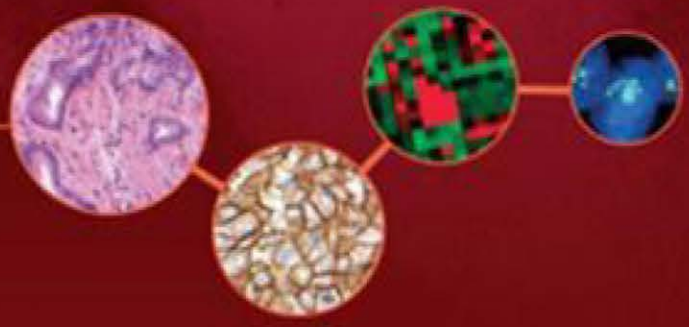
Robbins and Cotran

Review of Pathology

THIRD EDITION



KLATT
KUMAR

A Student CONSULT Title

Online + Print

SAUNDERS
ELSEVIER

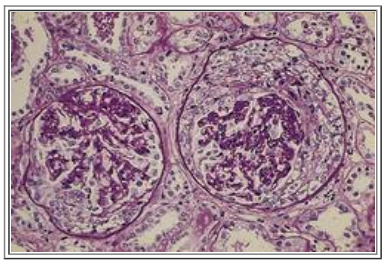
20. The Kidney

PBD7 and PBD8 Chapter 20: The Kidney

BP7 and BP8 Chapter 14: The Kidney and Its Collecting System

1 A 24-year-old man is awakened at night because of severe lower abdominal pain that radiates to the groin. The pain is very intense and comes in waves. The next morning, he notices blood in his urine. He has no underlying illnesses and has been healthy all his life. On physical examination, he is afebrile and has a blood pressure of 110/70 mm Hg. Laboratory studies show serum Na^+, 142 mmol/L; K^+, 4 mmol/L; Cl^-, 96 mmol/L; CO_2, 25 mmol/L; glucose, 74 mg/dL; creatinine, 1.1 mg/dL; calcium, 9.1 mg/dL; and phosphorus, 2.9 mg/dL. Urinalysis shows a pH of 7; specific gravity of 1.020; and no protein, glucose, ketones, or nitrite. The patient is advised to drink more water. He likes iced tea and consumes large quantities over the course of a hot summer. He continues to have similar episodes. Which of the following substances is most likely to be increased in his urine?

- □ (A) Calcium oxalate
- □ (B) Cystine
- □ (C) Magnesium ammonium phosphate
- □ (D) Mucoprotein
- □ (E) Uric acid



2 A 47-year-old man has had a decreased urine output over the past 10 days. On physical examination, he is afebrile. Urinalysis shows 1+ proteinuria, 4+ hematuria, urobilinogen, and no glucose or ketones. Microscopic examination of the urine shows few WBCs and some RBCs with RBC casts. A renal biopsy is done, and the light microscopic appearance of a PAS-stained specimen is shown in the figure. What is the most likely clinical course in this patient?

- □ (A) Acute renal failure that is reversible with supportive therapy
- □ (B) Slowly developing renal failure that is unresponsive to corticosteroid treatment
- □ (C) Rapidly progressive renal failure accompanied by hemoptysis
- □ (D) Stable clinical course with intermittent hematuria
- □ (E) Fever, leukocytosis, and endotoxic shock

3 A 63-year-old man has noted increasing back pain for 7 months. He has had three respiratory tract infections with *Streptococcus pneumoniae* within the past year. On examination, he has pitting edema to his thighs. Laboratory studies show total serum protein, 9.6 g/dL; albumin, 3.5 g/dL; creatinine, 3 mg/dL; urea nitrogen, 28 mg/dL; and glucose, 79 mg/dL. Urinalysis shows proteinuria of 4 g/24 hr, but no glucosuria or hematuria. Abdominal CT scan shows enlarged kidneys without cysts or masses. A renal biopsy specimen shows deposits of amorphous pink material within glomeruli, interstitium, and arteries with H&E stain. Which of the following diseases is he most likely to have?

- □ (A) Analgesic nephropathy
- □ (B) Diabetes mellitus
- □ (C) Membranous glomerulonephritis

□ (D) Multiple myeloma

□ (E) Systemic lupus erythematosus

□ (F) Wegener granulomatosis

4 A 58-year-old woman dies of a cerebral infarction. Laboratory findings before death included serum urea nitrogen level of 110 mg/dL and creatinine level of 9.8 mg/dL. At autopsy, the kidneys are small (75 g) and have a coarsely granular surface appearance. Microscopic examination shows sclerotic glomeruli, a fibrotic interstitium, tubular atrophy, arterial thickening, and scattered lymphocytic infiltrates. Which of the following clinical findings was most likely reported on the patient's medical history?

□ (A) Rash

□ (B) Hypertension

□ (C) Hemoptysis

□ (D) Lens dislocation

□ (E) Pharyngitis

5 For the past 6 months, a 72-year-old woman has noticed a slowly enlarging mass on the urethra. The mass causes local pain and irritation and is now bleeding. Physical examination shows a 2.5-cm warty, ulcerated mass protruding from the external urethral meatus. There are no lesions on the labia or vagina. A biopsy specimen of the lesion is most likely to identify which of the following?

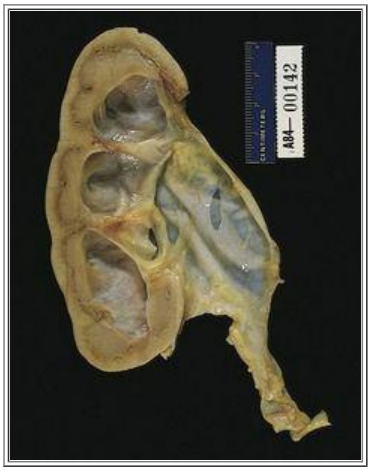
□ (A) Embryonal rhabdomyosarcoma

□ (B) Leiomyoma

□ (C) Papilloma

□ (D) Squamous cell carcinoma

□ (E) Syphilitic chancre



6 A 72-year-old man with Alzheimer disease dies of pneumonia. The gross appearance of the right kidney at autopsy is shown in the figure. The left kidney is normal in size, with a smooth cortical surface and a single 0.6-cm, fluid-filled cyst. The appearance of the right kidney is most suggestive of renal injury from which of the following?

□ (A) Ureteral obstruction

□ (B) Benign nephrosclerosis

□ (C) Analgesic abuse

□ (D) Chronic pyelonephritis

□ (E) Diabetes mellitus

7 A 25-year-old man has a 5-year history of celiac sprue. Several days after a mild upper respiratory infection, he begins passing dark red-brown urine. The dark urine persists for the next 3 days and then becomes clear and yellow, only to become red-brown again 1 month later. There are no remarkable findings on physical examination. Urinalysis shows a pH of 6.5; specific gravity 1.018; 3+ hematuria; 1+ proteinuria; and no glucose or ketones. Microscopic examination of the urine shows RBCs and no WBCs, casts, or crystals. A 24-hour urine protein level is 200 mg. A renal biopsy specimen from the glomeruli of this patient is most likely to show which of the following alterations?

□ (A) Subepithelial electron-dense deposits

□ (B) Granular staining of the basement membrane by anti-IgG antibodies

□ (C) Mesangial IgA staining by immunofluorescence

□ (D) Diffuse proliferation and basement membrane thickening

□ (E) Thrombosis in the glomerular capillaries

8 A 7-year-old boy is recovering from impetigo. Physical examination shows a few honey-colored crusts on his face. The crusts are removed, and a culture of the lesions grows group A *Streptococcus pyogenes*. He is treated with antibiotics. One week later, he develops malaise with nausea and a slight fever and passes dark brown urine. Laboratory studies show a serum antistreptolysin O titer of 1:1024. Which of the following is the most likely outcome?

□ (A) Development of rheumatic heart disease

□ (B) Chronic renal failure

□ (C) Lower urinary tract infection

□ (D) Complete recovery without treatment

□ (E) Progression to crescentic glomerulonephritis

9 A 28-year-old, previously healthy man suddenly develops severe abdominal pain and begins passing red urine. There are no abnormalities on physical examination. Urinalysis shows a pH of 7; specific gravity 1.015; 1+ hematuria; and no protein, glucose, or ketones. The patient is given a device to use in straining the urine for calculi. The next day, the patient recovers a 0.3-cm stone that is sent for analysis. The chemical composition is found to be calcium oxalate. What underlying condition is most likely to be present?

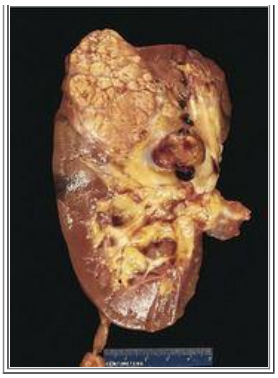
□ (A) Gout

□ (B) Acute cystitis

□ (C) Diabetes mellitus

□ (D) Primary hyperparathyroidism

□ (E) Idiopathic hypercalciuria



10 A 56-year-old man has had back pain and has passed dark-colored urine for the past month. On physical examination, there is right costovertebral angle tenderness. Urinalysis shows a pH of 6; specific gravity 1.015; 2+ hematuria; and no protein, glucose, or ketones. Microscopic examination of the urine shows numerous RBCs, few WBCs, and no casts or crystals. The figure shows the representative gross appearance of the renal lesion. Which of the following laboratory findings is most likely to be reported?

- □ (A) Elevated serum cortisol level
- □ (B) Elevated hematocrit
- □ (C) Ketonuria
- □ (D) Decreased creatinine clearance
- □ (E) lncreased plasma renin activity

11 A 15-year-old boy has been passing dark-colored urine for the past month. On physical examination, he has bilateral sensorineural hearing loss and corneal erosions. Urinalysis shows a pH of 6.5; specific gravity 1.015; 1+ hematuria; 1+ proteinuria; and no ketones, glucose, or leukocytes. The serum creatinine level is 2.5 mg/dL, and the urea nitrogen level is 24 mg/dL. A renal biopsy specimen shows tubular epithelial foam cells by light microscopy. By electron microscopy, the glomerular basement membrane shows areas of attenuation, with splitting and lamination of lamina densa in other thickened areas. What is the most likely diagnosis?

- □ (A) Acute tubular necrosis
- □ (B) Berger disease
- □ (C) Membranous glomerulonephritis
- □ (D) Diabetic nephropathy
- □ (E) Alport syndrome

12 A 32-year-old man has developed a fever and skin rash over the past 3 days. Five days later, he has increasing malaise and visits his physician. On physical examination, the maculopapular erythematous rash on his trunk has nearly faded away. His temperature is 37.1°C, and blood pressure is 135/85 mm Hg. Laboratory studies show a serum creatinine level of 2.8 mg/dL and blood urea nitrogen level of 29 mg/dL. Urinalysis shows 2+ proteinuria; 1+ hematuria; and no glucose, ketones, or nitrite. The leukocyte esterase result is positive. Microscopic examination of urine shows RBCs and WBCs, some of which are eosinophils. What is the most likely cause of this patient's condition?

- □ (A) Urinary tract infection
- □ (B) Congestive heart failure
- □ (C) Antibiotic use
- □ (D) Streptococcal pharyngitis
- □ (E) Poorly cooked ground beef

13 After eating a cheeseburger, French fries, and ice cream for dinner one night, a 6-year-old girl develops nausea, mild

abdominal cramping, and a slight fever. Three days later, her parents notice that she is passing dark stools and dark urine and appears fatigued and weak. On physical examination, she has a temperature of 37.9°C, pulse of 88/min, respirations of 18/min, and blood pressure of 140/90 mm Hg. Scattered petechiae are present on the extremities. Laboratory findings show a serum creatinine level of 2.2 mg/dL and urea nitrogen level of 20 mg/dL. Urinalysis shows a pH of 6; specific gravity 1.016; 2+ hematuria; and no protein or glucose. A renal biopsy specimen shows small thrombi within glomerular capillary loops. Which of the following diseases is most likely to produce these findings?

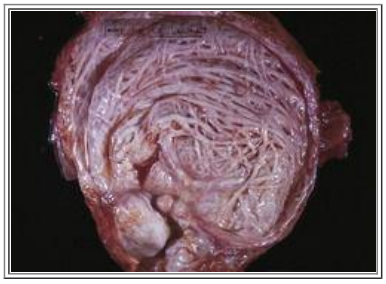
- □ (A) Postinfectious glomerulonephritis
- □ (B) Wegener granulomatosis
- □ (C) Hereditary nephritis
- □ (D) Hemolytic-uremic syndrome
- □ (E) IgA nephropathy

14 The parents of a 6-year-old girl notice that she has become increasingly lethargic over the past 2 weeks. On examination by the physician, she has puffiness around the eyes. Her temperature is 36.9°C, and blood pressure is 100/60 mm Hg. Laboratory findings show a serum creatinine level of 0.7 mg/dL and urea nitrogen level of 12 mg/dL. Urinalysis shows a pH of 6.5; specific gravity 1.011; 4+ proteinuria; and no blood or glucose. The 24-hour urine protein level is 3.8 g. The child's condition improves after glucocorticoid therapy. Which of the following findings by electron microscopy is most likely to characterize this disease process?

- □ (A) Subepithelial electron-dense humps
- □ (B) Reduplication of glomerular basement membrane
- □ (C) Areas of thickened and thinned basement membrane
- □ (D) Increased mesangial matrix
- □ (E) Effacement of podocyte foot processes

15 A 25-year-old woman experiences sudden onset of fever, malaise, and nausea. On physical examination, her temperature is 38.2°C, pulse is 85/min, respirations are 18/min, and blood pressure is 140/90 mm Hg. A routine urinalysis shows 1+ proteinuria, 4+ hematuria, and no ketones or glucose. RBC casts are seen on microscopic examination of the urine. A renal biopsy is performed, and light microscopic examination shows marked glomerular hypercellularity with neutrophils in glomerular capillary loops. Immunofluorescence microscopy shows granular deposition of IgG and C3 in glomerular capillary basement membranes. Electron microscopy shows electron-dense subepithelial “humps.” What is the most likely diagnosis?

- □ (A) Goodpasture syndrome
- □ (B) Systemic amyloidosis
- □ (C) Membranous glomerulonephritis
- □ (D) Diabetes mellitus
- □ (E) Postinfectious glomerulonephritis



16 A 77-year-old man has had increasing difficulties with urination for the past 2 years. He has difficulty starting and

stopping the urine stream. On physical examination, his temperature is 37°C, and blood pressure is 130/85 mm Hg. The figure shows the representative gross appearance of the bladder. Which of the following laboratory findings is most likely to be reported in this patient?

- □ (A) Positive ANA test result
- □ (B) Urine culture positive for *Mycobacterium tuberculosis*
- □ (C) Hemoglobin concentration of 22.5 g/dL
- □ (D) *Schistosoma haematobium* eggs in urine
- □ (E) Prostate-specific antigen level of 5 ng/mL

17 A 50-year-old woman with diabetic nephropathy receives a renal allograft. An episode of acute cellular rejection requires an increase in immunosuppressive therapy. She develops dysuria. On examination, she has suprapubic pain on palpation. A urinalysis shows hematuria. Cystoscopy is performed, and 3- to 4-cm soft, yellow, slightly raised mucosal plaques are seen. Biopsy specimens of these lesions are taken and microscopically show mucosal infiltration by foamy macrophages with abundant PAS-positive cytoplasmic granules and small, laminated mineralized concretions. Which of the following organisms is most likely to be found in her urine?

- □ (A) Adenovirus
- □ (B) *Candida albicans*
- □ (C) *Chlamydia trachomatis*
- □ (D) *Escherichia coli*
- □ (E) *Schistosoma haematobium*

18 A 26-year-old man is involved in a motor vehicle accident and sustains acute blood loss. He is hypotensive for several hours before paramedical personnel arrive. They stabilize the bleeding and transport him to a hospital, where he receives a transfusion of 3 U of packed RBCs. Over the next week, the serum urea nitrogen level increases to 48 mg/dL, the serum creatinine level increases to 5 mg/dL, and the urine output decreases. He undergoes hemodialysis for the next 2 weeks and then develops marked polyuria, with urine output of 2 to 3 L/day. His recovery is complicated by bronchopneumonia, but renal function gradually returns to normal. The patient's transient renal disease is best characterized by which of the following histologic features?

- □ (A) Glomerular crescents in Bowman space
- □ (B) Interstitial lymphocytic infiltrates
- □ (C) Arteriolar fibrinoid necrosis
- □ (D) Nodular glomerulosclerosis
- □ (E) Rupture of tubular basement membrane

19 A 60-year-old, previously healthy man sees his physician because he feels feverish and weak. He reports passing dark-colored urine on several occasions during the past month, but has no urinary frequency, dysuria, or nocturia. On physical examination, his temperature is 37.8°C, and blood pressure is 125/85 mm Hg. A dipstick urinalysis shows 4+ hematuria; 1+ proteinuria; and no glucose or ketones. Which of the following procedures is the most appropriate in management of this patient?

- □ (A) Straining of urine for calculi
- □ (B) Urine microbiologic culture
- □ (C) Abdominal CT scan for renal mass
- □ (D) Collection of a 24-hour urine specimen for protein

□ (E) Percutaneous renal biopsy

20 A 49-year-old man goes to his physician for a checkup and is found on physical examination to have a blood pressure of 160/110 mm Hg, but no other abnormalities. Laboratory studies show serum glucose of 75 mg/dL, creatinine of 1.3 mg/dL, and urea nitrogen of 20 mg/dL. His plasma renin is elevated. CT angiography shows marked stenosis of his renal arteries. He is treated with an angiotensin-converting enzyme inhibitor. A week later, he has a headache for which he takes ibuprofen. Over the next day, his urine output decreases. A reduction in which of the following chemical mediators most likely caused his reduced urine output?

□ (A) Aldosterone

□ (B) Histamine

□ (C) Nitric oxide

□ (D) Prostaglandin

□ (E) Tumor necrosis factor

21 A 50-year-old woman has had fever and flank pain for the past 2 days. On physical examination, her temperature is 38.2°C, pulse is 81/min, respirations are 16/min, and blood pressure is 130/80 mm Hg. Urinalysis shows no protein, glucose, or ketones. The leukocyte esterase test is positive. Microscopic examination of the urine shows numerous polymorphonuclear leukocytes and occasional WBC casts. Which of the following organisms is most likely to be found in the urine culture?

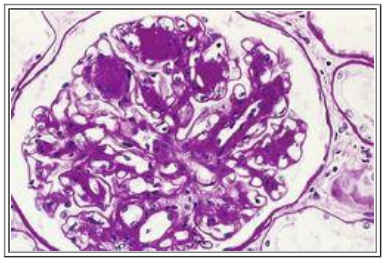
□ (A) *Mycobacterium tuberculosis*

□ (B) *Mycoplasma hominis*

□ (C) *Escherichia coli*

□ (D) Group A streptococcus

□ (E) *Cryptococcus neoformans*



22 A 58-year-old, relatively healthy man sees his physician for a routine health maintenance examination. Physical examination shows mild hypertension. Laboratory findings show a serum creatinine level of 2.2 mg/dL and urea nitrogen level of 25 mg/dL. Microalbuminuria is present, with excretion of 250 mg/day of albumin. Two years later, he returns for a follow-up visit. He is now hypertensive and has a serum creatinine level of 3.8 mg/dL, urea nitrogen level of 38 mg/dL, and 24-hour urine protein level of 2.8 g. A renal biopsy is done; the light microscopic appearance of a PAS-stained specimen is shown in the figure. Which of the following laboratory findings is most likely to be abnormal in this patient?

□ (A) Anti–glomerular basement membrane antibody

□ (B) ANA

□ (C) ANCA

□ (D) Antistreptolysin O

□ (E) C3 nephritic factor

□ (F) Hemoglobin A_{1c}

□ (G) Hepatitis B surface antigen

23 A 20-year-old woman, G1, P0, who is in the third trimester, has felt minimal fetal movement. An ultrasound scan shows a markedly decreased amniotic fluid index characteristic of oligohydramnios. She gives birth to a stillborn male fetus at 33 weeks' gestation. At autopsy, there are deformations resulting from marked oligohydramnios, including flattening of the facies, varus deformities of the feet, and marked pulmonary hypoplasia. Microscopic examination of the liver shows multiple epithelium-lined cysts and a proliferation of bile ducts. Which of the following best describes the appearance of the kidneys in this fetus?

□ (A) Bilaterally enlarged kidneys replaced by 1- to 4-cm, fluid-filled cysts

□ (B) Bilaterally shrunken kidneys with uniformly finely granular cortical surfaces

□ (C) Decreased overall size of the right kidney and normal-sized left kidney

□ (D) Irregular cortical scars in asymmetrically shrunken kidneys with marked calyceal dilation

□ (E) Marked bilateral renal pelvic and calyceal dilation with thinning of the cortices

□ (F) Normal-sized kidneys with smooth cortical surfaces

□ (G) Symmetrically enlarged kidneys composed of small, radially arranged cysts

24 A 65-year-old woman has experienced increasing malaise with nocturia and polyuria for the past year. On physical examination, her blood pressure is 170/95 mm Hg. Urinalysis shows a pH of 7.5; specific gravity 1.010; 1+ proteinuria; and no glucose, blood, or ketones. The tests for leukocyte esterase and nitrite yield positive results, and levels of serum urea nitrogen and serum creatinine are elevated. Her clinical course is characterized by worsening renal failure, and she dies of bronchopneumonia. At autopsy, the kidneys are shrunken but unequal in size, and have deep, irregular surface scars. On sectioning, the calyces underlying the cortical scars are blunted and deformed. What is the most likely cause of renal failure in this patient?

□ (A) Chronic glomerulonephritis

□ (B) Essential hypertension

□ (C) Reflux nephropathy

□ (D) Autosomal-dominant polycystic kidney disease

□ (E) Systemic lupus erythematosus

25 A 29-year-old woman sees her physician because she has had a fever and sore throat for the past 3 days. On physical examination, her temperature is 38°C. The pharynx is erythematous, with yellowish tonsillar exudate. Group A *Streptococcus pyogenes* is cultured. She is treated with ampicillin and recovers fully in 7 days. Two weeks later, she develops fever and a rash, and notices a slight decrease in urinary output. Her temperature is 37.7°C, and there is a diffuse erythematous rash on the trunk and extremities. Urinalysis shows a pH of 6; specific gravity 1.022; 1+ proteinuria; 1+ hematuria; and no glucose or ketones. Microscopic examination of the urine shows RBCs and WBCs, including eosinophils, but no casts or crystals. What is the most likely cause of her disease?

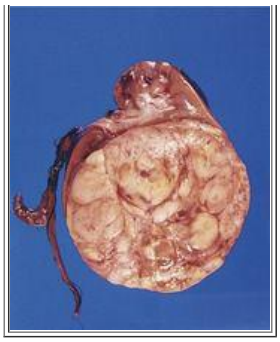
□ (A) Deposition of immune complexes with streptococcal antigens

□ (B) Hematogenous dissemination of septic emboli

□ (C) Renal tubular cell necrosis caused by bacterial toxins

□ (D) Hypersensitivity reaction to ampicillin

□ (E) Formation of antibodies against glomerular basement membrane



26 A 4-year-old girl has complained of abdominal pain for the past month. On physical examination, she is febrile, and palpation of the abdomen shows a tender mass on the right. Bowel sounds are present. Laboratory studies show hematuria without proteinuria. Abdominal CT scan shows a 12-cm, circumscribed, solid mass in the right kidney. A right nephrectomy is done; the gross appearance of the mass is shown in the figure. What is the most likely diagnosis?

- □ (A) Angiomyolipoma
- □ (B) Interstitial cell tumor
- □ (C) Renal cell carcinoma
- □ (D) Transitional cell carcinoma
- □ (E) Wilms tumor

27 One week after a mild flulike illness, a 9-year-old boy has an episode of hematuria that subsides within 2 days. One month later, he tells his parents that his urine is red again. On physical examination, there are no significant findings. Urinalysis shows a pH of 7; specific gravity 1.015; 1+ proteinuria; 1+ hematuria; and no ketones, glucose, or urobilinogen. The serum urea nitrogen level is 36 mg/dL, and the creatinine level is 3.2 mg/dL. A renal biopsy specimen shows diffuse mesangial proliferation and electron-dense deposits in the mesangium. Which of the following mechanisms is most likely to produce these findings?

- □ (A) Deposition of immune complexes containing IgA
- □ (B) Formation of antibodies against type IV collagen
- □ (C) Virus-mediated injury to the glomeruli
- □ (D) Cytokine-mediated injury to the glomerular capillaries
- □ (E) Congenital defects in the structure of glomerular basement membranes

28 The top of the diaper is often noted to be damp on a girl infant. Radiologic imaging with contrast enhancement shows that there is a connection from the bladder to umbilicus. What is the most likely diagnosis?

- □ (A) Congenital diverticulum
- □ (B) Exstrophy
- □ (C) Persistent urachus
- □ (D) Vesicoureteral reflux
- □ (E) Vitelline duct remnant

29 A 7-year-old boy is brought to the physician by his mother, who is concerned because he has become less active over the past 10 days. On physical examination, the boy has facial puffiness. Urinalysis shows no blood, glucose, or ketones, and microscopic examination shows no casts or crystals. The serum creatinine level is normal. A 24-hour urine collection yields 3.8 g of protein. He improves after corticosteroid therapy. He has two more episodes of proteinuria over the next few years, both of which respond to corticosteroid therapy. A renal biopsy is done. What is the most likely mechanism causing his disease?

- □ (A) Immune complex–mediated glomerular injury
- □ (B) Verocytotoxin-induced endothelial cell injury
- □ (C) Cytotoxic T cell–mediated tubular epithelial cell injury
- □ (D) Cytokine-mediated visceral epithelial cell injury
- □ (E) IgA-mediated mesangial cell injury

30 A 49-year-old man saw his physician because he had increased swelling in the extremities for 2 months. Physical examination showed generalized edema. A 24-hour urine collection yielded 4.1 g of protein and albumin and globulins. Extensive testing did not indicate the presence of a systemic disease, such as diabetes mellitus or systemic lupus erythematosus. He did not respond to a course of corticosteroid therapy. A renal biopsy was done, and microscopic examination showed diffuse thickening of the basement membrane. Immunofluorescence staining with antibody to the C3 component of complement was positive in a granular pattern in the glomerular capillary loops. Two years later, he experiences increasing malaise. Laboratory studies now show serum creatinine level of 4.5 mg/dL and urea nitrogen level of 44 mg/dL. Which of the following immunological mechanisms was most likely responsible for the glomerular changes observed in the biopsy specimen?

- □ (A) Antibodies that react with basement membrane collagen
- □ (B) Antibodies against streptococci that cross-react with the basement membrane
- □ (C) Release of cytokines by inflammatory cells
- □ (D) Cytotoxic T cells directed against renal antigens
- □ (E) Deposition of immune complexes on the basement membrane

31 A 31-year-old woman experiences abdominal pain and sees her physician 1 week later after noticing blood in her urine. She has had three episodes of urinary tract infection during the past year. There are no remarkable findings on physical examination. Urinalysis shows 2+ hematuria; 1+ proteinuria; hypercalciuria; and no glucose or ketones. Microscopic examination of the urine shows numerous RBCs and oxalate crystals. An intravenous pyelogram shows linear striations radiating into the renal papillae, along with small cystic collections of contrast material in dilated collecting ducts. She is advised to increase her daily intake of fluids, and her condition improves. Which of the following conditions is most likely to be associated with these findings?

- □ (A) Autosomal-dominant polycystic kidney disease
- □ (B) Gout
- □ (C) Medullary sponge kidney
- □ (D) Multicystic renal dysplasia
- □ (E) Autosomal-recessive polycystic kidney disease
- □ (F) Urothelial carcinoma
- □ (G) Vesicoureteral reflux

32 A 42-year-old man has had right flank pain for the past 2 days. On physical examination, his temperature is 37.4°C, pulse is 70/min, respirations are 14/min, and blood pressure is 130/85 mm Hg. Laboratory studies show a serum creatinine level of 1.1 mg/dL. Urinalysis shows no blood, protein, or glucose, and microscopic examination of the urine shows no WBCs or RBCs. Abdominal CT scan shows a 7-cm eccentric lesion of the upper pole of the right kidney. The lesion is well circumscribed and cystic with a thin wall and focal hemorrhage. What is the most likely diagnosis?

- □ (A) Acute pyelonephritis
- □ (B) Acute tubular necrosis
- □ (C) Diabetic nephropathy

□ (D) Hydronephrosis

□ (E) Simple renal cyst

□ (F) Rapidly progressive glomerulonephritis

□ (G) Renal cell carcinoma

□ (H) Urothelial carcinoma

33 A 51-year-old woman has had recurrent urinary tract infections for the past 15 years. On many of these occasions, *Proteus mirabilis* was cultured from her urine. For the past 4 days, she has had a burning pain on urination and urinary frequency. On physical examination, her temperature is 37.9°C, pulse is 70/min, respirations are 15/min, and blood pressure is 135/85 mm Hg. There is marked tenderness on deep pressure over the right costovertebral angle and on deep abdominal palpation. Urinalysis shows a pH of 7.5; specific gravity 1.020; 1+ hematuria; and no protein, glucose, or ketones. Microscopic examination of the urine shows many RBCs, WBCs, and triple-phosphate crystals. Which of the following renal lesions is most likely to be present?

□ (A) Renal cell carcinoma

□ (B) Acute tubular necrosis

□ (C) Malignant nephrosclerosis

□ (D) Staghorn calculus

□ (E) Papillary necrosis

34 A 53-year-old woman has had dysuria and urinary frequency for the past week. On physical examination, her temperature is 38°C, and she has pain on palpation over the left costovertebral angle. Laboratory findings show glucose, 177 mg/dL; hemoglobin A_{1c}, 9.8%; hemoglobin, 13.1 g/dL; platelet count, 232,200/mm^3; and WBC count, 11,320/mm^3. Urinalysis shows a pH of 6.5; specific gravity 1.016; 2+ glucosuria; and no blood, protein, or ketones. Microscopic examination of the urine shows numerous neutrophils, and a urine culture is positive for *Escherichia coli*. Which of the following complications is most likely to develop in this patient?

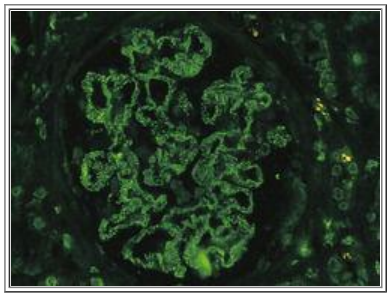
□ (A) Acute tubular necrosis

□ (B) Necrotizing papillitis

□ (C) Crescentic glomerulonephritis

□ (D) Hydronephrosis

□ (E) Renal calculi



35 A 42-year-old man has experienced increasing malaise for the past month. He is bothered by increasing swelling in the hands and legs. On physical examination, there is generalized edema. He is afebrile, and his blood pressure is 140/90 mm Hg. Urinalysis shows a pH of 6.5; specific gravity 1.017; 4+ proteinuria; and no blood, glucose, or ketones. Microscopic examination of the urine shows no casts or RBCs and 2 WBCs per high-power field. The 24-hour urine protein level is 4.2 g. A renal biopsy specimen is obtained, and immunofluorescence staining with antibody to the C3 component of complement produces the pattern shown in the figure. Which of the following underlying disease processes

is most likely to be present?

- □ (A) Chronic hepatitis B
- □ (B) AIDS
- □ (C) Multiple myeloma
- □ (D) Recurrent urinary tract infection
- □ (E) Nephrolithiasis

36 A 58-year-old man is in stable condition after an acute myocardial infarction. Two days later, his urine output decreases, and the serum urea nitrogen level increases to 3.3 mg/dL. Oliguria persists for 5 days, followed by polyuria for 2 days. He is discharged from the hospital. Which of the following renal lesions best explains these renal abnormalities?

