PATHOLOGY TEST BANK

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• Past papers

1. A 62-year-old man comes to his primary care physician for evaluation of daily headaches and blurry vision. These symptoms started two months ago. In addition, the patient reports feeling itchy over his body after bathing or visiting the sauna. Past medical history is notable for hypertension and asymptomatic gallstones were discovered on a recent ultrasound. The patient is a former smoker with a 20-pack-year smoking history. On the physical exam, the patient is observed to have a facial plethora and a spleen palpated 2 cm below the left costal margin. Laboratory testing is ordered and the results are as follows, what is the most likely cause of his symptoms?

Laboratory value	Result
Hemoglobin	18.1 g/dL
Hematocrit	54%
Erythrocytes	7.2 million/mm3
Leukocytes	12,500/mm3
Platelets	470,000/mm3
Uric Acid	7.9 mg/dL

A- Erythropoietin-independent proliferation of erythrocytes

B- Decreased blood plasma volume

C- Increased erythrocyte production secondary to hypoxia

D- Deposition of bile acids in the skin

E- Autoimmune destruction of myelin in the central nervous system

Answer: A

2. Which of the following is not a feature of anemia of acute blood loss?

A. Symptoms of hypotension
B. Increased erythropoiesis
C. Reticulocytosis
D. Normochromic normocytic RBCs
E. Hyperkalemia

Answer: E

3. A patient with anemia may have all these general symptoms, except:

A. Increased red cell 2,3-BPG
B. Headache
C. Fatigue
D. Dizziness
E. Bradycardia

Answer: E

4. Hb Bart means that you have:

A. 4 chains of gamma
B. 4 chains of beta

C. 3 chains of beta and 1 chain of alpha
D. 2 chains of beta and 2 chains of gamma
E. 4 chains of delta

Answer: A

5. Which of the following best describes a person with acute GIT hemorrhage?
A. Fluid is shifted from intravascular space to interstitial fluid
B. Iron deficiency might occur, causing complications
C. Erythropoietin is immediately secreted after hemorrhage has occurred
D. Erythrocytes may appear as hypochromic microcytic

Answer: B

6. Growth retardation can be observed in:
A. Chronic hemolytic anemia
B. Anemia of acute blood loss
C. Iron deficiency anemia
D. Thalassemia major

Answer: D

7. A patient showed up to the hospital with hair loss, spooned fingernails, and a tendency to eat dirt. Which of the following do you expect to see when examining a histological section of the patient's blood?
A. Microcytic hypochromic erythrocytes with reticulocytosis and thrombocytopenia
B. Ovalocytes with central pallor and low reticulocyte count
C. Lightly stained erythrocytes that have central & peripheral acidophilia with an area of pallor in between
D. Hypochromic microcytic anemia with anisopoikelocytosis that is densely stained with Perl's Prussian blue stain.

Answer: C

8. Wrong about Iron:
A. 20% of heme and 1% of non-heme iron are absorbed.
B. Is mostly absorbed in the jejunum.
C. Hepcidin inhibits iron absorption.

Answer: B

9. Which one of the following is NOT a cause of vitamin B12 deficiency?
A. Jejunal resection.
B. Gastrectomy.
C. Malabsorption.
D. Veganism.
E. Lack of gastric intrinsic factor

Answer: A

10. Which of the following causes pancytopenia:

A. Immune hemolytic anemia
B. Thalassemia
C. Iron deficiency anemia
D. Hereditary spherocytosis
E. B12 deficiency

Answer: E

11. Pernicious anemia is described as?

A. Macrocytic anemia
B. Autoimmune gastritis
C. Intrinsic factor deficiency
D. Vitamin B12 deficiency
E. All the answers are correct

Answer: E

12. A patient with a strict vegetarian diet is at risk for:

A. Thrombocytosis
B. Pancytopenia
C. Reticulocytosis
D. Severe coagulation

Answer: B

13. A 15-month-old girl is brought by her caretakers. Laboratory testing reveals a hemoglobin of 6.5 g/dL, a leukocyte count of 6,800/mm3, and a platelet count of 175,000/mm3. A peripheral smear reveals enlarged red blood cells. Which of the following is found in her case?

