

PEDIATRIC HEMATOLOGY

Approach to Anemia in Children

A Systematic Clinical Framework

Covering: Definition · Classification · Diagnosis · Management

Learning Objectives

By the end of this session, participants will be able to:

1

Define anemia:

Apply age-specific hemoglobin thresholds to correctly identify anemia in infants, children, and adolescents.

2

Classify anemia:

Use a systematic morphologic and pathophysiologic framework to categorize the type of anemia.

3

Build a differential:

Generate an appropriate differential diagnosis based on CBC, indices, smear, and clinical context.

4

Order rationally:

Select and interpret second-line investigations efficiently (iron studies, reticulocyte count, hemoglobin electrophoresis, etc.).

5

Manage & refer:

Initiate evidence-based treatment for common causes and identify red flags requiring hematology referral.

Definition of Anemia

WHO & age-specific hemoglobin thresholds

Anemia is defined as a hemoglobin (Hb) concentration below the lower limit of normal for age and sex, causing reduced oxygen-carrying capacity of the blood. No single threshold applies to all children — context and trend matter.

Age Group	Hb < (g/dL)	Hct < (%)	Clinical Note
Birth (term)	13.5	41	Physiologic nadir at 6–12 wks: Hb 9.5–11 normal
1–6 months	9.5	31	Physiologic anemia of infancy (↑ Hb F → Hb A switch)
6 mo – 2 yrs	10.5	33	Peak risk for iron deficiency
2 – 6 years	11.0	33	Screen at well-child visits
6 – 12 years	11.5	35	Screen girls entering puberty earlier
Girls ≥12 yrs	12.0	36	After menarche, menstrual losses key
Boys ≥12 yrs	13.0	40	Testosterone-driven erythropoiesis

⚡ Always compare Hb to age-appropriate norms. A Hb of 10.5 g/dL is normal at 3 months but severely anemic at 10 years.

Classification of Anemia

Two complementary frameworks — use both together

1. Morphologic (by MCV)

Microcytic MCV < age norm	Normocytic MCV normal	Macrocytic MCV > age norm
<ul style="list-style-type: none">• Iron deficiency• Thalassemia syndromes• Anemia of chronic disease• Lead poisoning• Sideroblastic anemia	<ul style="list-style-type: none">• Acute blood loss• Hemolytic anemias• Aplastic anemia• Anemia of chronic disease• Transient erythroblastopenia	<ul style="list-style-type: none">• B12 / Folate deficiency• Hypothyroidism• Liver disease• Diamond-Blackfan anemia• Drugs (methotrexate, AZT)

2. Pathophysiologic (by mechanism)

Decreased Production	Increased Destruction	Blood Loss
<p>Nutritional deficiencies (Fe, B12, folate, Cu)</p> <p>Bone marrow failure (aplasia, infiltration)</p> <p>Chronic disease / renal failure</p> <p>Congenital: DBA, Fanconi</p>	<p>Membrane defects (spherocytosis, elliptocytosis)</p> <p>Enzyme defects (G6PD, PK deficiency)</p> <p>Hemoglobinopathies (sickle cell, thalassemia)</p> <p>Immune hemolysis (AIHA, HDN)</p>	<p>GI bleeding (Meckel, IBD, polyps)</p> <p>Menorrhagia (adolescent girls)</p> <p>Trauma / surgical</p> <p>Pulmonary (rare)</p>

Clinical tip: Start with MCV to narrow the differential, then use reticulocyte count to distinguish production failure (low retics) from hemolysis/blood loss (high retics). *Reticulocyte Production Index (RPI) = Retic% × (Patient Hb / Normal Hb) ÷ Maturation factor. RPI <2 = hypoproliferative; RPI >3 = hyperproliferative.*

History & Physical Examination

The clinical context shapes the differential diagnosis

Key History Points

- Age of onset (neonatal vs infancy vs adolescence)
- Dietary history: cow's milk excess, vegetarian diet, pica
- Ethnic background: thalassemia, G6PD, sickle cell risk
- Family history: anemia, jaundice, splenectomy, transfusions
- Medication history: NSAIDs (GI blood loss), antimalarials (G6PD hemolysis)
- Stool/urine color: dark urine (hemolysis), melena (GI loss)
- Symptoms: fatigue, dyspnea, dizziness, palpitations, developmental delay

