CLINICAL REPORT Guidance for the Clinician in Rendering Pediatric Care

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Prevention, Screening, Diagnosis, and Treatment of Iron Deficiency and Iron Deficiency Anemia in Infants, Children, and Adolescents: Clinical Report

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This clinical report includes strategies for the prevention of iron deficiency (ID) and iron deficiency anemia (IDA), updates for screening, as well as diagnostic and treatment recommendations. It relates broadly to children, from birth through adolescence, affected by either nutritional ID or IDA attributable to insufficient dietary iron, malabsorption, or loss of iron from heavy menstrual, gastrointestinal, or other external blood loss. Recommended diagnostic strategies emphasize important features of the history, physical examination, and informative laboratory tests available to both generalists and subspecialists. Treatment of children with ID, mild IDA, and moderate or severe IDA or when IDA is refractory or recurrent is discussed. Recommendations regarding oral iron therapy and intravenous iron treatment options are described.

INTRODUCTION

Iron is a critical micronutrient that contributes to energy metabolism, neurodevelopment, and red blood cell production.[1] Ensuring that iron remains in balance, or being "iron sufficient," supports these important physiologic processes in developing infants, children, and adolescents.

Iron deficiency anemia (IDA) remains prevalent in the United States despite sustained prevention efforts.[2] Data from the National Health and Nutrition Examination Survey from 2003 to 2010 indicated that iron deficiency (ID), defined as low total body iron stores, affected approximately 15% of toddlers and 11% of nonpregnant female adolescents (Note: Throughout this report, the gender terminology in the cited

abstract

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literature is used; however, the American Academy of Pediatrics acknowledges that some adolescents who menstruate do not identify as female, and some adolescents who were assigned male sex at birth do not identify as male. Gender-neutral language is used where possible).[3] ID progresses to frank IDA in as many as 3% of toddlers and 5% of female adolescents.[4] Alaska Native toddlers, Latino/Latinx toddlers and adolescents, and African American adolescents are disproportionately affected, not directly related to their racial or ethnic group but rather to nonmedical drivers of health.[5,6]

The 2010 American Academy of Pediatrics (AAP) clinical report on screening and prevention of ID and IDA in children up to 3 years of age addressed appropriate iron intake for young children as well as prevention efforts and screening methods. This report replaces the previous version and reviews strategies to prevent ID, updates screening recommendations based on clinical risk factors by age and biological sex, and provides information on best practice, based on available literature and expert opinion, regarding both diagnostic and treatment approaches for infants, children, and adolescents with IDA.

DEFINITIONS

- Preterm infant: <37 weeks' gestational age at birth
- Term infant: ≥37 weeks' gestational age at birth
- Infancy: birth until <12 months of age
- Toddlers/early childhood: age ≥12 months until <5 years
- School age/middle childhood: age ≥5 until <11 years
- Adolescence: age ≥11 until <21 years
- Iron deficiency: low iron status, which may occur with or without anemia
- Anemia: hemoglobin (Hb) concentration below the normal threshold for age and sex
- Iron deficiency anemia: anemia attributable to low iron status

PREVENTION

Delayed cord clamping in vigorous term and preterm infants at the time of delivery may decrease the risk of ID in early childhood. This practice is recommended by the American College of Obstetrics and Gynecology (ACOG) and endorsed by the AAP.[7] Because data on long-term outcomes are limited, it is unknown whether delayed cord clamping alone is sufficient enough to alter current guidelines on iron supplementation for infants.[8]