A. Fanconi anemia
B. Iron deficiency anemia
C. Diamond-Blackfan anemia
D. Vitamin B12 deficiency anemia

Answer: C

14. Which one of the following is wrong about Myelodysplastic Syndrome?

A. Acquired neoplastic disease of bone marrow
B. Patients commonly develop neutropenia
C. RBCs are microcytes
D. Anemia is refractory to treatment
E. Primarily disease of old age

Answer: C

15. Which of the following is MOST likely required by a 5-year-old boy with Chronic Kidney Disease (CKD)? (Not sure if this is a past paper question)

A. Oprelvekin (IL-11)

B. Cyanocobalamin
C. Erythropoietin
D. Deferoxamine
E. Filgrastim (G-cSF)

Answer: C

16. The production of which of the following is primarily defective in iron deficiency anemia?
    A. Heme
    B. Alpha globin chains
    C. Protoporphyrin
    D. Beta globin chains
    E. None of the above

Answer: A

17. A 68-year-old male comes to his provider's office for evaluation of fatigue, weakness, and 8 kg (17.6 lb) unintentional weight loss over the past 2 months. Physical exam reveals oral mucosal pallor. Cardiac and pulmonary exams are non-contributory. Abdominal exam reveals hepatosplenomegaly. Biopsy of the bone marrow shows increased fibrosis and reduced cell count. Laboratory testing shows the finding below. Polymerase chain reaction testing reveals a mutation in:

Laboratory value	Result
Hemoglobin	9.5 g/dL
Hematocrit	28.5%
Leukocytes	2,700/mm3
Platelets	100,000/mm3

A. thr gene
B. tyrosine c7
C. jak 1 gene
D. jak 2 gene
E. RAS gene

Answer: D

18. Which of the following is NOT an expected finding in a patient with iron deficiency anemia?
A. Koilonychia (spoon nails)
B. Angular stomatitis
C. Hypochromic microcytic red blood cells
D. Pallor
E. Symmetric paresthesia in lower limbs

Answer: E

19. A 31-year-old woman comes to the clinic because of increasing fatigue and dizziness over the past several months. She started a vegan diet six months ago with heavy and prolonged menstrual bleeding. Physical examination shows conjunctival pallor. Laboratory investigations reveal a hemoglobin level of 10.3 g/dL. Which of the following sets of laboratory values is most likely to be present in this patient?
A. Normal serum iron and serum ferritin
B. Low serum iron and high serum ferritin

C. High serum iron and low serum ferritin
D. Low serum iron and low serum ferritin

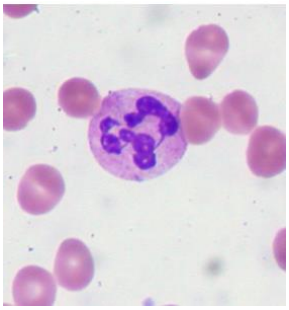
Answer: D

20. The best test to use for differential diagnosis between iron deficiency anemia and anemia of chronic inflammation is:

A. Serum iron level
B. Mean cell volume
C. Bone marrow iron stores
D. Reticulocyte count

Answer: C

21. A 75-year-old man comes to his primary care physician for a routine visit. Five months ago, his wife died from a stroke. The patient reports feeling depressed, and he has been consuming large quantities of vodka daily. He previously ate a balanced diet. However, he has had little motivation to cook since his wife passed away, and he currently eats crackers and beef jerky purchased from a convenience store. A complete blood count reveals a hemoglobin of 9.2 g/dL and a mean corpuscular volume (MCV) of 110 µm3. A peripheral smear is ordered, and the results are as follows, what is the pathogenesis of his condition?



A. Replacement of bone marrow by scar tissue
B. Defect in homologous DNA recombination
C. Iron deficiency secondary to bleeding in the gastrointestinal tract
D. Impaired DNA synthesis resulting from vitamin B12 deficiency
E. Impaired DNA synthesis resulting from vitamin B9 deficiency

Answer: D

22. Which of the following best corresponds to laboratory values in iron deficiency anemia?

A. Decreased ferritin, decreased serum iron, increased total iron binding capacity
B. Increased ferritin, decreased serum iron, increased total iron binding capacity
C. Normal ferritin, decreased serum iron, decreased total iron binding capacity
D. Decreased ferritin, increased serum iron, increased total iron binding capacity
E. Decreased ferritin, decreased serum iron, decreased total iron binding capacity

Answer: A

23. Which of the following is not a feature of megaloblastic anemia?

A. Reduced DNA synthesis
B. Mean corpuscular volume> 100
C. Reduced pyrimidine synthesis
D. Increased erythropoiesis
E. Pancytopenia

