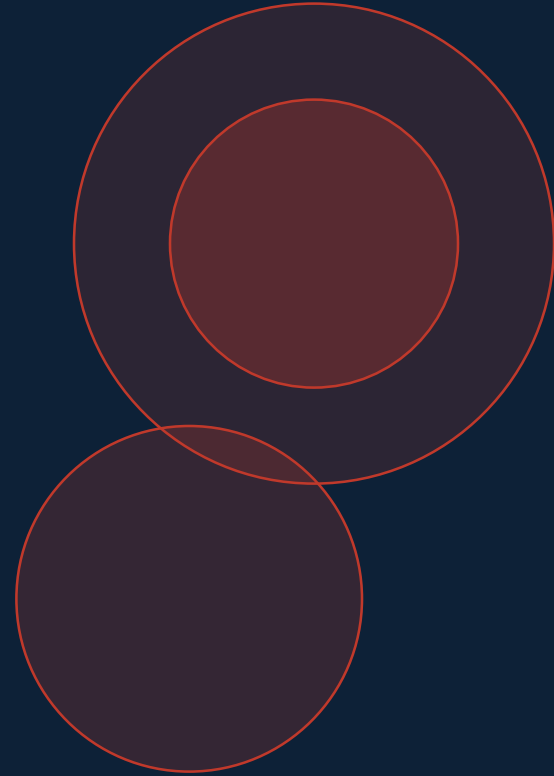


MICROCYTIC ANEMIA

in Children

A Comprehensive Clinical Review



Agenda

What we'll cover in 45 minutes

01

Overview & Definition

5 min

02

Etiology & Classification

7 min

03

Pathophysiology

7 min

04

Clinical Presentation

6 min

05

Diagnostic Approach

8 min

06

Management & Treatment

8 min

07

Complications & Follow-up

4 min

Overview & Definition

What is Microcytic Anemia?

A group of anemias characterized by small red blood cells ($MCV < 2$ SD below the mean for age), typically associated with impaired hemoglobin synthesis. The normal MCV in children is age-dependent, ranging from ~70 fl in infants to ~80 fl in adolescents.

#1

Most Common Nutritional
Deficiency Worldwide

25-50%

Prevalence of Iron-Deficiency
Anemia in Under-5s Globally

5 Types

Major Causes to Distinguish
in Pediatric Practice

Age-specific MCV thresholds for microcytosis: 6 mo–2 yr: <70 fl | 2–6 yr: <73 fl | 6–12 yr: <76 fl | >12 yr: <78 fl (females), <80 fl (males)

Always interpret MCV in the context of the patient's age. Reticulocyte count and RDW help further characterize the anemia.

Etiology & Classification

The '4 I's + Chronic Disease' Framework

Iron Deficiency

75-80%

Most common (75–80%)

- Inadequate dietary intake
- Poor absorption (cow's milk, celiac)
- Blood loss (GI, menstrual)
- Increased demand (prematurity, growth spurts)

Inflammation / ACD

10-15%

Anemia of Chronic Disease

- Infection, autoimmune disease
- IBD, JIA, malignancy
- Hepcidin-mediated iron sequestration
- Usually mild-moderate (Hb 8–10)

Inherited Disorders

5-10%

Thalassemia / Hemoglobin variants

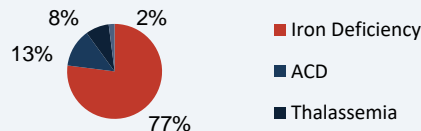
- α -thalassemia trait (silent, mild)
- β -thalassemia trait (target cells)
- HbE disease or HbC trait
- Family history, ethnic background key

