were resected. A week after the surgery, the patient begins to experience left-sided flank pain that radiates to the groin. Her temperature is 36.1 C (97 F), blood pressure is 120/70 mm Hg, and pulse is 84/min. On physical examination, there is a ballotable left flank mass. Which of the following most likely accounts for this physical examination finding?

- A. Hydronephrosis
- B. Interstitial nephritis
- C. Renal cell carcinoma
- D. Renal cystic disease
- E. Renal vein thrombosis
- F. Vesicoureteral reflux

Submit

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- A. Hydronephrosis [72%]
- B. Interstitial nephritis [1%]
- C. Renal cell carcinoma [5%]
- D. Renal cystic disease [2%]
- E. Renal vein thrombosis [11%]
- F. Vesicoureteral reflux [6%]

Omitted
Correct answer
A

72%
Answered correctly

3 Seconds
Time Spent

12/11/2018
Last Updated

Explanation

Ureteral anatomy

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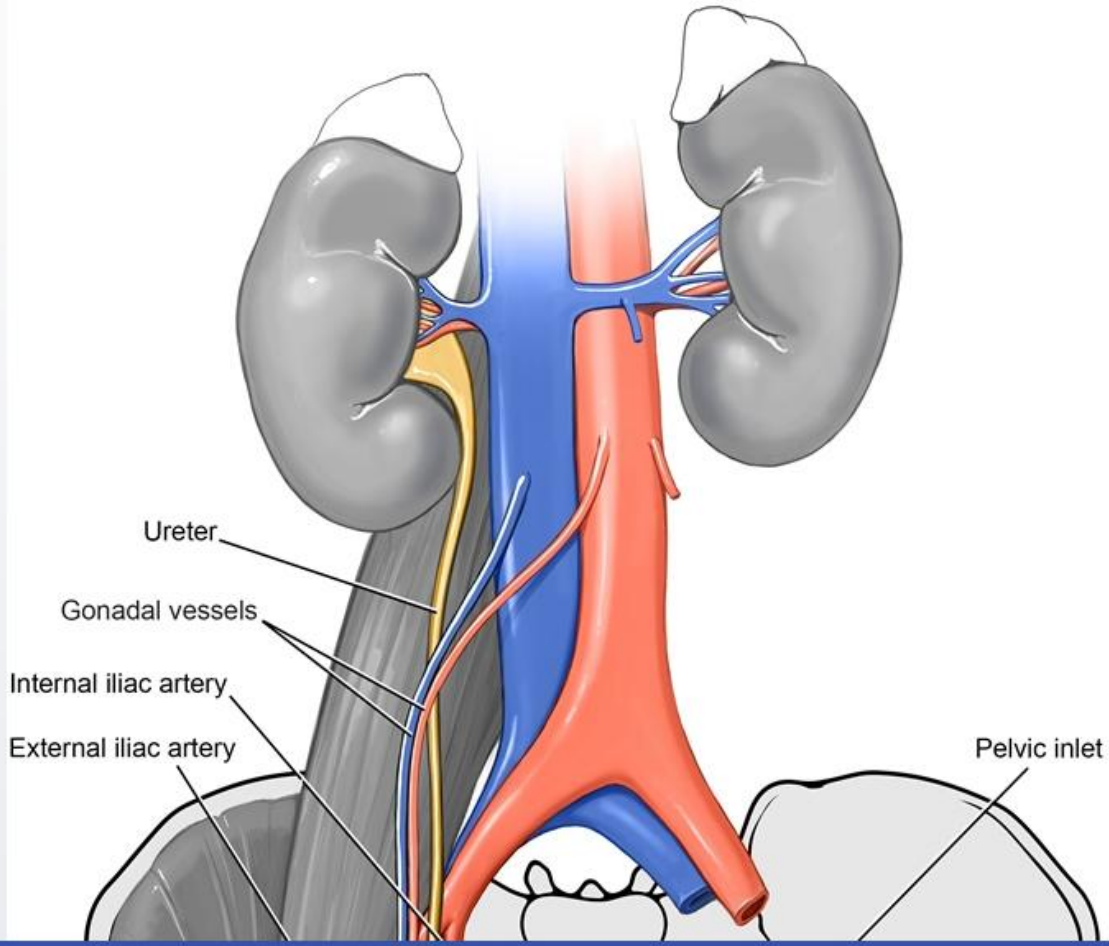
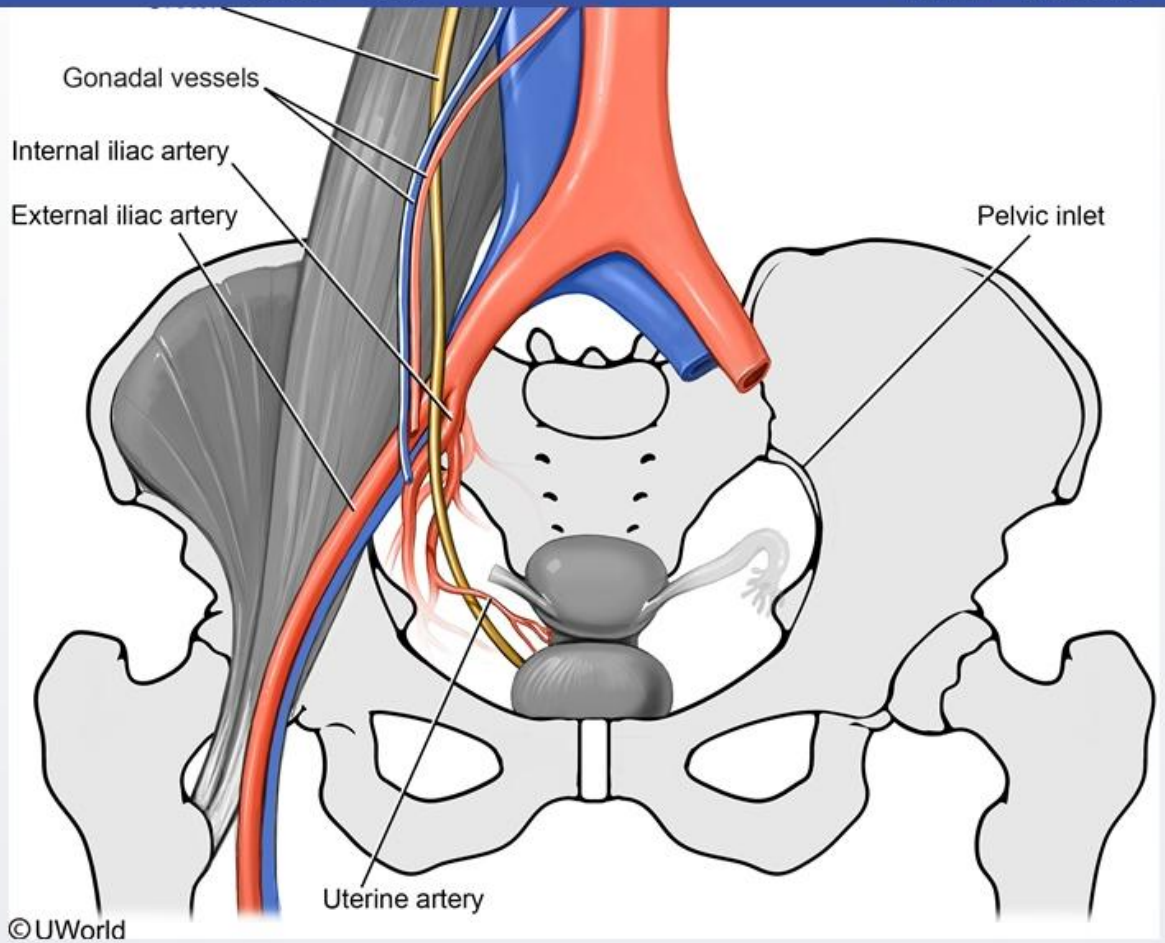
Ureteral anatomy





Flank pain radiating to the groin with a ballotable flank mass that develops within a week of pelvic surgery suggests **ureteric obstruction**. The

Flank pain radiating to the groin with a ballotable flank mass that develops within a week of pelvic surgery suggests **ureteric obstruction**. The ureter runs in close proximity to the pelvic vessels. It courses anterior to the iliac vessels (area of resection of the pelvic nodes, which drain the uterus and cervix) and just posterior to the uterine artery near the lateral fornix of the vagina. It is vulnerable to injury during **pelvic surgery**, such as that involved in hysterectomy with pelvic lymphadenectomy. Unintentional ureteral ligation causes obstruction with hydronephrosis and flank pain due to distension of the ureter and renal pelvis. Urine output and serum creatinine remain within normal limits in most individuals with unilateral obstruction because the contralateral kidney functions normally and compensates for decreased functioning of the affected kidney.

(Choice B) Acute interstitial nephritis is classically medication induced. Signs and symptoms include fever, transient rash, and acute renal failure.

(Choices C and D) Renal cell carcinoma classically causes hematuria, flank pain, and a palpable mass. Adult polycystic kidney disease is an autosomal dominant condition characterized by multiple renal, pancreatic, and hepatic cysts. This patient had no evidence of a renal mass prior to surgery, and these conditions would not develop over a period of a week.

(Choice E) Postsurgical patients are at increased risk for deep venous thrombosis, mostly in the lower extremities or pulmonary vasculature. Renal vein thrombosis is unusual postoperatively but may be seen in patients with nephrotic syndrome.

(Choice F) Vesicoureteral reflux can be a complication of prostatectomy or bladder surgery. It predisposes to pyelonephritis and hydroureteronephrosis.

Educational objective:
The ureters run in close proximity to the pelvic lymph nodes and the uterine artery in the female pelvis, which predisposes them to injury during pelvic surgery.

References

- Complications of hysterectomy.

A 26-year-old woman dies shortly after a sudden-onset, severe headache. She was recently diagnosed with hypertension but otherwise had no medical problems. The patient was a lifetime nonsmoker and did not use illicit drugs. Autopsy reveals evidence of intracranial hemorrhage. Both carotid arteries appear tortuous distally with alternating areas of fibrotic webs and aneurysmal dilation. On microscopic examination, the aneurysmal segments of the carotid arteries lack an internal elastic lamina. Which of the following is the most likely additional finding in this patient?

- A. Adrenal tumor
- B. Coarctation of the aorta
- C. Hypertrophic cardiomyopathy
- D. Renal artery stenosis
- E. Thyroid follicular hyperplasia

Submit

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- A. Adrenal tumor [6%]
- B. Coarctation of the aorta [33%]
- C. Hypertrophic cardiomyopathy [6%]
- ✔ D. Renal artery stenosis [51%]
- E. Thyroid follicular hyperplasia [1%]

Omitted
Correct answer
D

51%
Answered correctly

3 Seconds
Time Spent

11/06/2018
Last Updated

Explanation

Fibromuscular dysplasia	
Manifestations	• Fibromuscular webs (luminal stenosis) alternating with areas of aneurysmal dilation • Loss of the internal elastic lamina

Fibromuscular dysplasia	
Manifestations	• Fibromuscular webs (luminal stenosis) alternating with areas of aneurysmal dilation • Loss of the internal elastic lamina • Most common in women, age <55
Presentation	• Resistant hypertension (RAS) • CNS involvement: Headache, TIA, stroke, ruptured aneurysm
Diagnosis	• Angiography (CT, MRI, percutaneous) • String-of-beads appearance (multifocal disease)

RAS = renal artery stenosis; **TIA** = transient ischemic attack.

This young woman with recent-onset hypertension died of an intracranial hemorrhage, likely from a ruptured aneurysm. This, in conjunction with the characteristic pathology findings of **fibromuscular webs** alternating with **aneurysmal dilation** and loss of the internal elastic lamina, is consistent with **fibromuscular dysplasia** (FMD). FMD is a nonatherosclerotic disease characterized by abnormal tissue growth within arterial walls, leading to arterial stenosis, tortuosity, aneurysms, or dissections. FMD typically occurs in women age <55. Angiography (ie, percutaneous, CT, MRI) is diagnostic and typically demonstrates a **string-of-beads** appearance in multifocal disease.

FMD can involve any artery but most commonly the renal, cerebral (eg, carotid, vertebral), and visceral arteries. Up to 80% of patients develop **renal artery stenosis**, which limits renal perfusion and leads to activation of the renin-angiotensin-aldosterone system. The resultant **hypertension** is often the earliest sign of the disease. Other presentations are related to locations of the dysplastic artery; **cerebrovascular involvement** (ie, headache, stroke, aneurysm rupture), mesenteric ischemia, or extremity claudication may be seen.

(Choices A and B) Adrenal tumors that can present with severe hypertension include pheochromocytoma and aldosterone- or cortisol-secreting adrenocortical adenomas. Coarctation of the aorta also causes hypertension, with blood pressure higher in the upper versus lower extremities. Due to the elevated blood pressure, these diseases can cause headaches and intraparenchymal hemorrhage in predisposed individuals, but they

This young woman with recent-onset hypertension died of an intracranial hemorrhage, likely from a ruptured aneurysm. This, in conjunction with the characteristic pathology findings of **fibromuscular webs** alternating with **aneurysmal dilation** and loss of the internal elastic lamina, is consistent with **fibromuscular dysplasia** (FMD). FMD is a nonatherosclerotic disease characterized by abnormal tissue growth within arterial walls, leading to arterial stenosis, tortuosity, aneurysms, or dissections. FMD typically occurs in women age <55. Angiography (ie, percutaneous, CT, MRI) is diagnostic and typically demonstrates a **string-of-beads** appearance in multifocal disease.

FMD can involve any artery but most commonly the renal, cerebral (eg, carotid, vertebral), and visceral arteries. Up to 80% of patients develop **renal artery stenosis**, which limits renal perfusion and leads to activation of the renin-angiotensin-aldosterone system. The resultant **hypertension** is often the earliest sign of the disease. Other presentations are related to locations of the dysplastic artery; **cerebrovascular involvement** (ie, headache, stroke, aneurysm rupture), mesenteric ischemia, or extremity claudication may be seen.

(Choices A and B) Adrenal tumors that can present with severe hypertension include pheochromocytoma and aldosterone- or cortisol-secreting adrenocortical adenomas. Coarctation of the aorta also causes hypertension, with blood pressure higher in the upper versus lower extremities. Due to the elevated blood pressure, these diseases can cause headaches and intraparenchymal hemorrhage in predisposed individuals, but they are not associated with fibrotic webbing or aneurysm formation.

(Choice C) Hypertrophic cardiomyopathy may present with sudden death in young patients due to left ventricular outflow obstruction; histology demonstrates hypertrophied myocytes and interstitial fibrosis. However, hypertrophic cardiomyopathy is not associated with aneurysm formation.

(Choice E) Thyroid follicular hyperplasia can cause hyperthyroidism (eg, Graves disease, thyroid adenoma). This commonly causes tachycardia, tremor, and palpitations but would not cause aneurysm formation.

Educational objective:
Fibromuscular dysplasia is characterized by abnormal tissue growth within arterial walls, resulting in stenotic and tortuous arteries that can cause tissue ischemia and are prone to aneurysm formation. Pathology typically demonstrates alternating fibromuscular webs and aneurysmal dilation with absent internal elastic lamina (string-of-beads appearance). Renovascular hypertension occurs due to renal artery stenosis and activation of the renin-angiotensin-aldosterone system.

A 26-year-old previously healthy man comes to the office with a 3-week history of shortness of breath, cough, and hemoptysis preceded by an upper respiratory tract infection. He has no fever, night sweats, or weight loss. His blood pressure is 150/85 mm Hg and pulse is 86/min and regular. Physical examination reveals bilateral inspiratory crackles and lower extremity edema. His creatinine is 4.1 mg/dL. Urinalysis shows proteinuria and hematuria with dysmorphic red blood cells. Bilateral pulmonary infiltrates are seen on chest x-ray. He is also found to have an increased carbon monoxide diffusing capacity (DLCO) on pulmonary function testing. Antibodies directed against which of the following is most likely to be associated with this patient's condition?

- A. Alpha 3 chain of type IV collagen
- B. Beta-hemolytic streptococci
- C. Cardiolipin phospholipid
- D. Double-stranded DNA
- E. Topoisomerase I

Submit

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- A. Alpha 3 chain of type IV collagen [70%]
- B. Beta-hemolytic streptococci [16%]
- C. Cardiolipin phospholipid [6%]
- D. Double-stranded DNA [4%]
- E. Topoisomerase I [2%]

Omitted
Correct answer
A

70%
Answered correctly

3 Seconds
Time Spent

12/23/2018
Last Updated

Explanation

This patient has **Goodpasture syndrome**, which is caused by autoantibodies against the **alpha 3 chain of type IV collagen** found in the glomerular basement membrane (GBM) and pulmonary capillary membrane (**anti-GBM antibodies**). Antibody formation may be triggered by an antecedent viral respiratory infection, although most cases are idiopathic. These antibodies promote inflammatory injury of the glomerular and

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Explanation

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Rapidly progressive glomerulonephritis results in nephritic syndrome, characterized by hypertension, edema, acute renal failure, hematuria (eg, dysmorphic red cells and red cell casts), and proteinuria. On renal biopsy, **light microscopy** shows glomerular crescent formation and **immunofluorescence** shows linear deposition of IgG and C3 on the GBM. **Alveolar hemorrhage** manifests with shortness of breath and hemoptysis with infiltrates on chest x-ray. Hemoglobin in the alveoli leads to increased alveolar oxygen absorption and high carbon monoxide diffusing capacity (DLCO).

(Choice B) Patients with beta-hemolytic streptococci infection of the pharynx or skin can develop glomerular immune complex deposition resulting in poststreptococcal glomerulonephritis and nephritic syndrome; however, this usually occurs in children and pulmonary involvement with alveolar hemorrhage is not characteristic.

(Choice C) Anticardiolipin antibodies are characteristic of antiphospholipid antibody syndrome, which typically presents with unprovoked/recurrent arterial and venous thrombosis or recurrent spontaneous abortions.

(Choice D) Antibodies to double-stranded DNA (dsDNA) are typically seen in systemic lupus erythematosus (SLE), particularly in individuals with active lupus nephritis. Although this patient has findings of glomerulonephritis, other features of SLE such as constitutional symptoms (eg, fatigue, fever, weight loss), malar rash, arthritis, serositis, and cytopenias are not evident. Pulmonary hemorrhage is also not characteristic of SLE.

(Choice E) Anti-topoisomerase I (anti-Scl-70) antibodies are found in patients with systemic sclerosis, which typically presents with diffuse thickening/hardening of the skin, Raynaud phenomenon, and esophageal dysfunction. Acute renal failure and hypertension may occur during scleroderma renal crisis; however, glomerulonephritis is not characteristic. Lung involvement typically leads to pulmonary fibrosis and pulmonary

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Educational objective:
Goodpasture syndrome is caused by autoantibodies against the alpha 3 chain of type IV collagen in glomerular and alveolar basement membranes (anti-GBM antibodies). Patients typically present with rapidly progressive glomerulonephritis (nephritic syndrome) and alveolar hemorrhage (shortness of breath, hemoptysis).

References

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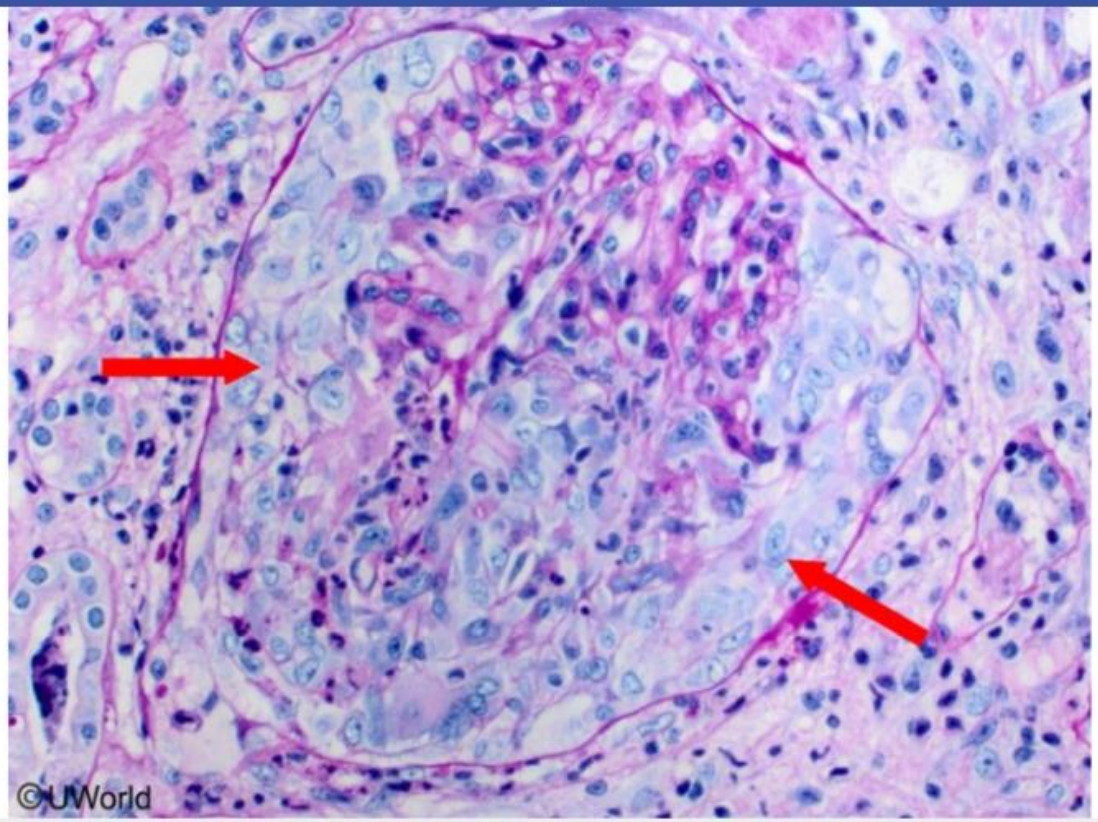

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2/11/2019

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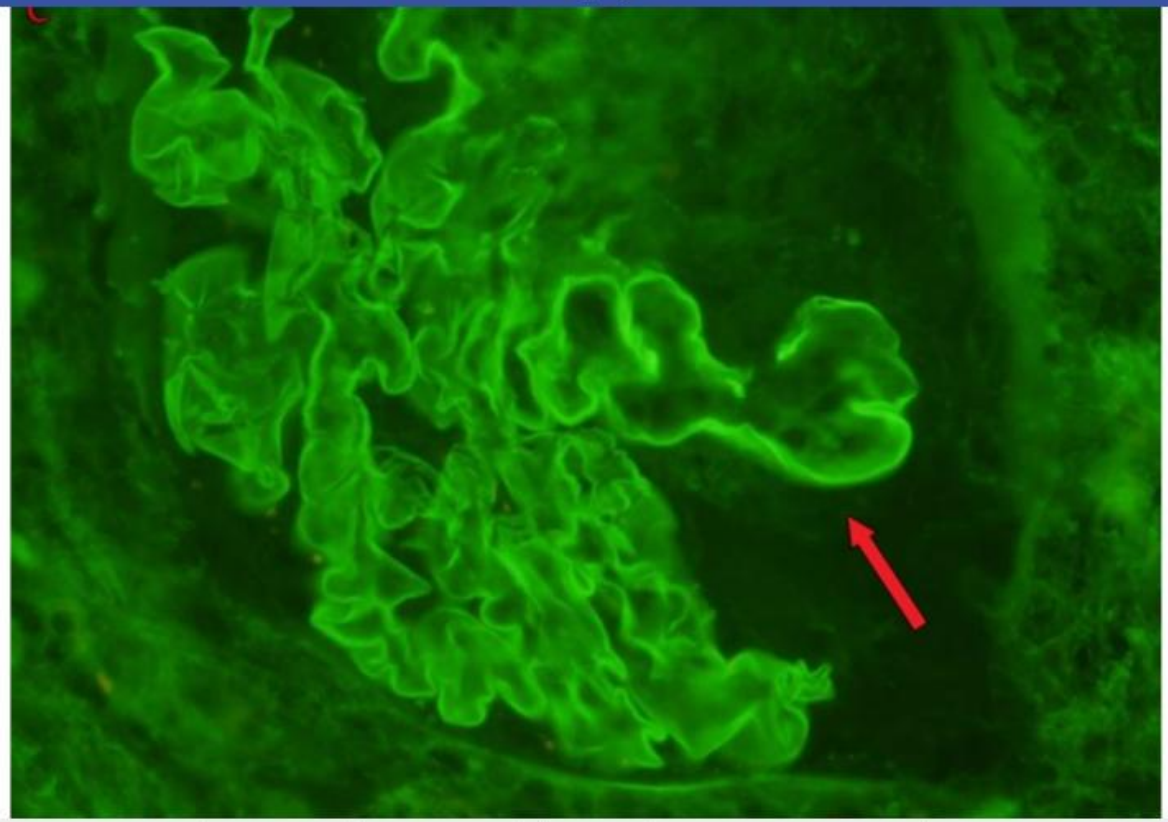

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fever, weight loss), malar rash, arthritis, serositis, and cytopenias are not evident. Pulmonary hemorrhage is also not characteristic of SLE.

A 46-year-old previously healthy woman comes to the emergency department due to 4 days of intermittent fever, abdominal pain, and vomiting. For the past 2 days she has also had decreased urine output, skin rash, and progressive lethargy. Her temperature is 38.3 C (101 F), blood pressure is 130/80 mm Hg, and pulse is 100/min. There is a scattered petechial rash, facial puffiness, and 1+ bilateral pedal edema on physical examination. Laboratory studies show hemoglobin of 8.9 g/dL with elevated reticulocyte count and a platelet count of 26,000/mm^3. Bleeding time is prolonged; prothrombin time and activated partial thromboplastin time are normal. The peripheral blood smear shows schistocytes and reduced platelets with presence of giant forms. Blood urea nitrogen is 46 mg/dL and serum creatinine is 2.3 mg/dL. Urinalysis is positive for proteinuria and hematuria. Which of the following is most likely to be seen on renal biopsy?

A. Collapse and sclerosis of glomerular tufts
B. Crescent-shaped mass of cellular proliferation and leukocytes
C. Diffuse proliferation and subepithelial immunoglobulin deposits
D. Mesangial IgA deposition and proliferation
E. Patchy necrosis of tubular epithelium and loss of basement membrane
F. Platelet-rich thrombi in glomeruli and arterioles

Submit

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- A. Collapse and sclerosis of glomerular tufts [1%]
- B. Crescent-shaped mass of cellular proliferation and leukocytes [14%]
- C. Diffuse proliferation and subepithelial immunoglobulin deposits [12%]
- D. Mesangial IgA deposition and proliferation [10%]
- E. Patchy necrosis of tubular epithelium and loss of basement membrane [10%]
- ✔ F. Platelet-rich thrombi in glomeruli and arterioles [50%]

Omitted
Correct answer
F

50%
Answered correctly

3 Seconds
Time Spent

08/24/2018
Last Updated

Explanation

This patient has the **pentad** of fever, neurologic symptoms (progressive lethargy), renal failure, anemia, and thrombocytopenia in the setting of a gastrointestinal illness. She most likely has **thrombocytopenic thrombotic purpura-hemolytic uremic syndrome** (TTP-HUS), one of the **thrombotic microangiopathy** (TMA) syndromes. These share common clinical and pathologic features, including:

- **Platelet activation** in arterioles and capillaries
- Diffuse **microvascular thrombosis** (most commonly affecting the brain, kidneys, and heart)
- Microangiopathic hemolytic anemia with schistocytes
- Thrombocytopenia

Unlike disseminated intravascular coagulation, in which coagulation cascade activation leads to prolongation of coagulation studies (prothrombin time [PT] and activated partial thromboplastin time [aPTT]), TTP is almost always characterized by **normal** PT and aPTT.

The pentad of symptoms described in this patient is classic for TTP.

(Choice A) Focal segmental glomerulosclerosis, including its collapsing variant, commonly manifests as heavy proteinuria.

(Choice B) Crescentic or **rapidly progressive glomerulonephritis (RPGN)** typically presents with macroscopic hematuria, hypertension, and progressive renal failure. It is classified as anti-glomerular basement membrane (with hemoptysis in Goodpasture syndrome), immune-complex mediated (eg, systemic lupus erythematous), or pauci-immune (with pulmonary, upper respiratory, and kidney involvement in granulomatosis with polyangiitis).

(Choice C) Poststreptococcal glomerulonephritis is typically a childhood disease that can follow streptococcal pharyngitis and lead to increased Coca-Cola-colored urine output and periorbital edema.

(Choice D) Henoch-Schönlein purpura is typically a childhood disease with nonthrombocytopenic palpable purpura and arthritis; IgA nephropathy commonly presents with recurrent hematuria and low-grade proteinuria following an upper respiratory tract infection. Both diseases have similar histopathologic findings with **IgA deposition in the mesangium**.

(Choice E) **Acute tubular necrosis** due to ischemia (eg, prolonged hypotension), nephrotoxins (eg, antibiotics), or pigment deposition (eg,

time [PT] and activated partial thromboplastin time [aPTT]), TTP is almost always characterized by **normal** PT and aPTT.

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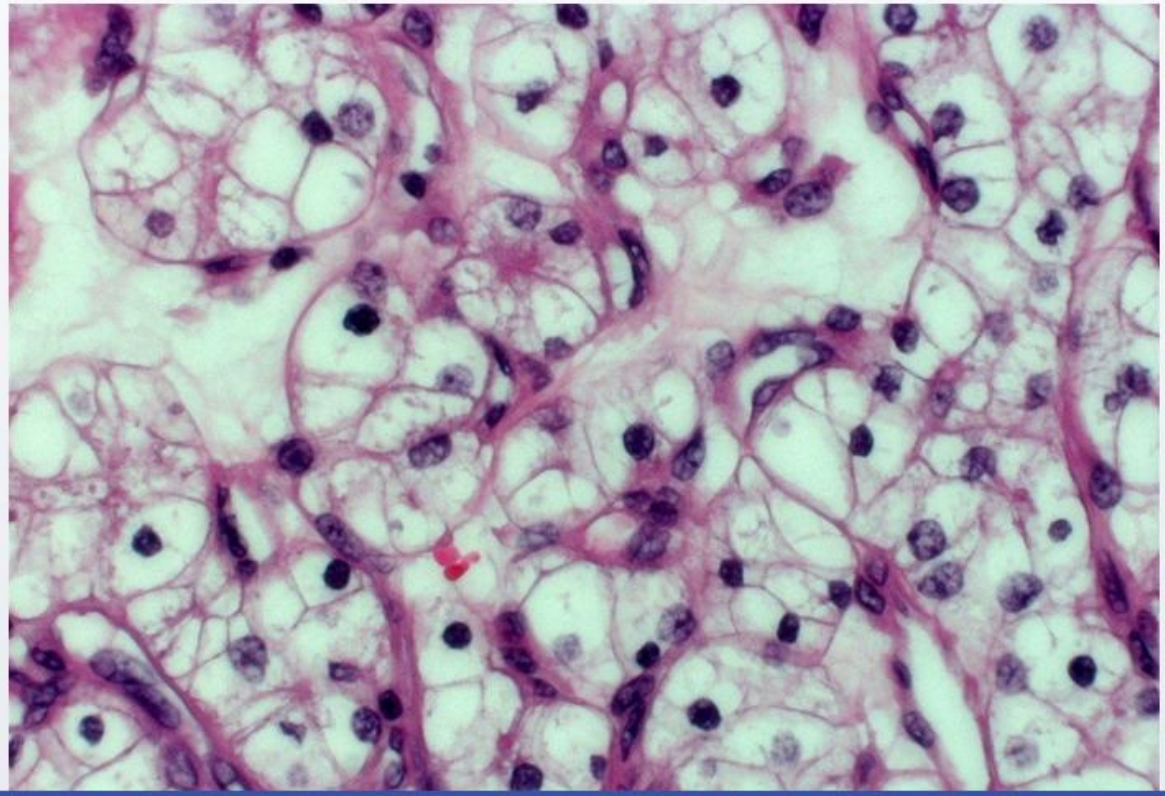
(Choice E) **Acute tubular necrosis** due to ischemia (eg, prolonged hypotension), nephrotoxins (eg, antibiotics), or pigment deposition (eg, myoglobinuria) generally presents with rising creatinine and muddy brown granular casts on urinalysis.

Educational objective:
Primary thrombotic microangiopathy (TMA) syndromes share common clinical and pathologic features and result in platelet activation and diffuse microthrombosis in arterioles and capillaries. TMA syndromes present with hemolytic anemia with schistocytes, thrombocytopenia, and organ injury (eg, brain, kidneys, heart).

References

- Thrombotic microangiopathy and associated renal disorders.
- Pathogenesis of thrombotic microangiopathies.

A 63-year-old man comes to the emergency department due to fever and loss of appetite. He also has chest pain with deep breaths. The patient has never had regular medical care and his medical history is unknown. He has smoked half a pack of cigarettes daily for 30 years. Laboratory evaluation shows a hematocrit of 56%. Chest imaging shows multiple round lesions in both lungs. Biopsy of one of the lesions reveals the findings shown below.



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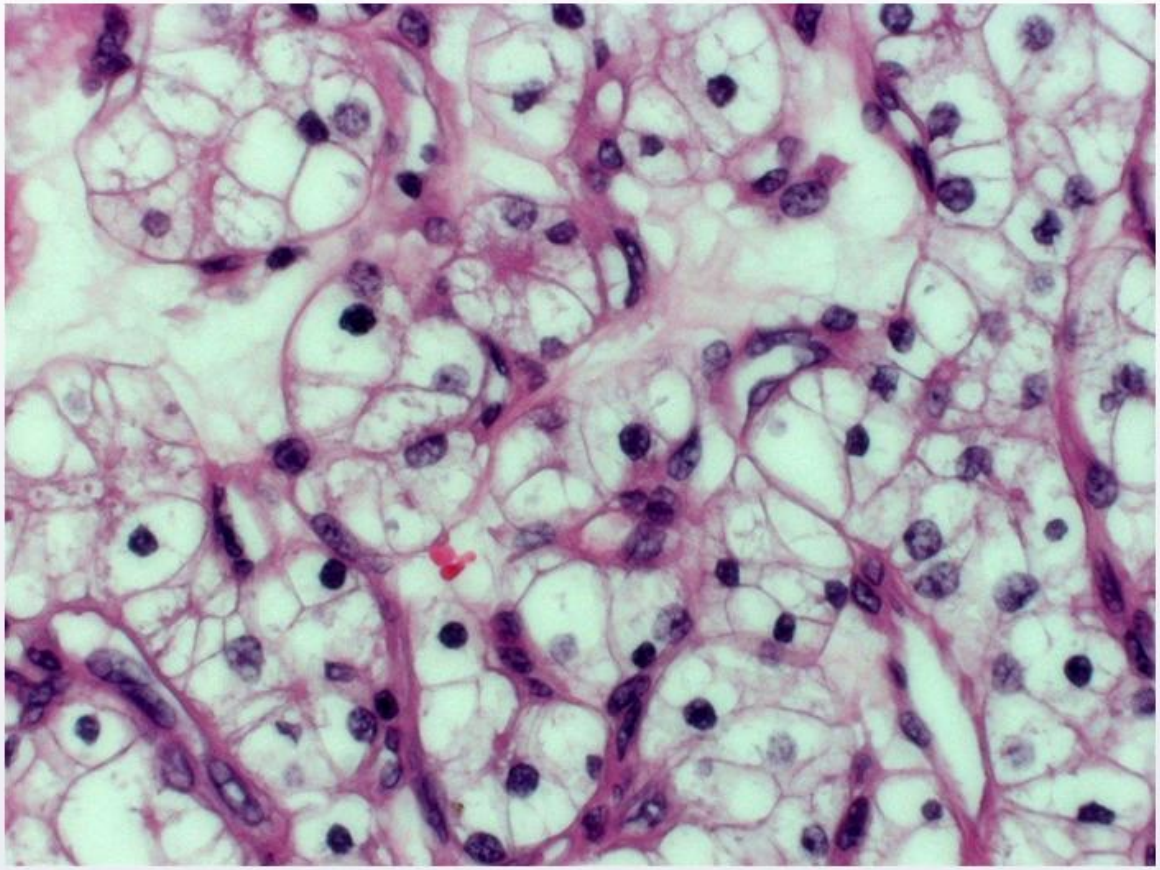
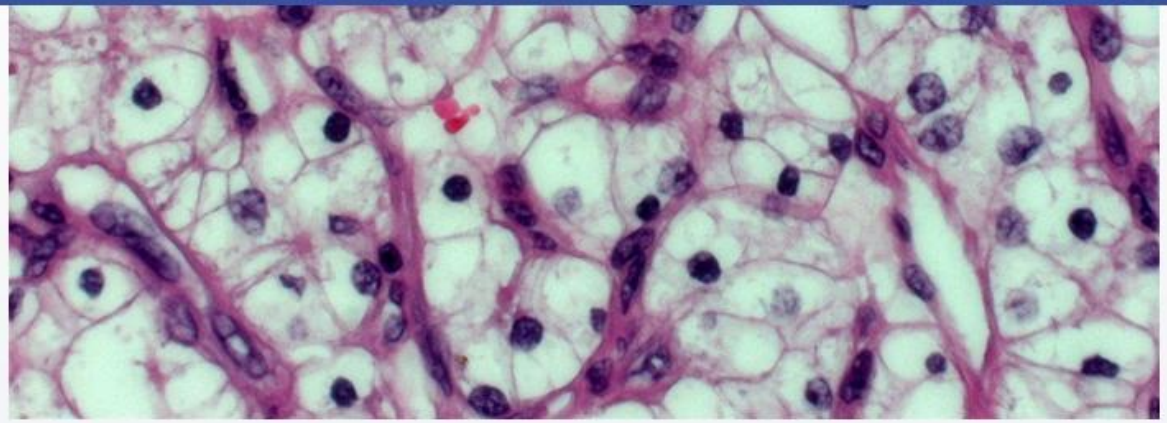
findings shown below.