Answer: D

24. Which of the following are not characteristic of iron deficiency anemia? **(Activity)**
    A. Low mean cell volume
    B. Can be caused by liver disease
    C. Absent Perl`s staining pattern
    D. Low total iron binding capacity
    E. Low reticulocyte hemoglobin content

Answer: D

25. Which of the following is not characteristic of megaloblastic anemia? **(Activity)**
    A. Severely high bilirubin levels
    B. Chronic course of disease
    C. Loss of proprioception
    D. Macroovalocytes
    E. Can be caused by a strict vegan diet

Answer: A

26. Hemoglobin H disease is caused by:
A. Deletion of 3 alpha genes
B. Deletion of 4 alpha genes
C. Mutation in 3 alpha genes
D. Mutation in 4 alpha genes

Answer: A

27. A 2-year-old boy is brought to the clinician by his parents due to easy fatigability and growth delay. He is at the 30th percentile for length and below the 10th percentile for weight. Hematological tests and hemoglobin electrophoresis are obtained Hb : 10.8 , high HbA2 , absent HbA1 , Which of the following is the most likely diagnosis?
A. α-thalassemia major
B. β-thalassemia minor
C. Sickle cell disease
D. Hemoglobin H disease
E. β-thalassemia major
F. Sickle cell trait

Answer: E

28. Which of the following does not worsen sickle cell trait?
A. Malarial infection
B. Hypoxia
C. Dehydration
D. Acidosis

Answer: A

29. Glutamic acid to valine (at position 6) is an amino acid substitution seen in the (----------) chain in sickle-cell disease:

A. alpha chain
B. beta chain
C. delta chain
D. gamma chain
E. epsilon chain

Answer: B

30. Newborns that have sickle-cell disease are initially asymptomatic because ------- levels are high, while hemoglobin S levels are low.

A. hemoglobin minor
B. hemoglobin C
C. hemoglobin F
D. hemoglobin y

Answer: C

31. The genetic inheritance of glucose-6-phosphate dehydrogenase deficiency is:

A. Autosomal recessive
B. X-linked
C. Acquired
D. Autosomal dominant
E. Autosomal co-dominant

Answer: B

32. Are pathological red blood cells that form as a result of the phagocytic removal of Heinz bodies in glucose-6-phosphate dehydrogenase deficiency:

A. Spur cells
B. Burr cells
C. Bite cells
D. Spherocytes
E. Schistocytes

Answer: C

33. A 19-year-old man presents to the clinic with low-grade fevers, fatigue, paleness, shortness of breath, and a nonproductive cough for the past 2 weeks. Chest X-ray shows bilateral patchy infiltrates. Direct Coombs test is positive, and agglutination of RBCs is observed. Which of the following classes of antibodies is most likely implicated in this disease process?

A. Immunoglobulin D (IgD)
B. Immunoglobulin M (IgM)
C. Immunoglobulin G (IgG)
D. Immunoglobulin E (IgE)
E. Immunoglobulin A (IgA)

Answer: B

34. The patient's total bilirubin is elevated, and hemoglobin levels are low. Peripheral blood smear shows microspherocytes and abundant reticulocytes. The patient's family history is non-contributory. Which of the following tests is most likely to be positive?

A. Schilling test
B. Direct Coombs test
C. Ristocetin test

Answer: B

35. B-cell lymphoma is a form of:

A. Warm type immune hemolytic anemia
B. Cold type immune hemolytic anemia
C. Iron deficiency

Answer: B

36. Polycythemia with low erythropoietin levels:

A. Renal cancer
B. Surreptitious
C. Polycythemia vera
D. Smokers
E. High altitude

Answer: C

37. Neuropathy is related to which type of anemia:

A. Aplastic anemia
B. Pernicious anemia
C. Thalassemia
D. Sickle cell anemia

Answer: B

38. Which type of anemia has abnormal osmolarity of blood cells?

A. Immune hemolytic anemia
B. Hereditary spherocytosis
C. Thalassemia
D. Aplastic anemia
E. Myelodysplastic syndrome
F. A+B

Answer: F

39. Which anemia is characterized by low levels of hepcidin?

A. Thalassemia minor
B. Iron deficiency anemia
C. Anemia of chronic inflammation

D. G6PD deficiency
E. Sickle cell anemia

Answer: B

40. Which anemia is characterized by splenomegaly and jaundice?
    A. Hereditary spherocytosis
    B. Megaloblastic anemia
    C. Aplastic anemia
    D. Iron deficiency anemia
    E. Anemia of chronic disease

