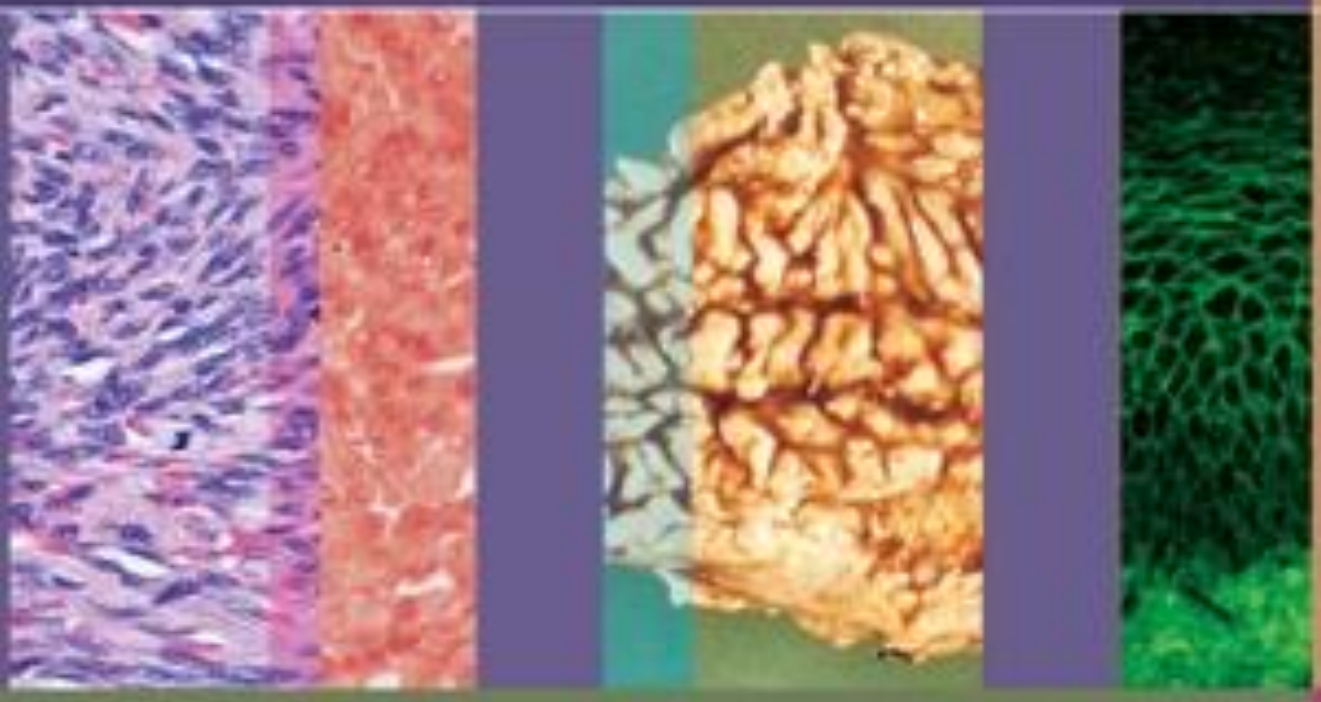
Lippincott's Illustrated Q&A Review of

Rubin's Pathology



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Wolters Kluwer Health | Lippincott Williams & Wilkins

Chapter 20

Hematopathology

QUESTIONS

Select the single best answer.

1 An 18-year-old man moves from sea level to an elevation of 2,400 m to train as a skier. The increased requirement for oxygen delivery to tissues at the higher elevation stimulates the synthesis of a renal hormone (erythropoietin), which targets hematopoietic stem cells in the bone marrow. Erythropoietin promotes the survival of early erythroid progenitor cells primarily through which of the following mechanisms?
(A) Altered cell-matrix adhesion
(B) Downregulation of p53
(C) Enhanced glucose uptake
(D) Inhibition of apoptosis
(E) Stimulation of globin biosynthesis

2 A 6-year-old girl is brought into the emergency room after an automobile accident. Physical examination shows bleeding from multiple wounds, and a CBC reveals a normocytic, normochromic anemia. Which of the following indices is most helpful in defining this patient's anemia as normocytic?
(A) Hematocrit
(B) Hemoglobin
(C) Mean corpuscular hemoglobin concentration
(D) Mean corpuscular volume
(E) Red blood cell count

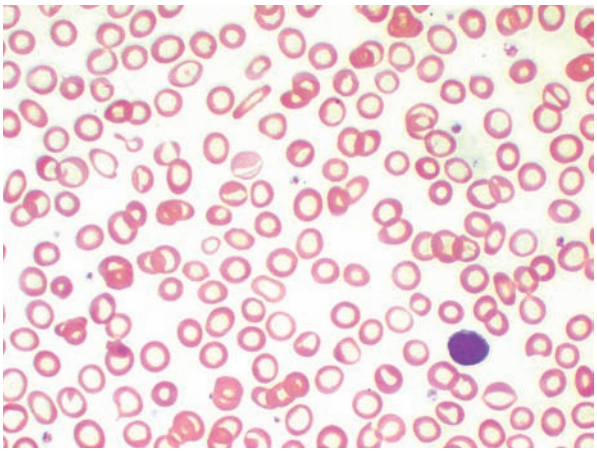
3 A 60-year-old man presents with a 6-month history of increasing fatigue. Physical examination reveals marked pallor, and a CBC shows a macrocytic anemia. Which of the following is the most likely cause of anemia in this patient?
(A) Alcoholism
(B) Chronic disease
(C) Iron deficiency
(D) Renal disease
(E) Thalassemia

4 A 43-year-old woman of Scandinavian descent complains of constant tiredness, light-headedness, and occasional palpitations and shortness of breath while ascending the stairs. Physical examination shows pallor of the oral mucosa and a raspberry-red tongue (glossitis). Neurologic examination reveals paresthesias, numbness, decreased vibration sensation, and loss of deep tendon reflexes. The results of laboratory studies include hemoglobin of 7.2 g/dL, WBC of 4,500/μL, platelets of 140,000/μL, erythrocyte folate of 220 ng/mL, serum vitamin B_{12} of 40 pg/mL (normal >200 pg/mL), serum anti-intrinsic factor of 1:128, and serum anti–parietal cell antibody of 1:64. Examination of peripheral blood shows macrocytic anemia, with poikilocytosis of RBCs and hypersegmented neutrophils. Atrophic gastritis is diagnosed by gastric biopsy. Bone marrow examination in this patient will reveal which of the following pathologic findings?
(A) Absent stainable bone marrow iron
(B) Atypical megakaryocytes with fibrosis
(C) Hypercellularity with megaloblastic erythroid maturation
(D) Hypocellularity with absence of erythroid precursors
(E) Myeloid hyperplasia with increased basophils

5 Which of the following mechanisms of disease best describes the pathogenesis of anemia in the patient described in Question 4?
(A) Bone marrow fibrosis
(B) Clonal stem cell abnormality
(C) Defective heme synthesis
(D) Immune destruction of circulating erythrocytes
(E) Impaired DNA synthesis

6 A 30-year-old woman complains of recent easy fatigability, bruising, and recurrent throat infections. Physical examination reveals numerous petechiae over her body and mouth. Abnormal laboratory findings include hemoglobin of 6 g/dL, WBC of 1,500/μL, and platelets of 20,000/μL. The bone marrow is hypocellular and displays increased fat. What is the appropriate diagnosis?
(A) Aplastic anemia
(B) Iron-deficiency anemia
(C) Megaloblastic anemia
(D) Myelofibrosis with myeloid metaplasia
(E) Pure red cell aplasia

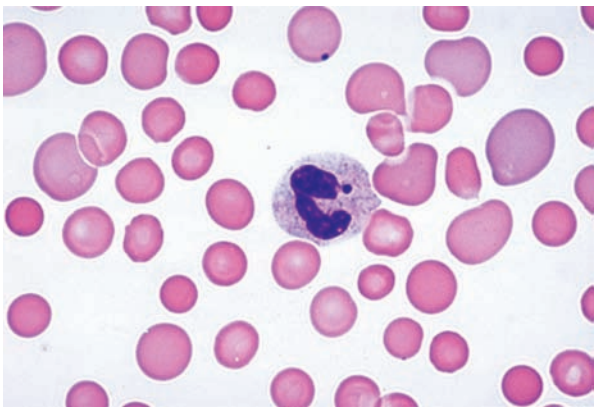
7 A 20-year-old thin fashion model complains that she cannot concentrate and is always tired. She has heavy menstrual bleeding every month but is otherwise healthy. The peripheral blood smear is shown in the image. Which of the following laboratory findings would be expected in this patient?



(A) Hyperbilirubinemia
(B) Increased serum ferritin
(C) Low plasma iron saturation
(D) Positive direct Coombs test
(E) Vitamin B_{12} deficiency

8 A 39-year-old woman presents with a 2-month history of upper abdominal pain, weakness, and fatigue. Physical examination reveals marked pallor. Laboratory studies show microcytic, hypochromic anemia (hemoglobin = 8.5 g/dL) and mild thrombocytosis. Gastroscopy discloses a mucosal defect in the antrum measuring 1.5 cm in diameter. Which of the following best describes the pathogenesis of anemia in this patient?
(A) Defective globin chain synthesis
(B) Impaired heme synthesis
(C) Poor utilization of iron stores
(D) Synthesis of structurally abnormal hemoglobin molecules
(E) Toxic damage to bone marrow stem cells

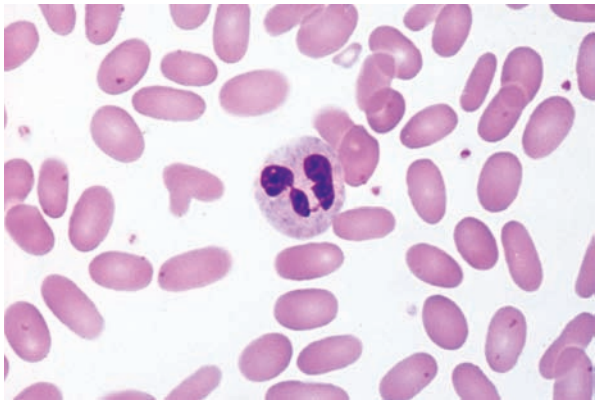
9 A 10-year-old boy presents with chronic fatigue. Physical examination reveals slight jaundice and splenomegaly. The results of laboratory studies include hemoglobin of 11.7 g/dL, hematocrit of 32%, total bilirubin of 2.6 mg/dL, and conjugated bilirubin of 0.8 mg/dL. The peripheral blood smear is shown in the image. The osmotic fragility of the patient's RBCs is increased, but the Coombs test is negative. Defects in which of the following are involved in the pathogenesis of this disorder?



(A) DNA synthesis
(B) Erythrocyte cytoskeleton
(C) Erythrocyte maturation
(D) Glucose-6-phosphate dehydrogenase (G6PD)
(E) Hemoglobin synthesis

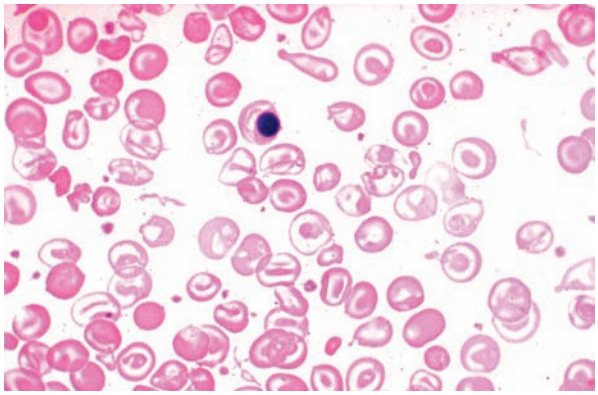
10 The patient described in Question 9 is at increased risk for development of which of the following conditions?
(A) Acute renal tubular necrosis
(B) Cholelithiasis
(C) Cirrhosis
(D) Nephrolithiasis
(E) Portal hypertension

11 A 27-year-old pregnant woman comes to the obstetrician for a prenatal check-up. Routine laboratory testing reveals a mild normocytic anemia. The peripheral blood smear is shown in the image. Which of the following best explains the pathogenesis of anemia seen in this patient?



(A) Abnormal membrane lipoprotein molecules
(B) Abnormal polymerization of spectrin molecules
(C) Decreased iron release in the bone marrow
(D) Destabilization of the lipid bilayer of the RBC membrane
(E) Oxidative denaturation of hemoglobin

12 A 10-month-old boy of Arabic extraction is brought to the physician by his parents who complain that their child is failing to thrive. Physical examination reveals splenomegaly and jaundice. A CBC shows a microcytic, hypochromic anemia (hemoglobin = 7.4 g/dL). Fetal hemoglobin accounts for most of the hemoglobin. A peripheral blood smear is shown in the image. Which of the following is the appropriate diagnosis?