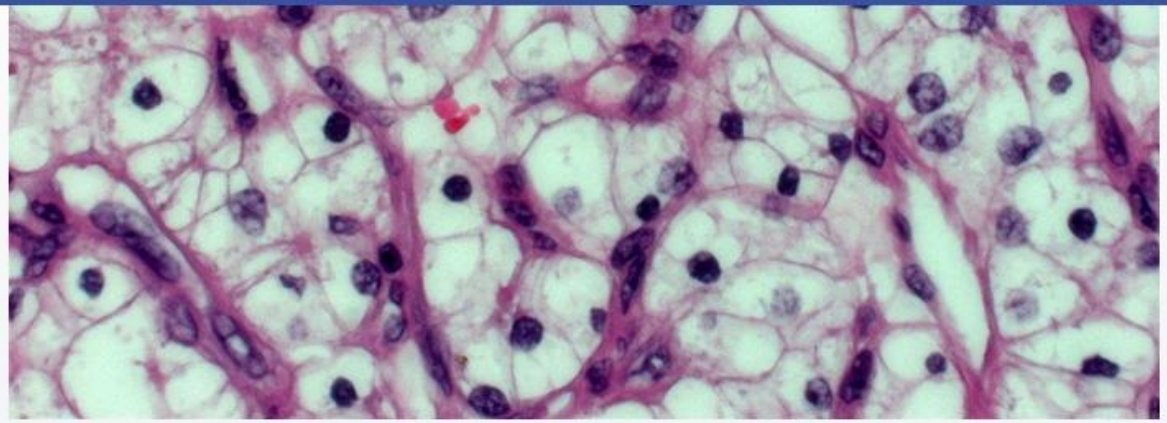
This patient's metastatic disease most likely originated from which of the following organs?



This patient's metastatic disease most likely originated from which of the following organs?

- A. Bone
- B. Brain
- C. Colon
- D. Kidney
- E. Stomach
- F. Testis

Submit



This patient's metastatic disease most likely originated from which of the following organs?

- A. Bone [5%]
- B. Brain [1%]
- C. Colon [8%]
- ✔ D. Kidney [75%]
- E. Stomach [5%]
- F. Testis [3%]

Omitted
Correct answer

75%
Answered correctly

10 Seconds
Time Spent

08/28/2018
Last Updated

Renal cell carcinoma	
Common presentation	• Asymptomatic (most common) • Hematuria, flank pain, palpable abdominal mass
Histopathology (clear cell)	• Rounded polygonal or cuboidal cells • Abundant clear or yellow cytoplasm
Common metastatic site	• Lungs ("cannonball metastases") • Bone (osteolytic)
Paraneoplastic syndromes	• Polycythemia (erythropoietin production) • Hypercalcemia (parathyroid hormone-related peptide production) • Hormone production (eg, ACTH, renin)

This patient has fevers, anorexia, and polycythemia. His evaluation shows multiple round lung lesions with histopathology revealing rounded polygonal cells with **abundant clear cytoplasm**. This presentation is consistent with metastatic clear cell carcinoma, the most common subtype of **renal cell carcinoma** (RCC). The cytoplasm appears clear due to the high glycogen and lipid content of the tumor. For the same reason, this neoplasm is often golden-yellow on macroscopic examination.

Patients with RCC are often asymptomatic; the classic triad of hematuria, flank pain, and palpable abdominal mass occur together in less than 10% of cases, often late in the course of the disease. **Nonspecific symptoms** such as fever and weight loss are more common. Paraneoplastic syndromes, including polycythemia (constitutive secretion of erythropoietin) and hypercalcemia (synthesis of parathyroid hormone-related protein), can also occur.

Renal cell carcinoma is often **detected incidentally** since localizing symptoms only develop in advanced disease; metastases are often discovered earlier than the primary neoplasm. RCC most commonly **metastasizes to the lungs**, where it often presents as large, rounded, well-circumscribed **"cannonball metastases"**. Osteolytic bone lesions and liver metastases also occur frequently.

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(Choice A) Osteosarcoma frequently metastasizes to the lungs, but most patients have localized pain at the primary site (eg, distal femur) and polycythemia is unexpected. Histologically, **spindle cells** with osteoid matrix production would be seen.

(Choice B) Primary brain neoplasms usually metastasize within the CNS, although rarely they can present with metastases outside the nervous system. These are not associated with polycythemia; histology varies by malignancy.

(Choices C and E) Colon and stomach cancers commonly metastasize to the lungs. Microscopy of **signet cell carcinoma** of the stomach demonstrates clear cytoplasm and eccentric nuclei (resembling a signet ring), whereas **colon cancer** forms glands and tubules. However, patients typically develop anemia due to occult bleeding, not polycythemia.

(Choice F) Testicular cancer also commonly metastasizes to the lung, but patients typically have a testicular mass. β-hCG or alpha-fetoprotein are often elevated; however, hematocrit elevations are unexpected. Histology varies by malignancy.

Educational objective:
Clear cell carcinoma is the most common subtype of renal cell carcinoma and is composed of large, rounded, or polygonal cells with clear cytoplasm. These tumors are often detected incidentally at an advanced stage; the lung is the most common site for metastasis, followed by osteolytic bone and liver.

neoplasm is often golden-yellow on macroscopic examination.

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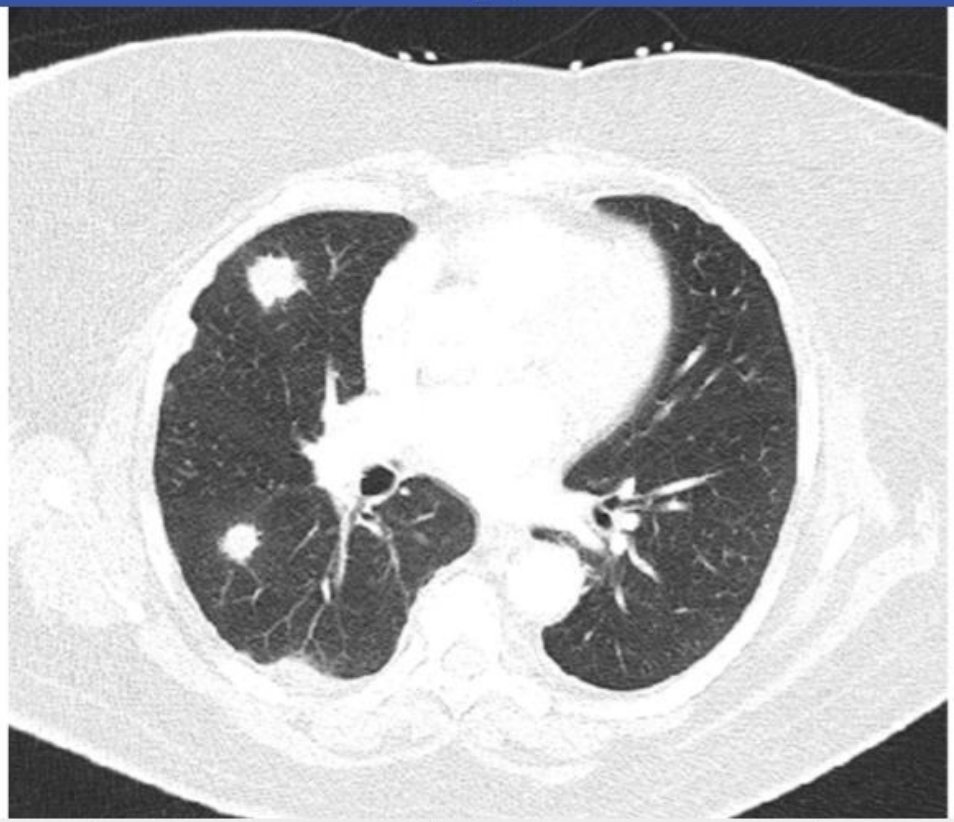

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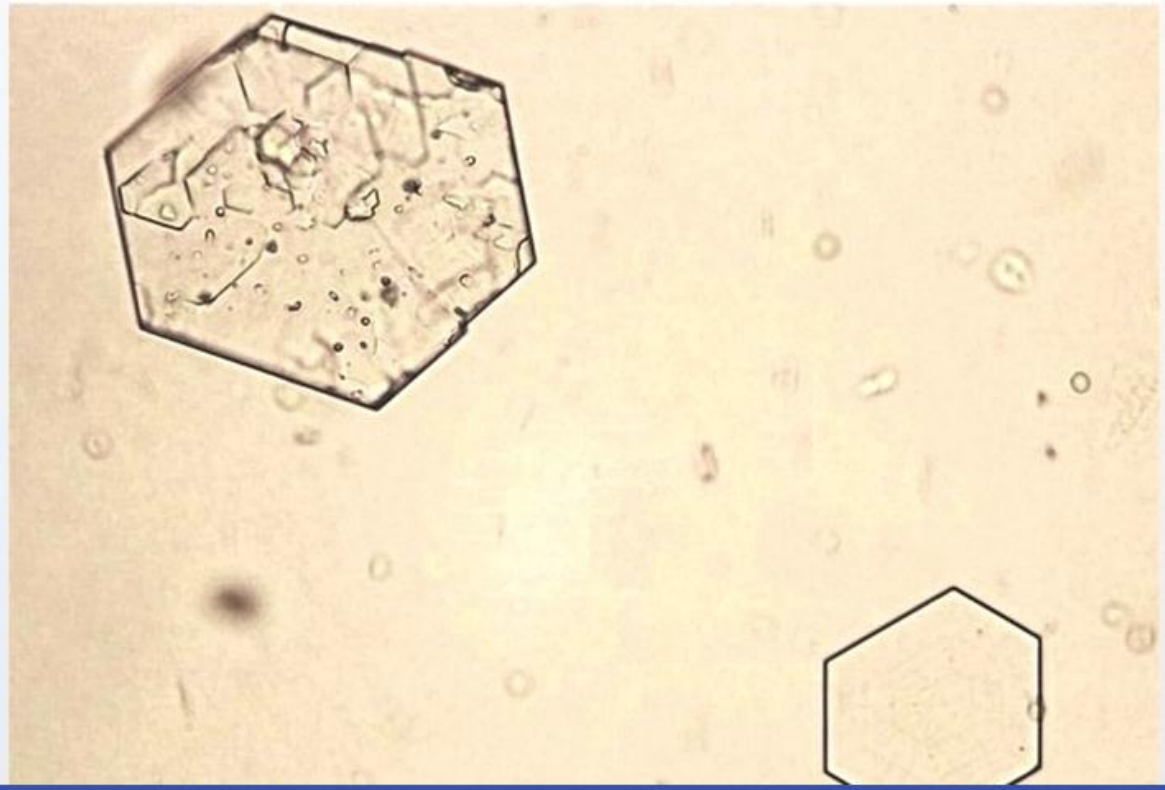
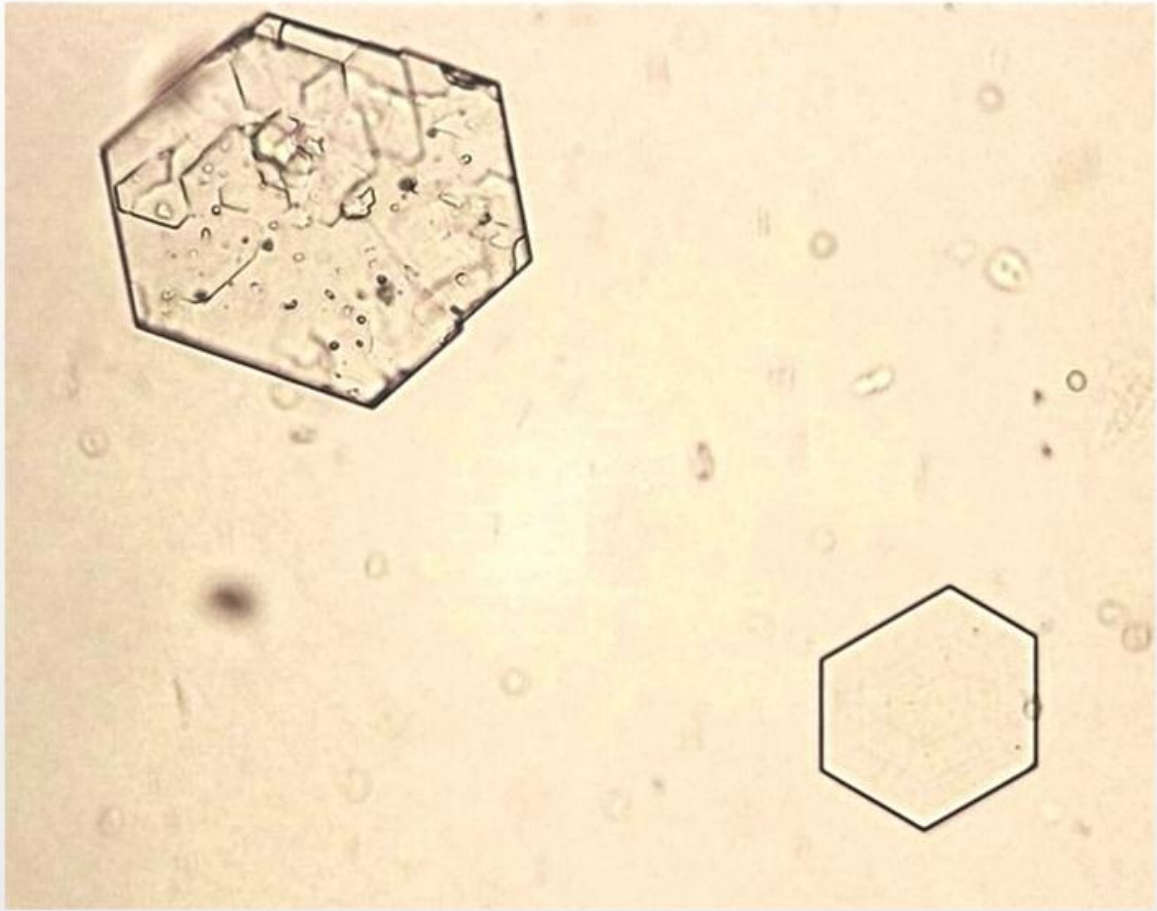
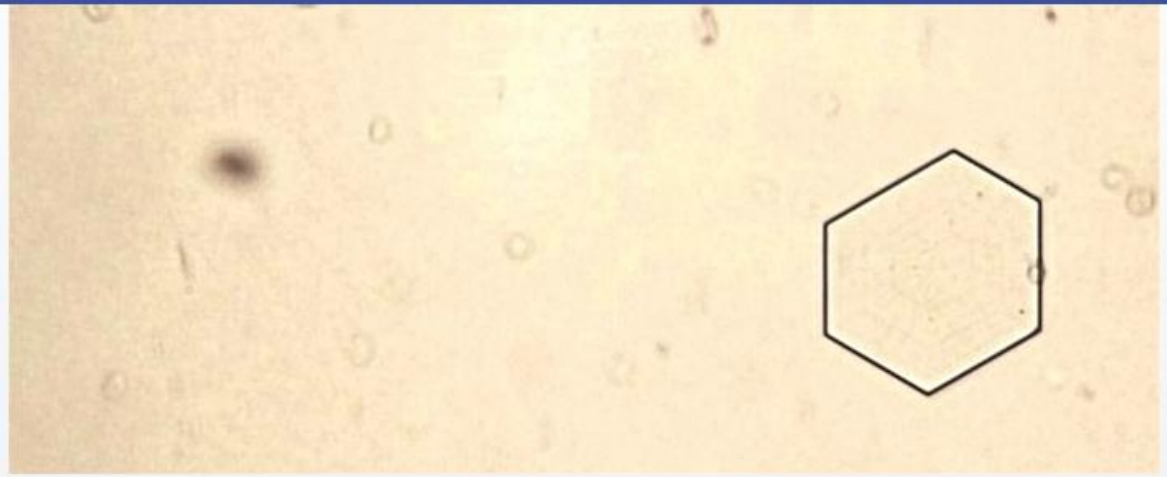
A 16-year-old boy is brought to the emergency department with sudden onset of left-sided abdominal pain and blood in his urine. The pain waxes and wanes in intensity and does not improve with rest or position changes. He has a lengthy history of similar pain episodes, but this is the first time he has had gross hematuria. Physical examination shows costovertebral angle tenderness on the left side. Microscopic examination of the urine is shown below.





Further quantitative laboratory evaluation is most likely to detect which of the following abnormalities in this patient?



Further quantitative laboratory evaluation is most likely to detect which of the following abnormalities in this patient?

- A. Aminoaciduria
- B. Hypercalciuria
- C. Hyperoxaluria
- D. Hyperuricosuria
- E. Hypocitraturia

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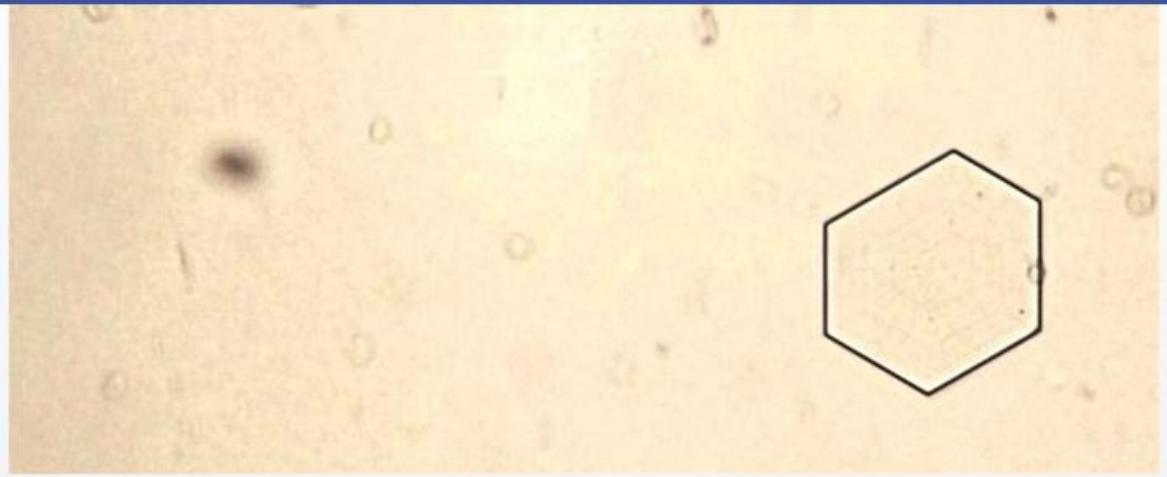


Further quantitative laboratory evaluation is most likely to detect which of the following abnormalities in this patient?

- A. Aminoaciduria [54%] ✔
- B. Hypercalciuria [10%]
- C. Hyperoxaluria [13%]
- D. Hyperuricosuria [11%]
- E. Hypocitraturia [9%]

Omitted
Correct answer

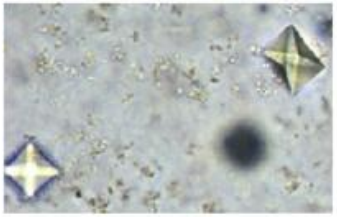
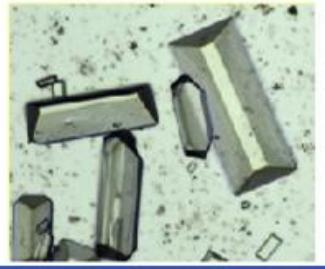
54%
Answered correctly

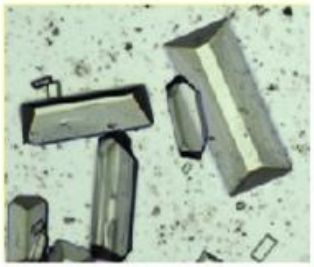
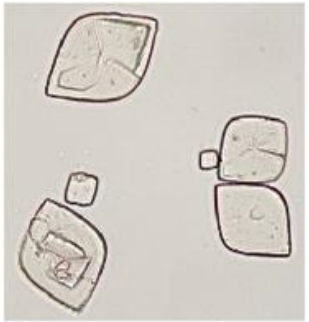
11 Seconds
Time Spent

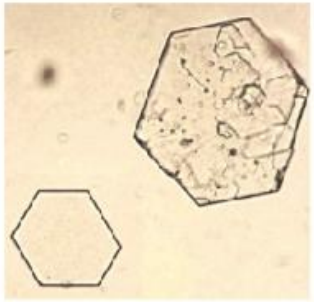
09/24/2018
Last Updated

Explanation

Nephrolithiasis

Content	Frequency	Radiograph opacity	pH	Microscopic appearance
Calcium oxalate	70%-80%	↑↑	--	 • Octahedron (square with an "X" in the center)
Calcium phosphate			>7.0	• Elongated, wedge-shaped • Forms rosettes
Magnesium ammonium phosphate (struvite or triple phosphate)	15%	↑	>7.0	

Magnesium ammonium phosphate (struvite or triple phosphate)	15%	↑	>7.0	 • Rectangular prism ("coffin lids")
Uric acid	5%	--	<7.0	 • Yellow or red-brown, diamond or rhombus
				

Cystine	1%	↑	<7.0	 • Flat, yellow, **hexagonal**

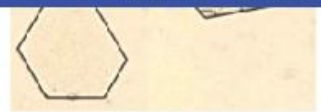
©UWorld

Recurrent nephrolithiasis in a young patient should raise suspicion for **cystinuria**, which is confirmed by the pathognomonic finding of **hexagonal-shaped crystals** on urinalysis. Cystinuria is an autosomal recessive disorder affecting the high-affinity, sodium-independent dibasic amino acid transporter found on the apical membrane of intestinal and proximal renal tubular epithelial cells. This prevents dibasic amino acids (eg, cysteine, ornithine, lysine, and arginine) from being reabsorbed in the proximal renal tubules, leading to urine supersaturation with cystine and formation of **cystine stones** (ornithine, lysine, and arginine are relatively soluble in the urine and do not form stones).

Patients with suspected cystinuria without cystine crystals on urinalysis can be diagnosed by detecting **elevated urinary cysteine levels** (ie, aminoaciduria). The **sodium cyanide-nitroprusside test** is a qualitive screening test that detects the presence of urinary cystine. Cyanide is initially added to the urine, converting cystine to cysteine. Afterward, nitroprusside is added and reacts with the sulfhydryl group on free cysteine, causing a red-purple discoloration (positive test). Treatment of cystinuria involves increasing hydration and **urinary alkalinization** (eg, acetazolamide).

(Choices B, C, D, and E) Hypercalciuria (eg, sarcoidosis), hyperoxaluria (eg, Crohn disease), hyperuricosuria (eg, gout), and hypocitraturia (eg, distal renal tubular acidosis) are risk factors for recurrent calcium stone formation. These abnormalities are not typically found in patients with cystinuria.

Educational objective:



- Flat, yellow, **hexagonal**

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Recurrent nephrolithiasis in a young patient should raise suspicion for **cystinuria**, which is confirmed by the pathognomonic finding of **hexagonal-shaped crystals** on urinalysis. Cystinuria is an autosomal recessive disorder affecting the high-affinity, sodium-independent dibasic amino acid transporter found on the apical membrane of intestinal and proximal renal tubular epithelial cells. This prevents dibasic amino acids (eg, cysteine, ornithine, lysine, and arginine) from being reabsorbed in the proximal renal tubules, leading to urine supersaturation with cystine and formation of **cystine stones** (ornithine, lysine, and arginine are relatively soluble in the urine and do not form stones).

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Educational objective:
Cystinuria results from defective dibasic amino acid transport in intestinal and proximal renal tubular epithelial cells. It most often presents with recurrent stone formation at a young age due to decreased reabsorption of cysteine from the urine. Urinalysis shows pathognomonic hexagonal cystine crystals, and the sodium cyanide-nitroprusside test can be used to detect excess cystine in the urine.

A 41-year-old woman is being evaluated for peripheral edema. The patient has gained 6.8 kg (15 lb) over the past 8 weeks. Her urine is "frothy." She has no other medical problems and takes no medications. The patient does not use tobacco, alcohol, or illicit drugs. Blood pressure is 140/90 mm Hg and pulse is 80/min. Examination shows generalized edema. Heart sounds are normal. The abdomen is soft and nontender. Serum creatinine is 1.1 mg/dL. Urinalysis shows 4+ protein, 0-3 leukocytes/hpf, and oval fat bodies. Serum contains IgG4 antibodies to the phospholipase A2 receptor (PLA2R), a transmembrane protein abundant on podocytes. Which of the following is the most likely diagnosis?

- A. Focal segmental glomerulosclerosis
- B. Membranous nephropathy
- C. Minimal change disease
- D. Mixed cryoglobulinemia
- E. Multiple myeloma

Submit

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- A. Focal segmental glomerulosclerosis [13%]
- ✔ B. Membranous nephropathy [73%]
- C. Minimal change disease [8%]
- D. Mixed cryoglobulinemia [2%]
- E. Multiple myeloma [1%]

Omitted
Correct answer
B

73%
Answered correctly

3 Seconds
Time Spent

10/02/2018
Last Updated

Explanation

This patient with weight gain and edema with 4+ protein and oval fat bodies on urinalysis has **nephrotic syndrome**. The presence of **phospholipase A2 receptor** (PLA2R) antibodies suggests a diagnosis of membranous nephropathy. Antibodies against PLA2R, primarily IgG4, can lead to immune deposition in the glomerulus and are thought to be a major factor in the pathogenesis of primary (idiopathic) **membranous nephropathy**, a common cause of nephrotic syndrome in adults.

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29

Explanation

This patient with weight gain and edema with 4+ protein and oval fat bodies on urinalysis has **nephrotic syndrome**. The presence of **phospholipase A2 receptor** (PLA2R) antibodies suggests a diagnosis of membranous nephropathy. Antibodies against PLA2R, primarily IgG4, can lead to immune deposition in the glomerulus and are thought to be a major factor in the pathogenesis of primary (idiopathic) **membranous nephropathy**, a common cause of nephrotic syndrome in adults.

Anti-PLA2R antibodies are highly specific for membranous nephropathy; positive titers effectively rule out other causes of nephrotic syndrome (eg, focal segmental glomerulosclerosis) and may eliminate the need for invasive renal biopsy. In addition, **titers correlate with disease activity**, and serial measurements can be used to determine the efficacy of immunosuppressive therapy.

(Choice A) Focal segmental glomerulosclerosis causes nephrotic syndrome but is caused by direct (eg, cytotoxic drugs) or indirect (eg, glomerular hyperfiltration) podocyte injury. It is not associated with anti-PLA2R antibodies.

(Choice C) Minimal change disease may be due to abnormal T-cell production of a glomerular permeability factor that affects the glomerular capillary wall, leading to fusion of the foot processes and marked proteinuria. There has been no association with anti-PLA2R antibodies.

(Choice D) Mixed cryoglobulinemia is associated with IgM deposition in the glomerulus, leading to basement membrane thickening and cellular proliferation. Renal disease typically presents as membranoproliferative glomerulonephritis with hematuria and red blood cell casts. It is most common in patients with chronic hepatitis C infection.

(Choice E) Renal disease in multiple myeloma is due to deposition of light chains (ie, cast nephropathy) and is not associated with anti-PLA2R antibodies.

Educational objective:
Primary (idiopathic) membranous nephropathy is associated with IgG4 antibodies to the phospholipase A2 receptor, which might play a role in development of the disease. Antibody titers are useful for diagnosis and correlate with disease activity.

The following vignette applies to the next **2** items. The items in the set must be answered in sequential order. Once you click **Proceed to Next Item**, you will not be able to add or change an answer.

A 54-year-old previously healthy man comes to the office due to several weeks of leg swelling. He has had no fever, chest pain, or dyspnea. The patient has a 40-pack-year smoking history but does not use alcohol or illicit drugs. He is afebrile and vital signs are within normal limits. On physical examination, there is symmetric pitting edema of the lower extremities bilaterally. The abdomen is soft and nondistended. A mobile left flank mass can be palpated. There are several vertically oriented tortuous veins on the lower abdominal wall.

Item 1 of 2

Which of the following structures is most likely obstructed in this patient?

- A. Femoral veins
- B. Iliac veins
- C. Inferior vena cava
- D. Portal vein
- E. Saphenous veins

Submit

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Item 1 of 2

Which of the following structures is most likely obstructed in this patient?

- A. Femoral veins [3%]
- B. Iliac veins [17%]
- ✔ C. Inferior vena cava [38%]
- D. Portal vein [38%]
- E. Saphenous veins [2%]

Omitted
Correct answer
C

38%
Answered correctly

3 Seconds
Time Spent

01/30/2019
Last Updated

Explanation

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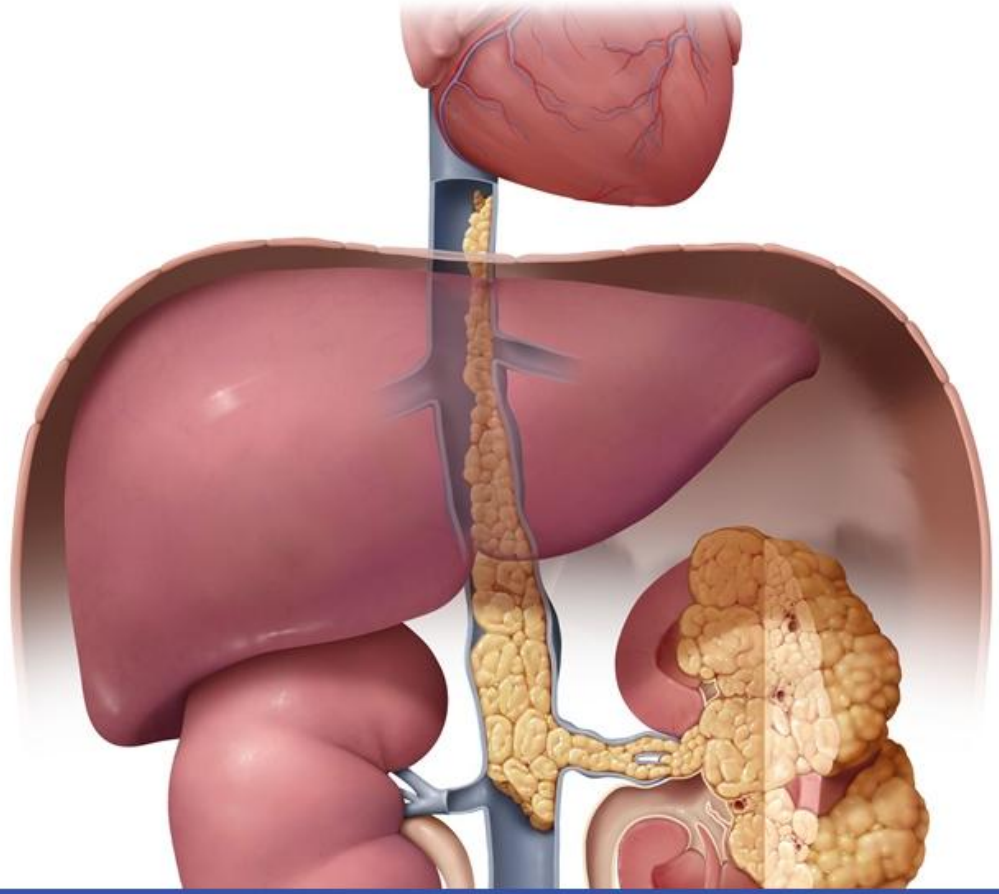
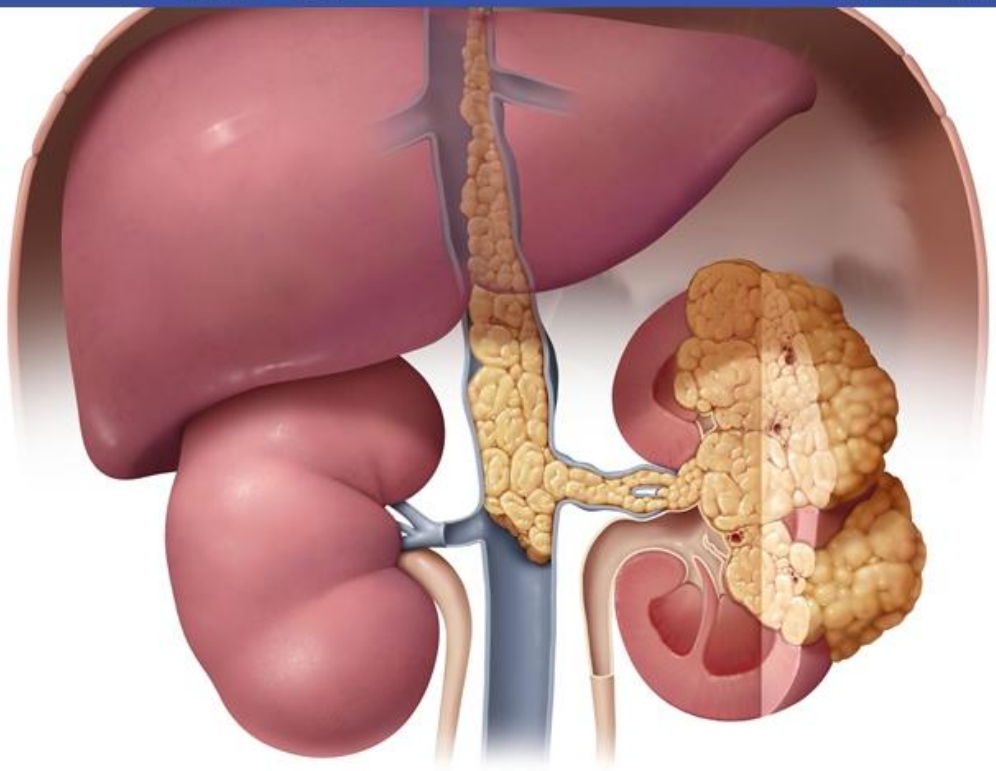
Renal cell carcinoma & IVC obstruction





This patient's symmetric bilateral lower extremity pitting edema and tortuous abdominal veins are concerning for an **inferior vena cava (IVC) obstruction**, which, in the setting of a left-sided flank mass, suggests **renal cell carcinoma** (RCC) with extension into the IVC. RCC accounts for >90% of all malignancies arising in the kidney and is highly associated with smoking. Patients with RCC classically have a triad of flank pain, palpable mass, and hematuria, although many remain asymptomatic until the disease is advanced.