- □ (A) Acute tubular necrosis
- □ (B) Benign nephrosclerosis
- □ (C) Acute renal infarction
- □ (D) Hemolytic-uremic syndrome
- □ (E) Rapidly progressive glomerulonephritis

37 Several members of a family developed chronic renal failure by age 50 years. Most are males. The affected individuals also developed visual problems. Some younger family members have proteinuria and hematuria on urinalysis. A renal biopsy specimen from a 20-year-old man shows prominent tubular foam cells and glomerular basement membrane thickening and thinning. Family members with this disease are most likely to have which of the following additional manifestations?

- □ (A) Watery diarrhea
- □ (B) Nerve deafness
- □ (C) Presenile dementia
- □ (D) Dilated cardiomyopathy
- □ (E) Infertility

38 A 65-year-old man recently retired after many years in a job that involved exposure to aniline dyes, including ß-naphthylamine. One month ago, he had an episode of hematuria that was not accompanied by abdominal pain. On physical examination, there are no abnormal findings. Urinalysis shows 4+ hematuria, and no ketones, glucose, or protein. Microscopic examination of the urine shows RBCs that are too numerous to count, 5 to 10 WBCs per high-power field, and no crystals or casts. The result of a urine culture is negative. What is the most likely diagnosis?

- □ (A) Renal cell carcinoma
- □ (B) Hemorrhagic cystitis
- □ (C) Tubercular cystitis
- □ (D) Urothelial carcinoma
- □ (E) Squamous cell carcinoma of the urethra

39 A 55-year-old woman has had poorly controlled hyperglycemia for many years. She sees her physician after experiencing burning pain on urination for 3 days. Physical examination shows a 2-cm ulceration on the skin of the heel and reduced sensation in the lower extremities. Her visual acuity is 20/100 bilaterally. Urinalysis shows 1+ proteinuria; 2+ glucosuria; and no blood, ketones, or urobilinogen. A urine culture contains more than 100,000 colony-forming units/mL of *Klebsiella pneumoniae*. Which of the following pathologic findings is most likely to be present in both kidneys?

- □ (A) Deposits of IgG and C3 in the glomerular basement membrane
- □ (B) Effacement of podocyte foot processes
- □ (C) Glomerular crescents
- □ (D) Mesangial deposits of IgA
- □ (E) Necrotizing granulomatous vasculitis
- □ (F) Nodular hyaline mesangial masses
- □ (G) Thickening and thinning of the glomerular basement membrane

40 A 17-year-old girl has had arthralgias and myalgias for several months. During the past week, she has noticed a decreased output of urine, which is reddish brown. On physical examination, her blood pressure is 160/100 mm Hg, and she has an erythematous malar skin rash. The ANA and anti–double-stranded DNA test results are positive. The serum urea nitrogen level is 52 mg/dL. Which of the following urinalysis findings is most likely to be reported for this patient?

- □ (A) Eosinophils
- □ (B) Glucose
- □ (C) Ketones
- □ (D) Myoglobin
- □ (E) Oval fat bodies
- □ (F) RBC casts
- □ (G) Triple phosphate crystals
- □ (H) Uric acid crystals
- □ (I) Waxy casts

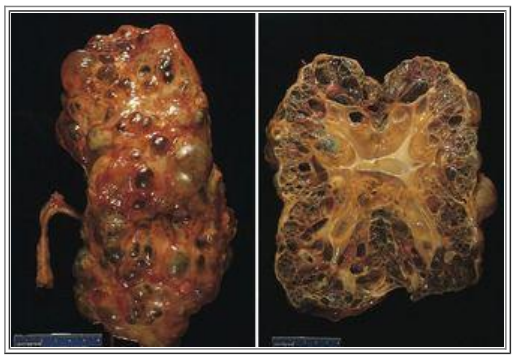
41 A 28-year-old woman has had dysuria, frequency, and urgency for the past 2 days. On physical examination, her temperature is 37.6°C. A urine culture grows greater than 100,000 colonies/mL of *Escherichia coli*. She is treated with antibiotic therapy. If the problem continues to recur, the patient is likely to be at greatest risk for development of which of the following renal diseases?

- □ (A) Diffuse glomerulosclerosis
- □ (B) Chronic glomerulonephritis
- □ (C) Amyloidosis
- □ (D) Membranous glomerulonephritis
- □ (E) Chronic pyelonephritis

42 A sexually active, 26-year-old man has had pain on urination for the past 4 days. On physical examination, there are no lesions on the penis. He is afebrile. Urinalysis shows no blood, ketones, protein, or glucose. Microscopic examination of the urine shows few WBCs and no casts or crystals. What infectious agent is most likely to produce these findings?

- □ (A) *Chlamydia trachomatis*
- □ (B) *Mycobacterium tuberculosis*
- □ (C) Herpes simplex virus
- □ (D) *Candida albicans*

□ (E) *Treponema pallidum*



43 A 61-year-old woman sees the physician because she has experienced increasing malaise for the past 5 years. On physical examination, there are no abnormalities other than a blood pressure of 150/95 mm Hg. One week later, she dies suddenly. At autopsy, both kidneys have the external (left panel) and bisected (right panel) appearance as shown in the figure. Which of the following conditions was the most probable cause of death?

□ (A) Metastatic Wilms tumor

□ (B) Ruptured berry aneurysm

□ (C) Acute tubular necrosis

□ (D) Disseminated intravascular coagulation

□ (E) Pneumothorax

44 For the past 20 years, a 69-year-old man with chronic arthritis has taken more than 3 g of analgesics per day, including phenacetin, aspirin, and acetaminophen. He sees his physician because of increasing malaise, nausea, and diminished mentation. On physical examination, his blood pressure is 156/92 mm Hg. Laboratory findings show serum urea nitrogen level of 68 mg/dL and creatinine level of 7.1 mg/dL. CBC shows hemoglobin, 11.7 g/dL; hematocrit, 35.1%; platelet count, 188,500/mm^3; and WBC count, 5385/mm^3. Which of the following renal diseases is this patient most likely to develop?

□ (A) Hydronephrosis

□ (B) Chronic glomerulonephritis

□ (C) Renal papillary necrosis

□ (D) Renal cell carcinoma

□ (E) Acute tubular necrosis

45 A 58-year-old woman sees her physician for a routine health maintenance examination. The only abnormality on physical examination is a blood pressure of 168/109 mm Hg. Urinalysis shows a pH of 7.0; specific gravity 1.020; 1+ proteinuria; and no blood, glucose, or ketones. An abdominal ultrasound scan shows bilaterally and symmetrically small kidneys with no masses. The ANA test result is negative. The serum urea nitrogen level is 51 mg/dL, and the creatinine level is 4.7 mg/dL. The hemoglobin A_{1c} concentration is within the reference range. What is the most likely diagnosis?

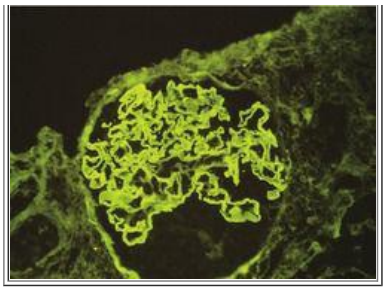
□ (A) Lupus nephritis

□ (B) Autosomal-dominant polycystic kidney disease

□ (C) Chronic glomerulonephritis

□ (D) Nodular glomerulosclerosis

□ (E) Amyloidosis

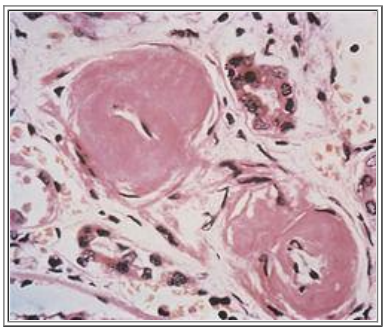


46 A previously healthy, 21-year-old man sees his physician because he notices blood in his urine. He reports no dysuria, frequency, or hesitancy of urination. On physical examination, there are no abnormal findings. Laboratory findings show a serum urea nitrogen level of 39 mg/dL and creatinine level of 4.1 mg/dL. A renal biopsy specimen is obtained; the immunofluorescence pattern of staining with antibody against human IgG is shown in the figure. Which of the following serum laboratory studies is most likely to be positive in this patient?

- □ (A) Antistreptolysin O antibody
- □ (B) HIV antibody
- □ (C) Anti–glomerular basement membrane antibody
- □ (D) Hepatitis B surface antibody
- □ (E) C3 nephritic factor

47 A 33-year-old woman has had fever and increasing fatigue for the past 2 months. Over the past year, she has noticed soreness of her muscles and joints and has had a 4-kg weight loss. On physical examination, her temperature is 37.5°C, pulse is 80/min, respirations are 15/min, and blood pressure is 145/95 mm Hg. She has pain on deep inspiration, and a friction rub is heard on auscultation of the chest. Laboratory findings show glucose, 73 mg/dL; total cholesterol, 160 mg/dL; total protein, 5.2 g/dL; albumin, 2.9 g/dL; total bilirubin, 0.9 mg/dL; and creatinine, 2.4 mg/dL. Serum complement levels are decreased. CBC shows hemoglobin of 9.7 g/dL, platelet count of 85,000/mm^3, and WBC count of 3560/mm^3. A renal biopsy specimen shows a diffuse proliferative glomerulonephritis with extensive granular immune deposits of IgG and C1q in capillary loops and mesangium. After being treated with immunosuppressive therapy consisting of prednisone and cyclophosphamide, her condition improves. Which of the following serologic studies is most likely to be positive in this patient?

- □ (A) Anticentromere antibody
- □ (B) Anti–double-stranded DNA antibody
- □ (C) Anti–DNA topoisomerase I antibody
- □ (D) Anti–glomerular basement membrane antibody
- □ (E) Antihistone antibody
- □ (F) ANCA
- □ (G) Antiribonucleoprotein



48 A 66-year-old woman died of an acute myocardial infarction. At autopsy, both kidneys were decreased in size (about

120 g each) with a finely granular cortical surface. The representative appearance of the kidney under high magnification is shown in the figure. Which of the following clinical abnormalities most likely accompanied this lesion?

- □ (A) Oliguria
- □ (B) Benign hypertension
- □ (C) Malignant hypertension
- □ (D) Hematuria
- □ (E) Flank pain

49 A 79-year-old man has had increasing back pain and fatigue for the past 6 months. On physical examination, there are no remarkable findings. Laboratory studies include a CBC with hemoglobin of 9.6 g/dL, platelet count of 241,600/mm^3, and WBC count of 7160/mm^3. The serum total protein is 9.8 g/dL, albumin is 3.6 g/dL, glucose is 72 mg/dL, creatinine is 3.3 mg/dL, and urea nitrogen is 30 mg/dL. A dipstick urinalysis shows a pH of 7; specific gravity 1.011; and no blood, protein, or glucose. One month later, he develops a cough with fever, and *Streptococcus pneumoniae* is cultured from his sputum. Despite antibiotic therapy, he develops sepsis and dies. At autopsy, the kidneys are normal in size, but microscopic examination shows dilated tubules filled with amorphous blue-to-pink casts and occasional multinucleated giant cells. What is the most likely underlying cause of this patient's death?

- □ (A) Cystinuria
- □ (B) Diabetes mellitus
- □ (C) Gout
- □ (D) Multiple myeloma
- □ (E) Parathyroid adenoma
- □ (F) Systemic lupus erythematosus

50 A 30-year-old woman with a history of recurrent urinary tract infections has had a high fever for the past 3 days. On physical examination, her temperature is 38.4°C. There is marked abdominal tenderness on deep palpation. A renal ultrasound scan shows an enlarged right kidney with pelvic and calyceal enlargement and cortical thinning; the left kidney appears normal. A right nephrectomy is done, and microscopic examination shows inflammatory infiltrates extending from the medulla to the cortex, with tubular destruction and extensive interstitial fibrosis. Lymphocytes, plasma cells, and neutrophils are abundant. Which of the following is most likely to produce these findings?

- □ (A) Benign nephrosclerosis
- □ (B) Vesicoureteral reflux
- □ (C) Lupus nephritis
- □ (D) Systemic amyloidosis
- □ (E) Congestive heart failure
- □ (F) Autosomal-dominant polycystic kidney disease

51 A 32-year-old man with a history of intravenous drug use comes to the emergency department because he has had a high fever for the past 2 days. On physical examination, his temperature is 38.4°C. He has a palpable spleen tip, bilateral costovertebral angle tenderness, and diastolic cardiac murmur. Laboratory findings show a serum urea nitrogen level of 15 mg/dL. Urinalysis shows 2+ hematuria, and no glucose, protein, or ketones. A blood culture is positive for *Staphylococcus aureus*. Which of the following best describes the kidneys in this patient?

- □ (A) Bilaterally enlarged kidneys replaced by 1- to 4-cm, fluid-filled cysts
- □ (B) Bilaterally shrunken kidneys with uniformly finely granular cortical surfaces

□ (C) Irregular cortical scars in asymmetrically shrunken kidneys with marked calyceal dilation

□ (D) Marked bilateral renal pelvic and calyceal dilation with thinning of the cortices

□ (E) Normal-sized kidneys with smooth cortical surfaces

□ (F) Scattered petechial hemorrhages in slightly swollen kidneys

□ (G) Wedge-shaped regions of yellow-white cortical necrosis involving both kidneys

52 Three years ago, a 47-year-old woman had a mastectomy of the right breast to remove an infiltrating ductal carcinoma. She now has bone pain, and a radionuclide scan shows multiple areas of increased uptake in the vertebrae, ribs, pelvis, and right femur. Urinalysis shows a specific gravity of 1.010, which remains unchanged after water deprivation for 12 hours. She undergoes several courses of chemotherapy over the next year. During this time, the serum urea nitrogen level progressively increases. Which of the following abnormal laboratory findings is most likely to be reported for this patient?

□ (A) Hepatitis B surface antigenemia

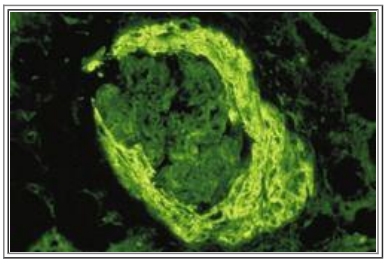
□ (B) Hypercalcemia

□ (C) Hypercholesterolemia

□ (D) Hypergammaglobulinemia

□ (E) Hyperglycemia

□ (F) Hyperuricemia



53 A 45-year-old man has experienced increasing malaise, nausea, and reduced urine output for the past 3 days. On physical examination, he is afebrile and normotensive. Laboratory findings show a serum creatinine level of 2.5 mg/dL. Urinalysis shows hematuria, but no pyuria or glucosuria. A renal biopsy is done; the immunofluorescence pattern with antifibrinogen is shown in the figure. Which of the following additional studies is most useful for classification and treatment of this disease?

□ (A) ANA titer

□ (B) Anti–glomerular basement membrane antibody test

□ (C) HIV titer

□ (D) Quantitative serum immunoglobulins

□ (E) Rheumatoid factor

□ (F) Urine immunoelectrophoresis

54 A 28-year-old man is diagnosed with acute myelogenous leukemia (M2). After induction with a multiagent chemotherapy protocol, he has an episode of lower abdominal pain accompanied by passage of red-colored urine. He has no fever, dysuria, or urinary frequency. On physical examination, there are no remarkable findings. Urinalysis shows a pH of 5.5; specific gravity 1.021; 2+ hematuria; and no protein, ketones, or glucose. There are no remarkable findings on an abdominal radiograph. Which of the following additional urinalysis findings is most likely to be reported for this patient?

□ (A) Bence Jones protein

- □ (B) Eosinophils
- □ (C) Myoglobin
- □ (D) Oval fat bodies
- □ (E) RBC casts
- □ (F) Triple phosphate crystals
- □ (G) Uric acid crystals
- □ (H) Waxy casts
- □ (I) WBC casts

55 A 44-year-old man has developed a fever, nonproductive cough, and decreased urine output over the past 3 days. On physical examination, his temperature is 37.7°C, and blood pressure is 145/95 mm Hg. He has sinusitis. On auscultation, crackles are heard over all lung fields. A chest radiograph shows bilateral patchy infiltrates and nodules. The serum creatinine level is 4.1 mg/dL, and the urea nitrogen level is 43 mg/dL. The results of serologic testing are negative for ANA, but positive for C-ANCA. A renal biopsy specimen shows glomerular crescents and granulomatous vasculitis. The result of immunofluorescence staining with anti-IgG and anti-C3 antibodies is negative. What is the most likely diagnosis?

- □ (A) Focal segmental glomerulosclerosis
- □ (B) Goodpasture syndrome
- □ (C) Lupus nephritis
- □ (D) Membranoproliferative glomerulonephritis type II
- □ (E) Membranous glomerulonephritis
- □ (F) Postinfectious glomerulonephritis
- □ (G) Wegener's granulomatosis

56 A 65-year-old woman has recently experienced several transient ischemic attacks. On physical examination, the only abnormal finding is a blood pressure of 150/95 mm Hg. Urinalysis shows 1+ proteinuria, and no glucose, blood, or ketones. Microscopic examination of the urine shows no RBCs or WBCs and few oxalate crystals. On abdominal ultrasound, the kidneys are slightly decreased in size. Which of the following renal lesions is most likely to be present in this patient?

- □ (A) Crescentic glomerulonephritis
- □ (B) Hyaline arteriolosclerosis
- □ (C) Mesangial cell proliferation
- □ (D) Arteriolar fibrinoid necrosis
- □ (E) Acute tubular necrosis
- □ (F) Interstitial nephritis

57 Over the past 72 hours, a 44-year-old man has experienced worsening headache, nausea, and vomiting. On physical examination, his blood pressure is 276/158 mm Hg, and there is bilateral papilledema. Urinalysis shows 2+ proteinuria; 1+ hematuria; and no glucose or ketones. Which of the following renal lesions is most likely to be present in this patient?

- □ (A) Papillary necrosis
- □ (B) Acute infarction
- □ (C) Necrotizing arteriolitis

□ (D) Acute tubular necrosis

□ (E) Acute pyelonephritis

58 A 35-year-old, previously healthy man is found dead in his home. At autopsy, the medical examiner notices bilaterally enlarged kidneys that contain multiple, irregularly arranged cysts of different shapes and sizes. There is a 0.5-cm nonruptured intracerebral berry aneurysm of the anterior communicating artery. There are scattered 1- to 2-cm, fluid-filled liver cysts involving 10% of the parenchymal volume. Postmortem laboratory testing of the urine and blood shows markedly elevated levels of cocaine and its metabolite, benzoylecgonine. Which of the following is the most appropriate conclusion to be drawn from these findings?

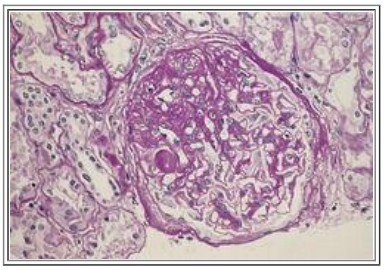
□ (A) He had lesions related to chronic use of cocaine

□ (B) He had autosomal-recessive polycystic kidney disease, but survived to adulthood

□ (C) His surviving family (children, siblings, and parents) should be evaluated for a similar condition

□ (D) The immediate cause of death is berry aneurysm

□ (E) The underlying cause of death is autosomal-dominant polycystic kidney disease



59 A 12-year-old girl has experienced increasing malaise for the past 2 weeks. On physical examination, she has periorbital edema. The child is afebrile. Laboratory findings show proteinuria on dipstick urinalysis, but no hematuria or glucosuria. Microscopic examination of the urine shows numerous oval fat bodies. The serum creatinine level is 2.3 mg/dL. She receives a course of corticosteroid therapy, but does not improve. A renal biopsy is done; the biopsy specimen shows that approximately 50% of the glomeruli in the specimen are affected by the lesion shown in the figure. What is the most likely diagnosis?

□ (A) Focal segmental glomerulosclerosis

□ (B) Lipoid nephrosis

□ (C) Membranoproliferative glomerulonephritis type I

□ (D) Membranoproliferative glomerulonephritis type II

□ (E) Nodular glomerulosclerosis

□ (F) Postinfectious glomerulonephritis

□ (G) Rapidly progressive glomerulonephritis

60 A 19-year-old woman has had a fever and chills accompanied by right flank pain for the past 3 days. On physical examination, her temperature is 38.3°C, her blood pressure is 150/90 mm Hg, and there is right costovertebral angle tenderness. Laboratory findings show a serum glucose level of 77 mg/dL and creatinine level of 1 mg/dL. Urinalysis shows a pH of 6.5; specific gravity 1.018; and no protein, blood, glucose, or ketones. Microscopic examination of the urine shows many WBCs and WBC casts. Which of the following factors is most important in the pathogenesis of the renal disease affecting this patient?

□ (A) Age

□ (B) Sex

□ (C) Vesicoureteral reflux

□ (D) Blood pressure

□ (E) Focus of infection in the lungs

61 Several days after eating a hamburger, chili, and ice cream at a home barbecue, a 5-year-old girl develops cramping abdominal pain and diarrhea. The next day, she has decreased urine output. On physical examination, there are petechial hemorrhages on the skin. Her temperature is 37°C, pulse is 90/min, respirations are 18/min, and blood pressure is 90/50 mm Hg. A stool sample is positive for occult blood. Laboratory findings show hemoglobin, 10.8 g/dL; hematocrit, 32.4%; platelet count, 64,300/mm^3; and WBC count, 6480/mm^3. The peripheral blood smear shows schistocytes, and the serum D-dimer level is elevated. Which of the following is the most likely causative organism?

□ (A) *Candida albicans*

□ (B) *Proteus mirabilis*

□ (C) *Clostridium difficile*

□ (D) *Escherichia coli*

□ (E) *Staphylococcus aureus*

62 A 17-year-old boy is involved in a motor vehicle accident in which he sustains severe blunt trauma to the extremities and abdomen. Over the next 3 days, he develops oliguria and dark brown urine. The urine dipstick analysis is positive for myoglobin and for blood, but microscopic examination of the urine shows no RBCs. His serum urea nitrogen level increases to 38 mg/dL, and he undergoes hemodialysis for 3 weeks. His condition improves, but the urine output remains greater than 3 L/day for 1 week before the urea nitrogen returns to normal. Which of the following renal lesions was most likely present in this patient?

□ (A) Malignant nephrosclerosis

□ (B) Renal vein thrombosis

□ (C) Membranous glomerulonephritis

□ (D) Acute pyelonephritis

□ (E) Acute tubular necrosis

63 A 45-year-old man has had headaches, nausea, and vomiting that have worsened over the past 5 days. He has started “seeing spots” before his eyes. On physical examination, his blood pressure is 268/150 mm Hg. Urinalysis shows 1+ proteinuria; 2+ hematuria; and no glucose, ketones, or leukocytes. The serum urea nitrogen and creatinine levels are elevated. Which of the following histologic findings is most likely to be seen in this patient's kidneys?

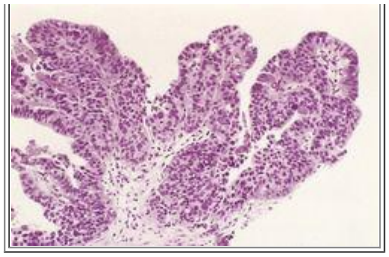
□ (A) Nodular glomerulosclerosis

□ (B) Segmental tubular necrosis

□ (C) Hyperplastic arteriolosclerosis

□ (D) Mesangial IgA deposition

□ (E) Glomerular crescents



64 A 62-year-old man has had several episodes of hematuria over the past week. He has not experienced increased urinary frequency or dysuria. On physical examination, there are no remarkable findings. Urinalysis shows 4+ hematuria. The urine culture is negative. A cystoscopy is performed, and a 2-cm sessile, friable mass is seen on the right bladder wall. A biopsy specimen is obtained; the microscopic appearance is shown in the figure. Which of the following risk factors is most important in the pathogenesis of this bladder lesion?

- □ (A) Smoking cigarettes
- □ (B) Schistosomiasis
- □ (C) Diabetes mellitus
- □ (D) Chronic bacterial cystitis
- □ (E) Nodular prostatic hyperplasia

65 A 38-year-old woman sees her physician because she has been feeling tired and lethargic for several months. On physical examination, she is afebrile, and her blood pressure is 140/90 mm Hg. Laboratory findings show hemoglobin, 10.3 g/dL; hematocrit, 30.9%; platelet count, 310,700/mm^3; and WBC count, 5585/mm^3. The serum creatinine level is 5.8 mg/dL. C3 nephritic factor is present in serum, and the ANA test result is negative. Urinalysis shows 2+ proteinuria. A renal biopsy is done; microscopic examination shows hypercellular glomeruli and prominent electron-dense deposits along the lamina densa of the glomerular basement membrane. Which of the following forms of glomerulonephritis is most likely to be present in this patient?

- □ (A) Postinfectious glomerulonephritis
- □ (B) Rapidly progressive glomerulonephritis
- □ (C) Membranoproliferative glomerulonephritis
- □ (D) Chronic glomerulonephritis
- □ (E) Membranous glomerulonephritis

66 A 60-year-old man presents with a feeling of fullness in his abdomen and a 5-kg weight loss over the past 6 months. Physical examination is normal. Laboratory studies show hemoglobin of 8.2 g/dL, hematocrit of 24%, and MCV of 70 μm^3. Urinalysis shows 3+ hematuria, but no protein, glucose, or leukocytes. Abdominal CT scan shows an 11-cm mass in the upper pole of the right kidney. A right nephrectomy is performed, and on gross examination the mass invades the renal vein. Microscopic examination of the mass shows cells with abundant clear cytoplasm. Which of the following molecular abnormalities is most likely to be found in tumor cell DNA?

- □ (A) Homozygous loss of the von Hippel–Lindau (*VHL*) gene
- □ (B) Mutational activation of the *MET* proto-oncogene
- □ (C) Trisomy of chromosome 7 associated genes
- □ (D) Integration of human papillomavirus-16 (HPV-16)
- □ (E) Microsatellite instability

67 A 45-year-old Hispanic man has had increasing malaise with headaches and easy fatigability for the past 3 months. Physical examination reveals his blood pressure is 200/100 mm Hg. There are no palpable abdominal masses and no costovertebral tenderness. Laboratory studies show hemoglobin, 9.5 g/dL; hematocrit, 28.3%; MCV, 92 μm^3; creatinine,

4.5 mg/dL; and urea nitrogen, 42 mg/dL. Urinalysis reveals 3+ hematuria and 3+ proteinuria, but no glucose or leukocytes. A renal biopsy is done; light microscopic examination of the biopsy specimen shows that approximately 50% of the glomeruli appear normal, but the rest show that a portion of the capillary tuft is sclerotic. Immunofluorescence staining shows IgM and C3 deposition in these sclerotic areas. Past history is significant for repeated episodes of passing dark brown urine, which failed to respond to corticosteroid therapy. Which of the following mechanisms is most likely responsible for his disease?

- □ (A) Deposition of immune complexes containing microbial antigens
- □ (B) Dysfunction of the podocyte slit diaphragm apparatus
- □ (C) Deposition of anti–glomerular basement membrane antibodies
- □ (D) Inherited defect in the basement membrane collagen
- □ (E) Deposition of C3 nephritic factor (C3NeF)

ANSWERS

1 **(A)** This patient has ureteral colic from the passage of a stone down the ureter. About 70% of all renal stones are composed of calcium oxalate crystals. Patients with these stones tend to have hypercalciuria without hypercalcemia. Uric acid stones and cystine stones are radiolucent and tend to form in acidic urine. Cystine stones are rare. Triple phosphate (magnesium ammonium phosphate) stones tend to occur in association with urinary tract infections, particularly infections caused by urease-positive bacteria, such as *Proteus*. Mucoproteins may coalesce into hyaline casts, which are too small to produce signs and symptoms.

BP7 536–537BP8 571–572PBD7 1014–1015PBD8 962–963

2 **(C)** The figure shows glomeruli with epithelial crescents that are the morphologic correlates of rapidly progressive glomerulonephritis. Patients with this condition rapidly develop renal failure. One cause of rapidly progressive renal failure is Goodpasture syndrome, in which anti–glomerular basement membrane antibodies damage the glomeruli and the pulmonary alveoli. Damage to the alveoli results in hemoptysis. Acute tubular necrosis is potentially reversible. Focal segmental glomerulosclerosis is typically nonresponsive to corticosteroids. IgA nephropathy can have intermittent hematuria. Acute pyelonephritis is accompanied by fever and leukocytosis.

BP7 523–524BP8 557–558PBD7 976–978PBD8 920–921

3 **(D)** There is a large amount of serum globulin, back pain from lytic lesions, immunosuppression with recurrent infections, and amyloid deposition enlarging the kidneys, all consistent with multiple myeloma. This AL amyloid deposition occurs in 6% to 24% of myeloma cases. Analgesic nephropathy can lead to tubulointerstitial nephritis and papillary necrosis. His serum glucose is not in the range for diabetes mellitus, and the pink deposits seen with nodular or diffuse glomerulosclerosis are not amyloid. The pink-staining, thickened capillary loops of membranous glomerulonephritis represent immune deposits, not amyloid. Systemic lupus erythematosus can result in immune deposits to produce “wire loop” thickening of glomerular capillaries.

BP7 159BP8 167PBD7 992, 1005–1006PBD8 252, 935

4 **(B)** These findings describe end-stage renal disease, the appearance of which is similar regardless of the cause (e.g., vascular disease or glomerular disease). With advanced renal destruction, hypertension almost always supervenes, even if it was absent at the onset of renal disease. Many such cases are referred to as “chronic glomerulonephritis” for want of a better term. A rash might have preceded the postinfectious glomerulonephritis. Hemoptysis occurs in Goodpasture's syndrome. Lens dislocation is a feature of Alport syndrome. Pharyngitis with group A streptococcal infection may precede postinfectious glomerulonephritis.

BP7 526BP8 559PBD7 960–961PBD8 932–933

5 **(D)** Carcinoma of the urethra is uncommon. It tends to occur in older women and is locally aggressive. An embryonal rhabdomyosarcoma (sarcoma botryoides) is a rare tumor that occurs in children. Benign tumors, such as a leiomyoma or papilloma, are typically well circumscribed and do not ulcerate. Syphilis produces indurated, painless lesions, rather than ulcerated, warty masses.

BP7 547BP8 575–577PBD7 1034PBD8 982

6 **(A)** The ureteral, pelvic, and calyceal dilation results from long-standing obstruction leading to hydroureter and hydronephrosis. With benign nephrosclerosis, the kidneys become smaller and develop granular surfaces, but there is no dilation. The scarring that accompanies analgesic nephropathy or chronic pyelonephritis can be marked; it is associated with significant loss of renal parenchyma, but not with pelvic dilation. There are many renal complications of diabetes mellitus, mostly from vascular, glomerular, or interstitial injury, but there is no obstruction. In some patients, diabetes is complicated by a neurogenic bladder, and this can lead to functional obstruction. In such cases, both kidneys and ureters would be affected.

BP7 537–538BP8 571–573PBD7 1012–1014PBD8 960–962

7 **(C)** IgA nephropathy, also known as Berger's disease, can explain the presence of recurrent hematuria in a young adult. Nephrotic syndrome is not present, and mesangial IgA deposition is characteristic. The initial episode of hematuria usually follows an upper respiratory infection. IgA nephropathy occurs with increased frequency in patients with celiac disease. Granular staining of basement membrane with IgG antibodies denotes immune complex deposition, which may occur in postinfectious glomerulonephritis. The subepithelial deposits are seen on electron microscopy. Patients with these changes have nephritic syndrome. Diffuse proliferation and basement membrane thickening denote membranoproliferative glomerulonephritis. In this condition, IgG and C3 are deposited in the glomeruli. Glomerular capillary thrombosis is typical of hemolytic-uremic syndrome.

BP7 524–525BP8 555–556PBD7 986–988PBD8 930–931

8 **(D)** These findings are characteristic of poststreptococcal glomerulonephritis. The strains of group A streptococci that cause poststreptococcal glomerulonephritis differ from the strains that cause rheumatic fever. Most children with poststreptococcal glomerulonephritis recover, although perhaps 1% develop a rapidly progressive glomerulonephritis. Progression to chronic renal failure occurs more frequently in affected adults. A urinary tract infection is not likely to accompany poststreptococcal glomerulonephritis because the organisms that caused the immunological reaction are no longer present when symptoms of glomerulonephritis appear.