Answer: A

41. All the following are general symptoms of anemia, except:
    A. Headache
    B. Hypoxia
    C. Fatigue
    D. Splenomegaly
    E. Dizziness

Answer: D

42. Which combination disorder would exhibit more severe symptoms:
    A. HbS and HbA
    B. HbS and α- thalassemia
    C. HbS and HbH
    D. HbS and HbF
    E. HbS and β-thalassemia minor

Answer: C

43. A 2-year-old child suspected to have thalassemia was found to have β/β+ genotype. Which of the following is true regarding his condition:
A. Nucleated RBCs in peripheral blood
B. Normal MCH (mean corpuscular hemoglobin)
C. Severe erythroid hyperplasia in bone marrow
D. Mild microcytic anemia
E. Normal HbA2 level

Answer: D

44. Osteomyelitis in sickle cell patients is commonly due to:
A. E. Coli infection
B. Pneumococcal infection
C. Klebsiella infection
D. Salmonella infection
E. Staphylococcal infection

Answer: D

45. What confirmatory test should be performed in suspected cases of pancytopenia:
A. Coombs test
B. Bone marrow examination
C. Serum iron and Total iron-binding capacity
D. Hemoglobin electrophoresis
E. Blood film

Answer: B

46. Absolute polycythemia can be caused by:
A. Diuretic drugs
B. Vomiting
C. Carcinoma in renal cells
D. Diarrhea

Answer: C

47. Which of the following is an adaptive mechanism in IDA?
A. Increased erythropoietin
B. Diminished hepcidin
C. Decreased erythropoietin

Answer: B

48. Recent research showed that patients with marked obesity have an increased level of IL-6 in blood that is mainly secreted from adipose tissue which results in anemia. Which of the following is an expected finding?
A. Absent haptoglobin level
B. High erythropoietin level
C. High reticulocyte count
D. Low total iron binding capacity
E. Presence of gall bladder stones

Answer: D

49. Chronic alcoholism is a risk factor for:
A. Megaloblastic anemia
B. Iron deficiency anemia
C. Aplastic anemia
D. Immune hemolytic anemia
E. Myelodysplastic syndrome

Answer: A

• Questions from Robbins

1. A healthy 19-year-old woman suffered blunt abdominal trauma in a motor vehicle accident. On admission to the hospital, her initial hematocrit was 33%, but over the next hour, it decreased to 28%. A paracentesis yielded serosanguineous fluid. She was taken to surgery, where a liver laceration was repaired, and 1 L of bloody fluid was removed from the peritoneal cavity. She remained stable. A CBC performed 3 days later is most likely to show which of the following morphologic findings in the peripheral blood?
    A. Basophilic stippling of red cells
    B. Hypochromic red cells
    C. Leukoerythroblastosis
    D. Reticulocytosis
    E. Schistocytosis

Answer: D The acute blood loss, in this case intraperitoneal hemorrhage, results in a reticulocytosis from marrow stimulation by anemia. Basophilic stippling of RBCs suggests a marrow injury, such as with a drug or toxin. Hypochromic RBCs occur in iron deficiency and thalassemias, both associated with reduced hemoglobin synthesis. Acute blood loss does not give rise to iron deficiency if iron stores and diet are adequate. Leukoerythroblastosis is typical of a myelophthisic process in the marrow, with both immature WBCs (myelocytes) and RBCs (nucleated forms) present. Schistocytes suggest a microangiopathic hemolytic anemia, which can accompany shock or sepsis.

2. A 65-year-old man has experienced worsening fatigue for the past 5 months. On physical examination, he is afebrile and has a pulse of 91/min, respirations of 18/min, and blood pressure of 105/60 mm Hg. There is no organomegaly. A stool sample is positive for occult blood. Laboratory findings include hemoglobin of 5.9 g/dL, hematocrit of 18.3%, MCV of 99 µm3, platelet count of 250,000/mm3, and WBC count of 7800/mm3. The reticulocyte concentration is 3.9%. No fibrin split products are detected, and direct and indirect Coombs test results are negative. A bone marrow biopsy specimen shows marked erythroid hyperplasia. Which of the following conditions best explains these findings?
    A. Aplastic anemia
    B. Autoimmune hemolytic anemia
    C. Chronic blood loss
    D. Iron deficiency anemia
    E. Metastatic carcinoma