Preterm infants receiving full enteral feeds should begin iron fortification or supplementation by 2 weeks of life to ensure iron intake of 2 to 3 mg/kg/d. Despite greater iron bioavailability from human milk vs formula and other forms of milk, prolonged exclusive breastfeeding greater than 6 months is associated with an increased risk of ID.[9] The AAP recommends that term infants who are exclusively breastfed receive iron supplementation (1 mg/kg/d) by 4 months of age. Alternatively, some caregivers may wish to wait with iron supplementation until 6 months of age when complementary foods containing iron are introduced. The role of high iron-containing solid foods in early childhood (eg, iron-fortified cereals, meats) should be reviewed with families when the infant is 6 months of age and older.[10,11] Cow milk (or milk alternatives) —in lieu of human milk or formula—should *not* be offered prior to 12 months of age to any infant (preterm or term). Children after their first birthday and younger than 5 years should receive a diet with sufficient quantities of iron–rich foods with milk (inclusive of both cow milk and plant-based milk alternatives) limited to less than 24 ounces per day.[12] Dietary recommendations for the prevention of ID should be discussed during well-child visits.[13] Early introduction of sources of heme iron, including meat (red meat, poultry, and fish) and/or non-heme iron (legumes, fortified cereals, and pastas) can be valuable in the prevention of ID in older infants and toddlers. Infants or children up to 5 years of age who are at nutritional risk may be referred to the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) to assist with provision of nutritious iron-rich foods and nutrition education. In resource-limited settings outside the United States, multinutrient fortification of foods and/or the use of iron-containing micronutrient powders may be recommended to reduce the prevalence of anemia and ID in young children.[14,15]

Older school-aged and adolescent children should be encouraged to consume a variety of iron-rich foods such as lean meat and poultry, beans, leafy green vegetables, and iron-fortified grains, cereals, and pastas. Adolescents who are nearing or have reached menarche, in particular, require higher iron intake given their risk of ID and IDA resulting from rapid growth and menstrual blood loss. Parents of children who follow vegetarian or vegan diets should be educated about including foods in the diet that are rich in non-heme iron. Additional dietary recommendations from the AAP for all pediatric age groups are provided in Chapter 18: Iron, in the 9th edition of *Pediatric Nutrition*.[16]

SCREENING

Rationale

ID is a multisystem condition with a wide range of clinical features and sequelae, including effects on neurologic, cardiac, and immunologic functioning.[1,17–19] Anemia, the extreme manifestation of ID, becomes apparent after tissue iron stores are depleted. Studies in the United States that evaluate the optimal timing for ID and IDA screening and outcomes of such screening, including the attainment of normal hematologic indices and effects on overall health and neurodevelopmental outcomes, are needed in young

children and female adolescents.[20] However, ID in infancy and early childhood, with or without frank anemia, has been associated with negative neurodevelopmental effects that may persist into adulthood.[19,21–23] Unrecognized ID can progress to anemia, and more severe and/or chronic IDA may be associated with poorer outcomes. Early identification and prompt treatment of ID and IDA with iron may mitigate its negative effects. In adolescents with ID, iron supplementation may improve verbal learning and concentration.[21,24] Iron treatment has also been associated with improvements in fatigue as well as some neurologic and sleep conditions such as restless legs syndrome or periodic limb movement disorder.[25–28] These observations provide the rationale for the AAP recommendations for screening and treatment of ID and IDA from infancy through adolescence.[2,29]

Infants and Young Children

Universal ID and IDA screening is recommended for all infants and young children between the ages of 9 and 18 months. Screening should occur at the age at which the child is most at risk for ID, on the basis of the primary source of nutrition (human milk vs iron-fortified formula) during the first year of life.

Screening at 9 to 12 Months

Infants receiving human milk as a primary source of nutrition during the first year of life, particularly if they have not received sufficient iron supplementation via iron drops or iron-fortified foods, are at risk for ID during this period. Therefore, screening for ID and IDA at 9 to 12 months of age is recommended for all infants receiving human milk as a primary source of nutrition.

Screening at 15 to 18 Months

Infants receiving an iron-fortified formula during the first year of life are at lower risk for ID and IDA at 1 year of age. The majority of these infants transition from iron-fortified formula, which provides 5 to 9 mg/d of iron, to cow milk, which provides <1 mg/d of iron, at 1 year of age, resulting in a significant reduction of iron intake. Plant-based milk alternatives, which include but are not limited to soy, oat, and almond milk, are similarly low in iron content. Assessments of dietary patterns in this age group have demonstrated inadequate iron intake at the time of this transition, creating a period during which a child is vulnerable for development of ID during the second year of life.[30]

Thus, for infants receiving iron-fortified formula as the primary source of nutrition during the first year of life, screening for ID and IDA is recommended at 15 to 18 months of age. Screening at this age is more likely to yield abnormal findings in toddlers who have transitioned from iron-fortified formula to milk (cow or plant-based) and drink in excess of 24 ounces of milk per day.[31]