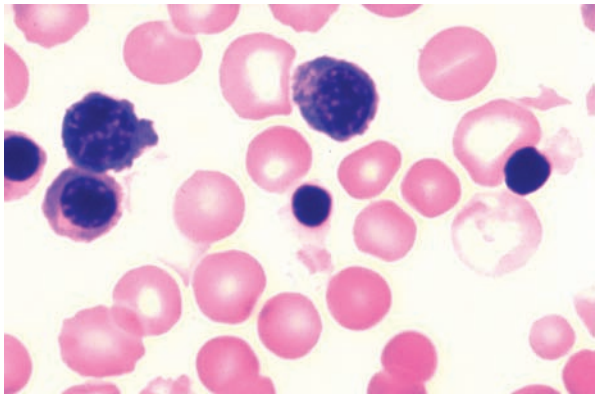


(A) G6PD deficiency
(B) Hereditary elliptocytosis
(C) Hereditary spherocytosis
(D) Iron deficiency anemia
(E) β-Thalassemia

13 Which of the following best describes the pathogenesis of splenomegaly seen in the patient described in Question 12?
(A) Amyloidosis
(B) Chronic malaria
(C) Extramedullary hematopoiesis
(D) Infectious mononucleosis
(E) Splenic vein thrombosis

14 A 22-year-old woman from a large Italian family is screened for a familial blood disorder. The results of laboratory studies include a hemoglobin of 9.5 g/dL and a smear displaying mild microcytosis, hypochromia, and a few target cells. Hemoglobin electrophoresis shows a mild increase in hemoglobin A2 (7.5%). What is the appropriate diagnosis?
(A) Anemia of chronic disease
(B) G6PD deficiency
(C) Heterozygous β-thalassemia
(D) Homozygous β-thalassemia
(E) Silent carrier α-thalassemia

15 A 28-year-old woman delivers a male neonate at 36 weeks of gestation. The mother has a history of poor prenatal care and several previous miscarriages. Examination of the neonate reveals marked pallor and generalized edema (anasarca), and the peripheral blood smear is shown in the image. The nucleated cells in this blood smear are which of the following?

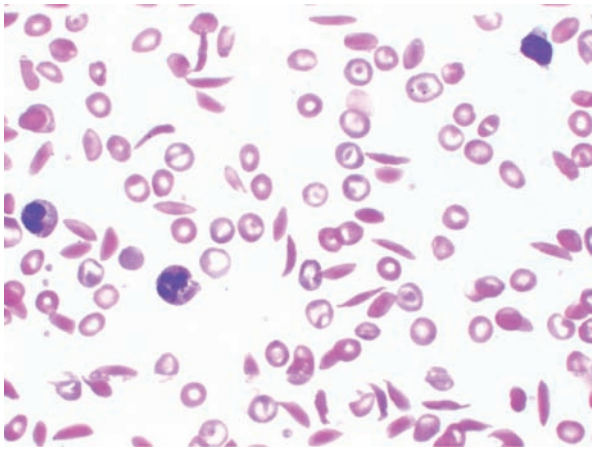


(A) B lymphocytes
(B) Eosinophils
(C) Erythroblasts
(D) Monocytes
(E) T lymphocytes

16 A 60-year-old man presents with headaches and pruritis. Physical examination reveals splenomegaly but no lymphadenopathy. A CBC demonstrates elevated hemoglobin of 19.5 g/dL, WBC of 12,800/μL, and platelets of 550,000/μL. The bone marrow displays hypercellularity of all lineages and depletion of marrow iron stores. Which of the following is the most likely diagnosis?
(A) Acute myelogenous leukemia
(B) Essential thrombocythemia
(C) Idiopathic myelofibrosis
(D) Occult infection
(E) Polycythemia vera

17 The patient described in Question 16 is at increased risk of developing which of the following conditions?
(A) Cerebral aneurysm
(B) Cerebrovascular accident
(C) Cholelithiasis
(D) Osteogenic sarcoma
(E) Raynaud phenomenon

18 A 10-year-old black girl is brought to the emergency room. She complains of severe pain in her chest, abdomen, and bones. Physical examination reveals jaundice and anemia. Her parents state that she has been anemic since birth. A CBC shows normocytic anemia with marked poikilocytosis. A peripheral blood smear is shown in the image. Hemoglobin electrophoresis demonstrates hemoglobin S. This child's chest and bone pain is most likely caused by which of the following mechanisms?



(A) Amyloidosis
(B) Coagulopathy
(C) Infection
(D) Ischemia
(E) Vasculitis

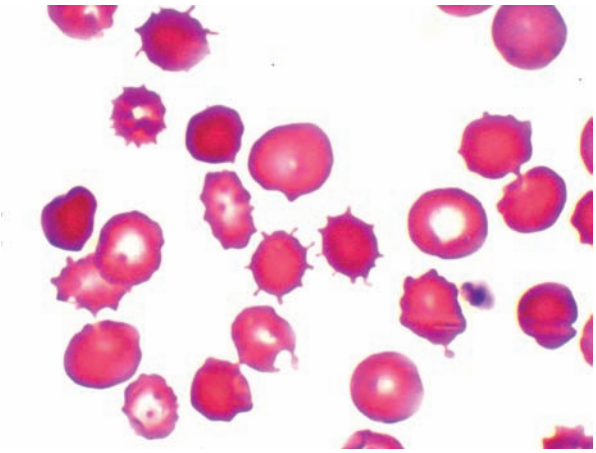
19 Over the next 6 years, the patient described in Question 18 develops multiple splenic infarcts. Which of the following is a common complication of autosplenectomy in this patient?
(A) Autoimmune gastritis
(B) Cholelithiasis
(C) Megaloblastic anemia
(D) Membranous nephropathy
(E) Pneumonia

20 A 24-year-old woman with sickle cell disease is seen in the emergency room for an acute upper respiratory tract infection. Laboratory findings include a severe, normocytic anemia. The patient develops a rapid drop in the hemoglobin level. However, the reticulocyte count is very low (<0.01%). This finding most likely reflects which of the following conditions?

(A) Bone marrow failure due to repeated infarction
(B) Expected result for the patient's underlying anemia
(C) Parvovirus B19 infection
(D) Retroperitoneal hemorrhage
(E) Vitamin B_{12} deficiency

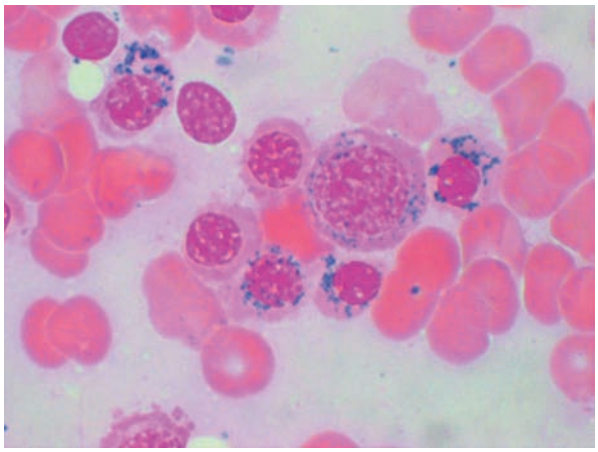
21 A 36-year-old man from China presents with increasing fatigue. He has a 3-year history of tuberculosis, and CBC shows a mild microcytic anemia. Blood work-up demonstrates low serum iron, low iron-binding capacity, and increased serum ferritin. The pathogenesis of anemia in this patient is most likely caused by which of the following mechanisms?
(A) Clonal stem cell defect
(B) Hypoxemia
(C) Impaired utilization of iron from storage sites
(D) Synthesis of structurally abnormal globin chains
(E) Toxic damage to bone marrow stem cells

22 A 45-year-old chronic alcoholic man presents with mental confusion. The peripheral blood smear is shown in the image. The morphologic abnormalities demonstrated in this blood smear are most likely associated with which of the following conditions?



(A) Abnormal spectrin in red cell membranes
(B) Chronic liver disease
(C) Chronic renal failure
(D) Microthrombi in capillaries
(E) Vitamin B_{12} deficiency

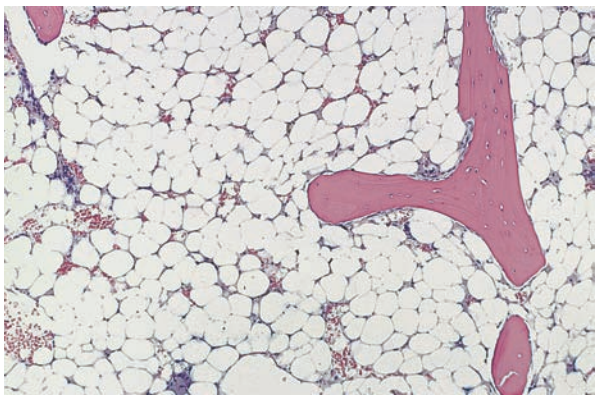
23 A 78-year-old man presents with increasing fatigue. A CBC shows pancytopenia, with moderate anemia (hemoglobin = 10.5 g/dL) and normochromic, hypochromic RBCs. Mild neutropenia and thrombocytopenia are noted. A bone marrow evaluation reveals erythroid hyperplasia with increased iron. A Prussian blue–stained bone marrow aspirate is shown in the image. Which of the following is the appropriate diagnosis?



(A) Hairy cell leukemia
(B) Multiple myeloma
(C) Myelodysplastic syndrome
(D) Polycythemia vera
(E) Promyelocytic leukemia

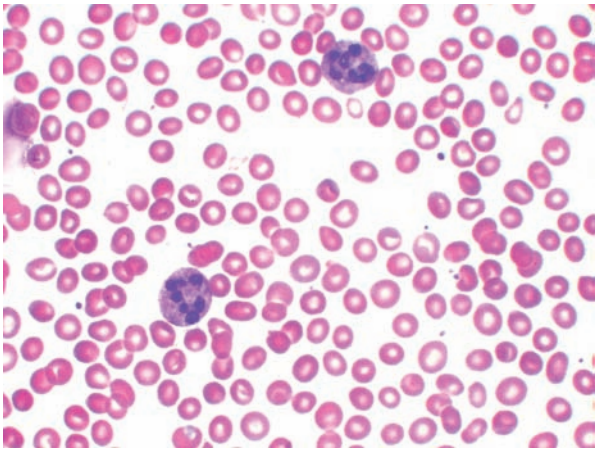
24 Which of the following best describes the pathogenesis of the hematologic disorder seen in the patient described in Question 23?
(A) Clonal stem cell defect
(B) C-*myc* translocation
(C) Deletion of a portion of the β-globin gene
(D) Functional asplenia
(E) Mutation of the T-cell receptor gene

25 A 32-year-old man presents with mild fever and increasing fatigue. He is an immigrant from Russia and worked in a benzene factory. Physical examination does not reveal lymphadenopathy or splenomegaly, but petechial skin lesions are noted. A CBC demonstrates severe pancytopenia, with normocytic red cell indices. A bone marrow biopsy is shown in the image. Which of the following is the most likely underlying mechanism in the development of this patient's anemia?



(A) Damage to stem cells
(B) Decreased erythropoietin production by the kidneys
(C) Folate deficiency
(D) Impaired globin chain synthesis
(E) Neoplastic proliferation of committed stem cells

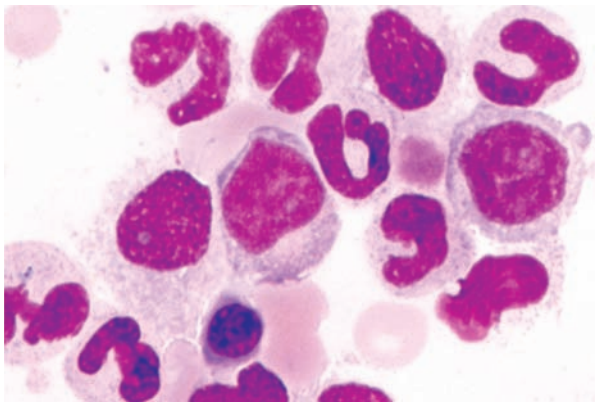
26 A patient with a history of chronic alcoholism presents with a macrocytic anemia and thrombocytopenia. Blood smear examination demonstrates numerous oval macrocytes and hypersegmented neutrophils (results shown in the image). A Schilling test is normal. Which of the following is the most likely diagnosis?



(A) Anemia of chronic disease
(B) Folic acid deficiency
(C) G6PD deficiency
(D) Iron deficiency anemia
(E) Sickle cell anemia

27 A 23-year-old, previously healthy man of Italian origin develops moderate to severe hemolytic anemia. The previous evening he had celebrated a Saint's day with a feast of beans and pasta. Urinalysis shows free hemoglobin, and the direct Coombs test is negative. Supravital staining of the blood smear demonstrates numerous membrane-bound inclusions (Heinz bodies) within erythrocytes. Which of the following is the most likely diagnosis?
(A) G6PD deficiency
(B) Paroxysmal nocturnal hemoglobinuria
(C) Sickle cell anemia
(D) β-Thalassemia minor
(E) Warm antibody autoimmune hemolytic anemia

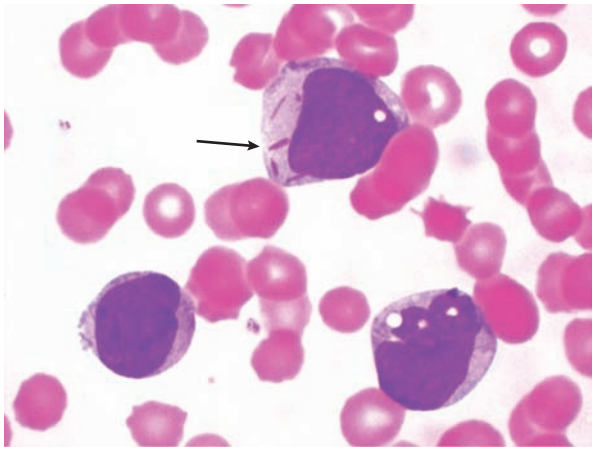
28 A 60-year-old man complains of night sweats, weight loss, easy fatigability, and discomfort in the left upper abdominal quadrant. Physical examination reveals splenomegaly. Laboratory studies show leukocytosis (40,000/μL). A peripheral blood smear demonstrates mature and maturing granulocytes, myelocytes, basophils, and occasional myeloblasts. The bone marrow is hypercellular and dominated by WBC precursors. Megakaryocytes are numerous, and RBC precursors are less prominent. A smear of the bone marrow aspirate is shown in the image. Cytogenetic studies disclose a monoclonal population of abnormal cells with a t(9;22)(q34;q11) chromosomal translocation. What is the appropriate diagnosis?