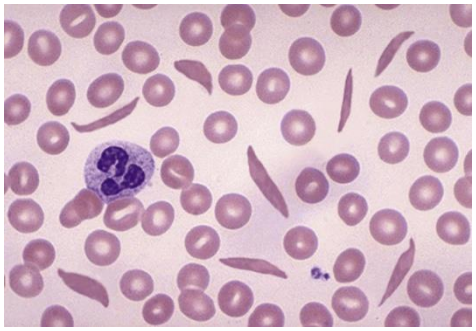
Answer: C The marked reticulocytosis and marrow hyperplasia indicate that the marrow is responding to a decrease in RBCs. The reticulocytes are larger RBCs that slightly increase the MCV. An aplastic marrow is very hypocellular and unable to respond to anemia; it is associated with pancytopenia. The normal Coombs test results exclude an autoimmune hemolytic anemia. Iron deficiency impairs the ability of the marrow to mount a significant and sustained reticulocytosis. Iron deficiency anemia is typically microcytic and hypochromic, but could be partially masked here

by reticulocytosis, which would not be as marked if iron were not available, but his diet is supplying needed iron. Infiltrative disorders, such as metastases in the marrow, would impair the ability to mount a reticulocytosis of this degree.

3. A 28-year-old woman has had a constant feeling of lethargy since childhood. On physical examination, she is afebrile and has a pulse of 80/min, respirations of 15/min, and blood pressure of 110/70 mm Hg. The spleen tip is palpable, but there is no abdominal pain or tenderness. Laboratory studies show hemoglobin of 11.7 g/dL, platelet count of 159,000/mm3, and WBC count of 5390/mm3. The peripheral blood smear shows small round erythrocytes that lack a zone of central pallor. An inherited abnormality in which of the following RBC components best accounts for these findings?
    A. α-Globin chain
    B. β-Globin chain
    C. Carbonic anhydrase
    D. Glucose-6-phosphate dehydrogenase
    E. Heme with porphyrin ring
    F. Spectrin cytoskeletal protein

Answer: F Hereditary spherocytosis is a condition in which a mutation affects one of several membrane cytoskeletal proteins. Spectrin and related proteins are cytoskeletal proteins that are important in maintaining the RBC shape. These proteins include ankyrin (most common) and band 4.2, which binds spectrin to the transmembrane ion transporter; band 3; and protein 4.1, which binds the "tail" of spectrin to another transmembrane protein, glycophorin A. The abnormal RBCs with such mutant proteins are less deformable, lack central pallor on a peripheral blood smear, and they are sequestered and destroyed in the spleen. Thalassemias with abnormal α-globin or β-globin chains are associated with hypochromic microcytic anemias. Iron deficiency affects the heme portion of hemoglobin, leading to hypochromia and to microcytosis. Carbonic anhydrase in RBCs helps to maintain buffering capacity. Glucose-6-phosphate dehydrogenase (G6PD) deficiency is an X-linked condition that most commonly affects black males. Porphyrias may affect the production of porphyrin rings and may lead to hemolytic anemia along with abdominal pain, neurologic problems, or skin findings.

4. A 13-year-old boy has the sudden onset of severe abdominal pain and cramping accompanied by chest pain, nonproductive cough, and fever. On physical examination, his temperature is 39° C, pulse is 110/min, respirations are 22/min, and blood pressure is 80/50 mm Hg. He has diffuse abdominal tenderness, but no masses or organomegaly. Laboratory studies show a hematocrit of 18%. The peripheral blood smear is shown in the figure. A chest radiograph shows bilateral pulmonary infiltrates. Which of the following is the most likely mechanism for initiation of his pulmonary problems?



    A. Chronic hypoxia of the pulmonary parenchyma
    B. Defects in the alternative pathway of complement activation

C. Extensive RBC adhesion to endothelium
D. Formation of autoantibodies to alveolar basement membrane
E. Intravascular antibody-induced hemolysis