BP7 522–523BP8 554–555PBD7 974–976PBD8 917–920

9 **(E)** Calcium oxalate stones are the most common type of urinary tract stone. Approximately 50% of patients with calcium oxalate stones have increased excretion of calcium without hypercalcemia. The basis of hypercalciuria is unclear. Most uric acid stones are formed in acidic urine and are not related to gout. It is thought that these patients have an unexplained tendency to excrete acidic urine. At low pH, uric acid is insoluble, and stones form. Infections can predispose to the formation of magnesium ammonium phosphate stones. Diabetes mellitus is an uncommon cause of urinary tract lithiasis; although infections are more common in diabetics, most are not caused by urea-splitting bacteria. Hyperparathyroidism predisposes affected individuals to form stones containing calcium, but few patients with urinary tract stones have this condition.

BP7 536–537BP8 571PBD7 1014–1015PBD8 962

10 **(B)** The figure shows a renal cell carcinoma. About 5% to 10% of these tumors secrete erythropoietin, giving rise to polycythemia. Other substances can be secreted—among them corticotropin (adrenocorticotropic hormone), resulting in hypercortisolism in Cushing's syndrome—but these cases are encountered less frequently than polycythemia. Ketonuria is a feature of type 1 diabetes mellitus, which is not associated with the development of renal neoplasms. Renal cell carcinomas are usually unilateral, and typically they do not destroy all of a kidney. There is no significant loss of renal function, and the serum urea nitrogen and creatinine levels are not elevated. Hypertension from hyperreninemia can occur in patients with some renal cell carcinomas, although this is uncommon. Ketonuria is seen in patients with decreased caloric intake and with type 1 diabetes mellitus. Renal cell carcinomas are usually unilateral and involve part of the kidney; renal failure is unlikely.

BP7 539–541BP8 573–575PBD7 1016–1018PBD8 964–966

11 **(E)** Alport syndrome is a form of hereditary nephritis. Hematuria is the most common presenting feature, but proteinuria is often present and may be in the nephrotic range. Patients progress to chronic renal failure in adulthood. Most patients have an X-linked dominant pattern of inheritance, but autosomal dominant and autosomal recessive pedigrees also exist. The foamy change in the tubular epithelial cells and ultrastructural alterations of the basement membrane are characteristic features. The genetic defect results from mutation in the gene for the α-5 chain of type IV collagen. Acute tubular necrosis follows ischemic or toxic injuries to the kidney and does not involve glomeruli. Berger disease, or IgA nephropathy, is a form of glomerulonephritis that does not produce tubular epithelial changes. Membranous

glomerulonephritis generally produces a nephrotic syndrome and deposition of immune complexes in glomerular basement membrane. Nodular and diffuse glomerulosclerosis are typical changes in diabetic nephropathy.

BP7 525–526BP8 556–557PBD7 988PBD8 931–932

12 **(C)** These findings are typical of drug-induced interstitial nephritis. Various drugs can cause this condition, including sulfonamides, penicillins, cephalosporins, the fluoroquinolone antibiotics ciprofloxacin and norfloxacin, and the antituberculous drugs isoniazid and rifampin. Acute tubulointerstitial nephritis also can occur with use of thiazide and loop diuretics, cimetidine, ranitidine, omeprazole, and nonsteroidal anti-inflammatory drugs. The disease manifests about 2 weeks after the patient begins to use the drug. Elements of type I (increased IgE) and type IV (skin test positivity to drug haptens) hypersensitivity are present. WBCs, but not eosinophils, may be present in the urine of a patient with a urinary tract infection. Congestive heart failure can lead to acute tubular necrosis, but it is not associated with a rash or proteinuria. Poststreptococcal glomerulonephritis could account for the proteinuria and hematuria seen in this patient, but not for the rash because the strains of group A β-hemolytic streptococci that cause a skin infection precede by weeks the development of glomerulonephritis. Hemolytic-uremic syndrome can occur after ingestion of strains of *Escherichia coli* that may be present in ground beef.

BP7 530BP8 563–564PBD7 1002PBD8 944–945

13 **(D)** Hemolytic-uremic syndrome is one of the most common causes of acute renal failure in children. It most commonly occurs after ingestion of meat infected with verocytotoxin-producing *Escherichia coli,* most often serotype O157:H7. The toxin damages endothelium, reducing nitric oxide, promoting vasoconstriction and necrosis, and promoting thrombosis. With supportive therapy, most patients recover in a few weeks, although perhaps one fourth progress to chronic renal failure. Postinfectious glomerulonephritis occurs several weeks after an infection, usually with group A β-hemolytic streptococci. Wegener granulomatosis is a vasculitis that most often occurs in adults. Hereditary nephritis may occur in childhood; it is progressive and is not related to vascular disease. An IgA nephropathy most often occurs in young adults; it is not accompanied by vascular changes.

BP7 534–535BP8 568PBD7 1009–1010PBD8 952–953

14 **(E)** A child with nephrotic syndrome and no other clinical findings is most likely to have lipoid nephrosis, also called minimal change disease. The term *minimal change disease* reflects the paucity of pathologic findings. There is fusion of foot processes, which can be seen only by electron microscopy. Subepithelial electron-dense humps represent immune complexes and are seen in postinfectious glomerulonephritis. Variability of basement membrane thickening may be seen in Alport syndrome. The mesangial matrix is expanded in some forms of glomerulonephritis (e.g., IgA nephropathy) and other diseases, such as diabetes mellitus, but not in minimal change disease.

BP7 518–519BP8 549–550PBD7 981–982PBD8 924–926

15 **(E)** Postinfectious glomerulonephritis is one of many causes of a nephritic syndrome characterized by hematuria and RBC casts. Most children recover completely, but one in six adults may progress to chronic renal failure. Some cases may occur after a streptococcal pharyngitis (poststreptococcal glomerulonephritis). In other cases, such as this one, the preceding infection is so mild that patients give no history. Goodpasture syndrome also may produce a nephritic syndrome, but there is linear deposition of antibody in the glomerular basement membrane. Amyloidosis of the kidney mainly produces proteinuria without hematuria, as does membranous glomerulonephritis. Nodular and diffuse glomerulosclerosis are characteristic of diabetic nephropathy.

BP7 522–523BP8 554–555PBD7 974–976PBD8 917–920

16 **(E)** This patient has bladder hypertrophy resulting from outlet obstruction. In an older man, this type of obstruction is most often caused by prostatic enlargement resulting from hyperplasia or carcinoma. Mild elevations in the prostate-specific antigen (PSA) level may occur in patients with prostatic hyperplasia, and greater increases in PSA suggest carcinoma. Autoimmune conditions may be associated with interstitial cystitis, but cystitis does not cause bladder neck obstruction. Bladder outlet obstruction can increase the risk of infection, typically with bacterial organisms such as *Escherichia coli,* not *Mycobacterium tuberculosis.* Polycythemia can be the result of a paraneoplastic syndrome, but urothelial malignancies are unlikely to produce this finding; renal cell carcinoma is a more likely cause. Schistosomiasis leads to chronic inflammation and scarring.

BP8 571–573PBD7 1033PBD8 981

17 **(D)** This woman has a peculiar form of cystitis known as malacoplakia, when macrophages have reduced phagocytic

function, and the concretions within macrophages are known as Michaelis-Gutman bodies. Malacoplakia is a reaction to chronic bacterial infections, usually *Escherichia coli* and *Proteus* species, and often in the setting of immunosuppression. The most common organism associated with cases of acute cystitis is *E. coli*. The other organisms listed are uncommon causes for cystitis and for malacoplakia.

PBD7 1027–1028PBD8 975–976

18 **(E)** This patient's history is typical of ischemic acute tubular necrosis, which is often accompanied by rupture of the basement membrane (tubulorrhexis). An initiating phase that lasts approximately 1 day is followed by a maintenance phase during which progressive oliguria and increasing blood urea nitrogen levels occur, with salt and water overload. This is followed by a recovery phase during which there is a steady increase in urinary output and hypokalemia. Eventually, tubular function is restored. Treatment of this acute renal failure results in recovery of nearly all patients. Crescents suggest a rapidly progressive glomerulonephritis that is unlikely to resolve. Interstitial infiltrates suggest a chronic tubulointerstitial process. Fibrinoid necrosis in arterioles is a feature of malignant nephrosclerosis, a serious condition that produces significant renal damage. Nodular glomerulosclerosis is a feature of diabetic nephropathy and is a progressive condition that leads to chronic renal failure.

BP7 531–533BP8 564–566PBD7 993–996PBD8 936–938

1 9 **(C)** Painless hematuria in an older adult suggests a renal neoplasm. The additional presence of constitutional symptoms, such as fever and weakness, should raise the suspicion of a renal cell carcinoma. Urinary tract calculi usually cause severe, colicky pain when they are passed. Urinary tract infections are not characterized by recurrent hematuria without fever or other signs of acute inflammation. Nephrotic syndrome, which manifests with proteinuria, typically is not associated with hematuria. A renal biopsy has a low yield in a patient without an acute-onset renal disease, and it is an ineffective way of diagnosing tumors.

BP7 539–541BP8 573–575PBD7 1016–1018PBD8 964–966

20 **(D)** This patient's hypertension is due to renal vascular constriction, typical for renal arterial atherosclerosis. In the face of reduced renal blood flow, his glomerular filtration rate (GFR) is maintained by prostaglandin-mediated vasodilation of afferent arterioles and angiotensin II–mediated vasoconstriction of efferent arterioles. The angiotensin-converting enzyme inhibitor decreases efferent arteriolar vasoconstriction and decreases glomerular capillary perfusion pressure. Nonsteroidal anti-inflammatory drugs such as ibuprofen inhibit prostaglandin synthesis and lead to vasoconstriction that reduces renal blood flow and reduces GFR. Aldosterone is increased with increased renin and angiotensin production and leads to reduced sodium excretion. Histamine is a vasodilator from mast cell granules that plays a role in acute inflammatory processes, but not blood pressure regulation. Tumor necrosis factor plays a role in many inflammatory processes, but not renal blood flow. Nitric oxide is a vasodilator, but does not have a significant effect on capillary blood flow.

PBD7 1004PBD8 950–951

21 **(C)** The clinical features in this patient are typical of urinary tract infection, and *Escherichia coli* is the most common cause. The WBCs are characteristic of an acute inflammatory process. The presence of WBC casts indicates that the infection must have occurred in the kidney because casts are formed in renal tubules. Most infections of the urinary tract begin in the lower urinary tract and ascend to the kidneys. Hematogenous spread is less common. *Mycobacterium tuberculosis* causes the rare “sterile pyuria”; however, renal tuberculosis typically does not manifest as an acute febrile illness. *Mycoplasma* and *Cryptococcus* are rare urinary tract pathogens. Group A streptococcus is best known as an antecedent infection to poststreptococcal glomerulonephritis, an immunologically mediated disease in which the organisms are not present at the site of glomerular injury.

BP7 527–529BP8 560PBD7 996–1000PBD8 939–942

2 2 **(F)** The figure shows nodular and diffuse glomerulosclerosis, a classic lesion in diabetes mellitus. Patients with diabetes mellitus have an elevated level of glycosylated hemoglobin (HbA_{1c}). Patients with type 1 diabetes mellitus may initially have microalbuminuria, which predicts development of future overt diabetic nephropathy. There is progressive loss of renal function. These patients are often hypertensive and have hyaline arteriolosclerosis. The presence of overt proteinuria suggests progression to end-stage renal disease within 5 years. Anti–glomerular basement membrane antibody is seen in Goodpasture syndrome, which manifests as a rapidly progressive glomerulonephritis. The ANA test is positive in a variety of autoimmune diseases, most typically systemic lupus erythematosus, which can be accompanied by glomerulonephritis. The ANCA test is positive in some forms of vasculitis, such as Wegener's granulomatosis, which can

involve the kidneys. The antistreptolysin O titer is elevated after streptococcal infections, which may cause postinfectious glomerulonephritis. The C3 nephritic factor may be present in type II membranoproliferative glomerulonephritis (dense deposit disease). Some patients with membranous glomerulonephritis have a positive serologic test result for HBsAg.

BP7 650BP8 783–784PBD7 991–992PBD8 934–935, 1141–1142

23 **(G)** Autosomal-recessive polycystic kidney disease (ARPKD) most often occurs in children and may involve the liver; most cases have mutations in the *PKHD1* gene encoding for fibrocystin expressed in kidney, liver, and pancreas. By contrast, autosomal-dominant polycystic kidney disease (ADPKD) manifests with renal failure in adults and involves *PKD1* and *PKD2* gene mutations encoding for polycystin proteins found in renal tubules. Some less common forms of ARPKD are accompanied by survival beyond infancy, and these patients develop congenital hepatic fibrosis. Enlarged kidneys with 1- to 4-cm cysts are characteristic of ADPKD in adults. Perhaps the most common renal cystic disease seen in fetuses and infants is multicystic renal dysplasia (multicystic dysplastic kidney), in which the cysts and kidneys are variably sized. This disease can be focal, unilateral, or bilateral; however, congenital hepatic fibrosis is not present. Small, shrunken, granular kidneys typify end-stage renal diseases in adults. For oligohydramnios to be present, both kidneys must be affected, not just one. Irregular cortical scars with pelvicaliceal dilation may represent hydronephrosis complicated by infection in chronic pyelonephritis, a process that occurs in adults. Dilation with calyceal thinning can occur with obstructions in utero, such as posterior urethral valves in males or urethral atresia in males or females; liver lesions are not present in these cases. A cause of oligohydramnios other than abnormalities of the urinary tract (e.g., leakage of amniotic fluid with premature and prolonged rupture of membranes) could be present if the kidneys appear normal, but in this case the distinctive finding of congenital hepatic fibrosis points to ARPKD.

BP7 536BP8 570PBD7 964–965PBD8 959

24 **(C)** This description of the gross appearance of the kidney is characteristic of chronic pyelonephritis, caused most often by reflux nephropathy. Typical features include coarse and irregular scarring resulting from ascending infection, blunting and deformity of calyces, and asymmetric involvement of the kidneys. The loss of tubules from scarring gives rise to reduced renal concentrating ability; the patient had polyuria with a low specific gravity of the urine. Chronic glomerulonephritis, benign nephrosclerosis (caused by essential hypertension), and systemic lupus erythematosus produce bilateral symmetric involvement, and the affected kidneys are shrunken and finely granular. Autosomal-dominant polycystic kidney disease is characterized by large cysts that replace the renal parenchyma and greatly increase the size of the kidneys bilaterally.

BP7 529–530BP8 562–563PBD7 1000–1001PBD8 942–944

25 **(D)** These findings point to an acute drug-induced interstitial nephritis caused by ampicillin. This is an immunological reaction, probably caused by a drug acting as a hapten. Poststreptococcal glomerulonephritis is unlikely to be accompanied by a rash or by eosinophils in the urine. Acute pyelonephritis is an ascending infection; it is uncommonly caused by hematogenous spread of bacteria from other sites. Acute tubular necrosis can cause acute renal failure. It is caused by hypoxia resulting from shock or from toxic injury caused by chemicals such as mercury, and only rarely, if ever, by bacterial toxins. Anti–glomerular basement membrane antibodies occur in Goodpasture's syndrome, with hemorrhages in lungs as well.

BP7 530BP8 563–564PBD7 1002PBD8 944–945

26 **(E)** Wilms' tumor is the most common renal neoplasm in children, and one of the most common childhood neoplasms. A complex staging, grading, and molecular analysis formula, and surgery, chemotherapy, and radiation result in a high cure rate. The microscopic pattern of Wilms tumor (nephroblastoma) resembles the fetal kidney nephrogenic zone. Angiomyolipomas may be sporadic or part of the genetic syndrome of tuberous sclerosis. They may be multiple and bilateral and have well-differentiated muscle, adipose tissue, and vascular components. Renomedullary interstitial cell tumors ("medullary fibromas") are generally less than 1 cm and are incidental findings. Renal cell carcinoma is rare in children, and the most common patterns are clear cell, papillary, and chromophobe. Transitional cell carcinomas arise in the urothelium in adults and microscopically resemble urothelium.

BP7 256–257, 541BP8 271–273PBD7 504–506PBD8 479–481

27 **(A)** Development of recurrent hematuria after a viral illness in a child or young adult is typically associated with IgA nephropathy. In these patients, some defect in immune regulation causes excessive mucosal IgA synthesis in response to viral or other environmental antigens. IgA complexes are deposited in the mesangium and initiate glomerular injury. Antibodies against type IV collagen are formed in Goodpasture syndrome. Although viruses induce IgA synthesis, they do not cause direct glomerular damage. Cytokine-mediated injury can occur in transplant rejection. Defects in the structure of

glomerular basement membrane are a feature of hereditary nephritis.

BP7 524–525BP8 555–557PBD7 986–988PBD8 930–931

28 **(C)** The embryologic urachus may not become obliterated, leaving a fistulous tract or a cyst between the bladder and abdominal wall at the umbilicus. Congenital diverticula result from either focal failure in formation of bladder musculature or bladder outlet obstruction, and there is no fistulous tract. Exstrophy refers to failure in development of the lower abdominal wall, leaving an open defect to the bladder. Abnormal reflux of bladder contents into the ureter defines vesicoureteral reflux, which may be due to congenital abnormalities of bladder development, but there is no fistulous tract. A vitelline duct remnant may account for a Meckel diverticulum, or rarely a fistulous tract from small intestine to umbilicus.

PBD7 1026PBD8 974

29 **(D)** Steroid-responsive proteinuria in a child is typical of minimal change disease, in which the kidney looks normal by light microscopy, but there is foot process fusion by electron microscopy. The most likely cause of foot process fusion is a primary injury to visceral epithelial cells caused by T cell–derived cytokines. Immune complex deposition in membranous glomerulopathy can cause nephrotic syndrome, but is less common in children than adults and is not steroid-responsive. Certain verocytotoxin-producing *Escherichia coli* strains can cause hemolytic-uremic syndrome by injury to capillary endothelium. Acute cellular renal transplant rejection is mediated by T cell injury with tubulitis. IgA nephropathy with mesangial IgA deposition and consequent glomerular injury causes recurrent gross or microscopic hematuria and, far less commonly, nephrotic syndrome.

BP7 518–519BP8 550–551PBD7 981–982PBD8 942–946

3 0 **(E)** This patient has idiopathic membranous glomerulopathy, producing nephrotic syndrome. Diffuse basement membrane thickening, in the absence of proliferative changes, and granular deposits of IgG and C3 are typical of this condition. It is caused by the deposition of immune complexes on the basement membrane, which activates complement. Antibodies that react with basement membrane give rise to a linear immunofluorescence pattern, as in Goodpasture syndrome. Membranous glomerulopathy has no association with streptococcal infections. There also is no evidence of cytokine-mediated or T cell–mediated damage in this disease. In 85% of patients with membranous glomerulopathy, the cause of immune complex deposition is unknown. In the remaining 15%, an associated systemic disease (e.g., systemic lupus erythematosus) or some known cause of immune complex formation (e.g., drug reaction) exists.

BP7 518–520BP8 551–552PBD7 979–981PBD8 922–923

31 **(C)** The congenital disorder known as medullary sponge kidney (MSK) is present to some degree in 1% of adults. In MSK, cystic dilation of 1 to 5 mm is present in the inner medullary and papillary collecting ducts. MSK is bilateral in 70% of cases. Not all papillae are equally affected, although calculi are often present in dilated collecting ducts. Patients usually develop kidney stones, infection, or recurrent hematuria in the third or fourth decade. More than 50% of patients have stones. Autosomal-dominant polycystic kidney disease produces much larger cysts that involve the entire kidney, eventually leading to massive renomegaly. Uric acid crystals are present in gout and may be deposited in the medulla, but cysts do not form. Multicystic renal dysplasia may occur sporadically or as part of various genetic syndromes, such as Meckel-Gruber syndrome, in fetuses and newborns. Autosomal-recessive polycystic kidney disease is rare and leads to bilateral, symmetric renal enlargement manifested in utero, with renal failure evident at birth. Transitional cell carcinoma may be multifocal, but it produces masses, not cysts. Vesicoureteral reflux can lead to hydroureter, hydronephrosis, and an increased risk of infection.

BP8 570–571PBD7 962, 965PBD8 957, 959

3 2 **(E)** Simple cysts are common in adults, and multiple cysts may occur. The cysts are not as numerous as cysts occurring in autosomal-dominant polycystic kidney disease (ADPKD), and there is no evidence of renal failure. Simple cysts may be 10 cm, and hemorrhage sometimes occurs into a cyst. Multiple cysts sometimes develop in patients receiving long-term hemodialysis. Acute pyelonephritis is unlikely in this patient because of the absence of fever and WBCs in the urine. Acute pyelonephritis may be associated with small abscesses, but not with cysts, although in patients with ADPKD, cysts may become infected. Acute tubular necrosis follows ischemic or toxic injury, and there is evidence of renal failure. Diabetic nephropathy includes vascular and glomerular disease, but not cysts. Hydronephrosis may produce a focal obstruction of a calyx with dilation, but it does not produce an eccentric cyst. Glomerulonephritis is not associated with cyst formation. Neoplasms usually produce solid masses, although sometimes a renal cell carcinoma is cystic. The latter is much less common than a simple cyst, however.

BP7 535BP8 569PBD7 962, 966PBD8 960

33 **(D)** Recurrent urinary tract infections with urea-splitting organisms such as *Proteus* can lead to formation of magnesium ammonium phosphate stones. These stones are large, and they fill the dilated calyceal system. Because of their large size and projections into the calyces, such stones are sometimes called "staghorn calculi." Infections are not a key feature of renal cell carcinoma. Cases of acute tubular necrosis typically occur from toxic or ischemic renal injuries. Malignant nephrosclerosis is primarily a vascular process that is not associated with infection. Papillary necrosis can complicate diabetes mellitus.

BP7 537BP8 571–572PBD7 1014–1015PBD8 962

34 **(B)** This patient has laboratory findings consistent with diabetes mellitus and clinical features of acute pyelonephritis caused by *Escherichia coli* infection. Necrotizing papillitis with papillary necrosis is a complication of acute pyelonephritis, and diabetic patients are particularly prone to this development. In the absence of diabetes mellitus, papillary necrosis develops when acute pyelonephritis occurs in combination with urinary tract obstruction. Papillary necrosis also can occur with long-term use of analgesics. Acute tubular necrosis typically occurs in acute renal failure caused by hypoxia (e.g., shock) or toxic injury (e.g., mercury). Crescentic glomerulonephritis causes rapidly progressive renal failure. Hydronephrosis occurs when urinary outflow is obstructed in the renal pelvis or in the ureter. Renal calculi can complicate conditions such as gout, but they do not complicate diabetes mellitus.

BP7 527–529BP8 560–562PBD7 990, 998–999PBD8 941–942

35 **(A)** One of the most common causes of nephrotic syndrome in adults is membranous glomerulopathy, caused by immune complex deposition, shown here as granular deposits with C3. About 85% of cases are idiopathic, but some cases follow infections (e.g., hepatitis, malaria), or are associated with causes such as malignancies or autoimmune diseases. In some cases of AIDS, a nephropathy resembling focal segmental glomerulosclerosis occurs. Multiple myeloma can be complicated by systemic amyloidosis, which can involve the kidney. Recurrent urinary tract infection can cause chronic pyelonephritis. Nephrolithiasis may lead to interstitial nephritis, but it does not cause glomerular injury.

BP7 518–520BP8 551–552PBD7 978–981PBD8 922–923

36 **(A)** The most common cause of acute tubular necrosis is ischemic injury. The hypotension that develops after myocardial infarction causes decreased renal blood flow. Benign nephrosclerosis takes years to develop and is associated with benign essential hypertension. Emboli from mural thrombosis after myocardial infarction could reach the kidney, causing renal infarction, but these infarctions are small and focal. Hemolytic-uremic syndrome is a thrombotic microangiopathy that most often occurs in children after infection with enterotoxigenic *Escherichia coli*. A rapidly progressive glomerulonephritis does not follow ischemic injury and would not resolve as quickly as in this patient.

BP7 531–533BP8 564–566PBD7 993–996PBD8 936–937

37 **(B)** These findings are characteristic of Alport syndrome, a form of hereditary nephritis. Most cases are inherited in an X-linked dominant pattern, but autosomal dominant and autosomal recessive patterns of inheritance also are seen. Most commonly, males are severely affected. Vision, hearing, and renal function are affected, but other organ systems are not affected.

BP7 525–526BP8 556–557PBD7 988PBD8 931–932

38 **(D)** Exposure to arylamines markedly increases the risk of bladder cancer, which can occur decades after the initial exposure. After absorption, aromatic amines are hydroxylated into an active form, which is detoxified by conjugation with glucuronic acid and then excreted. Urinary glucuronidase splits the nontoxic conjugated form into the active carcinogenic form. Renal cell carcinomas also may manifest as painless hematuria, but exposure to aniline dyes is not a risk factor. Hemorrhagic cystitis occurs after radiation injury or treatment with cytotoxic drugs such as cyclophosphamide. Tubercular cystitis is typically a complication of renal tuberculosis. Squamous cell carcinoma is the most common malignancy of the urethra, but it is rare and has no relation to carcinogens.

BP7 541–542BP8 575–576PBD7 1032PBD8 979–980

39 **(F)** This patient has diabetes mellitus. Nodular and diffuse glomerulosclerosis often occur in patients with long-standing diabetes mellitus. Infections with bacterial organisms also occur more frequently in patients with diabetes mellitus. Deposits of IgG and C3 in the glomerular basement membrane occur with forms of glomerulonephritis caused by immune complex deposition, including lupus nephritis and membranous glomerulonephritis. The only abnormality observed in minimal change disease is effacement of podocyte foot processes, but this change is not specific for minimal change

disease and may be seen in other disorders that produce proteinuria. Crescentic glomerulonephritis is not typically seen in diabetes mellitus. IgA deposition in the mesangium occurs in IgA nephropathy (Berger disease). A necrotizing granulomatous vasculitis can be present in the kidneys of patients with Wegener's granulomatosis. Thickening and thinning of glomerular basement membranes occurs in Alport syndrome.

BP7 650BP8 783–784PBD7 991–992PBD8 934–935, 1141–1142

40 **(F)** This patient has findings of systemic lupus erythematosus, an autoimmune disease that often manifests with renal involvement. There are several forms of lupus nephritis, and they tend to produce a nephritic pattern of involvement. Because these patients have leakage of RBCs from damaged glomeruli and proteinuria, RBC casts are found in the urine. Eosinophils may appear in the urine as a result of drug-induced interstitial nephritis. Glucosuria and ketonuria are features of type 1 diabetes mellitus. Myoglobinuria results most often from rhabdomyolysis, which can occur after severe crush injuries. Oval fat bodies are sloughed tubular cells containing abundant lipid that are characteristic of nephrotic syndromes. Triple phosphate crystals are typical findings in patients with infections caused by urease-positive bacteria, such as *Proteus*. Uric acid crystals form in acidic urine when uricosuria is present; this is a characteristic feature in some patients with gout. Waxy casts form in dilated, damaged tubules.

BP7 134–136BP8 142–144PBD7 231–233, 990PBD8 217–219, 913–914

4 1 **(E)** Most cases of pyelonephritis result from ascending bacterial infections, which are more common in women. Recurrent urinary tract infections complicated by vesicoureteral reflux cause progressive interstitial damage and scarring, which can lead to chronic pyelonephritis with renal failure. Diffuse glomerulosclerosis is a feature of diabetes mellitus. Glomerular injury is not the major consequence of renal infections. Some cases of membranous glomerulonephritis are preceded by chronic infections, such as hepatitis B or malaria, but recurrent urinary tract infections alone are unlikely antecedents. Some chronic infections (e.g., lung abscess, pulmonary tuberculosis) can lead to reactive systemic amyloidosis that may involve the kidney. Recurrent urinary tract infections do not cause amyloidosis, however.

BP7 527–529BP8 561–563PBD7 997–1000PBD8 939–941

42 **(A)** This patient has urethritis. The most common cause of nongonococcal urethritis in men is *Chlamydia trachomatis*. The condition is a nuisance; however, the behavior that led to the infection can place the patient at risk of other sexually transmitted diseases. Tuberculosis of the urinary tract is uncommon. Herpes simplex can produce painful vesicles on the skin. *Candida* infections typically occur in immunocompromised patients or in patients receiving long-term antibiotic therapy. A syphilitic chancre on the penis is an indicator of *Treponema pallidum* infection.

BP7 675BP8 705–706PBD7 1034PBD8 981

43 **(B)** These findings are characteristic of autosomal-dominant polycystic kidney disease (ADPKD). As seen in the figure, several large cysts have completely replaced the kidney. In autosomal-recessive polycystic kidney disease, which typically manifests in fetal and neonatal life, the kidneys have a smooth external appearance. On cut section, many small cysts give the kidney a spongelike appearance. About 10% to 30% of affected patients with ADPKD have an intracranial berry aneurysm, and some of these can rupture without warning. Wilms tumor does not arise in a polycystic kidney. Acute tubular necrosis is the result of ischemic or toxic renal injuries. Disseminated intravascular coagulation may complicate hemolytic-uremic syndrome. Pulmonary disease does not accompany adult polycystic kidney disease.

BP7 535–536BP8 569–570PBD7 962–964PBD8 956–959

4 4 **(C)** This patient has analgesic nephropathy, which damages the renal interstitium and can give rise to papillary necrosis. Hydronephrosis is unlikely to develop because there is no urinary tract obstruction in analgesic nephropathy. There is an increased risk of transitional cell carcinoma of the renal pelvis, however. The toxic injury that occurs with analgesic use is slowly progressive and not acute, in contrast to the course of acute tubular necrosis.

BP7 531BP8 564PBD7 1003–1004PBD8 945–946

4 5 **(C)** Chronic glomerulonephritis may follow specific forms of acute glomerulonephritis. In many cases, however, it develops insidiously with no known cause. With progressive glomerular injury and sclerosis, both kidneys become smaller, and their surfaces become granular. Hypertension often develops because of renal ischemia. Regardless of the initiating cause, these “end-stage” kidneys appear morphologically identical. They have sclerotic glomeruli, thickened arteries, and chronic inflammation of interstitium. Because the patient's ANA test result is negative, lupus is unlikely. Polycystic kidney disease and amyloidosis would cause the kidney size to increase, not decrease. The normal hemoglobin A_{1c} concentration indicates that the patient does not have diabetes mellitus. Nodular glomerulosclerosis is typical of diabetes mellitus with an

elevated hemoglobin A_{1c}.

BP7 526BP8 559PBD7 1000–1002PBD8 932–933

46 **(C)** The linear pattern of staining shown in the figure indicates the presence of anti–glomerular basement membrane antibodies. Such antibodies are typically seen in Goodpasture's syndrome. The antistreptolysin O titer is increased in poststreptococcal glomerulonephritis, which typically has a granular pattern of immune complex deposition. HIV infection can lead to a nephropathy that resembles focal segmental glomerulosclerosis, in which IgM and C3 are deposited in the mesangial areas of affected glomeruli. Some cases of membranous glomerulonephritis are associated with hepatitis B virus infection, but the immune complex deposition is granular, not linear. The C3 nephritic factor can be a marker for type II membranoproliferative glomerulonephritis.

BP7 513–514, 523–524BP8 557–558PBD7 968, 975PBD8 912

47 **(B)** This patient has findings characteristic of systemic lupus erythematosus (SLE) with lupus nephritis. Systemic problems include fever, arthralgias, myalgias, pancytopenia, and serositis with pericarditis and pleuritis. Renal disease is common in SLE, and a renal biopsy helps to determine the severity of involvement and the appropriate therapy. Anticentromere antibody is most specific for limited scleroderma (CREST syndrome), which is unlikely to have renal involvement. Anti–DNA topoisomerase I antibody is more specific for diffuse scleroderma, which does have renal involvement, although usually this manifests as vascular disease and not as glomerulonephritis. Anti–glomerular basement membrane antibody is characteristic of Goodpasture's syndrome, in which IgG antibody is deposited in a linear fashion along glomerular capillary basement membranes. Antihistone antibody may be present in drug-induced lupus. ANCAs can be seen in some forms of vasculitis, such as Wegener's granulomatosis or microscopic polyangiitis. Antiribonucleotide protein is present in mixed connective tissue disease, which has some features of SLE, but usually does not include severe renal involvement.