(A) Acute lymphoblastic leukemia
(B) Acute myeloid leukemia
(C) Chronic lymphocytic leukemia
(D) Chronic myelogenous leukemia
(E) Myelodysplastic syndrome

29 Which oncogene is located at the t(9;22) chromosomal breakpoint in the patient described in Question 28?
(A) *abl*
(B) *erb*
(C) *myb*
(D) *myc*
(E) *neu*

30 A 40-year-old woman complains of fatigue and nausea of 3 months in duration. Physical examination reveals numerous pustules on the face, as well as splenomegaly and hepatomegaly. Laboratory studies show hemoglobin of 6.3 g/dL and platelets of 50,000/μL. A peripheral smear shows malignant cells with Auer rods (arrow). The patient develops diffuse purpura, bleeding from the gums, and laboratory features of disseminated intravascular coagulation (DIC). Which of the following is the appropriate diagnosis?

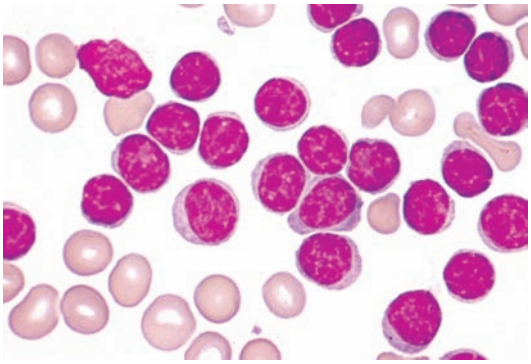


(A) Acute lymphoblastic leukemia
(B) Acute megakaryocytic leukemia
(C) Acute promyelocytic leukemia
(D) Chronic myelogenous leukemia
(E) Monocytic leukemia

31 Cytogenetic studies in malignant cells from the patient described in Question 30 demonstrate a chromosomal translocation. Which of the following genes is most likely found at the translocation site?

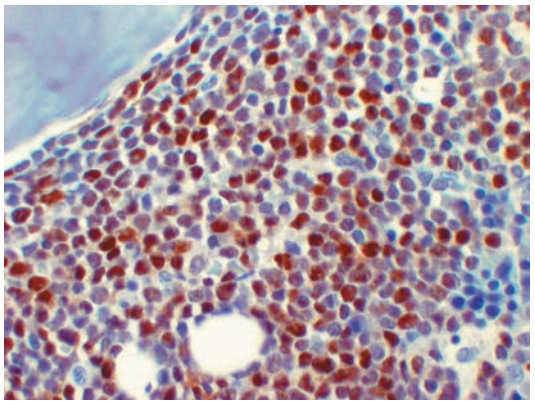
(A) *abl*
(B) *bcl-1*
(C) *bcl-2*
(D) *myc*
(E) Retinoic acid receptor

32 A 60-year-old man presents with a 3-week history of lymph node enlargement in his neck and axillae. A CBC reveals mild anemia, with a leukocytosis of 20,000/μL. The peripheral blood smear is shown in the image. More than 80% of WBCs are small lymphocytes, but there are also prominent "smudge cells." Examination of a bone marrow biopsy shows nodular and interstitial infiltrates of lymphocytes, which demonstrate clonal rearrangement of the IgG light-chain gene. Which of the following is the appropriate diagnosis?



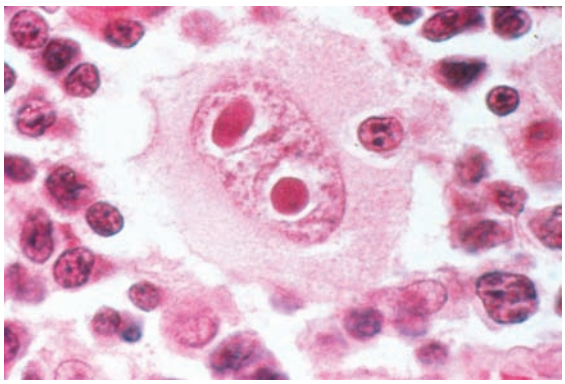
(A) Acute lymphoblastic lymphoma
(B) Chronic lymphocytic leukemia
(C) Chronic myelogenous leukemia with lymphoid blast crisis
(D) Multiple myeloma
(E) Waldenström macroglobulinemia

33 A 6-year-old boy presents with fatigue, fever, and night sweats. Physical examination reveals marked pallor. Palpation of his sternum demonstrates diffuse tenderness. Laboratory studies disclose anemia, thrombocytopenia, and leukocytosis. The WBC differential count shows that 90% blasts. A bone marrow biopsy stained immunohistochemically for terminal deoxynucleotidyl transferase (TdT) is shown in the image. Which of the following is the appropriate diagnosis?



(A) Acute lymphoblastic leukemia
(B) Acute myelogenous leukemia
(C) Acute promyelocytic leukemia
(D) Chronic lymphocytic leukemia
(E) Chronic myelogenous leukemia

34 A 27-year-old man presents with an 8-week history of fevers, chills, pruritis, and night sweats. Two months ago, he experienced a flu-like illness. A nagging cough with occasional hemoptysis persisted for several weeks following resolution of his other symptoms. Physical examination reveals moderately enlarged, firm, nontender lymph nodes located in the right supraclavicular region. A lymph node biopsy is shown in the image. What is the appropriate diagnosis?



(A) Acute myelogenous leukemia
(B) Burkitt lymphoma
(C) Hodgkin lymphoma
(D) Infectious mononucleosis
(E) Lymphoblastic lymphoma

35 Which of the following is the most common histologic subtype of the disease in the patient described in Question 34?

(A) Lymphocyte depleted
(B) Lymphocyte predominant
(C) Lymphocyte rich
(D) Mixed cellularity
(E) Nodular sclerosis

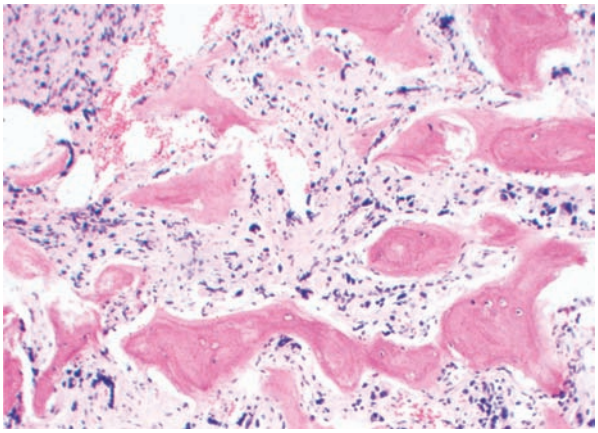
36 A 55-year-old man complains of pain in his back, fatigue and occasional confusion. He admits to polyuria and polydipsia. An X-ray examination reveals numerous lytic lesions in the lumbar vertebral bodies. Laboratory studies disclose hypoalbuminemia, mild anemia, and thrombocytopenia. A monoclonal Igκ peak is demonstrated by serum electrophoresis. Urinalysis shows 4+ proteinuria. A bone marrow biopsy discloses foci of plasma cells, which account for 18% of all hematopoietic cells. What is the appropriate diagnosis?

(A) Acute lymphoblastic lymphoma
(B) Chronic lymphocytic leukemia
(C) Extramedullary plasmacytoma
(D) Multiple myeloma
(E) Waldenström macroglobulinemia

37 For the patient described in Question 36, which of the following is the most common, and ultimately lethal, extramedullary complication?

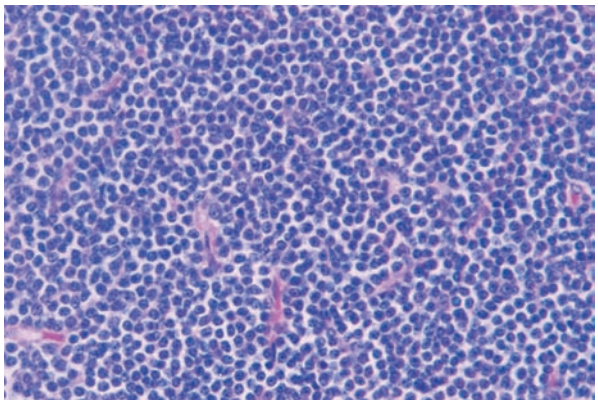
(A) Dementia
(B) Hepatic failure
(C) Pericarditis
(D) Peritonitis
(E) Renal failure

38 A 62-year-old man presents with a history of several months of vague abdominal pain and fatigue. Physical examination reveals marked splenomegaly but no evidence of lymphadenopathy. The patient subsequently develops bacterial sepsis and expires. A bone marrow biopsy at autopsy shows numerous atypical megakaryocytes and marked marrow fibrosis (results shown in the image). Which of the following is the most likely diagnosis?



(A) Acute myelogenous leukemia
(B) Acute promyelocytic leukemia
(C) Chronic idiopathic myelofibrosis
(D) Chronic lymphocytic leukemia
(E) Chronic myelogenous leukemia

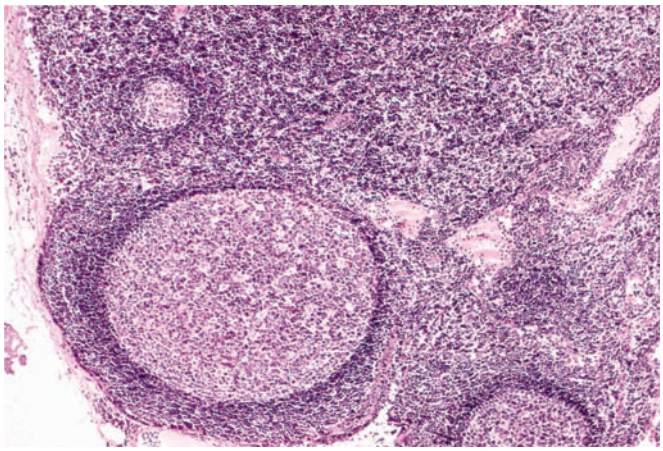
39 A 57-year-old man is admitted to the hospital with inguinal and cervical lymphadenopathy. He had noticed the first palpable nodule about 6 months ago. Upon physical examination, more palpable lymph nodes are found in the axillary and supraclavicular regions. Laboratory data show the serum proteins to be within normal limits, whereas the WBC count is 25,000/μL with many small abnormal lymphocytes. A cervical lymph node biopsy is shown in the image. The histologic features are most consistent with which of the following hematologic disorders?



(A) Burkitt lymphoma
(B) Hodgkin lymphoma
(C) Plasmacytoma
(D) Reactive follicular hyperplasia
(E) Small lymphocytic lymphoma

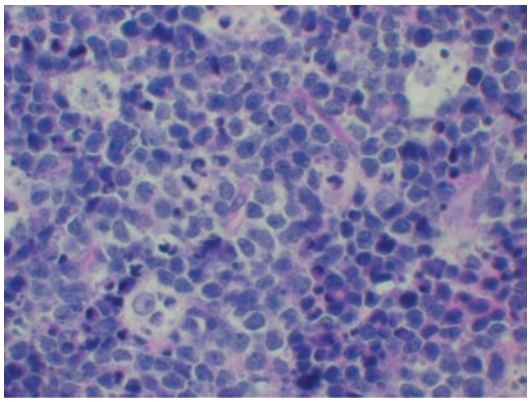
40 A 50-year-old man presents with fever and diffuse lymphadenopathy. A lymph node biopsy reveals non-Hodgkin follicular lymphoma. Immunohistochemical staining of neoplastic lymphoid cells within the nodular areas of the lymph node would be expected to stain positively for which of the following protein markers?
(A) Abl
(B) Bax
(C) Bcl-2
(D) Myc
(E) Retinoic acid receptor

41 A 12-year-old girl presents with a fever of 38°C (101°F) and a swollen lymph node of 6 days in duration. The CBC is normal. Biopsy of the swollen lymph node shows benign follicular hyperplasia (shown in the image). This pathologic finding is best interpreted as which of the following?



