FULL-LENGTH PRACTICE TEST 12

Practice Test 12: Hematology and Oncology

45 Questions — Recommended Time: 45 Minutes

1. A 25-year-old African American man presents with severe bone pain in his lower extremities, chest pain, and shortness of breath following a flight from New York to Los Angeles. His hemoglobin is 7.2 g/dL, and peripheral blood smear reveals sickle-shaped red blood cells and Howell-Jolly bodies. Hemoglobin electrophoresis shows HbS 85% and HbF 8%. Which of the following is the most likely diagnosis?

A. Sickle cell trait

B. Thalassemia major

C. Sickle cell disease with acute vaso-occlusive crisis

D. Glucose-6-phosphate dehydrogenase deficiency

2. A 65-year-old man presents with fatigue, pallor, and dyspnea on exertion. Laboratory studies reveal hemoglobin 8.5 g/dL, MCV 110 fL, and a peripheral blood smear showing hypersegmented neutrophils (6+ lobes) and macro-ovalocytes. Serum vitamin B12 level is markedly low at 95 pg/mL. He has a history of gastric bypass surgery 5 years ago. Which of the following is the most likely diagnosis?

A. Vitamin B12 deficiency (megaloblastic anemia)

B. Folate deficiency

C. Iron deficiency anemia

D. Myelodysplastic syndrome

3. A 30-year-old woman presents with heavy menstrual bleeding, fatigue, and pica (craving ice). Laboratory studies reveal hemoglobin 9.0 g/dL, MCV 68 fL, serum ferritin 8 ng/mL (low), serum iron 25 µg/dL (low), TIBC 450 µg/dL (elevated), and transferrin saturation 6% (low). Peripheral smear reveals microcytic, hypochromic red blood cells with anisocytosis and poikilocytosis. Which of the following is the most likely diagnosis?

A. Thalassemia trait

B. Iron deficiency anemia

C. Anemia of chronic disease

D. Sideroblastic anemia

4. A 70-year-old man presents with bone pain, fatigue, and recurrent infections. Laboratory studies reveal hemoglobin 9.2 g/dL, calcium 12.5 mg/dL, creatinine 2.8 mg/dL, and total protein 11.5 g/dL with a markedly elevated globulin fraction. Serum protein electrophoresis reveals a large monoclonal (M) spike in the gamma region. Urine analysis reveals Bence Jones proteinuria. Skeletal survey reveals multiple lytic ("punched-out") lesions in the skull, spine, and pelvis. Which of the following is the most likely diagnosis?

A. Waldenström macroglobulinemia

B. Metastatic bone disease

C. Primary hyperparathyroidism

D. Multiple myeloma

5. A 20-year-old woman presents with easy bruising, petechiae, and gingival bleeding for the past two weeks. She had a viral upper respiratory infection three weeks ago. Physical examination reveals petechiae on the lower extremities and oral mucosal bleeding. CBC reveals an isolated platelet count of 12,000/μL with normal hemoglobin and WBC. Peripheral smear reveals decreased platelets but is otherwise normal with no schistocytes. Which of the following is the most likely diagnosis?

A. Thrombotic thrombocytopenic purpura

B. Immune thrombocytopenic purpura (ITP)

C. Disseminated intravascular coagulation

D. Aplastic anemia

6. A 55-year-old man presents with progressive fatigue and an incidentally discovered WBC of 85,000/μL on routine blood work. He is asymptomatic with no lymphadenopathy or splenomegaly. Peripheral blood smear reveals a predominance of mature-appearing small lymphocytes with many "smudge cells." Flow cytometry reveals CD5+, CD19+, CD20 dim, CD23+ B-lymphocytes. Which of the following is the most likely diagnosis?

A. Chronic lymphocytic leukemia (CLL)

B. Acute lymphoblastic leukemia

C. Hairy cell leukemia

D. Mantle cell lymphoma

7. A 35-year-old woman presents with fatigue, jaundice, and dark urine. Laboratory studies reveal hemoglobin 7.5 g/dL, reticulocyte count 12% (elevated), indirect bilirubin 4.2 mg/dL, LDH 650 U/L (elevated), and haptoglobin less than 10 mg/dL (undetectable). Direct antiglobulin test (Coombs test) is positive. Peripheral smear reveals spherocytes. Which of the following is the most likely diagnosis?

A. Hereditary spherocytosis

B. Glucose-6-phosphate dehydrogenase deficiency

C. Autoimmune hemolytic anemia (warm antibody type)

D. Paroxysmal nocturnal hemoglobinuria

8. A 5-year-old boy presents with fatigue, pallor, fever, and bone pain. Physical examination reveals lymphadenopathy, hepatosplenomegaly, and petechiae. CBC reveals WBC 45,000/μL with 80% blasts, hemoglobin 6.8 g/dL, and platelet count 22,000/μL. Bone marrow biopsy reveals greater than 90% lymphoblasts that are TdT-positive, CD10-positive, and CD19-positive. Which of the following is the most likely diagnosis?

A. Acute myeloid leukemia

B. Chronic myeloid leukemia

C. Burkitt lymphoma

D. Acute lymphoblastic leukemia (ALL)

9. A 62-year-old man is admitted with acute onset of confusion, petechiae, fever, renal insufficiency, and microangiopathic hemolytic anemia. Laboratory studies reveal hemoglobin 7.8 g/dL, platelet count 18,000/μL, creatinine 2.5 mg/dL, LDH 1,200 U/L (markedly elevated), and schistocytes on peripheral blood smear. PT and PTT are normal. ADAMTS13 activity is severely deficient (less than 10%). Which of the following is the most likely diagnosis?

A. Thrombotic thrombocytopenic purpura (TTP)

B. Hemolytic uremic syndrome

C. Disseminated intravascular coagulation

D. Immune thrombocytopenic purpura

10. A 28-year-old man presents with a painless, enlarged lymph node in his left supraclavicular region. He also reports night sweats, unexplained weight loss of 15 pounds over 2 months, and pruritus. Excisional biopsy of the lymph node reveals Reed-Sternberg cells (large binucleated cells with prominent eosinophilic nucleoli creating an "owl's eye" appearance) in a background of reactive inflammatory cells. Which of the following is the most likely diagnosis?

A. Non-Hodgkin lymphoma

B. Hodgkin lymphoma

C. Reactive lymphadenopathy

D. Metastatic carcinoma

11. A 55-year-old woman presents with progressive fatigue, weight loss, and early satiety. Physical examination reveals massive splenomegaly with the splenic tip palpable 10 cm below the left costal margin. CBC reveals WBC 125,000/µL with a differential showing the full spectrum of myeloid maturation (myelocytes, metamyelocytes, bands, and segmented neutrophils), basophilia, and eosinophilia. Hemoglobin is 10.5 g/dL and platelet count is 650,000/µL. Which of the following cytogenetic abnormality is most likely present?

A. t(15;17)

B. t(14;18)

C. t(8;14)

D. t(9;22) — Philadelphia chromosome (BCR-ABL fusion gene)

12. A 72-year-old man presents with fatigue and is found to have a hemoglobin of 9.8 g/dL, MCV 105 fL, WBC 3,200/µL, and platelet count 95,000/µL. Peripheral smear reveals dysplastic neutrophils (bilobed, hyposegmented nuclei — pseudo-Pelger-Huët anomaly), oval macrocytes, and hypo-granular platelets. Bone marrow biopsy reveals hypercellular marrow with trilineage dysplasia and 8% blasts. Which of the following is the most likely diagnosis?

A. Aplastic anemia

B. Acute myeloid leukemia

C. Myelodysplastic syndrome

D. Vitamin B12 deficiency

13. A 45-year-old woman presents with deep vein thrombosis of the left lower extremity. She has no prior history of thrombosis, no recent surgery or immobilization, and no family history of clotting disorders. She is not on oral contraceptives and is not pregnant. Thrombophilia workup reveals a positive lupus anticoagulant, positive anticardiolipin antibodies, and positive anti-beta-2 glycoprotein I antibodies on two separate occasions 14 weeks apart. Which of the following is the most likely diagnosis?