BP7 134–136BP8 142–144PBD7 231–233, 990PBD8 217–219, 913–914

48 **(B)** The figure shows hyaline arteriolosclerosis, which typically occurs in patients with benign hypertension. Similar changes can be seen with aging in the absence of hypertension. Oliguria is a sign of acute renal failure that does not complicate benign essential hypertension, a slowly progressive disease that is often clinically silent. Blood pressure screening is an important method that can identify patients with hypertension before significant organ damage has occurred. Malignant hypertension causes distinctive renal vascular lesions that include fibrinoid necrosis and hyperplastic arteriosclerosis. Hematuria may be present in malignant hypertension from vascular injury, but it is not a feature of benign hypertension. Flank pain is a symptom of acute pyelonephritis and some renal neoplasms.

BP7 533BP8 566–567PBD7 1006–1007PBD8 949–950

49 **(D)** This patient has a high serum globulin level from the presence of a monoclonal protein, and the back pain is probably caused by lytic lesions in the spine. Patients with myeloma often have Bence Jones proteinuria (not detected by the standard dipstick urinalysis), and some have cast nephropathy (as in this case), which can cause acute or, more commonly, chronic renal failure (as in this case). Cystinuria is an uncommon condition arising from defective transport of the amino acids cystine, lysine, arginine, and ornithine by the brush borders of renal tubule and intestinal epithelial cells. Excessive amounts of these amino acids are lost in the urine, leading to stone formation (the distinctive crystals look like miniature “stop” signs). Diabetic nephropathy can take many forms, but cast nephropathy is not one of them. Gouty deposits in the kidney are not in the form of casts, and uric acid crystals form at acidic pH. Hypercalcemia from a parathyroid adenoma can increase urine calcium excretion, favoring formation of stones, but not casts. Systemic lupus erythematosus is more likely to cause glomerulonephritis.

BP7 430–431BP8 455–456PBD7 993, 1005–1006PBD8 252, 935

50 **(B)** These changes are characteristic of chronic pyelonephritis. Urinary tract obstruction favors recurrent urinary tract infection. Vesicoureteral reflux propels infected urine from the urinary bladder to the ureters and renal pelvis and predisposes to infection. Benign nephrosclerosis is a vascular disease that does not carry a risk of infection. Lupus nephritis is associated with extensive inflammatory changes of glomeruli that are noninfectious. Amyloidosis can lead to progressive renal failure as a result of amyloid deposition in the glomeruli; however, amyloid does not evoke an inflammatory response. Congestive heart failure may predispose to acute tubular necrosis. Autosomal-dominant polycystic kidney disease is a bilateral process; patients usually are not symptomatic until middle age.

BP7 529–530BP8 562–563PBD7 1000–1002PBD8 942–944

51 **(G)** This patient is septic, and the heart murmur strongly suggests infective endocarditis. Cardiac lesions are the source of emboli (from valvular vegetations or mural thrombi) that can lodge in renal artery branches, producing areas of coagulative necrosis. These areas of acute infarction typically are wedge-shaped on cut section because of the vascular flow pattern. Bilaterally enlarged, cystic kidneys are typical of autosomal-dominant polycystic kidney disease. Small, shrunken kidneys represent an end stage of many chronic renal diseases. Irregular cortical scars with pelvicaliceal dilation may represent hydronephrosis complicated by infection in chronic pyelonephritis, whereas dilation alone points to obstructive uropathy, such as occurs with nodular prostatic hyperplasia. This patient's kidneys may have been normal-sized and smooth-surfaced before this event. Petechiae and edema may be seen in hyperplastic arteriolosclerosis associated with malignant hypertension.

BP7 97–98BP8 560PBD7 997, 1012PBD8 955

52 **(B)** This patient has findings characteristic of nephrocalcinosis resulting from hypercalcemia. One of the most common causes of hypercalcemia in adults is metastatic disease. The hypercalcemia produces a chronic tubulointerstitial disease of the kidneys that is initially manifested by loss of concentrating ability. With continued hypercalcemia, there is progressive loss of renal function. Urinary tract stones formed of calcium oxalate also may be present. Some patients with membranous glomerulonephritis have a positive serologic test result for hepatitis B surface antigen. Hypercholesterolemia may be seen in some cases of minimal change disease, which can occur in Hodgkin lymphoma and other lymphoproliferative malignancies. Hypergammaglobulinemia with a monoclonal protein (M protein) may be present in multiple myeloma, but not in breast cancer. Hyperglycemia can occur in diabetes mellitus, but patients with cancer are not at increased risk of developing diabetes mellitus. Hyperuricemia occurs in some cases of gout. It also can occur in patients with neoplasms (particularly lymphomas and leukemias) that have a high proliferation rate and are treated with chemotherapy. In these cases, extensive cell death (lysis syndrome) causes acute elevations in uric acid levels, leading to urate nephropathy.

PBD7 1005PBD8 947

53 **(B)** The renal biopsy specimen shows glomerular crescents, which indicate rapidly progressive glomerulonephritis. Crescentic glomerulonephritis is divided into three groups on the basis of immunofluorescence: type I (anti–glomerular basement membrane [GBM] disease), type II (immune complex disease), and type III (characterized by absence of anti-GBM antibodies or immune complexes). Each type has a different cause and treatment. The presence of anti-GBM antibodies suggests Goodpasture's syndrome; patients with this disorder require plasmapheresis. Type II crescentic glomerulonephritis can occur in systemic lupus erythematosus, in Henoch-Schönlein purpura, and after infections. Causes of type III crescentic glomerulonephritis include Wegener's granulomatosis and microscopic polyangiitis. Immunofluorescence studies are crucial for the classification and treatment of crescentic glomerulonephritis. A positive ANA test result may be reported in patients with lupus nephritis, which uncommonly manifests with glomerular crescents. HIV nephropathy has features similar to those of focal segmental glomerulosclerosis, which is not rapidly progressive. Quantitative serum immunoglobulins are not helpful because the important consideration is the pattern of immune deposits in the kidney. Rheumatoid factor is present in rheumatoid arthritis, which is not associated with renal complications. Urine immunoelectrophoresis is useful in categorizing a monoclonal gammopathy.

BP7 523–524BP8 557–558PBD7 976–978PBD8 920–921

54 **(G)** The rapid cell turnover in acute leukemias and cell death from treatment cause the release of purines from the cellular DNA breakdown. The resulting hyperuricemia can predispose to the formation of uric acid stones. Renal stones can produce colicky pain when they pass down the ureter and through the urethra, and the local trauma to the urothelium can produce hematuria. Uric acid stones form in acidic urine. In contrast to stones containing calcium, uric acid stones are radiolucent and are not visible on a plain radiograph. The urine dipstick is sensitive to albumin, but not to globulins; a separate test for Bence Jones protein may be positive, although the dipstick protein result is negative. Bence Jones proteinuria is characteristic of multiple myeloma, however, not of leukemias or lymphomas. Eosinophils may appear in the urine in drug-induced interstitial nephritis. Myoglobin can cause the dipstick reagent for blood to become positive in the absence of RBCs or hemoglobin. Myoglobinuria results most often from rhabdomyolysis, which can occur after severe crush injuries. Oval fat bodies are sloughed tubular cells containing abundant lipid; they are characteristic of nephrotic syndromes. RBC casts appear in nephritic syndromes as a result of glomerular injury. Triple phosphate crystals are typical of infections with urease-positive bacteria, such as *Proteus*. Waxy casts form in dilated, damaged tubules. WBC casts alone are most indicative of acute pyelonephritis, but they can appear in conjunction with other cellular elements in severe glomerular injury.

BP7 537, 774BP8 571–572PBD7 1004–1005PBD8 947

55 **(G)** Wegener granulomatosis causes rapidly progressive glomerulonephritis characterized by epithelial crescents in Bowman space. Several features differentiate Wegener granulomatosis from other forms of crescentic glomerulonephritis (e.g., Goodpasture syndrome), including the presence of granulomatous vasculitis, the absence of immune complexes or anti–glomerular basement membrane (GBM) antibodies, and the presence of C-ANCA. Focal segmental glomerulosclerosis does not affect renal vessels and is unlikely to produce crescents with a rapidly progressive presentation. Goodpasture syndrome is a form of rapidly progressive glomerulonephritis with crescent formation, but a granulomatous vasculitis is not present, and there is anti-GBM antibody, not C-ANCA. Lupus nephritis, membranoproliferative glomerulonephritis, and postinfectious glomerulonephritis occasionally can have a rapidly progressive course with crescent formation, but they do not produce granulomatous vasculitis. In patients with lupus, the ANA test result is often positive. Membranous glomerulonephritis is most likely to produce nephrotic syndrome without crescents.

BP7 351–352, 524BP8 558PBD7 541–542, 977PBD8 517, 935

56 **(B)** Hyaline arteriosclerosis, characterized by thickening and hyalinization of small arteries and arterioles, is typically seen in patients with long-standing benign hypertension. Such a change also occurs with aging. Vascular narrowing causes ischemic changes that are slow and progressive. There is diffuse scarring and shrinkage of the kidneys. RBCs and RBC casts are a feature of crescentic glomerulonephritis, which typically is a rapidly progressive form of renal failure. Mesangial proliferation is a feature of some forms of glomerulonephritis. Fibrinoid necrosis in arterioles is seen in malignant hypertension. Acute tubular necrosis results from anoxic or toxic injury to the renal tubules. In interstitial nephritis, more cells would be seen in the urine sediment.

BP7 533BP8 566–567PBD7 1006–1007PBD8 949–950

5 7 **(C)** This patient has malignant hypertension. Necrotizing arteriolitis and hyperplastic arteriolosclerosis are the distinctive vascular lesions of malignant hypertension. Papillary necrosis is more likely to complicate diabetic nephropathy or analgesic nephropathy. Infarction of the kidney may result from emboli originating in the systemic circulation. Malignant hypertension does not damage the large systemic vessels, however. Acute tubular necrosis is seen in hypoxic or toxic injury to the renal tubules. Acute pyelonephritis is a febrile illness, without severe blood pressure elevation.

BP7 533–534BP9 567–568PBD7 1007–1008PBD8 950–951

5 8 **(C)** The combination of cysts in the kidney and berry aneurysms in the brain is characteristic of adult autosomal-dominant polycystic kidney disease (ADPKD). The cysts also may appear in the liver and pancreas. Because of the autosomal dominant pattern of inheritance, with high penetrance of the gene, first-degree relatives are at risk of having the same disorder, and should be evaluated by ultrasound or other imaging techniques. This evaluation is particularly important because many patients remain asymptomatic until the onset of renal failure as adults. Cocaine use can increase the risk of hemorrhages, but no hemorrhage was found in this case. The cause of death was cocaine intoxication. Autosomal-recessive polycystic kidney disease is unlikely to remain asymptomatic from birth. Because the berry aneurysm had not ruptured, it was not the cause of death. About 1% of all individuals have a berry aneurysm, whereas at least 10% of individuals with ADPKD have such an aneurysm. Most berry aneurysms do not rupture, however. The patient did not die as a consequence of ADPKD; had he lived, he might have developed complications from renal failure, leading to death decades later.

BP7 535–536BP8 569–570PBD7 962–964PBD8 956–959

59 **(A)** The biopsy specimen shows sclerosis of only a segment of the glomerulus (segmental lesion), and because only 50% of the glomeruli are affected, this is focal disease. Focal segmental glomerulosclerosis manifests clinically with nephrotic syndrome that does not respond to corticosteroid therapy. In contrast, corticosteroid-responsive nephrotic syndrome in children is typically caused by minimal change disease (lipoid nephrosis); this disease is not associated with any glomerular change seen under the light microscope. Type I or type II membranoproliferative glomerulonephritis is more likely to produce a nephritic syndrome in adults. A diabetic patient with nephrotic syndrome is likely to have nodular glomerulosclerosis or diffuse thickening of the basement membrane. Sore throat (pharyngitis) followed by nephritic syndrome is the typical clinical history of acute proliferative poststreptococcal (postinfectious) glomerulonephritis. A rapidly progressive glomerulonephritis is associated with hematuria, and glomerular crescents are present.

BP7 520–521BP8 550–551PBD7 982–984PBD8 916–917

60 **(C)** This patient has acute pyelonephritis. Acquired or congenital vesicoureteral reflux is extremely important in the pathogenesis of ascending urinary tract infections because it allows bacteria to ascend from the urinary bladder into the ureter and the pelvis. Urinary tract infections generally are more common in females because of their shorter urethra, but

in the absence of vesicoureteral reflux, the infections tend to remain localized in the urinary bladder. Older women and sexually active women are at increased risk of urinary tract infections. Hypertension can cause renal vascular narrowing and ultimately impair renal function, but it does not predispose to infections. Foci of infection in the lungs can seed the kidney hematogenously, but this route is far less common than ascending infection.

BP7 527–529BP8 560–562PBD7 997–998PBD8 940–941

61 **(D)** This girl has hemolytic-uremic syndrome. Some strains of *Escherichia coli,* which can contaminate ground beef products, may elaborate a toxin that damages endothelium, causing this syndrome. Hemolytic-uremic syndrome most often occurs in children and is one of the most common causes of acute renal failure in children. Candidal urinary tract infections typically affect the urinary bladder. *Proteus* is a common cause of bacterial urinary tract infections. *Clostridium difficile* is best known for causing a pseudomembranous enterocolitis, not renal lesions. *Staphylococcus aureus* can cause urinary tract infections.

BP7 534–535BP8 568PBD7 1009–1011PBD8 952–953

62 **(E)** This patient sustained muscle injury that resulted in myoglobinemia and myoglobinuria. The large amount of excreted myoglobin produces a toxic acute tubular necrosis. With supportive care, the tubular epithelium can regenerate, and renal function can be restored. During the recovery phase of acute tubular necrosis, patients excrete large volumes of urine because the glomerular filtrate cannot be adequately reabsorbed by the damaged tubular epithelium. Trauma is not a cause of malignant hypertension. A bilateral renal vein thrombosis is uncommon. Glomerulonephritis does not occur as a result of trauma. An infection with pyelonephritis is unlikely to be characterized by such a short course or such a marked loss of renal function.

BP7 531–533BP8 564–566PBD7 993PBD8 936–937

63 **(C)** This patient has malignant hypertension, which may follow long-standing benign hypertension. Two types of vascular lesions are found in malignant hypertension. Fibrinoid necrosis of the arterioles may be present; in addition, there is intimal thickening in interlobular arteries and arterioles, caused by proliferation of smooth muscle cells and collagen deposition. The proliferating smooth muscle cells are concentrically arranged, and these lesions, called hyperplastic arteriolosclerosis, cause severe narrowing of the lumen. The resultant ischemia elevates the renin level, which further promotes vasoconstriction to potentiate the injury. Nodular glomerulosclerosis is a feature of diabetes mellitus that slowly progresses over many years. Segmental tubular necrosis occurs in ischemic forms of acute tubular necrosis. An IgA nephropathy involves glomeruli, but not typically the interstitium or vasculature. Glomerular crescents are a feature of a rapidly progressive glomerulonephritis; however, the blood pressure elevation is not as marked as that seen in this patient.

BP7 533–534BP8 567–568PBD7 1007–1008PBD8 950–951

64 **(A)** The figure shows a high-grade urothelial carcinoma of the bladder. Cigarette smoking is the greatest risk factor in half of all men with such cancers. Schistosomiasis also is a risk factor for bladder cancer, although typically for squamous cell carcinoma. The increased risk of infection that occurs in diabetes mellitus and prostatic hyperplasia, with the resultant acute and chronic cystitis, does not predispose to urothelial carcinoma.

BP7 541–542BP8 575–577PBD7 1028–1032PBD8 976–979

65 **(C)** This patient has type II membranoproliferative glomerulonephritis, or dense-deposit disease, which usually leads to chronic renal failure. Postinfectious glomerulonephritis is often characterized by a hypercellular glomerulus with infiltration of polymorphonuclear leukocytes, but no basement membrane thickening. A rapidly progressive glomerulonephritis is marked by crescents. The term *chronic glomerulonephritis* often is used when sclerosis of many glomeruli is present with no clear cause. Membranous glomerulonephritis is characterized by thickening of only the basement membrane and small electron-dense deposits.

BP7 521–522BP8 552–554PBD7 984–986PBD8 928–929

66 **(A)** Clear cell carcinoma, the most common form of kidney cancer, often manifests with painless hematuria, most often in individuals in the sixth or seventh decade. Approximately 80% of sporadic clear cell carcinomas show loss of both alleles of the *VHL* gene. Germline inheritance of the *VHL* mutation can give rise to von Hippel–Lindau syndrome, with peak incidence of renal cell carcinoma in the fourth decade, and they may have other tumors, including cerebellar and retinal hemangioblastomas and adrenal pheochromocytomas. Mutation of the *MET* gene on chromosome 7 is associated with the papillary variant of renal cell carcinoma. HPV-16 infection is associated with carcinomas of the uterine cervix. Microsatellite instability is a feature of the Lynch syndrome, also called hereditary nonpolyposis colon cancer syndrome,

characterized by right-sided colon cancer and, in some cases, endometrial cancer.

BP7 539–540BP8 573–574PBD7 1016–1018PBD8 964–966

67 **(B)** Corticosteroid-resistant hematuria and proteinuria in a Hispanic man leading to hypertension and renal failure is typical for focal segmental glomerulosclerosis (FSGS). FSGS is now the most common cause of nephrotic syndrome in adults in the United States. Specialized extracellular areas overlying the glomerular basement membrane between adjacent foot processes of podocytes are called slit diaphragms, and these exert control over glomerular permeability. Mutations in genes affecting several proteins, including nephrin and podocin, have been found in inherited cases of FSGS, and their dysfunction, possibly caused by cytokines or unknown toxic factors, is believed to be responsible for acquired cases of FSGS. FSGS also is seen in patients with HIV-associated nephropathy. Immune complexes containing microbial antigens cause postinfectious glomerulonephritis. Anti–glomerular basement membrane antibodies are responsible for Goodpasture syndrome. Inherited defects in basement membrane collagen cause Alport syndrome, also characterized by hematuria, but other congenital abnormalities, such as deafness, are often present, and nephrotic syndrome is uncommon. C3NeF is an autoantibody directed against C3 convertase, and it is seen in membranoproliferative glomerulonephritis type II.

BP8 550–551 PBD7 959, 973PBD8 916–917

21. The Lower Urinary Tract and Male Genital System

PBD7 and PBD8 Chapter 21: The Lower Urinary Tract and Male Genital System

BP7 and BP8 Chapter 18: The Male Genital System

1 A 30-year-old man visits his physician because he has noticed increasing enlargement and a feeling of heaviness in his scrotum for the past year. On physical examination, the right testis is twice its normal size, and it is firm and slightly tender. An ultrasound examination shows a 3.5-cm solid mass in the right testis. Abdominal CT scan shows enlargement of the para-aortic lymph nodes. Multiple lung nodules are seen on a chest radiograph. Laboratory findings include markedly increased serum levels of chorionic gonadotropin and α-fetoprotein. Which of the following testicular neoplasms is the most likely diagnosis?

- □ (A) Leydig cell tumor
- □ (B) Mixed germ cell tumor
- □ (C) Pure spermatocytic seminoma
- □ (D) Choriocarcinoma
- □ (E) Metastatic adenocarcinoma of the prostate gland
- □ (F) Large diffuse B-cell lymphoma

2 For the past year, a 65-year-old man has had multiple, recurrent urinary tract infections. *Escherichia coli* and streptococcal organisms have been cultured from his urine during several of these episodes, with bacterial counts of more than 10^5/mL. He has difficulty with urination, including starting and stopping the urinary stream. Over the past week, he has again developed burning pain with urination. Urinalysis shows a pH of 6.5, and specific gravity of 1.020. No blood or protein is present in the urine. Tests for leukocyte esterase and nitrite are positive. Microscopic examination of the urine shows numerous WBCs and a few WBC casts. Which of the following is the most likely diagnosis?

- □ (A) *Neisseria gonorrhoeae* infection
- □ (B) Prostatic nodular hyperplasia
- □ (C) Phimosis
- □ (D) Epispadias
- □ (E) Adenocarcinoma of the prostate gland
- □ (F) Vesicoureteral reflux

3 A 35-year-old man has noticed bilateral breast enlargement over the past 6 months. On physical examination, both breasts are enlarged without masses. His right testis is 1.5 times larger than his left testis; both are firm and round. His serum estrogen is increased. An ultrasound scan shows a circumscribed 2-cm mass in the body of the right testis, and a right orchiectomy is performed. The mass has a grossly uniform, brown cut surface. On microscopic examination, the cells are large and round with granular eosinophilic cytoplasm along with rod-shaped crystalloids of Reinke. What is the most likely diagnosis?

- □ (A) Choriocarcinoma
- □ (B) Embryonal carcinoma
- □ (C) Gonadoblastoma
- □ (D) Leydig cell tumor
- □ (E) Seminoma
- □ (F) Teratoma

□ (G) Yolk sac tumor

4 A 23-year-old, sexually active man has been treated for *Neisseria gonorrhoeae* infection several times during the past 5 years. He now comes to the physician because of the increasing number and size of warty lesions slowly enlarging on his external genitalia during the past year. On physical examination, there are multiple 1- to 3-mm sessile, nonulcerated, papillary excrescences over the inner surface of the penile prepuce. These lesions are excised, but 2 years later, similar lesions appear. Which of the following conditions most likely predisposed him to development of these recurrent lesions?

□ (A) *Candida albicans* infection

□ (B) Circumcision

□ (C) Human papillomavirus infection

□ (D) *Neisseria gonorrhoeae* infection

□ (E) Paraphimosis

□ (F) Phimosis

5 A 55-year-old man has dysuria, increased frequency, and urgency of urination for the past 6 months. He has sometimes experienced mild lower back pain. On physical examination, he is afebrile. There is no costovertebral angle tenderness. The prostate gland feels normal in size; no nodules are palpable. Laboratory studies show that expressed prostatic secretions contain 30 leukocytes per high-power field. What is the most likely diagnosis?

□ (A) Benign prostatic hyperplasia

□ (B) Acute bacterial prostatitis

□ (C) Syphilitic prostatitis

□ (D) Chronic abacterial prostatitis

□ (E) Metastatic prostatic adenocarcinoma

6 A 32-year-old man has noticed an increased feeling of heaviness in his scrotum for the past 10 months. On physical examination, the left testis is three times the size of the right testis and is firm on palpation. An ultrasound scan shows a 6-cm solid mass within the body of the left testis. Laboratory studies include an elevated serum α-fetoprotein level. Which of the following cellular components is most likely to be present in this mass?

□ (A) Yolk sac cells

□ (B) Leydig cells

□ (C) Seminoma cells

□ (D) Cytotrophoblasts

□ (E) Embryonal carcinoma cells

□ (F) Lymphoblasts

7 A 25-year-old man has occasionally felt pain in the scrotum for the past 3 months. On physical examination, the right testis is more tender than the left, but does not appear to be appreciably enlarged. An ultrasound scan shows a 1.5-cm mass. A right orchiectomy is performed, and gross examination shows the mass to be hemorrhagic and soft. A retroperitoneal lymph node dissection is done. In sections of the lymph nodes, a neoplasm is seen with grossly extensive necrosis and hemorrhage. Microscopic examination shows that areas of viable tumor are composed of cuboidal cells intermingled with large eosinophilic syncytial cells containing multiple dark, pleomorphic nuclei. Immunohistochemical staining of the tumor is most likely to show which of the following antigenic components in the syncytial cells?

□ (A) Human chorionic gonadotropin

□ (B) α-Fetoprotein

- □ (C) Vimentin
- □ (D) CD20
- □ (E) Testosterone
- □ (F) Carcinoembryonic antigen
- □ (G) CA-125

8 A 70-year-old, previously healthy man comes to his physician for a routine health examination. On palpation, his prostate is normal in size. Laboratory studies show a serum prostate-specific antigen (PSA) level of 17 ng/mL, however, twice the value he had 1 year ago. A routine urinalysis shows no abnormalities. Which of the following histologic findings in a subsequent biopsy specimen of the prostate is most likely to account for the patient's current status?

- □ (A) Acute prostatitis
- □ (B) Adenocarcinoma
- □ (C) Chronic abacterial prostatitis
- □ (D) Nodular hyperplasia
- □ (E) Prostatic intraepithelial neoplasia

9 A 35-year-old man and his 33-year-old wife are childless. They have tried to conceive a child for 12 years, and now they undergo an infertility work-up. On physical examination, neither spouse has any remarkable findings. Laboratory studies show that the man has a sperm count in the low-normal range. On microscopic examination of the seminal fluid, the sperm have a normal morphologic appearance. A testicular biopsy is done. The biopsy specimen shows patchy atrophy of seminiferous tubules, but the remaining tubules show active spermatogenesis. Which of the following disorders is the most likely cause of these findings?

- □ (A) Mumps virus infection
- □ (B) Cryptorchidism
- □ (C) Hydrocele
- □ (D) Klinefelter syndrome
- □ (E) Prior chemotherapy

10 A 25-year-old, previously healthy man suddenly develops severe pain in the scrotum. The pain continues unabated for 6 hours, and he goes to the emergency department. On physical examination, he is afebrile. There is exquisite tenderness of a slightly enlarged right testis, but there are no other remarkable findings. The gross appearance of the right testis is shown in the figure. Which of the following conditions is most likely to cause these findings?

- □ (A) Disseminated tuberculosis
- □ (B) Invasive germ cell tumor
- □ (C) Lymphedema
- □ (D) Obstruction of blood flow

□ (E) Previous vasectomy

11 The mother of a 2-year-old boy notices that he has had increasing asymmetric enlargement of the scrotum over the past 6 months. On physical examination, there is a well-circumscribed, 2.5-cm mass in the left testis. A left orchiectomy is performed, and histologic examination of this mass shows sheets of cells and ill-defined glands composed of cuboidal cells, some of which contain eosinophilic hyaline globules. Microcysts and primitive glomeruloid structures also are seen. Immunohistochemical staining shows α-fetoprotein in the cytoplasm of the neoplastic cells. What is the most likely diagnosis?

□ (A) Choriocarcinoma

□ (B) Seminoma

□ (C) Yolk sac tumor

□ (D) Teratoma

□ (E) Leydig cell tumor

12 A 19-year-old man comes to his physician complaining of worsening local pain and irritation with difficult urination over the past 3 years. He has become more sexually active during the past year and describes his erections as painful. Physical examination shows that he is not circumcised. The prepuce (foreskin) cannot be easily retracted over the glans penis. What is the most likely diagnosis?

□ (A) Epispadias

□ (B) Bowenoid papulosis

□ (C) Phimosis

□ (D) Genital candidiasis

□ (E) Paraphimosis

13 A 19-year-old man comes to his physician for a routine health maintenance examination. On physical examination, there is no left testis palpable in the scrotum. The patient is healthy, has had no major illnesses, and has normal sexual function. In counseling this patient, which of the following statements regarding his condition would be most appropriate?

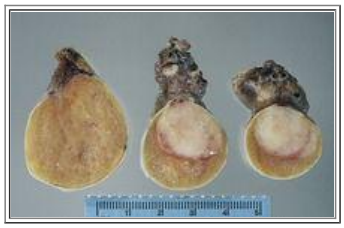
□ (A) You will be unable to father children

□ (B) You are at increased risk of developing a testicular tumor

□ (C) This is a common finding in more than half of all men

□ (D) This is an outcome of childhood mumps infection

□ (E) This is an inherited disorder



14 A 29-year-old man complains of a vague feeling of heaviness in the scrotum, but he has had no increase in pain for the past 5 months. He is otherwise healthy. Physical examination shows that the right testis is slightly larger than the left testis. An ultrasound scan shows the presence of a solid, circumscribed, 1.5-cm mass in the body of the right testis. The representative gross appearance of the mass is shown in the figure. A biopsy is done, and microscopic examination of the mass shows uniform nests of cells with distinct cell borders, glycogen-rich cytoplasm, and round nuclei with prominent nucleoli. There are aggregates of lymphocytes between these nests of cells. Which of the following features is most

characteristic of this lesion?

- □ (A) Excellent response to radiation therapy
- □ (B) Likelihood of extensive metastases early in the course of disease
- □ (C) Elevation of human chorionic gonadotropin levels in the serum
- □ (D) Elevation of α-fetoprotein levels in the serum
- □ (E) Elevation of serum testosterone levels
- □ (F) Association with 46,X(fra)Y karyotype
- □ (G) Association with 46,XXY karyotype

15 A 5-year-old boy has a history of recurrent urinary tract infections. Urine cultures have grown *Escherichia coli, Proteus mirabilis,* and enterococcus. Physical examination now shows an abnormal constricted opening of the urethra on the ventral aspect of the penis, about 1.5 cm from the tip of the glans penis. There also is a cryptorchid testis on the right and an inguinal hernia on the left. What term best describes the child's penile abnormality?

- □ (A) Hypospadias
- □ (B) Phimosis
- □ (C) Balanitis
- □ (D) Epispadias
- □ (E) Bowen disease

16 A 46-year-old man with a history of poorly controlled diabetes mellitus comes to the physician because he has had painful, erosive, markedly pruritic lesions on the glans penis, scrotum, and inguinal regions of the skin for the past 2 months. Physical examination shows irregular, shallow, 1- to 4-cm erythematous ulcerations. Scrapings of the lesions are examined under the microscope. Which of the following microscopic findings in the scrapings is most likely to be reported?

- □ (A) Eggs and excrement of *Sarcoptes scabiei*
- □ (B) Budding cells with pseudohyphae
- □ (C) Atypical cells with hyperchromatic nuclei
- □ (D) Enlarged cells with intranuclear inclusions
- □ (E) Spirochetes under dark-field examination

17 A clinical trial of two pharmacologic agents compares one agent that inhibits 5α-reductase and diminishes dihydrotestosterone (DHT) synthesis in the prostate with another agent that acts as an α_1-adrenergic receptor. The subjects are 40 to 80 years old. The study will determine whether symptoms of prostate disease are ameliorated in the individuals who take these drugs. Which of the following diseases of the prostate is most likely to benefit from one or both of these drugs?

- □ (A) Acute prostatitis
- □ (B) Adenocarcinoma
- □ (C) Leiomyoma
- □ (D) Chronic prostatitis
- □ (E) Nodular hyperplasia

18 A 33-year-old man has noted asymmetric enlargement of the scrotum over the past 4 months. On physical examination,

the right testis is twice its normal size and has increased tenderness to palpation. The right testis is removed. The epididymis and the upper aspect of the right testis have extensive granulomatous inflammation with epithelioid cells, Langhans giant cells, and caseous necrosis. Which of the following is the most likely cause of these findings?

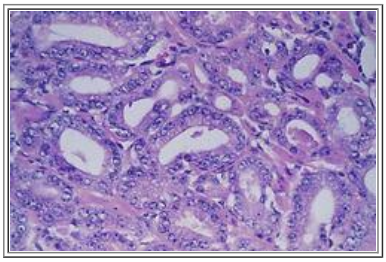
- □ (A) Mumps
- □ (B) Syphilis
- □ (C) Tuberculosis
- □ (D) Gonorrhea
- □ (E) Sarcoidosis

19 A 48-year-old man has noticed a reddish area on the penis for the past 3 months. He has had no sexual intercourse for more than 1 month. On physical examination, there is a solitary 0.8-cm, plaquelike, erythematous area on the distal shaft of the penis. A routine microbiologic culture with a Gram-stained smear of the lesion shows normal skin flora. Microscopic examination of a biopsy specimen of the lesion shows dysplasia involving the full thickness of the epithelium. What is the most likely diagnosis?