Answer: C The crescent-shaped RBCs (sickled RBCs) are characteristic of hemoglobin SS. This disease is most common in individuals of African and eastern Arabian descent. The sickled RBCs are susceptible to hemolysis (mainly vascular, in the spleen), but they also can cause microvascular occlusions anywhere in the body, most commonly bone, lungs, liver, and brain, leading to ischemia and severe pain. Vascular occlusions in the lungs are often accompanied by infection and lead to "acute chest syndrome." Abdominal pain and back pain are common and severe, requiring prompt and effective analgesia. The cell membranes of reversibly sickled cells are abnormally "sticky," and they adhere to capillary endothelium, especially in lungs. Vasoconstriction is caused by depletion of NO by free hemoglobin. Adhesion of RBCs to endothelium retards blood flow, creates hypoxia, and precipitates local sickling and vascular occlusion. Chronic tissue hypoxia does occur in sickle cell anemia, but it produces insidious impairment of function in organs such as heart, kidneys, and lungs. Defects in the alternative pathway of complement activation predispose to infection with encapsulated bacteria, such as Haemophilus influenzae and Streptococcus pneumoniae. Autoantibodies to alveolar basement membrane can be part of Goodpasture syndrome, which also affects kidneys. The most severe intravascular hemolysis occurs with major transfusion reactions.

5. A 30-year-old woman has had mild fatigue for many years. Physical examination reveals a palpable spleen tip. Laboratory studies show Hgb 11.1 g/dL, Hct 28.8%, MCV 77 fL, platelet count 229,000/microliter, and WBC count 7340/microliter. Her reticulocyte count is 3.9%. Examination of her peripheral blood smear shows small RBCs that lack central pallor. Which of the following patterns of inheritance is most likely present with her disease?

A. Autosomal dominant, European ancestry
B. Autosomal recessive, Asian ancestry
C. CX-linked recessive, Middle Eastern ancestry
D. Autosomal recessive, West African ancestry
E. Sporadic occurrence

Answer: A Hereditary spherocytosis is the most common inherited hemolytic anemia in persons of northern European descent. It has a frequency in this population of 1 in 5000. An abnormality in the structural membrane proteins ankyrin or spectrin accounts for the abnormality.

6. A clinical study of patients who inherit mutations that reduce the level of ankyrin, the principal binding site for spectrin, in the RBC membrane cytoskeleton shows an increased prevalence of chronic anemia with splenomegaly. For many patients, it is observed that splenectomy reduces the severity of anemia. This beneficial effect of splenectomy is most likely related to which of the following processes?

A. Decrease in opsonization of RBCs and lysis in spleen
B. Decrease in production of reactive oxygen species by splenic macrophages
C. Decrease in splenic RBC sequestration and lysis

D. Increase in deformability of RBCs within splenic sinusoids
E. Increase in splenic storage of iron

Answer: C In patients with hereditary spherocytosis, spheroidal cells are trapped and destroyed in the spleen because the abnormal RBCs have reduced deformability. Splenectomy is beneficial because the spherocytes are no longer detained by the spleen. Splenectomy has no effect on the synthesis of spectrin or RBC deformability; the RBCs in spherocytosis are not killed by opsonization. In warm antibody hemolytic anemias, opsonized RBCs are removed by the spleen. Reactive oxygen species do not play a role in anemias. Iron is not the rate-limiting step to RBC production when the iron can be recycled within the body.

7. A 3-year-old boy from Sicily has a poor appetite and is underweight for his age and height. Physical examination shows hepatosplenomegaly. The hemoglobin concentration is 6 g/dL, and the peripheral blood smear shows severely hypochromic and microcytic RBCs. The total serum iron level is normal, and the reticulocyte count is 10%. A radiograph of the skull shows maxillofacial deformities and expanded marrow spaces. Which of the following is the most likely cause of this child's illness?

    A. An Imbalance in α-globin and β-globin chain production
    B. Increased fragility of erythrocyte membranes
    C. Reduced synthesis of hemoglobin F
    D. Relative deficiency of vitamin B12
    E. Sequestration of iron in reticuloendothelial cells

Answer: A This patient of Mediterranean descent has β-thalassemia major. In this condition, there is a severe reduction in the synthesis of β-globin chains without impairment of α-globin synthesis. The free, unpaired α-globin chains form aggregates that precipitate within normoblasts and cause them to undergo apoptosis. The death of RBC precursors in the bone marrow is called "ineffective erythropoiesis." Not only does this cause anemia, but it also increases the absorption of dietary iron, giving rise to iron overload, which results in hemochromatosis with infiltrative cardiomyopathy, hepatic cirrhosis, and "bronze diabetes" from pancreatic islet dysfunction. The severe anemia triggers erythropoietin synthesis, which expands the erythropoietic marrow. The marrow expansion encroaches on the bones, causing maxillofacial deformities. Extramedullary hematopoiesis causes hepatosplenomegaly. In comparison, the hemolytic anemia is mild in β-thalassemia minor, and there is very little ineffective erythropoiesis. Hemochromatosis is particularly detrimental to the liver and heart. Patients with chronic anemia may require RBC transfusions, which adds even more iron to body stores. The other listed options do not lead to a marked expansion of hematopoiesis.