A. Antiphospholipid syndrome

B. Factor V Leiden mutation

C. Protein C deficiency

D. Prothrombin G20210A mutation

14. A 60-year-old man with a history of chronic myeloid leukemia on imatinib therapy presents with sudden onset of bleeding gums, petechiae, and fatigue. CBC reveals WBC 35,000/μL with 65% blasts, hemoglobin 7.2 g/dL, and platelet count 15,000/μL. Bone marrow biopsy reveals 70% myeloid blasts. Which of the following best describes this clinical scenario?

A. Chronic phase CML with good imatinib response

B. CML in accelerated phase

C. Secondary acute myeloid leukemia unrelated to CML

D. Blast crisis of CML (transformation to acute leukemia)

15. A 68-year-old man on warfarin therapy for atrial fibrillation presents with hematuria and easy bruising. His INR is 8.5. He is hemodynamically stable with no signs of active major bleeding. Which of the following is the most appropriate initial management?

A. Immediate administration of fresh frozen plasma

B. Hold warfarin and administer oral vitamin K

C. Continue warfarin at the current dose and recheck INR in 1 week

D. Administer IV prothrombin complex concentrate (PCC) emergently

16. A 50-year-old woman presents with a palpable breast mass in the upper outer quadrant of the right breast. Mammography reveals an irregular, spiculated mass with microcalcifications. Ultrasound confirms a solid, hypoechoic mass. Core needle biopsy reveals invasive ductal carcinoma, estrogen receptor-positive, progesterone receptor-positive, HER2-negative. Which of the following receptor profiles has the most favorable prognosis?

A. ER-negative, PR-negative, HER2-positive

B. ER-negative, PR-negative, HER2-negative (triple-negative)

C. ER-positive, PR-positive, HER2-negative (luminal A type)

D. ER-positive, PR-positive, HER2-positive

17. A 58-year-old man with a 40-pack-year smoking history presents with a persistent cough, hemoptysis, and weight loss. Chest X-ray reveals a central hilar mass. Biopsy reveals squamous cell carcinoma. He also has hypercalcemia with a calcium of 13.2 mg/dL. PTH is suppressed. PTHrP (parathyroid hormone-related peptide) is elevated. Which of the following best explains his hypercalcemia?

A. Humoral hypercalcemia of malignancy from PTHrP secretion by the tumor

B. Osteolytic bone metastases

C. Primary hyperparathyroidism

D. Vitamin D toxicity

18. A 40-year-old man presents with recurrent episodes of hemarthrosis affecting the knees and elbows since childhood. He also has a history of excessive bleeding after dental extractions. Family history reveals an affected maternal uncle. Laboratory studies reveal a prolonged PTT, normal PT, normal platelet count, and a factor VIII activity level of 3% (severely reduced). Which of the following is the most likely diagnosis?

A. Von Willebrand disease

B. Factor V Leiden

C. Vitamin K deficiency

D. Hemophilia A (factor VIII deficiency)

19. A 22-year-old African American man presents to the emergency department with severe abdominal pain, jaundice, and dark urine after taking the antimalarial drug primaquine. Laboratory studies reveal hemoglobin 7.0 g/dL, reticulocyte count 15%, indirect bilirubin 5.5 mg/dL, LDH 900 U/L, and undetectable haptoglobin. Peripheral smear reveals bite cells and Heinz bodies on supravital staining. Which of the following is the most likely diagnosis?

A. Sickle cell crisis

B. Glucose-6-phosphate dehydrogenase (G6PD) deficiency

C. Autoimmune hemolytic anemia

D. Hereditary spherocytosis

20. A 65-year-old man presents with fatigue, weight loss, and night sweats. Physical examination reveals generalized painless lymphadenopathy. Excisional lymph node biopsy reveals a follicular pattern with a predominance of small cleaved lymphocytes. Immunohistochemistry is positive for CD20, CD10, and BCL-2. Cytogenetics reveals t(14;18). Which of the following is the most likely diagnosis?

A. Hodgkin lymphoma

B. Mantle cell lymphoma

C. Follicular lymphoma

D. Diffuse large B-cell lymphoma

21. A 50-year-old man presents with progressively worsening fatigue and exertional dyspnea. He has a history of chronic kidney disease stage IV. Laboratory studies reveal hemoglobin 8.5 g/dL, MCV 88 fL (normocytic), serum iron 45 µg/dL (low-normal), TIBC 200 µg/dL (low), ferritin 350 ng/mL (elevated), and reticulocyte count 0.5% (inappropriately low). Which of the following is the most likely cause of his anemia?

A. Anemia of chronic kidney disease (erythropoietin deficiency)

B. Iron deficiency anemia

C. Aplastic anemia

D. Myelodysplastic syndrome

22. A 30-year-old woman at 32 weeks gestation presents with fatigue, jaundice, and dark urine. Laboratory studies reveal hemoglobin 7.0 g/dL, platelet count 45,000/μL, LDH 1,800 U/L, haptoglobin undetectable, AST 350 U/L, and schistocytes on peripheral blood smear. Blood pressure is 165/105 mmHg with 3+ proteinuria. Which of the following is the most likely diagnosis?

A. Thrombotic thrombocytopenic purpura

B. Immune thrombocytopenic purpura

C. Preeclampsia with normal liver enzymes

D. HELLP syndrome (hemolysis, elevated liver enzymes, low platelets)

23. A 75-year-old man with newly diagnosed extensive-stage small cell lung cancer develops acute onset of facial swelling, neck vein distension, upper extremity edema, and dyspnea. The symptoms are worse when he raises his arms above his head. CT scan reveals a large mediastinal mass compressing the superior vena cava. Which of the following is the most likely diagnosis?

A. Cardiac tamponade

B. Superior vena cava syndrome

C. Tension pneumothorax

D. Aortic dissection

24. A 55-year-old man undergoes a total knee replacement and develops acute onset of dyspnea, tachycardia, and pleuritic chest pain on postoperative day 3. His D-dimer is elevated. CT pulmonary angiography reveals a large filling defect in the right main pulmonary artery. He is hemodynamically stable. Which of the following is the most appropriate initial anticoagulation?

A. Oral warfarin alone as initial monotherapy

B. Aspirin 325 mg daily

C. Unfractionated heparin or low-molecular-weight heparin, bridged to warfarin or transitioned to a DOAC

D. Thrombolytic therapy (tPA) for hemodynamically stable PE

25. A 60-year-old woman presents with a left axillary mass. Fine needle aspiration reveals malignant cells consistent with adenocarcinoma. Mammography, breast MRI, and breast ultrasound are all normal. CT scan of the chest, abdomen, and pelvis reveals no other primary site. Upper and lower endoscopy are unremarkable. Which of the following best describes this clinical scenario?

A. Stage IV breast cancer with axillary metastasis

B. Occult primary breast cancer with normal imaging

C. Lymphoma of the axillary lymph node

D. Cancer of unknown primary (CUP)

26. A 45-year-old woman is diagnosed with a new unprovoked deep vein thrombosis. She has a personal history of two prior miscarriages and a prolonged PTT that does not correct with a mixing study. Anticardiolipin antibodies and lupus anticoagulant are positive. Which of the following is the most appropriate long-term anticoagulation strategy?

A. Low-dose aspirin alone

B. Rivaroxaban (direct oral anticoagulant) as preferred therapy

C. Warfarin with a target INR of 2.0-3.0

D. No anticoagulation needed after initial treatment

27. A 62-year-old man with a 50-pack-year smoking history presents with facial plethora, upper extremity cyanosis, and bilateral periorbital edema. He also has new-onset headaches. Chest CT reveals a large right hilar mass with compression of the superior vena cava. Biopsy reveals small cell lung carcinoma. In addition to treating the underlying malignancy, which of the following is the most appropriate immediate management of his SVC obstruction?

A. Endovascular SVC stent placement for rapid symptom relief

B. Surgical bypass of the SVC

C. Observation with head-of-bed elevation only

D. Oral diuretics as definitive therapy

28. A 35-year-old woman presents with menorrhagia, easy bruising, and a prolonged bleeding time. Laboratory studies reveal a prolonged PTT that corrects with mixing study, normal PT, normal platelet count, reduced factor VIII activity (35%), reduced von Willebrand factor antigen, and reduced ristocetin cofactor activity. Which of the following is the most likely diagnosis?

