Hematology Questions

"Questions and Answers at the end"

(1-71)

1. A 20-month-old toddler is brought to the emergency department for lethargy and poor feeding. The parents report the child drinks nearly 38 oz of whole milk daily and eats very little solid food. On exam, the child is pale, tachycardic, and appears fatigued. Laboratory testing reveals a hemoglobin of 4.5 g/dL.

What is the next best step in management?

A. Oral iron supplementation
B. Intravenous iron infusion
C. Packed red blood cell transfusion
D. Observation and dietary counseling

2. A 7-year-old boy with a known history of chronic inflammatory bowel disease presents with progressive fatigue and decreased activity over the past several weeks. He has no history of bleeding. Physical examination reveals mild pallor but is otherwise unremarkable. Laboratory studies show: hemoglobin: decreased, serum iron: low, total iron-binding capacity (TIBC): low to normal, ferritin: normal to elevated

What is the most likely diagnosis?

A. Iron deficiency anemia
B. Thalassemia trait
C. Sideroblastic anemia
D. Anemia of chronic disease

3. A 6-year-old boy is evaluated after routine screening reveals mild anemia. He is asymptomatic, with normal growth and development. There is no history of dietary deficiency or chronic illness. Laboratory studies show: Hemoglobin: mildly decreased, mean corpuscular volume (MCV): low, iron studies: normal, red cell distribution width (RDW): normal, Mentzer index: 11

What is the most likely diagnosis?

A. Iron deficiency anemia
B. Thalassemia trait
C. Lead poisoning
D. Sideroblastic anemia

4. A 5-year-old child has mild microcytic anemia. Iron studies are normal, RDW is normal, Mentzer index is 11, and hemoglobin electrophoresis is normal with no elevation in Hb A_2.

What is the most likely diagnosis?

A. Beta thalassemia minor
B. Iron deficiency anemia
C. Alpha thalassemia trait
D. Sickle cell trait

5. A 12-month-old boy adopted from China is brought for evaluation of poor weight gain and progressive abdominal distension. His caregivers report that he has required multiple blood transfusions since infancy. On examination, he appears pale and jaundiced. There is marked hepatosplenomegaly. Facial features include frontal bossing and maxillary overgrowth, giving a characteristic "chipmunk facies."

What is the most likely diagnosis?

A. Alpha thalassemia trait
B. Sickle cell disease
C. Beta thalassemia major
D. Iron deficiency anemia

6. A healthy 4-year-old child undergoes routine laboratory evaluation. Hemoglobin electrophoresis shows: Hb A >98% Small amount of Hb A_2 How should this result be interpreted?

A. Beta thalassemia minor
B. Alpha thalassemia
C. Iron deficiency anemia
D. Normal hemoglobin electrophoresis

7. A 3-year-old child is evaluated for mild anemia. Laboratory testing includes hemoglobin electrophoresis, which shows: Hb A: 93% Hb A_2: 6% Hb F: 1%

What is the most likely diagnosis?

A. Alpha thalassemia trait
B. Beta thalassemia minor
C. Iron deficiency anemia
D. Sickle cell disease

8. A 9-month-old boy is brought to the clinic for poor feeding and decreased activity. He appears pale and tired on examination. Laboratory studies show a hemoglobin of 6 g/dL with a normal red blood cell count of 5 million/μL. The Mentzer index is 9. Hemoglobin electrophoresis demonstrates absence of Hb A, Hb A_2 of 4%, and Hb F of 96%.

What is the most likely diagnosis?

A. Sickle cell disease
B. Alpha thalassemia trait
C. Beta thalassemia minor
D. Beta thalassemia major

9. A 2-year-old toddler is brought to clinic for fatigue and poor appetite. The parents report excessive cow's milk intake. Laboratory studies show low hemoglobin, low MCV, low serum iron, low ferritin, high TIBC, high RDW, low reticulocyte count, and elevated soluble transferrin receptor (sTfR). The Mentzer index is 15.

What is the most likely diagnosis?

A. Thalassemia trait
B. Anemia of chronic disease
C. Lead poisoning
D. Iron-deficiency anemia

10. A 15-month-old child is suspected of having iron-deficiency anemia based on dietary history and pallor on examination. Which of the following is the best initial diagnostic evaluation?

A. Hemoglobin electrophoresis
B. Bone marrow biopsy
C. CBC, reticulocyte count, ferritin, and soluble transferrin receptor (sTfR)
D. Serum transferrin saturation only

11. A 14-year-old menstruating adolescent female presents for routine health maintenance. She has no symptoms but is at risk for iron deficiency.

What is the recommended daily iron intake to prevent iron-deficiency anemia?

A. 5 mg/day
B. 10 mg/day
C. 15 mg/day
D. 30 mg/day

12. A 3-year-old child is evaluated for developmental concerns. Parents report fatigue and unusual cravings for dirt and ice. On exam, the child appears pale and inattentive. Which symptom is most consistent with iron-deficiency anemia?

A. Tremors
B. Pica and poor concentration
C. Hyperactivity
D. Polyuria

13. A 20-month-old toddler drinks 40 oz of cow's milk daily and presents with pallor and microcytic anemia on screening labs. What is the most likely cause of anemia?

A. Lead poisoning
B. Thalassemia
C. Anemia of chronic disease
D. Iron-deficiency anemia

14. A 2-year-old with iron-deficiency anemia is started on oral iron therapy. Follow-up labs are planned. What is the best indicator of response to iron therapy?

A. Rise in reticulocyte count and hemoglobin within 1–4 weeks
B. Normalization of TIBC
C. Increase in ferritin only
D. Resolution of pallor alone

15. A 3-year-old child with confirmed iron-deficiency anemia shows normalization of hemoglobin after 2 months of treatment. How long should iron therapy be continued?

A. Stop immediately
B. 2 weeks more
C. 1–2 months after hemoglobin normalization
D. Until ferritin becomes high

16. A 2-year-old child is diagnosed with iron-deficiency anemia. What is the standard therapeutic dose of elemental iron?

A. 1 mg/kg/day
B. 1 mg/kg/day
C. 2-3 mg/kg/day
D. 6-7 mg/kg/day

17. A 22-month-old toddler presents with severe microcytic anemia (hemoglobin 5 g/dL). He drinks 40 oz of whole milk daily. He is alert and active with normal vital signs and no signs of heart failure or cardiovascular compromise. Iron-deficiency anemia is confirmed.

What is the most appropriate next step?

A. Immediate packed RBC transfusion
B. Observation only
C. Iron replacement therapy (oral iron or IV iron if rapid repletion is needed) and restriction of cow's milk intake
D. Bone marrow biopsy

18. A 2-month-old premature infant born at 30 weeks' gestation is evaluated during routine follow-up. He appears well and feeds appropriately. Laboratory testing shows hemoglobin 9.0 g/dL with a normal MCV, normal bilirubin, and no evidence of hemolysis.

What is the most likely diagnosis?

A. Iron-deficiency anemia
B. Diamond–Blackfan anemia
C. Transient erythroblastopenia of childhood
D. Anemia of prematurity

19. A 2-year-old child presents with pallor but no jaundice or splenomegaly. Labs show hemoglobin 4 g/dL, normal MCV, low reticulocyte count, normal adenosine deaminase (ADA), negative direct Coombs test, and no evidence of hemolysis.

What is the most likely diagnosis?

A. Aplastic anemia
B. Diamond–Blackfan anemia
C. Transient erythroblastopenia of childhood
D. Fanconi anemia

20. A 7-year-old child presents with fatigue, recurrent infections, and easy bruising. Laboratory evaluation reveals pancytopenia. On physical examination, the child has: hypoplastic thumbs and absent radius, short stature, hyperpigmented skin with café-au-lait spots, microcephaly and abnormal facial features (small eyes, triangular face), renal anomaly (horseshoe kidney)

What is the most likely diagnosis?

A. Shwachman–Diamond syndrome
B. Fanconi anemia
C. Diamond–Blackfan anemia
D. Pearson syndrome

21. A 4-month-old infant presents with pallor and poor feeding. Laboratory studies reveal severe macrocytic anemia, low reticulocyte count, and elevated adenosine deaminase (ADA) levels. On physical examination, the infant is noted to have a triphalangeal thumb.

What is the most likely diagnosis?

A. Fanconi anemia
B. Diamond–Blackfan anemia
C. Transient erythroblastopenia of childhood (TEC)
D. Vitamin B12 deficiency

22. A child presents with pallor, recurrent infections, and failure to thrive. Laboratory evaluation reveals macrocytic anemia, neutropenia, and thrombocytopenia. Additional findings include: low stool elastase enzyme. Bone marrow biopsy showing ring sideroblasts

What is the most likely diagnosis?

A. Shwachman-Diamond syndrome
B. Fanconi anemia
C. Pearson marrow–pancreas syndrome
D. Diamond–Blackfan anemia

23. A short-statured child presents with frequent infections, imperforate anus, hypoplastic teeth, macrocytic anemia, neutropenia, thrombocytopenia, and exocrine pancreatic insufficiency.

Most likely diagnosis?

A. Pearson syndrome
B. Fanconi anemia
C. Shwachman-Diamond syndrome
D. Diamond–Blackfan anemia

24. A toddler fed exclusively goat's milk presents with pallor and fatigue. Labs show macrocytic anemia. What is the most likely cause?

A. Vitamin B12 deficiency
B. Folic acid deficiency
C. Iron-deficiency anemia
D. Diamond–Blackfan anemia

25. A child from a strictly vegan family presents with macrocytic anemia, paresthesias, and fatigue. What is the most appropriate next step?

A. Start folic acid
B. Bone marrow biopsy
C. Suspect vitamin B12 deficiency and supplement
D. Start iron therapy

26. A school-aged child presents with fatigue, pallor, and abdominal discomfort. Examination reveals glossitis and gait instability. Laboratory findings show: macrocytic anemia, low vitamin B12 levels, presence of anti–intrinsic factor antibodies.