Iron Transport Defects

<2%

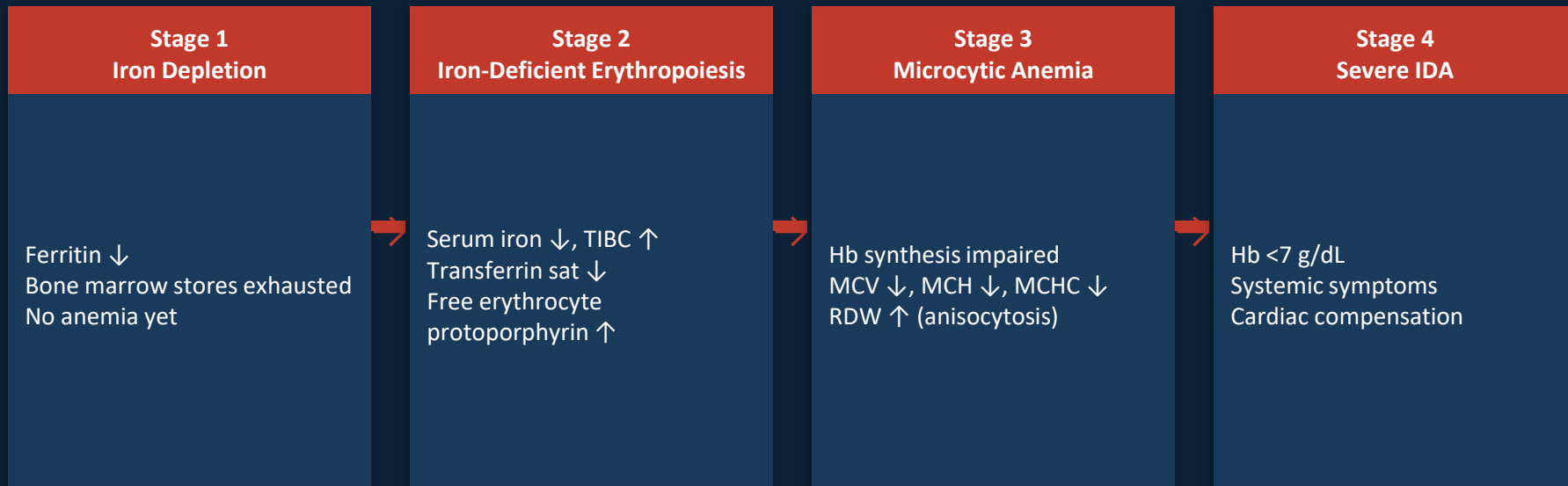
Rare causes

- Sideroblastic anemia (ring sideroblasts)
- Lead poisoning
- Copper deficiency
- IRIDA (TMPRSS6 mutation)



Pathophysiology

Iron Deficiency — The Core Mechanism



Hepcidin Regulation in ACD vs IDA:

IDA: Hepcidin LOW → iron absorption ↑ from gut, iron released from macrophages | **ACD:** Hepcidin HIGH (IL-6 driven) → iron trapped in RES, absorbed iron sequestered → functional iron deficiency

Pathophysiology

Thalassemia Syndromes — Globin Chain Imbalance

α-Thalassemia (HBA1 / HBA2 deletions)

Genotype	Lab Findings	Severity
Silent carrier (1 gene)	Hb A, normal MCV	None
α-thal trait (2 genes)	Mild microcytosis, normal Hb	Mild
HbH disease (3 genes)	HbH inclusions, hemolysis	Moderate
Hydrops fetalis (4 genes)	Hb Bart, incompatible with	Fatal

β-Thalassemia (HBB mutations)

Phenotype	Features	Severity
β-thal minor (trait)	↑ HbA2 >3.5%, mild anemia	Mild
β-thal intermedia	Hb 7–10, splenomegaly	Moderate
β-thal major	Hb <7, transfusion-dependent	Severe

⚡ Key Distinguishing Points

- Thalassemia trait: Low MCV but NORMAL or NEAR-NORMAL Hb (unlike IDA where Hb falls proportionally)
- Mentzer Index: $MCV \div RBC \text{ count}$ — <13 suggests thalassemia; >13 suggests IDA (sensitivity ~85%)
- Thalassemia trait: Low RDW (uniform small cells); IDA: HIGH RDW (heterogeneous population)

Clinical Presentation

Recognize the spectrum — from subtle to severe

General & Hematologic

- Pallor (conjunctival, palmar)
- Fatigue, decreased exercise tolerance
- Tachycardia, flow murmur
- Splenomegaly (thalassemia)

Neurodevelopmental

- Irritability, poor concentration
- Developmental delay (severe/chronic)
- Breath-holding spells
- Pica (ice, dirt, starch)

Nutritional Red Flags

- Excessive cow's milk (>24 oz/day)
- Poor dietary iron intake
- Exclusively breastfed >6 months without iron
- Prematurity / low birth weight

Severe / Thalassemia Major

- Frontal bossing, malar prominence
- Maxillary overgrowth, dental malocclusion
- Growth retardation
- Hepatosplenomegaly, jaundice

⚡ **Clinical Pearl: Conjunctival pallor is more sensitive than palmar pallor in darker-skinned children. Use it as your primary screening tool.**