- □ (A) Primary syphilis
- □ (B) Balanitis
- □ (C) Soft chancre
- □ (D) Bowen disease
- □ (E) Condyloma acuminatum

20 An 85-year-old man comes to the physician because he had experienced urinary hesitancy and nocturia for the past year. He has had increasing back pain for the past 6 months. On digital rectal examination, there is a hard, irregular prostate gland. A bone scan shows increased areas of uptake in the thoracic and lumbar vertebrae. Laboratory studies show a serum alkaline phosphatase level of 300 U/L, serum prostatic acid phosphatase level of 8 ng/mL, and serum prostate-specific antigen (PSA) level of 72 ng/mL. The blood urea nitrogen concentration is 44 mg/dL, and the serum creatinine level is 3.8 mg/dL. Transrectal biopsy specimens of all lobes of the prostate are obtained. Microscopic examination shows that more than 90% of the tissue has a pattern of cords and sheets of cells with hyperchromatic pleomorphic nuclei, prominent nuclei, and scant cytoplasm. Which of the following is the best classification for this patient's disease?

	Stage	Gleason grade
□ (A)	A1	1, 1
□ (B)	A2	1, 2
□ (C)	B1	2, 3
□ (D)	B2	3, 3
□ (E)	C1	3, 4
□ (F)	C2	4, 4
□ (G)	D1	4, 5
□ (H)	D2	5, 5



21 A 45-year-old man comes to the physician for a routine health maintenance examination. On physical examination,

there are no remarkable findings. Laboratory findings include serum creatinine, 1.1 mg/dL; urea nitrogen, 17 mg/dL; glucose, 76 mg/dL; alkaline phosphatase, 89 U/L; and prostate-specific antigen (PSA), 8 ng/mL. Prostate biopsies are performed and the high-power microscopic appearance of a biopsy specimen is shown in the figure. Which of the following is the most likely risk factor for his disease?

- □ (A) Epigenetic hypermethylation of *GSTP1* gene
- □ (B) Recurrent bacterial urinary tract infections
- □ (C) Exposure to naphthylamine compounds
- □ (D) Tobacco use
- □ (E) Overproduction of dihydrotestosterone

22 A 59-year-old man notices gradual enlargement of the scrotum over the course of 1 year. The growth is not painful, but produces a sensation of heaviness. He has no problems with sexual function. Physical examination shows no lesions of the overlying scrotal skin and no obvious masses, but the scrotum is enlarged, boggy, and soft bilaterally. The transillumination test result is positive. What is the most likely diagnosis?

- □ (A) Varicocele
- □ (B) Elephantiasis
- □ (C) Orchitis
- □ (D) Seminoma
- □ (E) Hydrocele

23 An otherwise healthy, 72-year-old man has had increasing difficulty with urination for the past 10 years. He now has to get up several times each night because of a feeling of urgency, but each time the urine volume is not great. He has difficulty starting and stopping urination. On physical examination, the prostate is enlarged to twice its normal size, but is not tender to palpation. One year ago, his serum prostate-specific antigen (PSA) level was 6 ng/mL, and it is still at that level when retested. Which of the following drugs is most likely to be effective in treatment of this man?

- □ (A) Estrogen (hormone)
- □ (B) Finasteride (5-α-reductase inhibitor)
- □ (C) Mitoxantrone (chemotherapy agent)
- □ (D) Nitrofurantoin (antibiotic)
- □ (E) Prednisone (corticosteroid)

24 Over the past 9 months, a 30-year-old man has noticed increased heaviness with enlargement of the scrotum. On physical examination, there is an enlarged, firm left testis, but no other remarkable findings. An ultrasound scan shows a 5-cm solid mass within the body of the left testis. An orchiectomy of the left testis is performed. Microscopic examination of the mass shows areas of mature cartilage, keratinizing squamous epithelium, and colonic glandular epithelium. Laboratory findings include elevated levels of serum human chorionic gonadotropin (hCG) and α-fetoprotein (AFP). Despite the appearance of the cells in the tumor, the surgeon tells the patient that he probably has a malignant testicular tumor. The surgeon's conclusion is most likely based on which of the following factors?

- □ (A) Size of the tumor
- □ (B) Age of the patient
- □ (C) Presence of colonic glandular epithelium
- □ (D) Elevation of hCG and AFP levels
- □ (E) Location of the mass in the left testis

25 A 71-year-old, currently healthy man visits his physician for a checkup because he is worried about his family history of prostate cancer. Physical examination does not indicate any abnormalities. Because of the patient's age and family history, his prostate-specific antigen (PSA) level is immediately measured, and the PSA level is 5 ng/mL. Six months later, the PSA level is 6 ng/mL. A urologist obtains transrectal biopsy specimens, and microscopic examination shows multifocal areas of prostatic intraepithelial neoplasia and glandular hyperplasia. Based on these findings, what is the most appropriate course of management for this patient?

- □ (A) Antibiotic therapy
- □ (B) Monitoring PSA levels
- □ (C) Multiagent chemotherapy
- □ (D) Radiation therapy
- □ (E) Radical prostatectomy
- □ (F) Transurethral prostate resection

ANSWERS

1 **(B)** Although a modest elevation of the human chorionic gonadotropin (hCG) concentration can occur when a seminoma contains some syncytial giant cells, significant elevation of the α-fetoprotein (AFP) level never occurs with pure seminomas. Elevated levels of AFP and hCG effectively exclude the diagnosis of a pure seminoma and indicate the presence of a nonseminomatous tumor of the mixed type. The most common form of testicular neoplasm combines multiple elements; the term *teratocarcinoma* is sometimes used to describe tumors with elements of teratoma, embryonal carcinoma, and yolk sac tumor. The yolk sac element explains the high AFP level. Mixed tumors may include seminoma. Leydig cell tumors are non–germ cell tumors derived from the interstitial (Leydig) cells; they may elaborate androgens. Choriocarcinomas secrete high levels of hCG, but no AFP. It is unusual for a tumor to metastasize to the testis; this patient is of an age at which a primary cancer of the testis should be considered when a testicular mass is present. Lymphomas may involve the testis, usually when there is systemic involvement by a high-grade lesion. Lymphomas do not elaborate hormones.

BP7 661–664BP8 690–695PBD7 1041–1042, 1046PBD8 992

2 **(B)** Of the diseases listed, prostatic nodular hyperplasia is the most common in older men. When it causes obstruction of the prostatic urethra, it can predispose to bacterial infections. Gonorrhea is more likely to be seen in younger, sexually active men, and obstruction is not a key feature. Phimosis can occur in uncircumcised men. It may be congenital or acquired from inflammation, usually at a much younger age. Epispadias is a congenital condition, observed at birth. Prostatic adenocarcinomas are less likely than hyperplasia to cause obstructive symptoms. Vesicoureteral reflux is more likely to be present at an earlier age, and it does not account for the obstructive symptoms the patient has on urination.

BP7 665–666BP8 696–697PBD7 1048–1050PBD8 994–996

3 **(D)** The patient has a Leydig cell tumor of the testis. These tumors are most often small, benign masses that may go unnoticed. Some patients have gynecomastia, however, caused by androgenic or estrogenic hormone production (or both) by the tumor. Most patients are young to middle-aged men; sexual precocity may occur in the few boys who have such tumors. Choriocarcinomas are grossly soft and hemorrhagic masses that have large bizarre syncytiotrophoblast and cytotrophoblast cells and are aggressive. Embryonal carcinomas are large, aggressive tumors that have a variegated gross appearance and primitive cells with large, hyperchromatic nuclei. Gonadoblastomas are rare testicular tumors that arise in the setting of gonadal dysgenesis. A pure seminoma can be uniformly brown on cut surface, but often has a lymphoid stroma, and is not likely to secrete androgens or estrogens. Pure teratomas are rare and contain elements of three germ layers. Yolk sac tumors have cells that organize into primitive endodermal sinuses (Schiller-Duval bodies).

BP8 690, 695PBD7 1046PBD8 982–983

4 **(C)** The patient's lesions are characteristic of condyloma acuminatum, which is typical of human papillomavirus (HPV) infection. A condyloma acuminatum is a benign, recurrent squamous epithelial proliferation resulting from infection with HPV, one of many sexually transmitted diseases that can occur in sexually active individuals. Koilocytosis is particularly characteristic of HPV infection. Candidiasis can be associated with inflammation, such as balanoposthitis, but not condylomata. Recurrent gonococcal infection indicates that the patient is sexually active and at risk for additional

infections, but is not the cause for the condylomata. Gonococcal infection causes suppurative lesions in which there may be liquefactive necrosis and a neutrophilic exudate or mixed inflammatory infiltrates with chancroid. Circumcision generally reduces risks for infections. Phimosis is a nonretractile prepuce, and paraphimosis refers to forcible retraction of the prepuce that produces pain and urinary obstruction.

BP7 677BP8 709PBD7 1035–1036PBD8 982–983

5 **(D)** The patient has more than 10 leukocytes per high-power field, indicating prostatitis. Chronic abacterial prostatitis is the most common form of the disorder. Patients typically do not have a history of recurrent urinary tract infections. Nodular prostatic hyperplasia by itself is not an inflammatory process. Patients with acute bacterial prostatitis, most often caused by *Escherichia coli* infection, have fever, chills, and dysuria; on rectal examination, the prostate is very tender. Syphilis is a disease of the external genitalia, although the testis may be involved. Prostate carcinomas generally do not have a significant amount of acute inflammation, and metastases are most often associated with pain; most prostatic conditions causing dysuria are benign.

BP7 664–665BP8 695–696PBD7 1047–1048PBD8 993–994

6 **(A)** α-Fetoprotein (AFP) is a product of yolk sac cells that can be shown by immunohistochemical testing. Pure yolk sac tumors are rare in adults, but yolk sac components are common in mixed nonseminomatous tumors. Leydig cells produce androgens. Pure seminomas do not produce AFP. Cytotrophoblasts do not produce a serum marker, but they may be present in a choriocarcinoma along with syncytiotrophoblasts, which do produce human chorionic gonadotropin. Embryonal carcinoma cells by themselves do not produce any specific marker. Embryonal carcinoma cells are common in nonseminomatous tumors, however, and are often mixed with other cell types. Lymphoblasts may be seen in high-grade non-Hodgkin lymphomas, which do not produce hormones.

BP7 661–664BP8 690–695PBD7 1043, 1045PBD8 989–990

7 **(A)** This patient has a choriocarcinoma, the most aggressive testicular carcinoma. It often metastasizes widely. The primitive syncytial cells mimic the syncytiotrophoblast of placental tissue and stain for human chorionic gonadotropin. α-Fetoprotein is a marker that is more likely to be found in mixed tumors with a yolk sac component. Vimentin is more likely to be seen in sarcomas, which are rare in the testicular region. CD20 is a lymphoid marker for B cells. Testosterone is found in Leydig cells. Carcinoembryonic antigen (CEA) is found in a variety of epithelial neoplasms, particularly adenocarcinomas. CA-125 is best known as a marker for ovarian epithelial malignant tumors.

BP7 661–664BP8 690–695PBD7 1043–1044, 1046PBD8 990

8 **(B)** The prostate-specific antigen (PSA) level is significantly elevated in this patient. The increase over time is more likely to be indicative of carcinoma. Typically, prostatic carcinomas are adenocarcinomas that form small glands packed back to back. Many adenocarcinomas of the prostate do not produce obstructive symptoms and may not be palpable on digital rectal examination. Inflammation and nodular hyperplasias can increase the PSA level, although not to a high level that increases significantly over time. Prostatic intraepithelial neoplasia, although an antecedent to adenocarcinoma, is not likely to increase the PSA significantly over time.

BP7 667–669BP8 698–700PBD7 1054–1056PBD8 1001–1002

9 **(A)** Mumps is a common childhood infection that can produce parotitis. Adults who have this infection more often develop orchitis. The orchitis is usually not severe, and its involvement of the testis is patchy; infertility is not a common outcome. Cryptorchidism results from failure of the testis to descend into the scrotum normally; the abnormally positioned testis becomes atrophic throughout. A hydrocele is a fluid collection outside the body of the testis that does not interfere with spermatogenesis. Klinefelter syndrome and estrogen therapy can cause tubular atrophy, although it is generalized in both cases. Patchy loss of seminiferous tubules indicates a local inflammatory process. Many chemotherapeutic agents are particularly harmful to rapidly and continuously proliferating testicular germ cells, but the effect would not be patchy within the testicular parenchyma. Patients who wish to father children may want to store sperm in a sperm bank before undergoing chemotherapy.

BP7 660BP8 690PBD7 1039PBD8 986

10 **(D)** The markedly hemorrhagic appearance results from testicular torsion that obstructs venous outflow to a greater extent than the arterial supply. Doppler ultrasound shows reduced or no vascular flow in the affected testis. An abnormally positioned or anchored testis in the scrotum is a risk factor for this condition. Tuberculosis can spread from the lung through the bloodstream, producing miliary tuberculosis, seen as multiple pale, millet-sized lesions, most often involving

the epididymis. Testicular carcinomas do not obstruct the blood flow. Parasitic infestation, typically filariasis, obstructs the flow of lymph, leading to gradual enlargement of the scrotum with thickening of the overlying skin. A previous vasectomy may lead to a small leakage of fluid and sperm, producing a localized sperm granuloma.

PBD7 1040PBD8 987

11 **(C)** Yolk sac tumors are typically seen in boys younger than 3 years old. The primitive glomeruloid structures are known as Schiller-Duval bodies. Choriocarcinomas contain large, hyperchromatic, syncytiotrophoblastic cells. Seminomas have sheets and nests of cells resembling primitive germ cells, often with an intervening lymphoid stroma. Teratomas contain elements of mature cartilage; bone; or other endodermal, mesodermal, or ectodermal structures. Embryonal carcinomas with yolk sac cells contain α-fetoprotein, but they are seen in adults. They are composed of cords and sheets of primitive cells. Leydig cell tumors may produce androgens or estrogens or both.

BP7 661–664BP8 690–695PBD7 1043–1044PBD8 989–990

12 **(C)** Phimosis can be congenital, but is more often a consequence of multiple episodes of balanitis (inflammation of the glans penis or foreskin). Balanitis leads to scarring that prevents retraction of the foreskin. Forcible retraction may result in vascular compromise, with further inflammation and swelling (paraphimosis). Epispadias is a congenital condition in which the penile urethra opens onto the dorsal surface of the penis. Bowenoid papulosis is a premalignant lesion of the penile shaft resulting from viral infection. Candidiasis is most likely to produce shallow ulcerations that are intensely pruritic.

BP7 658BP8 688PBD7 1035PBD8 982

13 **(B)** This patient has cryptorchidism, which results from failure of the testis to descend from the abdominal cavity into the scrotum during fetal development. One or both testes may be involved. It is associated with an increased risk of testicular cancer. An undescended testis eventually atrophies during childhood. Unilateral cryptorchidism usually does not lead to infertility, but it may be associated with atrophy of the contralateral descended testis. Mumps infection tends to produce patchy testicular atrophy, usually without infertility. Isolated cryptorchidism is a developmental defect that is usually sporadic and is not inherited in the germline.

BP7 659–660BP8 689–690PBD7 1037–1038PBD8 984–984

14 **(A)** This is the most common form of “pure” testicular germ cell tumor that may remain confined to the testis (stage I). The prognosis is good in most cases, even with metastases, because seminomas are radiosensitive. Human chorionic gonadotropin (hCG) levels may be slightly elevated in about 15% of patients with seminoma. Elevated hCG levels suggest a component of syncytial cells; very high levels suggest choriocarcinoma. α-Fetoprotein levels are elevated in testicular tumors with a yolk sac component, and many tumors with an embryonal cell component also contain yolk sac cells. Testosterone is a product of Leydig cells, not germ cells. Fragile X syndrome is associated with mental retardation. The testes are enlarged bilaterally. Klinefelter syndrome is associated with decreased testicular size and reduced fertility.

BP7 661–664BP8 690–695PBD7 1040–1042PBD8 988–989

1 5 **(A)** Hypospadias is a congenital condition seen in about 1 in 300 male infants. The inguinal hernia and the cryptorchidism are abnormalities that may accompany this condition. Phimosis is a constriction preventing retraction of the prepuce. It can be congenital, but more likely is the result of inflammation of the foreskin of the penis (e.g., balanitis, a form of local inflammation of the glans penis). Epispadias is a congenital condition in which the urethra opens on the dorsal aspect of the penis. Bowen disease, which is squamous cell carcinoma in situ of the penis, occurs in adults.

BP7 658BP8 687–688PBD7 1035PBD8 982

16 **(B)** Genital candidiasis can occur in individuals without underlying illnesses, but it is far more common in individuals with diabetes mellitus. Warm, moist conditions at these sites favor fungal growth. Scabies mites are more likely to be found in linear burrows in epidermis scraped from the extremities. Neoplasms may ulcerate, but such lesions are unlikely to be shallow or multiple without a mass lesion present. Intranuclear inclusions suggest a viral infection; however, diabetes is not a risk factor for genital viral infections. These lesions are too large and numerous to be syphilitic chancres.

BP7 658BP8 688PBD7 1035PBD8 982

17 **(E)** Androgens are the major hormonal stimuli of glandular and stromal proliferation resulting in nodular prostatic hyperplasia. Although testosterone production decreases with age, prostatic hyperplasia increases, probably because of an increased expression of hormonal receptors that enhance the effect of any dihydrotestosterone that is present. The 5α-

reductase inhibitors, such as finasteride, diminish the prostate volume, specifically the glandular component, leading to improved urine flow. The α_1-adrenergic receptor blockers, such as tamsulosin, cause smooth muscle in the bladder neck and prostate to relax, which relieves symptoms and improves urine flow immediately. The other listed conditions are not amenable to therapy with these drugs.

BP7 665–666BP8 696–698PBD7 1048–1049PBD8 994–995

18 **(C)** Tuberculosis is an uncommon infection in the testes, but it can occur with disseminated disease. The infection typically starts in the epididymis and spreads to the body of the testis. Mumps produces patchy orchitis with minimal inflammation, which heals with patchy fibrosis. Syphilis involves the body of the testis, and there can be gummatous inflammation with neutrophils, necrosis, and some mononuclear cells. Gonococcal infections produce acute inflammation. Sarcoidosis produces noncaseating granulomas that are not likely to be found in the testis.

BP7 660BP8 690PBD7 1039PBD8 986

19 **(D)** Bowen disease is a form of squamous cell carcinoma in situ. Similar to carcinoma in situ elsewhere, it has a natural history of progression to invasive cancer if untreated. Poor hygiene and infection with human papillomavirus (particularly types 16 and 18) are factors that favor development of dysplasias and cancer of the genital epithelia. Syphilis is a sexually transmitted disease that produces a hard chancre, which heals in a matter of weeks. Balanitis is an inflammatory condition without dysplasia. A soft chancre may be seen with *Haemophilus ducreyi* infections. Condylomas are raised, whitish lesions.

BP7 658BP8 688–689PBD7 1036PBD8 983–984

20 **(H)** The presence of a hard irregular nodule, along with the extremely high prostate-specific antigen (PSA) level, points most clearly to prostate carcinoma. Modest elevations of the PSA concentration can occur in nodular hyperplasia of the prostate and prostatitis. Symptoms of urinary obstruction are more prominent in nodular hyperplasia because the nodules are in the periurethral region, but this sign is insufficient to distinguish cancer from hyperplasia. Similarly, renal failure owing to obstruction or infiltration is most common with nodular hyperplasia, but can occur with cancer as well. Levels of alkaline phosphatase are elevated when prostate carcinoma gives rise to osteoblastic metastases. Although staging and grading schemes for malignant disease seem daunting, they are applied intuitively. The lowest stage is the smallest, most localized tumor; higher stages represent larger tumors or spread of the disease inside or outside of the primary organ site. Grading schemes also start with the lowest, most well-differentiated tumor, as seen with the microscope. Higher grade tumors have increasingly abnormal-appearing cells and structures so poorly differentiated that they hardly resemble their site of origin. In this case, the prostate cancer has the highest grade (it does not have glandular structures) and the highest stage (it has metastasized to the spine).

BP7 667–669BP8 698–700PBD7 1050–1056PBD8 997–1000

21 **(A)** He has prostatic adenocarcinoma with back-to-back glands and prominent nucleoli. Alterations of the *glutathione S-transferase* (*GSTP1*) gene allow damage from carcinogens. Other genetic abnormalities in prostate cancer include variations in CAG repeats in the *androgen receptor* gene, *BRCA2* mutations, and translocation of *ETS* family transcription genes. His prostate-specific antigen (PSA) level is twice the upper limit of normal. This is worrisome, but not an absolute indication of prostate cancer. Elevated PSA levels can occur with nodular hyperplasia or prostatitis. A higher level or a level that increases over time or an increased free PSA is more suggestive of carcinoma. Recurrent urinary tract infections and hydronephrosis are complications of obstruction more commonly from nodular prostatic hyperplasia. Naphthylamine compounds are linked to urothelial carcinomas. Tobacco use is associated with many cancers, including urothelial carcinoma and renal cell carcinoma. Increased dihydrotestosterone output from prostatic stromal cells drives nodular hyperplasia.

BP7 667–669BP8 698–700PBD7 1055PBD8 1001–1002

22 **(E)** Hydrocele is one of the most common causes of scrotal enlargement. It consists of a fluid collection within the tunica vaginalis. Most cases are idiopathic, although some may result from local inflammation. A varicocele is a collection of dilated veins (pampiniform plexus) that may produce increased warmth, which inhibits spermatogenesis. Elephantiasis is a complication of parasitic filarial infections involving the inguinal lymphatics. Orchitis involves the body of the testis without marked enlargement, but with tenderness. A seminoma is typically a firm unilateral mass.

BP7 659BP8 689PBD7 1047PBD8 993

23 **(B)** The clinical features are typical of nodular hyperplasia of the prostate, and slight elevation of the PSA level can

occur. A PSA level that remains unchanged for 1 year, as in this case, is less likely to be found with a prostate cancer. Finasteride is a 5-α reductase inhibitor that decreases formation of dihydrotestosterone (DHT) that binds to androgen receptors in prostatic stromal and epithelial cells, driving proliferation with prostate gland enlargement. However, α-1-adrenergic blockers that diminish smooth muscle tone are somewhat more effective in treating nodular hyperplasia. Estrogen therapy has been used as antihormonal therapy in prostate cancer. Mitoxantrone is a chemotherapy agent which when given with prednisone has been shown effective in treating advanced prostate cancers. Nitrofurantoin is an antibiotic that is often used in treating urinary tract infections.

BP7 665–666BP8 696–698PBD7 1047–1050PBD8 994–996

24 **(D)** The tumor has elements of all three germ layers and is a teratoma. It is uncommon for teratomas in men to be completely benign. The most common additional histologic component is embryonal carcinoma. The elevated levels of human chorionic gonadotropin and α-fetoprotein indicate that this is a mixed tumor with elements of choriocarcinoma and yolk sac cells. The size of the tumor, age of the patient, location of the tumor (e.g., right, left, cryptorchid), and differentiation of the glandular epithelium are not markers of malignancy. On examining more histologic sections from the mass, the pathologist would find the malignant elements.

BP7 661–664BP8 690–695PBD7 1044–1045PBD8 990–991

25 **(B)** Prostatic intraepithelial neoplasia (PIN) is a potential precursor of prostatic adenocarcinoma. By itself, it does not warrant therapy because only about one third of patients diagnosed with PIN develop invasive cancer within 10 years. Conversely, in about 80% of cases in which prostate cancer is present, PIN can be found in the surrounding tissue. PIN usually does not increase the PSA levels. In this case, the elevation in PSA levels was probably caused by the coexistent hyperplasia. Following the patient with PSA tests can aid in determining if cancer has developed. Antibiotic therapy is appropriate in the treatment of an infectious process, not for PIN. Radiation and chemotherapy are reserved for malignancies, not for a preneoplastic condition. Surgical resection of the prostate gland is considered when a diagnosis of adenocarcinoma is established.

BP7 668BP8 699PBD7 1053PBD8 999

22. The Female Genital Tract

PBD7 and PBD8 Chapter 22: The Female Genital Tract

BP7 and BP8 Chapter 19: Female Genital System and Breast

1 A 24-year-old woman experiences sudden onset of severe lower abdominal pain. Physical examination shows no masses, but there is severe tenderness in the right lower quadrant. A pelvic examination shows no lesions of the cervix or vagina. Bowel sounds are detected. An abdominal ultrasound scan shows a 4-cm focal enlargement of the proximal right fallopian tube. A dilation and curettage procedure shows only decidua from the endometrial cavity. Which of the following laboratory findings is most likely to be reported for this patient?

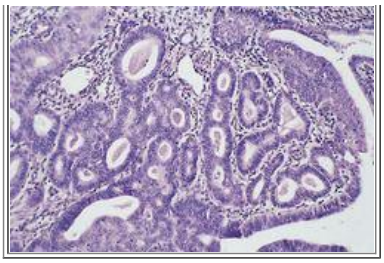
- □ (A) Cervical culture positive for *Neisseria gonorrhoeae*
- □ (B) 69,XXY karyotype on decidual tissue
- □ (C) Positive result of serum pregnancy test
- □ (D) Positive result of serologic testing for syphilis
- □ (E) Pap smear showing *Candida*

2 A 30-year-old, sexually active woman has had a mucopurulent vaginal discharge for 1 week. On pelvic examination, the cervix appears reddened around the os, but no erosions or mass lesions are present. A Pap smear shows numerous neutrophils, but no dysplastic cells. A cervical biopsy specimen shows marked follicular cervicitis. Which of the following infectious agents is most likely to produce these findings?

- □ (A) *Chlamydia trachomatis*
- □ (B) *Candida albicans*
- □ (C) *Gardnerella vaginalis*
- □ (D) Herpes simplex virus
- □ (E) Human papillomavirus
- □ (F) *Neisseria gonorrhoeae*
- □ (G) *Trichomonas vaginalis*

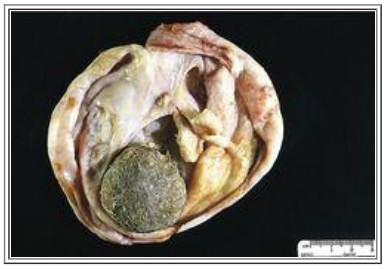
3 A 36-year-old woman has had menorrhagia and pelvic pain for several months. She had a normal, uncomplicated pregnancy 10 years ago. She has been sexually active with one partner for the past 20 years and has had no dyspareunia. On physical examination, she is afebrile. A pelvic examination shows a symmetrically enlarged uterus, with no apparent nodularity or palpable mass. A serum pregnancy test result is negative. What is the most likely diagnosis?

- □ (A) Endometriosis
- □ (B) Leiomyoma
- □ (C) Endometrial hyperplasia
- □ (D) Adenomyosis
- □ (E) Chronic endometritis



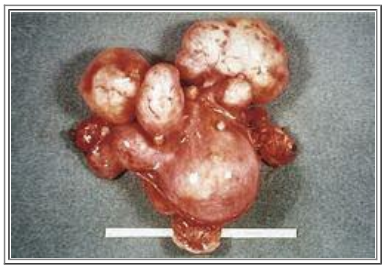
4 A 45-year-old woman has had menometrorrhagia for the past 3 months. On physical examination, there are no remarkable findings. The microscopic appearance of an endometrial biopsy specimen is shown in the figure. The patient undergoes a dilation and curettage, and the bleeding stops, with no further problems. What condition is most likely to produce these findings?

- □ (A) Ovarian mature cystic teratoma
- □ (B) Chronic endometritis
- □ (C) Failure of ovulation
- □ (D) Pregnancy
- □ (E) Use of oral contraceptives



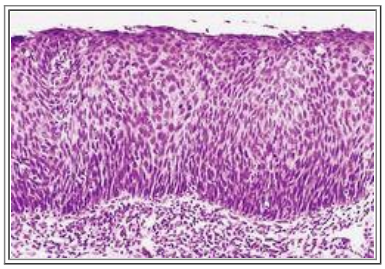
5 A 31-year-old woman has had dull, constant abdominal pain for 6 months. On physical examination, the only finding is a right adnexal mass. CT scan of the pelvis shows a 7-cm circumscribed mass that involves the right ovary and contains irregular calcifications. The right fallopian tube and ovary are surgically excised. The gross appearance of the ovary, which has been opened, is shown in the figure. What is the most likely diagnosis?

- □ (A) Mucinous cystadenoma
- □ (B) Choriocarcinoma
- □ (C) Dysgerminoma
- □ (D) Serous cystadenoma
- □ (E) Mature cystic teratoma



6 A healthy 52-year-old woman has had a feeling of pelvic heaviness for the past 11 months. There is no history of abnormal bleeding, and her last menstrual period was 8 years ago. Her physician palpates an enlarged nodular uterus on bimanual pelvic examination. A Pap smear shows no abnormalities. Pelvic CT scan shows multiple solid uterine masses; there is no evidence of necrosis or hemorrhage. A total abdominal hysterectomy is performed. Based on the gross appearance of the mass shown in the figure, what is the most likely diagnosis?

- □ (A) Metastases
- □ (B) Endometriosis
- □ (C) Infiltrative leiomyosarcoma
- □ (D) Multiple leiomyomas
- □ (E) Adenomyosis



7 A 33-year-old woman comes to the physician for a routine health maintenance examination. On physical examination, there are no abnormal findings. A Pap smear shows abnormalities; colposcopy and a biopsy are performed. The figure shows the microscopic appearance of the biopsy specimen. Which of the following factors is likely to have contributed most to the development of this lesion?

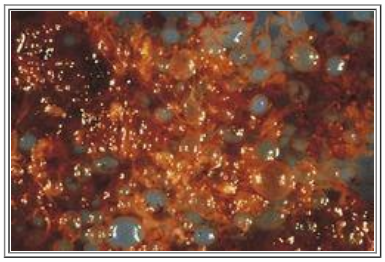
- □ (A) Diethylstilbestrol (DES) exposure
- □ (B) Recurrent *Candida* infections
- □ (C) Early age at first intercourse
- □ (D) Multiple pregnancies
- □ (E) Postmenopausal estrogen therapy

8 A 62-year-old, obese, nulliparous woman had an episode of vaginal bleeding, which produced only about 5 mL of blood. On pelvic examination, there appears to be no enlargement of the uterus, and the cervix appears normal. A Pap smear shows cells consistent with adenocarcinoma. Which of the following conditions is most likely to have contributed to the development of this malignancy?

- □ (A) Endometrial hyperplasia
- □ (B) Chronic endometritis
- □ (C) Use of oral contraceptives
- □ (D) Human papillomavirus infection
- □ (E) Adenomyosis

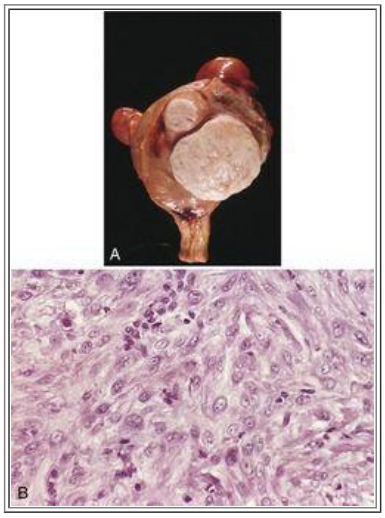
9 A 36-year-old primigravida developed peripheral edema late in the second trimester. On physical examination, her blood pressure was 155/95 mm Hg. Urinalysis showed 2+ proteinuria, but no blood, glucose, or ketones. At 36 weeks, the patient gives birth to a normal viable, but low-birth-weight, infant. Her blood pressure returns to normal, and she no longer has proteinuria. Which of the following is most likely to be found on examination of the placenta?

- □ (A) Chronic villitis
- □ (B) Partial mole
- □ (C) Hydrops
- □ (D) Multiple infarcts
- □ (E) Choriocarcinoma



10 A 22-year-old woman, G2, P1, is in the early second trimester. She has noted a small amount of vaginal bleeding for the past week and has had marked nausea and vomiting for several weeks. On physical examination, the uterus measures large for dates. Ultrasound shows intrauterine contents with a “snowstorm appearance,” and no fetus is identified. The gross appearance of tissue obtained by dilation and curettage is shown in the figure. Which of the following substances is most likely to be increased in the serum?