What is the most likely diagnosis?

A. Folate deficiency
B. Pernicious anemia

C. Diamond–Blackfan anemia
D. Fanconi anemia

27. A 6-year-old child presents with chronic pallor, intermittent jaundice, and fatigue. Parents report episodes of worsening jaundice during minor illnesses. On examination: splenomegaly, and mild scleral icterus. Laboratory findings: normocytic anemia, elevated reticulocyte count, increased indirect bilirubin, elevated MCHC, and peripheral smear shows small, dense red blood cells lacking central pallor.

What is the most likely diagnosis?

A. G6PD deficiency
B. Autoimmune hemolytic anemia
C. Hereditary spherocytosis
D. Sickle cell disease

28. An African-American boy develops dark urine, jaundice, pallor, and splenomegaly after starting nitrofurantoin for possible UTI infection. Labs show anemia, reticulocytosis, indirect hyperbilirubinemia, low haptoglobin, and normal G6PD activity during the episode. Smear shows Heinz bodies.

What is the most likely Diagnosis?

A. Autoimmune hemolytic anemia
B. G6PD deficiency
C. Sickle cell disease
D. Hereditary spherocytosis

29. A 9-month-old infant with known sickle cell disease presents with acute onset of painful swelling of both hands and feet. The child is irritable but afebrile.

What is the most likely diagnosis?

A. Acute chest syndrome
B. Splenic sequestration
C. Dactylitis
D. Aplastic crisis

30. A child with known sickle cell disease presents with fever and signs of sepsis. Due to functional asplenia, he is at increased risk for infection with encapsulated organisms. What is the most common cause of sepsis in children with sickle cell disease?

A. Escherichia coli
B. Staphylococcus aureus
C. Streptococcus pneumoniae
D. Haemophilus influenzae

31. A 2-year-old child with known sickle cell disease presents with sudden pallor, lethargy, and abdominal distension. Parents report rapid worsening over a few hours. On examination: marked splenomegaly, and tachycardia. Laboratory findings: severe anemia reticulocytosis, thrombocytopenia

What is the most likely diagnosis and next best step in management?

A. Aplastic crisis → steroids
B. Splenic sequestration → packed RBC transfusion
C. Acute chest syndrome → antibiotics
D. Transient erythroblastopenia of childhood (TEC) → observation

32. A 5-year-old child with known sickle cell disease presents with fever, malaise, and a mild rash. Over the past few days, the child has become increasingly pale and fatigued. Laboratory findings: severe anemia, marked reticulocytopenia

What is the most likely diagnosis?

A. Splenic sequestration
B. Aplastic crisis (parvovirus B19)
C. Acute chest syndrome
D. Hemolytic crisis

33. A 6-year-old child with sickle cell disease presents with fatigue and pallor after a viral prodrome. Laboratory studies show severe anemia with reticulocytopenia. PCR testing confirms infection with a DNA virus that selectively suppresses erythroid precursors.

Which virus is the most common cause of aplastic crisis?

A. Epstein–Barr virus
B. Cytomegalovirus
C. Parvovirus B19
D. Human herpesvirus 6

34. A 10-year-old child with sickle cell disease is followed in clinic. Parents ask about the most common causes of long-term illness and death associated with this condition. Which of the following are the most common causes of morbidity and mortality?

A. Renal failure and hypertension
B. Pulmonary embolism and cardiomyopathy
C. Infection, acute chest syndrome, and stroke
D. Malignancy and marrow failure

35. A 9-year-old child with sickle cell anemia presents with fever, chest pain, tachypnea, dyspnea, and hypoxia. Chest radiograph reveals a new pulmonary infiltrate.

What is the most appropriate management?

A. Adequate pain relief, oxygen, ceftriaxone and macrolide plus early simple transfusion
B. High-dose corticosteroids, and exchange transfusion
C. IV fluids and bronchodilators only
D. Chest CT scan with contrast

36. A 7-year-old with sickle cell disease is being counseled on infection prevention. Sickle cell patients are at highest risk for infection with which organisms?

A. Anaerobic bacteria
B. Intracellular parasites
C. Encapsulated organisms
D. Fungal pathogens

37. A 10-year-old child with sickle cell anemia presents to the ED with severe limb pain requiring hospitalization. What is the most common reason for hospitalization in children with sickle cell disease, and how is it treated?

A. Infection → IV antibiotics
B. Acute chest syndrome → oxygen and transfusion
C. Vaso-occlusive pain crisis → IV hydration, NSAIDs, and opioids
D. Splenic sequestration → splenectomy

38. A 6-year-old child with sickle cell disease is asymptomatic but undergoing routine screening. Which test reduces the risk of ischemic stroke in children with sickle cell anemia?

A. Brain MRI annually
B. Echocardiography
C. Transcranial Doppler ultrasound yearly (ages 2–16)
D. Coagulation panel

39. A 5-year-old with sickle cell disease presents with fever, positive parvovirus B19 testing, reticulocytopenia, hemoglobin 6 g/dL, and acute splenomegaly. What is the next best step?

A. Observation only
B. Exchange transfusion
C. Empiric antibiotics and packed RBC transfusion
D. Steroids

40. A 15-year-old male with sickle cell disease presents with a painful erection lasting 6 hours. What is the most appropriate management?

A. Oral analgesics and discharge

B. Cold compresses
C. Observation overnight
D. Immediate aspiration ± irrigation, phenylephrine, pain control

41. A 9-year-old child with sickle cell disease presents with fever and localized bone pain. Osteomyelitis is suspected. What is the most common causative organism?

A. Salmonella species
B. Streptococcus pyogenes
C. Staphylococcus aureus
D. Escherichia coli

42. A child with sickle cell disease presents with fever and bone pain suspicious for osteomyelitis. What is the next best step?

A. Plain radiographs only
B. Oral antibiotics
C. MRI, blood cultures, IV antibiotics covering Salmonella and S. aureus
D. Bone biopsy immediately

43. A 16-year-old adolescent presents with acute onset fatigue, pallor, and scleral icterus. On examination, he is tachycardic. Laboratory findings: Hemoglobin: 6 g/dL, hematocrit: 25%, elevated reticulocyte count, elevated indirect bilirubin, positive direct antiglobulin (Coombs) test.

What is the most likely diagnosis?

A. G6PD deficiency
B. Autoimmune hemolytic anemia (AIHA)
C. Hereditary spherocytosis
D. Sickle cell crisis

44. A 7-year-old child receiving chemotherapy presents to the emergency department with a temperature of 38.6°C (101.5°F). Laboratory studies show an absolute neutrophil count (ANC) of 300/μL. The child appears ill but hemodynamically stable. What is the next best step?

A. Hospital admission, blood cultures, and immediate IV broad-spectrum antibiotics
B. Repeat CBC in 24 hours
C. Oral antibiotics and outpatient follow-up
D. Observation only

45. A 5-year-old child has recurrent episodes of neutropenia occurring for about 1 week every 3 weeks. During these episodes, he develops gingivitis, pharyngitis, and skin infections. Between episodes, he is healthy.

What is the most likely diagnosis?

A. Kostmann syndrome
B. Autoimmune neutropenia
C. Cyclic neutropenia
D. Leukemia

46. A child diagnosed with cyclic neutropenia continues to have recurrent infections during neutropenic episodes. What is the best long-term management?

A. Daily oral antibiotics
B. Observation only
C. Prophylactic granulocyte colony-stimulating factor (G-CSF)
D. Bone marrow transplant

47. A 2-month-old infant presents with severe neutropenia since birth, recurrent skin and oral infections, gingivitis, and oral ulcers. ANC remains persistently low without recovery.

What is the most likely diagnosis?

A. Cyclic neutropenia
B. Autoimmune neutropenia
C. Viral bone marrow suppression
D. Kostmann syndrome (severe congenital neutropenia)

48. A 10-year-old child presents with a persistent cervical lymph node measuring 2.5 cm for 6 weeks. He has fever, weight loss, night sweats, and has not responded to oral antibiotics.

What is the next best step?

A. Extend antibiotics
B. Ultrasound surveillance
C. Reassurance
D. Referral to pediatric oncology for lymph node biopsy

49. A 6-year-old child is noted to have a supraclavicular lymph node present for 2 weeks. He is otherwise asymptomatic. What is the most appropriate next step?

A. Referral for further evaluation and biopsy
B. Oral antibiotics
C. Reassurance
D. Observe for 3 months

50. An infant presents with intracranial hemorrhage. PT, PTT, platelet count, fibrinogen, and von Willebrand panel are all normal. What is the most likely diagnosis?

A. Hemophilia A
B. von Willebrand disease
C. Factor XIII deficiency
D. Vitamin K deficiency

51. A 4-year-old has normal PT, markedly prolonged PTT, and no history of abnormal bleeding. Which factor deficiency explains this?

A. Factor VIII
B. Factor XII
C. Factor IX
D. Factor XI

52. A 5-year-old child develops petechiae, epistaxis, and oral mucosal bleeding 2 weeks after a viral URI. Platelet count is 12,000/μL, with large platelets on peripheral smear. WBCs, hemoglobin and hematocrit levels are within normal limits What is the most likely diagnosis?

A. Immune thrombocytopenic purpura (ITP)
B. Leukemia
C. Aplastic anemia
D. TTP

53. A 2-year-old boy presents with recurrent infections, eczema, severe thrombocytopenia, and small platelets. What is the most likely diagnosis?

A. ITP
B. Fanconi anemia
C. Wiskott–Aldrich syndrome
D. Leukemia

54. A term newborn is noted to have severe thrombocytopenia (platelet count <20,000/μL) on routine laboratory testing shortly after birth. The infant appears well with no active bleeding. The mother has a history of immune thrombocytopenic purpura (ITP). What is the most appropriate management?