Physical Examination

- Pallor: conjunctival, palmar creases, nail beds (most reliable in dark skin: conjunctiva)
- Jaundice + pallor → hemolytic anemia (check sclera, skin)
- Splenomegaly: hemolytic anemias, thalassemia, storage disorders
- Hepatomegaly: extramedullary hematopoiesis, storage disorders
- Frontal bossing / malar prominence: thalassemia major, severe chronic IDA
- Lymphadenopathy: malignancy, viral (EBV, CMV)
- Petechiae / bruising: bone marrow failure, thrombocytopenia

Initial Investigations

First-line workup — always start here

Complete Blood Count (CBC)

Hb / Hct — confirms anemia
MCV — microcytic / normocytic / macrocytic
MCH, MCHC — hypochromia
RDW — anisocytosis (↑ in IDA, heterogeneous populations)
WBC / Platelet — isolated vs pancytopenia

Peripheral Blood Smear

Hypochromic microcytes, pencil cells → IDA
Target cells, basophilic stippling → thalassemia
Spherocytes → HS or AIHA
Schistocytes → microangiopathy (TTP/HUS)
Blasts → leukemia

Reticulocyte Count

Essential to classify: production failure vs destruction
Raw count + reticulocyte production index (RPI)
RPI <2 → hypoproliferative
RPI >3 → hemolytic or acute loss

Additional First-Line

Serum ferritin + iron + TIBC (if microcytic)
Direct Coombs test (if hemolysis suspected)
Bilirubin, LDH, haptoglobin (hemolysis panel)
Renal function (CKD-related anemia)

★ Smear review is non-negotiable — it often reveals the diagnosis when numbers alone don't. Request it actively.

Diagnostic Algorithm

A step-by-step approach from CBC to diagnosis

CBC + Reticulocyte Count + Smear

MCV LOW → Microcytic

Iron Studies + Ferritin

Low ferritin → IDA
Normal ferritin → ACD / Thalassemia
High ferritin → Inflammation, sideroblastic
→ HPLC / Mentzer if thalassemia suspected

Treat IDA / Refer for Thal

Iron 3–6 mg/kg/day × 3 months
Genetic counseling if thalassemia
Transfuse if Hb <7 + symptomatic

MCV NORMAL → Normocytic

Retic Count + Coombs

Retic LOW → aplasia, TEC, malignancy
→ BMA if pancytopenic
Retic HIGH → hemolysis / blood loss
→ DCT, bilirubin, LDH, haptoglobin

Targeted Therapy

TEC → watchful waiting (resolves)
AIHA → steroids / IVIG
Aplasia → immunosuppression / HSCT

MCV HIGH → Macrocytic

B12 / Folate / TSH

B12/folate LOW → supplement
TSH abnormal → treat thyroid
Hypersegmented PMNs on smear →
megaloblastic
No deficiency → consider DBA / liver disease

Correct Deficiency / Refer

B12 IM / oral supplementation
Folate 1 mg/day
Rare cause → hematology referral

Iron Deficiency Anemia (IDA)

Most common anemia worldwide — a clinical deep dive

Epidemiology & Risk Factors

Age Group

- 6 months – 3 years (peak)
- Adolescent girls (menarche)
- Premature / LBW infants

Dietary Causes

- Excessive cow's milk (>24 oz/day)
- Low iron intake (vegan/vegetarian)
- No fortified foods, no iron drops

GI / Other

- Celiac disease, IBD
- Helicobacter pylori
- Chronic GI blood loss, Meckel's

Diagnostic Criteria

- Low Hb for age + MCV low
- Ferritin <12 µg/L (gold standard; <30 if CRP elevated)
- Serum iron ↓, TIBC ↑, transferrin sat <10%
- RDW ↑ (anisocytosis), smear: hypochromic pencil cells
- Therapeutic trial: Hb ↑ ≥1 g/dL after 4 weeks confirms IDA