(A) Proliferation in B-cell areas
(B) Proliferation of dendritic cells
(C) Proliferation of plasma cells
(D) Proliferation in T-cell areas
(E) Proliferation of marginal-zone lymphocytes

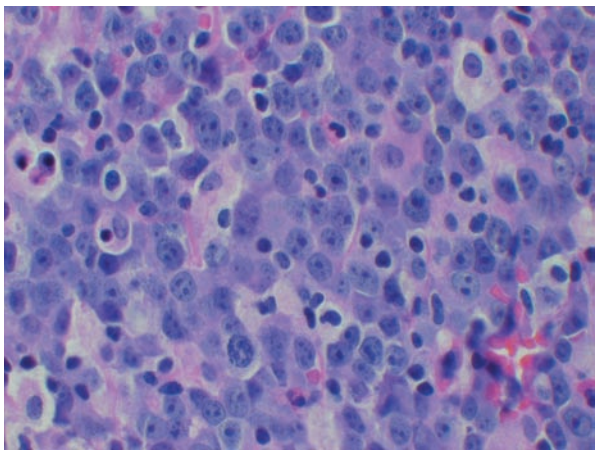
42 A 4-year-old boy from Kenya presents with a 3-week history of a rapidly expanding jaw. A biopsy of an enlarged cervical lymph node is shown in the image. Histologic examination reveals numerous mitotic figures and many macrophages containing nuclear and cytoplasmic debris. The cells express surface IgM and are positive for common B-cell antigens. Which of the following is the appropriate diagnosis?



(A) Acute myelogenous leukemia
(B) Burkitt lymphoma
(C) Plasmacytoma
(D) Reactive follicular hyperplasia
(E) Small lymphocytic lymphoma

43 A 24-year-old woman presents with an earache of 4 days in duration. She also reports increased urine production, a skin rash, and bone pain on her scalp. Physical examination reveals otitis media, dermatitis, and exophthalmos. An X-ray of the scalp shows calvarial bone defects. A fine-needle aspirate displays numerous eosinophils. Which of the following is the most likely diagnosis?
(A) Hodgkin lymphoma
(B) Langerhans cell histiocytosis
(C) Malignant melanoma
(D) Metastatic breast carcinoma
(E) Multiple myeloma

44 A 42-year-old woman presents with an enlarged supraclavicular lymph node. The patient is HIV positive and takes antiviral medications. A lymph node biopsy is shown in the image. The tumor cells express B cell antigens and are positive for Epstein-Barr virus (EBV). Which of the following is the most likely diagnosis?



(A) Follicular lymphoma
(B) Hodgkin lymphoma
(C) Large B-cell lymphoma
(D) MALT lymphoma
(E) Mantle cell lymphoma

45 A 55-year-old man presents with a 3-week history of abdominal discomfort. Physical examination demonstrates splenomegaly but no lymphadenopathy. A CBC shows pancytopenia. Examination of a peripheral blood smear reveals atypical lymphoid cells that exhibit tartrate-resistant acid phosphatase activity. Which of the following is the appropriate diagnosis?
(A) Acute lymphocytic leukemia
(B) Chronic lymphocytic leukemia
(C) Chronic myelogenous leukemia
(D) Hairy cell leukemia
(E) Hodgkin disease

46 A 55-year-old man presents with recurrent epigastric pain. Upper GI endoscopy and gastric biopsy reveal a neoplastic, lymphocytic infiltrate invading glandular tissue. Giemsa staining is positive for *Helicobacter pylori*. Which of the following is the most likely diagnosis?
(A) Burkitt lymphoma
(B) Follicular lymphoma
(C) Hodgkin lymphoma
(D) Mantle cell lymphoma
(E) Marginal zone lymphoma

47 A 58-year-old man presents with a 2-month history of erythematous, scaly plaques over his trunk and upper extremities. Biopsy of these lesions reveals an atypical lymphocytic infiltrate in the dermis, which extends into the overlying epidermis. Immunohistochemical staining demonstrates positive staining for CD4. Which of the following is the most likely diagnosis?
(A) Acute lymphoblastic lymphoma
(B) Chronic lymphoid leukemia
(C) Extramedullary plasmacytoma
(D) Hairy cell leukemia
(E) Mycosis fungoides

48 A 56-year-old man presents with enlarged lymph nodes. Physical examination reveals mild hepatosplenomegaly. A lymph node biopsy shows small lymphocytes, as well as plasmacytoid lymphocytes containing Dutcher and Russell bodies. Immunohistochemical studies demonstrate cytoplasmic accumulation of IgM. What is the appropriate diagnosis?
(A) Burkitt lymphoma
(B) Hodgkin lymphoma
(C) Richter syndrome
(D) Sézary syndrome
(E) Waldenström disease

49 A 9-year-old girl develops widespread pinpoint skin hemorrhages. She recovered from a flu-like illness 1 week earlier. Laboratory findings reveal a platelet count of 20,000/μL but no other abnormalities. Her bone marrow shows an increased number of megakaryocytes. The platelet count is normal after 2 months. Which of the following is the appropriate diagnosis?
(A) Antiphospholipid antibody syndrome
(B) Disseminated intravascular coagulation
(C) Hemolytic-uremic syndrome
(D) Idiopathic thrombocytopenic purpura
(E) Thrombotic thrombocytopenic purpura

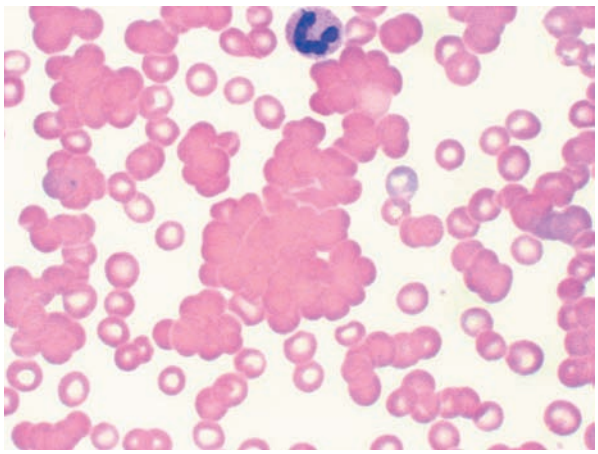
50 A 25-year-old woman with a history of systemic lupus erythematosus presents with diffuse petechiae and fatigue. Physical examination demonstrates lymphadenopathy and splenomegaly. Laboratory findings include normocytic anemia (hemoglobin = 6.1 g/dL) and thrombocytopenia (30,000/μL). Which of the following is the most likely underlying mechanism in the development of thrombocytopenia in this patient?

(A) Antibody-mediated platelet destruction
(B) Clonal plasma cell circulating paraprotein
(C) Decreased susceptibility to complement-mediated lysis
(D) Defect in the platelet cytoskeleton
(E) Increased activity of an enzyme in the glycolytic pathway

51 For the patient described in Question 50, a peripheral blood smear shows polychromasia with 10% reticulocytes. This patient most likely has which of the following hematologic diseases?

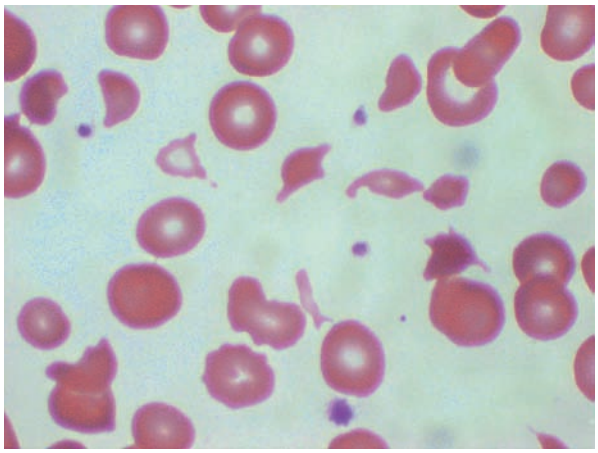
(A) Anemia of chronic renal failure
(B) Aplastic anemia
(C) Hemolytic anemia
(D) Iron deficiency anemia
(E) Myelophthisic anemia

52 A 22-year-old man presents with a 6-day history of sore throat, fever, and general malaise. Physical examination reveals generalized lymphadenopathy, which is most prominent in the cervical lymph nodes. A CBC demonstrates atypical lymphocytes. The monospot test is positive. Two weeks later, the patient complains of intermittent pain and tingling in the tips of his fingers. A CBC discloses a mild, macrocytic anemia. The peripheral blood smear is shown in the image. Which of the following is the most likely cause of anemia in this patient?



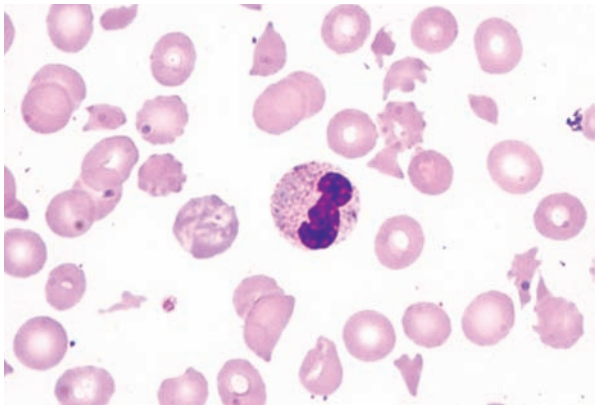
(A) Autoantibodies directed against the erythrocyte membrane
(B) Clonal plasma cell dyscrasia with circulating paraprotein
(C) Decreased activity of an enzyme in the glycolytic pathway
(D) Defect in the erythrocyte cytoskeleton
(E) Increased susceptibility to complement-mediated hemolysis

53 A 25-year-old previously healthy woman develops spontaneous vaginal bleeding. The following day, she experiences a tonic-clonic seizure. On physical examination, she is febrile and jaundiced and has widespread purpura. Laboratory findings include a hemoglobin of 5.3 g/dL with 8% reticulocytes, a platelet count of 10,000/μL, and a BUN of 48 mg/dL. The peripheral blood smear is shown in the image. Which of the following is the appropriate diagnosis?



(A) Drug-induced thrombocytopenia
(B) Henoch-Schönlein purpura
(C) Idiopathic thrombocytopenic purpura
(D) Thrombotic thrombocytopenic purpura
(E) von Willebrand disease

54 A 45-year-old man suffers severe third-degree burns in an industrial accident. During his hospital stay, the patient develops anemia, thrombocytopenia, and widespread purpura. Blood oozes from venipuncture sites. Laboratory studies show that fibrin split products are elevated. The peripheral blood smear is shown in the image. What is the appropriate diagnosis?



(A) Acanthocytosis
(B) Henoch-Schönlein purpura
(C) Idiopathic thrombocytopenic purpura
(D) Microangiopathic hemolytic anemia
(E) Paroxysmal nocturnal hemoglobinuria

55 A 67-year-old woman with a prosthetic aortic valve develops progressive anemia. Examination of a peripheral blood smear reveals reticulocytosis and schistocytes. What is the appropriate diagnosis?

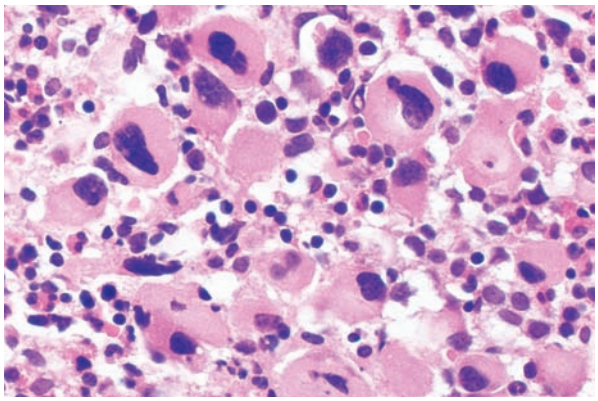
(A) Acanthocytosis
(B) Henoch-Schönlein purpura
(C) Idiopathic thrombocytopenic purpura
(D) Macroangiopathic hemolytic anemia
(E) Microangiopathic hemolytic anemia

56 A 14-year-old boy presents with acute onset of right flank pain, which developed after he helped his father paint the ceiling of his bedroom. Physical examination demonstrates an area of ecchymosis in the right flank that is tender to palpation. The patient has a lifelong history of easy bruising. His brother shows the same tendency. The serum level of clotting factor VIII is less than 2% of normal. Which of the following is the most likely underlying mechanism for bleeding tendency in this patient?
(A) Circulating antibodies directed against factor VIII
(B) Decreased hepatic synthesis of multiple coagulation factors
(C) Deficiency of vitamin K
(D) Genetic defect involving the factor VIII gene
(E) Nonimmune peripheral consumption of coagulation proteins

57 A 4-year-old boy develops severe bleeding into the knee joint. Laboratory studies show that serum levels of factor IX are reduced, but levels of factor VIII are normal. What is the appropriate diagnosis?
(A) Hemophilia A
(B) Hemophilia B
(C) Henoch-Schönlein purpura
(D) Idiopathic thrombocytopenic purpura
(E) von Willebrand disease

58 A 39-year-old man reports seeing red-colored urine in the morning. The CBC reveals anemia, low serum iron, and an elevated reticulocyte count. Laboratory studies show increased lysis of erythrocytes when incubated with either sucrose or acidified serum. Which of the following is the appropriate diagnosis?
(A) Anemia of chronic renal failure
(B) Hereditary spherocytosis
(C) Microangiopathic hemolytic anemia
(D) Paroxysmal nocturnal hemoglobinuria
(E) Vitamin B_{12} deficiency

59 A 46-year-old man presents with ataxia. MRI shows a cerebellar infarct. The platelet count is discovered to be 955,000/μL. The bone marrow biopsy reveals increased megakaryocytes with absent fibrosis (shown in the image). Cytogenetic studies are normal. Which of the following is the most likely diagnosis?



