

What is appropriate management of iron deficiency for young children?

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EVIDENCE-BASED ANSWER

Infants and toddlers with suspected iron-deficiency anemia (IDA) should begin treatment with oral ferrous sulfate (3 mg/kg/d of elemental iron). A rise in hemoglobin >1 g/dL after 4 weeks supports the diagnosis of iron deficiency, and supplementation should continue for 2 additional months to replenish iron stores. Recheck hemoglobin at the end of treatment and again 6 months

later (strength of recommendation [SOR]: **C**, based on expert opinion).

For primary prevention, counsel parents on the use of iron-fortified formula for non-breastfed infants until the age 12 months (SOR: **B**, based on randomized controlled study), and introduce iron-rich foods between 4 and 6 months to breastfed babies (SOR: **C**, based on expert opinion).

CLINICAL COMMENTARY

If you need reassurance, check CBC and reticulocytes 1 week after start of iron therapy

While the evidence supports the empiric approach, hemoglobin <11 g/dL has only a 29% positive predictive value for IDA. To obtain quick reassurance the diagnosis is correct, the pediatric faculty of our residency program advocates checking a complete blood count and a reticulocyte count 1 week after beginning iron therapy. By then, if the hemoglobin level stays the same or

shows a small increase and the reticulocyte level is elevated, the diagnosis is confirmed.

When advising parents on how much iron to give their child, remember that 3 mg of elemental iron is contained in 15 mg of ferrous sulfate. The common over-the-counter liquid ferrous sulfate product contains 15 mg of elemental iron per 0.6-mL dropper. Thus, a 10-kg child would require a 0.6-mL dropper twice a day.

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Evidence summary

Depletion of iron stores leads to IDA, which, among children, is associated with motor and cognitive deficits that may be irreversible. Little is known about whether iron deficiency, in the absence of anemia, results in physiologic sequelae. A Cochrane review of iron therapy for children with IDA aged >3 years found no

short-term (5–11 days) improvement in Bayley scores of mental and motor development following iron therapy.¹ A 10-year longitudinal cohort study in Costa Rica found that adolescents treated for severe chronic IDA in infancy (n=48) scored 0.4 to 0.7 standard deviations lower on cognitive and motor testing relative to controls (n=114).² In an Indonesian randomized

FAST TRACK**Iron deficiency should be the presumptive diagnosis in a child with anemia; give elemental iron because of its low cost and tolerability**

controlled trial (RCT), baseline Bayley scores were 10% to 15% lower ($P<.01$) for infants (12–18 months) with IDA compared with both nonanemic iron-deficient and iron-sufficient infants.³ Following treatment with ferrous sulfate (3 mg/kg/d of elemental iron) for 4 months, the IDA infants' Bayley scores improved compared with those of nonanemic children.

Consensus recommendations suggest that iron deficiency should be the presumptive diagnosis in a child with anemia, and that a trial of ferrous sulfate at a dose of 3 mg/kg/d of elemental iron be instituted because of low cost, tolerability, and relative simplicity.^{4,5} In a prospective study of 75 1-year-olds with anemia (hemoglobin <11.0 g/dL), 45% achieved an increase in hemoglobin ≥ 1 g/dL after 3 months of iron therapy (3 mg/kg/d).⁶ An RCT of 278 nonanemic 1-year-olds found no difference in adverse effects from this dose compared with placebo.⁷ However, an analysis of data from NHANES III showed that a Hgb <11.0 had a positive predictive value of just 29% and sensitivity of 30% for diagnosing iron-deficiency in children aged <3 years.⁸

The recommended dose of 3 mg/kg/d was derived from models of bioavailability and iron needs⁹; no studies compare alternative doses. An RCT of 557 anemic children under 24 months of age in Ghana demonstrated that ferrous sulfate (5 mg/kg/d) given once daily was equivalent to 3-times-daily dosing in terms of effectiveness (61% vs 56%) and tolerance.¹⁰ Less frequent dosing has been studied in developing countries with mixed results.

Because anemia may lead to developmental impairment, primary prevention is critical. In a cohort study, infants given iron-fortified formula ($n=98$) were less likely to become iron-deficient by their 12-month visit than infants fed whole cow milk ($n=69$) (11.2% vs 24.6%, number needed to treat [NNT]=8).¹¹ In a RCT of inner-city children who had been switched to cows' milk by 6 months, half ($n=50$) were randomized to receive iron-fortified formula for another year, resulting in a decreased risk of anemia at 24 months

(0% vs 26%, NNT=4), and smaller declines in developmental functioning compared with those on cows' milk.¹²

Recommendations from others

The CDC and the Institute of Medicine recommend parental dietary counseling, treatment with oral ferrous sulfate at 3 mg/kg/d for 3 months to restore iron stores, and monitoring of hemoglobin or hematocrit to assess response.^{4,5} To prevent IDA, the American Academy of Pediatrics (AAP) recommends that all infants who are not breastfed or are partially breastfed should receive an iron-fortified formula (containing between 4.0–12 mg/L of iron) from birth to 12 months. The AAP also recommends that parents should refrain from feeding cow's milk to infants until after age 12 months and introduce iron-enriched foods between ages 4 and 6 months.¹³

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