Diagnostic Approach

Step 1: CBC & Peripheral Smear Interpretation

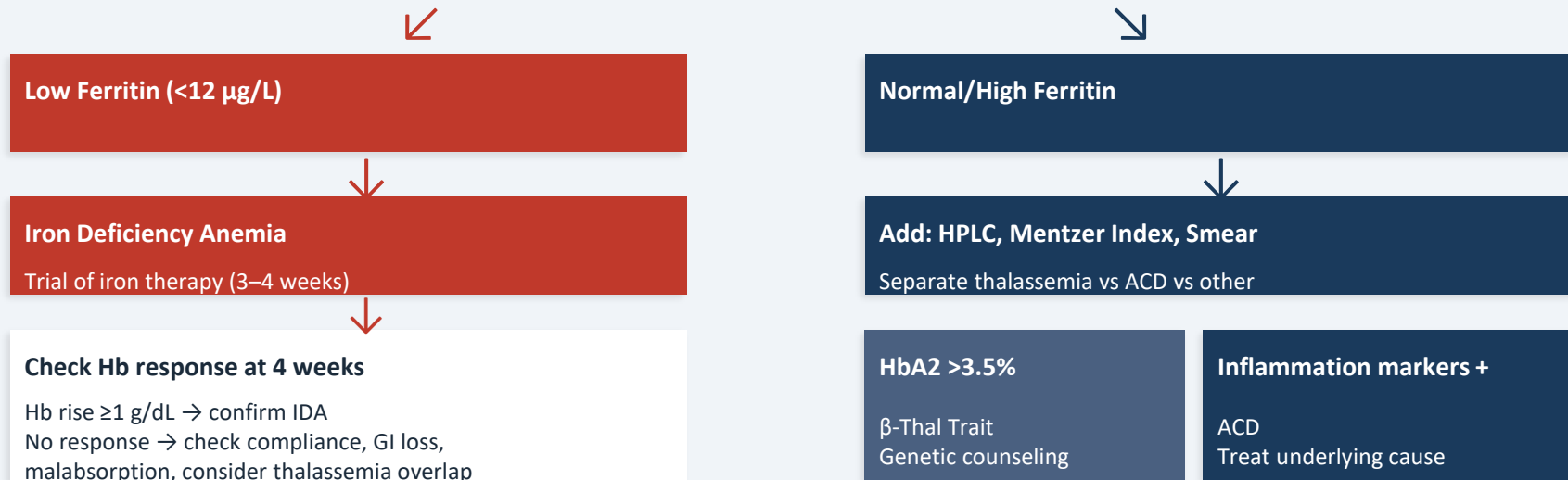
Parameter	IDA	ACD	β-Thal Trait	Lead Poisoning
MCV	↓↓	↓ or normal	↓↓	↓ or normal
Hb	↓	↓ (mild-mod)	Normal/↓	↓
RDW	↑↑ (>14%)	Normal/↑	Normal	↑
Serum Iron	↓↓	↓	Normal	↑↑
Ferritin	↓↓ (<12)	↑ or normal	Normal	Normal/↑
TIBC	↑↑	↓ or normal	Normal	Normal
Transferrin sat	↓ (<10%)	↓	Normal	↑
HbA2 (HPLC)	Normal	Normal	↑↑ (>3.5%)	Normal

Smear findings: IDA → hypochromia, pencil cells | Thalassemia → target cells, basophilic stippling | Lead → basophilic stippling prominent | Sideroblastic → dimorphic population

Diagnostic Algorithm

Step-by-step workup for microcytic anemia in children

Step 1: CBC + Reticulocyte Count



📌 When to refer to hematology: Hb <7 g/dL, failure to respond to iron, suspected thalassemia major/intermedia, Hb <10 in neonate, abnormal HPLC pattern, or family history of hemoglobinopathy.

Management & Treatment

Iron Deficiency Anemia — Evidence-Based Therapy

Oral Iron — First-Line Treatment

Dosing (elemental iron):

- Infants/toddlers: 3–6 mg/kg/day ÷ 1–2 doses
- Children: 3–6 mg/kg/day (max 150–200 mg/day)
- Adolescents: 60 mg TID or 120 mg twice daily

Administration tips:

- Give on empty stomach or with Vitamin C
- Avoid with milk, tea, antacids
- Duration: 3 months after Hb normalizes
- Alternate-day dosing may ↑ absorption (↓ hepcidin spike)

IV Iron — When Oral Fails

Indications:

- Malabsorption (celiac, IBD, post-surgical)
- Non-compliance or intolerance to oral iron
- Severe symptomatic anemia needing rapid correction
- Ongoing losses exceeding oral replacement

Agents used in children:

- Ferric carboxymaltose (FCM) — preferred
- Low-molecular-weight iron dextran
- Ferric gluconate (for infants)
- Monitor for hypersensitivity reactions

Blood Transfusion Thresholds

Symptomatic anemia (Hb <5–7 g/dL) with cardiorespiratory compromise | Packed RBCs 10–15 mL/kg over 3–4 hrs | *Avoid rapid transfusion in compensated chronic anemia (risk of cardiac overload)*