A. Observation only
B. Platelet transfusion
C. Exchange transfusion
D. Intravenous immunoglobulin (IVIG)

55. A term newborn is noted to have severe thrombocytopenia at birth (platelet count <20,000/μL). The infant is otherwise well-appearing. The mother has no history of autoimmune disease, but reports that previous siblings had similar neonatal thrombocytopenia. What is the most likely diagnosis and best treatment?

A. Neonatal ITP → IVIG
B. Neonatal alloimmune thrombocytopenia → washed maternal platelets
C. TAR syndrome → platelet transfusion
D. DIC → FFP

56. A newborn with severe thrombocytopenia has a normal physical examination and no signs of bleeding. What is the next best step?

A. Platelet transfusion
B. IVIG
C. Head ultrasonography
D. Bone marrow biopsy

57. A 6-year-old child has had easy bruising and recurrent mucosal bleeding since infancy. Platelet count is low-normal, PT and PTT are normal, fibrinogen is normal, and von Willebrand studies are normal. What is the most likely diagnosis?

A. Platelet function disorder
B. von Willebrand disease
C. Hemophilia
D. DIC

58. A 10-year-old boy presents with recurrent epistaxis, gingival bleeding, and easy bruising. Platelet count and size are normal. Platelets agglutinate to ristocetin, but show poor aggregation to ADP, epinephrine, and collagen. What is the diagnosis?

A. Bernard–Soulier syndrome
B. von Willebrand disease
C. Hemophilia A
D. Glanzmann thrombasthenia

59. A 10-year-old child with suspected bleeding disorder has mild thrombocytopenia with large platelets. Platelets do not agglutinate to ristocetin, but aggregate normally to ADP, epinephrine, and collagen. What is the most likely diagnosis?

A. Glanzmann thrombasthenia
B. von Willebrand disease
C. Bernard–Soulier syndrome
D. ITP

60. A child with a known platelet function disorder presents with life-threatening intracranial hemorrhage. What is the most appropriate immediate management?

A. IVIG
B. Desmopressin

C. Platelet transfusion
D. FFP

61. A 48-hour-old newborn presents with prolonged bleeding after circumcision. CBC reveals severe thrombocytopenia. Physical exam shows bilateral absence of the radius, but normal thumbs. What is the diagnosis?

A. Fanconi anemia
B. Thrombocytopenia with absent radii (TAR syndrome)
C. Neonatal ITP
D. Holt–Oram syndrome

62. A male newborn presents with prolonged bleeding after circumcision. Coagulation studies reveal a prolonged PTT. What is the most likely diagnosis?

A. von Willebrand disease
B. Platelet disorder
C. Vitamin K deficiency
D. Hemophilia

63. An 8-year-old boy develops severe knee swelling after minor trauma. Joint aspiration reveals blood. Imaging is normal. What is the next best step?

A. NSAIDs
B. MRI
C. Coagulation profile and mixing studies
D. Platelet transfusion

64. A 15-year-old girl reports heavy menstrual bleeding since menarche. PT and PTT are normal. Ristocetin cofactor activity is reduced. What is the most likely diagnosis?

A. Hemophilia carrier
B. von Willebrand disease
C. Platelet disorder
D. DIC

65. A 4-year-old child develops bloody diarrhea, followed by thrombocytopenia, elevated BUN/creatinine, and schistocytes on peripheral smear. What is the most likely diagnosis?

A. TTP
B. Hemolytic uremic syndrome (HUS)
C. DIC
D. ITP

66. A critically ill child in the PICU has prolonged PT and PTT, low fibrinogen, elevated D-dimer, and thrombocytopenia. What is the diagnosis and management?

A. TTP → plasma exchange
B. HUS → supportive care
C. DIC → treat underlying cause + blood products
D. Hemophilia → factor replacement

67. A 17-year-old Caucasian boy presents with recurrent episodes of deep vein thrombosis (DVT) involving the lower extremities. He has no history of malignancy, central venous catheter, or recent surgery. Family history is significant for multiple first-degree relatives with DVT at a young age.

What is the most likely underlying cause?

A. Antithrombin III deficiency
B. Protein C deficiency
C. Protein S deficiency
D. Factor V Leiden mutation

68. A 10-month-old infant is brought to the clinic for persistent rash and poor weight gain. Parents report that the rash has been present for several weeks and does not improve with topical treatments. On examination: Scaly, erythematous rash on the scalp and trunk (seborrheic-like), hepatosplenomegaly, pallor, petechiae. Laboratory findings: anemia and thrombocytopenia. Imaging: skull X-ray shows punched-out lytic lesions.

What is the most likely diagnosis?

A. Acute lymphoblastic leukemia
B. Osteomyelitis
C. Metastatic neuroblastoma
D. Langerhans cell histiocytosis

69. A 1-year-old child presents with persistent high fever, lethargy, and is toxic appearing. Examination reveals hepatosplenomegaly. Laboratory studies show pancytopenia, hypertriglyceridemia, and markedly elevated ferritin. Bone marrow biopsy demonstrates hemophagocytosis.

What is the most likely diagnosis?

A. Acute leukemia
B. Severe sepsis
C. Macrophage activation syndrome
D. Hemophagocytic lymphohistiocytosis (HLH)

70. An infant undergoing chemotherapy for leukemia presents with fever, diarrhea, and a diffuse macular, erythematous, blanching, nonpruritic rash. Liver enzymes are elevated. The infant received a packed red blood cell transfusion two weeks ago.

What is the most likely cause of these findings?

A. Viral exanthem
B. Drug hypersensitivity reaction
C. Sepsis-related rash
D. Transfusion-associated graft-versus-host disease

71. A 7-year-old boy is evaluated for persistent anemia despite 3 months of appropriate oral iron therapy. He initially presented with fatigue and pallor and was diagnosed with presumed iron deficiency anemia. Compliance with iron therapy is confirmed. On examination, he remains pale with no hepatosplenomegaly.

Laboratory findings:

- Hemoglobin: low
- MCV: low (microcytic anemia)
- Serum iron: elevated
- Ferritin: elevated
- Transferrin saturation: elevated
- TIBC: low-normal
- Peripheral smear: dimorphic RBC population

A bone marrow biopsy is performed

What is the most likely diagnosis?

A. Refractory iron deficiency anemia
B. Thalassemia trait
C. Anemia of chronic disease
D. Sideroblastic anemia

Hematology Questions and Answers

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1. A 20-month-old toddler is brought to the emergency department for lethargy and poor feeding. The parents report the child drinks nearly **38 oz of whole milk daily** and eats very little solid food. On exam, the child is pale, tachycardic, and appears fatigued. Laboratory testing reveals a **hemoglobin of 4.5 g/dL.**

What is the next best step in management?

A. Oral iron supplementation
B. Intravenous iron infusion
C. Packed red blood cell transfusion
D. Observation and dietary counseling

Correct Answer: C

Explanation:
Severe symptomatic anemia (Hb <6 g/dL) with signs of cardiovascular compensation requires urgent packed red blood cell transfusion, regardless of etiology. Each 10 mL/kg of packed RBCs raises hemoglobin by approximately 2 g/dL.

Board Pearl:
Severe anemia + tachycardia or lethargy → transfuse first
10 mL/kg PRBCs → ↑ Hb by ~2 g/dL

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2. A 7-year-old boy with a known history of **chronic inflammatory bowel disease** presents with progressive fatigue and decreased activity over the past several weeks. He has no history of bleeding. Physical examination reveals mild pallor but is otherwise unremarkable.

Laboratory studies show:

- **Hemoglobin: decreased**
- **Serum iron: low**
- **Total iron-binding capacity (TIBC): low to normal**
- **Ferritin: normal to elevated**

What is the most likely diagnosis?

A. Iron deficiency anemia
B. Thalassemia trait
C. Sideroblastic anemia
D. **Anemia of chronic disease**

Correct Answer: D
Explanation:
This child with chronic inflammatory bowel disease has laboratory findings consistent with **anemia of chronic disease (ACD)**.
In inflammatory states:

- Cytokines stimulate increased production of **hepcidin**

- Hepcidin inhibits iron release from macrophages and decreases intestinal iron absorption
- This results in:
    - **Low serum iron** (iron is trapped in storage sites)
    - **Normal or elevated ferritin** (reflects adequate stores or associated inflammation)
    - **Low or normal TIBC** (decreased transferrin production during inflammation)

Board Pearl:

Low serum iron + normal or high ferritin = anemia of chronic disease

Think **hepcidin-mediated iron trapping** in inflammatory conditions

Common in chronic infections, autoimmune diseases, and inflammatory bowel disease

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3. A 6-year-old boy is evaluated after routine screening reveals mild anemia. He is asymptomatic, with normal growth and development. There is no history of dietary deficiency or chronic illness.

Laboratory studies show:

- Hemoglobin: mildly decreased
- Mean corpuscular volume (MCV): low
- Iron studies: normal
- Red cell distribution width (RDW): normal
- Mentzer index: 11

What is the most likely diagnosis?

A. Iron deficiency anemia
B. Thalassemia trait
C. Lead poisoning
D. Sideroblastic anemia

Correct Answer: B

Explanation:

This child has **microcytic anemia with normal iron studies**, which strongly suggests **thalassemia trait**.

Key diagnostic clues:

- **Low MCV** with **normal iron studies** → not iron deficiency
- **Normal RDW** → uniform RBC size (typical of thalassemia)
- **Mentzer index < 13** → favors thalassemia over iron deficiency

Mentzer index = MCV / RBC count

- **< 13 → Thalassemia trait**
- **> 13 → Iron deficiency anemia**

Board Pearl:
Mentzer index <13 → think **thalassemia**, not iron deficiency.

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4. A 5-year-old child has mild microcytic anemia. Iron studies are normal, RDW is normal, Mentzer index is 11, and hemoglobin electrophoresis is **normal** with no elevation in Hb A_2.

What is the most likely diagnosis?