A. Hemophilia A

B. Von Willebrand disease (type 1)

C. Factor XI deficiency

D. Bernard-Soulier syndrome

29. A 45-year-old man presents with headache, dizziness, blurred vision, and facial plethora (ruddy complexion). Laboratory studies reveal hemoglobin 21 g/dL, hematocrit 63%, WBC 14,000/µL, platelet count 550,000/µL, and an erythropoietin level that is suppressed (below normal). JAK2 V617F mutation is positive. He has splenomegaly on examination. Which of the following is the most likely diagnosis?

A. Secondary polycythemia from chronic hypoxia

B. Dehydration-induced hemoconcentration

C. Chronic myeloid leukemia

D. Polycythemia vera

30. A 42-year-old woman undergoing chemotherapy for breast cancer presents with fever (101.8°F), chills, and malaise 10 days after her last chemotherapy cycle. CBC reveals an absolute neutrophil count (ANC) of 350 cells/µL. She appears stable but has no identifiable source of infection. Which of the following is the most appropriate initial management?

A. Empiric broad-spectrum IV antibiotics (antipseudomonal beta-lactam such as cefepime, piperacillin-tazobactam, or meropenem) after blood cultures

B. Observation with close monitoring and oral antibiotics only

C. Granulocyte transfusion as first-line therapy

D. Antipyretics alone and recheck CBC in 24 hours

31. A 55-year-old man presents with an incidentally discovered serum protein electrophoresis showing a small monoclonal (M) spike of 1.8 g/dL. He is asymptomatic with no bone pain, renal dysfunction, anemia, or hypercalcemia. Bone marrow biopsy reveals 8% clonal plasma cells. Skeletal survey is normal. Which of the following is the most likely diagnosis?

A. Multiple myeloma

B. Waldenström macroglobulinemia

C. Monoclonal gammopathy of undetermined significance (MGUS)

D. Smoldering myeloma

32. A 68-year-old man presents with progressive fatigue and a CBC revealing hemoglobin 8.0 g/dL, MCV 72 fL, and a positive fecal occult blood test. Iron studies reveal ferritin 10 ng/mL, serum iron 20 µg/dL, and elevated TIBC. He has no history of NSAID use or known bleeding. Colonoscopy reveals a large, ulcerated mass in the ascending colon. Which of the following is the most likely explanation for his anemia?

A. Anemia of chronic disease

B. Iron deficiency anemia from chronic occult gastrointestinal blood loss

C. Vitamin B12 deficiency

D. Thalassemia trait

33. A 58-year-old man presents with a new diagnosis of acute promyelocytic leukemia (APL). He develops sudden onset of diffuse bleeding from IV sites, mucosal surfaces, and petechiae. Laboratory studies reveal prolonged PT and PTT, elevated D-dimer, decreased fibrinogen (85 mg/dL), and thrombocytopenia. Peripheral smear reveals schistocytes. Which of the following is the most likely complication?

A. Thrombotic thrombocytopenic purpura

B. Immune thrombocytopenic purpura

C. Heparin-induced thrombocytopenia

D. Disseminated intravascular coagulation (DIC)

34. A 60-year-old woman presents with progressive shortness of breath, pallor, and tachycardia. She was diagnosed with non-Hodgkin lymphoma 3 months ago and has been receiving chemotherapy. CBC reveals hemoglobin 5.5 g/dL, MCV 90 fL, and reticulocyte count 0.3% (inappropriately low). WBC and platelet counts are mildly decreased. Bone marrow biopsy reveals hypocellular marrow with decreased erythroid precursors. Which of the following is the most likely cause of her anemia?

A. Chemotherapy-induced bone marrow suppression

B. Iron deficiency from chronic blood loss

C. Autoimmune hemolytic anemia

D. Pure red cell aplasia

35. A 40-year-old woman presents with gradually worsening fatigue. She has a history of Hashimoto thyroiditis and vitiligo. Laboratory studies reveal hemoglobin 9.0 g/dL, MCV 115 fL, reticulocyte count 1.0%, and a peripheral smear showing hypersegmented neutrophils and oval macrocytes. Serum B12 is low, and anti-intrinsic factor antibodies are positive. Which of the following is the most likely diagnosis?

A. Folate deficiency

B. Dietary vitamin B12 deficiency

C. Pernicious anemia

D. Myelodysplastic syndrome

36. A 65-year-old man presents with painless gross hematuria. CT urogram reveals a 4-centimeter solid mass in the right kidney with enhancement. No lymphadenopathy or distant metastases are identified. Which of the following is the most appropriate next step in management?

A. Observation with repeat CT in 6 months

B. Radical or partial nephrectomy

C. Systemic chemotherapy as first-line treatment

D. Radiation therapy as primary treatment

37. A 50-year-old woman presents with a rapidly enlarging neck mass, hoarseness, and dysphagia. She has a history of Hashimoto thyroiditis. Ultrasound reveals a 5-centimeter solid, hypoechoic thyroid mass with irregular borders and microcalcifications. Fine needle aspiration reveals papillary structures with "Orphan Annie eye" nuclei (optically clear nuclei), nuclear grooves, and psammoma bodies. Which of the following is the most likely diagnosis?

A. Follicular thyroid carcinoma

B. Papillary thyroid carcinoma

C. Medullary thyroid carcinoma

D. Anaplastic thyroid carcinoma

38. A 70-year-old man presents with progressive lower back pain, urinary hesitancy, and nocturia. Digital rectal examination reveals a firm, irregular, enlarged prostate. PSA is 45 ng/mL (markedly elevated). Bone scan reveals multiple areas of increased uptake in the lumbar spine, pelvis, and ribs consistent with osteoblastic metastases. Prostate biopsy confirms adenocarcinoma with a Gleason score of 9 (4+5). Which of the following is the most appropriate initial systemic treatment for metastatic hormone-sensitive prostate cancer?

A. Radical prostatectomy alone

B. Watchful waiting without treatment

C. Radiation therapy to the prostate only

D. Androgen deprivation therapy (ADT) combined with a novel hormonal agent or docetaxel

39. A 55-year-old woman undergoes surgery for colon cancer. Five days postoperatively, she develops unilateral left lower extremity swelling, warmth, and tenderness. Compression ultrasonography reveals a non-compressible left common femoral vein with absent flow. She has no contraindications to anticoagulation. Which of the following is the most appropriate initial treatment?

A. Anticoagulation with LMWH or unfractionated heparin, transitioned to warfarin or a DOAC

B. Aspirin 81 mg daily

C. Inferior vena cava filter as first-line therapy

D. Observation with compression stockings only

40. A 72-year-old man with a history of chronic alcohol use and cirrhosis presents for evaluation of a liver mass found on surveillance ultrasound. Triphasic CT reveals a 3.5-centimeter lesion with arterial phase hyperenhancement and portal venous phase washout. AFP is 650 ng/mL. He has Child-Pugh class A cirrhosis, no portal hypertension, and adequate liver function. Which of the following is the most likely diagnosis?

A. Hepatic hemangioma

B. Focal nodular hyperplasia

C. Hepatocellular carcinoma

D. Metastatic colorectal cancer

41. A 48-year-old woman presents with a changing mole on her right calf. Examination reveals an asymmetric, irregularly bordered, multicolored (brown, black, and red) lesion measuring 8 mm in diameter that has grown over the past 3 months. Excisional biopsy reveals malignant melanoma with a Breslow thickness of 2.5 mm and ulceration present. Which of the following is the most important prognostic factor?

A. Location on the lower extremity

B. Breslow thickness (tumor depth)

C. Patient age

D. Presence of satellite lesions

42. A 45-year-old man presents with painless testicular enlargement that he noticed 3 weeks ago. Testicular ultrasound reveals a solid, hypoechoic intratesticular mass. Serum tumor markers show AFP 350 ng/mL (elevated) and beta-hCG 5 mIU/mL (mildly elevated). CT scan of the abdomen and pelvis reveals no retroperitoneal lymphadenopathy. Which of the following is the most appropriate initial management?