Management & Treatment

Thalassemia Major & Anemia of Chronic Disease

β-Thalassemia Major

Regular transfusions:	Every 3–4 weeks; target pre-transfusion Hb 9–10.5 g/dL
Iron chelation:	Deferoxamine, deferasirox, deferiprone — start after 10–20 units transfused
Splenectomy:	Consider if transfusion requirement ↑ by >50% or massive splenomegaly
HSCT:	Curative — best outcomes in young, well-chelated patients with matched sibling donor
Gene therapy:	Betibeglogene — approved for non-β0/β0 genotype; emerging option

Anemia of Chronic Disease (ACD)

Primary strategy:

Treat the underlying condition (infection, IBD, JIA)
Anemia typically resolves with disease control

Adjunct:

Erythropoiesis-stimulating agents (ESAs) if CKD
IV iron if coexistent iron deficiency
Restrict transfusion unless Hb <7 or symptomatic

Prevention of IDA in Infants

- Term infants: iron-rich foods from 6 months; AAP recommends 1 mg/kg/day drops from 4 months
- Preterm (<34 wks): 2–4 mg/kg/day from 2 weeks of life
- Limit cow's milk to <24 oz/day in toddlers
- Universal screening at 12 months (AAP) and repeat at 15–18 months

Complications & Follow-up

Long-term consequences and monitoring plan

Cognitive & Behavioral

Irreversible neurodevelopmental impairment if chronic in <2 yrs
Poor academic performance, attention deficits
Altered dopamine neurotransmission

Cardiovascular

High-output cardiac failure (severe)
Hyperdynamic circulation, cardiomegaly
Flow murmur → resolves with treatment

Immune Function

Impaired T-cell proliferation
Decreased bactericidal activity
Increased susceptibility to infections

Follow-up & Monitoring Schedule

Test	Timing	Goal
CBC + Reticulocytes	2–4 weeks after treatment	Confirm ↑ Hb ≥ 1 g/dL → confirms diagnosis
CBC + Iron studies	3 months (mid-treatment)	Hb should normalize; iron stores rebuilding
CBC + Ferritin	3 months post-completion	Confirm replete stores (ferritin >20–30 $\mu\text{g/L}$)
Developmental screening	At each well-child visit	Especially for children diagnosed <2 years

Clinical Case Summary

Bringing it all together — a practical approach

Case Vignette

A 14-month-old boy is brought in for pallor and irritability. He drinks 32 oz of cow's milk daily and eats little solid food. Exam: pale conjunctivae, HR 130, soft systolic murmur. CBC: Hb 7.8 g/dL, MCV 62 fL, RDW 18.5%. Smear: hypochromic, microcytic cells, occasional pencil cells.

Diagnosis?

Iron Deficiency Anemia (classic presentation — excessive cow's milk, high RDW, hypochromic/microcytic smear)

Immediate workup?

Serum ferritin, serum iron, TIBC, transferrin saturation. (No HPLC needed yet — IDA is most likely)

Treatment?

Oral elemental iron 3–6 mg/kg/day + reduce cow's milk to <16 oz/day + iron-rich foods + Vitamin C with meals

Follow-up?

Recheck CBC + reticulocytes in 2–4 weeks. Expect Hb rise ≥ 1 g/dL. Treat for 3 months after Hb normalizes.

Key Takeaways

Remember these 6 clinical essentials

- 01 Iron deficiency is the most common cause (~75%) — always consider dietary history and cow's milk intake first.
- 02 MCV must be interpreted for age — a 'normal' MCV of 75 fl is microcytic in a 14-month-old.
- 03 Distinguish IDA from thalassemia trait: RDW high in IDA (anisocytosis), normal in thalassemia; Mentzer Index <13 suggests thalassemia.
- 04 Ferritin is the single best test for iron stores — but it's an acute-phase reactant; interpret with CRP in inflammation.
- 05 Check the Hb response at 4 weeks — a rise of ≥ 1 g/dL confirms IDA and adequate treatment adherence.
- 06 Chronic untreated IDA in children <2 years causes irreversible neurodevelopmental harm — screen and treat early.

Thank You

Questions & Discussion

Selected References

- Baker RD, et al. AAP Clinical Report: Diagnosis and Prevention of Iron Deficiency and IDA in Infants and Young Children. Pediatrics 2010.
- WHO. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. 2011.
- Cappellini MD, et al. Guidelines for the Management of Transfusion Dependent Thalassaemia (TDT). TIF 2021.
- Camaschella C. Iron-deficiency anemia. NEJM 2015; 372:1832–1843.