A. Beta thalassemia minor
B. Iron deficiency anemia
C. **Alpha thalassemia trait**
D. Sickle cell trait

Correct Answer: C

Explanation:
Alpha thalassemia trait often has **normal electrophoresis** because alpha chains are part of all hemoglobin types.

Board Pearl:
Normal electrophoresis + microcytosis → **alpha thalassemia trait**.

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5. A 12-month-old boy adopted from China is brought for evaluation of poor weight gain and progressive abdominal distension. His caregivers report that he has required multiple blood transfusions since infancy.
On examination, he appears pale and jaundiced. There is **marked hepatosplenomegaly. Facial features include frontal bossing and maxillary overgrowth, giving a characteristic "chipmunk facies."**

What is the most likely diagnosis?

A. Alpha thalassemia trait
B. Sickle cell disease
C. **Beta thalassemia major**
D. Iron deficiency anemia

Correct Answer: C

Explanation:
Beta thalassemia major presents after 6 months of age with severe anemia, extramedullary hematopoiesis, and transfusion dependence.

Board Pearl:
Chipmunk facies + transfusion-dependent anemia → **beta thalassemia major**.

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6. A **healthy 4-year-old child** undergoes routine laboratory evaluation. **Hemoglobin electrophoresis** shows:

- **Hb A >98%**
- **Small amount of Hb A_2**

How should this result be interpreted?

A. Beta thalassemia minor
B. Alpha thalassemia
C. Iron deficiency anemia
D. **Normal hemoglobin electrophoresis**

Correct Answer: D

Explanation:
In a **normal child older than 1 year**, hemoglobin electrophoresis typically shows:

- **Hb A: ~95–98% (major component)**
- **Hb A_2: ~2–3%**
- **Hb F: <1%**

This child's results (**Hb A >98% with a small amount of Hb A_2**) are consistent with a **normal adult hemoglobin pattern**.

Board Pearl:
Hb A >98% → **normal electrophoresis**.

---

7. A **3-year-old child** is evaluated for **mild anemia**. Laboratory testing includes **hemoglobin electrophoresis**, which shows:

- **Hb A: 93%**
- **Hb A_2: 6%**
- **Hb F: 1%**

What is the **most likely diagnosis**?

A. Alpha thalassemia trait
B. **Beta thalassemia minor**

C. Iron deficiency anemia
D. Sickle cell disease

Correct Answer: B

Explanation:

Elevated Hb A_2 (>3.5%) is diagnostic of **beta thalassemia minor**.

Board Pearl:

↑ Hb A_2 = **beta thalassemia trait**.

---

8. A 9-month-old boy is brought to the clinic for poor feeding and decreased activity. He appears pale and tired on examination. Laboratory studies show a **hemoglobin of 6 g/dL** with a **normal red blood cell count** of 5 million/μL. The **Mentzer index is 9**. Hemoglobin electrophoresis demonstrates **absence of Hb A**, **Hb A_2 of 4%**, and **Hb F of 96%**.
What is the most likely diagnosis?

A. Sickle cell disease
B. Alpha thalassemia trait
C. Beta thalassemia minor
D. **Beta thalassemia major**

Correct Answer: D

Explanation:

Severe anemia in infancy with absent Hb A and markedly elevated Hb F is characteristic of **beta thalassemia major**, which presents after fetal hemoglobin declines.

Board Pearl:

Absent Hb A + very high Hb F in infancy → **beta thalassemia major**.

---

9. A 2-year-old toddler is brought to clinic for fatigue and poor appetite. The parents report excessive cow's milk intake. Laboratory studies show **low hemoglobin**, **low MCV**, **low serum iron**, **low ferritin**, **high TIBC**, **high RDW**, **low reticulocyte count**, and **elevated soluble transferrin receptor (sTfR)**. The **Mentzer index is 15**.

What is the most likely diagnosis?

A. Thalassemia trait

B. Anemia of chronic disease
C. Lead poisoning
D. **Iron-deficiency anemia**

Correct Answer: D

Explanation:

Iron-deficiency anemia is characterized by low iron stores (low ferritin), increased iron binding capacity, high RDW, elevated sTfR, and a Mentzer index >13.

Board Pearls
Mentzer index **>13 + low ferritin** → iron-deficiency anemia.

---

10. A 15-month-old child is suspected of having iron-deficiency anemia based on dietary history and pallor on examination.

Which of the following is the **best initial diagnostic evaluation**?

A. Hemoglobin electrophoresis
B. Bone marrow biopsy
C. **CBC, reticulocyte count, ferritin, and soluble transferrin receptor (sTfR)**
D. Serum transferrin saturation only

Correct Answer: C

Explanation:
CBC evaluates anemia and MCV; reticulocyte count assesses marrow response; ferritin reflects iron stores; sTfR increases in iron deficiency and is unaffected by inflammation.

Board Pearl:
Ferritin + sTfR together help distinguish iron deficiency from anemia of chronic disease.

---

11. A 14-year-old menstruating adolescent female presents for routine health maintenance. She has no symptoms but is at risk for iron deficiency.

What is the recommended daily iron intake to **prevent iron-deficiency anemia**?

A. 5 mg/day
B. 10 mg/day
C. **15 mg/day**
D. 30 mg/day

Correct Answer: C

Explanation:

Menstruating adolescents require **15 mg of iron daily** to maintain iron stores and prevent anemia.

Board Pearl:

Menstruation = increased iron requirement.

---

12. A 3-year-old child is evaluated for developmental concerns. Parents report fatigue and unusual cravings for dirt and ice. On exam, the child appears pale and inattentive.

Which symptom is **most consistent with iron-deficiency anemia**?

A. Tremors
B. **Pica and poor concentration**
C. Hyperactivity
D. Polyuria

Correct Answer: B

Explanation:

Iron deficiency commonly causes fatigue, pica, impaired concentration, restless leg syndrome, and neurodevelopmental delay.

Board Pearl:

Pica + fatigue in toddlers → check iron studies.

---

13. A 20-month-old toddler drinks **40 oz of cow's milk daily** and presents with pallor and microcytic anemia on screening labs.

What is the most likely cause of anemia?

A. Lead poisoning
B. Thalassemia
C. Anemia of chronic disease
D. **Iron-deficiency anemia**

Correct Answer: D

Explanation:

Excessive cow's milk intake (>24 oz/day) leads to decreased iron intake, poor absorption, and occult intestinal blood loss.

Board Pearl:

Too much milk = too little iron.

---

14. A 2-year-old with iron-deficiency anemia is started on oral iron therapy. Follow-up labs are planned.

What is the **best indicator of response** to iron therapy?

A. **Rise in reticulocyte count and hemoglobin within 1–4 weeks**
B. Normalization of TIBC
C. Increase in ferritin only
D. Resolution of pallor alone

Correct Answer: A

Explanation:
Reticulocytosis occurs within days, followed by a rise in hemoglobin and MCV over weeks.

Board Pearl:
Reticulocyte rise = earliest sign of iron response.

---

15. A 3-year-old child with confirmed iron-deficiency anemia shows normalization of hemoglobin after 2 months of treatment.

How long should iron therapy be continued?

A. Stop immediately
B. 2 weeks more
C. **1–2 months after hemoglobin normalization**
D. Until ferritin becomes high

Correct Answer: C

Explanation:
Normalization of hemoglobin indicates correction of anemia, but **total body iron stores remain depleted**. Iron therapy must be continued beyond normalization to allow **repletion of iron stores**, primarily reflected by ferritin levels.

- Hemoglobin corrects first (within ~4–8 weeks)
- Iron stores (ferritin) take longer to replenish
- Stopping early → **high risk of relapse**

Board Pearl:
Correct anemia **first**, then replete iron stores.

---

16. A 2-year-old child is diagnosed with iron-deficiency anemia.

What is the **standard therapeutic dose** of elemental iron?

A. 1 mg/kg/day
B. 1 mg/kg/day
C. **2-3 mg/kg/day**
D. 6-7 mg/kg/day

Correct Answer: C

Explanation:

The recommended treatment dose is **2-3 mg/kg/day of elemental iron**, divided once or twice daily

Lower doses are equally effective as higher doses (4–6 mg/kg) at treating iron deficiency, while significantly reducing gastrointestinal side effects and toxicity risks

Board Pearl:
Therapeutic dose of oral iron is 2-3mg/kg of **elemental iron more effective, less side effects and more compliance**.

---

17. A 22-month-old toddler presents with severe microcytic anemia (hemoglobin 5 g/dL). He drinks 40 oz of whole milk daily. He is alert and active with normal vital signs and no signs of heart failure or cardiovascular compromise. **Iron-deficiency anemia is confirmed.**

What is the most appropriate next step?

A. Immediate packed RBC transfusion
B. Observation only
C. Iron replacement therapy (oral iron or IV iron if oral iron is not tolerated) and restriction of cow's milk intake
D. Bone marrow biopsy

Correct Answer: C

Explanation

Excessive cow's milk intake is the most common cause of iron-deficiency anemia in toddlers. In a hemodynamically stable child without symptoms of cardiovascular compromise, treatment focuses on iron replacement and limiting milk intake. Packed RBC transfusion is generally reserved for children with significant symptoms, heart failure, or hemodynamic instability.
Board Pearl

Severe iron-deficiency anemia with hemodynamic stability does not automatically require transfusion. Treat the iron deficiency and reserve transfusion for symptomatic or unstable patients.

---

18. A **2-month-old premature infant** born at 30 weeks' gestation is evaluated during routine follow-up. He appears well and feeds appropriately. Laboratory testing shows **hemoglobin 9.0 g/dL** with a **normal MCV**, normal bilirubin, and no evidence of hemolysis.

What is the most likely diagnosis?

A. Iron-deficiency anemia
B. Diamond–Blackfan anemia
C. Transient erythroblastopenia of childhood
D. **Anemia of prematurity**

Correct Answer: D

Explanation:
Anemia of prematurity occurs due to decreased erythropoietin production, shortened RBC lifespan, and frequent phlebotomy in preterm infants.