A. Testicular fine needle aspiration biopsy

B. Observation with repeat ultrasound in 3 months

C. External beam radiation to the testicle

D. Radical inguinal orchiectomy

43. A 62-year-old woman presents with a newly discovered pelvic mass, ascites, and an elevated CA-125 level of 850 U/mL. CT scan reveals bilateral ovarian masses with peritoneal implants and omental caking. She has no prior history of gynecologic disease. Which of the following is the most likely diagnosis?

A. Epithelial ovarian cancer (advanced stage)

B. Uterine fibroids with degeneration

C. Ovarian torsion

D. Endometriosis

44. A 65-year-old man who has been a lifelong smoker presents with persistent hoarseness for 6 weeks, throat discomfort, and referred otalgia. He drinks alcohol heavily. Direct laryngoscopy reveals an exophytic mass on the right vocal cord. Biopsy reveals squamous cell carcinoma. Which of the following is the most important risk factor for this malignancy?

A. Alcohol use alone

B. Human papillomavirus infection

C. Tobacco use (especially combined with alcohol)

D. Chronic laryngopharyngeal reflux

45. A 35-year-old woman presents with an anterior mediastinal mass discovered on chest X-ray obtained for persistent cough. CT scan reveals a well-circumscribed anterior mediastinal mass. She reports episodes of ptosis and diplopia that worsen with sustained activity and improve with rest. Acetylcholine receptor antibodies are positive. Which of the following is the most likely mediastinal tumor?

A. Teratoma

B. Thymoma

C. Lymphoma

D. Thyroid goiter

PRACTICE TEST 12: ANSWER KEY WITH EXPLANATIONS

Hematology and Oncology

1. C. Sickle cell disease with acute vaso-occlusive crisis. Sickle cell disease (HbSS) is an autosomal recessive hemoglobinopathy caused by a point mutation in the beta-globin gene substituting valine for glutamic acid at position 6, producing hemoglobin S that polymerizes under conditions of hypoxia, dehydration, acidosis, and cold temperatures. Hemoglobin electrophoresis showing HbS 85% with elevated HbF confirms sickle cell disease. Vaso-occlusive crisis (the most common acute complication) results from sickling of red blood cells causing microvascular occlusion, tissue ischemia, and severe bone pain. Triggers include high altitude, dehydration, infection, and hypoxia — this patient's long flight created a hypoxic environment. Howell-Jolly bodies indicate functional asplenia from autoinfarction. Acute chest syndrome (chest pain, dyspnea, pulmonary infiltrate) is a life-threatening complication. Treatment includes IV fluids, analgesics, supplemental oxygen, and exchange transfusion for severe complications.

2. A. Vitamin B12 deficiency (megaloblastic anemia). Megaloblastic anemia results from impaired DNA synthesis in rapidly dividing cells, causing nuclear-cytoplasmic dyssynchrony (delayed nuclear maturation with normal cytoplasmic development). Vitamin B12 deficiency produces macrocytic anemia (MCV greater than 100 fL) with characteristic peripheral smear findings of hypersegmented neutrophils (5 or more lobes in greater than 5% of neutrophils, or any neutrophil with 6 or more lobes) and macro-ovalocytes. Gastric bypass surgery causes B12 deficiency by eliminating intrinsic factor production from parietal cells and bypassing the duodenum where B12-IF complex is absorbed in the terminal ileum. Neurologic manifestations (subacute combined degeneration of the spinal cord) distinguish B12 deficiency from folate deficiency. Treatment is parenteral B12 (intramuscular cyanocobalamin or hydroxocobalamin) in patients with malabsorption.

3. B. Iron deficiency anemia. Iron deficiency is the most common cause of anemia worldwide. The classic laboratory profile includes low ferritin (the most sensitive and specific test for iron deficiency), low serum iron, elevated TIBC (reflecting the liver's compensatory increase in transferrin production to capture more iron), and low transferrin saturation (below 20%). Peripheral smear reveals microcytic (low MCV), hypochromic (pale-staining) red blood cells with anisocytosis (variation in size) and poikilocytosis (variation in shape including target cells and pencil cells). Pica (craving non-food items such as ice, dirt, or starch) is a characteristic but often overlooked symptom. Menorrhagia is the most common cause of iron deficiency in premenopausal women. Treatment is oral ferrous sulfate 325 mg two to three times daily on an empty stomach with vitamin C to enhance absorption.

4. D. Multiple myeloma. Multiple myeloma is a malignant clonal proliferation of plasma cells in the bone marrow producing a monoclonal immunoglobulin (M protein). The classic "CRAB" criteria define end-organ damage — Calcium elevation (hypercalcemia from osteoclast-activating cytokines), Renal insufficiency (from light chain deposition, hypercalcemia, or amyloidosis), Anemia (from marrow infiltration), and Bone disease (lytic lesions from osteoclast activation without compensatory osteoblast activity, which is why bone scan may be falsely negative). Bence Jones proteinuria represents monoclonal free light chains in the urine. SPEP showing an M spike greater than 3 g/dL with bone marrow plasma cells greater than 10% establishes the diagnosis. Treatment includes proteasome inhibitors (bortezomib), immunomodulatory agents (lenalidomide), dexamethasone, and autologous stem cell transplantation in eligible patients.

5. B. Immune thrombocytopenic purpura (ITP). ITP is an autoimmune disorder characterized by isolated thrombocytopenia (platelet count below 100,000/μL) caused by IgG autoantibodies directed against platelet surface glycoproteins (GPIIb/IIIa, GPIb/IX), leading to premature platelet destruction in the spleen. In children, ITP typically follows a viral infection and is self-limited. The hallmark is isolated severe thrombocytopenia with an otherwise normal CBC and peripheral smear (no schistocytes, excluding TTP/HUS; normal WBC and hemoglobin, excluding aplastic anemia and leukemia). Bleeding manifestations include petechiae, purpura, mucosal bleeding, and menorrhagia. First-line treatment for adults with platelets below 30,000/μL or significant bleeding includes corticosteroids (prednisone or dexamethasone), IVIG for rapid platelet count increase, and anti-Rh(D) immunoglobulin for Rh-positive patients.

6. A. Chronic lymphocytic leukemia (CLL). CLL is the most common leukemia in adults in Western countries, predominantly affecting elderly patients with a median age of diagnosis around 70 years. It is characterized by progressive accumulation of mature-appearing but functionally incompetent monoclonal B lymphocytes. Smudge cells (fragile lymphocytes that rupture during blood smear preparation) are a classic peripheral smear finding. Flow cytometry is the diagnostic gold standard, revealing the characteristic immunophenotype of CD5+, CD19+, CD20 (dim), and CD23+ B cells — co-expression of CD5 (a T-cell marker) with B-cell markers is distinctive. Rai staging (0-IV) and Binet staging (A-C) guide prognosis and treatment. Many patients have indolent disease requiring only observation ("watch and wait"), while treatment is indicated for symptomatic or progressive disease.

7. C. Autoimmune hemolytic anemia (warm antibody type). Warm autoimmune hemolytic anemia (WAIHA) is the most common type of autoimmune hemolytic anemia, caused by IgG autoantibodies that bind to red blood cell surface antigens at body temperature (37°C), leading to extravascular hemolysis primarily in the spleen. Laboratory findings of hemolysis include elevated reticulocyte count (bone marrow compensation), elevated indirect bilirubin and LDH (from RBC destruction), and undetectable haptoglobin (consumed by binding free hemoglobin). The positive direct antiglobulin test (DAT/direct Coombs test) is the key diagnostic finding, detecting IgG and/or complement (C3d) bound to the red blood cell surface. Spherocytes result from partial phagocytosis of antibody-coated RBCs by splenic macrophages. Treatment is corticosteroids (first-line), rituximab for refractory cases, and splenectomy for severe or relapsing disease.