This patient's symmetric bilateral lower extremity pitting edema and tortuous abdominal veins are concerning for an **inferior vena cava (IVC) obstruction**, which, in the setting of a left-sided flank mass, suggests **renal cell carcinoma** (RCC) with extension into the IVC. RCC accounts for >90% of all malignancies arising in the kidney and is highly associated with smoking. Patients with RCC classically have a triad of flank pain, palpable mass, and hematuria, although many remain asymptomatic until the disease is advanced.

RCC is a highly vascular tumor that **invades the renal vein** in up to 25% of cases. IVC obstruction can occur due to intraluminal extension and thrombus formation, rather than mass effect from the tumor itself. The obstruction can occur acutely or gradually over time. In chronic cases, collateral venous circulation may develop based on the site of the obstruction. Prominent abdominal wall **collateral veins**, as in this patient, suggest obstruction of the upper segment of the IVC.

(Choices A, B, and E) The femoral, iliac, and saphenous veins are too low in the legs to produce significant abdominal wall collateral veins if obstructed. Obstruction of these veins would be more likely to cause varices on the legs, thighs, and hips. In addition, unilateral (rather than bilateral) lower extremity edema would be expected.

(Choice D) Obstruction of the portal vein is most commonly associated with severe hepatic cirrhosis. Affected patients have shunting of blood through portocaval anastomoses, leading to hemorrhoids, esophageal varices, and caput medusae about the umbilicus. They may also have ascites.

Educational objective:
Renal cell carcinoma tends to invade the renal vein; inferior vena cava obstruction can occur by intraluminal extension of the tumor. Obstruction of the inferior vena cava produces symmetric bilateral lower extremity edema, often associated with prominent development of venous collaterals in the abdominal wall.

References

- Important surgical considerations in the management of renal cell carcinoma (RCC) with inferior vena cava (IVC) tumour thrombus.

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29

Item 2 of 2

Further evaluation of the patient reveals microscopic hematuria. Laboratory results are as follows:

Leukocytes	9,000/mm^3
Hemoglobin	19.2 g/dL
Platelets	230,000/mm^3

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

A. Arteriovenous malformation
B. Excess erythropoietin production
C. Extramedullary hematopoiesis
D. Myeloproliferative disorder
E. Reduced plasma volume

Submit

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29

Item 2 of 2

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Hemoglobin	19.2 g/dL
Platelets	230,000/mm^3

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

- A. Arteriovenous malformation [1%]
- ✔ B. Excess erythropoietin production [78%]
- C. Extramedullary hematopoiesis [5%]
- D. Myeloproliferative disorder [8%]
- E. Reduced plasma volume [5%]

Omitted
Correct answer
B

78%
Answered correctly

13 Seconds
Time Spent

01/30/2019
Last Updated

Explanation

Correct answer
B

78%
Answered correctly

13 Seconds
Time Spent

01/30/2019
Last Updated

Explanation

This patient most likely has **renal cell carcinoma** with an elevated hemoglobin level suggestive of erythrocytosis. Renal cell carcinoma causes a variety of paraneoplastic syndromes. **Erythrocytosis** is an uncommon but classic finding and is the result of excessive erythropoietin production by the renal cell tumor. Hypercalcemia may also occur due to overproduction of parathyroid hormone–related peptide or from lytic bone metastases.

(Choice A) Arteriovenous malformations have been associated with high-output cardiac failure, local bony hypertrophy, and local tissue compression and distortion. These lesions are typically congenital although they may not become clinically evident until puberty.

(Choice C) When intramedullary hematopoiesis is insufficient, blood cell formation can sometimes occur in extramedullary sites such as the liver, spleen, and thymus, resulting in enlargement of these organs. Extramedullary hematopoiesis typically occurs in the setting of myelofibrosis.

(Choice D) Myeloproliferative disorders such as polycythemia vera typically cause increases in all cell lines (leukocytosis and thrombocytosis would also be expected).

(Choice E) Reduced plasma volume can cause a pseudo-elevation in hemoglobin/hematocrit levels. However, hemoconcentration typically causes this pseudo-elevation in all cell lines. In addition, there is no other indication of a reduced plasma volume, and in this clinical setting, erythropoietin overproduction from a renal tumor is more likely.

Educational objective:
Renal cell carcinoma causes a variety of paraneoplastic syndromes including erythrocytosis (due to excessive erythropoietin production) and hypercalcemia (due to parathyroid hormone–related peptide).

A 17-year-old boy is brought to the office due to occasional blood in the urine. The first episode occurred 1 year ago, about 3 days after a flulike illness, and resolved spontaneously. The patient had a similar episode about 6 months ago, which also seemed to resolve. He has no other medical conditions and does not use tobacco or alcohol. There is no history of blood or kidney disorders in the family. Vital signs are normal. On laboratory evaluation, blood urea nitrogen level is 14 mg/dL and creatinine is 0.8 mg/dL. Urinalysis results are as follows:

Specific gravity	1.013
Protein	+2
Blood	trace
Glucose	negative
Ketones	negative
Leukocyte esterase	negative
Nitrites	negative
White blood cells	1-2/hpf
Red blood cells	20-30/hpf

A renal biopsy is performed. Which of the following findings is most likely to be seen on microscopic evaluation?

A. Apple-green birefringent mesangial deposits
B. Crescent formation with linear IgG deposits
C. Effacement of podocyte foot processes
D. Granular IgG and C3 deposits

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- D. Granular IgG and C3 deposits
- E. Lamellated basement membrane
- F. Mesangial deposition of IgA
- G. Sclerosis of a portion of some glomeruli
- H. Thin basement membrane

Submit

Glucose	negative
Ketones	negative
Leukocyte esterase	negative
Nitrites	negative
White blood cells	1-2/hpf
Red blood cells	20-30/hpf

A renal biopsy is performed. Which of the following findings is most likely to be seen on microscopic evaluation?

- A. Apple-green birefringent mesangial deposits [1%]
- B. Crescent formation with linear IgG deposits [3%]
- C. Effacement of podocyte foot processes [8%]
- D. Granular IgG and C3 deposits [20%]
- E. Lamellated basement membrane [0%]
- ✔ F. Mesangial deposition of IgA [61%]
- G. Sclerosis of a portion of some glomeruli [0%]
- H. Thin basement membrane [2%]

Omitted
Correct answer

61%
Answered correctly

8 Seconds
Time Spent

01/24/2019
Last Updated

Pathological findings in nephritic syndromes		
	Cause of glomerular injury	**Characteristic biopsy features**
Poststreptococcal glomerulonephritis	Antibodies against streptococcal antigens that deposit in GBM	IF - C3 granular staining along GBM EM - **Subepithelial humps**
Anti-GBM disease	Antibodies against type IV collagen in GBM	LM - Glomerular crescents IF - **Linear staining (IgG)** along GBM
Rapidly progressive glomerulonephritis	**Severe** immunologic injury (eg, anti-GBM antibodies, immune complex deposition)	LM - Glomerular **crescents** IF - Fibrin in crescents
IgA nephropathy	Deposition of IgA-containing complexes	LM - Mesangial hypercellularity IF - **IgA in mesangium**
Alport syndrome	Defective type IV collagen in GBM	EM - **Lamellated appearance of GBM**

EM = electron microscopy; **GBM** = glomerular basement membrane; **IF** = immunofluorescence; **LM** = light microscopy.

This patient likely has **IgA nephropathy** (Berger disease), the most common cause of **glomerulonephritis**. It typically affects older children and young adults and presents with **painless hematuria** within 5-7 days of an **upper respiratory tract infection**. The hematuria lasts for several days and then subsides temporarily, returning every few months or with another upper respiratory infection (syphargitic hematuria). Complement levels are usually normal. Renal biopsy will show **mesangial hypercellularity** with **mesangial IgA deposits** seen on immunohistochemical staining.

This patient likely has **IgA nephropathy** (Berger disease), the most common cause of **glomerulonephritis**. It typically affects older children and young adults and presents with **painless hematuria** within 5-7 days of an **upper respiratory tract infection**. The hematuria lasts for several days and then subsides temporarily, returning every few months or with another upper respiratory infection (synpharngitic hematuria). Complement levels are usually normal. Renal biopsy will show **mesangial hypercellularity** with **mesangial IgA deposits** seen on immunohistochemical staining.

When IgA nephropathy is accompanied by extrarenal symptoms (eg, abdominal pain, arthralgias, purpuric skin lesions), the syndrome is called Henoch-Schönlein purpura.

(Choice A) The kidney is often affected by amyloidosis. On Congo red staining, amyloid deposits appear red-pink under light microscopy and have an **apple-green birefringence** under polarized light. Amyloidosis typically presents in older adults as nephrotic syndrome with significant edema and proteinuria.

(Choice B) Crescent formation with **linear IgG deposits** occurs in patients with antiglomerular basement membrane antibody disease (Goodpasture disease). This condition generally presents as rapidly progressive glomerulonephritis associated with an acute rise in creatinine and decreased urine output; patients also often have hemoptysis. The disease is rare in children.

(Choice C) Minimal change disease (MCD) is characterized by **effacement of podocyte foot processes** on electron microscopy. MCD typically results in nephrotic syndrome with generalized edema and high levels of proteinuria; recurrent hematuria associated with an upper respiratory infection is more consistent with IgA nephropathy.

(Choice D) Poststreptococcal glomerulonephritis (PSGN) demonstrates granular IgG and C3 deposits along the glomerular basement membrane. However, hematuria in PSGN usually develops 1-3 weeks after streptococcal pharyngitis (postpharyngitic nephritis), and reoccurrence is rare.

(Choice E) Alport syndrome is a disorder of type IV collagen that causes a nephritic syndrome; however, it is associated with hearing loss and ocular abnormalities. Electron microscopy shows a lamellated basement membrane with irregular thinning and thickening ("basket-weave" appearance).

(Choice C) Focal segmental glomerular sclerosis also typically causes nephrotic syndrome. Recurrent episodes of macroscopic hematuria are

and decreased urine output; patients also often have hemoptysis. The disease is rare in children.

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(Choice G) Focal segmental glomerular sclerosis also typically causes nephrotic syndrome. Recurrent episodes of macroscopic hematuria are unexpected.

(Choice H) Thin basement membrane disease is an autosomal dominant disorder that results in a thin basement membrane with recurrent microscopic hematuria, gross hematuria, or flank pain. Due to the inheritance pattern, patients typically have a family history of hematuria.

Educational objective:
IgA nephropathy (Berger disease) frequently presents as recurrent, self-limited, painless hematuria within 5 days of an upper respiratory infection. Kidney biopsy will show mesangial IgA deposits on immunofluorescence. In contrast, poststreptococcal glomerulonephritis is seen 1-3 weeks after streptococcal pharyngitis and is usually not recurrent.

References

- The genetics and immunobiology of IgA nephropathy.
- Diagnosis and classification of IgA nephropathy.

Rapidly progressive glomerulonephriti	**Severe** immunologic injury (eg, anti-GBM antibodies, immune	LM - Glomerular **crescents**
IgA nephropathy		arity
Alport syndrome		nce

EM = electron microscopy; GI

This patient likely has **IgA neph** ren and young adults and presents with veral days and then subsides tempor Complement levels are usually immunohistochemical staining.

When IgA nephropathy is accor called Henoch-Schönlein purpura.

(Choice A) The kidney is often y and have an **apple-green birefring** ificant edema and proteinuria.

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Exhibit Display

Nephritic vs nephrotic syndrome

	Nephritic	Nephrotic
Onset	Abrupt	Insidious
GFR	Low	Normal or low
Serum albumin	Normal	Low
Edema	±	++
Hypertension	++	±
Casts	RBC casts	Fatty or none
Proteinuria	±	++
Hematuria	++	±
Pyuria	+	none

Add To Flash Card

Rapidly progressive glomerulonephriti	**Severe** immunologic injury (eg, anti-GBM antibodies, immune	LM - Glomerular **crescents**
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Exhibit Display

	Nephritic	Nephrotic
Onset	Abrupt	Insidious
GFR	Low	Normal or low
Serum albumin	Normal	Low
Edema	±	++
Hypertension	++	±
Casts	RBC casts	Fatty or none
Proteinuria	±	++
Hematuria	++	±
Pyuria	+	none

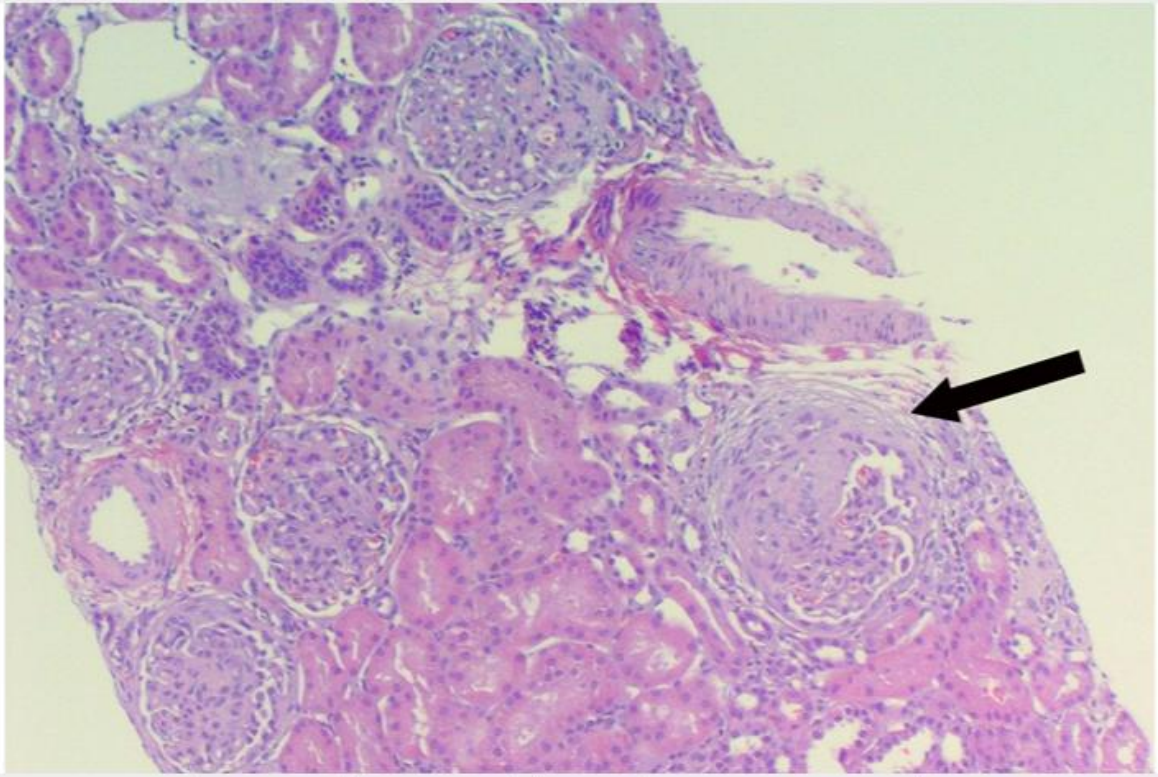
GFR = glomerular filtration rate; RBC = red blood cell.
+ = present; ++ = significant.

Add To Flash Card

Rapidly progressive	**Severe** immunologic injury (eg, anti-GBM antibodies, immune	LM - Glomerular **crescents**

Exhibit Display

Henoch-Schonlein purpura nephritis Henoch-Schonlein purpura nephritis



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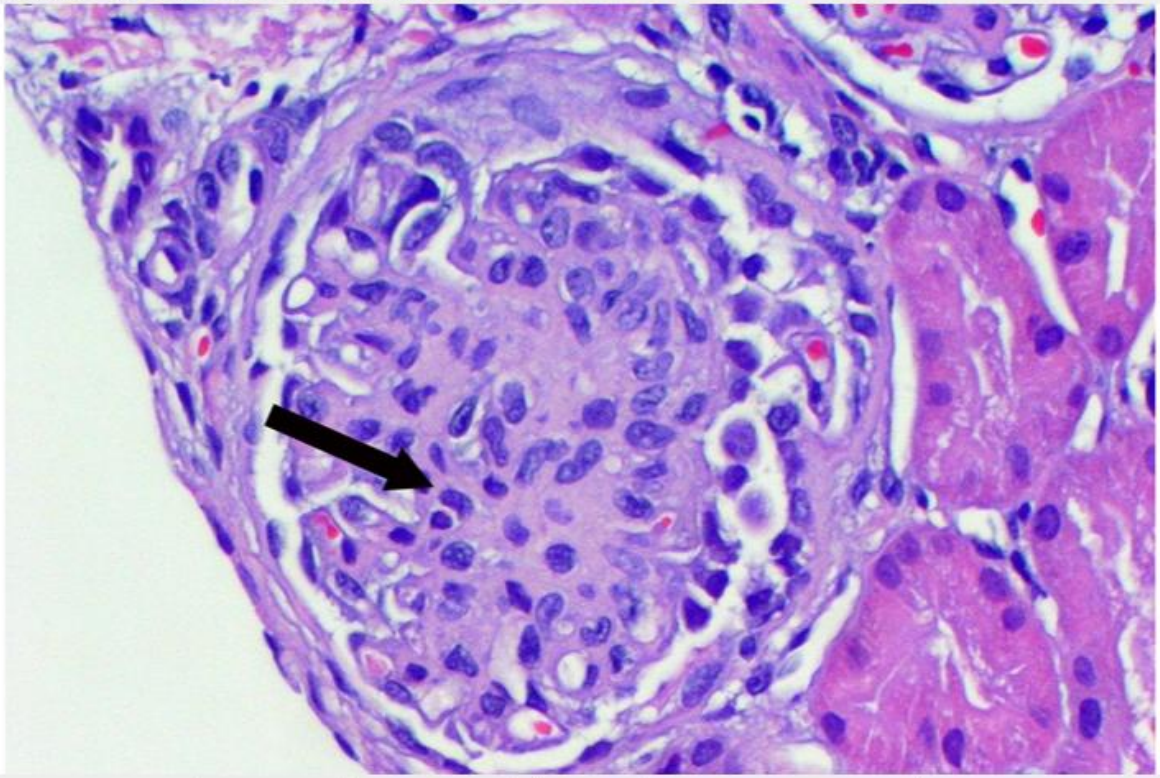
Rapidly progressive	**Severe** immunologic injury (eg, anti-GBM antibodies, immune	LM - Glomerular **crescents**

Exhibit Display

Henoch-Schonlein purpura nephritis Henoch-Schonlein purpura nephritis



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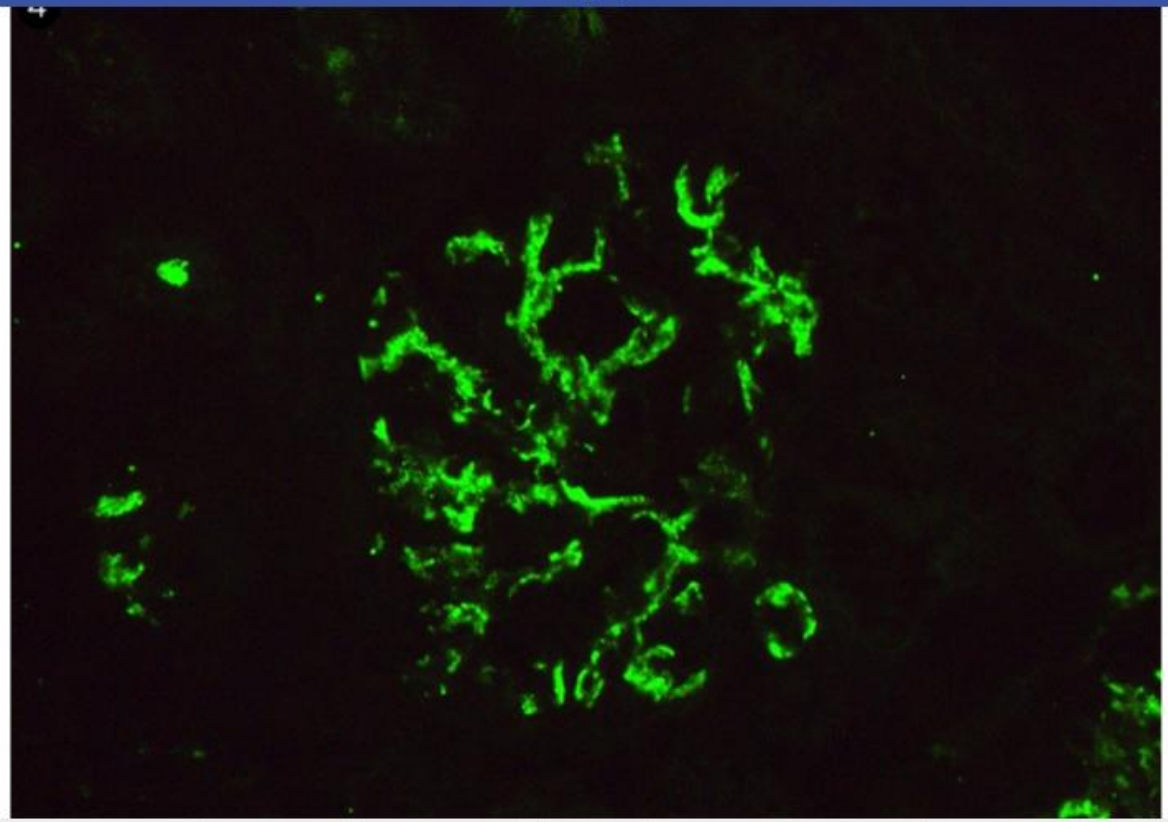
Rapidly progressive	**Severe** immunologic injury (eg, anti-GBM antibodies, immune	LM - Glomerular **crescents**

Exhibit Display



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A 21-year-old man is brought to the emergency department due to diffuse muscle aches and weakness. He has also noticed darkening of his urine. The patient recently joined the military and was participating in rigorous training exercises in hot weather earlier in the day. He has no significant medical conditions and takes no medications. Medical evaluation and laboratory testing performed prior to military enlistment showed no abnormalities. Temperature is 36.7 C (98 F), blood pressure is 100/60 mm Hg, pulse is 105/min, and respirations are 16/min. Physical examination shows dry mucous membranes and muscle tenderness over the bilateral thighs and calves. Laboratory results are as follows:

Sodium	136 mEq/L
Potassium	5.6 mEq/L
Chloride	100 mEq/L
Bicarbonate	18 mEq/L
Blood urea nitrogen	36 mg/dL
Creatinine	2.0 mg/dL
Calcium	6.8 mg/dL
Phosphorus	7.8 mg/dL
Creatine kinase	22,000 U/L (normal: 30-170)

Which of the following urine microscopy findings is most likely to be seen in this patient?

A. Dysmorphic red blood cells
B. Eosinophils
C. Granular casts

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- A. Dysmorphic red blood cells
- B. Eosinophils
- C. Granular casts
- D. Isomorphic red blood cells
- E. Polymorphonuclear leukocytes
- F. Red blood cell casts

Submit

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Creatine kinase	22,000 U/L (normal: 30-170)

Which of the following urine microscopy findings is most likely to be seen in this patient?

- A. Dysmorphic red blood cells [16%]
- B. Eosinophils [1%]
- ✔ C. Granular casts [54%]
- D. Isomorphic red blood cells [10%]
- E. Polymorphonuclear leukocytes [1%]
- F. Red blood cell casts [15%]

Omitted
Correct answer

54%
Answered correctly

9 Seconds
Time Spent

02/01/2019
Last Updated

Urinary casts	Composition	Associated conditions
Hyaline	Tamm-Horsfall protein	Nonspecific, concentrated urine
Fatty	Lipid droplets	Nephrotic syndrome
Waxy	Degenerated hyaline cast	Chronic kidney disease
Granular (muddy brown)	Sloughed tubular epithelial cells with pigmented granules	Acute tubular necrosis
WBC	White blood cells	Pyelonephritis, interstitial nephritis
RBC	Red blood cells	Glomerulonephritis

This patient's presentation is consistent with **rhabdomyolysis**, which is characterized by skeletal muscle necrosis and the release of intracellular breakdown products into the circulation. The condition is most commonly caused by trauma, sepsis, drugs/toxins (eg, statins, alcohol, cocaine), and **overexertion** (particularly in hot climates). Patients classically have **myalgia and weakness** (predominantly in the proximal muscles, lower back, and calves) and dark urine (due to **myoglobinuria**). Laboratory studies often show markedly **elevated creatine kinase** levels and acute kidney injury with electrolyte disturbances (eg, hyperkalemia, hyperphosphatemia, hypocalcemia, metabolic acidosis).

Acute kidney injury in rhabdomyolysis occurs due to myoglobin degradation and heme pigment release. Heme pigment causes acute tubular necrosis (ATN) through direct cytotoxicity and renal vasoconstriction (ie, ischemia). In ATN, injured tubular epithelial cells, with their deeply pigmented, granular contents, slough off into the tubular lumen, forming **granular, muddy brown casts**. Heme pigment in myoglobin cross-reacts with the urine dipstick reagent that detects hemoglobin, leading to a false-positive result for blood in urine; however, microscopy shows no red

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(Choices A, D, and F) Dysmorphic RBCs and RBC casts are typically seen in patients with glomerulonephritis. Dysmorphic RBCs have abnormal shapes due to deformation as they pass through the glomerular basement membrane and osmotic stress in the renal tubules. Normal-appearing (isomorphic) RBCs are seen in nonglomerular sources of hematuria, such as nephrolithiasis or urinary tract malignancies.

(Choice B) Urinary eosinophils are suggestive of acute interstitial nephritis (AIN), although they may be associated with other conditions (eg, kidney transplant rejection, pyelonephritis). AIN results from immune-mediated tubulointerstitial injury often caused by medications (eg, nonsteroidal anti-inflammatory drugs, penicillins). Patients classically have some combination of rash, fever, and eosinophilia.

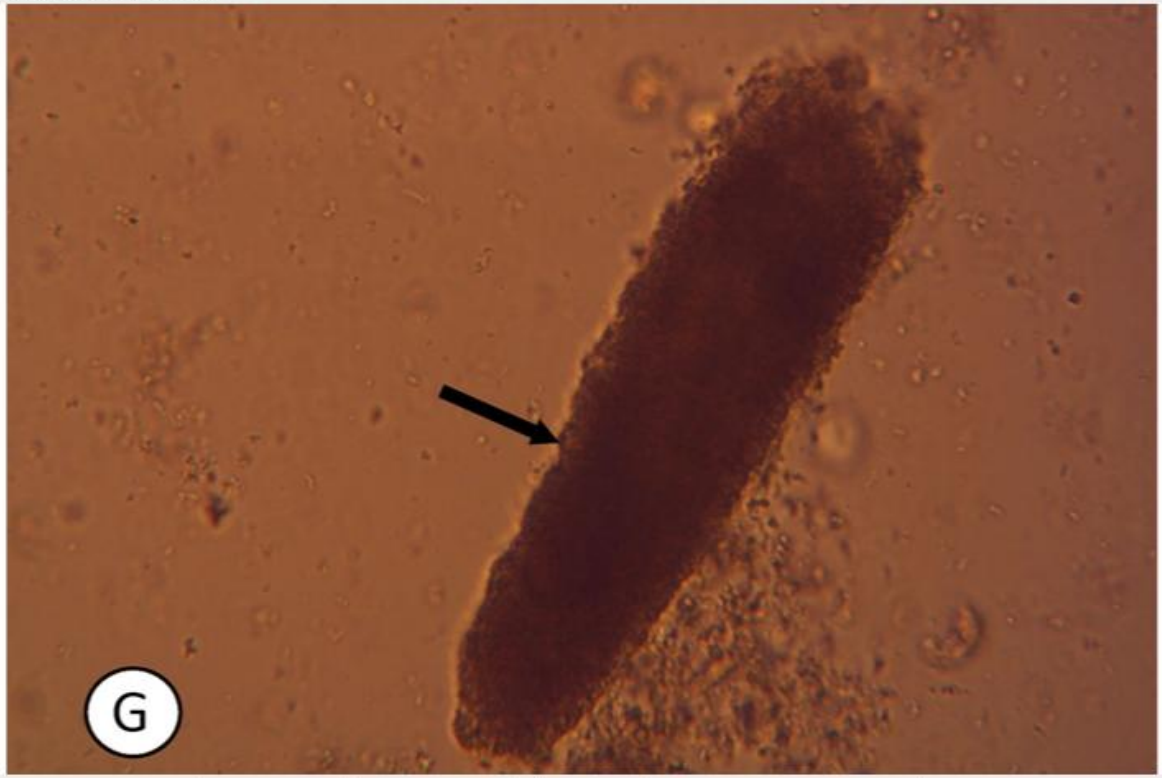
(Choice E) Polymorphonuclear leukocytes in the urine indicate inflammation, which most commonly occurs due to infection. Interstitial nephritis, renal tuberculosis, and gonorrhea/chlamydia urethritis should be considered in patients with negative urine cultures (sterile pyuria).

Educational objective:
Rhabdomyolysis usually presents with myalgia, proximal muscle weakness, and dark urine (myoglobinuria) in the setting of trauma, sepsis, or overexertion. Kidney injury occurs due to heme pigment-mediated tubular injury, leading to acute tubular necrosis. Urine microscopy typically reveals granular, muddy brown casts.

This patient's presentation is consistent with **rhabdomyolysis**, which is characterized by skeletal muscle necrosis and the release of intracellular

Exhibit Display

Acute tubular necrosis Acute tubular necrosis



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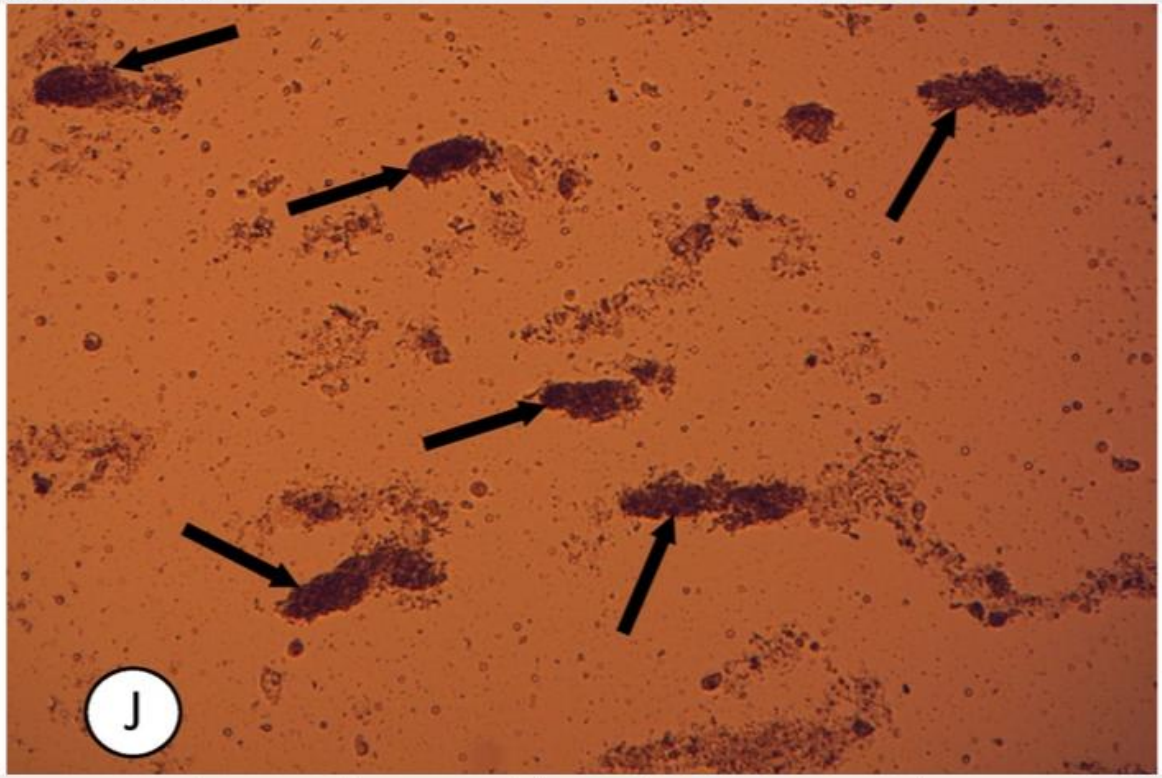
This patient's presentation is consistent with **rhabdomyolysis**, which is characterized by skeletal muscle necrosis and the release of intracellular

Exhibit Display

Acute tubular necrosis Acute tubular necrosis



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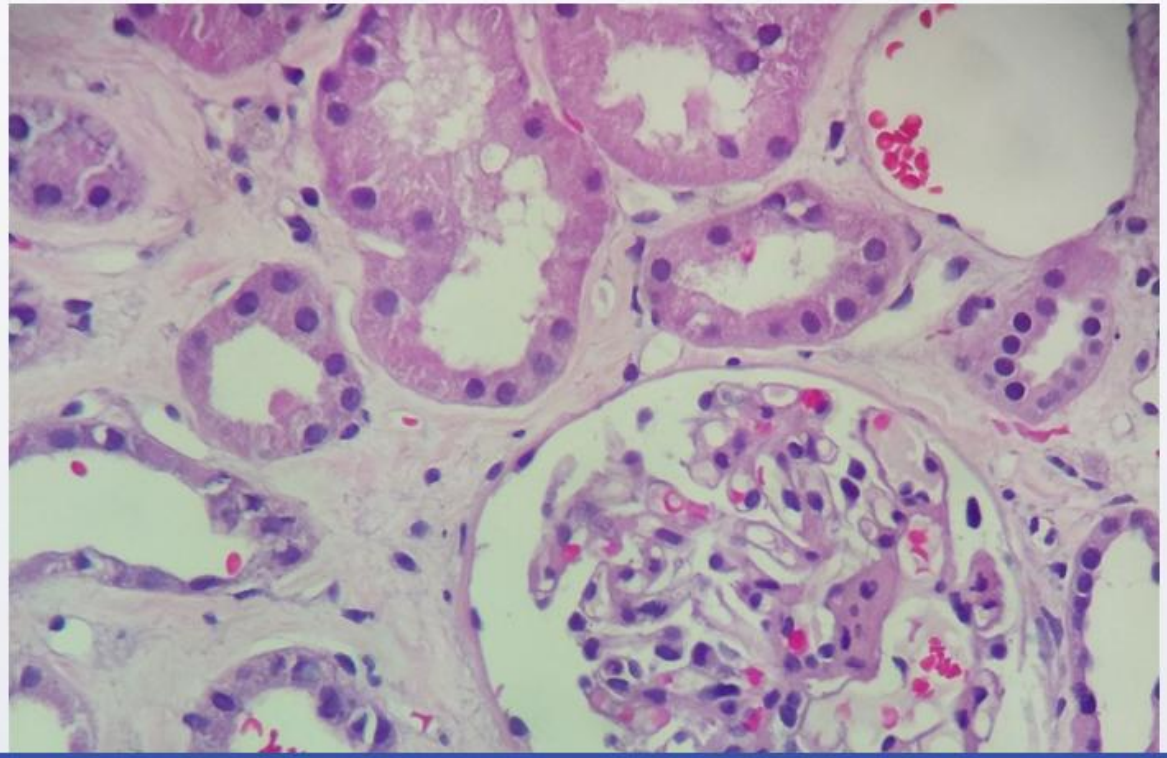
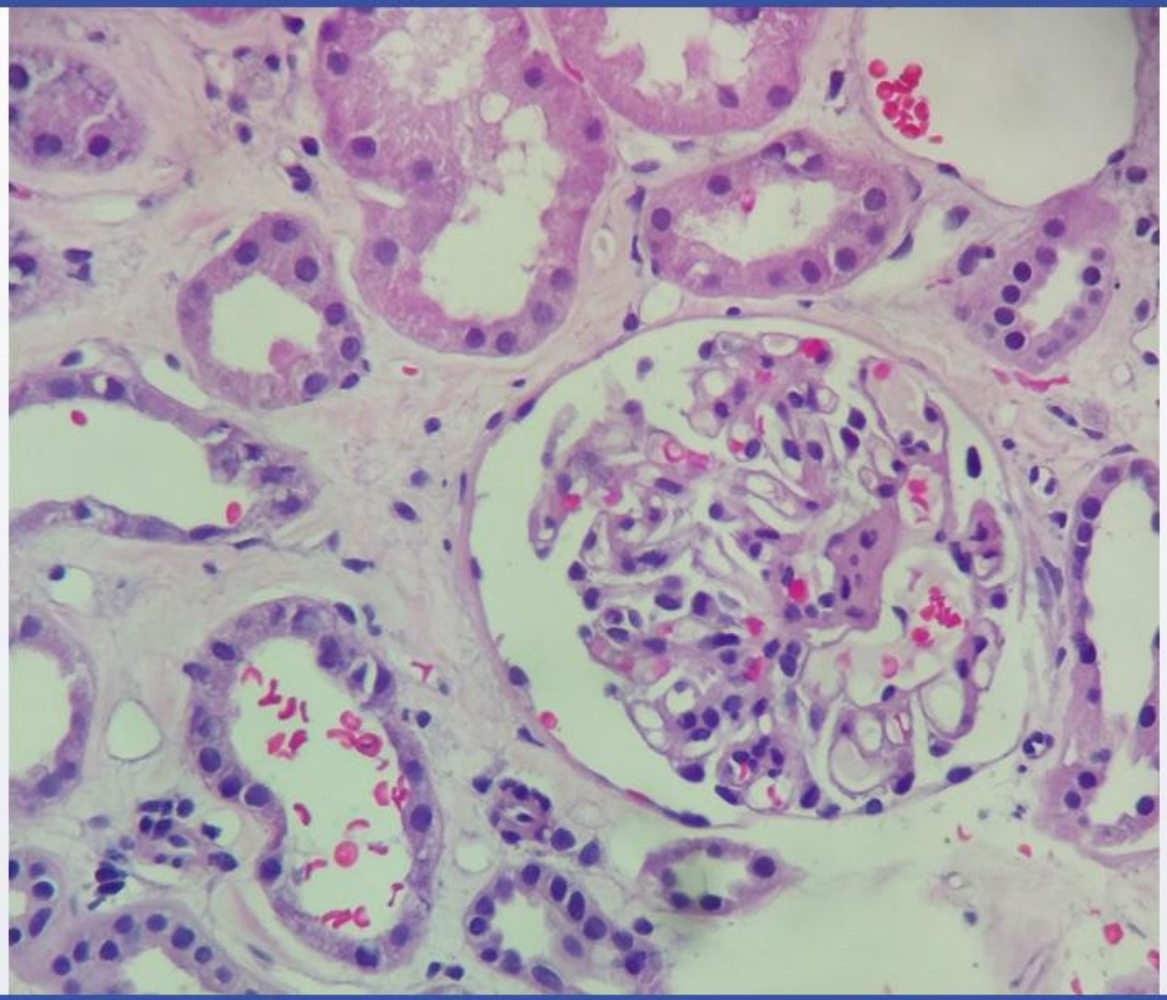
A 15-year-old girl is brought to the clinic for evaluation of swelling around her eyes that developed over the past week. The patient is a cheerleader, and she had been taking ibuprofen daily for the last 3 months for various sprains and aches after practice. She has no chronic medical conditions. Vital signs are normal. On physical examination, there is moderate periorbital edema with bilateral lower extremity pitting edema. Serum creatinine is 0.5 mg/dL and serum albumin is 2.1 g/dL. Urinalysis shows 4+ protein and negative blood. Multiple regions of the kidney are biopsied, and a representative image is shown below:





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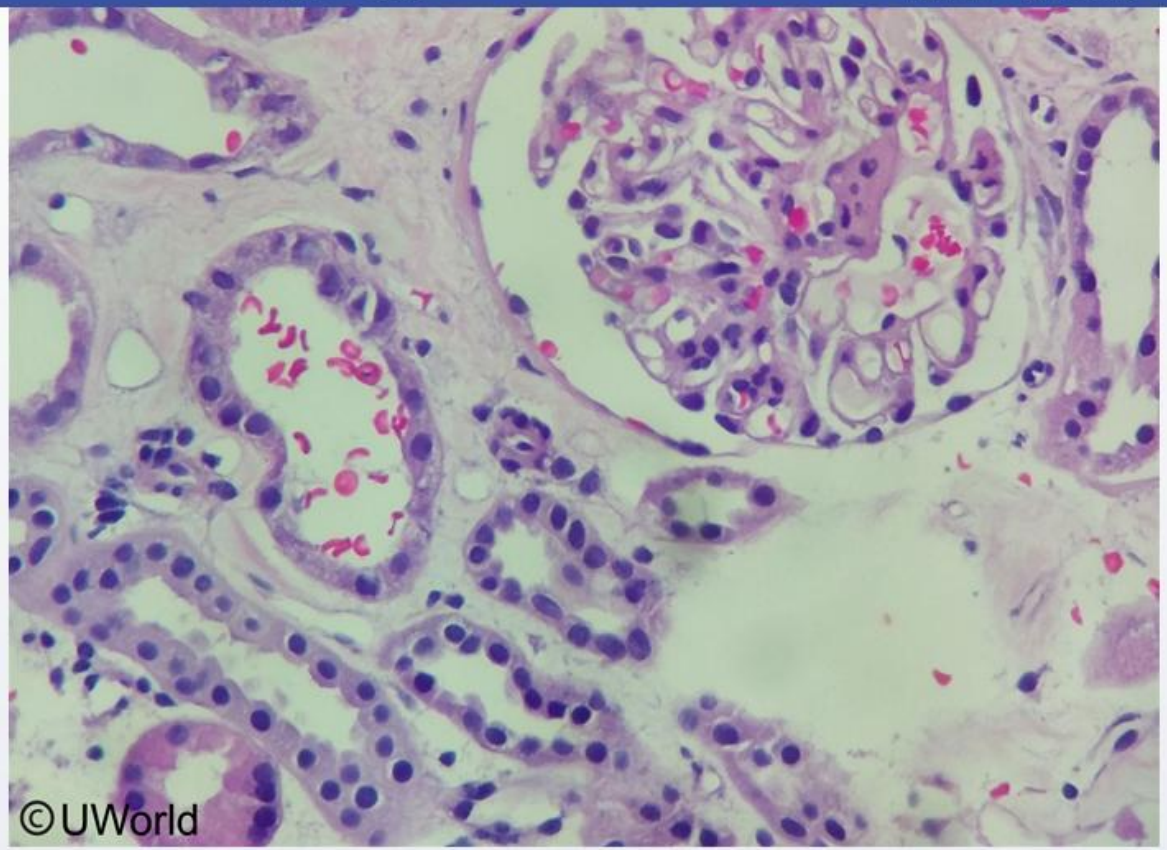
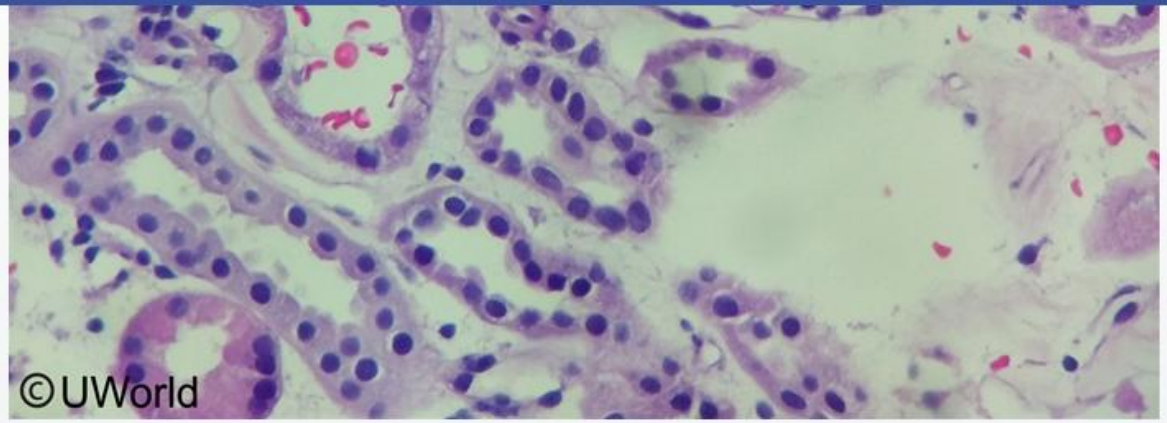


Which of the following is the most likely diagnosis?

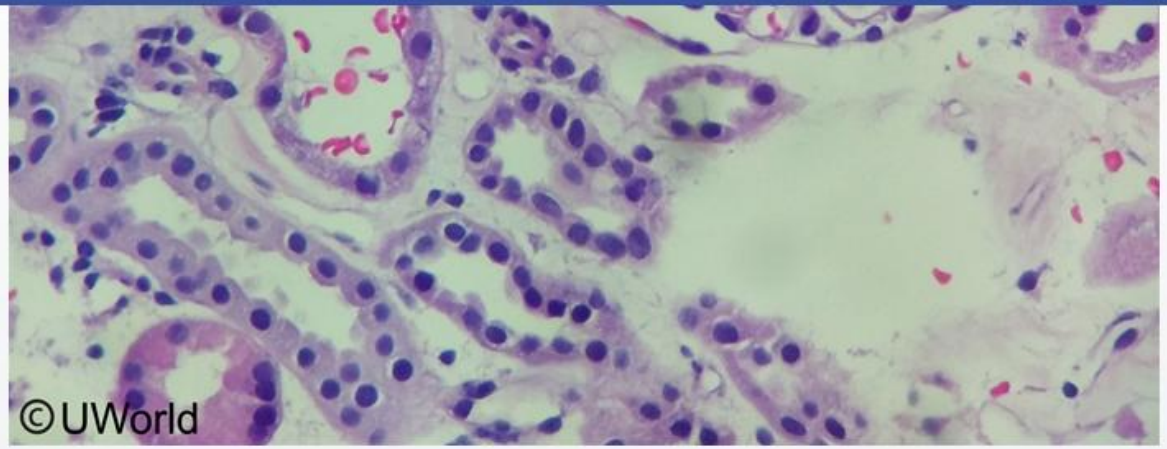
A. Acute interstitial nephritis



Which of the following is the most likely diagnosis?

- A. Acute interstitial nephritis
- B. Crescentic glomerulonephritis
- C. Focal segmental glomerulosclerosis
- D. Membranous nephropathy
- E. Minimal change disease
- F. Poststreptococcal glomerulonephritis

Submit



Which of the following is the most likely diagnosis?

- A. Acute interstitial nephritis [20%]
- B. Crescentic glomerulonephritis [1%]
- C. Focal segmental glomerulosclerosis [10%]
- D. Membranous nephropathy [17%]
- ✔ E. Minimal change disease [47%]
- F. Poststreptococcal glomerulonephritis [1%]

Omitted
47%
16 Seconds
01/29/2019

Minimal change disease	
Epidemiology	• Most common cause of nephrotic syndrome in children • Median age 2-3
Pathogenesis	• T cell–mediated injury to podocytes • Production of a glomerular permeability factor
Clinical features	• Edema, frothy urine • Proteinuria, hypoalbuminemia, hyperlipidemia
Diagnosis	• LM: normal glomeruli • IM: no immune deposits • EM: diffuse podocyte foot process effacement

EM = electron microscopy; **IM** = immunofluorescence microscopy; **LM** = light microcopy.

This patient with edema, proteinuria, and hypoalbuminemia has **nephrotic syndrome**. The histopathology demonstrating normal glomeruli on light microscopy (LM) suggests a diagnosis of **minimal change disease** (MCD). MCD is the most common cause of nephrotic syndrome in children. It is often idiopathic but may be triggered by drugs (eg, **nonsteroidal anti-inflammatory drugs** [NSAIDs], as in this patient), immunizations, or malignancy (eg, Hodgkin lymphoma). T-cell dysfunction results in the production of a glomerular permeability factor (possibly IL-13), which damages podocytes and decreases the anionic charge of the glomerular basement membrane (GBM), allowing for selective loss of albumin in the urine.

Clinical features include acute weight gain, diffuse edema, and "frothy urine" due to heavy proteinuria. Renal biopsy demonstrates **normal glomeruli on LM**, with no immunoglobulin or complement deposits visible on immunofluorescent microscopy. However, electron microscopy shows diffuse **effacement and fusion** of podocyte foot process.

(Choice A) Acute interstitial nephritis often occurs after initiation of new drugs (eg, NSAIDS, diuretics) but causes acute kidney injury with white

IL-13), which damages podocytes and decreases the anionic charge of the glomerular basement membrane (GBM), allowing for selective loss of albumin in the urine.

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(Choice A) Acute interstitial nephritis often occurs after initiation of new drugs (eg, NSAIDS, diuretics) but causes acute kidney injury with white blood cell casts on urinalysis; heavy proteinuria is unexpected. Although the glomeruli are often normal, patchy tubular necrosis will be seen on LM.

(Choices B and F) Crescentic glomerulonephritis and poststreptococcal glomerulonephritis cause nephritic syndrome (eg, hematuria, red blood cell casts, hypertension). Crescentic glomerulonephritis occurs in multiple renal diseases (eg, Goodpasture disease, microscopic polyangiitis) and demonstrates **hypercellular crescents** composed of parietal and inflammatory cells. Poststreptococcal glomerulonephritis, which occurs 2-4 weeks after a group A streptococcal infection, demonstrates **hypercellular glomeruli** on LM.

(Choice C) Focal segmental glomerular sclerosis causes nephrotic syndrome and also demonstrates similar podocyte foot process effacement on electron microscopy; however, LM demonstrates **sclerotic foci** within the glomerulus. This disease is more common in adults and typically has a slower onset of edema and weight gain.

(Choice D) Membranous nephropathy causes nephrotic syndrome, and is associated with NSAID use, but is more common in adults. LM demonstrates hypercellular glomeruli with **diffuse GBM thickening**.

Educational objective:
Minimal change disease is the most common cause of nephrotic syndrome in children. It is often idiopathic but may be triggered by drugs, immunizations, or malignancy. Light microscopy shows normal glomeruli, with no immunoglobulin or complement deposits on immunofluorescent staining. However, electron microscopy shows diffuse podocyte foot process effacement and fusion.

Explanation

Exhibit Display

Nephritic vs nephrotic syndrome		
	Nephritic	**Nephrotic**
Onset	Abrupt	Insidious
GFR	Low	Normal or low
Serum albumin	Normal	Low
Edema	±	++
Hypertension	++	±
Casts	RBC casts	Fatty or none
Proteinuria	±	++
Hematuria	++	±
Pyuria	+	none

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EM = ele

This patient with edema, protein… …uli on light microscopy (LM) suggests … …e in children. It is often idiopathic b… immunizations, or malignancy (eg, Hodgkin lymphoma). T-cell dysfunction results in the production of a glomerular permeability factor (possibly IL-13), which damages podocytes and decreases the anionic charge of the glomerular basement membrane (GBM), allowing for selective loss of albumin in the urine.

Clinical features include acute weight gain, diffuse edema, and "frothy urine" due to heavy proteinuria. Renal biopsy demonstrates **normal**

Explanation

Exhibit Display

	Nephritic	Nephrotic
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GFR	Low	Normal or low
Serum albumin	Normal	Low
Edema	±	++
Hypertension	++	±
Casts	RBC casts	Fatty or none
Proteinuria	±	++
Hematuria	++	±
Pyuria	+	none

GFR = glomerular filtration rate; RBC = red blood cell.
+ = present; ++ = significant.

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EM = ele

This patient with edema, protein… …uli on light microscopy (LM) suggests … …e in children. It is often idiopathic b… immunizations, or malignancy (eg, Hodgkin lymphoma). T-cell dysfunction results in the production of a glomerular permeability factor (possibly IL-13), which damages podocytes and decreases the anionic charge of the glomerular basement membrane (GBM), allowing for selective loss of albumin in the urine.

Clinical features include acute weight gain, diffuse edema, and "frothy urine" due to heavy proteinuria. Renal biopsy demonstrates **normal**

EM = electron microscopy; IM = immunofluorescence microscopy; LM = light microcopy.

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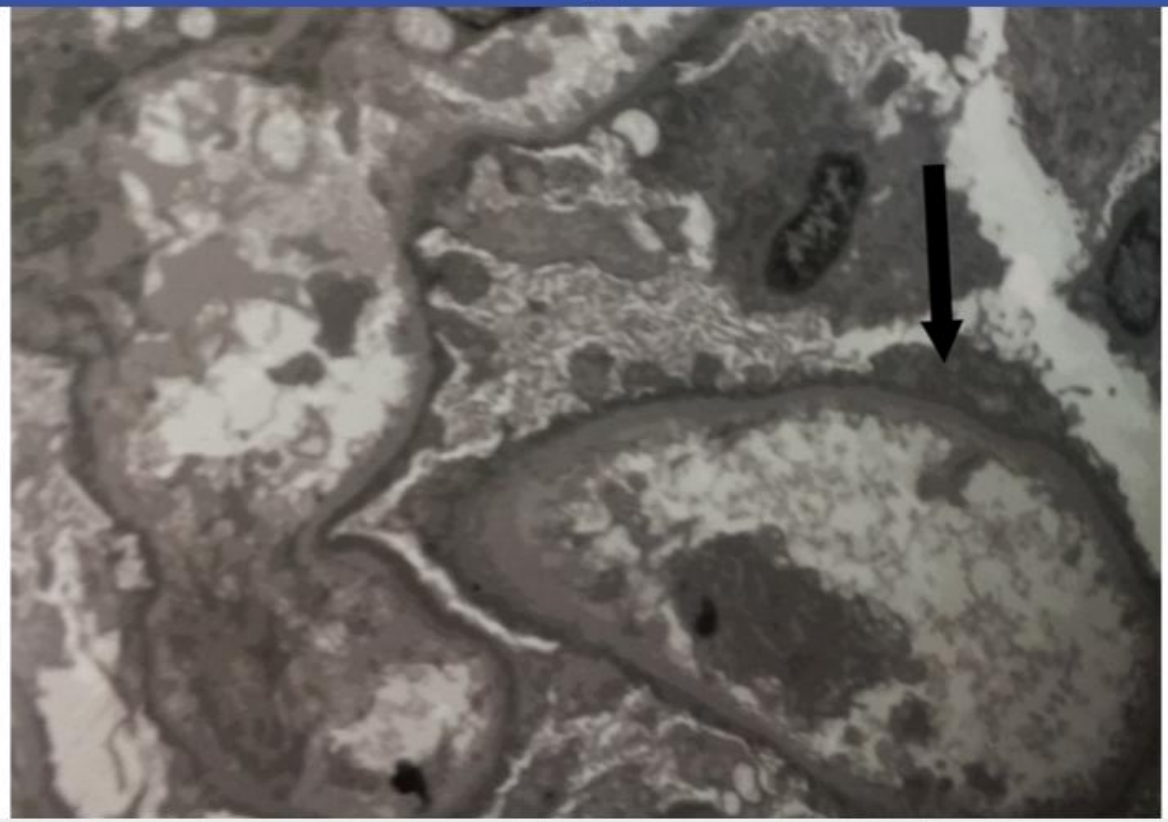

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Educational objective:

A 30-year-old man is admitted to the hospital due to seizures. The repeated, prolonged tonic-clonic seizures were terminated with intravenous lorazepam in the emergency department. Medical history is significant for amphetamine abuse. The patient develops decreased urine output 24 hours after hospital admission. Temperature is 37.1 C (98.8 F), blood pressure is 140/90 mm Hg, pulse is 88/min, and respirations are 18/min. Examination shows bibasilar lung crackles and mild edema of the lower extremities. Laboratory results are as follows:

Serum chemistry	
Blood urea nitrogen	40 mg/dL
Creatinine	4.2 mg/dL
Potassium	6.4 mEq/L
Urinalysis	
Protein	2+
Blood	3+
White blood cells	negative
Red blood cells	negative

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

A. Glomerular injury due to immune complexes
B. Inflammatory reaction of the tubular interstitium
C. Renal infarction due to arterial obstruction
D. Tubular injury due to light-chain deposition

Creatinine	4.2 mg/dL
Potassium	6.4 mEq/L

Urinalysis

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C. Renal infarction due to arterial obstruction
D. Tubular injury due to light-chain deposition
E. Tubular injury due to released hemoglobin
F. Tubular injury due to released myoglobin

Submit

Creatinine	4.2 mg/dL
Potassium	6.4 mEq/L

Urinalysis

Protein	2+
Blood	3+
White blood cells	negative
Red blood cells	negative

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

- A. Glomerular injury due to immune complexes [7%]
- B. Inflammatory reaction of the tubular interstitium [20%]
- C. Renal infarction due to arterial obstruction [10%]
- D. Tubular injury due to light-chain deposition [2%]
- E. Tubular injury due to released hemoglobin [4%]
- ✔ F. Tubular injury due to released myoglobin [54%]

Omitted
Correct answer

54%
Answered correctly

8 Seconds
Time Spent

11/01/2018
Last Updated

Rhabdomyolysis	
Risk factors	• Crush injury • Prolonged muscle activity (eg, seizure, marathon running) • Drug/medication use (eg, statins, amphetamines, heroin)
Etiology	• Myocyte necrosis, release of intracellular contents (eg, myoglobin) • Kidney injury: Heme pigment–induced acute tubular necrosis
Laboratory findings	• ↑↑ Creatine kinase • Myoglobinuria (UA with positive blood but no RBCs on microscopy) • Acute kidney injury & electrolyte abnormalities (eg, ↑ K, ↑ P, ↓ Ca)

Ca = calcium; **K** = potassium; **P** = phosphorus; **RBCs** = red blood cells; **UA** = urinalysis.

This patient with acute kidney injury, hyperkalemia, and urinalysis with 3+ blood but no red blood cells has **rhabdomyolysis**, likely induced by his prolonged seizure. Rhabdomyolysis is characterized by myocyte injury with the release of intracellular muscle contents (ie, myoglobin, electrolytes) into the circulation. It is common in crush injuries, prolonged muscle activity (eg, seizure), or drug use. **Positive blood** on urine dipstick (a reaction that detects the heme pigment in both hemoglobin and myoglobin) in the **absence of red blood cells** on microscopic urinalysis suggests **myoglobinuria**.

Renal injury in rhabdomyolysis results from **myoglobin** filtration and degradation within the glomeruli. **Heme pigment** is released, which causes **acute tubular necrosis** by direct cytotoxicity and renal vasoconstriction. Hyperkalemia, hyperphosphatemia, and hyperuricemia also occur due to myocyte lysis.

(Choice A) Immune complex–mediated glomerular injury is seen in a variety of diseases (eg, IgA nephropathy, poststreptococcal glomerulonephritis), but these diseases do not cause myoglobinuria. Urinary cast formation or severe proteinuria are more common manifestations.

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(Choice A) Immune complex–mediated glomerular injury is seen in a variety of diseases (eg, IgA nephropathy, poststreptococcal glomerulonephritis), but these diseases do not cause myoglobinuria. Urinary cast formation or severe proteinuria are more common manifestations.

(Choice B) Acute interstitial nephritis, an inflammatory reaction of the tubular interstitium, is typically associated with a medication exposure (eg, antibiotics) and presents with some combination of fever, eosinophilia, and rash. Urinalysis shows white blood cell casts, not myoglobinuria.

(Choice C) Renal infarctions can be due to thromboembolic or atheroembolic disease and typically occur in older patients with established atherosclerosis or hypercoagulability. Hematuria with red cells would be expected on urinalysis.

(Choice D) Multiple myeloma causes renal injury due to light chain–complex deposition in the renal tubules. This malignancy occurs in older patients and presents with hypercalcemia, anemia, and bone pain. It causes proteinuria (ie, Bence Jones protein), not myoglobinuria.

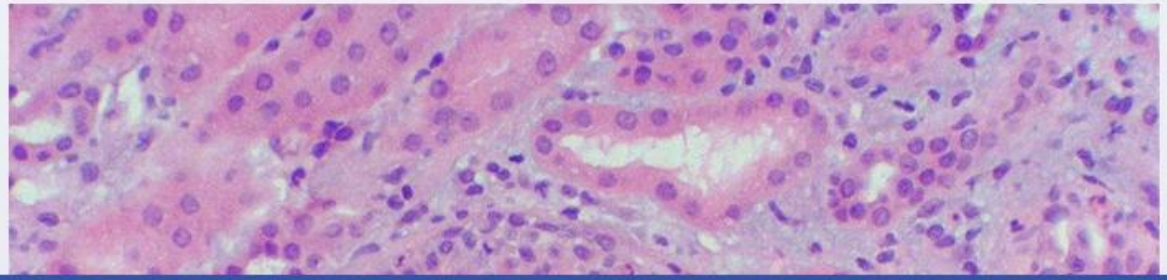
(Choice E) Tubular injury due to released hemoglobin can also cause a heme pigment–induced kidney injury and may occur with hemolytic diseases (eg, paroxysmal nocturnal hemoglobinuria) or incompatible blood transfusion. However, renal failure after a prolonged seizure is more suggestive of rhabdomyolysis.

Educational objective:
Rhabdomyolysis is characterized by the release of intracellular muscle contents (eg, myoglobin, electrolytes) due to myocyte injury; it is common with crush injuries, seizures, or drug use (eg, statins). Heme pigment (released from myoglobin after degradation in the kidney) is toxic to tubular cells and can cause acute tubular necrosis. Positive blood on urine dipstick in the absence of red blood cells on microscopic urinalysis suggests myoglobinuria.

A 12-year-old boy is brought to the physician because of fatigue. Physical examination is unremarkable. A urinalysis reveals:

Protein	1+
Blood	Trace
Glucose	Negative
Ketones	Negative
Esterase	Negative
Nitrites	Negative
WBC	3-5/hpf
RBC	20-30/hpf
Casts	RBC
Crystals	None

A kidney biopsy is performed and light microscopy of the tissue sample is shown below.



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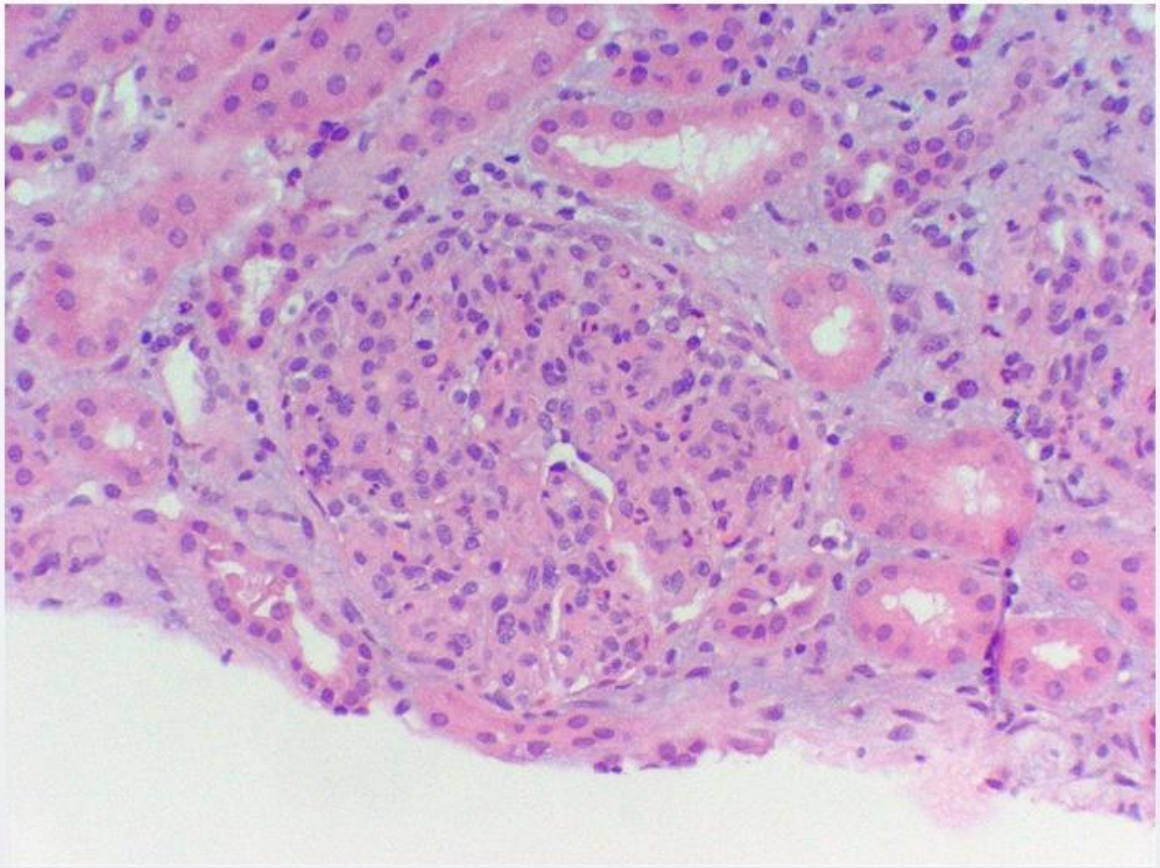

Which of the following additional findings is most likely to be present in this patient?

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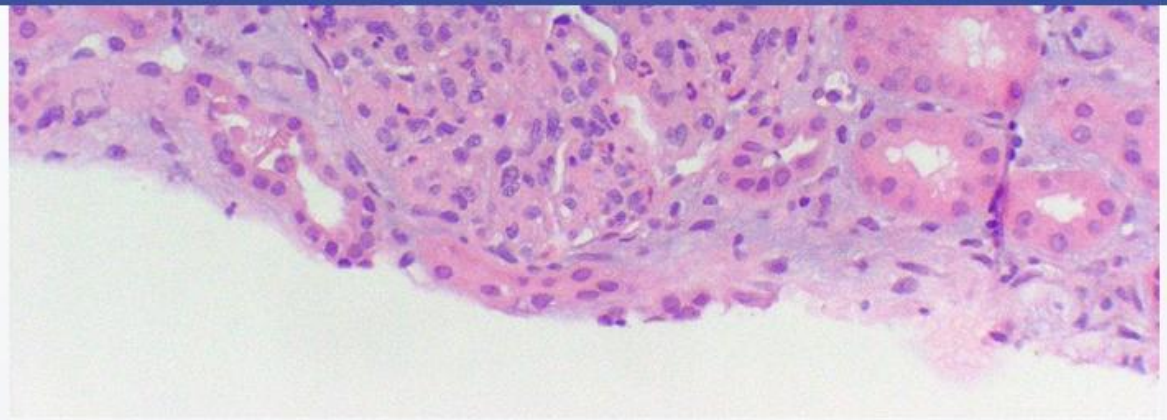

Which of the following additional findings is most likely to be present in this patient?

A. Serum anti-glomerular basement membrane antibodies
B. Serum anti-neutrophil cytoplasmic antibodies
C. Serum anti-phospholipid antibodies
D. Decreased serum C3 level
E. Decreased serum C4 level
F. High circulating eosinophil count

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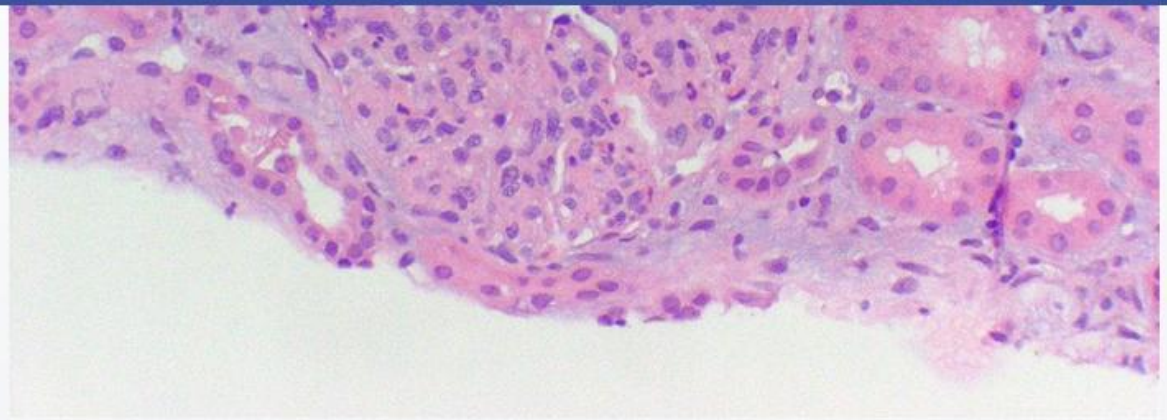


Which of the following additional findings is most likely to be present in this patient?

- A. Serum anti-glomerular basement membrane antibodies [17%]
- B. Serum anti-neutrophil cytoplasmic antibodies [8%]
- C. Serum anti-phospholipid antibodies [3%]
- ✔ D. Decreased serum C3 level [62%]
- E. Decreased serum C4 level [1%]
- F. High circulating eosinophil count [6%]

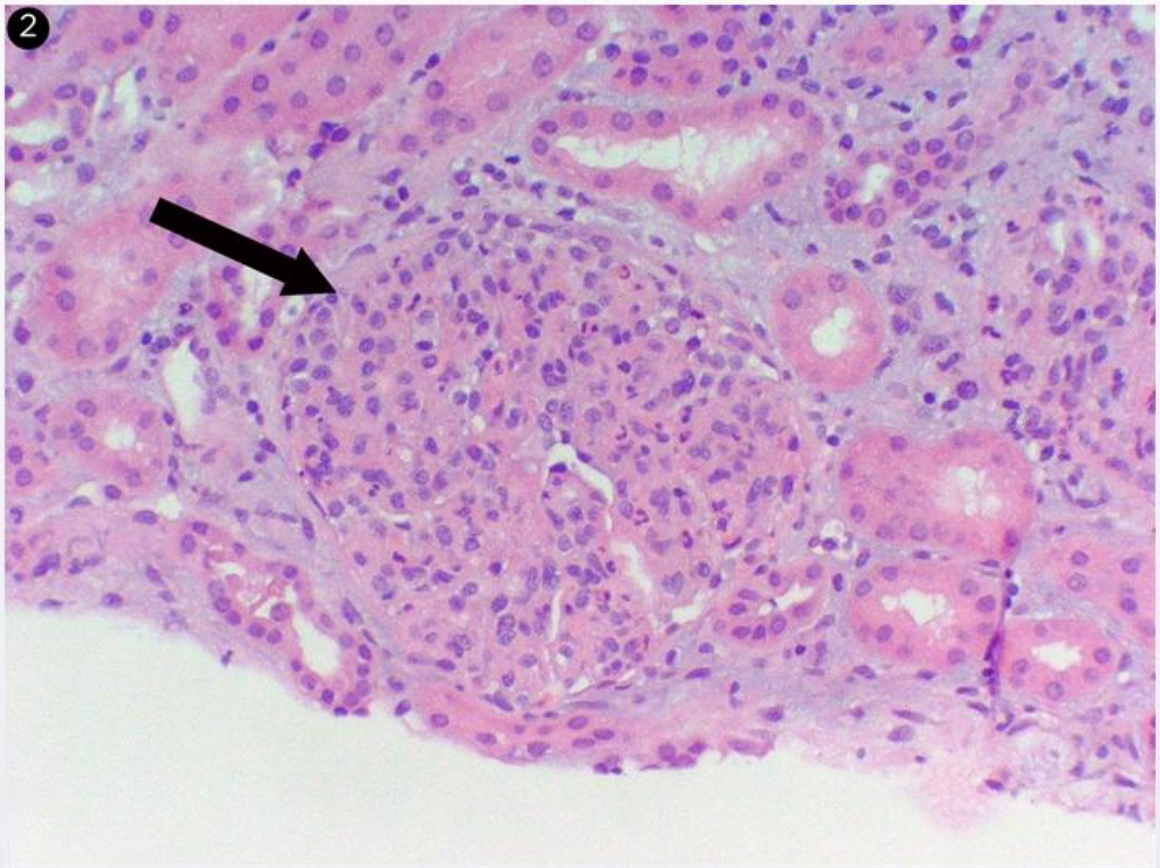
Omitted
Correct answer

62%
Answered correctly

11 Seconds
Time Spent

10/05/2018
Last Updated

Explanation



This image shows a hypercellular glomerulus typical of poststreptococcal glomerulonephritis (PSGN). When hematuria, proteinuria, and urine

This image shows a hypercellular glomerulus typical of poststreptococcal glomerulonephritis (PSGN). When hematuria, proteinuria, and urine RBC casts are present in a patient with hypercellular glomeruli on light microscopy, PSGN is the most likely diagnosis.