Board Pearl:
Preterm infant + normocytic anemia at 6–12 weeks → anemia of prematurity.

---

19. A **2-year-old child** presents with pallor but no jaundice or splenomegaly. Labs show **hemoglobin 4 g/dL**, **normal MCV**, **low reticulocyte count**, **normal adenosine deaminase (ADA)**, **negative direct Coombs test**, and no evidence of hemolysis.

What is the most likely diagnosis?

A. Aplastic anemia
B. Diamond–Blackfan anemia
C. **Transient erythroblastopenia of childhood**
D. Fanconi anemia

Correct Answer: C

Explanation:
Transient erythroblastopenia of childhood (TEC) is a benign, self-limited suppression of erythropoiesis, usually following a viral illness.

Board Pearl:
Toddler + severe normocytic anemia + low retic + normal ADA → TEC.

---

20. A 7-year-old child presents with fatigue, recurrent infections, and easy bruising. Laboratory evaluation reveals **pancytopenia**.

On physical examination, the child has:

- **Hypoplastic thumbs and absent radius**
- **Short stature**
- **Hyperpigmented skin with café-au-lait spots**
- **Microcephaly and abnormal facial features (small eyes, triangular face)**
- **Renal anomaly (horseshoe kidney)**

What is the most likely diagnosis?

A. Shwachman–Diamond syndrome
B. **Fanconi anemia**
C. Diamond–Blackfan anemia
D. Pearson syndrome

Correct Answer: B

Explanation:
Fanconi anemia is an inherited bone marrow failure syndrome associated with congenital anomalies and pancytopenia.

Board Pearl:
Pancytopenia + radial ray defects + hyperpigmentation = Fanconi anemia until proven otherwise.

Think DNA repair defect + high malignancy risk (AML).

---

21. A 4-month-old infant presents with pallor and poor feeding. Laboratory studies reveal **severe macrocytic anemia**, **low reticulocyte count**, and **elevated adenosine deaminase (ADA)** levels.

On physical examination, the infant is noted to have a **triphalangeal thumb**.

What is the most likely diagnosis?

A. Fanconi anemia
B. **Diamond–Blackfan anemia**
C. Transient erythroblastopenia of childhood (TEC)
D. Vitamin B12 deficiency

Correct Answer: B

Explanation:
Diamond–Blackfan anemia presents in infancy with macrocytic anemia, elevated ADA, congenital anomalies, and pure red cell aplasia.

Key diagnostic features (high-yield):

- **Severe macrocytic anemia**
- **Low reticulocyte count** (bone marrow fails to produce RBCs)
- **Normal WBCs and platelets** (isolated anemia)
- **Elevated ADA** (very characteristic finding)
- **Congenital anomalies**, especially:
    - **Triphalangeal thumb**
    - Craniofacial abnormalities
    - Short stature

Board Pearl:
Macrocytic anemia + low retic + ↑ADA + thumb anomaly = Diamond–Blackfan anemia.
If it's infancy + isolated anemia → think pure red cell aplasia.

---

22. A child presents with pallor, recurrent infections, and failure to thrive. Laboratory evaluation reveals **macrocytic anemia**, **neutropenia**, and **thrombocytopenia**.

Additional findings include:

- **Low stool elastase enzyme**
- Bone marrow biopsy showing **ring sideroblasts**

What is the most likely diagnosis?

A. Shwachman-Diamond syndrome
B. Fanconi anemia
C. **Pearson marrow–pancreas syndrome**
D. Diamond–Blackfan anemia

Correct Answer: C

Explanation:
Pearson syndrome is a mitochondrial disorder causing marrow failure and pancreatic dysfunction.

Board Pearl:
Marrow failure + pancreatic insufficiency → think mitochondrial (Pearson).

---

23. A **short-statured child** presents with **frequent infections**, **imperforate anus**, **hypoplastic teeth**, **macrocytic anemia**, **neutropenia**, **thrombocytopenia**, and **exocrine pancreatic insufficiency**.

Most likely diagnosis?

A. Pearson syndrome
B. Fanconi anemia
C. **Shwachman-Diamond syndrome**
D. Diamond–Blackfan anemia

Correct Answer: C

Explanation:
Shwachman–Diamond syndrome causes bone marrow dysfunction and pancreatic insufficiency with skeletal anomalies.

Board Pearl:
Pancreatic insufficiency + marrow failure + infections → Shwachman–Diamond.

---

24. A **toddler fed exclusively goat's milk** presents with pallor and fatigue. Labs show **macrocytic anemia**.

What is the most likely cause?

A. Vitamin B12 deficiency
B. **Folic acid deficiency**
C. Iron-deficiency anemia
D. Diamond–Blackfan anemia

Correct Answer: B

Explanation:
Goat's milk is deficient in folate, leading to macrocytic anemia.

Key facts:

- Goat's milk is **very low in folate**
- Leads to **megaloblastic (macrocytic) anemia**
- Symptoms: pallor, fatigue, poor growth

Board Pearl:
Goat's milk → folate deficiency.

---

25. A **child from a strictly vegan family** presents with **macrocytic anemia**, paresthesias, and fatigue.

What is the most appropriate next step?

A. Start folic acid
B. Bone marrow biopsy
C. **Suspect vitamin B12 deficiency and supplement**
D. Start iron therapy

Correct Answer: C

Explanation:
Vitamin B12 is found in animal products; deficiency causes macrocytic anemia and neurologic symptoms.

Board Pearl:
Vegan diet + macrocytosis → check B12.

---

26. A school-aged child presents with **fatigue**, **pallor**, and **abdominal discomfort**. Examination reveals **glossitis** and **gait instability**.

Laboratory findings show:

- **Macrocytic anemia**
- Low vitamin B12 levels
- Presence of **anti–intrinsic factor antibodies**

What is the most likely diagnosis?

A. Folate deficiency
B. **Pernicious anemia**
C. Diamond–Blackfan anemia
D. Fanconi anemia

Correct Answer: B

Explanation:
Pernicious anemia results from autoimmune destruction of intrinsic factor, impairing B12 absorption.

Key diagnostic features:

- **Macrocytic (megaloblastic) anemia**
- **Neurologic symptoms** → gait instability, paresthesia (due to demyelination)
- **Glossitis** (beefy red tongue)
- **Positive anti–intrinsic factor antibodies** (highly specific)

Pathophysiology:

- Lack of intrinsic factor → impaired **B12 absorption in terminal ileum**
- Leads to **ineffective DNA synthesis** → macrocytosis
- Causes **neurologic dysfunction** (not seen in folate deficiency)

Board Pearl:
Anti-IF antibodies → pernicious anemia.

---

27. A 6-year-old child presents with **chronic pallor**, intermittent **jaundice**, and **fatigue**. Parents report episodes of worsening jaundice during minor illnesses.

On examination:

- **Splenomegaly**
- Mild scleral icterus

Laboratory findings:

- **Normocytic anemia**
- **Elevated reticulocyte count**
- **Increased indirect bilirubin**
- **Elevated MCHC**

Peripheral smear shows **small, dense red blood cells lacking central pallor**.

What is the most likely diagnosis?

A. G6PD deficiency
B. Autoimmune hemolytic anemia
C. **Hereditary spherocytosis**
D. Sickle cell disease

Correct Answer: C

Explanation:
Hereditary spherocytosis causes extravascular hemolysis and spherocytes on smear.

Board Pearl:

Spherocytes + ↑MCHC + splenomegaly = hereditary spherocytosis.
If RBCs have NO central pallor → think spherocytes immediately.
Watch for aplastic crisis after parvovirus infection on the exam.

---

28. An **African-American boy** develops **dark urine, jaundice, pallor**, and **splenomegaly** after starting **nitrofurantoin for** possible UTI infection. Labs show anemia, reticulocytosis, indirect hyperbilirubinemia, low haptoglobin, and **normal G6PD activity during the episode**. Smear shows **Heinz bodies**.

What is the most likely Diagnosis?

A. Autoimmune hemolytic anemia
B. **G6PD deficiency**
C. Sickle cell disease
D. Hereditary spherocytosis

Correct Answer: B

Explanation:
G6PD levels can be falsely normal during hemolysis due to destruction of older RBCs.

Exposure to **fava beans, primaquine, sulfa drugs, or nitrofurantoin** exacerbates G6PD deficiency

Board Pearl:
Suspected G6PD + normal enzyme during crisis → repeat later.
Oxidative stress triggers hemolysis in G6PD deficiency.

---

29. A 9-month-old infant with known sickle cell disease presents with **acute onset of painful swelling of both hands and feet**. The child is irritable but afebrile.

What is the most likely diagnosis?

A. Acute chest syndrome
B. Splenic sequestration
C. **Dactylitis**
D. Aplastic crisis

Correct Answer: C

Explanation:
Dactylitis is often the first manifestation of sickle cell disease in infants.

Board Pearl:

Painful swollen hands/feet in an infant with sickle cell = dactylitis.
First presentation of sickle cell disease on the boards.

---

30. A child with known sickle cell disease presents with fever and signs of sepsis. Due to functional asplenia, he is at increased risk for infection with encapsulated organisms.

What is the most common cause of sepsis in children with sickle cell disease?

A. *Escherichia coli*
B. *Staphylococcus aureus*

C. ***Streptococcus pneumoniae***
D. *Haemophilus influenzae*

Correct Answer: C

Board Pearl:
Sickle cell disease + sepsis = think encapsulated organisms → #1 is Streptococcus pneumoniae.
Functional asplenia = loss of opsonization → high risk of pneumococcal sepsis.

---

31. A 2-year-old child with known sickle cell disease presents with **sudden pallor**, lethargy, and abdominal distension. Parents report rapid worsening over a few hours.

On examination:
- **Marked splenomegaly**
- Tachycardia

Laboratory findings:
- **Severe anemia**
- **Reticulocytosis**
- **Thrombocytopenia**

What is the most likely diagnosis and next best step in management?