- □ (A) α-Fetoprotein
- □ (B) Thyroxine
- □ (C) Estradiol
- □ (D) Lactate dehydrogenase
- □ (E) Human chorionic gonadotropin
- □ (F) Human placental lactogen
- □ (G) Acetylcholinesterase



11 A 46-year-old perimenopausal woman has had pelvic discomfort for 5 months. On physical examination, the uterus appears slightly enlarged, and there are no adnexal masses. The cervix and vagina appear normal. A total abdominal hysterectomy is performed. The figure shows the gross (A) and microscopic (B) features of the uterus. Which of the following is most likely prevented by the hysterectomy performed on this patient?

- □ (A) Iron deficiency
- □ (B) Malignant transformation
- □ (C) Endometriosis
- □ (D) Osteoporosis
- □ (E) Invasive mole
- □ (F) Preeclampsia

12 A 62-year-old childless woman noticed a blood-tinged vaginal discharge twice during the past month. Her last menstrual period was 14 years ago. Bimanual pelvic examination shows that the uterus is normal in size, with no palpable adnexal masses. There are no cervical erosions or masses. Her body mass index is 33. Her medical history indicates that for the past 30 years she has had hypertension and type 2 diabetes mellitus. An endometrial biopsy specimen is most likely to show which of the following?

- □ (A) Adenomyosis
- □ (B) Leiomyosarcoma
- □ (C) Adenocarcinoma
- □ (D) Squamous cell carcinoma
- □ (E) Choriocarcinoma
- □ (F) Malignant mixed müllerian tumor

13 A 23-year-old woman, G3, P2, has a spontaneous abortion at 15 weeks' gestation. The male fetus is small for gestational age and is malformed and has syndactyly of the third and fourth digits of each hand. The placenta also is small, and shows 0.5-cm grapelike villi scattered among morphologically normal villi. Chromosomal analysis of placental tissue is most likely to show which of the following karyotypes?

- □ (A) 69,XXY
- □ (B) 46,XX
- □ (C) 23,Y
- □ (D) 45,X
- □ (E) 47,XXY
- □ (F) 47,XY,+18

14 A 54-year-old woman has had weight loss accompanied by abdominal enlargement for the past 6 months. She is concerned because of a family history of ovarian carcinoma. On physical examination, there are no lesions of the cervix, and the uterus is normal in size, but there is a left adnexal mass. An abdominal ultrasound scan shows a 10-cm cystic mass in the left adnexal region, with scattered 1-cm peritoneal nodules. Cytologic studies of peritoneal fluid show malignant cells consistent with a cystadenocarcinoma. Which of the following mutated genes is most likely a factor in the development of this neoplasm?

- □ (A) *RAS*
- □ (B) *BRCA1*
- □ (C) *ERBB2* (*HER2*)
- □ (D) *MYC*
- □ (E) *RB1*

15 A 4-year-old girl is brought to the physician by her parents, who noticed blood-stained underwear and "something" protruding from her external genitalia. On physical examination, there are polypoid, grapelike masses projecting from the vagina. Histologic examination of a biopsy specimen from the lesion shows small, round tumor cells, some of which have eosinophilic straplike cytoplasm. Immunohistochemical staining shows desmin in these cells. What is the most likely diagnosis?

- □ (A) Neuroblastoma
- □ (B) Embryonal rhabdomyosarcoma

□ (C) Condyloma acuminatum

□ (D) Vulvar intraepithelial neoplasm

□ (E) Infiltrating squamous cell carcinoma

16 A 42-year-old woman has had menometrorrhagia for the past 2 months. She has no history of irregular menstrual bleeding, and she has not yet reached menopause. On physical examination, there are no vaginal or cervical lesions, and the uterus appears normal in size, but there is a right adnexal mass. An abdominal ultrasound scan shows the presence of a 7-cm solid right adnexal mass. Endometrial biopsy shows hyperplastic endometrium, but no cellular atypia. What is the most likely diagnosis?

□ (A) Mature cystic teratoma

□ (B) Endometrioma

□ (C) Corpus luteum cyst

□ (D) Metastasis

□ (E) Granulosa-theca cell tumor

□ (F) Struma ovarii

17 A 19-year-old woman has had pelvic pain for 1 week. A pelvic examination shows mild erythema of the ectocervix. A Pap smear shows many neutrophils, but no dysplastic cells. A cervical culture grows *Neisseria gonorrhoeae*. If the infection is not adequately treated, the patient will be at increased risk for which of the following complications?

□ (A) Ectopic pregnancy

□ (B) Dysfunctional uterine bleeding

□ (C) Cervical carcinoma

□ (D) Endometrial hyperplasia

□ (E) Endometriosis

□ (F) Placenta previa

18 A 28-year-old, sexually active woman comes to her physician for a routine health maintenance examination. There are no abnormal findings on physical examination. The patient has been taking oral contraceptives for the past 10 years. A Pap smear shows a moderate dysplasia, or cervical intraepithelial neoplasia (CIN) II. What is the major significance of this finding?

□ (A) A cervicitis needs to be treated

□ (B) The patient has an increased risk of cervical carcinoma

□ (C) Condylomata acuminata are probably present

□ (D) An endocervical polyp needs to be excised

□ (E) The patient should stop taking oral contraceptives

19 A 40-year-old, G5, P5 woman has noticed lower abdominal pain with fever for the past 2 days. She delivered a normal term infant 1 week ago. On examination, she has a temperature of 37.4°C. There is a foul-smelling vaginal discharge. Which of the following pathologic findings is she most likely to have?

□ (A) Cervical epithelial dysplasia

□ (B) Endometrial neutrophilic infiltrates

□ (C) Myometrial smooth muscle neoplasm

□ (D) Ovarian endometrioma

□ (E) Tubal granulomatous inflammation

□ (F) Vaginal trichomonads

20 A 25-year-old woman has experienced discomfort during sexual intercourse for the past month. On physical examination, there are no lesions of the external genitalia. Pelvic examination shows a focal area of swelling on the left posterolateral inner labium that is very tender on palpation. A 3-cm cystic lesion filled with purulent exudate is excised. In which of the following structures is this lesion most likely to develop?

□ (A) Bartholin's gland

□ (B) Gartner duct

□ (C) Hair follicle

□ (D) Urogenital diaphragm

□ (E) Vestibular bulb

21 A 58-year-old woman has had dull pain in the lower abdomen for the past 6 months and minimal vaginal bleeding on three occasions. Her last menstrual period was 14 years ago. Pelvic examination shows a right adnexal mass, and the uterus appears normal in size. An abdominal ultrasound scan shows an 8-cm solid mass. A total abdominal hysterectomy is performed, and the mass is diagnosed as an ovarian granulosa-theca cell tumor. Which of the following additional lesions is most likely to be found in the excised specimen?

□ (A) Condylomata acuminata of the cervix

□ (B) Endometrial hyperplasia

□ (C) Metastases to the uterine serosa

□ (D) Bilateral chronic salpingitis

□ (E) Partial mole of the uterus

22 A 43-year-old woman has had postcoital bleeding for 6 months. She experienced menarche at age 11 and has had 12 sexual partners during her life. She continues to have regular menstrual cycles without abnormal intermenstrual bleeding. Pelvic examination shows a focal, slightly raised area of erythema on the cervix at the 5 o’clock position. A Pap smear shows high-grade cervical intraepithelial neoplasia (CIN III). In situ hybridization performed on cells from the cervix shows the presence of human papillomavirus type 16. If the cervical lesion is not treated, which of the following malignancies is she at greatest risk of developing?

□ (A) Clear cell carcinoma

□ (B) Immature teratoma

□ (C) Krukenberg tumor

□ (D) Leiomyosarcoma

□ (E) Papillary serous cystadenocarcinoma

□ (F) Sarcoma botryoides

□ (G) Squamous cell carcinoma

23 An 18-year-old woman has had pelvic discomfort for several months. On pelvic examination, there is a 10-cm right adnexal mass. An abdominal CT scan shows the mass to be solid and circumscribed. On surgical removal, the mass is solid and white, with small areas of necrosis. Microscopically, it contains mostly primitive mesenchymal cells along with some cartilage, muscle, and foci of neuroepithelial differentiation. What is the most likely diagnosis?

- □ (A) Brenner tumor
- □ (B) Dysgerminoma
- □ (C) Granulosa cell tumor
- □ (D) Immature teratoma
- □ (E) Leiomyosarcoma
- □ (F) Malignant mixed müllerian tumor
- □ (G) Sarcoma botryoides

24 A 32-year-old woman has cyclic abdominal pain that coincides with her menses. Attempts to become pregnant have failed over the past 5 years. There are no abnormal findings on physical examination. Laparoscopic examination shows numerous hemorrhagic 0.2- to 0.5-cm lesions over the peritoneal surfaces of the uterus and ovaries. Which of the following ovarian lesions is most likely to be seen during the laparoscopic procedure?

- □ (A) Fibroma
- □ (B) Brenner tumor
- □ (C) Endometriotic cyst
- □ (D) Krukenberg tumor
- □ (E) Mature cystic teratoma
- □ (F) Mucinous cystadenocarcinoma

25 A 37-year-old woman has noted increasing size of a red, pruritic lesion on her left labium over the past 7 months. On examination, this rough, scaly lesion is 0.4 × 0.9 cm. On physical examination, the lesions are slightly raised, soft pink to white in color, and 0.2 to 1 cm in diameter. The perineum appears normal; there is no lymphadenopathy, and there are no rectal lesions. A Pap smear shows no abnormal findings. The lesion is excised; on microscopic examination, there is infiltration of the lower dermis by large cells having pale blue to granular cytoplasm. What is the most likely diagnosis?

- □ (A) Condylomata acuminata
- □ (B) Extramammary Paget disease
- □ (C) Lichen sclerosus et atrophicus
- □ (D) Lichen simplex chronicus
- □ (E) Vulvar intraepithelial neoplasia

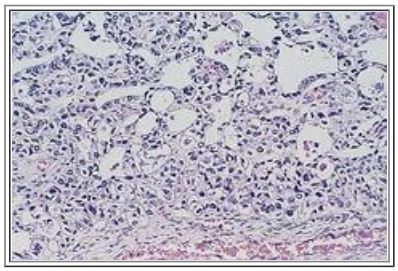
26 A 31-year-old woman has had a whitish, globular, vaginal discharge for the past week. On pelvic examination, the cervix appears erythematous, but there are no erosions or masses. A Pap smear shows budding cells and pseudohyphae. No dysplastic cells are present. Which of the following infectious agents is most likely to produce these findings?

- □ (A) *Trichomonas vaginalis*
- □ (B) *Ureaplasma urealyticum*
- □ (C) *Candida albicans*
- □ (D) *Chlamydia trachomatis*
- □ (E) *Neisseria gonorrhoeae*

27 A 57-year-old woman comes to the physician because she recently noticed a pale area of discoloration on the labia. Pelvic examination shows the presence of a 0.7-cm flat, white area on the right labia majora. A biopsy specimen shows

dysplastic cells that occupy about half the thickness of the squamous epithelium, with minimal underlying chronic inflammation. In situ hybridization shows human papillomavirus type 16 DNA in the epithelial cells. What is the most likely diagnosis?

- □ (A) Lichen sclerosus et atrophicus
- □ (B) Condyloma acuminatum
- □ (C) Squamous hyperplasia
- □ (D) Vulvar intraepithelial neoplasia
- □ (E) Chronic vulvitis
- □ (F) Contact dermatitis

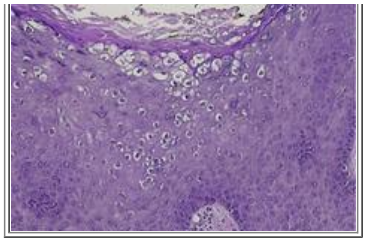


28 A 19-year-old, sexually active woman has had dyspareunia followed by vaginal bleeding for the past month. On pelvic examination, a red, friable, 2.5-cm nodular mass is seen on the anterior wall of the upper third of the vagina. The microscopic appearance of a biopsy specimen is shown in the figure. Which of the following conditions is likely to have contributed most to the origin of this neoplasm?

- □ (A) Diethylstilbestrol (DES) exposure
- □ (B) *Trichomonas* vaginitis
- □ (C) Polycystic ovaries
- □ (D) Human papillomavirus infection
- □ (E) Congenital adrenal hyperplasia

29 A 35-year-old woman presents with infertility. She has had dysmenorrhea, dyspareunia and pelvic pain on defecation for 4 years. Laparoscopic examination reveals red-blue nodules on the surface of the uterus and extensive adhesions between ovaries and the fallopian tubes. Histologic examination of a biopsy from one of the nodules shows hyperplastic endometrial glands and hemorrhage in the stroma. Molecular analysis of the biopsy material reveals hypomethylation of the promoter regions of the genes that encode steroidogenic factor-1 and estrogen receptor-β. There are no mutations in the *PTEN*, *KRAS* and *hMLH1* genes. Which of the following is an appropriate treatment modality in this case?

- □ (A) Aromatase inhibitors
- □ (B) Chemotherapy
- □ (C) Estrogen
- □ (D) Progesterone
- □ (E) Surgical removal



30 A 36-year-old woman has noticed that warty vulvar lesions have been increasing in size and number over the past 5 years. On physical examination, there are several 0.5- to 2-cm, red-pink, flattened lesions with rough surfaces present on the vulva and perineum. One of the larger lesions is excised; its microscopic appearance is shown in the figure. Which of the following infectious agents is most likely to produce these lesions?

- □ (A) Human papillomavirus
- □ (B) *Chlamydia trachomatis*
- □ (C) *Treponema pallidum*
- □ (D) *Haemophilus ducreyi*
- □ (E) *Candida albicans*

31 A 35-year-old woman has a routine Pap smear for the first time. The results indicate that dysplastic cells are present, and the lesion is consistent with cervical intraepithelial neoplasia (CIN) III. The patient is referred to a gynecologist, who performs colposcopy and takes several biopsy specimens that all show CIN III. Conization of the cervix shows a focus of microinvasion at the squamocolumnar junction. Based on these findings, what is the next step in treating this patient?

- □ (A) Course of radiation therapy
- □ (B) Hysterectomy
- □ (C) Bone scan for metastatic lesions
- □ (D) Pelvic exenteration
- □ (E) No further therapy is indicated

32 A 20-year-old woman experienced menarche at age 14 and had regular menstrual cycles for several years. For the past year, she has had oligomenorrhea and has developed hirsutism. She has noticed a 10-kg weight gain in the past 4 months. On pelvic examination, there are no vaginal or cervical lesions, the uterus is normal in size, and the adnexa are prominent. A pelvic ultrasound scan shows that each ovary is about twice normal size, whereas the uterus is normal in size. Which of the following conditions is most likely to be present?

- □ (A) Immature teratomas
- □ (B) Polycystic ovaries
- □ (C) Krukenberg tumors
- □ (D) Tubo-ovarian abscesses
- □ (E) Ovarian cystadenocarcinomas

33 A 28-year-old woman sees her physician because she has had fever, pelvic pain, and a feeling of pelvic heaviness for the past week. Pelvic examination shows a palpable left adnexal mass. Laparoscopy shows an indistinct left fallopian tube that is part of a 5-cm circumscribed, red-tan mass involving the left adnexal region. Which of the following infectious agents is most likely to produce these findings?

- □ (A) Human papillomavirus
- □ (B) *Mycobacterium tuberculosis*

□ (C) *Treponema pallidum*

□ (D) *Chlamydia trachomatis*

□ (E) *Candida albicans*

□ (F) Herpes simplex virus

□ (G) *Haemophilus ducreyi*

34 A 42-year-old woman has a Pap smear as part of a routine health maintenance examination. There are no remarkable findings on physical examination. The Pap smear shows cells consistent with a high-grade squamous intraepithelial lesion (HSIL) with human papillomavirus subtype 18. Cervical biopsy specimens are obtained, and microscopic examination confirms the presence of extensive moderate dysplasia (CIN II) along with intense chronic inflammation with squamous metaplasia in the endocervical canal. What is the most likely explanation for proceeding with cervical conization for this patient?

□ (A) She is at risk for invasive carcinoma

□ (B) Human papillomavirus infection cannot be treated

□ (C) She is perimenopausal

□ (D) She has chronic cervicitis

□ (E) Her reproductive years are over

35 A 20-year-old woman notices a bloody, brownish vaginal discharge. The next day, she sees a physician because of shortness of breath. On physical examination, a 3-cm, red-brown mass is seen on the lateral wall of the vagina. A chest radiograph shows numerous 2- to 5-cm nodules in both lungs. A biopsy specimen of the vaginal mass shows malignant cells resembling syncytiotrophoblasts. Which the following proteins is most likely to be elevated in the serum?

□ (A) Human chorionic gonadotropin

□ (B) α-Fetoprotein

□ (C) Estradiol

□ (D) Testosterone

□ (E) Thyroxine

□ (F) Carcinoembryonic antigen

36 A 14-year-old girl began menstruation 1 year ago. She now has abnormal uterine bleeding, with menstrual periods that are 2 to 7 days long and 2 to 6 weeks apart. The amount of bleeding varies from minimal spotting to a very heavy flow. On physical examination, there are no remarkable findings. A pelvic ultrasound scan shows no abnormalities. Which of the following is most likely to produce these findings?

□ (A) Endometrial polyp

□ (B) Anovulatory cycles

□ (C) Ectopic pregnancy

□ (D) Uterine leiomyomata

□ (E) Endometrial carcinoma

37 A 51-year-old woman is concerned about pale areas on her labia that have been slowly enlarging for the past year. The areas cause discomfort and become easily irritated. Physical examination shows pale gray to parchment-like areas of skin that involve most of the labia majora, labia minora, and introitus. The introitus is narrowed. A biopsy specimen shows thinning of the squamous epithelium, a dense band of upper dermal hyaline collagen, and scattered upper dermal

mononuclear inflammatory cells. What is the most likely diagnosis?

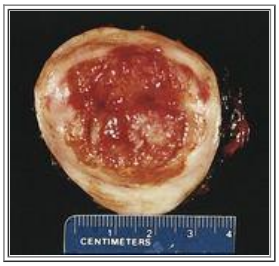
- □ (A) Pelvic inflammatory disease
- □ (B) Lichen sclerosus et atrophicus
- □ (C) Vulvar intraepithelial neoplasia
- □ (D) Extramammary Paget disease
- □ (E) Human papillomavirus infection

38 A 40-year-old, nulliparous woman has had menorrhagia for the past 6 months. On physical examination her blood pressure is 150/90 mm Hg: there are no cervical lesions or adnexal masses, and the uterus is normal in size. She is 155 cm (5 feet 1 inch) tall and weighs 74.5 kg (body mass index 38). A Pap smear shows atypical glandular cells of uncertain significance. Hemoglobin A1c concentration is 9.8%. Endometrial biopsy shows complex hyperplasia with atypia; molecular analysis detects loss of *PTEN* gene heterozygosity and enhanced AKT phosphorylation. What is further biochemical analysis of her endometrium most likely to reveal?

- □ (A) Decreased glucose uptake
- □ (B) Decreased prostaglandin synthesis
- □ (C) Increased aerobic glycolysis
- □ (D) Increased glycogen storage
- □ (E) Increased oxidative phosphorylation

39 A 35-year-old woman has had increasing abdominal enlargement for the past 6 months. She states that she feels like she is pregnant, but results of a pregnancy test are negative. On physical examination, there is abdominal distention with a fluid wave. A pelvic ultrasound scan shows bilateral cystic ovarian masses, 10 cm on the right and 7 cm on the left. The masses are surgically removed. On gross examination, the excised masses are unilocular cysts filled with clear fluid, and papillary projections extend into the central lumen of the cyst. Microscopic examination shows that the papillae are covered with atypical cuboidal cells that invade underlying stroma. Psammoma bodies are present. What is the most likely diagnosis?

- □ (A) Endometrioid tumor
- □ (B) Clear cell carcinoma
- □ (C) Cystadenocarcinoma
- □ (D) Dysgerminoma
- □ (E) Granulosa cell tumor
- □ (F) Malignant mixed müllerian tumor
- □ (G) Mature cystic teratoma
- □ (H) Sertoli-Leydig cell tumor



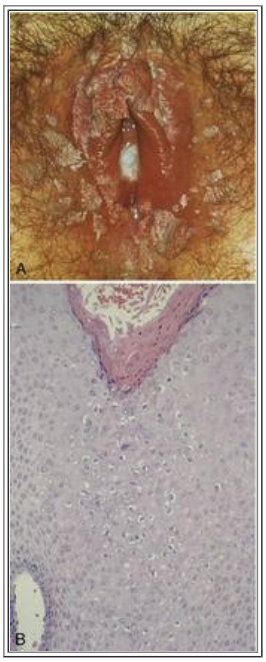
40 A 45-year-old woman has had a small amount of vaginal bleeding and a brownish, foul-smelling discharge for the past

month. On pelvic examination, there is a 3-cm lesion on the ectocervix, shown in the figure. Microscopic examination of the lesion is most likely to show which of the following?

- □ (A) Adenocarcinoma
- □ (B) Cervical intraepithelial neoplasia
- □ (C) Chronic cervicitis
- □ (D) Clear cell carcinoma
- □ (E) Extramammary Paget disease
- □ (F) Squamous cell carcinoma

41 A healthy 30-year-old woman comes to the physician for a routine health maintenance examination. No abnormalities are found on physical examination. A screening Pap smear shows cells consistent with a low-grade squamous intraepithelial lesion (LSIL). Subsequent cervical biopsy specimens confirm the presence of cervical intraepithelial neoplasia (CIN) I. Which of the following risk factors is most likely related to her Pap smear findings?

- □ (A) Oral contraceptive use
- □ (B) Diethylstilbestrol (DES) exposure
- □ (C) Vitamin B_{12} (cobalamin) deficiency
- □ (D) Prior treatment for squamous cell carcinoma
- □ (E) Multiple sexual partners



42 A 24-year-old woman has had lesions of the external genitalia that first appeared several years ago, after she vacationed at a resort near Negril, Jamaica, where she goes every year. The figure shows the gross appearance of the external genitalia (A) and histologic features (B) of an excised lesion. Which of the following factors is likely to have contributed most to the development of these lesions?

- □ (A) Lack of menstrual cycles
- □ (B) Inheritance of a faulty tumor-suppressor gene
- □ (C) Poorly controlled diabetes mellitus

□ (D) Exposure to ultraviolet light

□ (E) Sexual intercourse

43 A 40-year-old woman has noticed progressive enlargement of the abdomen over the past 5 months, although her diet has not changed, and she has been exercising more. Physical examination shows no palpable masses, but a fluid wave is present. Paracentesis yields 500 mL of slightly cloudy fluid. Cytologic examination of the fluid shows malignant cells. An abdominal ultrasound scan shows a 15-cm multilobular mass that involves the right adnexal region. The uterus is normal in size. The mass is surgically removed; the figure shows the gross features of a section of the excised mass. What is the most likely diagnosis?

□ (A) Immature teratoma

□ (B) Mucinous cystadenocarcinoma

□ (C) Granulosa cell tumor

□ (D) Choriocarcinoma

□ (E) Dysgerminoma

44 A 35-year-old primigravid woman is in the seventh month of an otherwise unremarkable pregnancy when she develops worsening headaches along with a 3-kg weight gain over 1 week. This morning she had a generalized seizure. On physical examination, she is afebrile, but her blood pressure is 190/110 mm Hg (it was 120/80 mm Hg at a prenatal visit 1 month ago). She has edema involving her head and all extremities. Fetal heart tones of 140/min and fetal movement are present. Laboratory studies show hemoglobin, 12.5 g/dL; hematocrit, 37.6%; MCV, 92 μm^3; platelet count, 199,000/mm^3; serum creatinine, 1 mg/dL; potassium, 4.2 mmol/L; and glucose, 101 mg/dL. Urinalysis shows 2+ proteinuria, but no hematuria, RBCs, WBCs, or casts. Which of the following is the most likely underlying factor in the causation of her disease?

□ (A) Gestational trophoblastic disease

□ (B) Disseminated intravascular coagulation

□ (C) Adrenal cortical hyperplasia

□ (D) Placenta ischemia

□ (E) Ovarian neoplasm producing estrogen

45 A study of patients with postmenopausal uterine bleeding reveals that some of them have malignant neoplasms that arise from prior atypical hyperplastic lesions. The peak incidence is between 55 and 65 years of age in women who have obesity, hypertension, and/or diabetes mellitus. Molecular analysis reveals mutations of the *PTEN* tumor suppressor gene in most of them. Their malignancies tend to remain localized for years before spread to local lymphatics. Which of the following neoplasms is most likely to have these characteristics?

□ (A) Clear cell carcinoma

□ (B) Endometrioid carcinoma

□ (C) Leiomyosarcoma

□ (D) Mixed mullerian tumor

□ (E) Serous carcinoma

□ (F) Stromal sarcoma

ANSWERS

1 **(C)** The patient has an ectopic pregnancy. Conditions predisposing to ectopic pregnancy include chronic salpingitis (which may be caused by gonorrhea, but a culture would be positive only with acute infection), intrauterine tumors, and endometriosis. In about half of cases, there is no identifiable cause. Gestational trophoblastic disease associated with a triploid karyotype, such as a complete or partial mole developing outside the uterus, is rare. Syphilis is not likely to produce a tubal mass with acute symptoms (a gumma is a rare finding). *Candida* produces cervicitis and vaginitis and is rarely invasive or extensive in immunocompetent patients.

BP7 701BP8 734–735PBD7 1105PBD8 1053–1054

2 **(A)** The redness of the cervix, the inflammatory cells in the cervical discharge, and the biopsy findings indicate that the patient has cervicitis. *Chlamydia trachomatis* is the most common cause of cervicitis in sexually active women. Candidiasis, gonorrhea, and trichomoniasis also are common. Candidiasis often produces a scant, white, curdlike vaginal discharge; gonorrhea may have an associated urethritis; and *Trichomonas* may produce a profuse homogeneous, frothy, and adherent yellow or green vaginal discharge. *Gardnerella* is found in bacterial vaginosis, a common condition caused by overgrowth of bacteria. *Gardnerella* infection produces a moderate, homogeneous, low-viscosity, adherent vaginal discharge that is white or gray and has a characteristic “fishy” odor; “clue” cells are seen on a wet mount. Herpetic infections are more likely to manifest as clear vesicles on the skin in the perineal region. Infection with human papillomavirus is associated with condylomata, dysplasias, and carcinoma.

BP7 685BP8 716–717PBD7 1062–1063, 1072–1073PBD8 1017

3 **(D)** In adenomyosis, endometrial glands extend from the endometrium down into the myometrium. The process may be superficial, but occasionally it is extensive, and the uterus becomes enlarged two to four times its normal size because of a reactive thickening of the myometrium. In endometriosis, endometrial glands and stroma are found outside the uterus in such sites as peritoneum, ovaries, and ligaments. A leiomyoma is a myometrial tumor mass that, if large, produces an asymmetric mass. Endometrial hyperplasias do not increase the size of the uterus. Chronic endometritis does not extend to the myometrium and does not increase uterine size.

BP7 689–690BP8 721PBD7 1083PBD8 1028–1029

4 **(C)** This patient has endometrial hyperplasia, which results from excessive estrogenic stimulation. This lesion often occurs with failure of ovulation about the time of menopause. Estrogen-secreting ovarian tumors also may produce endometrial hyperplasia, but teratomas are not known for this phenomenon. Hyperplasias do not develop from endometritis. A secretory pattern of the endometrium is seen in pregnancy, not the proliferative pattern shown in the figure. Oral contraceptives contain small doses of estrogenic compounds that do not lead to hyperplasia.

BP7 691BP8 723–724PBD7 1085–1086PBD8 1030–1031

5 **(E)** This patient has a cystic tumor with a mass of hair in the lumen. This is the typical appearance of a mature cystic teratoma. This tumor also is known as a dermoid cyst because it is cystic and filled with hair and sebum derived from ectodermal structures. Dermoid cysts are benign tumors of germ cell origin, and they can contain various ectodermally, endodermally, and mesodermally derived tissues. A mucinous cystadenoma is often multiloculated and filled with mucoid fluid, but it does not contain hair or calcifications. A choriocarcinoma is gestational in origin and is an aggressive neoplasm that usually has a hemorrhagic appearance. A dysgerminoma is a solid, lobulated, tan-white mass; it is the female equivalent of a male testicular seminoma. A serous cystadenoma is usually a unilocular cyst filled with clear fluid and little else.

BP7 698–700BP8 733PBD7 1099–1100PBD8 1047–1048

6 **(D)** The masses shown are well circumscribed, suggesting the presence of multiple benign tumors. Leiomyomas (“fibroids”) can be present in one third to one half of all women. They tend to enlarge during the reproductive years, and

then stop growing or involute after menopause. Most are asymptomatic. They are a common incidental finding in a uterus removed for another reason. Metastases of this size and location are unlikely to occur in a healthy-appearing individual. The small implants of endometriosis rarely exceed 1 to 2 cm in diameter; when a large mass forms, it is cystic and filled with "old" blood ("chocolate cyst"). A leiomyosarcoma is a rare tumor and is usually a large, solitary mass. Endometrial glands and stroma that extend into the myometrium constitute adenomyosis, a process that tends to enlarge the uterus diffusely, without nodularity.

BP7 692–693BP8 724–725PBD7 1089–1090PBD8 1036–1037

7 **(C)** The figure shows cervical intraepithelial neoplasia (CIN) III because the dysplasia involves the full thickness of the cervical epithelium. Such lesions arise more frequently in women who have had first intercourse at an early age, have multiple sexual partners, or have a male partner with multiple sexual partners. These factors are believed to increase the risk of infection with human papillomavirus (HPV), particularly types 16 and 18. HPV-16 and HPV-18 are associated with dysplasias and carcinomas of the cervix. Diethylstilbestrol (DES) exposure in utero is strongly associated with clear cell adenocarcinomas of the vagina and cervix. Recurrent *Candida* infections are a nuisance, but they are not premalignant. Pregnancy does not play a role in the development of cervical neoplasia. Most cervical dysplasias occur in premenopausal women. Estrogen therapy and the use of oral contraceptives do not increase the risk of cervical dysplasia.

BP7 686–688BP8 718–719PBD7 1073–1076PBD8 1019–1021

8 **(A)** The patient has an endometrial carcinoma. Estrogenic stimulation from anovulatory cycles, nulliparity, obesity, and exogenous estrogens (in higher amounts than found in birth control pills) gives rise to endometrial hyperplasia and can progress to endometrial carcinoma if the estrogenic stimulation continues. Atypical endometrial hyperplasias progress to endometrial cancer in about 25% of cases. Chronic endometritis and human papillomavirus infection (which is associated with squamous epithelial dysplasias and neoplasia) do not cause cancer. Adenomyosis increases the size of the uterus and is not a risk for endometrial carcinoma.

BP7 693–694BP8 725–727PBD7 1086–1088PBD8 1031–1034

9 **(D)** This patient has toxemia of pregnancy. Her condition is best classified as preeclampsia because she has hypertension, proteinuria, and edema, but no seizures. The placenta tends to be small because of reduced maternal blood flow and uteroplacental insufficiency; infarct and retroplacental hemorrhages can occur. Microscopically, the decidual arterioles may show acute atherosis and fibrinoid necrosis. A chronic villitis is characteristic of a congenital infection such as cytomegalovirus. In a partial mole, a fetus is present, but it is malformed and rarely liveborn. Placental hydrops often accompanies fetal hydrops in conditions such as infections and fetal anemias. A fetus is not present in a choriocarcinoma.