Laboratory findings typically found in PSGN include: elevated titers of anti-streptococcal antibodies (anti-streptolysin O, anti-DNase B, anti-cationic proteinase) and low C3 concentration. Cryoglobulins may also be present in the serum.

On light microscopy, enlarged, hypercellular glomeruli are seen (compare to **normal glomerulus**). The hypercellularity, which involves all lobules of all glomeruli, is the result of leukocyte infiltration and endothelial and mesangial cell proliferation. Electron microscopy typically shows electron-dense deposits ("humps") on the epithelial side of the basement membrane. These deposits are composed of immune complexes. On immunofluorescent microscopy, there are coarse granular deposits of IgG and C3 with the characteristic "starry sky" appearance.

(Choice A) Serum anti-glomerular basement membrane antibodies are found in Goodpasture syndrome, a condition characterized clinically by renal failure and pulmonary involvement. Crescent formation is often seen on light microscopy.

(Choice B) Serum anti-neutrophil cytoplasmic antibodies are present in patients that have granulomatosis with polyangiitis (Wegener's). In this condition, renal involvement may progress to rapidly progressive glomerulonephritis (RPGN) type 3 (pauci-immune). Additionally, there may be pulmonary symptoms (cough, hemoptysis) and upper respiratory tract symptoms (sinusitis, epistaxis). As in all types of RPGN, crescents are seen on light microscopy.

(Choice C) Serum anti-phospholipid antibodies are detected in patients with autoimmune disorders such as systemic lupus erythematosus. They are not present in PSGN.

(Choice E) Whereas C3 levels are decreased in almost all patients with PSGN (suggesting activation of the alternative complement pathway), C4 levels are usually normal. In some patients, however, C4 levels are slightly low (suggesting the possibility of classical pathway activation as well).

(Choice F) A high serum eosinophil count is seen with drug-induced interstitial nephritis. The most common offenders include beta-lactam antibiotics, NSAIDs, diuretics, and anticonvulsants.

Laboratory findings typically found in PSGN include: elevated titers of anti-streptococcal antibodies (anti-streptolysin O, anti-DNase B, anti-cationic proteinase) and low C3 concentration. Cryoglobulins may also be present in the serum.

On light microscopy, enlarged, hypercellular glomeruli are seen (compare to **normal glomerulus**). The hypercellularity, which involves all lobules of all glomeruli, is the result of leukocyte infiltration and endothelial and mesangial cell proliferation. Electron microscopy typically shows electron-dense deposits ("humps") on the epithelial side of the basement membrane. These deposits are composed of immune complexes. On immunofluorescent microscopy, there are coarse granular deposits of IgG and C3 with the characteristic "starry sky" appearance.

(Choice A) Serum anti-glomerular basement membrane antibodies are found in Goodpasture syndrome, a condition characterized clinically by renal failure and pulmonary involvement. Crescent formation is often seen on light microscopy.

(Choice B) Serum anti-neutrophil cytoplasmic antibodies are present in patients that have granulomatosis with polyangiitis (Wegener's). In this condition, renal involvement may progress to rapidly progressive glomerulonephritis (RPGN) type 3 (pauci-immune). Additionally, there may be pulmonary symptoms (cough, hemoptysis) and upper respiratory tract symptoms (sinusitis, epistaxis). As in all types of RPGN, crescents are seen on light microscopy.

(Choice C) Serum anti-phospholipid antibodies are detected in patients with autoimmune disorders such as systemic lupus erythematosus. They are not present in PSGN.

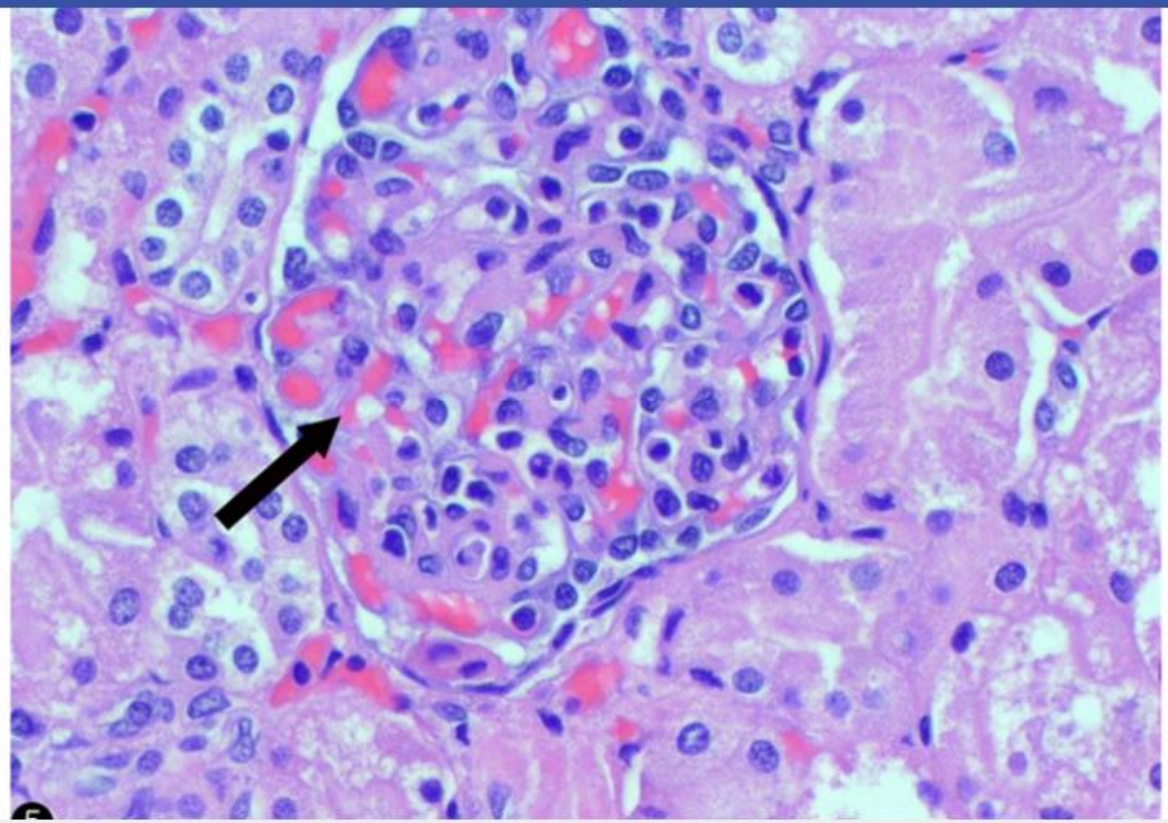
(Choice E) Whereas C3 levels are decreased in almost all patients with PSGN (suggesting activation of the alternative complement pathway), C4 levels are usually normal. In some patients, however, C4 levels are slightly low (suggesting the possibility of classical pathway activation as well).

(Choice F) A high serum eosinophil count is seen with drug-induced interstitial nephritis. The most common offenders include beta-lactam antibiotics, NSAIDs, diuretics, and anticonvulsants.

Educational objective:
Laboratory findings in poststreptococcal glomerulonephritis include: elevated anti-streptolysin O (ASO) titers, elevated anti-DNase B titers, decreased C3 and total complement levels, and the presence of cryoglobulins. C4 level is usually normal.

Laboratory findings typically found in PSGN include: elevated titers of anti-streptococcal antibodies (anti-streptolysin O, anti-DNase B, anti-cationic

Exhibit Display



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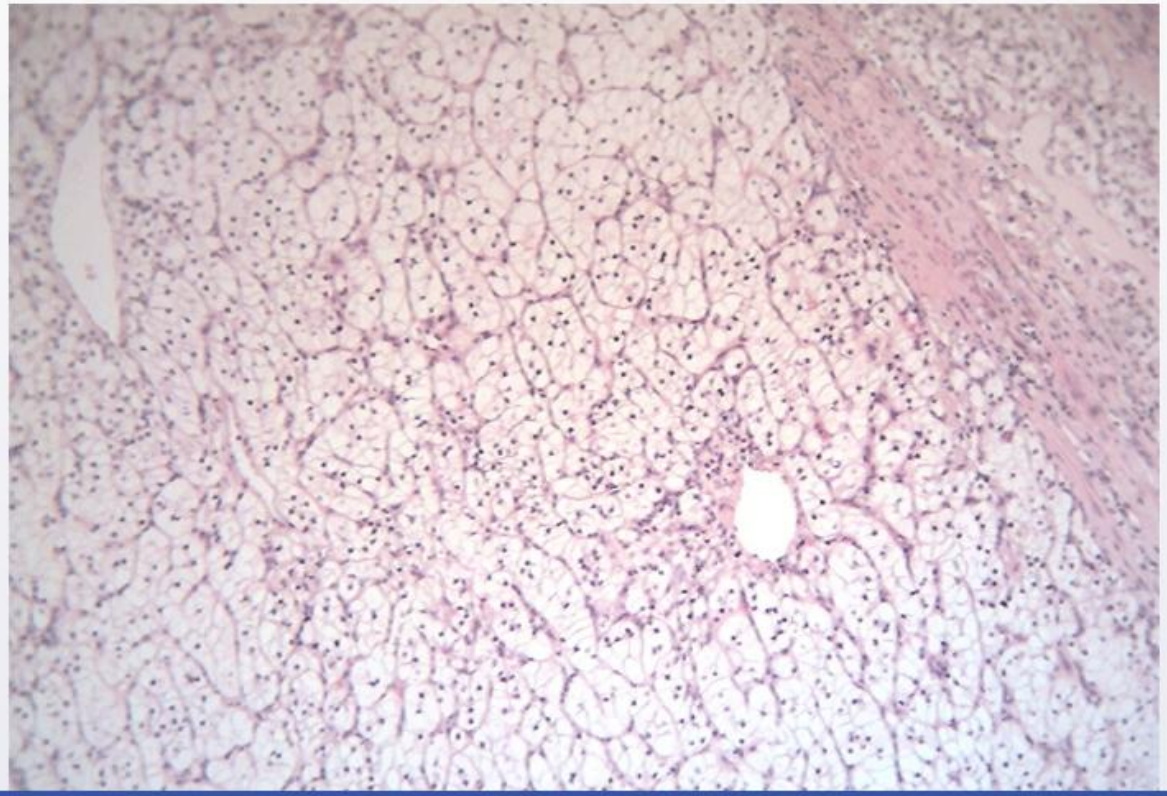
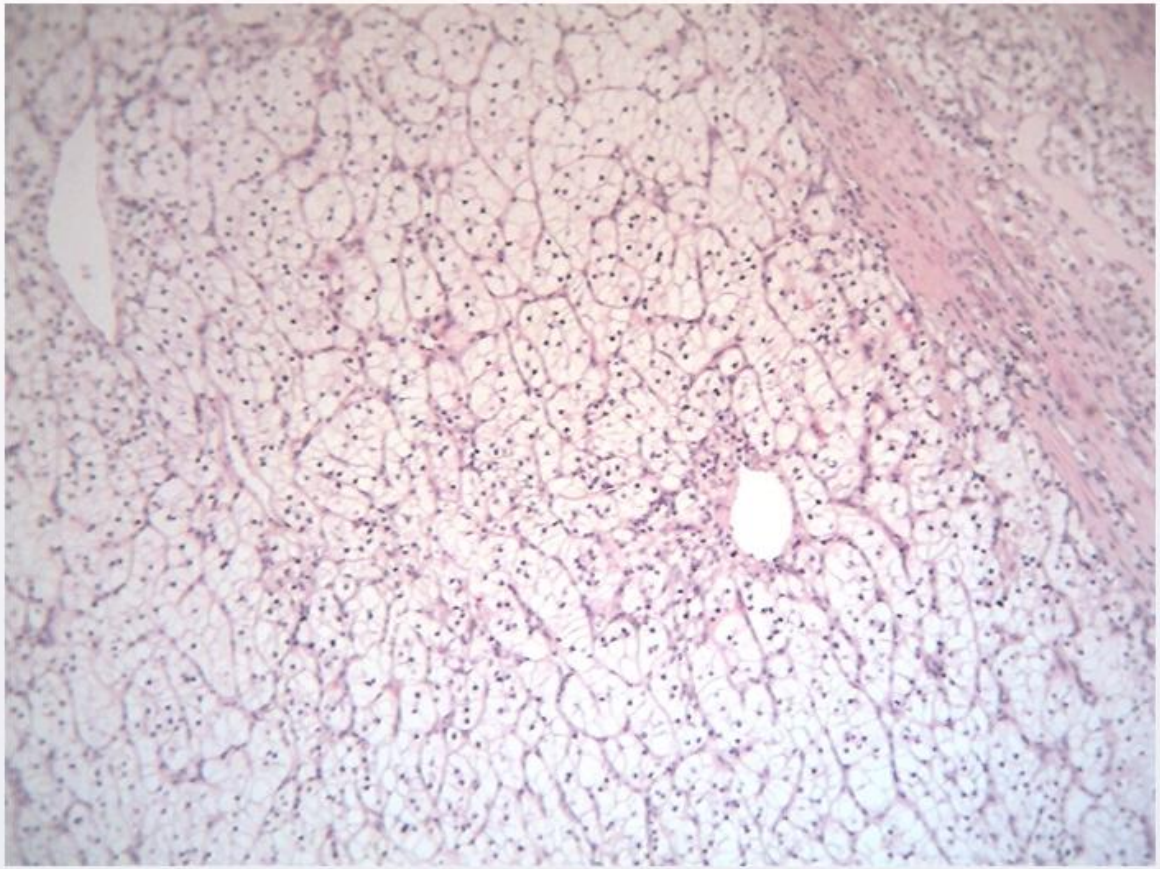
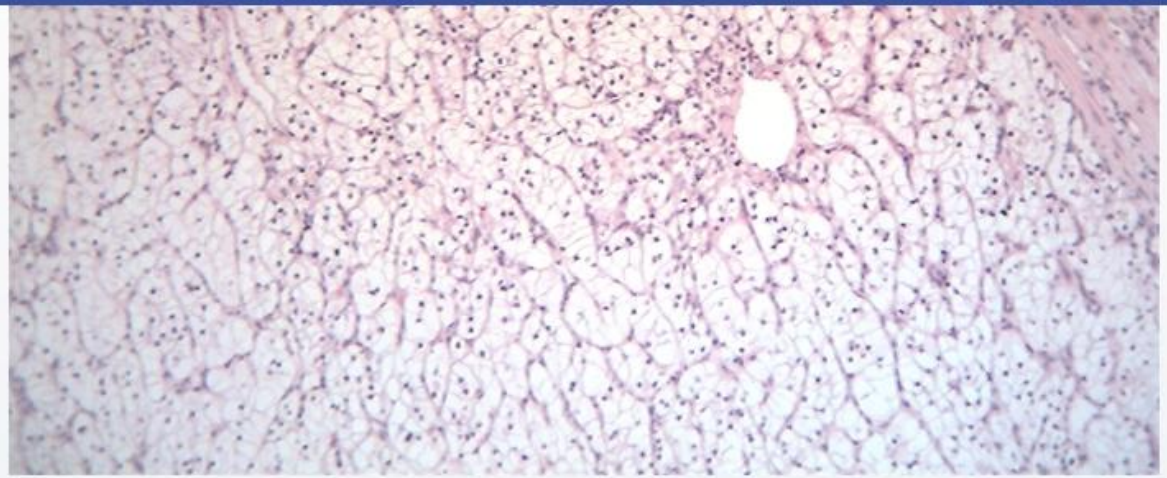
A 65-year-old man comes to the office for evaluation of blood in the urine. The patient has no abdominal pain, urinary frequency, or urgency. He has hypertension, type 2 diabetes mellitus, and stage II chronic kidney disease. He quit smoking 10 years ago and had smoked a pack of cigarettes daily for 30 years. On examination, vital signs are within normal limits. The patient's BMI is 33 kg/m^2. Appropriate work-up is performed, and he undergoes a renal biopsy. The histopathologic findings are displayed on the slide below.





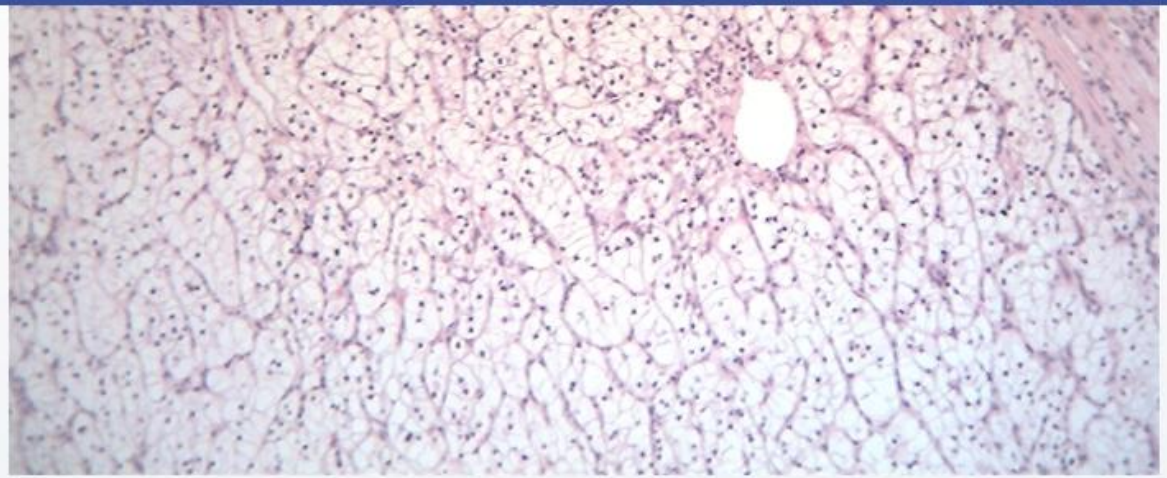
Which of the following processes most likely accounts for the abnormal appearance of these cells?



Which of the following processes most likely accounts for the abnormal appearance of these cells?

A. Glycogen and lipid accumulation
B. Karyorrhexis
C. Membrane lipid peroxidation
D. Mitochondrial swelling
E. Pigment accumulation

Submit



Which of the following processes most likely accounts for the abnormal appearance of these cells?

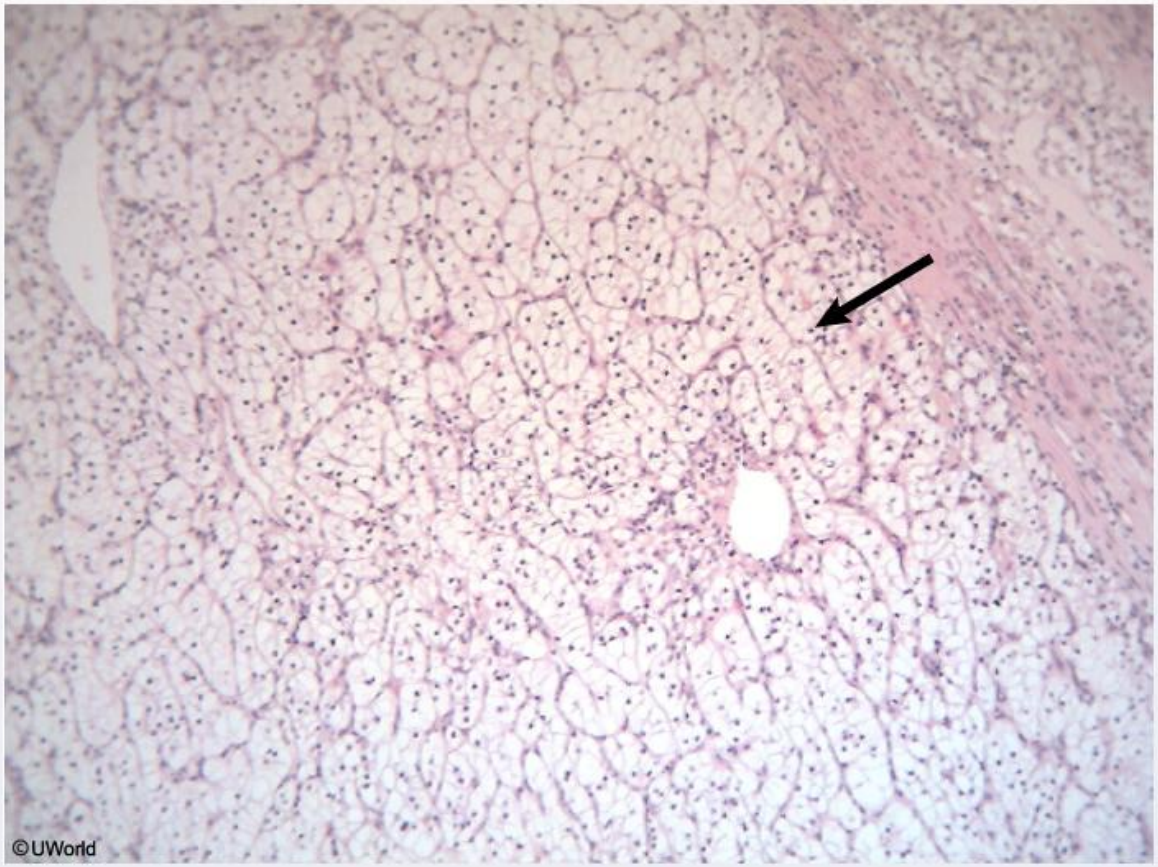
- A. Glycogen and lipid accumulation [76%] ✔
- B. Karyorrhexis [8%]
- C. Membrane lipid peroxidation [9%]
- D. Mitochondrial swelling [4%]
- E. Pigment accumulation [1%]

Omitted
Correct answer

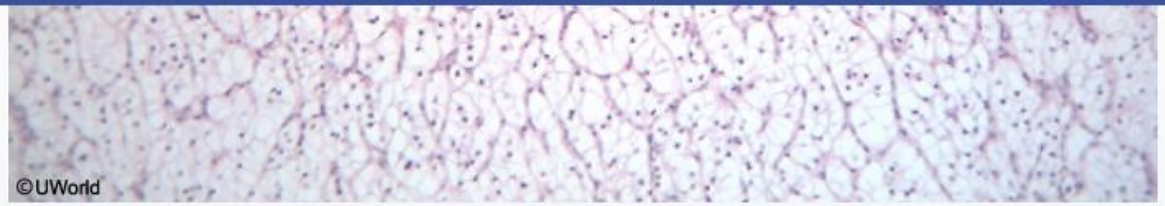
76%
Answered correctly

10 Seconds
Time Spent

09/20/2018
Last Updated



Gross painless hematuria in an older adult should be considered a sign of urinary tract cancer (urothelial or renal cell carcinoma) until proven otherwise. This patient's renal biopsy shows **rounded/polygonal cells** with abundant **clear cytoplasm**, which is characteristic of **clear cell**



Gross painless hematuria in an older adult should be considered a sign of urinary tract cancer (urothelial or renal cell carcinoma) until proven otherwise. This patient's renal biopsy shows **rounded/polygonal cells** with abundant **clear cytoplasm**, which is characteristic of **clear cell carcinoma**, the most common form of renal cell carcinoma. Clear cell carcinoma originates from proximal tubular epithelial cells and contains copious amounts of intracellular glycogen and lipids. Standard tissue fixation and staining techniques typically dissolve glycogen and lipids from pathologic specimens, leaving **clear spaces**, as seen in the slide.

(Choice B) Karyorrhexis is fragmentation of pyknotic (condensed) nuclei during apoptotic cell death. The cells in this slide have intact nuclei.

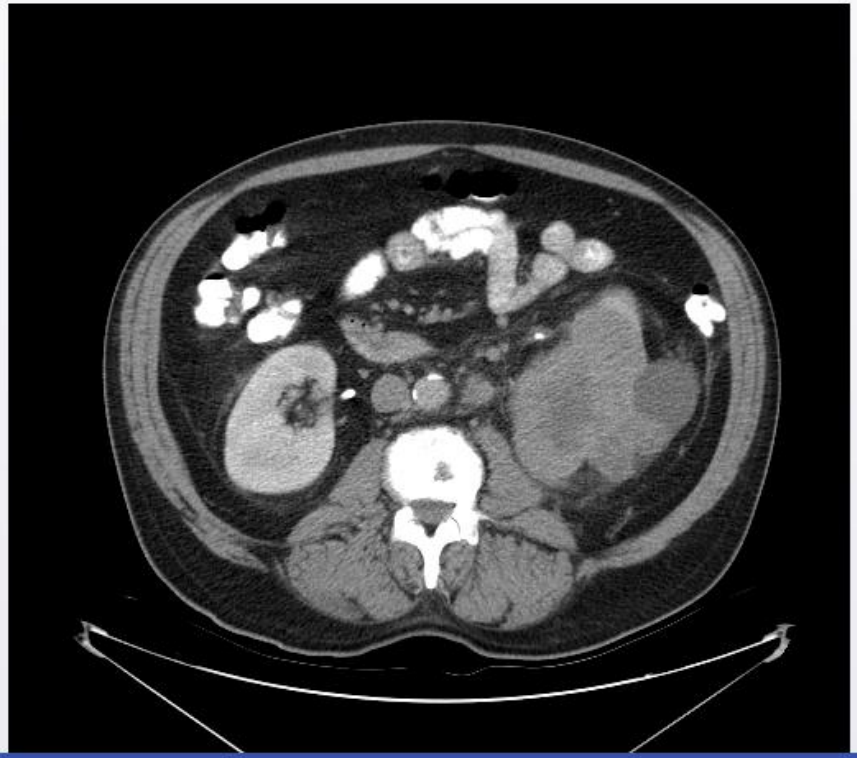
(Choice C) Plasma membrane damage caused by lipid peroxidation can be visualized using immunofluorescent microscopy. Lipid peroxidation is a form of free radical damage and is associated with inflammation, atherosclerosis, and tumorigenesis.

(Choice D) Mitochondrial swelling usually occurs during cell injury and would not be expected to render the cell cytoplasm completely clear on routine hematoxylin and eosin stain.

(Choice E) Melanin and hemosiderin are pigments commonly seen on histologic specimens. Hemosiderin is an iron oxide pigment that stains tissues at sites of bleeding.

Educational objective:
The most common renal malignancy is clear cell carcinoma, which arises from renal proximal tubular cells. Rounded or polygonal cells with abundant clear cytoplasm are seen on light microscopy. "Clear cells" are generally those with a high glycogen or lipid content that dissolves during routine tissue preparation.

A 64-year-old man comes to the office due to several episodes of intermittent hematuria over the past 2 months. He has had no abdominal pain, burning on urination, or fever but has lost 4.5 kg (10 lb) since the onset of symptoms. The patient has smoked a pack of cigarettes daily for 30 years. Vital signs are within normal limits. The abdomen is soft, nontender, and nondistended. An enlarged and firm prostate is palpated on digital rectal examination. Serum calcium is 12.3 mg/dL. Urinalysis shows 30-40 red blood cells/hpf, negative protein, and no casts. A CT scan of the abdomen is shown below.



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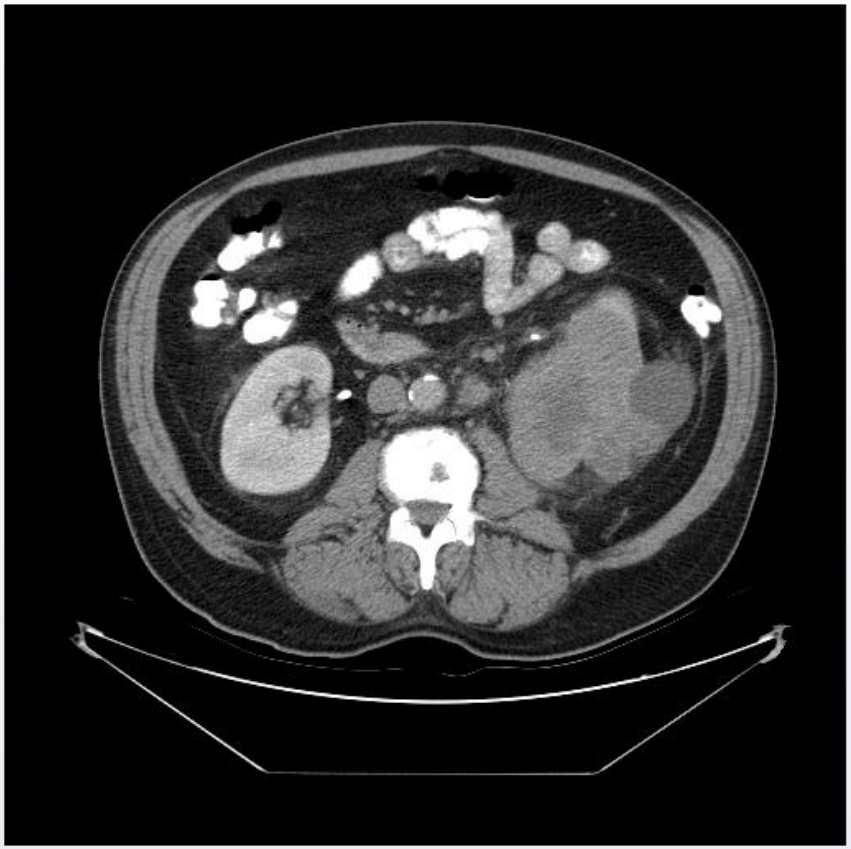
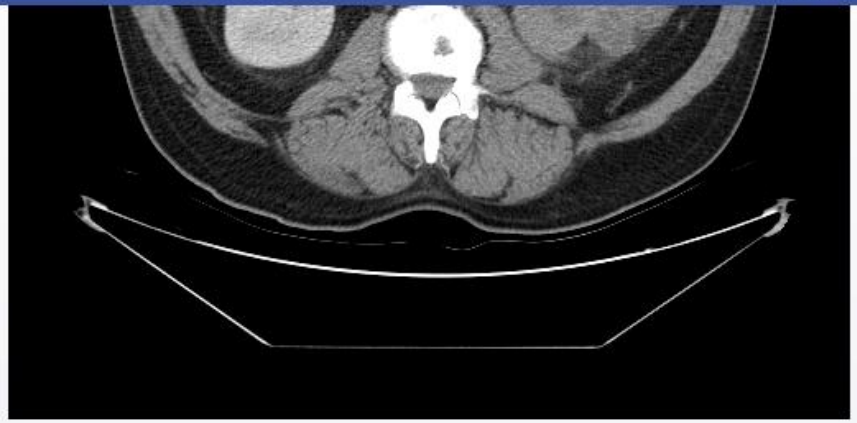


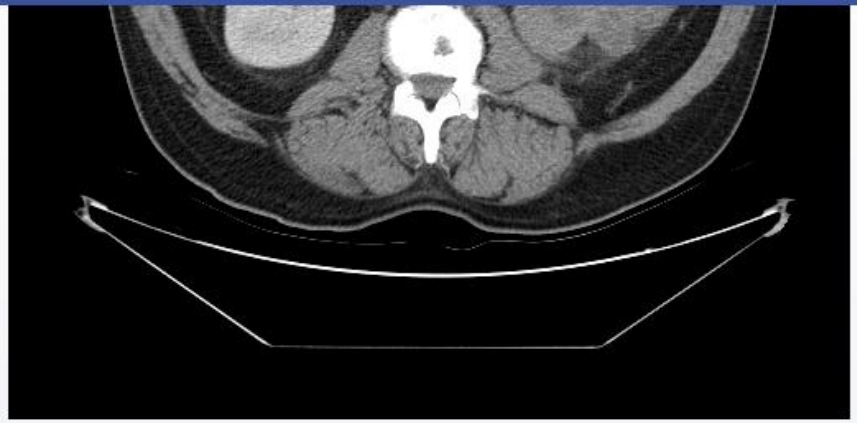
Which of the following is the most likely diagnosis?



Which of the following is the most likely diagnosis?

- A. Bladder cancer
- B. Pheochromocytoma
- C. Polycystic kidney disease
- D. Prostate cancer
- E. Renal cell carcinoma
- F. Ureterolithiasis

Submit



Which of the following is the most likely diagnosis?

- A. Bladder cancer [7%]
- B. Pheochromocytoma [0%]
- C. Polycystic kidney disease [6%]
- D. Prostate cancer [13%]
- ✔ E. Renal cell carcinoma [69%]
- F. Ureterolithiasis [2%]

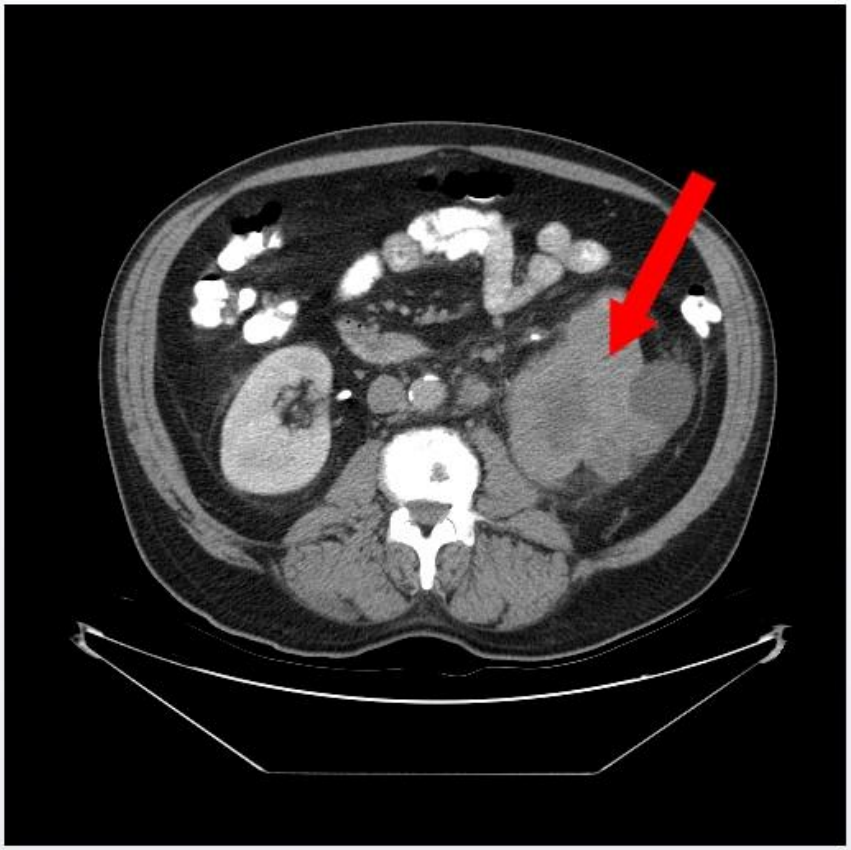
Omitted
Correct answer

69%
Answered correctly

10 Seconds
Time Spent

02/10/2019
Last Updated

Explanation



This patient with an extensive smoking history, 4.5-kg weight loss, painless hematuria, hypercalcemia, and renal mass (arrow) likely has **renal cell**

This patient with an extensive smoking history, 4.5-kg weight loss, painless hematuria, hypercalcemia, and renal mass (arrow) likely has **renal cell carcinoma** (RCC). RCC originates in the renal cortex and accounts for up to 90% of primary renal tumors. It is often identified incidentally on radiographic imaging, and many individuals remain **asymptomatic** until the disease is relatively advanced. Hematuria is the most common symptom, and **painless hematuria** in an adult should raise suspicion for a genitourinary malignancy. Patients may also have **flank pain** and a palpable **abdominal mass** at the time of presentation.

Paraneoplastic syndromes are common in RCC due to the secretion of biologically active substances by the tumor cells. **Hypercalcemia** is frequently seen due to increased production of parathyroid hormone–related peptide or overproduction of prostaglandins that promote bony resorption. **Erythrocytosis** (due to ectopic erythropoietin production) and hepatic dysfunction unrelated to liver metastases may also be seen.

(Choice A) Bladder cancer is another common cause of hematuria and weight loss; however, CT scan would demonstrate a **bladder mass**. This malignancy tends to metastasize to the liver, bones, and lungs, not the kidney. Although hypercalcemia may occur occasionally, it is more strongly associated with RCC.

(Choice B) Pheochromocytoma can cause severe, episodic hypertension associated with headaches, anxiety, palpitations, and sweating. A CT scan would reveal a suprarenal mass, and urine catecholamines and metanephrine would be elevated. Hematuria is not seen.

(Choice C) Polycystic kidney disease can cause hematuria; however, flank pain is common, and imaging would show **bilateral renal cysts**, not a unilateral mass. In addition, weight loss and hypercalcemia would be unexpected.