A. Aplastic crisis → steroids
B. **Splenic sequestration → packed RBC transfusion**
C. Acute chest syndrome → antibiotics
D. Transient erythroblastopenia of childhood (TEC) → observation

Correct Answer: B

Explanation:
Splenic sequestration is life-threatening and requires urgent transfusion.

Board Pearl:
Sickle cell + sudden splenomegaly + anemia + ↑retic = splenic sequestration → transfuse immediately.

Reticulocytosis = NOT aplastic crisis.
This is a pediatric emergency—don't delay transfusion.

---

32. A 5-year-old child with known sickle cell disease presents with **fever**, **malaise**, and a mild **rash**. Over the past few days, the child has become increasingly pale and fatigued.

Laboratory findings:

- **Severe anemia**
- **Marked reticulocytopenia**

What is the most likely diagnosis?

A. Splenic sequestration
B. **Aplastic crisis (parvovirus B19)**
C. Acute chest syndrome
D. Hemolytic crisis

Correct Answer: B

Explanation:
Parvovirus B19 suppresses erythropoiesis, causing reticulocytopenia.

Board Pearl:
Low retic in SCD anemia → aplastic crisis.

---

33. A **6-year-old child with sickle cell disease** presents with fatigue and pallor after a viral prodrome. Laboratory studies show **severe anemia with reticulocytopenia**. PCR testing confirms infection with a DNA virus that selectively suppresses erythroid precursors.

Which virus is the most common cause of aplastic crisis?

A. Epstein–Barr virus
B. Cytomegalovirus
C. **Parvovirus B19**
D. Human herpesvirus 6

Correct Answer: C

Explanation:
Parvovirus B19 infects erythroid precursor cells, causing transient cessation of red blood cell production and resulting in aplastic crisis in patients with chronic hemolytic anemia.

Board Pearl:
Reticulocytopenia + acute anemia in SCD → Parvovirus B19.

---

34. A **10-year-old child with sickle cell disease** is followed in clinic. Parents ask about the most common causes of long-term illness and death associated with this condition.

Which of the following are the most common causes of morbidity and mortality?

A. Renal failure and hypertension
B. Pulmonary embolism and cardiomyopathy
C. **Infection, acute chest syndrome, and stroke**
D. Malignancy and marrow failure

Correct Answer: C

Explanation:
Functional asplenia predisposes to severe infections; vaso-occlusion causes acute chest syndrome and ischemic stroke.

Board Pearl:
Infection + ACS + stroke = top killers in SCD.

---

35. A **9-year-old child with sickle cell anemia** presents with **fever, chest pain, tachypnea, dyspnea**, and hypoxia. Chest radiograph reveals a **new pulmonary infiltrate**.

What is the most appropriate management?

A. **Adequate pain relief, oxygen, ceftriaxone and macrolide plus early simple transfusion**
B. High-dose corticosteroids, and exchange transfusion
C. IV fluids and bronchodilators only
D. Chest CT scan with contrast

Correct Answer: A

Explanation:
Acute chest syndrome is managed with adequate pain relief, incentive spirometry, broad-spectrum antibiotics covering typical and atypical organisms, oxygen, early simple transfusion, pain control, and cautious hydration.

Exchange transfusion is necessary in patients with severe clinical features or evidence of progression despite initial simple transfusion

Board Pearl:
New infiltrate + fever + chest pain in SCD = ACS.

---

36. A **7-year-old with sickle cell disease** is being counseled on infection prevention.

Sickle cell patients are at highest risk for infection with which organisms?

A. Anaerobic bacteria
B. Intracellular parasites
C. **Encapsulated organisms**
D. Fungal pathogens

Correct Answer: C

Explanation:
Functional asplenia impairs clearance of encapsulated bacteria such as *Streptococcus pneumoniae*.

Board Pearl:
SCD → functional asplenia → encapsulated bacteria.

---

37. A **10-year-old child with sickle cell anemia** presents to the ED with severe limb pain requiring hospitalization.

What is the most common reason for hospitalization in children with sickle cell disease, and how is it treated?

A. Infection → IV antibiotics
B. Acute chest syndrome → oxygen and transfusion
C. **Vaso-occlusive pain crisis → IV hydration, NSAIDs, and opioids**
D. Splenic sequestration → splenectomy

Correct Answer: C

Explanation:
Vaso-occlusive pain crises are the most frequent cause of hospitalization and are treated with aggressive pain control and hydration.

Board Pearl:
Pain crisis = most common admission in SCD.

---

38. A **6-year-old child with sickle cell disease** is asymptomatic but undergoing routine screening.

Which test reduces the risk of ischemic stroke in children with sickle cell anemia?

A. Brain MRI annually
B. Echocardiography
C. **Transcranial Doppler ultrasound yearly (ages 2–16)**
D. Coagulation panel

Correct Answer: C

Explanation:
Elevated cerebral blood flow velocities predict stroke risk; chronic transfusion reduces this risk.

Board Pearl:
TCD saves brains in SCD.

---

39. A **5-year-old with sickle cell disease** presents with **fever**, **positive parvovirus B19 testing**, **reticulocytopenia**, **hemoglobin 6 g/dL**, and **acute splenomegaly**.

What is the next best step?

A. Observation only
B. Exchange transfusion
C. **Empiric antibiotics and packed RBC transfusion**
D. Steroids

Correct Answer: C

Explanation:
This presentation suggests acute splenic sequestration with aplastic crisis—both life-threatening.

Board Pearl:
Splenic enlargement + falling Hb = transfuse.

---

40. A **15-year-old male with sickle cell disease** presents with a **painful erection lasting 6 hours**.

What is the most appropriate management?

A. Oral analgesics and discharge
B. Cold compresses
C. Observation overnight
D. **Immediate aspiration ± irrigation, phenylephrine, pain control**

Correct Answer: D

Explanation:
Prolonged priapism is a urologic emergency due to ischemic injury risk.

Board Pearl:
Priapism >4 hours = emergency.

---

41. A **9-year-old child with sickle cell disease** presents with fever and localized bone pain. Osteomyelitis is suspected.

What is the most common causative organism?

A. **Salmonella species**
B. Streptococcus pyogenes
C. Staphylococcus aureus
D. Escherichia coli

Correct Answer: A

Explanation:
Salmonella osteomyelitis is uniquely associated with sickle cell disease.

Board Pearl:
Bone pain + SCD → think Salmonella.

---

42. A **child with sickle cell disease** presents with fever and bone pain suspicious for osteomyelitis.

What is the next best step?

A. Plain radiographs only
B. Oral antibiotics
C. **MRI, blood cultures, IV antibiotics covering Salmonella and S. aureus**
D. Bone biopsy immediately

Correct Answer: C

Explanation:
MRI is most sensitive early; empiric antibiotics should cover Salmonella and Gram-positive organisms.

Board Pearl:
MRI is the imaging of choice for osteomyelitis.

---

43. A 16-year-old adolescent presents with **acute onset fatigue**, **pallor**, and **scleral icterus**. On examination, he is tachycardic.

Laboratory findings:

- **Hemoglobin: 6 g/dL**

- **Hematocrit: 25%**
- **Elevated reticulocyte count**
- **Elevated indirect bilirubin**
- **Positive direct antiglobulin (Coombs) test**

What is the most likely diagnosis?

A. G6PD deficiency
B. **Autoimmune hemolytic anemia (AIHA)**
C. Hereditary spherocytosis
D. Sickle cell crisis

Correct Answer: B

Explanation:
AIHA causes immune-mediated RBC destruction and a positive direct Coombs test.

Key diagnostic features in this case:
- **Severe anemia (Hb 6 g/dL, Hct 25%)**
- **Reticulocytosis** → bone marrow compensation
- **Indirect hyperbilirubinemia** → hemolysis
- **Positive Coombs test** → confirms autoimmune cause

Start corticosteroids and transfuse least-incompatible RBCs if needed

Board Pearl:
Positive Coombs + hemolysis → AIHA.
AIHA → steroids first, then transfusion if unstable

---

44. A **7-year-old child receiving chemotherapy** presents to the emergency department with a **temperature of 38.6°C (101.5°F)**. Laboratory studies show an **absolute neutrophil count (ANC) of 300/µL**. The child appears ill but hemodynamically stable.

What is the next best step?

A. **Hospital admission, blood cultures, and immediate IV broad-spectrum antibiotics**
B. Repeat CBC in 24 hours
C. Oral antibiotics and outpatient follow-up
D. Observation only

Correct Answer: A

Explanation:
Febrile neutropenia is a medical emergency due to the high risk of sepsis. Empiric IV antibiotics must be started promptly after blood cultures.

Board Pearl:
Fever + ANC < 500 = admit and start IV antibiotics.

---

45. A **5-year-old child** has **recurrent episodes of neutropenia occurring for about 1 week every 3 weeks**. During these episodes, he develops **gingivitis, pharyngitis, and skin infections**. Between episodes, he is healthy.

What is the most likely diagnosis?

A. Kostmann syndrome
B. Autoimmune neutropenia
C. **Cyclic neutropenia**
D. Leukemia

Correct Answer: C

Explanation:
Cyclic neutropenia is characterized by periodic neutrophil nadirs approximately every 21 days.
Serial CBC monitoring demonstrates the cyclical pattern of neutrophil counts.
CBC 2–3 times per week for 6–8 weeks will establish the diagnosis of cyclic neutropenia

Board Pearl:
Neutropenia every 3 weeks with infections → cyclic neutropenia.

---

46. A **child diagnosed with cyclic neutropenia** continues to have recurrent infections during neutropenic episodes.

What is the best long-term management?

A. Daily oral antibiotics
B. Observation only
C. **Prophylactic granulocyte colony-stimulating factor (G-CSF)**
D. Bone marrow transplant

Correct Answer: C

Explanation:
G-CSF reduces the depth and duration of neutropenia and decreases infection risk.

Board Pearl:
Cyclic neutropenia → G-CSF + urgent care for fever.