Treatment

Oral iron: 3–6 mg/kg/day elemental iron (max 150–200 mg)

Give: Between meals + Vitamin C; avoid with milk/tea

Duration: 3 months AFTER Hb normalizes (to replete stores)

IV iron: Malabsorption, non-compliance, severe anemia

Transfuse: Hb <5–7 g/dL with cardiorespiratory compromise

Prevention: 1 mg/kg/day drops from 4 months (term); 2–4 mg/kg from 2 wks (preterm)

Hemolytic Anemia

Recognize the triad: anemia + jaundice + splenomegaly

Classic Triad: Pallor (anemia) + Jaundice (↑ indirect bilirubin) + Splenomegaly | *Lab:* ↑ LDH, ↑ retics, ↓ haptoglobin, ↑ urine urobilinogen

Membrane Defects

Hereditary spherocytosis (HS)

- spherocytes, ↑ MCHC, osmotic fragility ↑
- Splenectomy if severe

Hereditary elliptocytosis

- mild hemolysis usually

Enzyme Defects

G6PD deficiency

- X-linked, crisis after oxidant stress (infection, fava beans, drugs)
- Heinz bodies, bite cells

Pyruvate kinase deficiency

- AR, chronic hemolysis
- echinocytes (spiculated cells)

Immune Hemolysis (AIHA)

Warm AIHA (IgG)

- Positive DCT, spherocytes
- Treat: steroids, IVIG, rituximab

Cold agglutinin disease (IgM)

- Cold-triggered, intravascular
- Mycoplasma, EBV associated

Microangiopathic (MAHA)

HUS: schistocytes + thrombocytopenia + AKI

- E. coli O157:H7, post-diarrheal
- Supportive; avoid antibiotics

TTP: rare in children

- ADAMTS13 deficiency

✂ **Direct Coombs test (DCT): KEY differentiator** — positive = immune hemolysis; negative = intrinsic RBC defect or MAHA.

Hypoproliferative Anemias

Low reticulocyte count — the bone marrow is failing

Transient Erythroblastopenia of Childhood (TEC)

Most common acquired pure red cell aplasia in children (1–4 yrs)
Follows viral illness; self-limiting (resolves in 1–2 months)
Normocytic, retics low, WBC/PLT normal
Management: watchful waiting; transfuse if symptomatic (Hb <5)

Aplastic Anemia

Pancytopenia + hypocellular bone marrow
Acquired (immune-mediated) > congenital (Fanconi)
Fanconi: chromosomal fragility test (DEB/MMC), radial ray defects
Management: IST (ATG + cyclosporine) or HSCT if matched sibling

Diamond-Blackfan Anemia (DBA)

Congenital pure red cell aplasia (presents in first year of life)
Macrocytic anemia, low retics, elevated HbF, ↑ adenosine deaminase
Physical anomalies (thumb, craniofacial) in ~50%
Treatment: steroids (70% respond), chronic transfusions, HSCT

Anemia of Chronic Disease / CKD

Normocytic normochromic, low retics, normal-high ferritin
Hepcidin ↑ → iron sequestration in macrophages
Underlying disease drives the anemia — treat the cause
CKD: erythropoietin-stimulating agents + IV iron supplementation

★ Any pancytopenia with low retics requires urgent bone marrow aspiration/biopsy to rule out leukemia and aplasia.

Special Populations

Neonatal anemia & adolescent girls — unique considerations

Neonatal Anemia

Hemorrhagic

Fetomaternal hemorrhage (most common)
Twin-twin transfusion syndrome
Internal hemorrhage (liver, adrenal, cephalohematoma)
Umbilical cord complications
→ Low retics, normocytic in acute loss

Hemolytic (HDN)

Rh incompatibility (most severe)
ABO incompatibility (most common)
Minor blood group (Kell, Duffy, Kidd)
G6PD deficiency (triggered by bilirubin lights!)
→ Positive DCT, ↑ bilirubin, ↑ retics