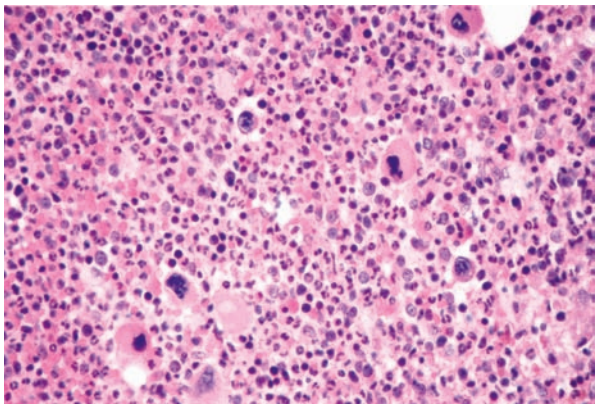
(A) Chronic myelogenous leukemia
(B) Essential thrombocythemia
(C) Myelofibrosis with myeloid metaplasia
(D) Polycythemia vera
(E) Thrombotic thrombocytopenic purpura

60 An 18-year-old man is rushed to the emergency room in shock following a motor vehicle accident. He is transfused with 5 U of blood. Following the transfusion the patient complains of fever, nausea, vomiting, and chest pain. Laboratory data show elevated indirect serum bilirubin, decreased serum haptoglobin, and a positive Coombs test. Which of the following is the most likely diagnosis?
(A) Autoimmune hemolytic anemia
(B) Disseminated intravascular coagulation
(C) Hemolytic transfusion reaction
(D) Hemolytic uremic syndrome
(E) Microangiopathic hemolysis

61 A 60-year-old woman complains of weakness and hematuria. Physical examination shows marked pallor, hepatosplenomegaly, and numerous ecchymoses of the upper and lower extremities. A CBC reveals a normocytic normochromic anemia, thrombocytopenia, neutropenia, and a marked leukocytosis, which is composed mainly of myeloblasts. The major clinical problems associated with this patient's condition are most directly related to which of the following?
(A) Avascular necrosis of bone
(B) Disseminated intravascular coagulation
(C) Hypersplenism
(D) Microangiopathic hemolytic anemia
(E) Suppression of hematopoiesis

62 A 69-year-old man is scheduled for surgery, but the procedure is canceled because of abnormal findings in the preoperative blood work. A CBC shows leukocytosis (WBC = 124,000/μL), consisting mainly of maturing neutrophils. Basophilia and

eosinophilia are also observed. The platelet count is 820,000/μL. A t(9;22)(q34;q11) translocation is documented. A bone marrow biopsy is shown in the image. Which of the following best characterizes the pathogenesis of the hematologic condition encountered in this patient?



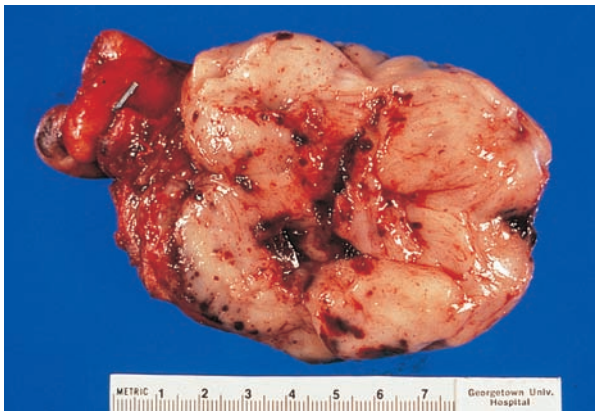
(A) Blocked differentiation of pre-B cells
(B) Blocked differentiation of pre-T cells
(C) Maturational arrest of lymphoid progenitor stem cells
(D) Transformation of a lymphoplasmacytic cell
(E) Transformation of a pluripotent bone marrow stem cell

63 A 48-year-old alcoholic man presents with a 6-day history of productive cough and fever. The temperature is 38.7°C (103°F), respirations are 32 per minute, and blood pressure is 125/85 mm Hg. The patient's cough worsens, and he begins expectorating large amounts of foul-smelling sputum. A chest X-ray shows a right upper and middle lobe infiltrate. A CBC demonstrates leukocytosis (WBC = 38,000/μL), with 80% slightly immature neutrophils and toxic granulation. Laboratory studies reveal elevated leukocyte alkaline phosphatase. Which of the following best describes this patient's hematologic condition?
(A) Acute myelogenous leukemia
(B) Chronic lymphocytic leukemia
(C) Chronic myelogenous leukemia
(D) Leukemoid reaction
(E) Richter syndrome

64 A 20-year-old carpenter with a wound infection on his left thumb presents with an enlarged and tender lymph node in the axilla. A lymph node biopsy shows follicular enlargement and hyperemia. The sinuses are filled with neutrophils. Which of the following is the most likely diagnosis?
(A) Castleman disease
(B) Histiocytosis X
(C) Interfollicular hyperplasia
(D) Sinus histiocytosis
(E) Suppurative lymphadenitis

65 A 56-year-old man with 3-year history of B-cell chronic lymphocytic leukemia complains of the recent onset of fever, weight loss, abdominal pain, and enlargement of lymph nodes. Physical examination reveals hepatosplenomegaly and generalized lymphadenopathy. A lymph node biopsy shows a high-grade, large-cell lymphoma. This patient has which of the following diseases?
(A) Acute lymphoblastic lymphoma
(B) Chronic myelogenous leukemia
(C) Hodgkin lymphoma
(D) Leukemoid reaction
(E) Richter syndrome

66 A 21-year-old woman complains of generalized weakness, blurred vision, and difficulty swallowing. Physical examination shows bilateral ptosis and facial muscle weakness. A CT scan of the chest reveals a mass in the anterior mediastinum. The patient's mass is surgically removed (shown in the image). A microscopic examination demonstrates epithelial cells and normal lymphocytes. What is the most likely diagnosis?

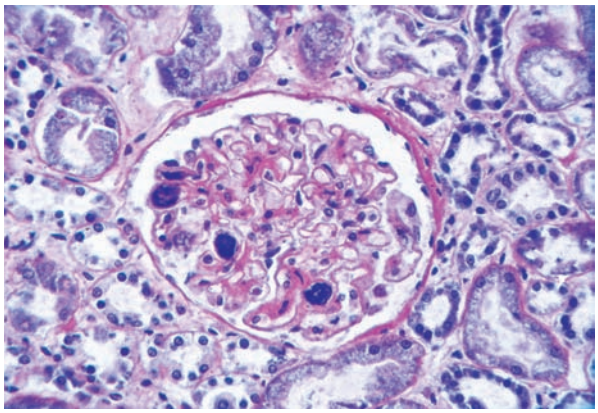


(A) Carcinoid tumor
(B) Hodgkin lymphoma
(C) Lymphocytic lymphoma
(D) Squamous cell carcinoma
(E) Thymoma

67 A 47-year-old man with a history of a heart-lung transplant 3 years ago complains of fever, malaise, and abdominal pain. The patient has been taking cyclosporine for immunosuppression. Physical examination reveals an abdominal mass. A CT-guided biopsy of the mass shows atypical lymphocytes that are positive for latent membrane proteins of Epstein-Barr virus (EBV). What is the most likely diagnosis?
(A) Acute suppurative lymphadenitis
(B) Burkitt lymphoma
(C) Graft-versus-host disease
(D) Infectious mononucleosis
(E) Posttransplant lymphoproliferative disorder

68 A 56-year-old man presents with a 2-week history of fatigue. The patient's past medical history is significant for aortic and mitral valve replacement 5 months ago. A CBC shows moderate anemia with an increased reticulocyte count. Which of the following best explains the pathogenesis of anemia in this patient?
(A) Complement-mediated hemolysis
(B) Decreased blood flow
(C) Direct red cell trauma
(D) Sludging of erythrocytes
(E) Thrombin activation

69 A 46-year-old man is rushed to the hospital after suffering massive trauma in an automobile accident. Two days later the patient suffers a clonic-tonic seizure. Blood cultures are positive for Gram-negative bacteria, and the patient is started on intravenous antibiotics. Laboratory studies show prolonged prothrombin time (PT) and partial thromboplastin time (PTT), low levels of fibrinogen, a positive D-dimer test, and thrombocytopenia. The patient develops renal failure and expires. A section of the kidney at autopsy is stained with phosphotungstic acid hematoxylin (shown in the image). The dark purple objects within the glomeruli are best identified as which of the following?



(A) Arteriovenous malformations
(B) Fat emboli
(C) Fibrin thrombi
(D) Psammoma bodies
(E) Vascular calcifications

ANSWERS

1 **The answer is D: Inhibition of apoptosis.** Recent studies indicate that erythropoietin promotes the survival of early erythroid progenitor cells through an inhibition of the default apoptosis pathway. Thus, this hormone rescues stem cells that are otherwise fated to undergo programmed cell death. None of the other choices are known to control the expansion of hematopoietic stem cell colonies in the bone marrow.
Diagnosis: Erythropoiesis

2 **The answer is D: Mean corpuscular volume (MCV).** MCV is the index used to measure the volume of a red blood cell. It categorizes RBCs by size. Cells with normal size are called normocytic, smaller cells are termed microcytic, and larger cells are referred to as macrocytic. Mean corpuscular hemoglobin concentration (choice C) measures hemoglobin content.
Diagnosis: Anemia

3 **The answer is A: Alcoholism.** Macrocytic anemia may be caused by impaired DNA synthesis due to a deficiency of folic acid or vitamin B_{12}. This results in abnormal nuclear development, which, in turn, leads to ineffective erythrocyte maturation and macrocytic anemia. Folic acid deficiency is most commonly due to inadequate dietary intake, which often develops in patients with poorly balanced diets (e.g., alcoholics). Other possible causes of macrocytic anemia include liver disease, hypothyroidism, and primary bone marrow disease. None of the other choices are associated with macrocytic anemia. Chronic disease (choice B) and renal disease (choice D) cause normochromic, normocytic anemia. Iron deficiency (choice C) and thalassemia (choice E) are microcytic anemias.
Diagnosis: Macrocytic anemia

4 **The answer is C: Hypercellularity with megaloblastic erythroid maturation.** Pernicious anemia is an autoimmune disorder in which patients develop antibodies directed against gastric parietal cells and intrinsic factor. Parietal cell antibodies lead to atrophic gastritis with achlorhydria. Deficiency of vitamin B_{12} or folic acid results in megaloblastic anemia. The peripheral blood smear shows macrocytosis and hypersegmentation of neutrophils. Megaloblastic maturation, characterized by cellular enlargement with asynchronous maturation between the nucleus and cytoplasm, is noted in bone marrow precursors from all lineages. Although the bone marrow tends to be hypercellular, the blood demonstrates pancytopenia because of ineffective hematopoiesis. Neurologic symptoms develop in vitamin B_{12} deficiency, secondary to degeneration of the posterior and lateral columns of the spinal cord. The other choices are not seen in pernicious anemia.
Diagnosis: Megaloblastic anemia, pernicious anemia

5 **The answer is E: Impaired DNA synthesis.** Megaloblastic anemias are caused by impaired DNA synthesis, usually due to a deficiency of either vitamin B_{12} or folic acid. In the face of defective DNA synthesis, nuclear development is impaired, whereas cytoplasmic maturation proceeds normally. This situation, termed nuclear to cytoplasmic asynchrony, results in the formation of megaloblasts. Because the megaloblastic precursors do not mature enough to be released into the blood, they undergo intramedullary destruction. Pernicious anemia is not related to any of the other choices.
Diagnosis: Megaloblastic anemia

6 **The answer is A: Aplastic anemia.** Aplastic anemia is a disorder of pluripotential stem cells that leads to bone marrow failure. The disorder features hypocellular bone marrow and pancytopenia (decreased circulating levels of all formed elements in the blood). Most cases are idiopathic. The bone marrow in aplastic anemia shows variably reduced cellularity, depending on the clinical stage of the disease. There is a decrease in the number of cells of myeloid, erythroid, and megakaryocytic lineages, with a relative increase in lymphocytes and plasma cells. As the cellularity decreases, there is a corresponding increase in bone marrow fat. Anemia, leukopenia (primarily granulocytopenia), and thrombocytopenia characterize aplastic anemia. Patients with aplastic anemia present with weakness, fatigue, infection, and bleeding. Iron-deficiency anemia (choice B) and megaloblastic anemia (choice C) are not characterized by a hypoplastic bone marrow. Myelofibrosis (choice D) shows increased connective tissue. Megakaryocytes and myeloid cells are not decreased in pure red cell aplasia (choice E).
Diagnosis: Aplastic anemia

7 **The answer is C: Low plasma iron saturation.** The blood smear reveals microcytic, hypochromic erythrocytes, characteristic of iron deficiency anemia caused by inadequate uptake or, more

often, excessive loss of iron. Women who have menorrhagia, especially those who consume restricted diets, are especially prone to iron deficiency anemia. Iron stores of the body are reduced, as evidenced by reduced levels of serum ferritin (not increased ferritin, choice B) and low iron saturation (iron/total iron binding capacity). None of the other laboratory findings would be expected in a patient with iron deficiency anemia.
Diagnosis: Iron deficiency anemia