---

47. A **2-month-old infant** presents with **severe neutropenia since birth**, recurrent skin and oral infections, **gingivitis**, and **oral ulcers**. ANC remains persistently low without recovery.

What is the most likely diagnosis?

A. Cyclic neutropenia
B. Autoimmune neutropenia
C. Viral bone marrow suppression
D. **Kostmann syndrome (severe congenital neutropenia)**

Correct Answer: D

Explanation:
Kostmann syndrome is a congenital disorder with persistent severe neutropenia and high risk of life-threatening infections.

Board Pearl:
Neutropenia from birth + recurrent infections → Kostmann syndrome.

---

48. A **10-year-old child** presents with a **persistent cervical lymph node measuring 2.5 cm** for 6 weeks. He has **fever, weight loss, night sweats**, and has **not responded to oral antibiotics**.

What is the next best step?

A. Extend antibiotics
B. Ultrasound surveillance
C. Reassurance
D. **Referral to pediatric oncology for lymph node biopsy**

Correct Answer: D

Explanation:
Systemic "B symptoms" and persistent lymphadenopathy raise concern for malignancy.

Board Pearl:
Large, persistent node + B symptoms = biopsy.

---

49. A **6-year-old child** is noted to have a **supraclavicular lymph node** present for 2 weeks. He is otherwise asymptomatic.

What is the most appropriate next step?

A. **Referral for further evaluation and biopsy**
B. Oral antibiotics
C. Reassurance
D. Observe for 3 months

Correct Answer: A

Explanation:
Supraclavicular lymphadenopathy is always pathologic until proven otherwise.

Board Pearl:
Supraclavicular nodes = malignancy until proven otherwise.

---

50. An infant presents with **intracranial hemorrhage**. PT, PTT, platelet count, fibrinogen, and von Willebrand panel are all normal.

What is the most likely diagnosis?

A. Hemophilia A
B. von Willebrand disease
C. **Factor XIII deficiency**
D. Vitamin K deficiency

Correct Answer: C

Explanation:
Factor XIII stabilizes fibrin clots; deficiency causes delayed bleeding.

Board Pearl:
Normal PT/PTT + bleeding → factor XIII deficiency.

---

51. A 4-year-old has **normal PT**, **markedly prolonged PTT**, and **no history of abnormal bleeding**.

Which factor deficiency explains this?

A. Factor VIII
B. **Factor XII**
C. Factor IX
D. Factor XI

Correct Answer: B

Explanation:
Factor XII deficiency prolongs PTT but does not cause bleeding.

Board Pearl:
Factor XII → abnormal labs, no bleeding.

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52. A **5-year-old child** develops **petechiae**, epistaxis, and oral mucosal bleeding 2 weeks after a viral URI. Platelet count is **12,000/µL**, with **large platelets on peripheral smear**. WBCs, hemoglobin and hematocrit levels are within normal limits

What is the most likely diagnosis?

A. **Immune thrombocytopenic purpura (ITP)**
B. Leukemia
C. Aplastic anemia
D. TTP

Correct Answer: A

Explanation

- ITP is an immune-mediated disorder characterized by isolated thrombocytopenia, often occurring after a viral infection.
- Children typically present with petechiae, bruising, epistaxis, or other mild mucosal bleeding.
- **The diagnosis is supported by:**
    - **Isolated thrombocytopenia**
    - **Normal hemoglobin and white blood cell count**
    - **Large platelets on peripheral smear indicating increased platelet production**
- **Children with no bleeding or only mild bleeding are usually managed with observation, even when the platelet count is very low.**
- Treatment is considered for clinically significant mucosal bleeding, impaired quality of life, or severe bleeding. First-line therapies include a short course of corticosteroids or IVIG.

Board Pearl
Petechiae + isolated thrombocytopenia + normal hemoglobin and WBC count after a recent viral illness = ITP until proven otherwise.
Management is guided by bleeding severity, not the platelet count alone.

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53. A **2-year-old boy** presents with **recurrent infections**, **eczema**, **severe thrombocytopenia**, and **small platelets**.

What is the most likely diagnosis?

A. ITP
B. Fanconi anemia

C. **Wiskott–Aldrich syndrome**
D. Leukemia

Correct Answer: C

Explanation:
Wiskott–Aldrich is an X-linked disorder affecting platelets and immunity.

Board Pearl:
Eczema + infections + small platelets = Wiskott–Aldrich.

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54. A term newborn is noted to have **severe thrombocytopenia (platelet count <20,000/µL)** on routine laboratory testing shortly after birth. The infant appears well with no active bleeding.

The mother has a history of **immune thrombocytopenic purpura (ITP)**.

What is the most appropriate management?

A. Observation only
B. Platelet transfusion
C. Exchange transfusion
D. **Intravenous immunoglobulin (IVIG)**

Correct Answer: D

Explanation:
Neonatal thrombocytopenia in this case is due to **transplacental passage of maternal antiplatelet IgG antibodies**, causing **immune-mediated platelet destruction** (neonatal ITP).

Management depends on platelet level and bleeding risk:

- **Platelets <30,000/µL (even without bleeding) → IVIG is indicated**
- IVIG helps **reduce antibody-mediated destruction**
- Goal: prevent **intracranial hemorrhage (IVH)**

When to use platelet transfusion:

- **Life-threatening bleeding** OR extremely low platelets with instability
- Often given **with IVIG**, not alone

Board Pearl:
Maternal ITP → neonatal thrombocytopenia → treat with IVIG if platelets <30,000.
If platelets >50,000 and no bleeding → observe.
Always think: prevent intracranial hemorrhage in neonates

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55. A term newborn is noted to have **severe thrombocytopenia at birth** (platelet count <20,000/μL). The infant is otherwise well-appearing.

The mother has **no history of autoimmune disease**, but reports that **previous siblings had similar neonatal thrombocytopenia**.

What is the most likely diagnosis and best treatment?

A. Neonatal ITP → IVIG
B. **Neonatal alloimmune thrombocytopenia → washed maternal platelets**
C. TAR syndrome → platelet transfusion
D. DIC → FFP

Correct Answer: B

Explanation:
Neonatal alloimmune thrombocytopenia (NAIT) results from maternal antibodies against fetal platelet antigens inherited from the father.

Key distinguishing features:

- **Severe thrombocytopenia at birth**
- **Mother is healthy (no ITP)**
- **History of previously affected siblings**
- High risk of **intracranial hemorrhage (even in utero)**

Best treatment:

- **Washed maternal platelets** (lack the targeted antigen → not destroyed)
- IVIG may also be used, but **platelets are first-line in severe cases**

Board Pearl:
Severe neonatal thrombocytopenia + healthy mother + prior affected siblings = NAIT.
Gold standard treatment = washed maternal platelets.
Highest risk = intracranial hemorrhage—even before birth.

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56. A **newborn with severe thrombocytopenia** has a **normal physical examination** and no signs of bleeding.

What is the next best step?

A. Platelet transfusion
B. IVIG
C. **Head ultrasonography**
D. Bone marrow biopsy

Correct Answer: C

Explanation:
Severe neonatal thrombocytopenia places the infant at high risk for **intracranial hemorrhage**, even without external bleeding.

Board Pearl:
Severe thrombocytopenia in newborn → always rule out ICH.

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57. A **6-year-old child** has had **easy bruising and recurrent mucosal bleeding since infancy**. Platelet count is **low-normal**, PT and PTT are normal, fibrinogen is normal, and von Willebrand studies are normal.

What is the most likely diagnosis?

A. **Platelet function disorder**
B. von Willebrand disease
C. Hemophilia
D. DIC

Correct Answer: A

Explanation:
his child has **primary hemostasis defect**:

- **Mucosal bleeding** (epistaxis, gum bleeding)
- **Normal platelet count (or near normal)**
- **Normal PT/PTT**

This pattern is classic for a **platelet function disorder**, where platelet number is adequate but function is impaired.

High-Yield Examples of Platelet Function Disorders
1. Glanzmann thrombasthenia
- Defect: **GpIIb/IIIa → impaired platelet aggregation**
- Key clue: **No aggregation with ADP, collagen, or epinephrine**
- Platelet count: **normal**

2. Bernard-Soulier syndrome
- Defect: **GpIb → impaired adhesion to vWF**
- Key clue: **Large platelets (giant platelets) + thrombocytopenia**
- Abnormal **ristocetin test (does not correct)**

Why not the other choices?
- **A. Hemophilia:** Deep tissue bleeding (joints), **↑PTT**
- **B. von Willebrand disease:** Abnormal vWF studies ± ↑PTT
- **D. DIC:** Abnormal PT/PTT, ↓ fibrinogen, ill-appearing

Board Pearl:
Mucosal bleeding + normal PT/PTT + normal vWF = platelet function disorder.
Think: "Platelets are present but not working."

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58. A **10-year-old boy** presents with **recurrent epistaxis, gingival bleeding, and easy bruising**. Platelet count and size are normal. Platelets **agglutinate to ristocetin**, but show **poor aggregation to ADP, epinephrine, and collagen**.

What is the diagnosis?

A. Bernard–Soulier syndrome
B. von Willebrand disease
C. Hemophilia A
D. **Glanzmann thrombasthenia**

Correct Answer: D

Explanation:
Glanzmann thrombasthenia is due to defective GPIIb/IIIa, causing impaired aggregation.

Board Pearl:
Normal platelets + failed aggregation (except ristocetin) → Glanzmann.

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59. A **10-year-old child** with suspected bleeding disorder has **mild thrombocytopenia** with **large platelets**. Platelets **do not agglutinate to ristocetin**, but aggregate normally to ADP, epinephrine, and collagen.

What is the most likely diagnosis?

A. Glanzmann thrombasthenia
B. von Willebrand disease
C. **Bernard–Soulier syndrome**
D. ITP

Correct Answer: C

Explanation:
Bernard–Soulier syndrome involves defective GPIb, preventing ristocetin-mediated aggregation.