Hypoproliferative

Physiologic anemia of prematurity
(2–8 wks in preterm; Hb nadir ~8–10)
Diamond-Blackfan anemia (rare)
Congenital infections (TORCH)
→ Low retics, usually normocytic

Adolescent Girls — Menstrual Iron Loss

- Screen all adolescent girls annually once menarche begins (AAP recommendation)
- Heavy menstrual bleeding (HMB) affects ~1 in 5 teens; underlying bleeding disorder (vWD) in ~13% of HMB cases
- Evaluate for vWD (PFA-100, von Willebrand factor antigen/activity, FVIII) if IDA + HMB in adolescent
- Treat: oral iron + assess contraceptive options (hormonal therapy ↓ menstrual loss); IV iron if severe or non-compliant

When to Refer / Admit

Recognize the limits of primary care management

Admit / Emergency Referral

- Hb <5 g/dL with any symptoms (tachycardia, poor perfusion, altered consciousness)
- Acute severe hemolysis with rapidly falling Hb
- Aplastic anemia with pancytopenia / febrile neutropenia
- Suspected leukemia or bone marrow infiltration (blasts on smear)
- Hemolytic uremic syndrome (schistocytes + thrombocytopenia + AKI)

Non-Urgent Hematology Referral

- No response to 4–6 weeks of appropriate oral iron therapy
- Thalassemia intermedia or major (confirmed on HPLC)
- Diamond-Blackfan anemia, aplastic anemia workup
- Hereditary hemolytic anemia (spherocytosis, G6PD, PK deficiency)
- Recurrent or chronic hemolysis of unclear etiology
- Suspected sideroblastic anemia or rare congenital disorder

Follow-up Monitoring for IDA Treatment

Timepoint	Test	Expected Finding
2–4 weeks	CBC + retics	Hb ↑ ≥1 g/dL confirms IDA & compliance

Clinical Case Discussion

Apply the framework — think before you turn the page

Case Vignette

A 9-year-old girl presents with 3 months of fatigue and pallor. She is a vegetarian. Exam: pale conjunctivae, mild tachycardia (HR 108), no jaundice, no organomegaly. CBC: Hb 8.1 g/dL, MCV 74 fL, RDW 17.2%, WBC 6.8, Plt 320. Retics 0.9%. Smear: hypochromic cells, anisocytosis.

Step 1: Classify

Microcytic (MCV 74) + normochromic/hypochromic → microcytic anemia. Low retics (0.9%) → hypoproliferative / production problem. No jaundice/organomegaly → not hemolytic.

Step 2: Differential

IDA most likely (vegetarian diet, RDW ↑↑ = anisocytosis). β -Thalassemia trait possible (but RDW usually normal). ACD less likely (no chronic disease).

Step 3: Next test

Serum ferritin + iron + TIBC. If ferritin low (<12 $\mu\text{g/L}$): confirms IDA. If ferritin normal/elevated: consider thalassemia → HPLC + Mentzer Index.

Step 4: Management

Ferritin 4 $\mu\text{g/L}$ → IDA confirmed. Start oral iron 3–6 mg/kg/day + dietary counseling (iron-rich foods + Vitamin C). Recheck CBC in 4 weeks. Treat for 3 months after Hb normalizes.

Key Takeaways

The essentials every clinician must know

- 01 Always use age-specific Hb thresholds — a Hb of 11 g/dL is normal at 2 years but anemic at birth.
- 02 Start with MCV to classify morphologically, then reticulocyte count to distinguish production failure from destruction.
- 03 Iron deficiency is the most common cause globally — but always look for an underlying cause (dietary, GI loss, malabsorption).
- 04 Ferritin is the best single test for iron stores — but it's an acute-phase reactant; interpret alongside CRP.
- 05 Peripheral blood smear is irreplaceable — request it routinely; it often points directly to the diagnosis.
- 06 Pancytopenia + low retics = bone marrow problem until proven otherwise — bone marrow aspiration is indicated.
- 07 Check for Hb response ($\uparrow \geq 1$ g/dL) at 4 weeks after starting iron — this confirms IDA and adequate adherence.

Thank You

Questions & Discussion

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