8. A 10-year-old child has experienced multiple episodes of pneumonia and meningitis with septicemia since infancy. Causative organisms include Streptococcus pneumoniae and Haemophilus influenzae. On physical examination, the child has no organomegaly and no deformities. Laboratory studies show hemoglobin of 9.2 g/dL, hematocrit of 27.8%, platelet count of 372,000/mm3, and WBC count of 10,300/mm3. A hemoglobin electrophoresis shows 1% hemoglobin A2, 7% hemoglobin F, and 92% hemoglobin S. Which of the following is the most likely cause of the repeated infections in this child?

    A. Absent endothelial cell expression of adhesion molecules

B. Diminished hepatic synthesis of complement proteins
C. Impaired neutrophil production
D. Loss of normal splenic function
E. Reduced synthesis of immunoglobulin

Answer: D In sickle cell anemia, the cumulative ischemic damage to the spleen results in autosplenectomy, leaving behind a small fibrotic remnant of this organ. The impaired splenic function and resultant inability to clear bacteria from the bloodstream can occur early in childhood, leading to risk for infection with encapsulated bacterial organisms. Immunodeficiency results from lack of splenic function, not from lack of immunoglobulins. Endothelium can be damaged with sickling, and adhesion between endothelial cells and RBCs is increased in sickle cell anemia. Complement proteins are part of innate immune responses in acute inflammation. There is no impairment in production or function of neutrophils.

9. A 32-year-old woman from Hanoi, Vietnam, gives birth at 34 weeks' gestation to a markedly hydropic stillborn male infant. Autopsy findings include hepatosplenomegaly and cardiomegaly, serous effusions in all body cavities, and generalized hydrops. No congenital anomalies are noted. There is marked extramedullary hematopoiesis in visceral organs. Which of the following hemoglobins is most likely predominant on hemoglobin electrophoresis of the fetal RBCs?

   A. Hemoglobin A1
   B. Hemoglobin A2
   C. Hemoglobin Bart's
   D. Hemoglobin E
   E. Hemoglobin F
   F. Hemoglobin H

Answer: C The infant had α-thalassemia major, which is most likely to occur in individuals of Southeast Asian ancestry, each of whose parents could have two abnormal α-globin genes on chromosome 16. A complete lack of α-globin chains precludes formation of hemoglobins A1, A2, and F. Only a tetramer of γ chains (Bart's hemoglobin) can be made, leading to severe fetal anemia. Inheritance of three abnormal α-globin chains leads to hemoglobin H disease, with tetramers of β chains; survival to adulthood is possible. Hemoglobin E disease produces mild hemolytic anemias.

10. A 23-year-old African American man passes dark reddish brown urine 3 days after taking an anti-inflammatory medication that includes phenacetin. He is surprised, because he has been healthy all his life and has had no major illnesses. On physical examination, he is afebrile, and there are no remarkable findings. CBC shows a mild normocytic anemia, but the peripheral blood smear shows precipitates of denatured globin (Heinz bodies) with supravital staining and scattered "bite cells" in the population of RBCs. Which of the following is the most likely diagnosis?

    A. α-Thalassemia minor
    B. β-Thalassemia minor
    C. Glucose-6-phosphate dehydrogenase deficiency
    D. Sickle cell trait
    E. Abnormal ankyrin in RBC cytoskeletal membrane

F. Warm antibody autoimmune hemolytic anemia

Answer: C Glucose-6-phosphate dehydrogenase (G6PD) deficiency is an X-linked disorder that affects about 10% of African American males. The lack of this enzyme subjects hemoglobin to damage by oxidants, including drugs such as primaquine, sulfonamides, nitrofurantoin, phenacetin, and aspirin (in large doses). Infection can also cause oxidative damage to hemoglobin. Heinz bodies are denatured hemoglobin, and they damage the RBC membrane, giving rise to intravascular hemolysis. The "bite cells" result from the attempts of overeager splenic macrophages to pluck out the Heinz bodies, adding an element of extravascular hemolysis. Heterozygotes with α-thalassemia (1 or 2 abnormal genes out of 4 total α-globin genes) have no major problems, but in cases of α-thalassemia major, perinatal death is the rule. Likewise, β-thalassemia minor and sickle cell trait are conditions usually with no major problems and no relation to drug usage. RBC membrane abnormalities, such as hereditary spherocytosis (caused by abnormal spectrin), typically produce a mild anemia without significant hemolysis, and there is no drug sensitivity. Some autoimmune hemolytic anemias can be drug related, but the hemolysis is predominantly extravascular.