8 **The answer is B: Impaired heme synthesis.** The presence of a peptic ulcer incriminates gastrointestinal bleeding as the cause of anemia. The resulting iron deficiency interferes with heme synthesis and thus leads to impaired hemoglobin production and anemia. Defective globin chain synthesis (choice A) and synthesis of structurally abnormal hemoglobin molecules (choice D) are hemoglobinopathies. Poor utilization of iron stores (choice C) reflects sideroblastic anemia and anemia of chronic disease.
Diagnosis: Iron deficiency anemia, peptic ulcer disease

9 **The answer is B: Erythrocyte cytoskeleton.** The smear shows many RBCs to be spherocytes, with decreased diameter and no central pallor. Hereditary spherocytosis (HS) represents a heterogeneous group of inherited disorders of the erythrocyte cytoskeleton, characterized by a deficiency of spectrin or other cytoskeletal components (ankyrin, protein 4.2, band 3). Most forms of HS are inherited as autosomal dominant traits, and most patients have a moderate normocytic anemia. The bone marrow demonstrates erythroid hyperplasia (erythroid maturation is not affected). The deficiency of a cytoskeletal protein in HS leads to uncoupling of the lipid bilayer from the underlying cytoskeleton. The defect results in progressive loss of membrane surface area and formation of spherocytes, which show increased osmotic fragility and are susceptible to chronic extravascular hemolysis. The osmotic fragility test is not abnormal in G6PD deficiency (choice D).
Diagnosis: Hereditary spherocytosis

10 **The answer is B: Cholelithiasis.** While circulating through the spleen, spherocytes lose additional surface membrane before they ultimately succumb to extravascular hemolysis and produce hyperbilirubinemia. Up to 50% of patients with spherocytosis develop cholelithiasis, with pigmented (bilirubin) gallstones due to the increased supply of bilirubin. Kidney stones (choice D) do not contain bilirubin. The liver (choices C and E) and kidney (choice A) are not affected by hereditary spherocytosis.
Diagnosis: Hereditary spherocytosis

11 **The answer is B: Abnormal polymerization of spectrin molecules.** The smear displays elliptical erythrocytes. Hereditary elliptocytosis (HE) refers to a heterogeneous group of inherited disorders involving the erythrocyte cytoskeleton, all of which feature a horizontal abnormality within the cytoskeleton. Variants of HE include defects in self-assembly of spectrin, spectrin-ankyrin binding, protein 4.1, and glycophorin C.
Diagnosis: Hereditary elliptocytosis

12 **The answer is E: β-Thalassemia.** The β-thalassemias are a heterogeneous group of disorders that most often arise secondary to point mutations affecting the β-globin gene. Accordingly, hemoglobin A ($\alpha_2\beta_2$) is not formed. Unpaired α-chains precipitate in red blood cells, accounting for ineffective erythropoiesis and increased hemolysis. The blood smear shows features characteristic of thalassemia, including hypochromic and microcytic RBCs, with anisocytosis, poikilocytosis, and target cells. In homozygous β-thalassemia, fetal hemoglobin (hemoglobin F) accounts for most of the hemoglobin, although increased levels of hemoglobin A2 are also present. Symptoms of the disease appear early in life, and affected children require constant transfusions. A heterozygous state for thalassemia may provide a protective effect against malaria and increase the reproductive potential of heterozygotes, thereby explaining the persistence of thalassemic disorders. Hemoglobin F is not increased in choices A, B, or C.
Diagnosis: Homozygous β-thalassemia

13 **The answer is C: Extramedullary hematopoiesis.** Increased oxygen affinity of hemoglobin F and the underlying anemia impair oxygen delivery and lead to marked bone marrow erythroid hyperplasia. The marrow space is expanded, causing facial and cranial bone deformities. Extramedullary hematopoiesis contributes to splenomegaly and the formation of soft tissue masses. Excess erythropoiesis leads to increased iron absorption, which, together with repeated transfusions, creates iron overload. Excess iron deposition in tissues is a major cause of morbidity and mortality in thalassemic patients. The other choices may cause splenomegaly, but they are not related to β-thalassemia.
Diagnosis: Homozygous β-thalassemia, splenomegaly

14 **The answer is C: Heterozygous β-thalassemia.** A normal hemoglobin molecule contains four globin chains, consisting of two α- and two non–α-chains. Three normal variants of hemoglobin are encountered, based on the nature of the non–α-chains. Hemoglobin A ($\alpha_2\beta_2$) accounts for 95% to 98% of the total hemoglobin in adults; only minor amounts of hemoglobin F ($\alpha_2\gamma_2$) and hemoglobin A2 ($\alpha_2\delta_2$) are present. Heterozygous β-thalassemia is associated with microcytosis and hypochromia, and the degree of microcytosis is disproportionate to the severity of the anemia, which is generally mild. Target cells, basophilic stippling, and a mild increase in hemoglobin A2 are present. Most patients are asymptomatic. Choice D (homozygous β-thalassemia) is a more serious disease and choice E (silent carrier for α-thalassemia) is asymptomatic.
Diagnosis: Heterozygous β-thalassemia

15 **The answer is C: Erythroblasts.** The peripheral blood smear displays erythroid precursors, which are normally confined to the bone marrow. Hemolytic disease of the newborn reflects a histoincompatibility between the mother and the developing fetus. The mother lacks an antigen that is expressed by the fetus. Maternal IgG alloantibodies cross the placenta, causing complement-mediated hemolysis of fetal erythrocytes and resulting in the release of numerous erythroid precursors (erythroblasts). The other choices represent normal immune cells.
Diagnosis: Hemolytic disease of newborn, erythroblastosis fetalis

16 **The answer is E: Polycythemia vera (PV).** PV is a myeloproliferative disease that arises from a single clonal hematopoietic stem cell and results in uncontrolled production of RBCs. The increase in erythrocytes in PV is autonomous and is not regulated by erythropoietin. PV derives from the malignant transformation of a single, hematopoietic stem cell with primary commitment to the erythroid lineage. Proliferation of the neoplastic clone occurs predominantly in the bone marrow but may involve extramedullary sites including the spleen, lymph nodes, and liver (myeloid metaplasia). The bone marrow is hypercellular with hyperplasia of all elements. The spleen is moderately enlarged, and its cut surface is uniformly dark red, with expansion of the red pulp and obliteration of the white pulp. Acute myelogenous leukemia (choice A) and essential thrombocythemia (choice B) involve the myeloid and megakaryocytic lines, respectively. Idiopathic myelofibrosis (choice C) features marrow collagen deposition (fibrosis).
Diagnosis: Polycythemia vera

17 **The answer is B: Cerebrovascular accident.** The patient has polycythemia vera (PV). Hyperviscosity associated with PV increases the risk for thrombotic stroke. The other choices are not associated with PV.
Diagnosis: Polycythemia vera

18 **The answer is D: Ischemia.** Sickle cell disease is characterized by the presence of an abnormal hemoglobin (hemoglobin S). Erythrocyte sickling is initially reversible with reoxygenation, but after several cycles of sickling and unsickling, the process becomes irreversible. Irreversibly sickled cells display a rearrangement of phospholipids between the outer and inner monolayers of the cell membrane. The erythrocytes are no longer deformable and are more adherent to endothelial cells, which are properties that predispose to thrombosis of small blood vessels. The resulting vascular occlusions lead to widespread ischemic complications, which are associated with severe pain, especially in the chest, abdomen, and bones.
Diagnosis: Sickle cell disease

19 **The answer is E: Pneumonia.** The asplenic state associated with sickle cell anemia renders the patient susceptible to infections by encapsulated bacteria, especially *Streptococcus pneumoniae*. In addtion to splenic infarcts, patients with sickle cell disease frequently develop renal papillary necrosis due to conditions of low oxygen, low pH, and high osmolality in the renal medulla. None of the other choices represent complications of splenectomy.
Diagnosis: Sickle cell disease

20 **The answer is C: Parvovirus B19 infection.** Patients with sickle cell anemia may undergo an aplastic crisis because of infection of the bone marrow by parvovirus B19, which suppresses erythrocyte production. None of the other choices are complications of sickle cell anemia.
Diagnosis: Sickle cell anemia, aplastic crisis

21 **The answer is C: Impaired utilization of iron from storage sites.** Anemia of chronic disease arises in association with chronic inflammatory diseases (e.g., tuberculosis and rheumatoid arthritis) and malignant conditions. Chronic disease leads to ineffective use of iron from macrophage stores in the bone marrow, resulting in a functional iron deficiency, although storage iron is normal or even increased. The anemia of chronic disease is mild to moderate, and the red cells are often microcytic. Serum iron levels tend to be reduced. However, in contrast to iron deficiency anemia, total iron-binding capacity also tends to be decreased (as is the serum albumin level). The other choices are not related to anemia of chronic disease.
Diagnosis: Anemia of chronic disease

22 **The answer is B: Chronic liver disease.** Acanthocytosis (shown in the photomicrograph) results from a defect within the lipid bilayer of the red cell membrane and features spiny projections of the surface, which may be associated with hemolysis. The most common cause of acanthocytosis is chronic liver disease, in which increased free cholesterol is deposited within the cell membrane. Abnormalities in the lipid membrane cause erythrocytes to become deformed and develop irregular spiny surface projections and centrally dense cytoplasm (acanthocytes or spur cells). Chronic renal failure (choice C) features burr cells. Abnormal spectrin (choice A) causes hereditary spherocytosis.
Diagnosis: Acanthocytosis

23 **The answer is C: Myelodysplastic syndrome (MDS).** MDS exhibits dysplastic morphologic features in one or more hematopoietic lineages and is accompanied by ineffective hematopoiesis. The disease is most common in the elderly and presents with anemia, neutropenia, and thrombocytopenia. The morphologic classification of MDS is based on the presence of abnormally shaped hematopoietic cells and an increased proportion of myeloblasts. Dysplastic features may be present in one or more hematopoietic lineages. Ringed sideroblasts are common. In this case, a smear of a bone marrow aspirate stained with Prussian blue shows erythroid precursor cells containing iron-laden mitochondria that encircle the nuclei. Ringed sideroblasts are not a feature of the other choices.
Diagnosis: Myelodysplastic syndrome

24 **The answer is A: Clonal stem cell defect.** Myelodysplastic syndromes (MDS) are hematopoietic stem cell disorders that are characterized by a discrepancy between the paucity of peripheral blood elements and marked hyperplasia in the bone marrow. MDS may be either primary (de novo) or secondary (therapy related). Patients with secondary myelodysplasia usually have a history of chemotherapy, especially alkylating agents, or radiation therapy for the treatment of cancer. Other risk factors for MDS include viruses, benzene exposure, cigarette smoking, and Fanconi anemia.
Diagnosis: Myelodysplasia

25 **The answer is A: Damage to stem cells.** The bone marrow is aplastic, consisting largely of fat cells and lacking normal hematopoietic activity. Patients with aplastic anemia present with severe pancytopenia and clinical symptoms related to the various cytopenias, including fatigue (anemia), fever (neutropenia), and petechiae (thrombocytopenia). The lack of an appropriate reticulocyte response to the anemia indicates decreased or ineffective hematopoiesis as the mechanism for the pancytopenia. Injury to bone marrow stem cells is

idiopathic (two thirds of cases), toxic (as in this case), immunologic, or hereditary (Fanconi anemia).
Diagnosis: Aplastic anemia

26 **The answer is B: Folic acid deficiency.** Folic acid deficiency commonly occurs in alcoholics who have poor nutrition. Macrocytosis, hypersegmented neutrophils, and a normal Schilling test (vitamin B_{12} absorption) point to folic acid deficiency. Folic acid and vitamin B_{12} are required for synthesis of DNA, and deficiency of either factor leads to megaloblastic transformation of hematopoietic cells. Macrocytosis and hypersegmented neutrophils are not features of the other choices.
Diagnosis: Megaloblastic anemia

27 **The answer is A: G6PD deficiency.** G6PD deficiency is an X-linked disorder that causes a hemolytic anemia characterized by abnormal sensitivity of red cells to oxidative stress. The highest prevalence is in Africa and the Mediterranean region. Because of the role of G6PD in recycling reduced glutathione, red cells deficient in this enzyme are susceptible to oxidative stress, which, in this case, is fava bean ingestion (favism). In quiescent periods, the erythrocytes of G6PD deficiency appear normal. However, during a hemolytic episode precipitated by oxidative stress, Heinz bodies can be demonstrated by supravital staining. Full expression of G6PD deficiency is seen only in males, with females being asymptomatic carriers. Heinz bodies are not characteristic of the other choices.
Diagnosis: Glucose-6-phosphate dehydrogenase deficiency