8. D. Acute lymphoblastic leukemia (ALL). ALL is the most common malignancy in children (peak incidence 2-5 years), characterized by clonal proliferation of lymphoid progenitor cells (lymphoblasts) in the bone marrow. Pancytopenia results from marrow replacement — anemia (fatigue, pallor), thrombocytopenia (petechiae, bleeding), and functional leukopenia despite elevated WBC (infections). Hepatosplenomegaly and lymphadenopathy reflect extramedullary blast infiltration. The immunophenotype TdT+, CD10+ (CALLA), CD19+ identifies B-cell precursor ALL (the most common subtype, approximately 85%). TdT (terminal deoxynucleotidyl transferase) is a marker of immature lymphoid cells. The Philadelphia chromosome t(9;22) is present in approximately 25% of adult ALL and confers a poorer prognosis. Prognosis in children is excellent with cure rates exceeding 85% with modern multi-agent chemotherapy protocols.

9. A. Thrombotic thrombocytopenic purpura (TTP). TTP is a thrombotic microangiopathy caused by severe deficiency of ADAMTS13 (a von Willebrand factor-cleaving protease), either acquired (autoantibody-mediated, most common) or inherited. Without ADAMTS13, ultra-large VWF multimers accumulate, causing platelet aggregation in the microvasculature, leading to microthrombi formation, consumptive thrombocytopenia, and microangiopathic hemolytic anemia (schistocytes from mechanical shearing). The classic pentad includes thrombocytopenia, microangiopathic hemolytic anemia, neurologic symptoms, renal dysfunction, and fever — though the full pentad is present in only approximately 5% of cases. Normal PT and PTT distinguish TTP from DIC. ADAMTS13 activity less than 10% confirms the diagnosis. Treatment is emergent therapeutic plasma exchange (TPE), which removes the inhibitory antibody and replenishes ADAMTS13.

10. B. Hodgkin lymphoma. Hodgkin lymphoma is characterized by the presence of Reed-Sternberg cells — large, binucleated or multinucleated cells with prominent eosinophilic nucleoli creating the pathognomonic "owl's eye" appearance — in a background of reactive inflammatory cells (lymphocytes, eosinophils, histiocytes, plasma cells). It typically presents in young adults (bimodal distribution with peaks at 15-35 and over 55 years) with painless cervical or supraclavicular lymphadenopathy. "B symptoms" (fever, drenching night sweats, greater than 10% unintentional weight loss over 6 months) are present in approximately 40% of patients and confer a worse prognosis. Pruritus is another common symptom. Nodular sclerosis is the most common histologic subtype. Staging uses the Ann Arbor/Lugano system (I-IV). Hodgkin lymphoma is highly curable with combination chemotherapy (ABVD) with or without radiation, achieving cure rates exceeding 80%.

11. D. t(9;22) — Philadelphia chromosome (BCR-ABL fusion gene). The Philadelphia chromosome results from a reciprocal translocation between chromosomes 9 and 22, creating the BCR-ABL fusion gene that encodes a constitutively active tyrosine kinase driving uncontrolled myeloid cell proliferation. It is present in greater than 95% of CML cases and is the diagnostic hallmark. CML characteristically presents in chronic phase with leukocytosis showing the entire spectrum of myeloid maturation (a "left shift" with myelocytes, metamyelocytes, bands, and segmented neutrophils), basophilia, eosinophilia, splenomegaly, and thrombocytosis. The leukocyte alkaline phosphatase (LAP) score is low in CML (distinguishing it from leukemoid reactions). Imatinib (Gleevec), a tyrosine kinase inhibitor targeting BCR-ABL, revolutionized CML treatment with complete cytogenetic response rates exceeding 80%.

12. C. Myelodysplastic syndrome. MDS encompasses a group of clonal hematopoietic stem cell disorders characterized by ineffective hematopoiesis, peripheral blood cytopenias, and dysplastic morphologic changes in one or more cell lineages, with a risk of transformation to acute myeloid leukemia (approximately 30%). Peripheral smear findings include pseudo-Pelger-Huët anomaly (bilobed, hyposegmented neutrophils), oval macrocytes, and hypogranular platelets. Bone marrow is typically hypercellular with dysplasia and blast percentage between 5-19% (20% or greater blasts defines AML). MDS primarily affects elderly patients (median age 65-70 years). The Revised International Prognostic Scoring System (IPSS-R) classifies risk. Treatment ranges from supportive care (transfusions, erythropoiesis-stimulating agents) to hypomethylating agents (azacitidine, decitabine) and allogeneic stem cell transplantation for eligible patients.

13. A. Antiphospholipid syndrome. APS is an autoimmune prothrombotic disorder defined by the combination of clinical events (arterial or venous thrombosis, or pregnancy morbidity) and persistent laboratory evidence of antiphospholipid antibodies — lupus anticoagulant, anticardiolipin antibodies, and/or anti-beta-2 glycoprotein I antibodies — confirmed on two or more occasions at least 12 weeks apart. Despite the name "lupus anticoagulant," it causes thrombosis in vivo (by activating endothelial cells, platelets, and complement) while paradoxically prolonging the PTT in vitro. APS can be primary (isolated) or secondary (associated with SLE in approximately 30-40% of cases). Pregnancy complications include recurrent miscarriages, preeclampsia, and placental insufficiency. Treatment of thrombotic APS is long-term anticoagulation with warfarin (target INR 2.0-3.0).

14. D. Blast crisis of CML (transformation to acute leukemia). Blast crisis represents the terminal phase of CML, defined by 20% or more blasts in the peripheral blood or bone marrow, or the presence of extramedullary blast proliferation. CML progresses through three phases — chronic phase (most patients at diagnosis, manageable with TKI therapy), accelerated phase (10-19% blasts, worsening cytopenias, increasing basophilia, additional cytogenetic abnormalities), and blast crisis (transformation to acute leukemia). Blast crisis can be myeloid (60-70%) or lymphoid (20-30%), with lymphoid blast crisis responding better to treatment. This patient on imatinib developed blast crisis despite TKI therapy, indicating treatment failure or disease progression. Management includes second-generation TKIs (dasatinib, nilotinib, ponatinib) and consideration for allogeneic stem cell transplantation.

15. B. Hold warfarin and administer oral vitamin K. For supratherapeutic INR greater than 4.5-10 without major bleeding, the appropriate management is to hold warfarin and administer low-dose oral vitamin K (2.5-5 mg). Oral vitamin K is preferred over IV vitamin K for non-emergency situations because it produces a more predictable, gradual correction of the INR with lower risk of anaphylactoid reactions. INR typically begins to decrease within 6-12 hours and normalizes within 24-48 hours. Fresh frozen plasma (FFP) or prothrombin complex concentrate (PCC) is reserved for active major bleeding or need for emergent surgical intervention (4-factor PCC is preferred for warfarin reversal). Simply holding warfarin without vitamin K for INR greater than 9 risks ongoing bleeding. The warfarin dose should be adjusted downward upon resumption.

16. C. ER-positive, PR-positive, HER2-negative (luminal A type). Breast cancer molecular subtypes are classified by receptor status and have distinct prognoses and treatment implications. Luminal A (ER+, PR+, HER2-, low Ki-67) has the best prognosis, characterized by slow proliferation and excellent responsiveness to hormonal therapy (tamoxifen in premenopausal women, aromatase inhibitors in postmenopausal women). Luminal B (ER+, PR±, HER2±, high Ki-67) has intermediate prognosis. HER2-enriched (ER-, PR-, HER2+) benefits from targeted anti-HER2 therapy (trastuzumab). Triple-negative (ER-, PR-, HER2-) has the worst prognosis with no targeted therapies available (relies on chemotherapy and emerging immunotherapy). Hormone receptor positivity is the strongest predictor of response to endocrine therapy and correlates with more indolent tumor biology.

17. A. Humoral hypercalcemia of malignancy from PTHrP secretion by the tumor. Squamous cell carcinoma of the lung (and other squamous cell cancers) is the classic cause of humoral hypercalcemia of malignancy (HHM) through secretion of parathyroid hormone-related peptide (PTHrP). PTHrP mimics PTH by binding to PTH receptors, increasing bone resorption and renal calcium reabsorption. However, unlike primary hyperparathyroidism where PTH is elevated, HHM produces elevated PTHrP with appropriately suppressed PTH. HHM accounts for approximately 80% of malignancy-associated hypercalcemia. The remaining 20% is caused by local osteolytic metastases (most common with breast cancer and myeloma) or tumor production of 1,25-dihydroxyvitamin D (lymphomas). Treatment of acute hypercalcemia includes IV normal saline, calcitonin (rapid but temporary effect), bisphosphonates (zoledronic acid for sustained effect), and denosumab for refractory cases.

