Revision Sheet

Hemolytic Anemia in Children

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1. Definition

Hemolytic anemia is anemia caused by **premature destruction of red blood cells (RBCs)** exceeding the bone marrow's ability to replace them.

Clinical clue:

Anemia + jaundice ± dark urine ± splenomegaly = Think hemolysis.

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2. Clinical Presentation

History

Ask about:

- Pallor
- Fatigue
- Jaundice
- Dark ("tea-colored") urine
- Abdominal pain
- Back pain (acute hemolysis)
- Fever or recent infection
- Drug exposure
    - Sulfonamides
    - Antimalarials
    - Nitrofurantoin
- Family history of anemia, jaundice, splenectomy, gallstones

- Previous transfusions
- Neonatal jaundice
- Ethnicity (risk of inherited hemolytic disorders)

Physical Examination

Look for:

- Pallor
- Scleral icterus
- Jaundice
- Tachycardia
- Splenomegaly
- Hepatomegaly
- Gallstones (older children)
- Growth failure (chronic hemolysis)

Signs of severe anemia

- Shock
- Altered mental status
- Heart failure
- Respiratory distress

→ Emergency management required.

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3. Diagnostic Approach

Step 1

Confirm anemia

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CBC

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Low Hb

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Step 2

Is hemolysis present?

Look for:

✓ Elevated reticulocyte count

✓ Elevated indirect bilirubin

✓ Elevated LDH

✓ Low haptoglobin (if available)

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If YES

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Peripheral blood smear

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Determine cause

- Immune
- Membrane defect
- Enzyme deficiency
- Hemoglobinopathy
- Microangiopathy

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4. Differential Diagnosis

Cause	Typical Clues
Autoimmune hemolytic anemia (AIHA)	Acute onset, positive Coombs test
Glucose-6-phosphate dehydrogenase deficiency	Oxidative drugs, fava beans, infection
Hereditary spherocytosis	Family history, splenomegaly, gallstones
Sickle cell disease	Pain crisis, African ancestry
Thalassemia	Chronic anemia, family history
Hemolytic uremic syndrome	Bloody diarrhea + thrombocytopenia + AKI
Infection-associated hemolysis	Malaria, sepsis
Drug-induced hemolysis	Recent medication exposure

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5. Investigations

First-line investigations

✓ CBC

✓ Reticulocyte count

✓ Peripheral smear

✓ Bilirubin (direct/indirect)

✓ LDH

✓ Haptoglobin (if available)

✓ Blood group & crossmatch (if severe)

Second-line investigations (guided by suspicion)

Test	Indication
Direct antiglobulin (Coombs) test	Suspected AIHA
G6PD assay*	Suspected G6PD deficiency
Hemoglobin electrophoresis	Suspected sickle cell disease or thalassemia
Osmotic fragility or EMA binding test	Suspected hereditary spherocytosis
Renal function	Suspected HUS
Urinalysis	Hemoglobinuria

*Avoid testing during acute hemolysis or shortly after transfusion if possible, as false-normal results may occur.

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6. Management Algorithm

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Child with anemia

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Evidence of hemolysis?

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Yes

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Assess severity

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Hemodynamically unstable?

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YES
Hospitalize
IV access
Blood transfusion if indicated
Treat underlying cause

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NO

Identify cause

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Immune?
Steroids

↓

G6PD?
Stop trigger
Supportive care

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Hereditary spherocytosis?
Folic acid
Follow-up

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Sickle cell disease?
Hydration
Pain control
Treat complications

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Refer when diagnosis uncertain or severe disease
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7. Drug Summary Table

Condition	First-line treatment
Autoimmune hemolytic anemia	Corticosteroids (Prednisolone **2 mg/kg/day**, max 60 mg/day)
G6PD deficiency	Stop offending drug, hydration, treat infection
Hereditary spherocytosis	Folic acid **1 mg/day**
Sickle cell disease	Hydration, analgesia, antibiotics if febrile
Severe anemia	Packed RBC transfusion (typically **10–15 mL/kg**, guided by clinical status and local transfusion protocols)

Avoid iron therapy unless iron deficiency is confirmed.

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8. Admission Criteria

Admit if:

- Hb <7 g/dL (or symptomatic severe anemia)
- Hemodynamic instability

- Rapidly falling Hb
- Severe jaundice
- Hemoglobinuria
- Acute kidney injury
- Suspected HUS
- Need for transfusion
- AIHA requiring steroids
- Diagnostic uncertainty
- Poor oral intake
- Inadequate outpatient follow-up

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9. Referral Criteria

Refer to pediatric hematology if:

- Newly diagnosed inherited hemolytic anemia
- Positive Coombs test
- Recurrent hemolysis
- Transfusion-dependent anemia
- Splenectomy consideration
- Severe hereditary spherocytosis
- Sickle cell disease
- Unclear diagnosis

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10. Follow-up

Monitor:

- Symptoms
- Hb
- Reticulocyte count
- Bilirubin
- Growth
- Splenic size
- Gallstone symptoms

Long-term:

- Vaccination review (especially if splenectomy is planned or performed)
- Folic acid supplementation for chronic hemolysis

- Family education on triggers (especially G6PD deficiency)
- Genetic counseling when appropriate

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11. Clinical Pearls

Clinical Pearl 1

Reticulocytosis strongly suggests hemolysis or blood loss rather than decreased RBC production.

Clinical Pearl 2

Dark urine indicates intravascular hemolysis until proven otherwise.

Clinical Pearl 3

A positive Direct Coombs test supports autoimmune hemolytic anemia.

Clinical Pearl 4

Splenomegaly favors extravascular hemolysis (e.g., hereditary spherocytosis).

Clinical Pearl 5

Acute hemolysis after infection or certain medications strongly suggests G6PD deficiency.

Clinical Pearl 6

Do not delay transfusion in a child with severe symptomatic anemia while awaiting the final diagnosis.

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12. Common Mistakes in Exams and Practice

❌ Treating every anemia with iron

❌ Forgetting to check the reticulocyte count

❌ Missing a drug history

❌ Missing family history

❌ Forgetting the peripheral blood smear

❌ Ordering a G6PD assay during an acute hemolytic episode without recognizing the possibility of a false-normal result

❌ Delaying transfusion in unstable patients

❌ Missing HUS in a child with anemia after bloody diarrhea

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13. Key Take-Home Messages

1. Think of hemolysis in any child with **anemia + jaundice + elevated reticulocyte count**.
2. The initial workup includes **CBC, reticulocyte count, peripheral smear, bilirubin, LDH, and Coombs test (if immune hemolysis is suspected)**.
3. A careful **drug, infection, and family history** often identifies the underlying cause.
4. **Peripheral blood smear** provides major diagnostic clues (e.g., spherocytes, sickled cells, schistocytes, bite cells).
5. Do **not** prescribe iron unless iron deficiency is proven.
6. **Autoimmune hemolytic anemia** is treated initially with corticosteroids.
7. In **G6PD deficiency**, remove oxidative triggers and provide supportive care.
8. Severe symptomatic anemia requires **urgent hospital admission** and may need packed RBC transfusion.
9. Children with recurrent or inherited hemolytic anemia require **pediatric hematology follow-up**.
10. Always assess for **red flags** such as shock, heart failure, acute kidney injury, or HUS, as these require immediate intervention.