Screening Based on Clinical Risk Factors

Children should be assessed for the presence of clinical risk factors for ID and IDA, specifically excessive milk intake (cow and/or plant-based) and/or inadequate intake of iron-containing complementary foods, and obesity, at each subsequent well child assessment until 4 years of age. Nonmedical drivers of health can also increase the risk of ID and IDA, such as low socioeconomic status, refugee status, or food insecurity.[3,5,32–34]

Female Adolescents

Screening at 14 Years

Of all children, female adolescents have the highest prevalence of ID and IDA, with the most common cause being excessive menstrual blood loss.[24,35] Current anemia screening questionnaires may lack sensitivity to predict who is at particular risk of being iron deficient.[36] Large case series have demonstrated that unrecognized ID or mild IDA may progress to severe anemia resulting in the need for emergent care and/or inpatient hospitalization.[6,37] Therefore, the AAP recommends universal laboratory screening for ID in all adolescents who are at least 1 year postmenarche but no later than 14 years of age.[38]

Subsequent laboratory screening should be performed based on the presence of clinical symptoms (eg, pica, fatigue) and/or risk factors (eg, low-iron diet, abnormal uterine bleeding including heavy menstrual bleeding, history of blood donation) assessed at annual well-child visits in all female adolescents and young adults.[39]

School-Aged Children and Male Adolescents

There is low prevalence of ID in school-aged children and male adolescents. In children with concerns or the presence of an underlying gastrointestinal condition or blood loss, other external blood loss, low-iron diet, and/or history of blood donation, laboratory screening for ID may be considered.

Laboratory Screening

Screening to identify children and adolescents with ID and IDA includes (1) a complete blood cell count (CBC), which measures the Hb and red blood cell indices such as mean corpuscular volume (MCV) and red blood cell distribution width (RDW); and (2) serum ferritin (SF), an indirect estimate of iron stores.[20,40] Performing both studies allows for appropriate treatment initiation in patients with IDA as well as in those patients with ID prior to onset of anemia.[41] If a CBC and SF cannot be obtained given the potential barriers in performing such laboratory studies, then screening Hb should be performed, at a minimum. If initial screening by CBC or Hb alone is abnormal, additional testing with SF should be performed to confirm ID. A table of normal CBC parameters is provided (Table 1).[42]

TABLE 1. Normal Hematologic Parameters in Infants, Children, and Adolescents by Age and Sex, From Age 9 Months to 18 Years[42]								
	6 to 24 mo		2 to 6 y		6 to 12 y		12 to <18 y	
	Females	Males	Females	Males	Females	Males	Females	Males
Hemoglobin, g/dL	11.0–13.5	11.0–13.4	11.0–13.6	11.0–13.7	11.2–14.5	11.3–14.6	11.4–14.7	12.4–16.4
Mean corpuscular volume, fl	73.3–83.2	71.1–82.2	75.2–85.0	74.1–84.3	78.3–87.7	77.8–86.5	80.5–91.8	80.4–90.1
Red cell distribution width, %	12.2–15.4	12.4–15.9	11.9–14.5	12.1–14.7	11.9–13.9	11.9–13.7	11.9–14.6	11.9–13.7

Therapeutic Trial of Iron

If it is not feasible to conduct SF testing, children with mild anemia may be started on a trial of therapeutically dosed oral iron therapy with assessment in response after 1 month. An appropriate response is the normalization of Hb (in mild anemia) or an improvement of at least 2 g/dL (in moderate or severe anemia). In children who do not demonstrate such a response, assessment of SF or other evaluations to identify the cause of anemia is indicated prior to continuing iron therapy.

DIAGNOSIS

Clinical History, Risk Factors, and Symptoms

A patient's clinical history—specifically symptoms of pallor, fatigue, or pica—as well as dietary history (low intake of iron-rich foods) and an assessment for external blood loss (menstrual, gastrointestinal, blood donation) can provide important information about risk factors for development of ID and IDA (Table 2). Obesity is also associated with ID, which may be attributable to impaired iron absorption from higher hepcidin levels, increased iron demands to support higher body mass, and/or insufficient dietary iron intake.[43,44] One or more positive risk factors or symptoms associated with ID and IDA, such as progressive fatigue (increased naps or fussiness in young children), shortness of breath, headache or dizziness (in adolescents), should prompt laboratory assessment. Symptoms of pica may include eating or chewing on dirt, rocks, paper, wipes, and cardboard in young children and ice, tissue, or other starchy nonfood items in older adolescents. Although also experienced by children with sickle cell disease and neurodevelopmental disorders, assessment of iron status is prudent for any child experiencing pica. For most affected children and adolescents, a positive clinical history of ID risk factors combined with microcytic anemia confirms the diagnosis.