28 **The answer is D: Chronic myelogenous leukemia (CML).** Chronic myeloproliferative diseases are defined as clonal hematogenous stem cell disorders with increased proliferation of one or more myeloid lineages. CML is derived from an abnormal pluripotent bone marrow stem cell and results in prominent neutrophilic leukocytosis over the full range of myeloid maturation. CML is the most common myeloproliferative disease and accounts for 15% to 20% of all cases of leukemia. It affects middle-aged or older adults. Replacement of the bone marrow by neoplastic cells causes anemia and thrombocytopenia and a predisposition to infections. In 95% of all CML cases, the Philadelphia chromosome can be demonstrated by conventional cytogenetics. The initial symptoms are nonspecific and include weakness, malaise, fever, and splenomegaly. Acute lymphoblastic leukemia (choice A) and acute myeloid leukemia (choice B) feature clonal expansion of lymphoblasts and myeloblasts, respectively. Although myelodysplastic syndrome (choice E) features hyperplastic bone marrow, the Philadelphia chromosome does not occur, and there is peripheral cytopenia in various cell lines.
Diagnosis: Chronic myelogenous leukemia

29 **The answer is A: *abl*.** Presence of the Philadelphia chromosome or molecular demonstration of the *bcr/abl* fusion gene is required to establish the diagnosis of chronic myelogenous leukemia (CML). The *bcr/abl* gene encodes a fusion protein, p210, which acts as a constitutively activated tyrosine kinase. The other choices may be involved in malignant transformations but they are not related to CML.
Diagnosis: Chronic myelogenous leukemia

30 **The answer is C: Acute promyelocytic leukemia (APL).** In APL, the bone marrow is packed with tumor cells that have promyelocytic features, with abundant Auer rods. Patients with APL frequently present with DIC. Senescent leukemic cells degranulate and activate the coagulation cascade. The presence of Auer rods excludes acute lymphoblastic leukemia (choice A), acute megakaryocytic leukemia (choice B), and chronic myelogenous leukemia (choice D). DIC is not characteristic of the other choices.
Diagnosis: Acute promyelocytic leukemia

31 **The answer is E: Retinoic acid receptor (RAR).** The underlying genetic defect in acute promyelocytic leukemia is a translocation involving the *PML* gene on chromosome 15 and the RAR (*RAR*α) gene on chromosome 17. The resulting *PML/RAR*α fusion gene encodes a functional RAR. The receptor can be targeted by all-*trans*-retinoic acid, which mediates maturation of the tumor cells. Complete remissions have been obtained in some patients. The other choices may be involved in other translocations.
Diagnosis: Acute promyelocytic leukemia

32 **The answer is B: Chronic lymphocytic leukemia (CLL).** CLL is characterized by clonal proliferation of small, mature-appearing lymphocytes in the bone marrow, lymph nodes, and spleen, with an expression in the peripheral blood. In most instances, the leukemic cells belong to B-cell lineage and show clonal Ig gene rearrangements and activation of the *bcl* protooncogene. Most patients are over 50 years of age. The symptoms tend to be nonspecific, but 80% of patients have lymph node enlargement, and 50% show splenomegaly. CLL usually has an indolent and protracted course. Acute lymphoblastic lymphoma (choice A) is principally a leukemia of childhood. Multiple myeloma (choice D) is a neoplasm of plasma cells. Waldenström macroglobulinemia (choice E) is a neoplasm of small lymphocytes and a variable number of IgM-secreting plasma cells of the same malignant clone.
Diagnosis: Chronic lymphocytic leukemia

33 **The answer is A: Acute lymphoblastic leukemia (ALL).** Most precursor B-cell malignancies involve primarily bone marrow and peripheral blood and are termed B-cell acute lymphoblastic leukemias (B-ALL). Only 15% of childhood ALLs) are derived from T cells, and 75% of B-ALL cases occur in children under the age of 6 years. B-ALL features numerical aberrations and chromosomal translocations, including the Philadelphia chromosome. In childhood ALL, a *bcr/abl* fusion protein, P190, is produced. B-ALLs are positive for nuclear expression of TdT. The demonstration of TdT activity suggests that a leukemic blast is of lymphoid rather than myeloid lineage. The other choices are rarely, if ever, encountered in this age group.
Diagnosis: Acute lymphocytic leukemia

34 **The answer is C: Hodgkin lymphoma (HL).** The lymph node biopsy shows a Reed-Sternberg cell. These large atypical mononuclear or multinucleated tumor cells in an inflammatory background are the diagnostic hallmark of HL. HL is the most common malignant neoplasm of Americans between the ages of 10 and 30 years. There is a distinctive bimodal

age distribution in developed countries. Most patients with HL present with lymphadenopathy. Constitutional symptoms include night sweats, fever, and weight loss exceeding 10% of body weight. Pruritus may occur with disease progression. Reed-Sternberg cells do not occur in the other choices.
Diagnosis: Hodgkin lymphoma

35 **The answer is E: Nodular sclerosis.** Nodular sclerosis accounts for 70% of classical Hodgkin lymphoma, with most cases occurring between the ages of 20 and 30 years. Histologic examination shows dense, band-like collagenous fibrosis that envelops cellular aggregates of lymphoid and inflammatory cells, as well as the specific lacunar cell variant of the Reed-Sternberg cell.
Diagnosis: Hodgkin lymphoma, nodular sclerosis subtype

36 **The answer is D: Multiple myeloma.** Plasma cell myeloma (multiple myeloma) is characterized by a multifocal infiltration of malignant plasma cells in the bone marrow. There are typically multiple destructive lytic lesions or diffuse demineralization of bone. Major diagnostic criteria for plasma cell myeloma include marrow plasmacytosis (>30%), plasmacytoma on biopsy, and immunoglobulin paraprotein (M-component). Neoplastic cells typically secrete a homogeneous complete or partial immunoglobulin chain, which can be seen in serum or urine electrophoresis. In this patient, the neoplastic clone secretes excess kappa light chains. Waldenström macroglobulinemia (choice E) is a neoplastic disorder of small lymphocytes that secrete IgM.
Diagnosis: Multiple myeloma

37 **The answer is E: Renal failure.** The most common and important extramedullary complication of multiple myeloma is amyloid nephropathy, which accounts for more than half of all deaths. Other complications include bone fractures and infection.
Diagnosis: Multiple myeloma

38 **The answer is C: Chronic idiopathic myelofibrosis.** Chronic idiopathic myelofibrosis is a clonal myeloproliferative disease in which marrow fibrosis is accompanied by prominent megakaryopoiesis and granulopoiesis. A prefibrotic stage is recognized wherein the bone marrow is hypercellular, with predominant neutrophilic and megakaryocytic proliferation. In the fibrotic stage, the peripheral blood shows either leukopenia or marked leukocytosis, and myeloid precursors and nucleated RBCs are usually present. Conspicuous reticulin or collagen fibrosis in the marrow defines this stage. Transformation to acute myelogenous leukemia (choice A) occurs in 15% of cases. The other choices do not feature marrow fibrosis.
Diagnosis: Myelofibrosis

39 **The answer is E: Small lymphocytic lymphoma (SLLs).** Chronic lymphocytic leukemias (CLLs) as well as SLLs are malignant B-cell proliferations of small, mature-appearing lymphocytes and a variable number of large cells. A diagnosis of CLL is made if bone marrow and peripheral blood are primarily involved. If the tumor cells give rise to lymphadenopathy or solid tumor masses, the term small lymphocytic lymphoma is used. Reactive follicular hyperplasia (choice D) is excluded in this case by the peripheral lymphocytosis and by the lack of reactive follicles in the lymph node biopsy. Hodgkin lymphoma (choice B) features Reed-Sternberg cells.
Diagnosis: Small lymphocytic lymphoma

40 **The answer is C: Bcl-2.** Follicular lymphoma is a clonal lymphoid proliferation derived from germinal-center B cells. The most common cytogenetic translocation in follicular lymphoma is t(14;18)(q32;q21), with *IgH* and *bcl-2* as partner genes. The bcl-2 protein, expressed in follicular lymphoma, is localized in the mitochondrial membrane and functions as an apoptosis inhibitor. Choices A, D, and E (abl, myc, and retinoic acid receptor) represent translocations in other disorders. Bax (choice B) is a pro-apoptotic protein.
Diagnosis: Follicular lymphoma

41 **The answer is A: Proliferation in B-cell areas.** Follicular hyperplasia refers to enlarged lymph follicles (principally in the cortex of the lymph node), which consist of B lymphocytes. Reactive follicular hyperplasia of lymph nodes represents a response to infections, inflammation, or tumors. Hyperplasia of the secondary follicles, germinal centers, and plasmacytosis of the medullary cords indicate B-lymphocyte immunoreactivity. Hyperplasia of the deep cortex or paracortex (interfollicular of diffuse hyperplasia) is characteristic of T-lymphocyte immunoreactivity (choice D).
Diagnosis: Follicular hyperplasia

42 **The answer is B: Burkitt lymphoma (BL).** BL, one of the most rapidly growing malignancies, is defined by a chromosomal translocation involving 8q24, which harbors the *myc* oncogene. Endemic BL is the most common childhood malignancy in Central Africa. Sporadic BL affects mainly children and young adults in the Western world, where it accounts for 1% to 2% of all lymphomas. Immunodeficiency-associated BL mainly occurs in HIV-infected persons. The cellular debris of apoptotic tumor cells is cleared by macrophages, whose scattered appearance is termed "starry sky macrophage." Most patients present with extranodal tumors that emerge in a short period of time and respond to aggressive chemotherapy. Choices A, C, and E are not endemic in Africa, and choice D (reactive follicular hyperplasia) is a nonmalignant disorder.
Diagnosis: Burkitt lymphoma

43 **The answer is B: Langerhans cell histiocytosis (LCH).** LCH refers to a spectrum of uncommon proliferative disorders of Langerhans cells. The disease ranges from asymptomatic involvement of a single site, such as bone or lymph nodes, to an aggressive systemic disorder that involves multiple organs. There is clinical heterogeneity of LCH; eosinophilic granuloma (75% of all cases) is a localized, usually self-limited disorder of older children and young adults; Hand-Schuller-Christian disease is a multifocal and typically indolent disorder, usually in children between 2 and 5 years of age; and Letterer-Siwe disease (fewer than 10% of cases) is an acute, disseminated variant of LCH in infants and children younger than 2 years of age. Organs involved by LCH include the skin (seborrheic or eczematoid dermatitis), lymph nodes, spleen, liver, lungs, and bone marrow. Otitis media is a common finding. Painful lytic lesions of bone are common. Proptosis may complicate infiltration

of the orbit. The classic triad of diabetes insipidus, proptosis, and defects in membranous bones characterizes Hand-Schuller-Christian disease. Hodgkin lymphoma (choice A) often features eosinophils but does not have this clinical presentation.

Diagnosis: Langerhans cell histiocytosis

44 **The answer is C: Large B-cell lymphoma.** Most lymphomas in patients who have AIDS are high-grade B-cell lymphomas. These aggressive, but potentially curable neoplasms include Burkitt lymphoma and diffuse large-cell B-cell lymphoma. As in follicular lymphoma, *bcl2* gene rearrangements are often seen, suggesting a potential germinal center origin. Diffuse large-cell B-cell lymphomas associated with immunodeficiency are usually positive for EBV. The other choices are not complications of HIV infection.

Diagnosis: Large B-cell lymphoma

45 **The answer is D: Hairy cell leukemia.** Hairy cell leukemia is a clonal B-cell proliferation of small- to medium-sized lymphocytes that display abundant cytoplasm and hair-like protrusions of the cell membrane. The disease involves primarily the monocyte/macrophage system of the bone marrow, spleen, and liver. Hairy cell leukemia is rare and affects mainly middle-aged to elderly persons, with a markedly increased male-to-female ratio of 5:1. Unlike the other choices, hairy cell leukemia expresses tartrate-resistant acid phosphatase.

Diagnosis: Hairy cell leukemia

46 **The answer is E: Marginal zone lymphoma.** Extranodal marginal-zone B-cell lymphomas that originate in mucosa-associated lymphoid tissue are referred to as MALT lymphomas. MALT lymphomas are indolent, malignant lymphocyte proliferations that consist of small- to medium-sized lymphocytes with frequent monocytoid features and variable admixtures of plasma cells. The malignant lymphocytes appear to originate from marginal-zone B cells. Most primary gastric lymphomas are MALT lymphomas. MALT lymphomas occur either in granular organs or along mucosal surfaces. They commonly arise in the context of a chronic inflammatory process or autoimmune disease. The other choices may rarely affect organs such as the stomach, but unlike MALT lymphoma, they are unrelated to *H. pylori* infection.

Diagnosis: Marginal zone lymphoma, MALT lymphoma

47 **The answer is E: Mycosis fungoides.** Mycosis fungoides represents a cutaneous T-cell lymphoma, composed of mature, postthymic T-helper ($CD4^+$) lymphocytes. Mycosis fungoides displays lymphocytic infiltrates at the dermal-epidermal junction and, in some cases, intraepidermal accumulations of tumor cells (Pautrier microabscesses). The other choices are not characteristically seen as skin lesions.

Diagnosis: Mycosis fungoides

48 **The answer is E: Waldenström disease.** Waldenström disease (lymphoplasmacytic lymphoma) is a neoplastic proliferation of small lymphocytes and a variable number of IgM-secreting plasma cells of the same malignant clone. Waldenström disease is not a variant of multiple myeloma, but rather, is an indolent malignant lymphoma that mainly affects the elderly. Eighty percent of patients with Waldenström macroglobulinemia present with a monoclonal IgM spike on serum electrophoresis (>3 g/dL). Many of the clinical symptoms are associated with hyperviscosity of the blood. The other choices do not feature IgM-producing lymphocytes.