Board Pearl:
Large platelets + failed ristocetin response → Bernard–Soulier.

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60. A child with a **known platelet function disorder** presents with **life-threatening intracranial hemorrhage**.

What is the most appropriate immediate management?

A. IVIG
B. Desmopressin
C. **Platelet transfusion**
D. FFP

Correct Answer: C

Explanation:
Transfusion of normally functioning platelets is required in severe bleeding.

Board Pearl:
Severe bleeding + platelet disorder → transfuse platelets.

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61. A **48-hour-old newborn** presents with **prolonged bleeding after circumcision**. CBC reveals **severe thrombocytopenia**. Physical exam shows **bilateral absence of the radius**, but **normal thumbs**.

What is the diagnosis?

A. Fanconi anemia
B. **Thrombocytopenia with absent radii (TAR syndrome)**
C. Neonatal ITP
D. Holt–Oram syndrome

Correct Answer: B

Explanation:
TAR syndrome is characterized by thrombocytopenia and absent radii with preserved thumbs.

The best treatment for **severe thrombocytopenia in TAR syndrome is platelet transfusion (irradiated, single-donor)**

Board Pearl:
Absent radius + thumbs present + thrombocytopenia = TAR.

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62. A **male newborn** presents with **prolonged bleeding after circumcision**. Coagulation studies reveal a **prolonged PTT**.

What is the most likely diagnosis?

A. von Willebrand disease
B. Platelet disorder
C. Vitamin K deficiency
D. **Hemophilia**

Correct Answer: D

Explanation:
Hemophilia A or B causes isolated prolonged PTT with normal platelets.

Board Pearl:
Male infant + bleeding + ↑PTT → hemophilia.

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63. An **8-year-old boy** develops **severe knee swelling** after minor trauma. Joint aspiration reveals blood. Imaging is normal.

What is the next best step?

A. NSAIDs
B. MRI
C. **Coagulation profile and mixing studies**
D. Platelet transfusion

Correct Answer: C

Explanation:
Hemarthrosis strongly suggests a coagulation factor deficiency.

Board Pearl:
Hemarthrosis → evaluate coagulation factors.

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64. A **15-year-old girl** reports **heavy menstrual bleeding since menarche**. PT and PTT are normal. Ristocetin cofactor activity is reduced.

What is the most likely diagnosis?

A. Hemophilia carrier
B. **von Willebrand disease**
C. Platelet disorder
D. DIC

Correct Answer: B

Explanation:

von Willebrand disease is the **most common inherited bleeding disorder**, especially presenting in **adolescent females with menorrhagia**.

Key diagnostic features:

- **Mucosal bleeding** → epistaxis, menorrhagia
- **Normal platelet count**
- **Normal PT**
- **PTT: normal or mildly prolonged** (due to ↓ factor VIII stability)
- **↓ Ristocetin cofactor activity** → impaired platelet adhesion

Pathophysiology:

- Deficiency or dysfunction of **von Willebrand factor (vWF)**
- Leads to:
    - Impaired **platelet adhesion**
    - Reduced **factor VIII stabilization**

Board Pearl:

Menorrhagia + normal PT/PTT + ↓ ristocetin activity = von Willebrand disease.

Most common cause of heavy menstrual bleeding in adolescents.

Think vWD first in any teenage girl with unexplained menorrhagia.

---

65. A **4-year-old child** develops **bloody diarrhea**, followed by **thrombocytopenia, elevated BUN/creatinine, and schistocytes** on peripheral smear.

What is the most likely diagnosis?

A. TTP
B. **Hemolytic uremic syndrome (HUS)**
C. DIC
D. ITP

Correct Answer: B

Explanation:

HUS follows diarrheal illness, commonly due to E. coli O157:H7.

Board Pearl:

Bloody diarrhea + AKI + thrombocytopenia → HUS.

---

66. A **critically ill child in the PICU** has **prolonged PT and PTT**, **low fibrinogen**, **elevated D-dimer**, and **thrombocytopenia**.

What is the diagnosis and management?

A. TTP → plasma exchange
B. HUS → supportive care
C. **DIC → treat underlying cause + blood products**
D. Hemophilia → factor replacement

Correct Answer: C

Explanation:
DIC is a consumptive coagulopathy triggered by severe illness (e.g., sepsis).

Board Pearl:
DIC = treat cause + FFP ± cryoprecipitate.

---

67. A **17-year-old Caucasian boy** presents with **recurrent episodes of deep vein thrombosis (DVT)** involving the lower extremities. He has no history of malignancy, central venous catheter, or recent surgery. Family history is significant for **multiple first-degree relatives with DVT at a young age**.

What is the most likely underlying cause?

A. Antithrombin III deficiency
B. Protein C deficiency
C. Protein S deficiency
D. **Factor V Leiden mutation**

Correct Answer: D

Explanation:
Factor V Leiden is the most common inherited thrombophilia in Caucasians. The mutation causes **resistance to activated protein C**, leading to a hypercoagulable state and recurrent venous thrombosis, especially in adolescents and young adults.

Board Pearl:
Recurrent DVT + strong family history → think **Factor V Leiden**, especially in Caucasians.

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68. A 10-month-old infant is brought to the clinic for **persistent rash** and poor weight gain. Parents report that the rash has been present for several weeks and does not improve with topical treatments.

On examination:

- **Scaly, erythematous rash on the scalp and trunk** (seborrheic-like)
- **Hepatosplenomegaly**

- **Pallor**
- **Petechiae**

Laboratory findings:

- **Anemia and thrombocytopenia**

Imaging:

- Skull X-ray shows **punched-out lytic lesions**

What is the most likely diagnosis?

A. Acute lymphoblastic leukemia
B. Osteomyelitis
C. Metastatic neuroblastoma
D. **Langerhans cell histiocytosis**

Correct Answer: D

Explanation:

Langerhans cell histiocytosis is a disorder characterized by **clonal proliferation of Langerhans cells**.
Classic infant presentation:

- **Seborrheic-like rash** (refractory to treatment)
- **Bone lesions** → "punched-out" lytic skull lesions
- **Hepatosplenomegaly**
- **Cytopenias** (bone marrow involvement)

Additional features:

- May cause **diabetes insipidus** (pituitary involvement)
- Can involve skin, bone, liver, spleen, and marrow

Board Pearl:
Infant + persistent seborrheic-like rash + lytic skull lesions = Langerhans cell histiocytosis.
If "rash that doesn't improve" + bone lesions → think LCH immediately.

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69. A **1-year-old child** presents with **persistent high fever**, lethargy, and is toxic appearing. Examination reveals **hepatosplenomegaly**. Laboratory studies show **pancytopenia**, **hypertriglyceridemia**, and **markedly elevated ferritin**. Bone marrow biopsy demonstrates **hemophagocytosis**.

What is the most likely diagnosis?

A. Acute leukemia
B. Severe sepsis
C. Macrophage activation syndrome
D. **Hemophagocytic lymphohistiocytosis (HLH)**

Correct Answer: D

Explanation:
Hemophagocytic lymphohistiocytosis is a **life-threatening hyperinflammatory syndrome** caused by **uncontrolled activation of macrophages and T cells**.

Key diagnostic features (HLH criteria – high yield):

- **Persistent fever**
- **Splenomegaly**
- **Cytopenias (≥2 cell lines)**
- **Hyperferritinemia (often >10,000)**
- **Hypertriglyceridemia and/or hypofibrinogenemia**
- **Hemophagocytosis in bone marrow/spleen**
- ↓ NK cell activity, ↑ soluble IL-2 receptor (advanced tests)

Triggers:

- **Infections (especially EBV)**
- Malignancy
- Genetic (familial HLH)

Board Pearl:
Fever + pancytopenia + very high ferritin → **HLH** (medical emergency).

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70. An **infant undergoing chemotherapy for leukemia** presents with **fever, diarrhea**, and a **diffuse macular, erythematous, blanching, nonpruritic rash**. Liver enzymes are elevated. The infant received a **packed red blood cell transfusion two weeks ago**.

What is the most likely cause of these findings?

A. Viral exanthem
B. Drug hypersensitivity reaction
C. Sepsis-related rash
D. **Transfusion-associated graft-versus-host disease**

Correct Answer: D

Explanation:
Transfusion-associated graft-versus-host disease (TA-GVHD) occurs when viable donor lymphocytes engraft in an immunocompromised host. It presents with **fever, diarrhea, rash, hepatitis, and bone marrow suppression** and is often fatal. It is **prevented by irradiating blood products**.

Board Pearl:
Immunocompromised + transfusion + rash + diarrhea → think **TA-GVHD**.
Prevention = **irradiated blood products**.

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71. A 7-year-old boy is evaluated for persistent anemia despite 3 months of appropriate oral iron therapy. He initially presented with fatigue and pallor and was diagnosed with presumed iron deficiency anemia. Compliance with iron therapy is confirmed.
On examination, he remains pale with no hepatosplenomegaly.
Laboratory findings:

- Hemoglobin: low
- MCV: low (microcytic anemia)
- Serum iron: elevated
- Ferritin: elevated
- Transferrin saturation: elevated
- TIBC: low-normal
- Peripheral smear: dimorphic RBC population

A bone marrow biopsy is performed

What is the most likely diagnosis?

A. Refractory iron deficiency anemia
B. Thalassemia trait
C. Anemia of chronic disease
D. Sideroblastic anemia

Correct Answer: D. Sideroblastic anemia

Explanation (High-Yield):
Failure to respond to iron therapy + paradoxically high iron stores = think sideroblastic anemia.
Key diagnostic clue:

- Bone marrow shows ring sideroblasts (iron-laden mitochondria encircling the nucleus)

Board Pearl:
If microcytic anemia does NOT improve with iron and labs show ↑ iron + ↑ ferritin + ↑ transferrin saturation, the diagnosis is sideroblastic anemia—not iron deficiency.