(Choice D) Prostate cancer typically presents with discrete nodules or asymmetric induration of the prostate on digital rectal examination. Diffuse, symmetric enlargement and firmness of the prostate are more suggestive of benign prostatic hyperplasia.

(Choice F) Ureterolithiasis is a common cause of hematuria, and patients with hypercalcemia from other causes (eg, hyperparathyroidism) are predisposed to stone formation. Although there are small kidney stones on this patient's imaging, this would not explain the large renal mass and unintended weight loss, which are highly suggestive of malignancy.

Educational objective:

Classic signs and symptoms of renal cell carcinoma (RCC) include hematuria, an abdominal mass, flank pain, and weight loss. Hypercalcemia

radiographic imaging, and many individuals remain **asymptomatic** until the disease is relatively advanced. Hematuria is the most common symptom, and **painless hematuria** in an adult should raise suspicion for a genitourinary malignancy. Patients may also have **flank pain** and a palpable **abdominal mass** at the time of presentation.

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Educational objective:
Classic signs and symptoms of renal cell carcinoma (RCC) include hematuria, an abdominal mass, flank pain, and weight loss. Hypercalcemia and erythrocytosis are common paraneoplastic syndromes associated with RCC.

A 44-year-old woman comes to the emergency department due to acute-onset, severe, right lower quadrant abdominal pain, nausea, vomiting, and hematuria over the last 4 hours. She had a similar episode of acute pain a year ago, but it resolved in a few hours and she did not seek medical intervention. The patient has no other medical conditions and takes no medication. She smokes a pack of cigarettes daily. She is sexually active and has never been pregnant. Temperature is 36.9 C (98.4 F), blood pressure is 140/90 mm Hg, and pulse is 102/min. There is mild tenderness to deep palpation in the right lower quadrant. Laboratory results are as follows:

Serum chemistry

Urea nitrogen	15 mg/dL
Creatinine	1.0 mg/dL
Glucose	90 mg/dL
Calcium	11 mg/dL
Phosphorus	2.5 mg/dL

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

A. Appendicitis
B. Diverticulitis
C. Glomerulonephritis
D. Ovarian torsion
E. Renal cell carcinoma
F. Renal infarction

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C. Glomerulonephritis
D. Ovarian torsion
E. Renal cell carcinoma
F. Renal infarction
G. Ureterolithiasis

Submit

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Glucose	90 mg/dL
Calcium	11 mg/dL
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Which of the following is the most likely cause of this patient's current condition?

- A. Appendicitis [3%]
- B. Diverticulitis [1%]
- C. Glomerulonephritis [1%]
- D. Ovarian torsion [5%]
- E. Renal cell carcinoma [8%]
- F. Renal infarction [2%]
- ✔ G. Ureterolithiasis [76%]

Omitted
Correct answer

76%
Answered correctly

9 Seconds
Time Spent

02/08/2019
Last Updated

Risk & prevention of kidney stones		
Stone type	**Risk factors**	**Prevention**
Calcium stones (oxalate, phosphate)	• Hypercalciuria (eg, hyperparathyroidism) • Hyperoxaluria (eg, malabsorption, low-calcium diet) • Hypocitraturia (eg, distal RTA) • Diet: ↑ sodium, ↑ protein, ↑ oxalate, ↓ calcium	• Reduce sodium, animal protein, oxalate intake • Increase potassium intake; moderate calcium intake • Thiazide diuretics
Uric acid	• Gout • Myeloproliferative disorders	• Urine alkalinization • Allopurinol
Magnesium ammonium phosphate (struvite)	• Recurrent upper urinary infection (eg, *Klebsiella*, *Proteus*)	• Stone removal • Suppressive antibiotics
All types	• Dehydration	• Increase fluid intake

RTA = renal tubular acidosis.

This patient has recurrent **abdominal pain**, vomiting, and **hematuria**. In conjunction with hypercalcemia and hypophosphatemia, this presentation suggests **ureterolithiasis** due to **hyperparathyroidism**. Most kidney stones are made up of calcium salts and are idiopathic, but conditions that increase calcium excretion increase the risk of stone formation. Primary hyperparathyroidism leads to increased bone resorption, decreased urinary phosphate reabsorption, and increased 1,25-dihydroxyvitamin D formation, all of which result in **hypercalcemia** and **hypophosphatemia**. Despite the increased fractional reabsorption of calcium induced by PTH, net urinary **calcium excretion is elevated** due to the increased filtered calcium load, raising the risk for stone formation.

Pain from ureterolithiasis, which occurs when the stone **obstructs renal drainage**, typically waxes and wanes. Obstruction at the ureteropelvic

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Pain from ureterolithiasis, which occurs when the stone **obstructs renal drainage**, typically waxes and wanes. Obstruction at the ureteropelvic junction normally presents with flank or upper abdominal pain, whereas an obstructing stone at the ureterovesical junction usually presents with lower abdominal or groin pain. Other common symptoms include hematuria, nausea, and vomiting.

(Choices A and B) Appendicitis presents with acute periumbilical or right lower quadrant pain and tenderness, but it would not usually cause recurrent symptoms. Acute diverticulitis can cause recurrent lower abdominal symptoms but is much more common on the left and typically occurs in older (age >60) patients. Neither of these conditions are associated with hematuria or hypercalcemia.

(Choice C) Glomerulonephritis is a category of kidney disorders characterized by hematuria, typically with red cell casts. Common associated features include hypertension, oliguria, and acute renal failure. Patients with various nephritic syndromes may have moderate flank pain, but acute, severe lower abdominal pain is not consistent with glomerulonephritis.

(Choice D) Ovarian torsion can present with acute, severe lower abdominal or pelvic pain. It can be recurrent but would not cause hematuria.

(Choice E) Renal cell cancer can cause hematuria and hypercalcemia; however, pain (if present) typically presents in the flank rather than the lower abdomen.

(Choice F) Renal infarction typically occurs due to acute obstruction of the renal arteries (eg, cardiac thromboembolism, aortic dissection). Patients often develop abdominal pain and hematuria but also typically have fever and marked hypertension (due to renin release). In addition, renal infarction is not associated with hypercalcemia or hypophosphatemia.

Educational objective:
Most kidney stones are made of calcium salts and are idiopathic, but conditions that increase renal calcium excretion can increase the risk of

lower abdominal or groin pain. Other common symptoms include hematuria, nausea, and vomiting.

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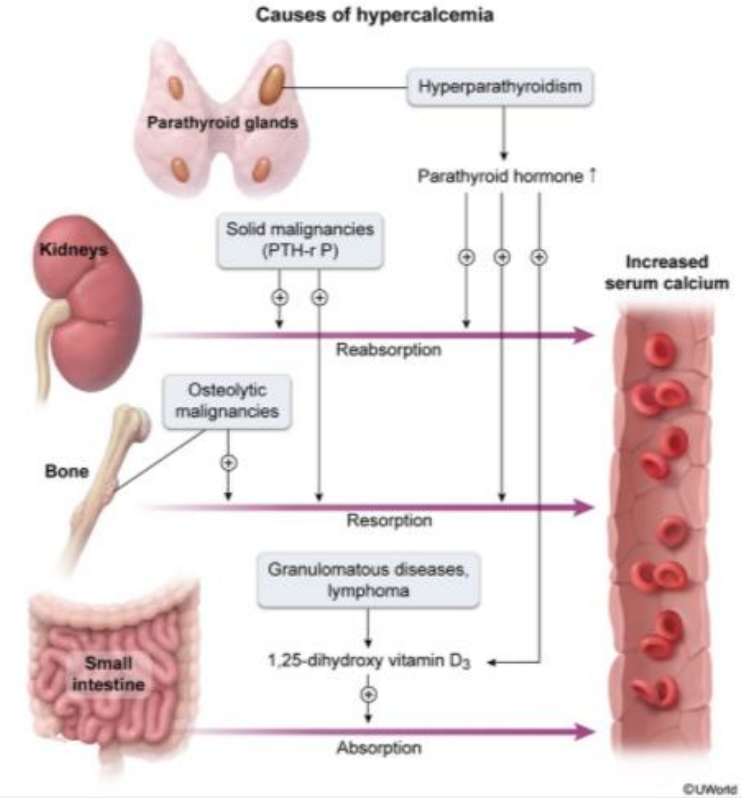
Educational objective:
Most kidney stones are made of calcium salts and are idiopathic, but conditions that increase renal calcium excretion can increase the risk of stones. Hyperparathyroidism is a common cause of recurrent kidney stones and is typically associated with mild hypercalcemia and hypophosphatemia.

References

- Renal stones and calcifications in patients with primary hyperparathyroidism: associations with biochemical variables.

Stone type | Risk factors | Prevention

Exhibit Display



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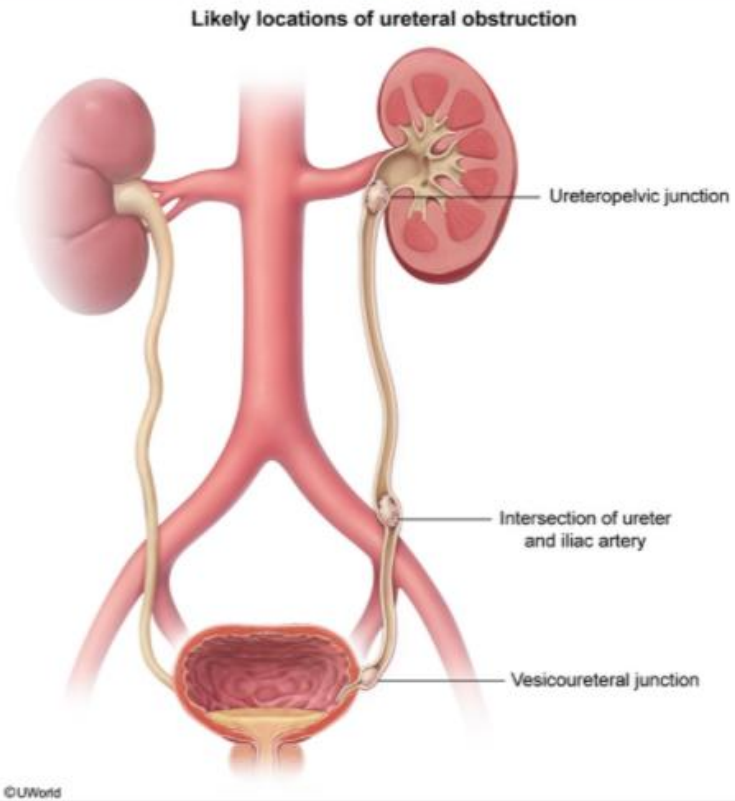
Stone type	Risk factors	Prevention

Exhibit Display



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A nephrology researcher conducts a clinical study to determine the risk factors for the development of renal calculi. He recruits a number of patients with a history of idiopathic calcium oxalate kidney stones, along with age- and sex-matched healthy subjects. Detailed medical, surgical, and nutritional histories are obtained, and several serum and urine laboratory tests are performed. Which of the following is most likely to be seen in affected patients compared with healthy individuals?

A. Higher dietary calcium
B. Higher dietary potassium
C. Higher fluid intake
D. Lower dietary oxalate
E. Lower urinary citrate

Submit

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- A. Higher dietary calcium [23%]
- B. Higher dietary potassium [3%]
- C. Higher fluid intake [2%]
- D. Lower dietary oxalate [7%]
- ✔ E. Lower urinary citrate [62%]

Omitted
Correct answer
E

62%
Answered correctly

3 Seconds
Time Spent

01/23/2019
Last Updated

Explanation

Risk & prevention of kidney stones		
Stone type	**Risk factors**	**Prevention**
	• Hypercalciuria (eg, hyperparathyroidism)	Reduce sodium, animal protein, oxalate

Risk & prevention of kidney stones		
Stone type	**Risk factors**	**Prevention**
Calcium stones (oxalate, phosphate)	• Hypercalciuria (eg, hyperparathyroidism) • Hyperoxaluria (eg, malabsorption, low-calcium diet) • Hypocitraturia (eg, distal RTA) • Diet: ↑ sodium, ↑ protein, ↑ oxalate, ↓ calcium	• Reduce sodium, animal protein, oxalate intake • Increase potassium intake; moderate calcium intake • Thiazide diuretics
Uric acid	• Gout • Myeloproliferative disorders	• Urine alkalinization • Allopurinol
Magnesium ammonium phosphate (struvite)	• Recurrent upper urinary infection (eg, *Klebsiella*, *Proteus*)	• Stone removal • Suppressive antibiotics
All types	• Dehydration	• Increase fluid intake

RTA = renal tubular acidosis.

Renal calculi occur due to an imbalance of the factors that facilitate or prevent stone formation. Overall, increased urinary concentrations of calcium (hypercalciuria), oxalate (hyperoxaluria), and uric acid (hyperuricosuria) promote salt crystallization, whereas increased urinary citrate and high fluid intake inhibit calculi formation.

Normally, **citrate** excreted by the kidneys **binds to ionized calcium** in the urine, **preventing** the formation of **insoluble calcium-oxalate complexes**. When urinary citrate is low (**hypocitraturia**), increased calcium availability leads to increased formation of calcium-oxalate complexes that can precipitate and form **calcium oxalate stones**. Hypocitraturia often occurs in the setting of chronic metabolic acidosis (eg,

Renal calculi occur due to an imbalance of the factors that facilitate or prevent stone formation. Overall, increased urinary concentrations of calcium (hypercalciuria), oxalate (hyperoxaluria), and uric acid (hyperuricosuria) promote salt crystallization, whereas increased urinary citrate and high fluid intake inhibit calculi formation.

Normally, **citrate** excreted by the kidneys **binds to ionized calcium** in the urine, **preventing** the formation of **insoluble calcium-oxalate complexes**. When urinary citrate is low (**hypocitraturia**), increased calcium availability leads to increased formation of calcium-oxalate complexes that can precipitate and form **calcium oxalate stones**. Hypocitraturia often occurs in the setting of chronic metabolic acidosis (eg, distal renal tubular acidosis, chronic diarrhea) due to enhanced renal citrate reabsorption. Supplemental oral potassium citrate is often prescribed to prevent recurrent calcium stones.

(Choice A) Individuals with higher (but not excessive) calcium intake paradoxically have a lower risk of calcium oxalate stone formation. Dietary calcium binds oxalate in the gut to form insoluble calcium oxalate, which is eliminated in the feces. This reduces the amount of oxalate absorbed into the body and excreted in the urine, reducing stone formation.

(Choice B) Higher potassium intake promotes urinary excretion of citrate and lowers urinary calcium excretion, leading to a lower risk of calcium oxalate stones.

(Choice C) High fluid intake prevents supersaturation of urine with stone-forming ingredients. Low fluid intake increases the urinary concentration of these ions regardless of their absolute amounts, promoting stone formation.

(Choice D) Excessive oxalate intake (eg, chocolate, spinach, rhubarb) leads to increased intestinal absorption of free oxalate, which is then excreted in the urine where it promotes formation of calcium oxalate stones. Intestinal malabsorption syndromes (eg, Crohn disease) can also cause hyperoxaluria because calcium becomes bound by unabsorbed lipids in the gut.

Educational objective:
Renal calculi occur due to an imbalance of the factors that facilitate or inhibit stone formation. Increased urinary concentrations of calcium, oxalate, and uric acid promote salt crystallization, whereas increased urinary citrate concentration and high fluid intake prevent calculi formation.

A 20-year-old woman develops gross hematuria. She otherwise feels well and has had no recent illnesses. The patient was diagnosed with type 1 diabetes mellitus approximately 1 year ago and is taking daily insulin injections. She works in a day care center and does not use tobacco, alcohol, or illicit drugs. Temperature is 37 C (98.6 F), blood pressure is 120/80 mm Hg, and pulse is 80/min. Physical examination shows no abnormalities. Laboratory results are as follows:

Serum creatinine	1.0 mg/dL
Serum albumin	4.0 mg/dL
Urinalysis	numerous red blood cells (RBCs) and few RBC casts; 1+ protein
Serum complement	normal

Which of the following is the most likely diagnosis?

A. Diabetic nephropathy
B. IgA nephropathy
C. Membranous nephropathy
D. Minimal change disease
E. Poststreptococcal glomerulonephritis

Submit

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Serum creatinine	1.0 mg/dL
Serum albumin	4.0 mg/dL
Urinalysis	numerous red blood cells (RBCs) and few RBC casts; 1+ protein
Serum complement	normal

Which of the following is the most likely diagnosis?

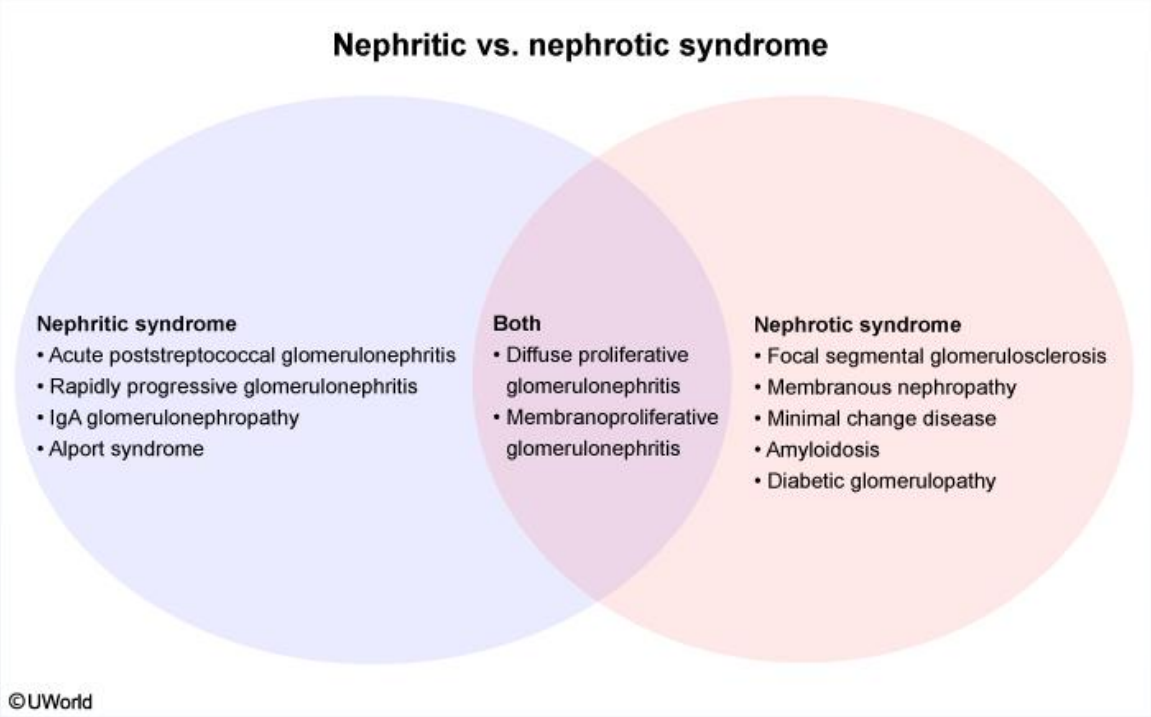
- A. Diabetic nephropathy [18%]
- ✔ B. IgA nephropathy [46%]
- C. Membranous nephropathy [14%]
- D. Minimal change disease [6%]
- E. Poststreptococcal glomerulonephritis [14%]

Omitted
Correct answer
B

46%
Answered correctly

3 Seconds
Time Spent

01/26/2019
Last Updated



Nephritic syndromes (ie, glomerulonephritis) are characterized by glomerular inflammation, resulting in hematuria and **red blood cell casts** on urinalysis. Renal dysfunction (eg, azotemia) and hypertension are common but not always present in early disease. Patients may also have mild to moderate proteinuria and edema, although typically not as severe as in nephrotic syndrome.

The most common cause of nephritic syndrome is **immune complex deposition**. Most immune complex–related nephritic syndromes (eg, poststreptococcal glomerulonephritis [PSGN], membranoproliferative glomerulonephritis, lupus nephritis) are associated with IgG and/or IgM

Nephritic syndromes (ie, glomerulonephritis) are characterized by glomerular inflammation, resulting in hematuria and **red blood cell casts** on urinalysis. Renal dysfunction (eg, azotemia) and hypertension are common but not always present in early disease. Patients may also have mild to moderate proteinuria and edema, although typically not as severe as in nephrotic syndrome.

The most common cause of nephritic syndrome is **immune complex deposition**. Most immune complex–related nephritic syndromes (eg, poststreptococcal glomerulonephritis [PSGN], membranoproliferative glomerulonephritis, lupus nephritis) are associated with IgG and/or IgM complexes and have heavy glomerular complement deposition and subsequent serum hypocomplementemia (consumption). However, **IgA nephropathy** is typically associated with **normal serum complement levels**, likely due to the weak complement-fixing activity of IgA as compared to IgG and IgM.

IgA nephropathy is characterized as recurrent gross hematuria that typically occurs **spontaneously** (as in this patient) or within 5-7 days of an upper respiratory or pharyngeal infection (synpharyngitic hematuria). When IgA nephropathy is accompanied by extrarenal symptoms (eg, abdominal pain, arthralgias, skin purpura), the syndrome is called Henoch-Schönlein purpura.

(Choices A, C, and D) Nephrotic syndromes typically cause *heavy proteinuria with low albumin levels* and edema, rather than hematuria and red blood cell casts; etiologies include diabetic nephropathy, membranous nephropathy, and minimal change disease. Diabetic nephropathy typically takes >5 years to develop in type 1 diabetes (although it can be present at the time of diagnosis in type 2).

(Choice E) PSGN presents with nephritic syndrome 2-4 weeks after infection with group A *Streptococcus* (postpharyngitic hematuria). Over 90% of patients with PSGN develop marked hypocomplementemia.

Educational objective:
IgA nephropathy is characterized as recurrent hematuria that occurs spontaneously or within 5-7 days of an upper respiratory or pharyngeal infection (synpharyngitic hematuria). Unlike other causes of immune complex–mediated nephritic syndromes (eg, poststreptococcal glomerulonephritis), IgA nephropathy is associated with normal serum complement levels.

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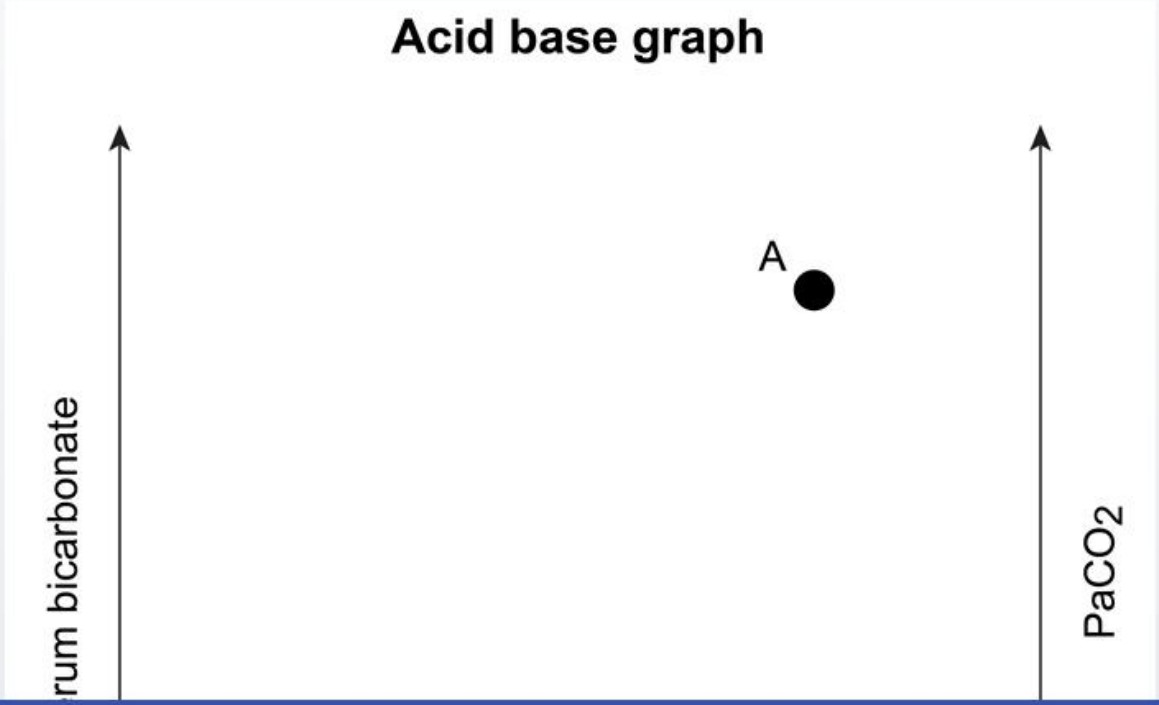
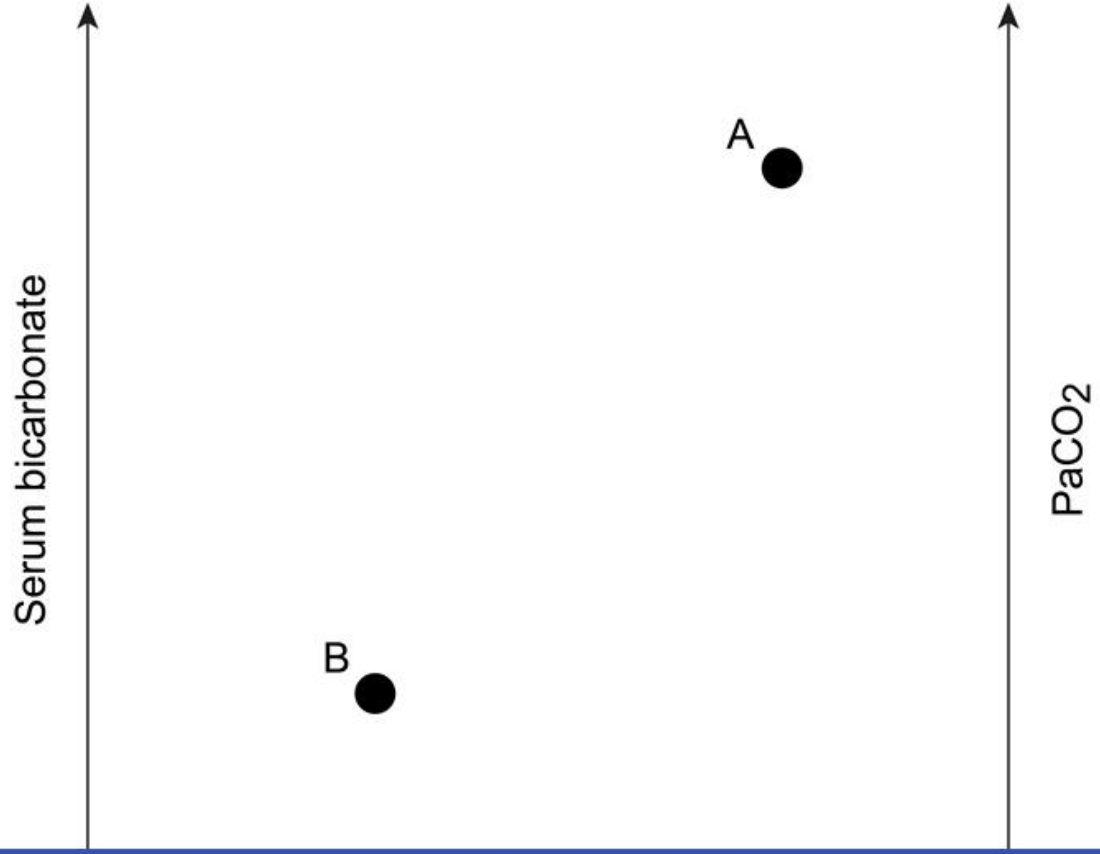
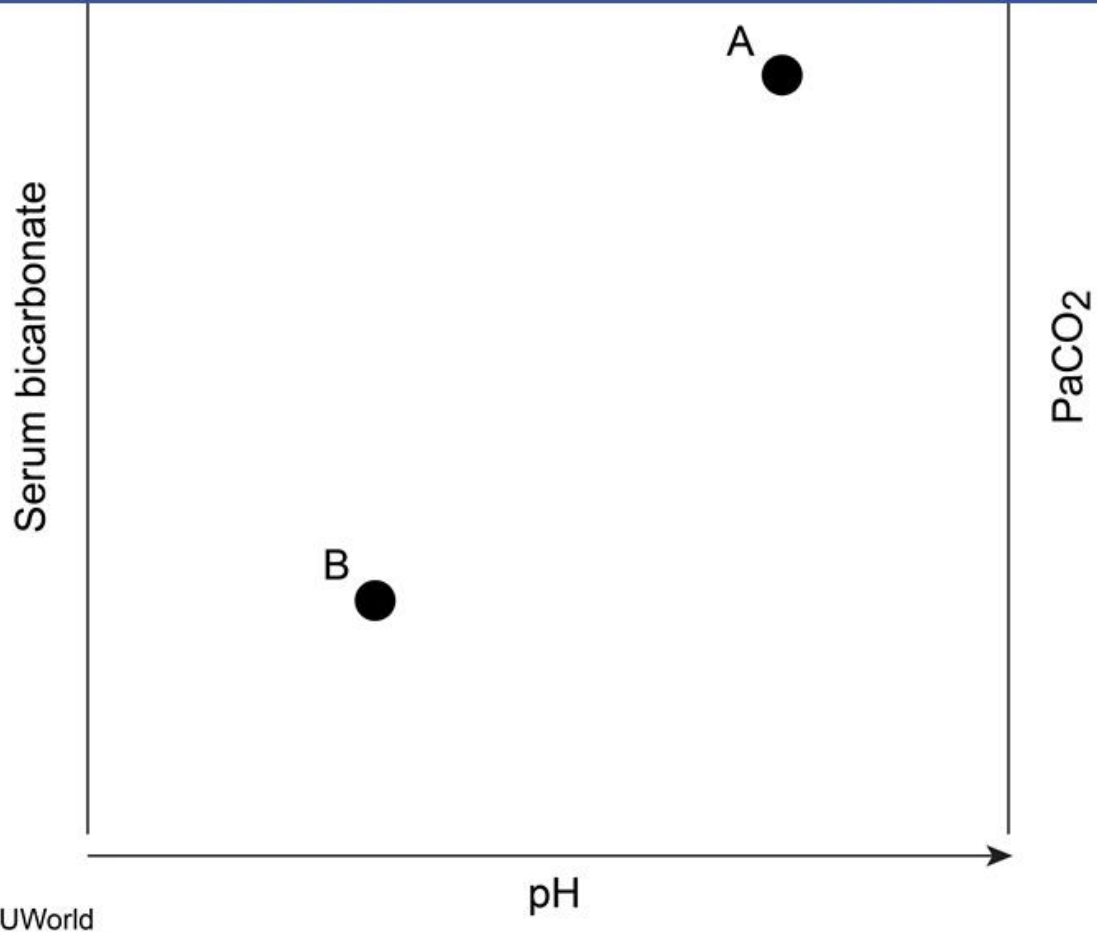
The following vignette applies to the next **2** items. The items in the set must be answered in sequential order. Once you click **Proceed to Next Item**, you will not be able to add or change an answer.

A 34-year-old man is brought to the emergency department with new-onset confusion and lethargy. Laboratory studies, including an arterial blood gas, are obtained. The changes in his blood gas parameters are shown in the graph below. Point A represents these parameters at the patient's physiologic baseline, and point B indicates his state on arrival in the emergency department.



Acid base graph





Item 1 of 2

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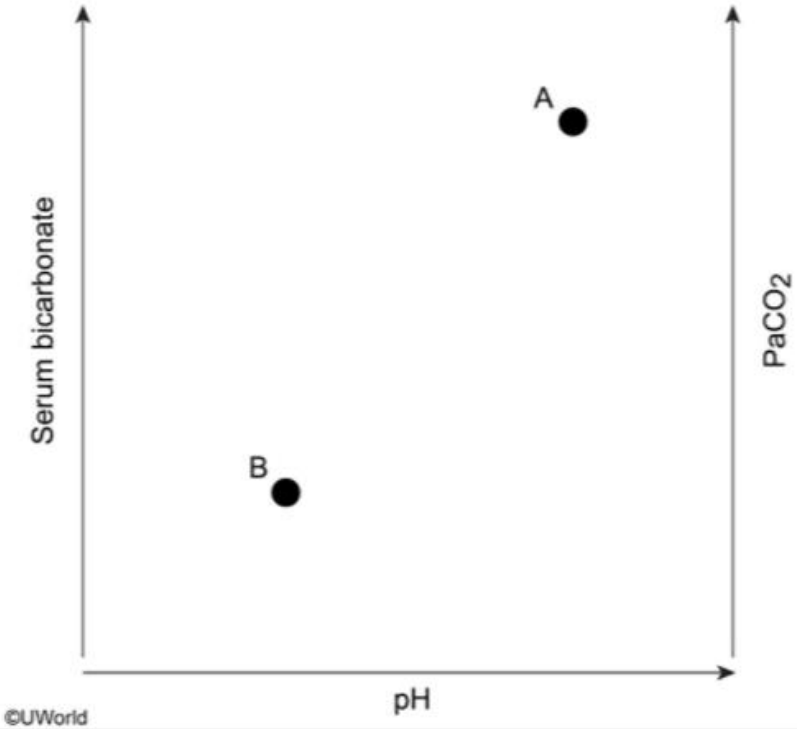
Exhibit Display

Acid base graph



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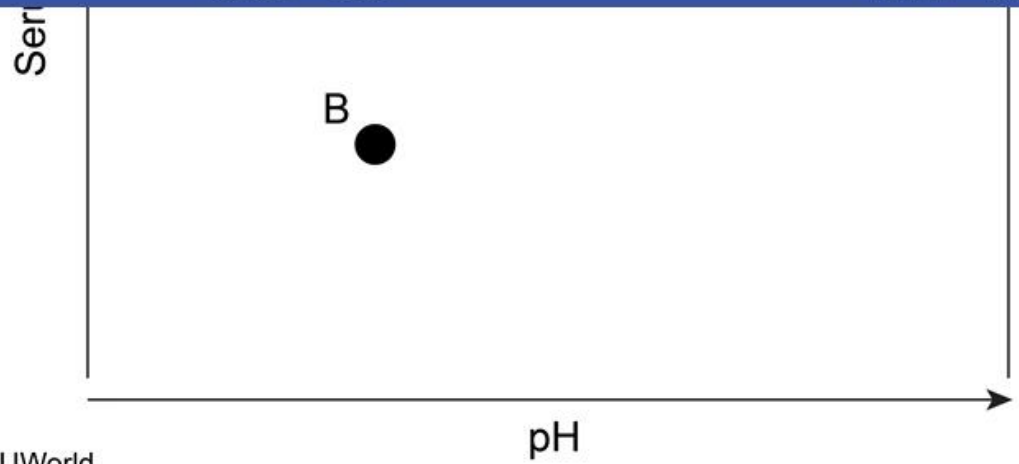
Item 1 of 2



Item 1 of 2

Which of the following is the most likely diagnosis?

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

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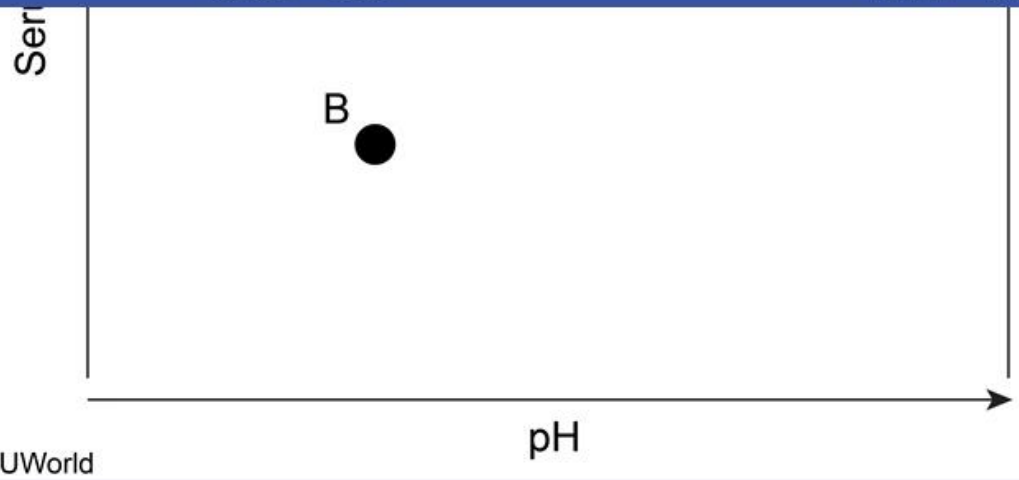

Item 1 of 2

Which of the following is the most likely diagnosis?