Diagnosis: Waldenström macroglobulinemia

49 **The answer is D: Idiopathic thrombocytopenic purpura (ITP).** ITP is a quantitative disorder of platelets caused by antibodies directed against platelet or megakaryocytic antigens. Similar to autoimmune hemolytic anemia, the etiology of ITP is related to antibody-mediated immune destruction of platelets or their precursors. In adults with acute ITP, the platelet count is typically less than 20,000/μL. In chronic adult ITP, the platelet count varies from a few thousand to 100,000/μL. The peripheral blood smear in ITP exhibits numerous large platelets, and the bone marrow shows a compensatory increase in megakaryocytes. Acute ITP in children typically appears after a viral illness and presents with sudden onset of petechiae and purpura without other symptoms. Spontaneous recovery can be expected in more than 80% of cases within 6 months. Thrombocytopenia may be observed in the other choices but is usually associated with other systemic signs and symptoms.

Diagnosis: Idiopathic thrombocytopenic purpura

50 **The answer is A: Antibody-mediated platelet destruction.** In common with idiopathic thrombocytopenic purpura and certain drug-induced thrombocytopenias, systemic lupus erythematosus is associated with increased platelet destruction due to immune-mediated damage and removal of circulating platelets (antibody-mediated platelet destruction). The other choices do not represent immune destruction of platelets.

Diagnosis: Idiopathic thrombocytopenic purpura, systemic lupus erythematosus

51 **The answer is C: Hemolytic anemia.** Reticulocytes are nonnucleated cells that represent the last stage before mature erythrocytes. The nucleus is extruded from the orthochromatic erythroblast, leaving mitochondria and hemoglobin-producing polyribosomes in the reticulocyte. After release from the bone marrow, the reticulocyte loses its capacity for aerobic metabolism and hemoglobin synthesis, and after 1 to 2 days, it becomes a mature erythrocyte. Hemolytic anemias are characterized by a compensatory increase in production and release of red cells by the bone marrow, manifested in the blood by polychromasia of red cells and an increased reticulocyte count. Increased peripheral reticulocytes are not observed in the other choices.

Diagnosis: Hemolytic anemia, idiopathic thrombocytopenic purpura

52 **The answer is A: Autoantibodies directed against the erythrocyte membrane.** The peripheral blood smear from this patient shows clumped red cells caused by cold agglutinins (autoantibodies). Cold agglutinins are mostly IgM, are directed against the I/I antigen system, and act optimally at 4°C. Cold agglutinins may be idiopathic or develop secondary to an underlying condition, most frequently infections (Epstein-Barr virus) or lymphoproliferative disorders. However, most autoimmune

hemolytic anemias are mediated by IgG antibodies that exert their maximal effect at body temperature (warm agglutinins). Choices D and E are associated with hemolysis rather than clumping of red blood cells.
Diagnosis: Autoimmune hemolytic anemia

53 **The answer is D: Thrombotic thrombocytopenic purpura (TTP).** TTP occurs in acute or chronic form and presents with a pentad that includes fever, thrombocytopenia, microangiopathic hemolytic anemia, renal impairment, and neurologic symptoms. The morphologic hallmark of TTP is the deposition throughout the body of PAS-positive hyaline microthrombi in arterioles and capillaries, principally in the heart, brain, and kidneys. The microthrombi contain platelet aggregates, fibrin, and a few erythrocytes and leukocytes. The peripheral blood smear displays microangiopathic hemolytic anemia. The peripheral blood smear shows numerous schistocytes. TTP resembles hemolytic uremic syndrome, which occurs more often in children than adults. The other choices are not associated with microangiopathic changes (e.g., schistocytes).
Diagnosis: Thrombotic thrombocytopenic purpura

54 **The answer is D: Microangiopathic hemolytic anemia.** Microangiopathic hemolytic anemia results from abnormalities in the microcirculation that cause turbulent blood flow patterns. The classic examples of this type of hemolytic anemia are DIC (this case) and TTP; both of which feature generalized thrombosis of capillary vessels. Long-distance running or walking or prolonged vigorous exercise can cause repetitive trauma to red blood cells in the microcirculation leading to hemolysis. Alterations in blood flow, as are encountered in malignant hypertension or vasculitis syndromes, may also produce mechanical fragmentation of erythrocytes. Microangiopathic features are not observed in the other choices.
Diagnosis: Microangiopathic hemolytic anemia

55 **The answer is D: Macroangiopathic hemolytic anemia.** Macroangiopathic hemolytic anemia most commonly results from direct erythrocyte trauma due to an abnormal vascular surface (e.g., prosthetic heart valve, synthetic vascular graft). Anemia is mild to moderate and is accompanied by an appropriate reticulocyte response. Blood smear examination reveals fragmented red blood cells (schistocytes) and polychromasia. Although choice E (microangiopathic hemolytic anemia) results in morphologically-similar red blood cells, it reflects changes in small blood vessels.
Diagnosis: Macroangiopathic hemolytic anemia

56 **The answer is D: Genetic defect involving the factor VIII gene.** Hemophilia A is an X-linked recessive disorder of blood clotting that results in spontaneous bleeding, particularly into joints, muscles, and internal organs. Classic hemophilia results from mutations in the gene encoding factor VIII (hemophilia A). Hemophilia A is the most frequently encountered sex-linked inherited bleeding disorder (1 per 5,000 to 10,000 males). Choices C and E represent acquired disorders.
Diagnosis: Hemophilia A

57 **The answer is B: Hemophilia B.** Hemophilia B is an X-linked recessive disease caused by mutations in the gene encoding factor IX. It accounts for only 10% of all cases of hemophilia. One third of all cases represent new mutations. It is clinically indistinguishable from hemophilia A (factor VIII deficiency) (choice A). In both forms of hemophilia, the partial thromboplastin time (PTT) is prolonged. Mixing of a patient's blood with that of a normal donor normalizes the PTT.
Diagnosis: Hemophilia B

58 **The answer is D: Paroxysmal nocturnal hemoglobinuria (PNH).** Despite its name, the disorder is nocturnal in only a minority of cases. PNH is a clonal stem cell disorder characterized by episodic intravascular hemolytic anemia that is secondary to increased sensitivity of erythrocytes to complement-mediated lysis. The underlying defect involves somatic mutation of the phosphatidylinositol glycan-class A (*PIG-A*) gene. PNH may develop as a primary disorder or evolve from preexisting cases of aplastic anemia. During hemolytic episodes, patients develop normocytic or macrocytic anemia, accompanied by an appropriate reticulocyte response. The traditional diagnostic tests for PNH, hemolysis in sucrose (sucrose hemolysis test) or acidified serum (Ham test), are now more easily diagnosed by demonstrating loss of GPI-anchored proteins on blood cells by flow cytofluorometry. Choices B and C, which are hemolytic conditions, do not show increased lysis in the described laboratory studies.
Diagnosis: Paroxysmal nocturnal hemoglobinuria

59 **The answer is B: Essential thrombocythemia.** Essential thrombocythemia is an uncommon neoplastic disorder of hematopoietic stem cells that is characterized by uncontrolled proliferation of megakaryocytes. A marked increase in circulating platelets is accompanied by recurrent episodes of thrombosis and hemorrhage. The WHO criteria require a sustained platelet count above 600,000/μL and prominent megakaryocytic proliferation in the bone marrow. Essential thrombocythemia is believed to derive from the malignant transformation of a hematopoietic stem cell with principal commitment to the megakaryocytic lineage. Increased megakaryocytes are a feature of chronic myelogenous leukemia (choice A) but in the context of multilineage expansion. Megakaryocytosis is also seen in myelofibrosis (choice C), but the marrow is fibrotic.
Diagnosis: Essential thrombocythemia

60 **The answer is C: Hemolytic transfusion reaction.** An immediate hemolytic transfusion reaction occurs when grossly incompatible blood is administered to patients with preformed alloantibodies, usually because of clerical errors. Massive hemolysis of the transfused blood may be associated with severe complications, including hypotension, renal failure, and even death. Choices B, D, and E are not characterized by a positive Coombs test. Choice A is not related to blood transfusions.
Diagnosis: Acute hemolytic transfusion reaction

61 **The answer is E: Suppression of hematopoiesis.** The presence of myeloblasts in the peripheral blood is indicative of acute myelogenous leukemia (AML). In AML, there is an accumula-

tion in the marrow of immature myeloid cells that lack the potential for further differentiation and maturation, which leads to suppression of normal hematopoiesis. As a consequence, the major clinical problems associated with AML are granulocytopenia, thrombocytopenia, and anemia. Promyelocytic leukemia causes disseminated intravascular coagulation (choice B).

Diagnosis: Acute myelogenous leukemia

62 **The answer is E: Transformation of a pluripotent bone marrow stem cell.** The patient exhibits the Philadelphia chromosome and clinicopathologic features of chronic myelogenous leukemia (CML). The neoplastic cells in CML are derived from an abnormal pluripotent bone marrow stem cell, which results in prominent neutrophilic leukocytosis over the full range of myeloid maturation. The other choices relate to cells in the lymphoid lineage.

Diagnosis: Chronic myelogenous leukemia

63 **The answer is D: Leukemoid reaction.** Neutrophilia is an absolute neutrophil count above 7,000/μL. In acute infections, neutrophilia may be so pronounced that it may be mistaken for leukemia, especially, chronic myelogenous leukemia (CML), in which case it is termed a leukemoid reaction. Clues to the benign (or reactive) nature of a leukemoid reaction include the following: (1) the cells in the peripheral blood smear are more mature than myelocytes; (2) leukocyte alkaline phosphatase activity is high in benign conditions and low in patients with CML; and (3) benign neutrophils often contain large blue cytoplasmic inclusions referred to as "Dohle bodies" or toxic granulation. The other choices are incorrect because the neutrophils in these disorders do not display these morphologic features, and they are usually associated with other hematologic abnormalities.

Diagnosis: Leukemoid reaction

64 **The answer is E: Suppurative lymphadenitis.** Acute suppurative lymphadenitis occurs in the lymph nodes that drain a site of acute bacterial infection. Suppurative lymph nodes enlarge rapidly because of edema and hyperemia and are tender due to distention of the capsule. Microscopically, infiltration of the lymph node sinuses and stroma by polymorphonuclear leukocytes and prominent follicular hyperplasia are noted. Neutrophils are not a morphologic feature of the other choices.

Diagnosis: Suppurative lymphadenitis

65 **The answer is E: Richter syndrome.** Five percent of patients with B-cell chronic lymphocytic leukemia (B-CLL) develop a large-cell lymphoma. Patients with this complication present with a rapid onset of fever, abdominal pain, and progressive lymphadenopathy and hepatosplenomegaly. Richter syndrome is aggressive and refractory to therapy, with a mean survival of 2 months. The other choices are not associated with B-CLL.

Diagnosis: Richter syndrome, B-cell chronic lymphocytic leukemia

66 **The answer is E: Thymoma.** Thymoma is a neoplasm of thymic epithelial cells, without regard to the number of lymphocytes. This tumor of adults is usually benign, but malignant examples occur. Fifteen percent of patients with myasthenia gravis have thymoma, as in this case. Conversely, one third to one half of patients with thymoma develop myasthenia gravis. Myasthenia gravis is not associated with the other choices, although mediastinal presentations occur.

Diagnosis: Thymoma, myasthenia gravis

67 **The answer is E: Posttransplant lymphoproliferative disorder (PTLD).** PTLD results from immunosuppression and is often associated with EBV infection. In most cases, the disease is an EBV-driven, monoclonal, lymphocyte proliferation with variable morphology. The incidence of PTLD parallels the extent of immunosuppression. In this connection, liver transplant recipients have a higher incidence of PTLD than do patients who receive kidney transplants. Burkitt lymphoma (choice B) has been related to EBV infection but is not a complication of immunosuppression. Infectious mononucleosis (choice D) does not present with an abdominal mass.

Diagnosis: Posttransplant lymphoproliferative disorder

68 **The answer is C: Direct red cell trauma.** Red cell fragmentation syndromes are disorders in which erythrocytes are subjected to mechanical disruption as they circulate in the blood (intravascular hemolysis). These disorders are classified as either macroangiopathic (large vessels), as in this case, or microangiopathic (capillaries), according to the site of hemolysis. Mechanical fragmentation of red cells is primarily due either to alteration of the endothelial surface of blood vessels or disturbances in blood flow patterns that lead to turbulence and increased shear stress. Macroangiopathic hemolytic anemia most commonly results from direct red cell trauma due to an abnormal vascular surface (e.g., prosthetic heart valve). The other choices are not an expected complication of a prosthetic valve.

Diagnosis: Macroangiopathic hemolysis

69 **The answer is C: Fibrin thrombi.** Disseminated intravascular coagulation (DIC) refers to widespread ischemic changes secondary to microvascular fibrin thrombi, which are accompanied by the consumption of platelets and coagulation factors and a hemorrhagic diathesis. DIC typically occurs as a complication of massive trauma, septicemia, and obstetric emergencies. It is also associated with metastatic cancer, hematopoietic malignancies, cardiovascular and liver diseases, and numerous other conditions. The other choices are not directly associated with DIC.

Diagnosis: Disseminated intravascular coagulation