18. D. Hemophilia A (factor VIII deficiency). Hemophilia A is an X-linked recessive bleeding disorder caused by deficiency of factor VIII. The X-linked inheritance pattern explains why males are affected and the disease is transmitted through carrier females (affected maternal uncle confirms this pattern). Hemarthrosis (bleeding into joints, especially knees, elbows, and ankles) is the hallmark clinical manifestation and the most common cause of morbidity, leading to chronic arthropathy if untreated. Laboratory findings include prolonged PTT (factor VIII is in the intrinsic pathway), normal PT (extrinsic pathway is intact), and normal platelet count and bleeding time. Severity classification is based on factor VIII activity — severe (less than 1%), moderate (1-5%), and mild (5-40%). This patient's level of 3% indicates moderate-severe disease. Treatment is factor VIII replacement (recombinant or plasma-derived) for acute bleeding and prophylaxis.

19. B. Glucose-6-phosphate dehydrogenase (G6PD) deficiency. G6PD deficiency is the most common enzymatic red blood cell disorder worldwide, with X-linked recessive inheritance predominantly affecting males of African, Mediterranean, and Asian descent. G6PD is essential for the pentose phosphate pathway, generating NADPH needed to maintain reduced glutathione, which protects red blood cells from oxidative damage. When exposed to oxidative stressors (primaquine, dapsone, sulfonamides, fava beans, infection, DKA), deficient red blood cells undergo oxidative hemolysis. Heinz bodies (denatured hemoglobin precipitates seen with supravital staining, such as crystal violet) and bite cells (red blood cells with a portion "bitten" away by splenic macrophages removing Heinz bodies) are pathognomonic peripheral smear findings. G6PD enzyme activity levels should be measured after the acute hemolytic episode

resolves, as levels may be falsely normal during active hemolysis when reticulocytes (which have higher G6PD activity) predominate.

20. C. Follicular lymphoma. Follicular lymphoma is the most common indolent (low-grade) non-Hodgkin lymphoma, accounting for approximately 20-30% of all NHL cases. The hallmark cytogenetic abnormality is t(14;18), which juxtaposes the BCL-2 anti-apoptotic gene on chromosome 18 with the immunoglobulin heavy chain promoter on chromosome 14, resulting in constitutive BCL-2 overexpression and resistance to apoptosis. Histologically, it displays a follicular (nodular) growth pattern with a predominance of centrocytes (small cleaved cells) and centroblasts (large cells). Immunophenotype is CD20+, CD10+, BCL-2+. Follicular lymphoma is generally incurable with standard therapy but has an indolent course with median survival exceeding 10-15 years. Treatment ranges from watchful waiting for asymptomatic patients to rituximab-based chemoimmunotherapy for symptomatic disease.

21. A. Anemia of chronic kidney disease (erythropoietin deficiency). The kidneys are the primary source of erythropoietin (EPO), the hormone that stimulates red blood cell production in the bone marrow. As renal function declines, EPO production decreases, resulting in normocytic, normochromic anemia with an inappropriately low reticulocyte count. This anemia typically becomes clinically significant when GFR falls below 30 mL/min (CKD stage IV-V). The iron studies show a pattern consistent with functional iron deficiency or anemia of chronic disease (low serum iron, low TIBC, elevated ferritin reflecting inflammation and impaired iron utilization). Treatment includes erythropoiesis-stimulating agents (ESAs — epoetin alfa or darbepoetin alfa) targeting hemoglobin 10-11.5 g/dL (higher targets increase cardiovascular risk) and IV iron supplementation to ensure adequate iron stores for erythropoiesis.

22. D. HELLP syndrome. HELLP syndrome (Hemolysis, Elevated Liver enzymes, Low Platelets) is a severe variant of preeclampsia occurring in the third trimester or early postpartum period. Diagnostic criteria include microangiopathic hemolytic anemia (schistocytes, elevated LDH above 600 U/L, elevated indirect bilirubin, undetectable haptoglobin), elevated hepatic transaminases (AST and ALT), and thrombocytopenia (below 100,000/μL). Hypertension and proteinuria distinguish HELLP from TTP and HUS. The pathophysiology involves endothelial dysfunction, platelet activation, and fibrin deposition in the hepatic microvasculature causing periportal hemorrhage and hepatocyte necrosis. Complications include hepatic rupture, DIC, placental abruption, and renal failure. Definitive treatment is delivery of the fetus and placenta. Magnesium sulfate is administered for seizure prophylaxis.

23. B. Superior vena cava syndrome. SVC syndrome results from obstruction of the superior vena cava, most commonly caused by malignancy (lung cancer, particularly small cell, accounts for approximately 70% of cases; lymphoma accounts for approximately 10%). Obstruction impairs venous drainage from the head, neck, and upper extremities, producing facial swelling (facial plethora), neck vein distension, upper extremity edema, dyspnea, and headache. Symptoms worsen with bending forward or raising the arms (Pemberton sign). CT with contrast is the diagnostic study of choice, identifying the site and cause of obstruction. Treatment is directed at the underlying malignancy — small cell lung cancer and lymphoma are highly chemoresponsive. Endovascular SVC stenting provides rapid symptomatic relief. Radiation therapy is used for chemoresistant tumors.

24. C. Unfractionated heparin or low-molecular-weight heparin, bridged to warfarin or transitioned to a DOAC. Acute pulmonary embolism in a hemodynamically stable patient requires immediate anticoagulation to prevent clot propagation. Initial parenteral anticoagulation with IV unfractionated heparin (UFH — preferred when there is a need for rapid dose adjustment or potential procedures) or subcutaneous LMWH (enoxaparin — preferred for most patients due to predictable pharmacokinetics without monitoring) is the standard approach. Anticoagulation is bridged to warfarin (target INR 2.0-3.0, with a minimum 5-day overlap with heparin) or transitioned to a DOAC (rivaroxaban or apixaban can be initiated without heparin bridge). Systemic thrombolysis (tPA) is reserved for massive PE with hemodynamic instability (hypotension, shock). Duration of anticoagulation is typically 3-6 months for provoked PE and indefinite for unprovoked or recurrent PE.

25. D. Cancer of unknown primary (CUP). Cancer of unknown primary is defined as a metastatic malignancy for which no primary site can be identified after a comprehensive diagnostic workup including history, physical examination, laboratory studies, imaging (CT chest/abdomen/pelvis), and pathologic evaluation. CUP accounts for approximately 3-5% of all cancer diagnoses. Adenocarcinoma in an axillary lymph node in a woman raises strong suspicion for an occult breast primary, but when mammography, breast MRI, and ultrasound are all normal, the diagnosis technically remains CUP with probable breast origin. Immunohistochemistry (ER, PR, HER2, GATA3, mammaglobin) on the biopsy specimen can help identify likely breast origin. Treatment may follow breast cancer protocols if immunohistochemistry suggests breast origin, including consideration of ipsilateral mastectomy or breast radiation.

26. C. Warfarin with a target INR of 2.0-3.0. Antiphospholipid syndrome with thrombosis requires long-term anticoagulation with warfarin (target INR 2.0-3.0). Warfarin remains the preferred anticoagulant for APS based on current evidence because direct oral anticoagulants (DOACs, particularly rivaroxaban) have shown inferior outcomes in randomized trials (TRAPS trial demonstrated increased thrombotic events with rivaroxaban compared to warfarin in high-risk triple-positive APS). Low-dose aspirin alone is insufficient for secondary prevention in patients with prior thrombosis (it may be used for primary prevention in obstetric APS). Duration of anticoagulation is typically indefinite given the high recurrence risk. In obstetric APS without prior thrombosis, treatment during pregnancy is LMWH plus low-dose aspirin.