- A. Metabolic acidosis [86%] ✔
- B. Metabolic alkalosis [6%]
- C. Respiratory acidosis [5%]
- D. Respiratory alkalosis [1%]

Omitted
Correct answer

86%
Answered correctly

21 Seconds
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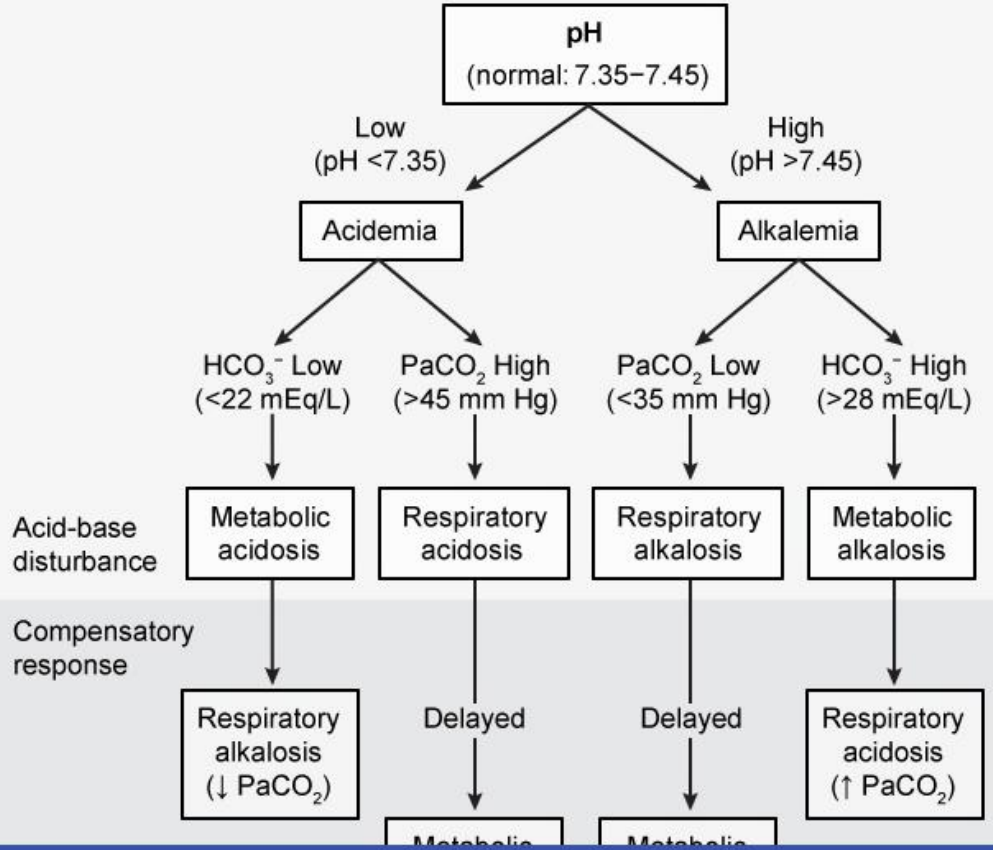
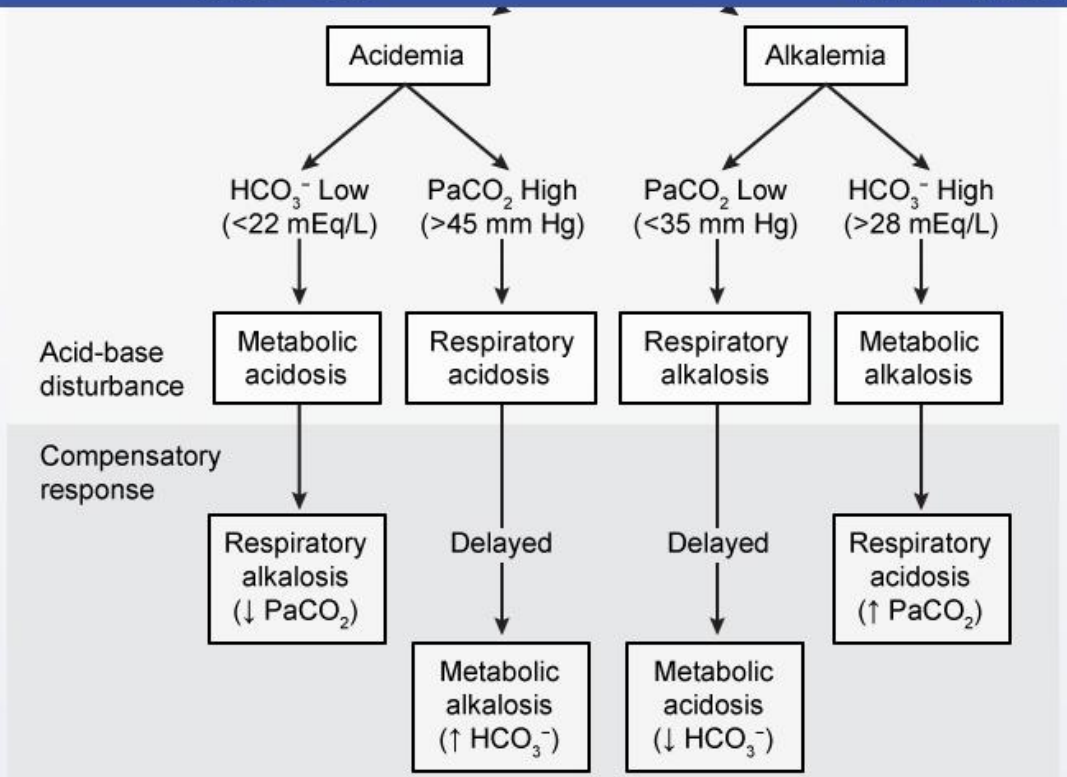
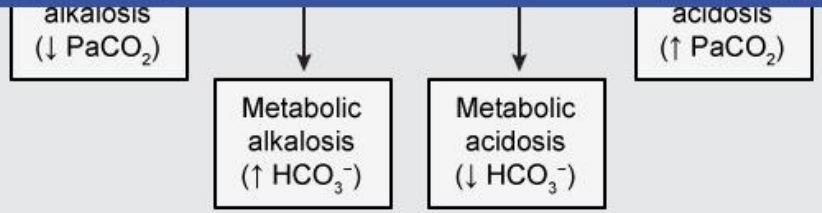
Arterial blood gas interpretation of primary acid-base disorders





HCO_3^- = bicarbonate; $PaCO_2$ = partial pressure of carbon dioxide in arterial blood.

Point B on the graph above shows that this patient has a **decreased pH** compared to his baseline physiologic state, which indicates acidosis. The next step is to assess whether his acidosis is primarily metabolic or respiratory. A **decrease in serum bicarbonate** is characteristic of **metabolic acidosis**. It is usually associated with a **decrease in $PaCO_2$** as a result of respiratory compensation for the primary **metabolic acidosis**.



HCO_3^- = bicarbonate; $PaCO_2$ = partial pressure of carbon dioxide in arterial blood.
©UWorld

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(Choice B) Metabolic alkalosis would be characterized by increased pH and serum bicarbonate. The $PaCO_2$ would also increase due to respiratory compensation.

(Choice C) Respiratory acidosis is characterized by decreased pH and increased $PaCO_2$. Plasma bicarbonate gradually increases to compensate for the primary respiratory acidosis (renal compensation). However, unlike respiratory compensation, this is a delayed response that occurs over 3-5 days.

(Choice D) Respiratory alkalosis is characterized by increased pH and decreased $PaCO_2$. Plasma bicarbonate gradually decreases to compensate for the primary respiratory alkalosis (renal compensation). However, unlike respiratory compensation, this is a delayed response that occurs over 3-5 days.

Educational objective:
Metabolic acidosis is characterized by a decrease in serum pH and serum bicarbonate. $PaCO_2$ will also decrease as a result of respiratory compensation for primary metabolic acidosis.

alkalosis | acidosis

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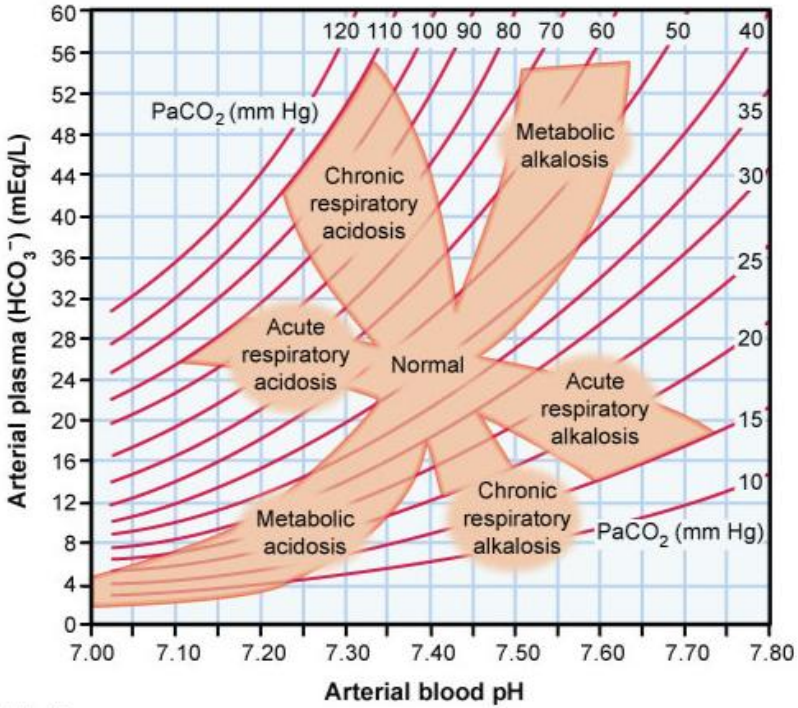

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Item 2 of 2

After determining that the patient has an increased anion gap metabolic acidosis, an appropriate treatment is instituted. Within several hours, the patient's mental status improves significantly. Repeat laboratory studies show an increase in serum bicarbonate and sodium levels, a decrease in serum osmolality, and a drop in the serum potassium level. Which of the following treatments was most likely given to this patient?

A. Insulin and normal saline
B. Loop diuretics
C. Mineralocorticoid injection
D. Opioid antagonists
E. Thyroxine supplementation

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Item 2 of 2

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- A. Insulin and normal saline [65%] ✔
- B. Loop diuretics [14%]
- C. Mineralocorticoid injection [19%]
- D. Opioid antagonists [0%]
- E. Thyroxine supplementation [0%]

Omitted
Correct answer
A

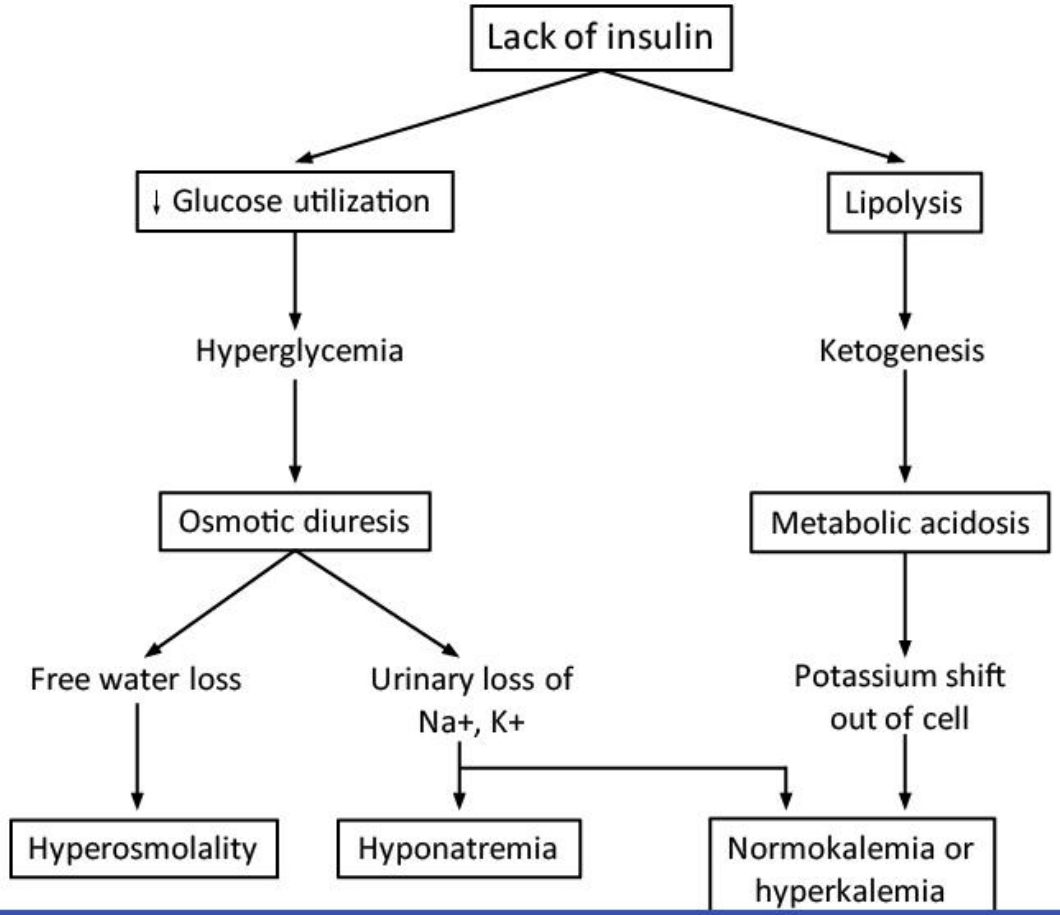
65%
Answered correctly

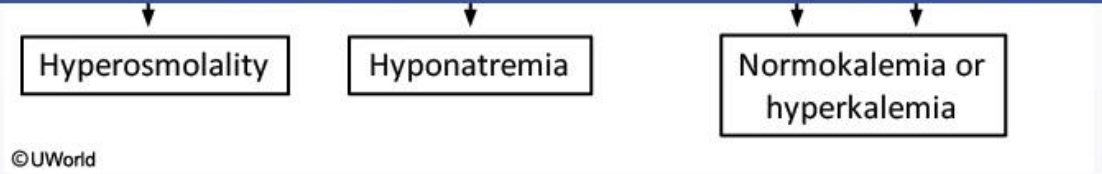
3 Seconds
Time Spent

10/31/2018
Last Updated

Explanation

Diabetic ketoacidosis





Based on the laboratory changes, this patient with an increased **anion gap metabolic acidosis** was most likely suffering from **diabetic ketoacidosis** (DKA). Patients classically have a fruity odor to the breath and often present with mental status changes, dehydration, abdominal pain, and tachypnea. Laboratory findings include hyperglycemia, ketosis, mild hyponatremia, normal or elevated serum potassium (despite a total body deficit), and increased plasma osmolality.

Insulin and hydration are the primary treatments for DKA. Insulin allows the cells to use glucose as an energy source, thereby decreasing lipolysis and production of ketone bodies. Because ketones are the principal acid produced in excess in patients with DKA, decreased production of ketone bodies will result in **increased serum bicarbonate**. Insulin also causes an **intracellular shift of potassium**, resulting in a decrease in the serum potassium level (which necessitates potassium repletion). In addition to insulin-induced changes, rehydration with normal saline will help normalize serum sodium concentration and decrease serum osmolality.

(Choice B) Loop diuretics could cause a decrease in potassium concentration as well as an increase in the serum concentration of bicarbonate. However, they also increase (not decrease) serum osmolality due to increased free water excretion (loop diuretics decrease the medullary concentration gradient, limiting the maximum tonicity of the urine).

(Choice C) Metabolic acidosis may develop in hypoaldosteronism (type 4 renal tubular acidosis), which is treated with exogenous mineralocorticoids. However, the combination of an increased anion gap and impaired mental status is not characteristic for hypoaldosteronism. Treatment with mineralocorticoids causes sodium and water retention with a mild increase in serum osmolality. Mineralocorticoids also decrease serum potassium and increase serum bicarbonate due to urinary K^+ and H^+ loss.

(Choice D) Opioid antagonists are useful in treating opioid overdoses, which typically cause respiratory acidosis (not anion gap metabolic acidosis) due to hypoventilation.

(Choice E) Thyroxine supplementation is useful in treating severe hypothyroidism, which may present with hyponatremia, extracellular volume

pain, and tachypnea. Laboratory findings include hyperglycemia, ketosis, mild hyponatremia, normal or elevated serum potassium (despite a total body deficit), and increased plasma osmolality.

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(Choice E) Thyroxine supplementation is useful in treating severe hypothyroidism, which may present with hyponatremia, extracellular volume expansion, and hypoglycemia.

Educational objective:
The treatment of choice for diabetic ketoacidosis is intravenous normal saline and insulin. These therapies increase serum bicarbonate and sodium and decrease serum glucose, osmolality, and potassium.

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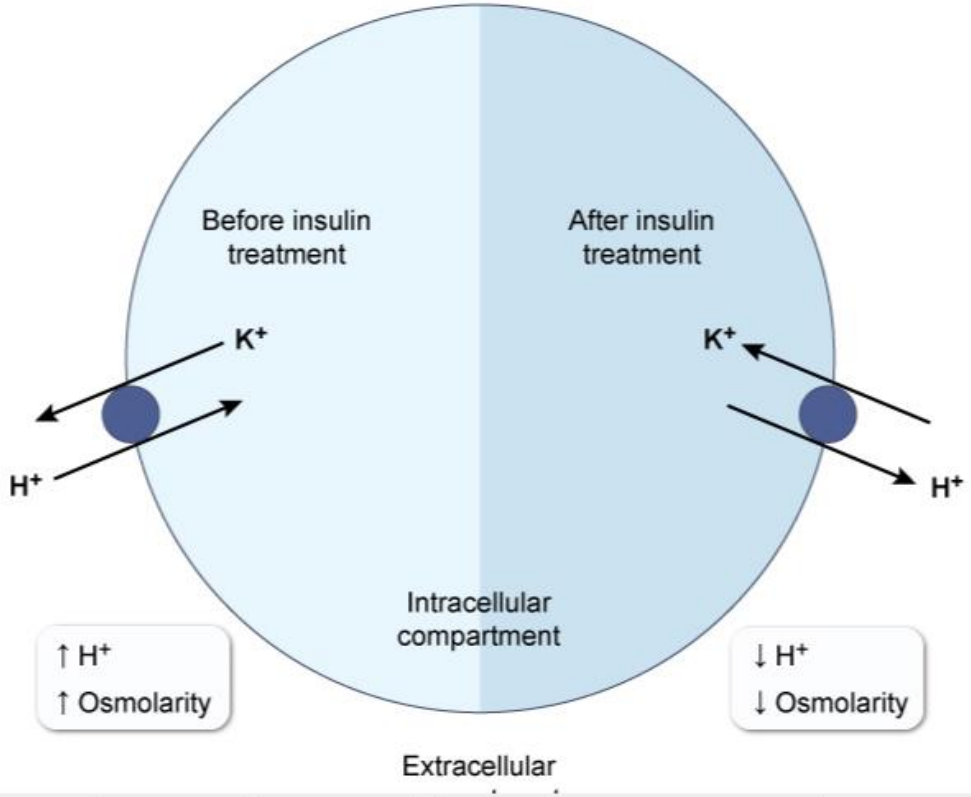

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A 76-year-old man comes to the office due to bilateral flank pain and nausea. The patient has not urinated for 24 hours. His medical history is significant for diet-controlled type 2 diabetes and degenerative arthritis of the knee. He occasionally takes naproxen for pain. Temperature is 37.3 C (99.1 F), blood pressure is 140/90 mm Hg, and pulse is 90/min. Cardiopulmonary examination shows no abnormalities. Abdominal examination shows suprapubic fullness. Laboratory results show a blood urea nitrogen level of 32 mg/dL and creatinine level of 2.6 mg/dL. Four weeks ago, his laboratory studies were normal. Which of the following is the most likely cause of this patient's renal dysfunction?

- A. Diabetic nephropathy
- B. Interstitial nephritis
- C. Renal tubule injury due to ischemia
- D. Renal tubule injury due to protein casts
- E. Urethral compression

Submit

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- A. Diabetic nephropathy [6%]
- B. Interstitial nephritis [21%]
- C. Renal tubule injury due to ischemia [11%]
- D. Renal tubule injury due to protein casts [2%]
- ✔ E. Urethral compression [58%]

Omitted
Correct answer
E

58%
Answered correctly

15 Seconds
Time Spent

01/19/2019
Last Updated

Explanation

This patient with **anuria** and **suprapubic fullness** (suggesting a distended bladder) has **acute urinary retention** (AUR). AUR is characterized by the inability to voluntarily micturate, which leads to suprapubic pain with **bladder distension**, often palpable above the pelvic brim. As urine refluxes into the ureters and kidneys, dilation of the ureters, renal pelvis, and calyces (hydronephrosis) results in **acute kidney injury**, bilateral flank pain, and costovertebral angle tenderness. Elevations in creatinine and blood urea nitrogen are also common, but the ratio between the two

the inability to voluntarily micturate, which leads to suprapubic pain with **bladder distension**, often palpable above the pelvic brim. As urine refluxes into the ureters and kidneys, dilation of the ureters, renal pelvis, and calyces (hydronephrosis) results in **acute kidney injury**, bilateral flank pain, and costovertebral angle tenderness. Elevations in creatinine and blood urea nitrogen are also common, but the ratio between the two is variable.

Etiologies of AUR include:

- Bladder outlet obstruction: By far the most common cause of urinary retention, bladder outlet obstructions are precipitated by **urethral compression**, typically due to **benign prostatic hyperplasia** (particularly in men age >50). Other etiologies include transitional cell carcinoma, and rectal or uterine malignancy.
- Medications: AUR is commonly caused by anticholinergic medications (eg, oxybutynin, atropine) and sympathomimetics (eg, pseudoephedrine).
- Neurologic dysfunction: Diabetic neuropathy, spinal cord injury, and stroke can result in a neurogenic bladder.

(Choice A) Diabetic nephropathy typically presents with proteinuria and chronic kidney disease rather than acute anuria with bilateral flank pain. This patient had normal baseline renal function 4 weeks ago, ruling out chronic kidney disease.

(Choice B) Interstitial nephritis typically occurs after introduction of new medications and is often accompanied by fever and rash. It can cause impaired urine production (oliguria), but an overly distended bladder and flank pain would be unexpected.

(Choices C and D) Ischemia (eg, due to hypotension) can cause tubular necrosis. Abundant protein casts can form in multiple myeloma, leading to obstruction and necrosis of the renal tubules. Both cause intrinsic renal injury with an elevation in creatinine; however, a distended bladder would be unexpected.

Educational objective:
Acute urinary retention is characterized by anuria and bladder distension, and can result in hydronephrosis and acute kidney injury. A palpable, distended bladder is present on examination, and abdominal and flank pain may be present. The most common cause of urinary retention is bladder outlet obstruction (urethral compression) due to benign prostatic hyperplasia.

A 5-year-old girl is brought to the clinic due to 2 days of dark red urine. The patient was treated for facial impetigo 1 month ago. Blood pressure is 140/90 mm Hg. Urinalysis reveals hematuria, mild proteinuria, and occasional red blood cell casts. Which of the following changes would most likely be present on this patient's renal biopsy?

A. Diffuse capillary wall thickening on light microscopy
B. Discrete subepithelial humps on electron microscopy
C. Glomerular basement membrane fibrin deposition on electron microscopy
D. Glomerular basement membrane splitting on light microscopy
E. Linear IgG and C3 deposits on immunofluorescent microscopy

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- A. Diffuse capillary wall thickening on light microscopy [2%]
- ✔ B. Discrete subepithelial humps on electron microscopy [72%]
- C. Glomerular basement membrane fibrin deposition on electron microscopy [4%]
- D. Glomerular basement membrane splitting on light microscopy [2%]
- E. Linear IgG and C3 deposits on immunofluorescent microscopy [17%]

Omitted
Correct answer
B

72%
Answered correctly

4 Seconds
Time Spent

09/26/2018
Last Updated

Explanation

Pathological findings in nephritic syndromes		
	Cause of glomerular injury	Characteristic biopsy features
Poststreptococcal		IF - C3 granular staining along

Pathological findings in nephritic syndromes		
	Cause of glomerular injury	**Characteristic biopsy features**
Poststreptococcal glomerulonephritis	Antibodies against streptococcal antigens that deposit in GBM	IF - C3 granular staining along GBM EM - **Subepithelial humps**
Anti-GBM disease	Antibodies against type IV collagen in GBM	LM - Glomerular crescents IF - **Linear staining (IgG)** along GBM
Rapidly progressive glomerulonephritis	**Severe** immunologic injury (eg, anti-GBM antibodies, immune complex deposition)	LM - Glomerular **crescents** IF - Fibrin in crescents
IgA nephropathy	Deposition of IgA-containing complexes	LM - Mesangial hypercellularity IF - **IgA in mesangium**
Alport syndrome	Defective type IV collagen in GBM	EM - **Lamellated appearance of GBM**

EM = electron microscopy; **GBM** = glomerular basement membrane; **IF** = immunofluorescence; **LM** = light microscopy.

This patient has **nephritic syndrome**, characterized by hypertension, mild proteinuria, and hematuria with red blood cell casts in the urine sediment. In association with a recent skin infection, this presentation suggests **poststreptococcal glomerulonephritis** (PSGN), the most common cause of nephritic syndrome in children. PSGN is an **immune complex–mediated** disease that occurs 2-4 weeks after exposure to group A beta-hemolytic *Streptococcus* (eg, pharyngitis, skin infection). Antigens expressed on nephritogenic streptococcal species combine with antibodies to form immune complexes, which are later deposited on the glomerular basement membrane (GBM).

This patient has **nephritic syndrome**, characterized by hypertension, mild proteinuria, and hematuria with red blood cell casts in the urine sediment. In association with a recent skin infection, this presentation suggests **poststreptococcal glomerulonephritis** (PSGN), the most common cause of nephritic syndrome in children. PSGN is an **immune complex–mediated** disease that occurs 2-4 weeks after exposure to group A beta-hemolytic *Streptococcus* (eg, pharyngitis, skin infection). Antigens expressed on nephritogenic streptococcal species combine with antibodies to form immune complexes, which are later deposited on the glomerular basement membrane (GBM).

On light microscopy, all glomeruli are enlarged and hypercellular due to leukocyte infiltration and proliferation of endothelial and mesangial cells. On electron microscopy, **electron-dense deposits** ("humps") on the epithelial side of the GBM are seen. Immunofluorescence reveals coarse, **granular deposits of IgG and C3** that have a characteristic "lumpy-bumpy" appearance.

(Choice A) Uniform, diffuse thickening of glomerular capillary walls on light microscopy is characteristic of **membranous glomerulopathy**, one of the most common causes of nephrotic syndrome in adults. Manifestations of nephrotic syndrome include generalized edema, marked proteinuria (>3.5 g/day), hypoalbuminemia, hyperlipidemia, and lipiduria.

(Choices C and E) In contrast to PSGN, which demonstrates granular deposits of IgG and C3 along the GBM, **linear IgG and C3 deposits** on immunofluorescence microscopy are characteristic of Goodpasture syndrome (anti-GBM disease). This commonly presents with rapidly progressive (crescentic) glomerulonephritis. Damage to the GBM results in leakage of plasma proteins and heavy fibrin deposition in the glomerulus, resulting in parietal cell proliferation and crescent formation. This disease is uncommon in children, and renal involvement is often accompanied by pulmonary symptoms (eg, hemoptysis).

(Choice D) GBM splitting is seen in membranoproliferative glomerulonephritis (MPGN) and Alport syndrome. Alport syndrome causes nephritic syndrome but is most commonly X-linked and therefore more common in males; it is not associated with recent streptococcal infections. MPGN causes nephrotic syndrome.

Educational objective:
Poststreptococcal glomerulonephritis is an immune complex–deposition disease that occurs 2-4 weeks after exposure to group A beta-hemolytic *Streptococcus* species (eg, pharyngitis, skin infection). Light microscopy shows enlarged, hypercellular glomeruli. Immunofluorescence demonstrates a "lumpy-bumpy" granular deposits of IgG and C3 on the glomerular basement membrane, and subepithelial, electron-dense deposits are seen on electron microscopy.

A 4-year-old girl developed acute-onset colicky abdominal pain, vomiting, and loose bloody stools during a family vacation. She was treated with supportive care and began to feel better. A few days later, her parents bring her to the emergency department because she has urinated only once in the past 10 hours and the urine was red. Physical examination shows conjunctival pallor but is otherwise normal. Laboratory studies are as follows:

Hemoglobin	7.8 g/dL
Platelets	80,000/mm^3
Creatinine	1.7 mg/dL

Urinalysis shows proteinuria and hematuria. Which of the following mechanisms is the most likely cause of this patient's condition?

A. Microthrombi in small blood vessels
B. Streptococcal antigen-associated glomerular damage
C. Systemic IgA-mediated vasculitis
D. Vasculitis involving medium arteries
E. Widespread activation of the coagulation cascade

Submit

A 4-year-old girl developed acute-onset colicky abdominal pain, vomiting, and loose bloody stools during a family vacation. She was treated with supportive care and began to feel better. A few days later, her parents bring her to the emergency department because she has urinated only once in the past 10 hours and the urine was red. Physical examination shows conjunctival pallor but is otherwise normal. Laboratory studies are as follows:

Hemoglobin	7.8 g/dL
Platelets	80,000/mm^3
Creatinine	1.7 mg/dL

Urinalysis shows proteinuria and hematuria. Which of the following mechanisms is the most likely cause of this patient's condition?

- ✔ A. Microthrombi in small blood vessels [48%]
- B. Streptococcal antigen-associated glomerular damage [11%]
- C. Systemic IgA-mediated vasculitis [27%]
- D. Vasculitis involving medium arteries [3%]
- E. Widespread activation of the coagulation cascade [9%]

Omitted
Correct answer
A

48%
Answered correctly

3 Seconds
Time Spent

02/04/2019
Last Updated

Explanation

Hemolytic uremic syndrome	
Etiology	Shiga toxin-producing bacteria • *Escherichia coli* O157:H7 • *Shigella*
Clinical features	• Antecedent diarrheal illness (often bloody) • Hemolytic anemia with schistocytes • Thrombocytopenia • Acute kidney injury

This patient has diarrhea-associated **hemolytic uremic syndrome (HUS)**, a major cause of acute renal failure in young children. Most cases are due to intestinal infection by **Shiga toxin (verotoxin)-producing organisms** (eg, *Escherichia coli* O157:H7, *Shigella dysenteriae*). These toxins injure the endothelium of preglomerular arterioles and glomerular capillaries, leading to platelet activation and aggregation and the formation of microthrombi. Platelet consumption causes **thrombocytopenia** (platelets <140,000/mm^3), but there is typically no purpura or active bleeding. Erythrocytes passing through the damaged capillaries suffer shear injury and are broken down to schistocytes, causing **microangiopathic hemolytic anemia** (conjunctival pallor). Extensive damage to the renal vasculature results in **acute kidney injury** (oliguria/anuria, hematuria, increased creatinine).

(Choice B) Poststreptococcal glomerulonephritis develops approximately 1-3 weeks following a cutaneous or pharyngeal infection by a nephritogenic strain of group A β-hemolytic streptococci. It is caused by an immune response against streptococcal antigens that deposit in the glomerulus. Patients have oliguria, hematuria, proteinuria, edema, and hypertension. Anemia is not commonly seen.

(Choice C) Henoch-Schönlein purpura (HSP) is a systemic leukocytoclastic vasculitis caused by IgA immune complex deposition within small

injure the endothelium of preglomerular arterioles and glomerular capillaries, leading to platelet activation and aggregation and the formation of microthrombi. Platelet consumption causes **thrombocytopenia** (platelets <140,000/mm^3), but there is typically no purpura or active bleeding. Erythrocytes passing through the damaged capillaries suffer shear injury and are broken down to schistocytes, causing **microangiopathic hemolytic anemia** (conjunctival pallor). Extensive damage to the renal vasculature results in **acute kidney injury** (oliguria/anuria, hematuria, increased creatinine).

(Choice B) Poststreptococcal glomerulonephritis develops approximately 1-3 weeks following a cutaneous or pharyngeal infection by a nephritogenic strain of group A β-hemolytic streptococci. It is caused by an immune response against streptococcal antigens that deposit in the glomerulus. Patients have oliguria, hematuria, proteinuria, edema, and hypertension. Anemia is not commonly seen.

(Choice C) Henoch-Schönlein purpura (HSP) is a systemic leukocytoclastic vasculitis caused by IgA immune complex deposition within small blood vessels of the skin, kidneys, intestines, and joints. Symptoms include palpable purpura, abdominal pain, arthralgias, and acute glomerulonephritis. Platelet count and coagulation studies are normal in HSP. In addition, the absence of palpable purpura and joint symptoms makes HSP an unlikely diagnosis in this patient.

(Choice D) Kawasaki disease (mucocutaneous lymph node syndrome) is a vasculitis of medium arteries that classically affects young children. The main symptoms are high fever, conjunctivitis, cervical lymphadenopathy, periungual desquamation, and mucocutaneous changes (eg, strawberry tongue).

(Choice E) Disseminated intravascular coagulation refers to massive, widespread activation of the coagulation cascade due to release of procoagulant substances caused by sepsis, malignancy, or trauma. These patients usually have bleeding, petechiae, and bruising due to concomitant fibrinolysis and consumption of platelets and coagulation factors.

Educational objective:
Hemolytic uremic syndrome is a common cause of acute renal failure in children. It is characterized by the triad of microangiopathic hemolytic anemia, thrombocytopenia, and acute kidney injury. Most cases develop following a diarrheal illness caused by Shiga toxin-producing organisms (eg, *Escherichia coli* O157:H7, *Shigella dysenteriae*).