BP7 704–705BP8 737–738PBD7 1106–1110PBD8 1055–1057

10 **(E)** The figure shows a hydatidiform mole, or complete mole, with enlarged, grapelike villi that form the tumor mass in the endometrial cavity. These trophoblastic tumors secrete human chorionic gonadotropin. Molar pregnancies result from abnormal fertilization. In a complete mole, only paternal chromosomes are present. α-Fetoprotein is a marker for some germ cell tumors that contain yolk sac elements. Thyroxine can be produced by the rare struma ovarii, which is a teratoma composed predominantly of thyroid tissue. Estrogens can be elaborated by various ovarian stromal tumors, including thecomas and granulosa cell tumors. More ominously, a decrease in maternal serum estriol suggests incipient abortion. Lactate dehydrogenase may be increased in many conditions, such as liver and cardiac disease, but it is unknown as a marker for genital tract lesions. Human placental lactogen is produced in small quantities in the developing placenta, and serum levels typically are not measured. Neural tube defects can be distinguished from other fetal defects (e.g., abdominal wall defects) by use of the acetylcholinesterase test on amniotic fluid obtained by amniocentesis. If acetylcholinesterase and maternal serum α-fetoprotein are elevated, a neural tube defect is likely. If the acetylcholinesterase is not detectable, another fetal defect is suggested.

BP7 702–703BP8 735–736PBD7 1110–1112PBD8 1057–1059

11 **(A)** The figure shows a uterus with two well-circumscribed, gray-white masses in the myometrium. Microscopically, the lesions show spindle-shaped cells in whorled bundles. The cells are uniform in size and shape, and mitotic figures are scarce. These features are characteristic of a benign neoplasm—a leiomyoma. A leiomyosarcoma is not as well demarcated, and its cut surface is not as homogeneous as that of a leiomyoma. Although leiomyomas are often asymptomatic, leiomyomas that are submucosal in location may produce menometrorrhagia and chronic blood loss, leading to iron deficiency anemia. A leiomyosarcoma arises de novo, not from a leiomyoma, and is usually a larger, more irregular mass composed of more pleomorphic spindle cells with many mitoses. Endometriosis may cause pelvic pain, but usually has an onset at an earlier age, and the hemorrhagic lesions are located outside the uterus. Decreased ovarian

function after menopause accelerates bone loss, which may be severe enough to be termed *osteoporosis*, but this process is not related to female genital tract neoplasia. About 10% of complete moles are complicated by invasive mole, which is unlikely to produce a large, circumscribed mass. Preeclampsia with hypertension and proteinuria is associated with abnormal decidual vascularization and placental ischemia.

BP7 692–693BP8 724–725PBD7 1089–1090PBD8 1036–1037

12 **(C)** Postmenopausal vaginal bleeding is a "red flag" for endometrial carcinoma. Such carcinomas often arise in the setting of endometrial hyperplasia. Increased estrogenic stimulation is thought to drive this process, and risk factors include obesity, type 2 diabetes mellitus, hypertension, and infertility. Adenomyosis is an extension of endometrial glands and stroma into the myometrium, generally resulting in symmetric uterine enlargement. A submucosal leiomyosarcoma could produce vaginal bleeding, but the uterus would be enlarged because leiomyosarcomas tend to be large masses. Squamous carcinomas of the endometrium are rare. Choriocarcinomas are gestational in origin. Malignant mixed müllerian tumors are much less common than endometrial carcinomas, but they could produce similar findings.

BP7 693–694BP8 725–727PBD7 1086–1088PBD8 1031–1034

13 **(A)** This patient has a partial hydatidiform mole, which results from triploidy (69 chromosomes). In contrast to a complete mole, in which no fetus is present, a partial mole has a fetus because maternal chromosomes are present. Survival of the fetus to term is rare. A partial mole may contain some grapelike villi or none. The fetus is usually malformed. A 46,XX karyotype could be present in a complete mole or a normal male fetus. The 23,Y karyotype is typical of a sperm. A fetus with Turner syndrome has a 45,X karyotype. Most female fetuses with loss of an X chromosome undergo spontaneous abortion. Klinefelter syndrome has a 47,XXY karyotype, and male infants are liveborn. A 47,XY,+18 karyotype of trisomy 18 is associated with multiple congenital malformations, but not with a partial mole.

BP7 702–703BP8 735–736PBD7 1110–1112PBD8 1058–1059

14 **(B)** Some familial cases of ovarian carcinoma (usually serous cystadenocarcinoma) are associated with the homozygous loss of the *BRCA1* gene. This tumor-suppressor gene also plays a role in the development of familial breast cancers. Familial syndromes account for less than 5% of all ovarian cancers, however. Mutations of the *RAS* and *MYC* oncogenes occur sporadically in cancers. The *ERBB2* gene may be overexpressed in ovarian cancers; however, mutations of this gene do not give rise to familial tumors. The *RB1* gene can be involved in familial forms of retinoblastoma and osteosarcoma.

BP7 696BP8 729–730PBD7 1093PBD8 1042

15 **(B)** Embryonal rhabdomyosarcoma is an uncommon vaginal tumor found in girls younger than 5 years old. Because it forms polypoid, grapelike masses, it is sometimes called sarcoma botryoides. Histologically, it is a small, round, blue-cell tumor that shows skeletal muscle differentiation in the presence of muscle-specific proteins such as desmin. Neuroblastomas also are small blue-cell tumors, but they occur in the adrenal glands or extra-adrenal sympathetic chain. Condylomata acuminata are caused by sexually transmitted human papillomavirus and rarely occur in such young patients. Vulvar intraepithelial neoplasm is a carcinoma in situ of the vulvar skin. It occurs in older patients. Invasive squamous cell carcinomas are rare in very young patients, and they show histologic evidence of squamous epithelial differentiation.

BP7 786BP8 716PBD7 1071–1072PBD8 1017

16 **(E)** The mass is probably producing estrogen, which has led to endometrial hyperplasia. Estrogen-producing tumors of the ovary are typically sex cord tumors, such as a granulosa-theca cell tumor or a thecoma-fibroma, the former more often being functional. Teratomas can contain various histologic elements, but not estrogen-producing tissues. Endometriosis can give rise to an adnexal mass called an endometrioma, which enlarges over time. Endometrial glands are hormonally sensitive, but they do not produce hormones. Corpus luteum cysts are common, but they are unlikely to produce estrogens. Metastases to the ovary do not cause increased estrogen production. A struma ovarii is a variant of a teratoma in which more than half the mass is thyroid tissue, which may be functional and cause hyperthyroidism.

BP7 691BP8 723, 732PBD7 1085, 1102–1104PBD8 1050–1051

17 **(A)** Gonorrheal infections can lead to salpingitis and pelvic inflammatory disease with scarring. This predisposes to ectopic pregnancy. Gonorrhea and other genital tract infections do not cause dysfunctional bleeding. Gonorrhea does not carry the risk of dysplasias or carcinomas that human papillomavirus infection does. Gonorrhea and other infections do not contribute to endometrial hyperplasia. The actual cause of endometriosis is unknown, but infection does not seem to play

a role in this process. Placenta previa results from low-lying implantation of the placenta and is not related to sexually transmitted diseases.

BP7 673–675, 685BP8 715–717, 727–728PBD7 1064–1065PBD8 1009–1010

18 **(B)** Dysplasias of the cervix should not be ignored because they naturally progress to more severe dysplasias and to invasive carcinomas. Although not all cases progress, the physician should not take this chance. Dysplasias are strongly related to human papillomavirus (HPV) infections, and HPV DNA can be found in about 90% of cases. In about 10% to 15% of cases, there is no evidence of HPV, and other factors may play a role in the development of the dysplasia. A condyloma acuminatum also is an HPV-associated lesion, but it is usually caused by a distinct, low-risk type of HPV. With such HPV infection, the Pap smear may show changes of cervical intraepithelial carcinoma (CIN) I. Cervicitis usually is due to bacterial or fungal organisms and is not a significant risk of dysplasia or carcinoma. Endocervical polyps may produce some bleeding, but typically show no dysplasia. Oral contraceptive use does not increase the risk of dysplasia significantly.

BP7 686–688BP8 717–719PBD7 1073–1076PBD8 1018–1019

19 **(B)** Acute endometritis in this case is the result of retained products of conception after delivery. Endometritis may follow premature rupture of membranes with ascending infection to the uterine cavity. There is often polymicrobial infection with organisms found in the vagina. Some cases of chronic endometritis may be associated with *Neisseria* and *Chlamydia* infections and produce lymphoplasmacytic infiltrates within the endometrium. Cervical dysplasias are confined to the epithelium and are asymptomatic so that detection is by Pap smear. A myometrial neoplasm is unlikely to produce acute inflammation. An ovarian endometrioma is a mass lesion resulting from continued hemorrhage into a focus of endometriosis, but this mass lesion is not associated with pregnancy, and endometriosis is a cause for infertility. *Mycobacterium tuberculosis* infection may spread to the female genital tract, most often the fallopian tube, but acute signs are unlikely to be present, and inflammation of the tube can be a cause for infertility. Vaginitis may produce acute inflammation with discharge, but trichomonal infections typically are associated with a watery gray-to-green discharge.

BP7 689BP8 721PBD7 1083PBD8 1027

20 **(A)** Bartholin's glands may become obstructed, inflamed, and cystic because of abscess formation. A Gartner duct cyst may form in the lateral vaginal wall from the remnant of a wolffian duct; the cyst is filled with fluid and is not inflamed. Hair follicles are not present at the inner labia. The Bartholin's gland lies just inferior to the fascia of the urogenital diaphragm and just anterior to the vestibular bulb, which is not glandular and does not become cystic.

BP8 712PBD7 1065PBD8 1011

2 1 **(B)** Most granulosa-theca cell tumors are hormonally active and secrete estrogens that can lead to endometrial hyperplasia or carcinoma. Most of these tumors also are benign and do not metastasize. A condyloma acuminatum is related to infection with human papillomavirus and is more likely to occur in younger, sexually active women. In most cases, chronic salpingitis is related to sexually transmitted infections, such as gonorrhea. A partial mole is an uncommon form of gestational trophoblastic disease and occurs only in reproductive-age women.

BP7 699BP8 732PBD7 1085, 1102PBD8 1050–1051

22 **(G)** This woman has several risk factors for the development of cervical squamous cell carcinoma, including multiple sexual partners, documented infection of the cervix with high-risk human papillomavirus (HPV) type 16, and diagnosis of a high-grade squamous intraepithelial neoplasm. The remaining choices are not related to HPV infection. Clear cell carcinomas of the cervix are uncommon; some are associated with maternal use of diethylstilbestrol (DES) in pregnancy. An immature teratoma arises in the ovary. A Krukenberg tumor is a form of metastasis to the ovary. Leiomyosarcomas are rare and typically arise in the myometrium, although they can form in the cervix. Cystadenocarcinomas arise in the ovary. Sarcoma botryoides is a vaginal lesion that typically occurs in young girls.

BP7 686–688BP8 719–721PBD7 1076–1079PBD8 1018

23 **(D)** Immature teratomas are not cystic similar to mature teratomas. Tissues derived from multiple germ cell layers are present, however, as in all teratomas. The presence of neuroectodermal tissues in immature teratomas is typical. The less differentiated and more numerous the neuroepithelial elements, the worse is the prognosis. Brenner tumors of the ovary are uncommon solid tumors that contain epithelial nests resembling transitional cells of the urinary tract; most are benign. Dysgerminomas are the female equivalent of male testicular seminomas. Granulosa cell tumors have cells that resemble those in ovarian follicles and may secrete estrogens. Leiomyosarcomas are solid tumors of smooth muscle origin that are

found most often in the myometrium. Malignant mixed müllerian tumors are typically uterine neoplasms that have glandular and stromal elements; the malignant stromal component can be “heterologous” and may resemble mesenchymal cells not ordinarily found in the myometrium, such as cartilage. Sarcoma botryoides resembles an embryonal rhabdomyosarcoma and is typically a vaginal tumor of young girls.

BP7 700BP8 733PBD7 1100–1101PBD8 1048

24 **(C)** This woman has endometriosis, a condition in which functional endometrial glands are found outside the uterus. Common sites include ovaries, uterine ligaments, rectovaginal septum, and pelvic peritoneum. These glands respond to ovarian hormones; cyclic abdominal pain coincides with menstruation. Recurrent hemorrhages are followed by scarring and the formation of fibrous adhesions in the pelvis. This may cause distortion of the ovaries and fallopian tubes and may lead to infertility. One common variation is formation of an endometrioma, or “chocolate cyst,” which represents a focus of endometriosis that becomes a cystic lesion, its center filled with chocolate-brown sludge from the recurrent hemorrhage. The remaining choices are not associated with endometriosis, although endometrioid tumors may form in foci of endometriosis.

BP7 690BP8 722–723PBD7 1083–1084PBD8 1028–1029

25 **(B)** In most cases, extramammary Paget disease is not associated with an underlying malignancy, in contrast to Paget disease of the breast. In many cases, the Paget cells remain in the epithelium, often for years, creating an annoying itchy red lesion, but local invasion and even metastases are possible. A condyloma is the result of HPV infection and leads to koilocytotic atypia, but the cells of a condyloma are not malignant. Lichen sclerosis is a white patch of epithelial thinning with dermal fibrosis and chronic inflammation that can be extensive enough to constrict the vaginal orifice; it may have an autoimmune basis, and there is an increased risk for future development of a squamous carcinoma. Lichen simplex chronicus is an area of epithelial hyperplasia that has no atypia and no association with malignancy. Vulvar intraepithelial neoplasia has neoplastic cells extending the full thickness of the epithelium; it is related to HPV infection.

BP7 683BP8 714–715PBD7 1068–1069PBD8 1015

26 **(C)** The presence of pseudohyphae indicates a fungal infection. Candidal (monilial) vaginitis is common; this organism is present in about 5% to 10% of women. The inflammation tends to be superficial, and there is typically no invasion of underlying tissues. Infection with *Trichomonas vaginalis* can produce a purulent vaginal discharge, but the organisms are protozoa and do not produce hyphae. *Ureaplasma* is a bacterial agent, as is *Chlamydia,* and both can produce cervicitis. *Neisseria gonorrhoeae,* a gram-negative diplococcus, is the causative agent of gonorrhea.

BP7 685BP8 712, 715–716PBD7 1062–1063PBD8 1008–1009

27 **(D)** The presence of dysplastic cells occupying half of the thickness of the epithelium suggests vulvar intraepithelial neoplasia (VIN). The incidence of these lesions has been increasing, probably because of more cases of human papillomavirus (HPV) infections. Some VIN lesions may progress to invasive cancers. Lichen sclerosus is a vulvar dystrophy characterized by thinning of the squamous epithelium and sclerosis of the dermis. A condyloma is usually a raised, nodular lesion. It also is caused by HPV, principally HPV-6 and HPV-11. Similar to VIN, squamous hyperplasia, another form of vulvar dystrophy, can appear as an area of leukoplakia, but no dysplastic changes are present. Chronic inflammation does not produce dysplasia. A contact dermatitis typically produces reddish “bumps” of various sizes, with irritation and itching that may persist for days or as long as 2 weeks.

BP7 682–683BP8 714PBD7 1067–1068PBD8 1012–1014

28 **(A)** The microscopic appearance is that of a malignant tumor containing cells with a clear cytoplasm. Vaginal clear cell carcinomas are associated with exposure of the patient's mother to diethylstilbestrol (DES) during pregnancy. These tumors are generally first diagnosed in the late teenage years. Trichomonal infections do not give rise to neoplasia. Polycystic ovary disease can lead to hormonal imbalances from excess androgen production, but vaginal neoplasms do not arise in this setting. Infection with human papillomavirus is associated with squamous epithelial dysplasias and malignancies, not with clear cell adenocarcinomas. Congenital adrenal hyperplasia can produce masculinization in girls, manifesting in early childhood.

BP7 684BP8 716PBD7 1071PBD8 1016–1017

29 **(A)** This woman has classical symptoms and signs of endometriosis. Thirty to 40% of women present with infertility, menstrual irregularities, and pelvic pain. The presence of endometrial tissue in the nodules confirms this diagnosis. The glands in the nodules are hyperplastic but show no evidence of malignancy; in addition all the genes implicated in

endometrial cancer are normal. Hypomethylation of the two genes, *steroidogenic factor-1* and *estrogen receptor-β* is found in endometriosis. These lead to over-production of prostaglandins and estrogens. Aromatase inhibitors are used to suppress estrogen production. Lesions of endometriosis are not neoplastic and chemotherapy is not indicated.

PBD8 1028–1029

30 **(A)** The epithelium shows typical features of infection with human papillomavirus—specifically, prominent perinuclear vacuolization (koilocytosis) and angulation of nuclei. These lesions, called condylomata acuminata, may occur anywhere on the anogenital surface, as single lesions or, more commonly, as multiple lesions. They are not precancerous. Condylomata are associated with HPV infection, often types 6 and 11. Chlamydial infections may produce urethritis, cervicitis, and pelvic inflammatory disease. *Treponema pallidum* is the infectious agent of syphilis, characterized by the gross appearance of a "hard" chancre. *Haemophilus ducreyi* is the agent that produces the "soft" chancre of chancroid. Candidal infections produce a vaginitis or cervicitis with exudate and erythema.

BP7 681–682BP8 712–714PBD7 1067PBD8 1012

31 **(E)** Microinvasive squamous cell carcinomas of the cervix are stage I lesions that have a survival rate similar to that of in situ lesions. Such minimal invasiveness does not warrant more aggressive therapies. The likelihood of metastasis or recurrence is minimal.

BP7 686–688BP8 719–720PBD7 1076–1079PBD8 1022–1023

32 **(B)** Polycystic ovarian disease is a disorder of unknown origin that is typically associated with oligomenorrhea, obesity, and hirsutism. It is thought to be caused by abnormal regulation of androgen synthesis. Teratomas are mass lesions that can be bilateral, but usually are not symmetric. Krukenberg tumors represent metastatic disease involving the ovaries, usually from a primary site in the gastrointestinal tract, and are rare among patients of this age. Abscesses are usually unilateral and do not account for the hormonal changes seen in this patient. Cystadenocarcinoma can be bilateral; however, androgen production by ovarian tumors is rare except by the rare Sertoli-Leydig cell tumors.

BP7 695BP8 728PBD7 1092–1093PBD8 1039–1040

3 3 **(D)** Sexually transmitted diseases are the most common cause of inflammation of the fallopian tube. When the incidence of gonorrhea caused by *Neisseria gonorrhoeae* decreases in a population, the proportion of cases of salpingitis caused by *Chlamydia* and *Mycoplasma* increases. The fallopian tube can become distended and adherent to the ovary and may form a tubo-ovarian abscess. These are features of pelvic inflammatory disease. Infection with human papillomavirus is associated with squamous epithelial dysplasia and neoplasia of the genital tract. *Mycobacterium tuberculosis* is an uncommon cause of salpingitis. *Treponema pallidum* infection causes syphilis, which does not produce florid inflammation with mass effect. *Candida* infections are typically limited to the vagina and cervix and are superficial, without invasion. Herpes simplex virus most often involves the external genitalia, but it may produce vaginal or cervical lesions; it is unlikely to advance farther. *Haemophilus ducreyi* causes chancroid, which can produce erythematous papules of the external genitalia or vagina, but grossly visible lesions may not be present in women.

BP7 694BP8 727–728PBD7 1063, 1091PBD8 1008, 1038

34 **(A)** This patient's cervical intraepithelial neoplasia (CIN) II may progress to invasive carcinoma in several years if not treated, particularly because she has a high-risk subtype of HPV. Infection with HPV often drives this process, but the presence of HPV alone does not determine therapy. HPV infection cannot be eradicated. Chronic cervicitis with squamous metaplasia is not a malignant lesion and does not determine therapy in this case. The conization can preserve fertility in women who are of childbearing age.

BP7 686–688BP8 718–719PBD7 1075–1076PBD8 1020–1021

35 **(A)** This patient has a choriocarcinoma, an aggressive malignant trophoblastic tumor. Some of these tumors can arise without evidence of pregnancy. Metastases in the vaginal wall and lungs and a hemorrhagic appearance are characteristic. The syncytiotrophoblastic cells produce human chorionic gonadotropin. The α-fetoprotein level is elevated in yolk sac tumors; estrogens are elevated in granulosa-theca cell tumors; androgens such as testosterone are elevated in Leydig cell tumors; and thyroxine can be elevated in specialized teratomas that contain thyroid tissue (e.g., struma ovarii). Carcinoembryonic antigen is a tumor marker that is more characteristic of visceral malignancies, such as colonic adenocarcinoma.

BP7 703–704BP8 736–737PBD7 1101–1102, 1113–1114PBD8 1059–1061

36 **(B)** Anovulatory cycles are a common cause of dysfunctional uterine bleeding in young women who are beginning menstruation and in women approaching menopause. There is prolonged estrogenic stimulation that is not followed by secretion of progesterone. Polyps are more common in older women. An ectopic pregnancy has acute findings and does not have a prolonged course. Submucosal leiomyomas are a cause of less variable bleeding and are more likely to be seen in older women. Endometrial carcinomas are rare in patients this age.

BP7 691BP8 723PBD7 1081–1082PBD8 1026–1027

37 **(B)** This patient has lichen sclerosus et atrophicus, which is most common in postmenopausal women. Although this lesion is not premalignant, there is a 1% to 4% risk for women with this condition developing a squamous cell carcinoma. In contrast, lichen simplex chronicus appears grossly as leukoplakia from squamous hyperplasia and is not associated with malignancy. Pelvic inflammatory disease results from infection of internal genital organs with organisms such as *Neisseria gonorrhoeae* and *Chlamydia trachomatis*. Vulvar intraepithelial neoplasia is marked by dysplastic squamous epithelial changes. Extramammary Paget disease is rare; it produces reddish areas of scaling and is caused by the presence of adenocarcinoma-like cells at the dermal-epidermal junction. Human papillomavirus infection is associated with condylomata acuminata and with squamous epithelial dysplasias.

BP7 681BP8 712–713PBD7 1066PBD8 1011

3 8 **(C)** She has obesity, diabetes mellitus, and nulliparity—factors that contribute to development of endometrial hyperplasias and carcinomas caused by hyperestrinism. She has complex endometrial hyperplasia with atypicality of cells —a precursor for type I endometrial carcinoma. These lesions often have loss of *PTEN* tumor suppressor genes. In many, if not all, cancers there is activation of aerobic glycolysis (i.e. glycolysis even in the presence of enough oxygen)—the so-called “Warburg effect.” This is linked to loss of *PTEN* and offers a growth advantage to tumor cells. When aerobic glycolysis is stimulated there is a reciprocal decrease in oxidative phosphorylation. Tumors are metabolically active, so glucose uptake and glycogen utilization is enhanced and not reduced. In many cancers the COX-2 enzyme is upregulated (e.g. colon cancer) and this leads to increased prostaglandins, but this is not related to *PTEN* loss.

BP7 693-694BP8 725–727PBD7 1086–1088PBD8 1031–1032

39 **(C)** Cystadenocarcinomas are common ovarian tumors that are often bilateral. The serous type occurs more frequently than the mucinous type and is typically unilocular, whereas mucinous tumors are multilocular. Serous cystadenocarcinomas account for more than half of ovarian cancers. As the name indicates, they are cystic in appearance. They may be benign, borderline, or malignant. Benign tumors have a smooth cyst wall with small or absent papillary projections. Borderline tumors have increasing amounts of papillary projections. Endometrioid tumors resemble endometrial carcinomas and may arise in foci of endometriosis. Clear cell carcinomas are uncommon malignancies of the vagina and cervix. Dysgerminomas are solid tumors of germ cell origin. Granulosa cell tumors can be solid and cystic and may produce estrogens. Malignant mixed müllerian tumors are typically uterine neoplasms that have glandular and stromal elements; the malignant stromal component can be “heterologous” and may resemble mesenchymal cells that are not ordinarily found in the myometrium, such as cartilage. Mature cystic teratomas typically contain abundant hair and gooey sebaceous fluid within the cystic cavity; surrounding tissues are formed from various germ layers. Sertoli-Leydig cell tumors are rare, yellow-brown, solid masses; they may secrete androgens or estrogens.

BP7 697–699BP8 730PBD7 1095–1097PBD8 1042–1044

4 0 **(F)** The lesion shown in the figure is large and ulcerative and projects into the vagina. It is most likely an invasive squamous cell carcinoma that has infiltrated into the subepithelial region. Dysplastic changes confined to the epithelium represent cervical intraepithelial neoplasia and do not form mass lesions. Glandular invasive lesions indicate an adenocarcinoma, which is much less common than squamous cell carcinoma of the cervix. Chronic cervicitis has erythema, but no mass effect. Clear cell carcinomas are uncommon and most likely found arising in the vagina. Extramammary Paget disease usually arises on the vulva, producing an eczematous lesion, not a mass, because the neoplastic cells are confined to the epithelium and to adjacent skin adnexa.

BP7 684BP8 719–721PBD7 1076–1079PBD8 1021–1023

41 **(E)** Cervical intraepithelial neoplasia (CIN) I represents minimal (mild) dysplasia and is a potentially reversible process. Dysplasias are preneoplastic and may progress to carcinomas if not treated. Risk factors for cervical dysplasias and carcinoma include early age at first intercourse, multiple sexual partners, and a male partner with multiple previous sexual partners. These factors all increase the potential for infection with human papillomavirus. Use of oral contraceptives does not cause cervical dysplasia or carcinoma. Diethylstilbestrol (DES) exposure is a factor in the development of clear cell

carcinomas of the vagina and cervix. A vitamin B_{12} deficiency may produce some megaloblastic epithelial changes, but not dysplasia. Treatment of carcinomas does not result in dysplasia.

BP7 686–688BP8 717–719PBD7 1075–1076PBD8 1020–1021

42 **(E)** The lesions shown are condylomata acuminata, which are often multiple and can become several centimeters in diameter. They also are known as genital or venereal warts and are the result of infection with human papillomavirus (HPV) acquired during sexual intercourse. The presence of HPV-infected cells is indicated by koilocytotic change. These cells have cytoplasmic vacuolation. Although not premalignant, condylomata acuminata can be present along with other lesions caused by HPV, such as squamous dysplasias and carcinomas. Anovulatory cycles can lead to irregular menstrual periods, but not to vulvar skin changes. The best-known association of a faulty tumor-suppressor gene and a genital tract cancer is the *BRCA1* gene and ovarian carcinoma. Diabetic patients are more prone to infections, typically bacterial or fungal, that do not produce nodular masses. Portions of this data are best left to the imagination of the reader to interpret.

BP7 681–682BP8 712–714PBD7 1067PBD8 1012

43 **(B)** Mucinous tumors of the ovary are of epithelial origin, are less common than serous tumors, and tend to be multiloculated. The appearance of ascites suggests metastases, which is most common with surface epithelial neoplasms of the ovary. Immature teratomas tend to be solid masses, as do granulosa cell tumors and dysgerminomas. Choriocarcinomas rarely reach this size because they metastasize early; they are typically hemorrhagic.

BP7 697–699BP8 730–731PBD7 1097PBD8 1044–1045

44 **(D)** This woman has classic features of eclampsia defined by hypertension, edema, and proteinuria, typically with onset in the third trimester. The addition of seizures defines eclampsia. Primigravid women are at greater risk. There is no evidence in this case that primary renal disease could cause her hypertension, and the onset was sudden. Although the precise cause of preeclampsia/eclampsia is unknown, placental ischemia is believed to be the underlying mechanism. This is associated with shallow placentation and incomplete conversion of decidual vessels into high-volume channels required to perfuse the placenta adequately. Untreated patients may go on to DIC. Gestational trophoblastic disease predisposes patients to preeclampsia, but hydatidiform mole is excluded by the presence of a fetus, and a partial mole would be unlikely to persist into the third trimester. Cushing syndrome with adrenal cortical hyperplasia could lead to hypertension with sodium retention, but she does not have hypokalemia or hyperglycemia. Functional ovarian tumors, most commonly estrogen-secreting, such as a granulosa cell tumor or thecoma, do not produce hypertension and proteinuria.

BP7 704–705BP8 737–738PBD7 1106–1110PBD8 1055–1057

45 **(B)** Most endometrial cancers have the endometrioid pattern and are classified as type I endometrial carcinomas. They arise in the setting of unopposed estrogen stimulation and may also have *KRAS* and β-*catenin* mutations as well as microsatellite instability. In contrast, type II endometrial carcinomas occur at an older age in the background of atrophic endometrium; they usually have a serous carcinoma pattern, but may also exhibit clear cell and mixed mullerian patterns, and *p53* mutations are common. Leiomyosarcomas and stromal sarcomas are far less common than endometrial carcinomas, and they have no known risk factors.

BP7 693BP8 726PBD7 1087PBD8 1031–1034

23. The Breast

PBD7 and PBD8 Chapter 23: The Breast

BP7 and BP8 Chapter 19: Female Genital System and Breast

1 A 36-year-old woman has noticed a bloody discharge from the nipple of her right breast for the past 3 days. On physical examination, the skin of the breasts appears normal, and no masses are palpable. There is no axillary lymphadenopathy. The patient has regular menstrual cycles and is using oral contraceptives. Excisional biopsy is most likely to show which of the following lesions in her right breast?

- □ (A) Fibroadenoma
- □ (B) Phyllodes tumor
- □ (C) Acute mastitis
- □ (D) Intraductal papilloma
- □ (E) Sclerosing adenosis

2 A 28-year-old woman in the third trimester of her third pregnancy discovered a lump in her left breast. The physician palpated a 2-cm, discrete, freely movable mass beneath the nipple. After the birth of a term infant, the mass appears to decrease slightly in size. The infant breastfeeds without difficulty. What is the most likely diagnosis?

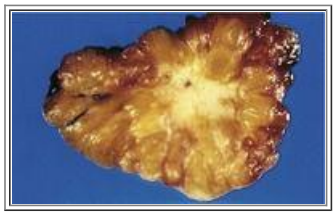
- □ (A) Intraductal papilloma
- □ (B) Phyllodes tumor
- □ (C) Lobular carcinoma in situ
- □ (D) Fibroadenoma
- □ (E) Medullary carcinoma

3 A 30-year-old woman sustained a traumatic blow to her right breast. Initially, there was a 3-cm contusion that resolved within 3 weeks, but she then felt a firm lump that persisted below the site of the bruise 1 month later. What is the most likely diagnosis for this lump?

- □ (A) Fibroadenoma
- □ (B) Sclerosing adenosis
- □ (C) Fat necrosis
- □ (D) Ductal carcinoma in situ
- □ (E) Mammary duct ectasia

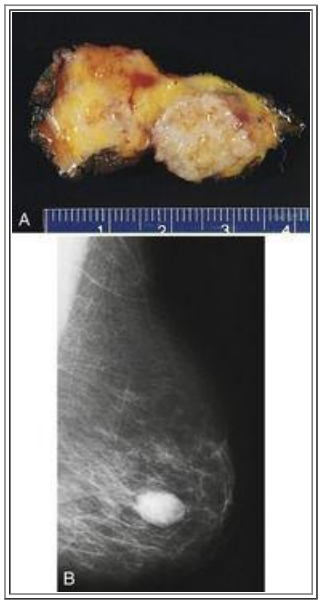
4 A 55-year-old man has developed bilateral breast enlargement over the past year. On physical examination, the enlargement is symmetric and is not painful to palpation. There are no masses. The patient is not obese and is not taking any medications. Which of the following underlying conditions best accounts for these findings?

- □ (A) Micronodular cirrhosis
- □ (B) Chronic glomerulonephritis
- □ (C) Choriocarcinoma of the testis
- □ (D) ACTH-secreting pituitary adenoma
- □ (E) Rheumatoid arthritis



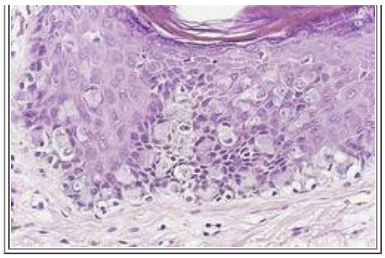
5 A 44-year-old woman sees her physician because she felt a lump in her left breast 1 week ago. The physician palpates a firm, irregular mass in the upper outer quadrant of the left breast. There are no overlying skin lesions. The gross appearance of the excisional biopsy specimen is shown in the figure. Which of the following additional findings is most likely to be present on physical examination?