27. A. Endovascular SVC stent placement for rapid symptom relief. While definitive treatment of SVC syndrome targets the underlying malignancy (chemotherapy for small cell lung cancer, which is highly chemoresponsive), endovascular SVC stent placement provides the most rapid symptomatic relief, typically within 24-72 hours. Stent placement has become the first-line intervention for symptomatic relief in SVC syndrome regardless of etiology, with technical success rates exceeding 95% and rapid resolution of symptoms. Supportive measures including head-of-bed elevation, supplemental oxygen, and diuretics provide temporary symptomatic improvement but are not definitive. Surgical bypass is rarely performed due to the availability of less invasive endovascular techniques. Concurrent initiation of systemic chemotherapy and/or radiation addresses the underlying malignancy.

28. B. Von Willebrand disease (type 1). Von Willebrand disease is the most common inherited bleeding disorder, affecting approximately 1% of the population. VWF is a multimeric glycoprotein that mediates platelet adhesion to damaged endothelium and serves as a carrier protein for factor VIII, protecting it from premature degradation. Type 1 VWD (approximately 70-80% of cases) is a quantitative partial deficiency (autosomal dominant with variable penetrance). The laboratory profile shows prolonged PTT (due to reduced factor VIII), reduced VWF antigen, reduced ristocetin cofactor activity (measures VWF function), and reduced factor VIII activity. Platelet count is normal (unlike Bernard-Soulier). The prolonged PTT corrects with mixing study because the deficiency is factor-based, not inhibitor-based. Treatment is desmopressin (DDAVP), which stimulates VWF and factor VIII release from endothelial stores, for mild bleeding, and VWF-containing factor VIII concentrates for severe bleeding.

29. D. Polycythemia vera. Polycythemia vera is a myeloproliferative neoplasm characterized by clonal proliferation of hematopoietic stem cells with primary overproduction of red blood cells and variable increases in white blood cells and platelets. The JAK2 V617F mutation is present in approximately 95% of PV cases and is essentially diagnostic. Suppressed erythropoietin distinguishes PV (primary polycythemia) from secondary polycythemia (where EPO is elevated in response to chronic hypoxia, EPO-secreting tumors, etc.). Symptoms result from hyperviscosity — headache, dizziness, visual disturbances, facial plethora, and pruritus (especially after bathing, due to histamine release from basophils). Thrombosis (arterial and venous) is the major cause of morbidity and mortality. Treatment is phlebotomy (target hematocrit below 45%), low-dose aspirin, and cytoreductive therapy (hydroxyurea) for high-risk patients.

30. A. Empiric broad-spectrum IV antibiotics after blood cultures. Febrile neutropenia (temperature greater than 100.4°F/38.3°C with ANC below 500 cells/μL or expected to fall below 500) is an oncologic emergency requiring immediate empiric broad-spectrum antibiotic therapy after obtaining blood cultures (at least 2 sets from different sites). Treatment must not be delayed for culture results because neutropenic patients lack adequate immune response and can rapidly develop sepsis and death. Monotherapy with an antipseudomonal beta-lactam (cefepime, piperacillin-tazobactam, or meropenem) is the standard initial empiric regimen. Vancomycin is added for suspected catheter-related infection, skin/soft tissue infection, hemodynamic instability, or known MRSA colonization. G-CSF (filgrastim) may be considered to shorten the duration of neutropenia. Mortality from untreated febrile neutropenia approaches 50% within 48 hours.

31. C. Monoclonal gammopathy of undetermined significance (MGUS). MGUS is a premalignant plasma cell dyscrasia defined by the presence of a monoclonal M protein less than 3 g/dL, bone marrow clonal plasma cells less than 10%, and absence of end-organ damage (no CRAB criteria — no hypercalcemia, renal insufficiency, anemia, or bone lesions). MGUS is present in approximately 3-4% of the general population over age 50 and progresses to multiple myeloma or related malignancy at a rate of approximately 1% per year. This distinguishes it from smoldering myeloma (M protein greater than 3 g/dL or bone marrow plasma cells 10-60% without CRAB criteria) and overt multiple myeloma (CRAB criteria present or specific biomarkers of malignancy). MGUS requires no treatment but necessitates indefinite monitoring with SPEP, CBC, calcium, and creatinine every 6-12 months.

32. B. Iron deficiency anemia from chronic occult gastrointestinal blood loss. Iron deficiency anemia in an elderly man with a positive fecal occult blood test and microcytic anemia (MCV 72 fL) should be considered gastrointestinal malignancy until proven otherwise. The iron studies (low ferritin, low serum iron, elevated TIBC) confirm iron deficiency as the mechanism. The ascending colon mass represents the source of chronic occult blood loss leading to progressive iron depletion. Right-sided colon cancers classically present with iron deficiency anemia and occult blood loss rather than overt rectal bleeding (which is more characteristic of left-sided lesions). This underscores the importance of completing a full gastrointestinal evaluation (colonoscopy) in any patient over 40 with unexplained iron deficiency anemia, even without overt bleeding symptoms.

33. D. Disseminated intravascular coagulation (DIC). DIC is a consumptive coagulopathy characterized by systemic activation of the coagulation cascade, leading to widespread microthrombi formation with simultaneous consumption of coagulation factors, platelets, and fibrinogen, resulting in both thrombosis and hemorrhage. Acute promyelocytic leukemia (APL, associated with t(15;17) producing PML-RARA fusion) is notorious for DIC at presentation and represents the most common cause of early death in APL. Laboratory findings include prolonged PT and PTT, elevated D-dimer and fibrin degradation products, decreased fibrinogen (below 100 mg/dL), thrombocytopenia, and schistocytes on peripheral smear. Treatment includes supportive care (cryoprecipitate for fibrinogen less than 100 mg/dL, platelet transfusions, FFP) and all-trans retinoic acid (ATRA) as the specific treatment for APL that rapidly reverses the coagulopathy.

34. A. Chemotherapy-induced bone marrow suppression. Myelosuppression is the most common dose-limiting toxicity of cytotoxic chemotherapy, resulting from direct damage to rapidly dividing hematopoietic progenitor cells in the bone marrow. It typically manifests 7-14 days after chemotherapy administration (nadir period) and affects all three lineages — anemia (fatigue, dyspnea), neutropenia (infection risk), and thrombocytopenia (bleeding risk). The severely low hemoglobin with inappropriately low reticulocyte count indicates impaired erythropoiesis from bone marrow suppression rather than hemolysis or blood loss (which would produce elevated reticulocyte counts). Hypocellular bone marrow with decreased erythroid precursors confirms the diagnosis. Management includes transfusion support, G-CSF for neutropenia, dose reduction or delay for subsequent chemotherapy cycles, and EPO-stimulating agents for persistent chemotherapy-induced anemia.

35. C. Pernicious anemia. Pernicious anemia is an autoimmune condition characterized by destruction of gastric parietal cells by autoantibodies, leading to absent intrinsic factor production and subsequent inability to absorb vitamin B12 in the terminal ileum. Anti-intrinsic factor antibodies are highly specific (though less sensitive) for pernicious anemia, while anti-parietal cell antibodies are sensitive but less specific. Pernicious anemia is strongly associated with other autoimmune conditions (Hashimoto thyroiditis, vitiligo, type 1 diabetes, Addison disease), as demonstrated in this patient. The macrocytic anemia (MCV 115 fL) with hypersegmented neutrophils and low B12 reflects megaloblastic anemia from impaired DNA synthesis. Unlike dietary B12 deficiency (which takes years to develop given large hepatic stores), pernicious anemia requires lifelong parenteral B12 replacement because the absorption defect is permanent.

36. B. Radical or partial nephrectomy. Renal cell carcinoma (RCC) is the most common malignant tumor of the kidney in adults, with clear cell carcinoma being the most common histologic subtype (70-80%). The classic triad of flank pain, hematuria, and palpable abdominal mass is present in only 10% of patients. Surgery is the only curative treatment for localized RCC — partial nephrectomy is preferred for tumors 4 cm or less (T1a) to preserve renal function, while radical nephrectomy is performed for larger tumors. RCC is notoriously resistant to conventional chemotherapy and radiation therapy. For metastatic disease, targeted therapies (tyrosine kinase inhibitors — sunitinib, pazopanib) and immunotherapy (nivolumab, ipilimumab combinations) are the primary treatment modalities. Paraneoplastic syndromes associated with RCC include polycythemia (EPO production), hypercalcemia (PTHrP), and Stauffer syndrome (hepatic dysfunction).