11. A 34-year-old woman reports becoming increasingly tired for the past 5 months. On physical examination, she is afebrile and has mild splenomegaly. Laboratory studies show a hemoglobin concentration of 10.7 g/dL and hematocrit of 32.3%. The peripheral blood smear shows spherocytes and rare nucleated RBCs. Direct and indirect Coombs test results are positive at 37° C, although not at 4° C. Which of the following underlying diseases is most likely to be diagnosed in this patient?
    A. Escherichia coli septicemia
    B. Hereditary spherocytosis
    C. Infectious mononucleosis
    D. Mycoplasma pneumoniae infection
    E. Systemic lupus erythematosus

Answer: E This patient has a warm autoimmune hemolytic anemia secondary to systemic lupus erythematosus (SLE). A positive Coombs test result indicates the presence of anti-RBC antibodies in the serum and on the RBC surface. Most cases of warm autoimmune hemolytic anemia are idiopathic, but one fourth occur in individuals with an identifiable autoimmune disease, such as SLE; in other cases, drugs are the cause. The immunoglobulin coating the RBCs acts as an opsonin to promote splenic phagocytosis. Nucleated RBCs can be seen in active hemolysis because the marrow compensates by releasing immature RBCs. Septicemia is more likely to lead to a microangiopathic hemolytic anemia. The increased RBC destruction in hereditary spherocytosis is extravascular and not immune mediated. Infections such as mononucleosis and Mycoplasma are associated with cold autoimmune hemolytic anemia (with an elevated cold agglutinin titer).

12. A 22-year-old woman has experienced malaise and a sore throat for 2 weeks. Her fingers turn white on exposure to cold. On physical examination, she has a temperature of 37.8° C, and the pharynx is erythematous. Laboratory findings include a positive monospot (heterophile antibody) test result. Direct and indirect Coombs test results are positive at 4°

C, although not at 37° C. Which of the following molecules bound on the surfaces of the RBCs most likely accounts for these findings?

A. α2-Macroglobulin
B. Complement C3b
C. Fibronectin
D. Histamine
E. IgE

Answer: B Cold agglutinin disease has antibody (usually IgM) coating RBCs. The IgM antibodies bind to the RBCs at low temperature at peripheral body sites and fix complement; however, complement is not lytic at this temperature. With an increase in temperature within core internal organs, the IgM is dissociated from the cell, leaving behind C3b. Most of the hemolysis occurs extravascularly in the cells of the mononuclear phagocyte system, such as Kupffer cells in the liver, or splenic macrophages, because the coating of complement C3b acts as an opsonin. IgG is typically involved in warm antibody hemolytic anemia, which is chronic and is not triggered by cold. Raynaud phenomenon occurs in exposed, colder areas of the body, such as the fingers and toes. The patient probably has an elevated cold agglutinin titer. Histamine is released in type I hypersensitivity reactions. Fibronectin is an adhesive cell surface glycoprotein that aids in tissue healing. IgE is present in allergic conditions.

13. 29-year-old rugby player takes part in a particularly contentious game between New Zealand and South Africa. He is the forward prop in the scrums, hitting hard and being hit hard by other players. He feels better after downing several pints of beer following the game, but notes darker urine. Urinalysis is positive for blood. Which of the following pathogenic mechanisms underlies change in the color of urine?

A. Complement lysis
B. Intravascular disruption
C. Osmotic fragility
D. Sinusoidal sickling
E. Splenic sequestration

Answer: B Mechanical trauma to RBCs is possible, but typically is not severe. It can follow strenuous exercises involving repeated blows to body parts. Complement-mediated lysis is a feature of immunohemolytic anemias. Increased osmotic fragility is noted in spherocytes. Sickle cell anemia is not likely to be found in the population groups in the countries noted, and persons with this disease are not likely to be playing rugby. Splenic sequestration is a feature of hemolytic anemias due to membrane defects and antibodies.

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جندك، والأمر أمرك، وأنت القويّ
العزيز، فانصرهم نصرًا عزيزًا مؤزّرًا
تشفي به صدور قوم مؤمنين.

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