- □ (A) Axillary lymphadenopathy
- □ (B) Bloody discharge from the nipple
- □ (C) Painful breast enlargement
- □ (D) Mass in the opposite breast
- □ (E) Cushingoid face



6 A 25-year-old woman sees her physician because she has noticed a lump in her right breast. The physician palpates a 2-cm, firm, circumscribed mass in the lower outer quadrant. The figure shows the excised mass (A) and the mammogram (B). What is the most likely diagnosis?

- □ (A) Phyllodes tumor
- □ (B) Fibrocystic changes
- □ (C) Fibroadenoma
- □ (D) Fat necrosis
- □ (E) Infiltrating ductal carcinoma
- □ (F) Mastitis



7 A 47-year-old woman has noticed a red, scaly area of skin on her left breast that has grown slightly larger over the past 4 months. On physical examination, there is a 1-cm area of eczematous skin just lateral to the areola. The figure shows the microscopic appearance of the skin biopsy specimen. What is the most likely diagnosis?

- □ (A) Apocrine metaplasia
- □ (B) Paget disease of the breast
- □ (C) Inflammatory carcinoma
- □ (D) Lobular carcinoma in situ
- □ (E) Fat necrosis

8 Three weeks after giving birth to a normal term infant, a 24-year-old woman is breastfeeding the infant and notices fissures in the skin around her left nipple. Over the next 3 days, the region around the nipple becomes erythematous and tender. Purulent exudate from a small abscess drains through a fissure. Which of the following organisms is most likely to be cultured from the exudate?

- □ (A) *Listeria monocytogenes*
- □ (B) *Streptococcus viridans*
- □ (C) *Candida albicans*
- □ (D) *Staphylococcus aureus*
- □ (E) *Lactobacillus acidophilus*

9 A 27-year-old woman feels a lump in her right breast. She has normal menstrual cycles, she is G3, P3, and her last child was born 5 years ago. The physician palpates a 2-cm, irregular, firm area beneath the lateral edge of the areola. The mass is not painful and does not feel firm. There are no lesions of the overlying skin and no axillary lymphadenopathy. A biopsy specimen shows microscopic evidence of an increased number of ducts, which are compressed because of proliferation of fibrous connective tissue. Dilated ducts with apocrine metaplasia also are present. What is the most likely diagnosis?

- □ (A) Traumatic fat necrosis
- □ (B) Fibrocystic changes
- □ (C) Mammary duct ectasia
- □ (D) Fibroadenoma
- □ (E) Infiltrating ductal carcinoma

10 A 44-year-old woman noticed a lump in her right breast. On examination, she has an ill-defined, 1-cm mass in the upper outer quadrant. The mass is cystic on ultrasound. An excision is done, and the mass shows predominantly fibrocystic changes, but carcinoma also is present. Fine-needle aspirates of both breasts reveal additional foci of similar malignant cells. Which of the following breast carcinomas is most likely to produce these findings?

- □ (A) Ductal carcinoma
- □ (B) Lobular carcinoma

□ (C) Malignant phyllodes tumor

□ (D) Medullary carcinoma

□ (E) Mucinous (colloid) carcinoma

11 A 56-year-old woman sees her physician for a routine health examination. There are no remarkable findings on physical examination. A mammogram shows a 0.5-cm irregular area of increased density with scattered microcalcifications in the upper outer quadrant of the left breast. Excisional biopsy shows atypical lobular hyperplasia. The patient has been on postmenopausal estrogen-progesterone therapy for the past 10 years. She has smoked 1 pack of cigarettes per day for the past 35 years. Which of the following conclusions is most pertinent to these findings?

□ (A) She has the *BRCA1* gene mutation

□ (B) The postmenopausal estrogen replacement therapy should be stopped

□ (C) Her risk of breast carcinoma is increased

□ (D) She should undergo bilateral simple mastectomies

□ (E) She should stop smoking

12 A 54-year-old woman sees her physician after feeling a lump in her left breast. The physician palpates a firm, irregular mass in the lower outer quadrant just beneath the lateral margin of the areola. A mammogram shows a 2-cm density with focal microcalcifications. Excisional biopsy shows intraductal and invasive components of a breast carcinoma. Immunohistochemical staining shows that the cells are positive for *HER2/neu* expression, but negative for estrogen receptor and progesterone receptor expression. Flow cytometry shows a small aneuploid peak and a low S-phase. When combined with doxorubicin, which of the following drugs is most likely to be useful in treating this patient?

□ (A) Hydroxyurea

□ (B) Celecoxib

□ (C) Raloxifene

□ (D) Tamoxifen

□ (E) Trastuzumab

13 A 55-year-old woman has felt a poorly defined lump in her right breast for the past year. On examination, she has a nontender, firm, 6-cm mass in the upper inner quadrant. There are no lesions of the overlying skin and no axillary lymphadenopathy. Needle biopsy is done, and microscopic examination of the specimen shows cellular stroma protruding into spaces lined by a single-layer cuboidal epithelium. The mass is excised with a wide margin, but recurs 1 year later. After further excision, the lesion does not recur. What is the most likely diagnosis?

□ (A) Fibroadenoma

□ (B) Fibrocystic changes

□ (C) Lobular carcinoma

□ (D) Phyllodes tumor

□ (E) Tubular carcinoma

14 A 51-year-old woman has noticed an area of swelling with tenderness in her right breast that has worsened over the past 2 months. On physical examination, the 7-cm area of erythematous skin is tender and firm. There is swelling of the right breast, nipple retraction, and right axillary lymphadenopathy. Excisional biopsy is most likely to show which of the following lesions?

□ (A) Atypical epithelial hyperplasia

□ (B) Phyllodes tumor

□ (C) Fat necrosis

□ (D) Sclerosing adenosis

□ (E) Infiltrating ductal carcinoma

15 A 39-year-old woman has noticed an enlarging mass in her left breast for the past 2 years. The physician palpates a 4-cm firm mass. A simple mastectomy is performed with axillary lymph node sampling and plastic reconstruction of the breast. On gross sectioning, the mass has a soft, tan, fleshy surface. Histologically, the mass is composed of large cells with vesicular nuclei and prominent nucleoli. There is a marked lymphocytic infiltrate within the tumor, and the tumor has a discrete, noninfiltrative border. No axillary node metastases are present. The tumor cells are negative for estrogen receptor and progesterone receptor. What is the most likely diagnosis?

□ (A) Colloid carcinoma

□ (B) Fibroadenoma

□ (C) Infiltrating ductal carcinoma

□ (D) Infiltrating lobular carcinoma

□ (E) Intraductal papilloma

□ (F) Medullary carcinoma

□ (G) Papillary carcinoma

□ (H) Phyllodes tumor

16 A 47-year-old woman has a routine health examination. There are no remarkable findings except for a barely palpable mass in the right breast. A mammogram shows an irregular, 1.5-cm area of density in the upper outer quadrant. Scattered microcalcifications are present in the density. A biopsy specimen from this area shows atypical ductal hyperplasia. Which of the following is the most appropriate advice to give to this patient?

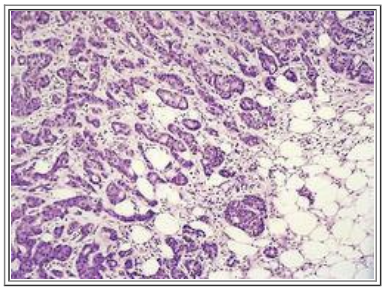
□ (A) There is a risk of cancer in the opposite breast

□ (B) A mastectomy should be performed

□ (C) These changes are related to smoking cigarettes

□ (D) Antibiotic therapy is indicated to treat the lesion

□ (E) The *BRCA1* oncogene has been inherited



17 A 25-year-old Jewish woman sees her physician after finding a lump in her right breast. On physical examination, a 2-cm, firm, nonmovable mass is palpated in the upper outer quadrant. No overlying skin lesions and no axillary lymphadenopathy are present. The figure shows an excisional biopsy specimen. The family history indicates that the patient's mother, maternal aunt, and maternal grandmother have had similar lesions. Her 18-year-old sister has asked a physician to determine whether she is genetically at risk of developing a similar disease. The physician is most likely to order an analysis of which of the following genes?

□ (A) *HER2/neu*

□ (B) *MYC*

□ (C) *BRCA1*

□ (D) *RB*

□ (E) Estrogen receptor gene

18 A study of women with breast carcinoma is done to determine the presence and amount of estrogen receptor (ER) and progesterone receptor (PR) in the carcinoma cells. Large amounts of ER and PR are found in the carcinoma cells of some patients. These receptors are not present in the cells of other patients. The patients with positivity for ER-PR are likely to exhibit which of the following traits?

□ (A) Higher response to therapy

□ (B) Increased immunogenicity

□ (C) Greater risk of familial breast cancer

□ (D) Higher tumor stage

□ (E) Greater likelihood of metastases

□ (F) Greater aneuploidy with flow cytometry

□ (G) Higher tumor grade

19 A 50-year-old woman has a routine health examination. There are no remarkable findings on physical examination, but a mammogram shows a 1-cm, irregular density in the right breast. A fine-needle aspirate of the lesion contains malignant cells. The mass is excised, and axillary lymph node sampling is performed. The microscopic features of the neoplasm are consistent with ductal carcinoma in situ. There are no lymph node metastases. She receives radiation therapy. Which of the following statements provides the most appropriate advice to the patient?

□ (A) You will probably survive less than 5 years

□ (B) Another cancer is probably present in the opposite breast

□ (C) Distant metastases are unlikely to be found

□ (D) Your family members should be screened for *BRCA1* and *BRCA2* mutations

□ (E) Flow cytometry can determine whether chemotherapy is warranted

20 A 79-year-old, previously healthy woman feels a lump in her right breast. The physician palpates a 2-cm firm mass in the upper outer quadrant. Nontender right axillary lymphadenopathy is present. A lumpectomy with axillary lymph node dissection is performed. Microscopic examination shows that the mass is an infiltrating ductal carcinoma. Two of 10 axillary nodes contain metastases. Flow cytometry on the carcinoma cells shows a small aneuploid peak and high S-phase. Immunohistochemical tests show that the tumor cells are positive for estrogen receptor, negative for *HER2/neu* expression, and positive for cathepsin D expression. What is the most important prognostic factor for this patient?

□ (A) Age

□ (B) Histologic subtype of carcinoma

□ (C) DNA content in the carcinoma

□ (D) Presence of lymph node metastases

□ (E) Expression of stromal proteases in the carcinoma

□ (F) Estrogen receptor positivity

□ (G) Lack of *HER2/neu* expression in the carcinoma.

21 A 29-year-old woman and her 32-year-old sister were diagnosed with infiltrating ductal carcinoma of the breast, and both had bilateral mastectomies. Which of the following risk factors is most significant for this type of cancer?

- □ (A) Oral contraceptive use
- □ (B) Inheritance of a mutant *p53* allele
- □ (C) Obesity
- □ (D) Multiparity
- □ (E) Smoking cigarettes

22 A 63-year-old woman feels a small lump in her right breast. The physician palpates a firm area that has a cordlike feel. No lesions of the overlying skin are present, and there is no axillary lymphadenopathy. A mammogram shows a density that contains microcalcifications. An excisional biopsy specimen contains soft, white material that is extruded from small ducts when pressure is applied. Microscopic examination shows ducts that contain large, atypical cells in a cribriform pattern. What is the most likely diagnosis?

- □ (A) Colloid carcinoma
- □ (B) Infiltrating ductal carcinoma
- □ (C) Infiltrating lobular carcinoma
- □ (D) Comedocarcinoma
- □ (E) Medullary carcinoma
- □ (F) Paget disease of the breast
- □ (G) Papillary carcinoma
- □ (H) Phyllodes tumor

23 An epidemiologic study is conducted with male subjects who have been diagnosed with breast carcinoma. Their demographic data, past medical histories, family histories, and laboratory data are examined to identify factors that increase the risk of cancer. Which of the following factors is most likely to increase significantly the risk of developing male breast carcinoma?

- □ (A) Gynecomastia
- □ (B) Age older than 70 years
- □ (C) Asian ancestry
- □ (D) Chronic alcoholism
- □ (E) *BRCA1* gene mutation

24 A clinical study is performed on postmenopausal women living in Tampa, Florida, who are between the ages of 45 and 70 years. All have been diagnosed with infiltrating ductal carcinoma positive for estrogen receptor (ER) and progesterone receptor (PR), which has been confirmed by biopsy and microscopic examination of tissue. None has the *BRCA1* or *BRCA2* mutation. Which of the following is most likely to indicate the highest relative risk of developing the carcinomas seen in this group of women?

- □ (A) Age at menarche older than 16 years
- □ (B) Age at menopause younger than 45 years
- □ (C) First-degree relative with breast cancer
- □ (D) Smoking cigarettes (>40 pack-years)

□ (E) Multiparity

□ (F) Prior diagnosis of mastitis

25 A 26-year-old woman has felt a breast lump for the past month and is worried because she has a family history of early-onset and bilateral breast cancers. On physical examination, there is a firm, 2-cm mass in the upper outer quadrant of her left breast. A biopsy is done, and the specimen microscopically shows carcinoma. Genetic analysis shows that she is a carrier of the *BRCA1* gene mutation, as are her mother and sister. Which of the following histologic types of breast carcinoma has the highest incidence in families such as hers?

□ (A) Lobular carcinoma

□ (B) Tubular carcinoma

□ (C) Metaplastic carcinoma

□ (D) Papillary carcinoma

□ (E) Medullary carcinoma

26 A study of gene expression profiling involving breast biopsies showing invasive carcinoma of no specific type (NST) is performed. A subset of these cases, comprising about 15% of all cases, has the following characteristics: estrogen receptor (ER) and progesterone receptor (PR) negative, HER2/neu negative, basal keratin positive, flow cytometry showing aneuploidy and high proliferation rate, and association with *BRCA1* mutations. Which of the following therapies is most likely to be effective in women with this subset of NST breast cancer?

□ (A) Chemotherapy

□ (B) Radiation

□ (C) Surgery alone

□ (D) Tamoxifen

□ (E) Trastuzumab

27 A Tumor Registry tracks patients diagnosed with breast cancer. Statistical analyses are performed regarding survival of these patients. Which of the following parameters recorded for these breast cancers is most likely to show the strongest correlation with longer patient survival?

□ (A) Dietary intake

□ (B) Family history

□ (C) Gene expression profile

□ (D) Histologic type

□ (E) Place of birth

□ (F) Tumor size

ANSWERS

1 **(D)** Intraductal papillomas are usually solitary and smaller than 1 cm. They are located in large lactiferous sinuses or ducts, and have a tendency to bleed. Fibroadenomas contain ducts with stroma and are not highly vascular; these lesions are not located in ducts. Phyllodes tumors also arise from intralobular stroma and can be malignant. They do not invade ducts to cause bleeding. Abscesses complicating mastitis organize with a fibrous wall. Sclerosing adenosis, a lesion occurring with fibrocystic changes, has abundant collagen, not vascularity.

BP7 710BP8 743PBD7 1129PBD8 1072–1073

2 **(D)** Fibroadenomas are common and may enlarge during pregnancy or late in each menstrual cycle. Most intraductal papillomas are smaller than 1 cm and are not influenced by hormonal changes. Phyllodes tumors are uncommon and tend to be larger than 4 cm. Lobular carcinoma in situ is typically an ill-defined lesion without a mass effect. Medullary carcinomas tend to be large; they account for only about 1% of all breast carcinomas.

BP7 709–710BP8 742–743PBD7 1149–1150PBD8 1091–1092

3 **(C)** Fat necrosis is typically caused by trauma to the breast. The damaged, necrotic fat is phagocytosed by macrophages, which become lipid laden. The lesion resolves as a collagenous scar within weeks to months. The firm scar can mammographically and grossly resemble a carcinoma, however. A fibroadenoma is a neoplasm, and tumors are not induced by trauma. Sclerosing adenosis is a feature of fibrocystic changes, a common cause of nontraumatic breast lumps. An intraductal carcinoma may not form a palpable mass lesion. Mammary duct ectasia from inspissated secretions can induce chronic inflammation and fibrosis, which mimic a carcinoma.

BP7 709BP8 742PBD7 1126PBD8 1070

4 **(A)** Micronodular cirrhosis is most often a consequence of chronic alcoholism and impairs hepatic estrogen metabolism, which can lead to gynecomastia. Chronic renal failure is unlikely to have this consequence. Choriocarcinomas of the testis produce human chorionic gonadotropin, not estrogens. ACTH-secreting pituitary adenomas cause truncal obesity because of Cushing syndrome. Rheumatoid nodules can appear in various locations along with rheumatoid arthritis, but they rarely occur in the breast and are unlikely to be bilateral.

BP7 716BP8 750PBD7 1151–1152PBD8 1093

5 **(A)** This irregular, infiltrative mass is an infiltrating (invasive) ductal carcinoma, the most common form of breast cancer. Breast carcinomas are most likely to metastasize to regional lymph nodes. By the time a breast cancer becomes palpable, lymph node metastases are present in more than 50% of patients. A bloody discharge from the nipple most often results from an intraductal papilloma. Pain with breast enlargement suggests inflammation. Lobular carcinomas are more often bilateral, but they are less common than infiltrating ductal carcinomas. Breast cancers are associated in rare cases with ectopic corticotropin secretion or Cushing syndrome.

BP7 713–714BP8 743–749PBD7 1142–1144PBD8 1083–1085

6 **(C)** Grossly and radiographically, this patient has a discrete mass that in a woman her age is most likely a fibroadenoma. Phyllodes tumors are typically much larger and are far less common. Fibrocystic changes are generally irregular lesions, not discrete masses. Fat necrosis and infiltrating cancers are masses with irregular outlines. Mastitis has a more diffuse involvement, without mass effect.

BP7 709–710BP8 742–743PBD7 1149–1150PBD8 1091–1092

7 **(B)** Paget cells are large cells that have clear, mucinous cytoplasm and infiltrate the skin. They are malignant and extend to the skin from an underlying breast carcinoma. Apocrine metaplasia affects the cells lining the cystically dilated ducts in fibrocystic change. “Inflammatory carcinoma” does not refer to a specific histologic type of breast cancer; rather, it describes the involvement of dermal lymphatics by infiltrating carcinoma. In lobular carcinoma in situ, terminal ducts or acini are filled with neoplastic cells. The overlying skin is unaffected. The macrophages in fat necrosis do not infiltrate the skin and do not have the atypical nuclei seen in the figure.

BP7 713BP8 745–746PBD7 1140–1141PBD8 1080–1081

8 **(D)** Staphylococcal acute mastitis typically produces localized abscesses, whereas streptococcal infections tend to spread throughout the breast. Listeriosis can be spread by contaminated food, including milk products, not by human milk. *Candida* may cause some local skin irritation, but is likely to become invasive only in immunosuppressed patients. *Lactobacillus acidophilus* is the organism used to produce fermented nonhuman milk.

BP7 708–709BP8 742PBD7 1125PBD8 1069

9 **(B)** Fibrocystic changes account for the largest category of breast lumps, statistically about 40% of all breast “lumps.” These lesions are probably related to cyclic breast changes that occur during the menstrual cycle. In about 30% of cases of breast lumps, no specific pathologic diagnosis can be made. Fibrocystic changes include ductal proliferation, ductal dilation (sometimes with apocrine metaplasia), and fibrosis. Fat necrosis may produce a localized, firm lesion that mimics carcinoma, but histology shows macrophages and neutrophils surrounding necrotic adipocytes, and healing leaves a

fibrous scar. Inspissated duct secretions may produce duct ectasia with a surrounding lymphoplasmacytic infiltrate. A fibroadenoma is a discrete mass formed by a proliferation of fibrous stroma with compressed ductules. Carcinomas have proliferations of atypical neoplastic cells that fill ducts and can invade stroma.

BP7 705–708BP8 739–741PBD7 1127–1129PBD8 1071

10 **(B)** Among primary malignancies of the breast, lobular carcinoma in situ (LCIS) is most likely to be bilateral. LCIS may precede invasive lesions by several years. Lobular carcinoma may be mixed with ductal carcinoma, and it may be difficult to distinguish them histologically. The other neoplasms listed are less likely to be bilateral and more likely to produce a mass effect.

BP7 714BP8 745–747PBD7 1141–1142PBD8 1082–1083

11 **(C)** Atypical lobular hyperplasia and atypical ductal hyperplasia increase the risk of breast cancer fivefold; the risk affects both breasts and is higher in premenopausal women or women who have a family history of breast cancer. The *BRCA1* mutation accounts for about 10% to 20% of familial breast carcinomas and only a few percent of all breast cancers. Mastectomies are probably not warranted at this time, but close follow-up is needed. Smoking and exogenous estrogen therapy are not well-established risk factors for breast cancer.

BP7 707BP8 740–741PBD7 1129PBD8 1073

12 **(E)** The expression of *HER2/neu* suggests that biotherapy with trastuzumab may have some effectiveness. Drug names with the suffix *-mab* are monoclonal antibodies that target a specific biochemical component of cells. This form of biotherapy is useful because normal breast cells do not have *HER2/neu* expression. Doxorubicin is a standard chemotherapeutic agent that is part of various multiagent protocols. Hydroxyurea is a cycle-acting agent that is not useful in breast cancer. Celecoxib is an inhibitor of cyclooxygenase-2 in the arachidonic acid pathway that forms prostaglandins as part of an inflammatory reaction. Tamoxifen is an antiestrogenic compound that has effectiveness in the treatment of breast cancers positive for estrogen receptor.

BP7 711–712BP8 745, 747, 749PBD7 1136–1137, 1148PBD8 1090

13 **(D)** Phyllodes tumors, although grossly and microscopically similar to fibroadenomas, occur at an older age, are larger, and are more cellular; they can recur locally, but rarely metastasize. Fibrocystic changes can produce a breast lump, but usually not as large as 6 cm, and without firm areas of cellular stroma. A lobular carcinoma has malignant-appearing epithelial cells in clusters and rows and may not even produce a mass effect. Tubular carcinomas of the breast are uncommon, most are less than 1 cm in diameter, and most have small tubular structures in a noncellular stroma.

BP7 710BP8 743PBD7 1150PBD8 1092–1093

14 **(E)** The gross appearance of the skin is consistent with invasion of dermal lymphatics by carcinoma—the so-called inflammatory carcinoma. Nipple retraction and axillary lymphadenopathy also suggest invasive ductal carcinoma. Atypical ductal hyperplasia may increase the risk of carcinoma, but it does not produce visible surface skin changes. A phyllodes tumor can be large and sometimes tender, but the overlying skin is typically not affected, and spread to lymph nodes is uncommon. The feel of fat necrosis on palpation can mimic that of carcinoma, but the skin is not involved. Sclerosing adenosis is a feature of benign fibrocystic changes and has no skin involvement.

BP7 714BP8 747PBD7 1142, 1146PBD8 1083, 1089

15 **(F)** Medullary carcinomas account for about 1% to 5% of all breast carcinomas. They tend to occur in women at younger ages than do most other breast cancers. Despite poor prognostic indicators, such as absence of estrogen receptors and progesterone receptors (ER-PR), medullary carcinomas have a better prognosis than most other breast cancers. Perhaps the infiltrating lymphocytes are helpful. Colloid carcinomas occur about as frequently as medullary carcinomas, but they are often positive for ER-PR, and the prognosis is better than average. Fibroadenomas are small benign lesions that tend to stop enlarging after menopause, when hormonal stimulation has ceased. Infiltrating ductal and infiltrating lobular carcinomas tend not to produce large, localized lesions because they are more invasive, and they lack a distinct lymphoid infiltrate. Intraductal papillomas are unlikely to be larger than 1 cm. True papillary carcinomas are quite rare, although other types of breast carcinoma may have a papillary component. The phyllodes tumor is typically large, but it has stromal and glandular components.

BP7 714BP8 747–748PBD7 1145PBD8 1087

16 **(A)** Fibrocystic changes without epithelial hyperplasia do not suggest an increased risk of breast cancer. Moderate to florid hyperplasia increases the risk twofold, and atypical ductal or lobular hyperplasias increase the risk fivefold. The risk in this patient is not great enough to suggest radical or simple mastectomy at this time. Breast cancers are not associated with tobacco use. These changes are not the result of infection. The *BRCA1* gene accounts for a small percentage of breast cancers, primarily in families in which cancer onset occurs at a young age.

BP7 706–708BP8 739–741PBD7 1127–1129PBD8 1071–1073

17 **(C)** The biopsy specimen shows an invasive breast cancer. Given the young age of the patient and the strong family history of breast cancer, it is reasonable to assume that she has inherited an altered gene that predisposes to breast cancer. There are two known breast cancer susceptibility genes: *BRCA1* and *BRCA2*. Both are cancer suppressor genes. Specific mutations of *BRCA1* are common in some ethnic groups, such as Ashkenazi Jews. *HER2/neu* is a growth factor receptor gene that is amplified in certain breast cancers and is a marker of poor prognosis, not susceptibility. Inheritance of *RB1* mutations predisposes to retinoblastoma and osteosarcomas, not breast carcinomas. Estrogen receptors are expressed in 50% to 75% of breast cancers. Their presence bodes well for therapy with receptor antagonists. There is no known relationship between the structure of the estrogen receptor gene and susceptibility to breast cancer.

BP7 710–714BP8 744PBD7 1131–1134PBD8 1077–1078

18 **(A)** The estrogen receptor and progesterone receptor (ER-PR) status helps predict whether chemotherapy with antiestrogen compounds such as tamoxifen would be effective; however, the correlation is not perfect. The ER and PR do not affect immunogenicity and are not targets for immunotherapy. In contrast, immunotherapy targeted to the overexpressed *HER2/neu* gene is being used. The overall prognosis may be predicted from several factors, including histologic type, histologic grade, presence of metastases, degree of aneuploidy, and tumor stage. A family history and the presence of specific mutations such as *BRCA1* or *BRCA2* correlate with familial risk of breast cancer.

BP7 716BP8 745PBD7 1136–1137PBD8 1076

19 **(C)** At least half of mammographically detected breast cancers are ductal carcinoma in situ (DCIS). This in situ carcinoma is highly unlikely to metastasize because the cells lack the ability to invade basement membrane. With surgical excision and radiotherapy, the 5-year survival rate is high, although some tumors may progress to invasive lesions over time. Lobular carcinomas are most likely to be present in the opposite breast. Patients with *BRCA1* or *BRCA2* mutations can have familial breast carcinomas. In these patients, there is usually a strong family history, and the age of onset may be early. The occurrence of a sporadic breast cancer in a racial group that is not at high risk of familial cancer does not warrant mutational analysis of *BRCA1* and *BRCA2*. Flow cytometry is useful to suggest prognosis, not treatment.

BP7 712–713BP8 745–748PBD7 1139–1141PBD8 1074–1075

20 **(D)** Many factors affect the course of breast cancer. The involvement of axillary lymph nodes is the most important prognostic factor. If there is no spread to axillary nodes, the 10-year survival rate is almost 80%. It decreases to 35% to 40% with 1 to 3 positive nodes and to 15% with more than 10 positive nodes. Increasing age is a risk of breast cancer, but age alone does not indicate a prognosis, and treatment of cancers in the elderly can be successful. Some histologic types of breast cancer have a better prognosis than others, but staging is a more important factor than histologic type. An increased DNA content with aneuploidy and a high S-phase suggests a worse prognosis, but staging is still a more important determinant of prognosis. The expression of stromal proteases, such as cathepsin D, predicts metastases, but in this case “the horse is out of the barn,” and metastasis has occurred. Estrogen receptor positivity suggests a better response to hormonal manipulation of the tumor, whereas expression of *HER2/neu* suggests responsiveness to biotherapy with the monoclonal antibody trastuzumab.

BP7 716BP8 748–749PBD7 1146–1148PBD8 1089–1090

21 **(B)** Bilateral breast cancer in very young women in the same family suggests a germline mutation in a tumor-suppressor gene. The affected genes may be *BRCA1, BRCA2,* or *p53.* The *BRCA1* and *BRCA2* genes account for most hereditary breast cancers. Establishment of other risk factors is not as secure. Multiparity reduces the risk of breast cancer.

BP7 711–712BP8 744–745PBD7 1133–1135PBD8 1077–1078

22 **(D)** An intraductal carcinoma, or ductal carcinoma in situ (DCIS), may not produce a palpable mass. The necrosis of the neoplastic cells in the ducts leads to calcification, and the necrotic cells can be extruded from the ducts, giving rise to the term *comedocarcinoma*. Such intraductal carcinomas represent about one fourth of all breast cancers. If not excised,

such lesions become invasive. Intraductal carcinoma has several other histologic patterns, including noncomedo DCIS and Paget disease of the nipple, in which extension of the malignant cells to the skin of the nipple and areola produces the appearance of a seborrheic dermatitis. Colloid carcinomas occur about as frequently as medullary carcinomas, but they are often positive for estrogen receptor and progesterone receptor, and the prognosis is better than average. Infiltrating ductal carcinomas tend to produce irregular, firm, mass lesions because they are more invasive. Infiltrating lobular carcinomas can have a diffuse pattern without significant mass effect. Medullary carcinomas tend to be large masses; microscopically, they have nests of large cells with a surrounding lymphoid infiltrate. True papillary carcinomas are rare, although a papillary component may be present in other types of breast carcinoma. The phyllodes tumor is typically large, but it has stromal and glandular components.

BP7 712–713BP8 745–748PBD7 1138–1141PBD8 1080–1081

23 **(B)** Male breast cancers are rare, and they occur primarily among the elderly. Additional risk factors include first-degree relatives with breast cancer, decreased testicular function, exposure to exogenous estrogens, infertility, obesity, prior benign breast disease, exposure to ionizing radiation, and residency in Western countries. Gynecomastia does not seem to be a risk factor. Of cases in men, 4% to 14% are attributed to germline *BRCA2* mutations.

BP7 717BP8 750PBD7 1152PBD8 1093–1094

24 **(C)** The relative risk of breast cancer increases with various factors, but family history is one of the strongest. A history of bilateral breast disease and earlier age of onset of cancer increase the risk. The earlier age of onset increases the risk of *BRCA1* or *BRCA2*. A longer reproductive life, with early menarche (<11 years old) and late menopause (>55 years old), and nulliparity increase the risk of breast cancer, probably because of increased estrogen exposure. “Soft” risk factors include exogenous estrogens, obesity, and smoking. Mastitis does not affect the risk of breast cancer.

BP7 710–712BP8 743–745PBD7 1130–1133PBD8 1076–1077

25 **(E)** Patients with the *BRCA1* gene mutation have a high incidence of medullary carcinomas that are poorly differentiated, do not express the HER2/neu protein, and are negative for estrogen and progesterone receptors.

BP8 747PBD7 1134, 1145PBD8 1087

26 **(A)** This is the “basal-like” subset of NST breast cancers that is “triple negative” for the usual immunohistochemical markers. Hence, lack of ER positivity predicts antihormonal therapy with tamoxifen will not be of benefit, and lack of HER2/neu indicates that trastuzumab will be ineffective. The basal-like cancers are highly aggressive and tend to metastasize early, so containment with surgery or radiation is unlikely. However, some of them are cured by chemotherapy. This emphasizes the importance of gene expression profiling, so that treatment is individualized to each cancer patient for the best chance of success.

BP8 745PBD7 1136PBD8 1084–1085

27 **(F)** The earlier a cancer can be detected, the smaller it is, the less chance it has had to acquire mutations giving it more aggressive characteristics, and the better the prognosis—simple but profound, and the rationale for cancer screening. However, broad population screening is difficult to institute in practice. Breast self examination is important, but too insensitive to detect cancers smaller than 2 cm, so regular mammographic screening is the best tool. Family history and geography are major influences, and diet a minor influence, on likelihood of developing breast cancer, but don't predict prognosis. Once a cancer is diagnosed, the gene expression profile along with histologic type are most important in determining therapy, but may also help in predicting prognosis. Presence of metastasis is the best (but undesirable) prognostic factor Finding a breast cancer <1 cm with no metastases predicts a >90% 10-year survival.

BP7 711BP8 748PBD7 1132PBD8 1076–1077