37. B. Papillary thyroid carcinoma. Papillary thyroid carcinoma is the most common thyroid malignancy (80-85% of cases), with the best overall prognosis. Histologic hallmarks include papillary architecture, "Orphan Annie eye" nuclei (optically clear, ground-glass nuclei from chromatin clearing), nuclear grooves (longitudinal indentations), intranuclear pseudoinclusions, and psammoma bodies (concentrically laminated calcifications that appear as microcalcifications on ultrasound). Papillary thyroid cancer is associated with prior radiation exposure and Hashimoto thyroiditis. It spreads primarily via lymphatic invasion to cervical lymph nodes. Treatment is total thyroidectomy (for tumors greater than 1-4 cm depending on risk factors) followed by radioactive iodine ablation (I-131) for intermediate and high-risk patients, and TSH suppression with levothyroxine. Ten-year survival exceeds 95%.

38. D. Androgen deprivation therapy (ADT) combined with a novel hormonal agent or docetaxel. Metastatic hormone-sensitive prostate cancer with high-volume disease (visceral metastases or multiple bone metastases) requires intensified systemic therapy beyond ADT alone. Current evidence-based standard of care is ADT (GnRH agonist such as leuprolide or GnRH antagonist such as degarelix) combined with either a novel androgen receptor pathway inhibitor (abiraterone, enzalutamide, apalutamide, or darolutamide) or docetaxel chemotherapy. Multiple landmark trials (CHAARTED, LATITUDE, STAMPEDE, ENZAMET, TITAN, ARCHES) demonstrated significant overall survival benefit with combination therapy compared to ADT alone. The Gleason score of 9 indicates high-grade, aggressive disease. Osteoblastic (sclerotic) metastases are characteristic of prostate cancer (in contrast to the osteolytic metastases of multiple myeloma and most solid tumors). PSA serves as a tumor marker for monitoring treatment response.

39. A. Anticoagulation with LMWH or unfractionated heparin, transitioned to warfarin or a DOAC. Acute deep vein thrombosis requires prompt anticoagulation to prevent clot propagation, pulmonary embolism, and post-thrombotic syndrome. Initial treatment follows the same approach as PE — parenteral anticoagulation with LMWH or UFH, transitioned to warfarin (target INR 2.0-3.0 with minimum 5-day heparin overlap) or a DOAC. For cancer-associated thrombosis (as in this postoperative colon cancer patient), LMWH has traditionally been preferred for the full treatment duration, though recent trials (SELECT-D, HOKUSAI VTE Cancer) have demonstrated comparable efficacy of DOACs (edoxaban, rivaroxaban) with a caveat of increased GI bleeding risk in GI malignancies. IVC filters are reserved for

patients with absolute contraindications to anticoagulation or who develop PE despite therapeutic anticoagulation.

40. C. Hepatocellular carcinoma. HCC is the most common primary liver malignancy, arising predominantly in the setting of cirrhosis regardless of etiology (alcohol, hepatitis B, hepatitis C, NAFLD/NASH). The characteristic imaging pattern on multiphasic contrast-enhanced CT or MRI is arterial phase hyperenhancement (HCC is supplied by the hepatic artery) followed by "washout" in the portal venous or delayed phase — this pattern is highly specific and allows non-invasive diagnosis in cirrhotic patients without biopsy (LI-RADS 5 classification). Markedly elevated AFP (above 200-400 ng/mL) further supports the diagnosis. Treatment depends on staging — Barcelona Clinic Liver Cancer (BCLC) staging system guides management from surgical resection and transplantation (early stage) to locoregional therapies (TACE, ablation for intermediate stage) and systemic therapy (atezolizumab-bevacizumab for advanced disease).

41. B. Breslow thickness (tumor depth). Breslow thickness, measuring the depth of tumor invasion from the granular layer of the epidermis to the deepest point of tumor penetration in millimeters, is the single most important prognostic factor in cutaneous melanoma. It directly correlates with the risk of metastasis and overall survival and is the primary determinant of T-staging in the AJCC melanoma staging system. Breslow thickness of 2.5 mm with ulceration classifies this melanoma as at least T3b (2.01-4.0 mm with ulceration), which carries a significant risk of regional and distant metastasis. Ulceration is the second most important histologic prognostic factor, independently worsening stage-for-stage prognosis. Sentinel lymph node biopsy is recommended for melanomas with Breslow thickness greater than 0.8 mm or those with ulceration. The ABCDE criteria (Asymmetry, Border irregularity, Color variation, Diameter greater than 6 mm, Evolution) guide clinical recognition.

42. D. Radical inguinal orchiectomy. A solid intratesticular mass in a young man is testicular cancer until proven otherwise. Radical inguinal orchiectomy (NOT transscrotal biopsy or orchiectomy, which violates surgical planes and risks scrotal seeding and altered lymphatic drainage patterns) is both the diagnostic and initial therapeutic procedure. The inguinal approach allows early control of the spermatic cord with high ligation at the internal inguinal ring. Elevated AFP indicates a non-seminomatous germ cell tumor (NSGCT) component — AFP is produced by yolk sac tumors and is never elevated in pure seminoma. Beta-hCG can be elevated in both seminoma and non-seminoma (particularly choriocarcinoma). Post-orchiectomy staging with CT and tumor markers guides further treatment — surveillance, retroperitoneal lymph node dissection, or chemotherapy (BEP — bleomycin, etoposide, cisplatin). Testicular cancer is one of the most curable solid tumors with cure rates exceeding 95%.

43. A. Epithelial ovarian cancer (advanced stage). Epithelial ovarian cancer is the most lethal gynecologic malignancy, primarily because the majority of cases (approximately 70%) are diagnosed at advanced stages (III-IV) due to the absence of early symptoms and lack of effective screening. Classic presentation includes abdominal/pelvic mass, ascites, and elevated CA-125 (a glycoprotein tumor marker elevated in approximately 80% of epithelial ovarian cancers). "Omental caking" (thickened, nodular omentum from tumor implants) and peritoneal carcinomatosis are characteristic of advanced disease.

Serous carcinoma is the most common histologic subtype. Treatment is primary cytoreductive (debulking) surgery aiming for no residual disease followed by platinum-based combination chemotherapy (carboplatin plus paclitaxel). BRCA1/2 mutations significantly increase ovarian cancer risk and have therapeutic implications (PARP inhibitor sensitivity).

44. C. Tobacco use (especially combined with alcohol). Tobacco use is the most important risk factor for laryngeal squamous cell carcinoma, with a dose-dependent relationship that increases risk 10-15 fold in heavy smokers. The combination of tobacco and heavy alcohol use produces a synergistic effect (multiplicative rather than additive), increasing risk 40-fold or more compared to non-users of either substance. Alcohol alone is a weaker independent risk factor. HPV (particularly HPV-16) is an increasingly recognized risk factor for oropharyngeal squamous cell carcinoma (base of tongue, tonsils) but is less strongly associated with laryngeal cancer specifically. Persistent hoarseness lasting more than 2-3 weeks in a smoker is an alarm symptom requiring direct laryngoscopy. Early-stage laryngeal cancer (T1-T2) is highly curable with radiation therapy or limited surgery, with voice preservation being a primary goal.

45. B. Thymoma. Thymoma is the most common primary tumor of the anterior mediastinum and has a well-established association with myasthenia gravis (MG) — approximately 30-50% of thymoma patients develop MG, and 10-15% of MG patients have a thymoma. Myasthenia gravis is an autoimmune disorder caused by acetylcholine receptor antibodies (positive in approximately 85% of generalized MG) that block neuromuscular transmission, producing fatigable weakness that worsens with sustained activity and improves with rest. Ptosis and diplopia (ocular involvement) are the most common presenting symptoms. The anterior mediastinal mass differential (the "4 T's") includes Thymoma, Teratoma (and other germ cell tumors), Terrible lymphoma, and Thyroid (retrosternal goiter). Thymectomy is recommended for all thymoma patients regardless of MG status, and is also therapeutic for MG even without thymoma in appropriate candidates.