References

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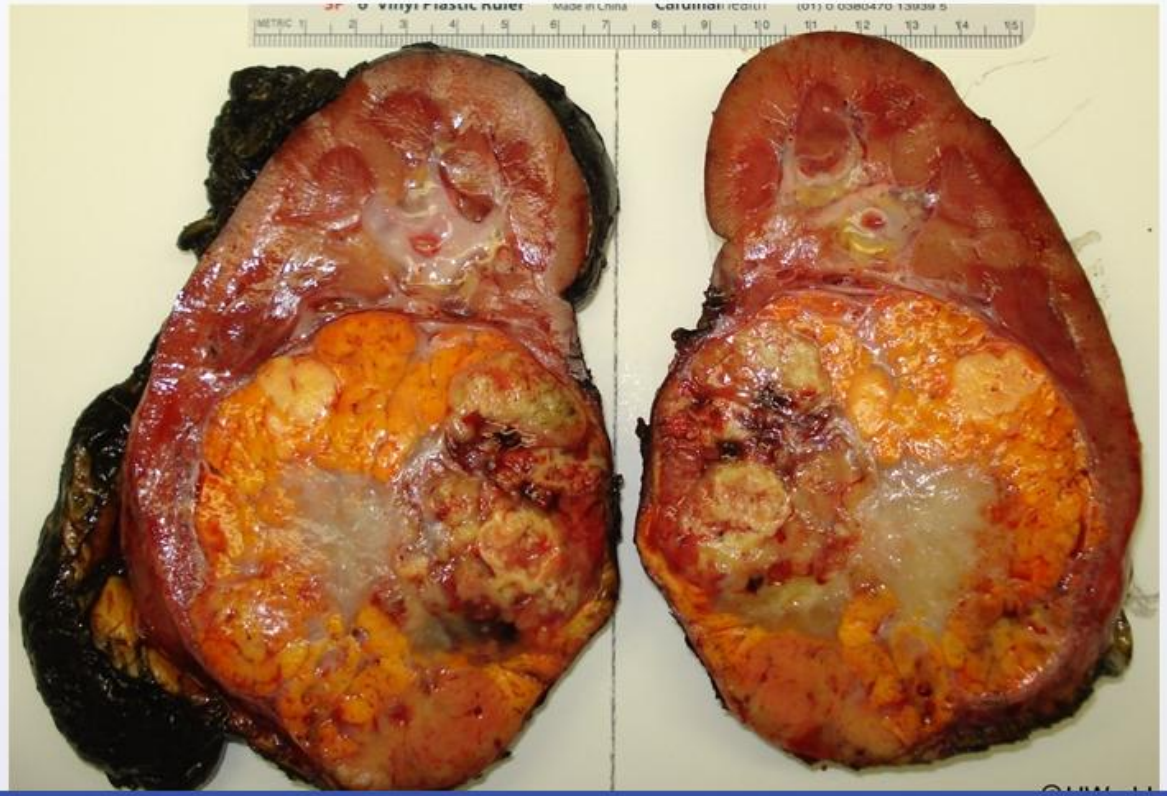
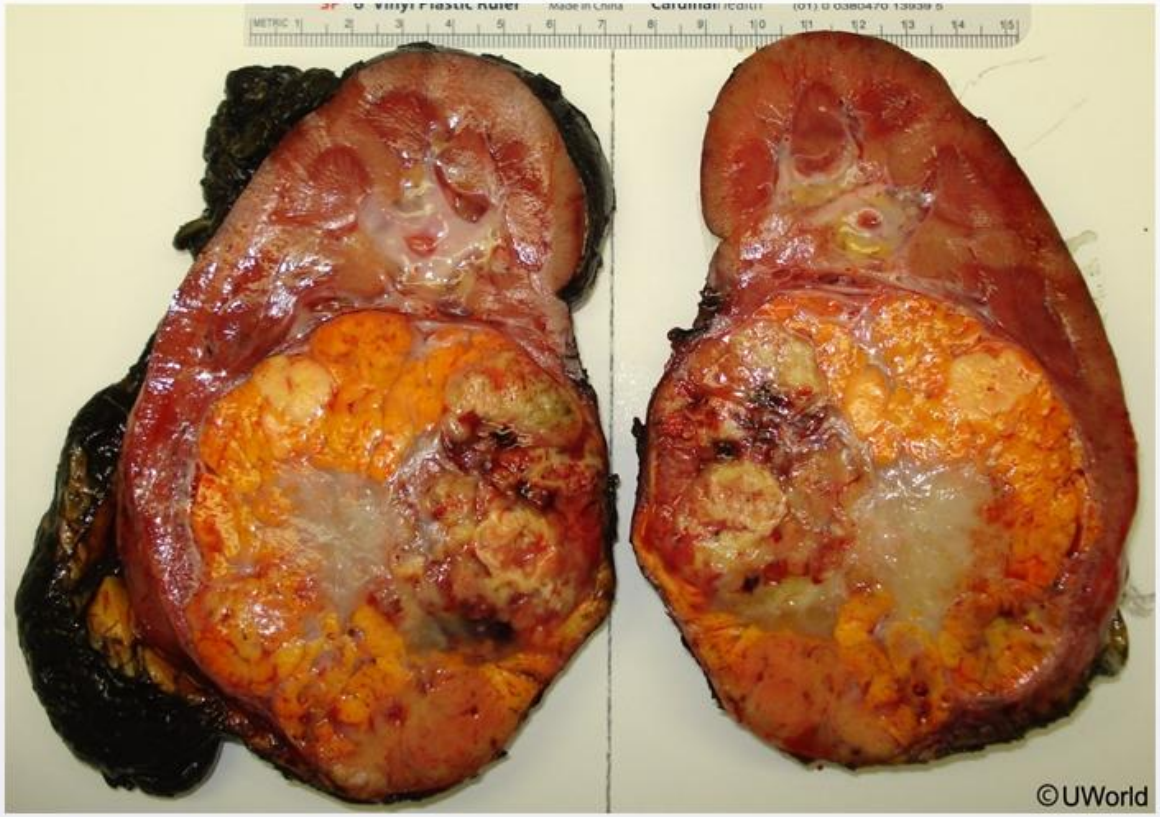
A 50-year-old man comes to the office for evaluation of abdominal fullness and mild right flank pain. He also reports a weight loss of 4.5 kg (10 lb) over the past 2 months. The patient has no other medical issues and works in a local industrial chemical manufacturing facility. Examination shows a soft abdomen. Ultrasound reveals a mass in the right kidney. A subsequent abdominal CT scan confirms the presence of a large right renal mass with evidence of necrosis. The patient undergoes a right total nephrectomy. The specimen is shown below.

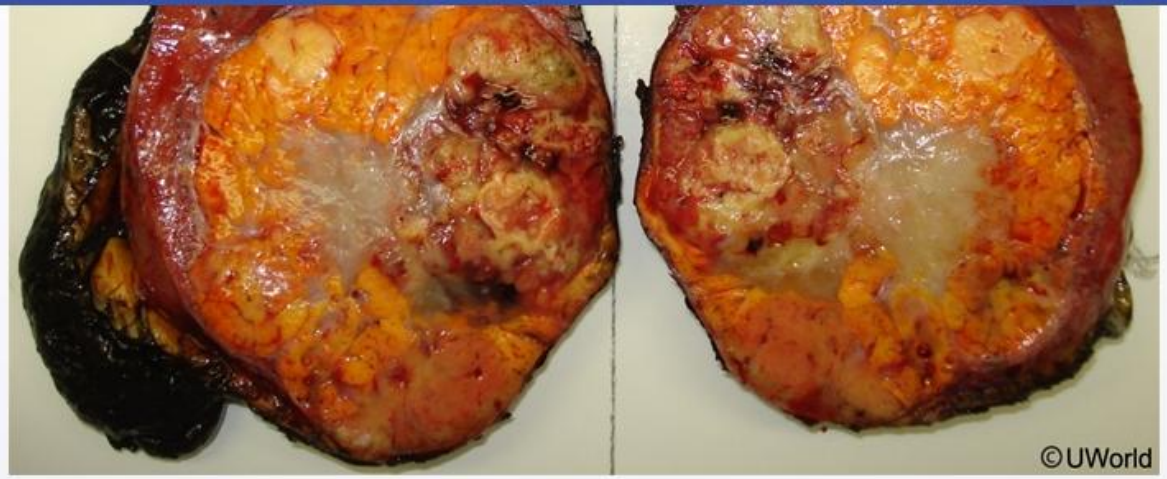


renal mass with evidence of necrosis. The patient undergoes a right total nephrectomy. The specimen is shown below.



This patient's lesion most likely originated from which of the following portions of the kidney?

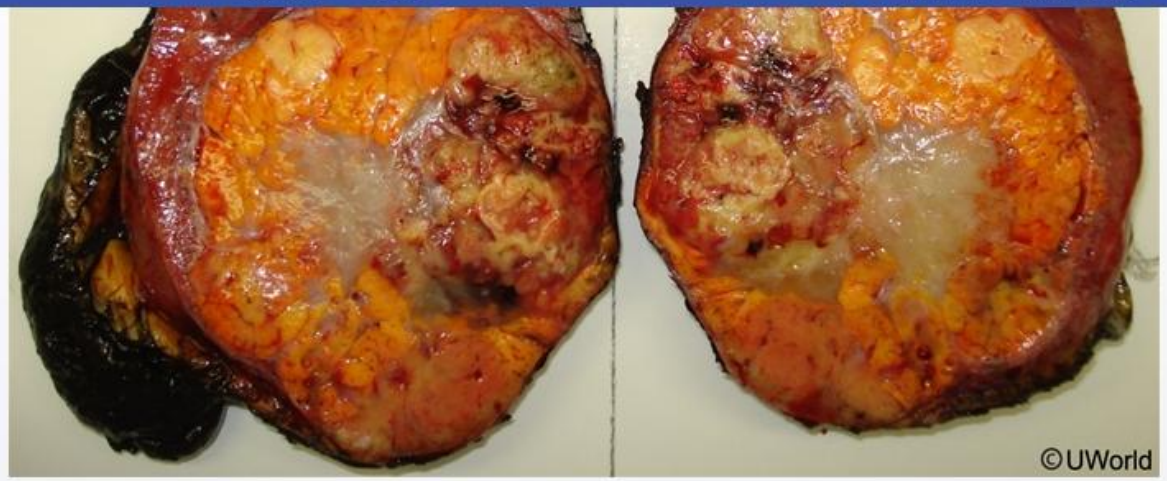
A. Blood vessels



This patient's lesion most likely originated from which of the following portions of the kidney?

- A. Blood vessels
- B. Collecting duct cells
- C. Glomeruli
- D. Proximal renal tubules
- E. Renal pelvis lining

Submit



This patient's lesion most likely originated from which of the following portions of the kidney?

- A. Blood vessels [7%]
- B. Collecting duct cells [14%]
- C. Glomeruli [6%]
- ✔ D. Proximal renal tubules [45%]
- E. Renal pelvis lining [25%]

Omitted
Correct answer

45%
Answered correctly

9 Seconds
Time Spent

01/06/2019
Last Updated

Renal cell carcinoma	
Presentation	• Hematuria, flank pain, palpable abdominal mass • Paraneoplastic syndrome (eg, polycythemia, hypercalcemia)
Risk factors	• Smoking, hypertension, obesity • Toxin exposure (eg, heavy metal, petroleum by-products)
Gross examination	• Spherical mass, often with invasion of the renal vein • Golden-yellow tissue (due to high lipid content)
Histology (Clear cell)	• Cuboidal or polygonal cells with abundant, clear cytoplasm • Branching, "chicken-wire" vasculature

This patient with a history of chemical exposure and a necrotic kidney mass likely has renal cell carcinoma (RCC), the most common renal malignancy. RCC originates in the renal cortex and occurs most commonly in patients age 60-70. Risk factors include **smoking**, obesity, hypertension and **toxin exposure** (eg, heavy metal, petroleum by-products, asbestos).

RCC is classified into subtypes based on cellular origin; **clear cell carcinoma** (CCC) is the most common type and accounts for up to 85% of RCCs. CCC originates from the epithelium of the **proximal renal tubules**. Gross pathology typically demonstrates a **sphere-like** mass composed of **golden-yellow tissue** (due to high lipid content) with areas of focal **necrosis** and **hemorrhage**. It often invades the renal vein and may extend into the inferior vena cava. On microscopy, CCC appears as cuboidal or polygonal cells with abundant clear cytoplasm and eccentric nuclei.

(Choice A) Angiomyolipomas are rare tumors that arise from blood vessel epithelial cells. Gross pathology demonstrates a well-circumscribed tumor composed of 3 different cell types: Yellow adipose tissue, red vascular components, and grayish smooth muscle. Angiomyolipomas are benign neoplasms often associated with tuberous sclerosis.

(Choice B) Renal oncocytomas are rare tumors that originate from collecting duct cells. Gross pathology often demonstrates a homogenous

This patient with a history of chemical exposure and a necrotic kidney mass likely has renal cell carcinoma (RCC), the most common renal malignancy. RCC originates in the renal cortex and occurs most commonly in patients age 60-70. Risk factors include **smoking**, obesity, hypertension and **toxin exposure** (eg, heavy metal, petroleum by-products, asbestos).

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(Choice A) Angiomyolipomas are rare tumors that arise from blood vessel epithelial cells. Gross pathology demonstrates a well-circumscribed tumor composed of 3 different cell types: Yellow adipose tissue, red vascular components, and grayish smooth muscle. Angiomyolipomas are benign neoplasms often associated with tuberous sclerosis.

(Choice B) Renal oncocytomas are rare tumors that originate from collecting duct cells. Gross pathology often demonstrates a homogenous brown tumor with a central stellate scar that is often visible on imaging; focal areas of necrosis are rare.

(Choice C) Glomerular diseases (eg, membranous nephropathy, minimal change disease) can be seen as a paraneoplastic syndrome associated with certain malignancies (eg, lung, gastrointestinal tumors), but the glomeruli are not the site of origin of RCC.

(Choice E) Urothelial carcinoma arises from the epithelium of the renal pelvis, ureters, or bladder and may be multifocal in nature. It often forms papillary tumors composed of urothelium supported by a thin fibrovascular stalk.

Educational objective:
Clear cell carcinoma is the most common type of renal cell carcinoma and originates from the epithelial cells of the proximal renal tubules. Gross pathology typically demonstrates a sphere-like mass composed of golden-yellow cells (due to high lipid content) with areas of necrotic cells and focal hemorrhage.

A 50-year-old man with polycystic kidney disease comes to the office due to constant, deep pain in his shoulders, arms, and legs. Medical history includes long-standing hypertension treated with ramipril. Blood pressure is 150/85 mm Hg and pulse is 78/min. Cardiopulmonary examination is normal. Abdominal examination shows large, palpable renal masses. Trace bilateral lower-extremity edema is present. Laboratory results from 2 years ago showed a blood urea nitrogen level of 25 mg/dL and a creatinine level of 2.3 mg/dL. Current laboratory results are as follows:

Sodium	136 mEq/L
Potassium	4.8 mEq/L
Chloride	104 mEq/L
Bicarbonate	22 mEq/L
Blood urea nitrogen	66 mg/dL
Creatinine	5.5 mg/dL
Calcium	7.5 mg/dL

Which of the following metabolic states is most likely present in this patient?

	Phosphate	Parathyroid Hormone	Calcitriol
A.	↓	↑	↑
B.	↑	↓	↑
C.	↑	↑	↓
D.	↓	↑	↓

Sodium	136 mEq/L
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A.	↓	↑	↑
B.	↑	↓	↑
C.	↑	↑	↓
D.	↓	↑	↓
E.	↑	↓	↓

Submit

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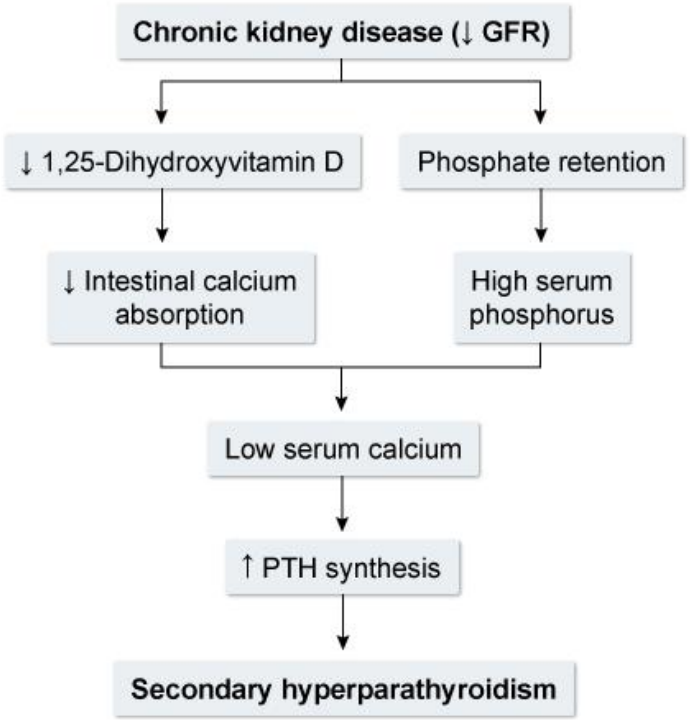
Creatinine	5.5 mg/dL
Calcium	7.5 mg/dL

Which of the following metabolic states is most likely present in this patient?

	Phosphate	Parathyroid Hormone	Calcitriol
A. [9%]	↓	↑	↑
B. [4%]	↑	↓	↑
✔ C. [61%]	↑	↑	↓
D. [18%]	↓	↑	↓
E. [5%]	↑	↓	↓



GFR = glomerular filtration rate; **PTH** = parathyroid hormone.

This patient's presentation is consistent with **metabolic bone disease** due to chronic kidney disease (CKD). CKD decreases the glomerular filtration rate (GFR), which decreases the filtered phosphate load and causes **elevated serum phosphate levels**. Hyperphosphatemia reduces serum free calcium and stimulates osteocytes and osteoclasts to release fibroblast growth factor-23 (FGF-23), a circulating peptide that decreases

This patient's presentation is consistent with **metabolic bone disease** due to chronic kidney disease (CKD). CKD decreases the glomerular filtration rate (GFR), which decreases the filtered phosphate load and causes **elevated serum phosphate levels**. Hyperphosphatemia reduces serum free calcium and stimulates osteocytes and osteoclasts to release fibroblast growth factor-23 (FGF-23), a circulating peptide that decreases proximal tubule phosphate reabsorption. Elevated levels of phosphate and FGF-23 also **reduce calcitriol synthesis** by inhibiting the proximal tubular expression of 1-alpha-hydroxylase, resulting in decreased intestinal calcium and phosphate absorption. This worsens hypocalcemia but does not significantly improve hyperphosphatemia due to the low GFR, which is the limiting factor for phosphate excretion in patients with advanced CKD.

Hypocalcemia and hyperphosphatemia also **increase parathyroid hormone (PTH) secretion**, which stimulates osteoclasts to increase bone turnover. Long-term elevation in PTH (secondary hyperparathyroidism) can eventually lead to friable bones and **osteitis fibrosa**. Affected patients can develop weakness, **bone pain**, and fractures.

(Choice A) Primary hyperparathyroidism causes hypercalcemia and decreased serum phosphate due to inappropriately elevated PTH. Renal synthesis of calcitriol is also increased by PTH. In contrast, calcitriol levels remain low in patients with CKD due to the reduction in renal mass and the inhibitory effects of FGF-23 and phosphate.

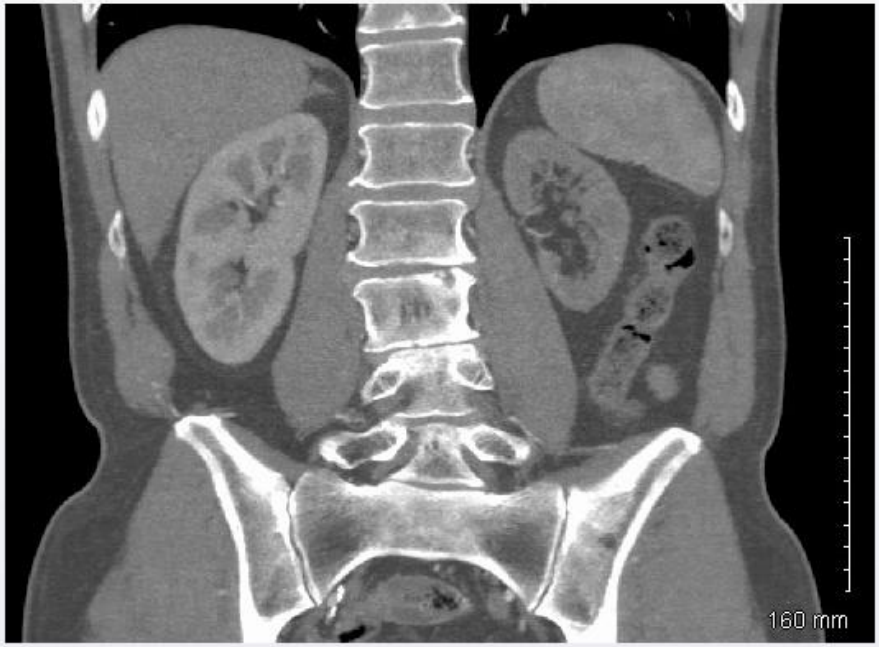
(Choice B) Vitamin D toxicity raises calcitriol levels, which increases calcium and phosphate absorption causing hypercalcemia and hyperphosphatemia. Hypercalcemia inhibits PTH release, lowering serum PTH.

(Choice D) Vitamin D deficiency in patients with normally functioning kidneys decreases intestinal calcium and phosphate absorption, leading to lower serum phosphate and calcium levels. The resulting hypocalcemia stimulates PTH release from the parathyroid glands.

(Choice E) Primary hypoparathyroidism causes hypocalcemia and hyperphosphatemia due to decreased PTH. Calcitriol levels can also be low due to decreased PTH-mediated stimulation of renal 1-alpha-hydroxylase.

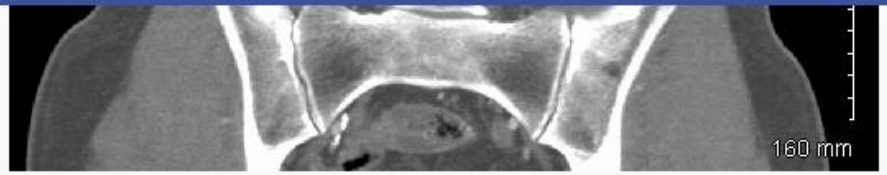
Educational objective:
Chronic kidney disease causes disordered mineralization and bone metabolism that usually presents with hyperphosphatemia, secondary hyperparathyroidism, and decreased calcitriol levels. Patients can be asymptomatic or develop weakness, bone pain, and fractures.

A 62-year-old man comes to the office due to poorly localized, intermittent abdominal pain that is triggered by eating and slowly subsides over the ensuing several hours. The patient has also lost 4.5 kg (10 lb) over the past 2 months. He has a history of hypertension and hyperlipidemia and has smoked a pack of cigarettes daily for 40 years. Blood pressure is 175/105 mm Hg and pulse is 70/min and regular. The abdomen is soft and nontender. CT scan of the abdomen reveals the renal findings shown in the image below.



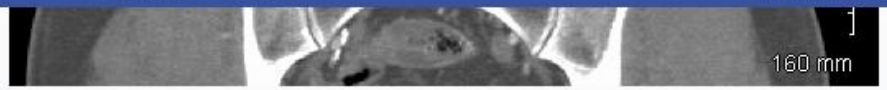
This patient most likely suffers from which of the following conditions?

A. Acute glomerulonephritis



This patient most likely suffers from which of the following conditions?

- A. Acute glomerulonephritis
- B. Acute pyelonephritis
- C. Amyloidosis
- D. Fanconi syndrome
- E. Hemolytic uremic syndrome
- F. Hypersensitivity interstitial nephritis
- G. Ischemic tubular necrosis
- H. Myeloma kidney
- I. NSAID-associated nephropathy
- J. Papillary necrosis
- K. Renal artery stenosis
- L. Urate nephropathy



This patient most likely suffers from which of the following conditions?

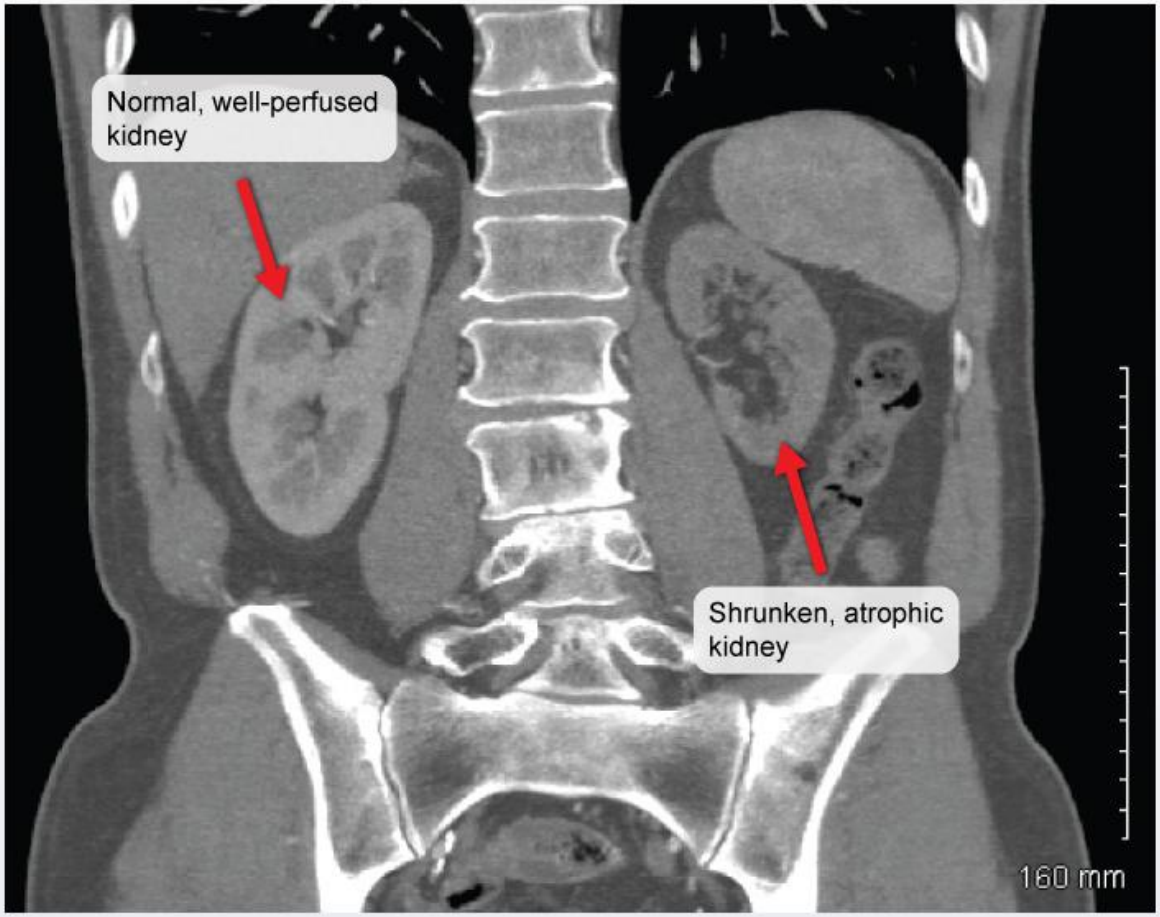
- A. Acute glomerulonephritis [0%]
- B. Acute pyelonephritis [1%]
- C. Amyloidosis [2%]
- D. Fanconi syndrome [2%]
- E. Hemolytic uremic syndrome [0%]
- F. Hypersensitivity interstitial nephritis [0%]
- G. Ischemic tubular necrosis [5%]
- H. Myeloma kidney [9%]
- I. NSAID-associated nephropathy [3%]
- J. Papillary necrosis [6%]
- ✔ K. Renal artery stenosis [62%]
- L. Urate nephropathy [3%]

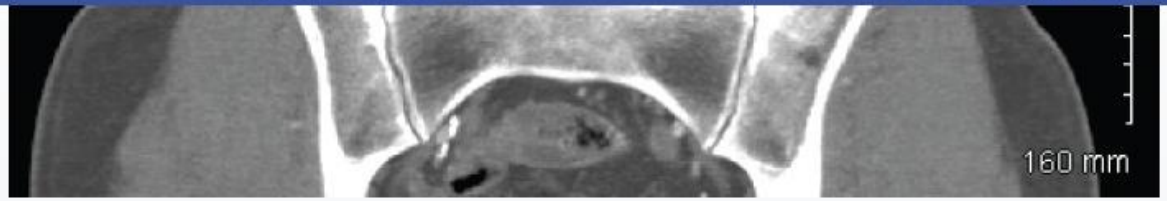
Omitted
Correct answer

62%
Answered correctly

10 Seconds
Time Spent

11/01/2018
Last Updated


Normal, well-perfused kidney
Shrunken, atrophic kidney
160 mm



This patient has postprandial pain and a 4.5-kg (10-lb) weight loss as well as multiple risk factors for **atherosclerosis** (eg, advanced age, hypertension, smoking). This presentation is highly suggestive of **chronic mesenteric (intestinal) ischemia**. Atherosclerotic narrowing of the abdominal (superior mesenteric or celiac) arteries results in reduced blood flow to the intestine; during periods of high metabolic requirement (ie, after eating), patients can develop "intestinal angina" (dull, cramping abdominal pain that resolves 2-3 hours after meals).

Atherosclerosis is a multiorgan disease, and patients often have involvement of other major vessels, including coronary artery disease, carotid stenosis, peripheral vascular disease, and **renal artery stenosis** (RAS). Atherosclerotic RAS often becomes apparent at age 60-70 and is typically associated with prominent atherosclerotic plaques at the junction of the aorta and the renal artery. Less frequently, nonatherosclerotic RAS occurs secondary to fibromuscular dysplasia, a disease that affects predominantly younger women and causes narrowing of multiple renal artery segments (string-of-beads appearance).

In **unilateral RAS**, chronic ischemia atrophies the affected kidney while the contralateral kidney undergoes compensatory hypertrophy, leading to **renal size discrepancy**, as seen in this patient. Renal hypoperfusion also activates the renin-angiotensin-aldosterone system, resulting in hypertension that is often refractory to medications. Abdominal and flank bruits are highly suggestive of RAS. Light microscopy of the atrophic kidney reveals tubular atrophy with decreased tubular epithelial size, patchy inflammation, and tubulointerstitial and glomerular fibrosis.

Educational objective:
Marked unilateral kidney atrophy is suggestive of renal artery stenosis. It occurs in elderly individuals due to atherosclerotic narrowing of the renal artery and is often seen in association with other atherosclerotic risk factors or diseases (eg, chronic mesenteric ischemia, coronary artery disease, peripheral vascular disease). Hypertension and abdominal and flank bruits are often present.

A 65-year-old woman is treated with gentamicin for an abdominal infection complicated by multidrug-resistant organisms. After a week of treatment, the patient's urine output decreases noticeably, and serum creatinine rises to 2.3 mg/dL. She has no previous kidney disease, and baseline kidney function was normal prior to the initiation of therapy. The patient has remained afebrile for 24 hours. Blood pressure is 130/80 mm Hg and pulse is 80/min. Examination shows moist mucous membranes. There is no rash. Results of urinalysis are as follows:

Protein	+1
White blood cells	1-2/hpf
Red blood cells	none
Microscopy	granular casts

Fractional excretion of sodium is >2%. Histologic examination of the patient's kidneys would most likely show which of the following?

A. Focal tubular epithelial necrosis
B. Leukocytic infiltration of the glomerular capillaries
C. Leukocytic infiltration of the interstitium and tubules
D. Preservation of normal renal architecture
E. Replacement of glomeruli with collagen

Submit

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Protein	+1
White blood cells	1-2/hpf
Red blood cells	none
Microscopy	granular casts

Fractional excretion of sodium is >2%. Histologic examination of the patient's kidneys would most likely show which of the following?

- A. Focal tubular epithelial necrosis [70%]
- B. Leukocytic infiltration of the glomerular capillaries [2%]
- C. Leukocytic infiltration of the interstitium and tubules [22%]
- D. Preservation of normal renal architecture [3%]
- E. Replacement of glomeruli with collagen [0%]

Omitted
Correct answer
A

70%
Answered correctly

3 Seconds
Time Spent

02/01/2019
Last Updated

Acute tubular necrosis due to nephrotoxins	
Common nephrotoxins	• Antibiotics: aminoglycosides (eg, gentamicin), vancomycin • Antivirals: cidofovir, foscarnet • Other: intravenous radiocontrast dye, cisplatin, heme pigment
Histology	• Tubular epithelial necrosis with casts obstructing the tubular lumens and rupture of basement membrane • Extensive involvement of the proximal tubules
Presentation	• BUN/creatinine ratio <20:1, FENa >2%, • Muddy brown granular casts, low urine osmolality • Oliguria or polyuria, ± electrolyte abnormalities

BUN = blood urea nitrogen; **FENa** = fractional excretion of sodium.

Aminoglycosides (eg, gentamicin, tobramycin) are bactericidal antibiotics that bind to the 30S ribosomal subunit and inhibit protein synthesis. They are commonly used for severe gram-negative infections but carry a significant risk of acute kidney injury. Aminoglycosides are filtered across the glomerulus and concentrate within the **proximal renal tubules**, where they impair lysosomal function, protein synthesis, and mitochondrial activity, leading to **acute tubular necrosis** (ATN). This is visualized histologically as **focal tubular epithelial necrosis**, often with extensive granular casts that obstruct the tubular lumen and lead to rupture of the basement membrane.

Aminoglycoside-induced kidney injury typically manifests within 1 week of therapy initiation. Due to the high intratubular drug concentrations, ATN can occur despite normal serum drug levels. Proximal tubular dysfunction results in loss of resorptive capacity and **electrolyte wasting** (eg, hypomagnesemia, hypophosphatemia); severe disease can result in Fanconi syndrome (ie, aminoaciduria, glucosuria, uricosuria, phosphaturia). Distal tubular injury may also occur and results in loss of concentrating capacity with polyuria (nonoliguric renal failure). Urinalysis typically demonstrates mild proteinuria with granular or hyaline casts. Consistent with other causes of ATN, the **fractional excretion of sodium** (FENa) **is >2%**.

Aminoglycosides (eg, gentamicin, tobramycin) are bactericidal antibiotics that bind to the 30S ribosomal subunit and inhibit protein synthesis. They are commonly used for severe gram-negative infections but carry a significant risk of acute kidney injury. Aminoglycosides are filtered across the glomerulus and concentrate within the **proximal renal tubules**, where they impair lysosomal function, protein synthesis, and mitochondrial activity, leading to **acute tubular necrosis** (ATN). This is visualized histologically as **focal tubular epithelial necrosis**, often with extensive granular casts that obstruct the tubular lumen and lead to rupture of the basement membrane.

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(Choices B and E) Leukocytic infiltration of the glomerular capillaries is seen with vasculitides (eg, granulomatosis with polyangiitis) that cause glomerulonephritis. Chronic glomerulonephritis is characterized by protracted inflammation with collagenous replacement of the glomeruli. However, nephritic diseases typically cause hypertension, hematuria, and red blood cell casts on urinalysis.

(Choice C) Leukocytic infiltration of the interstitium and tubules is seen in acute interstitial nephritis, a common cause of kidney injury that often occurs after introduction of a new drug. However, patients typically have fever and rash, and urinalysis shows pyuria and white blood cell casts.

(Choice D) Patients with prerenal causes of kidney injury (eg, dehydration, blood loss) have normal renal architecture. However, the FENa in prerenal disease is <1%, and the patient would be expected to have signs of hypovolemia (eg, dry mucous membranes).

Educational objective:
Aminoglycosides are filtered across the glomerulus and concentrate in the renal tubules, leading to proximal tubular injury and acute tubular necrosis. This is visualized histologically as focal tubular epithelial necrosis, often with extensive granular casts that obstruct the tubular lumen and lead to rupture of the basement membrane.

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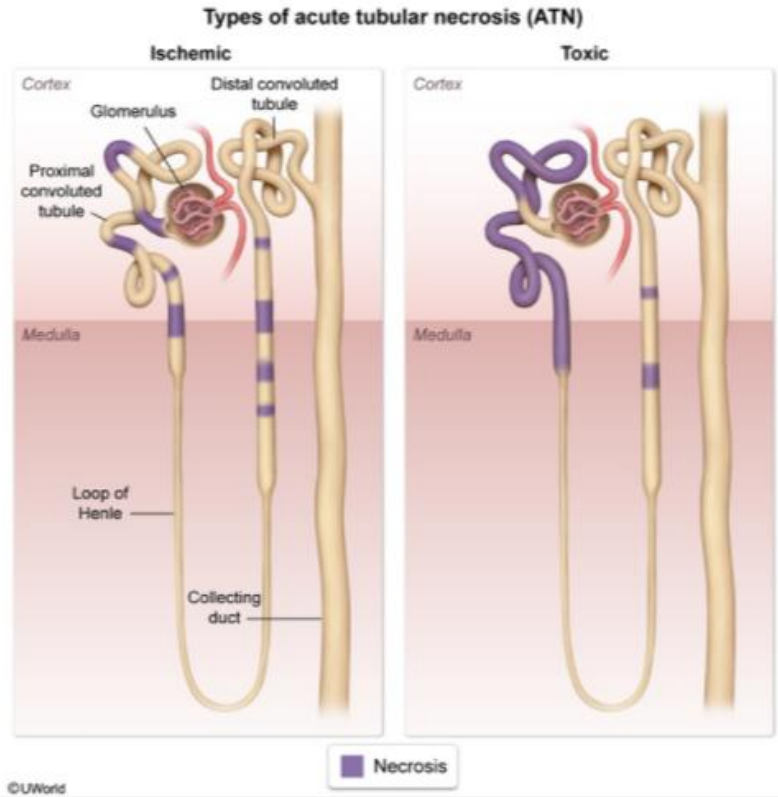
Exhibit Display



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