Physical Examination

Children with IDA share some nonspecific physical findings with other forms of anemia (including tachycardia and conjunctival, nail bed, and skin pallor), especially when it is moderate to severe. Parents of children with olive skin tones may report that their child appears pale, sallow, or more yellow than usual. Because IDA usually develops gradually over time, many parents may not notice changes

TABLE 2. Clinical History Consistent With or Concerning for Iron Deficiency or Iron Deficiency Anemia	
Clinical History	**Comment or Examples**
Diet	
Excessive milk intake	>24 ounces per day of cow milk and/or plant-based milk alternatives
Early introduction of cow milk	Prior to 12 mos; cow milk and/or plant-based milk alternatives
Low-iron fortification formula	"Lower iron" branded formula
Vegetarian or vegan diet	Assess for inclusion of nonheme iron-rich foods within diet
Blood Loss	
Gastrointestinal	Gross or occult
Menstrual	Heavy and/or irregular menstrual bleeding
Donation	Risk increases in regular adolescent blood donors
Other external sites	Recurrent epistaxis
Symptoms of IDA	
Pica	Craving for ice (pagophagia), dirt, paper, starch, or other, often crunchy, nonfood items
Fatigue	May be present with ID with or without anemia
Syncope	Moderate to severe anemia
Irritability	Usually associated with other manifestations
Poor concentration/attention difficulties	Poor school performance; inattention; lack of interest in activities
Sleep or neurologic conditions	Restless legs syndrome or periodic limb movement disorder

TABLE 3. Differential Diagnosis of Children With Microcytic Anemia

Diagnosis	Clinical History	Laboratory Measurements	Distinguishing Features
Iron deficiency anemia	Low-iron diet Blood loss	Elevated RDW Low SF	Improvement with oral iron
Alpha thalassemia trait	Not consistent with IDA Family history Ancestry	Normal iron panel Presence of Hb Bart's on newborn screen	Minimal to no change with oral iron
Beta thalassemia trait	Not consistent with IDA Family history Ancestry	Normal iron panel Elevated Hb A2 on hemoglobin analysis	Minimal to no change with oral iron
Anemia of inflammation or chronic disease	Recent acute and/or chronic illness Tissue injury Severe and/or chronic inflammation	MCV may be normal or low Elevated SF; transferrin or TIBC may be low Soluble transferrin receptor (sTfR)/$\log_{10}$ ferritin index low	May benefit from IV iron if symptomatic or anemia severe

Children with a mild microcytic anemia and normal RDW may have a form of thalassemia trait. Alpha thalassemia trait may be diagnosed during the newborn period by the presence of hemoglobin Bart's on newborn screening. In contrast, beta thalassemia trait is diagnosed after 6 months of age by hemoglobin analysis by the presence of elevated Hb A2. In patients with concomitant iron deficiency and suspected thalassemia trait, the iron deficiency should be fully corrected prior to performing hemoglobin analysis.

in skin color. In the setting of severe anemia, cardiac examination often reveals a systolic flow murmur associated with tachycardia. In extreme cases, patients may develop high-output cardiac failure. However, many children with chronic well-compensated anemia demonstrate few findings and may have a normal physical examination. A normal examination should not be used to exclude a diagnosis of IDA. Lymphadenopathy, hepatosplenomegaly, bruising, petechiae, or jaundice are not features of IDA, so if present, should prompt evaluation for other etiologies of the anemia.

Laboratory Diagnosis of IDA

Complete Blood Cell Count

The most valuable laboratory test in children with suspected IDA is the CBC, in which the blood cells are measured using an automated cell counter. Hb values should be interpreted in the context of normal values for age, and the effect of altitude on Hb should be considered in areas of high elevation. Anemia along with microcytosis, a reduced MCV, and an elevated RDW is most consistent with the diagnosis of IDA. Thalassemia trait or chronic inflammation may also result in microcytic anemia with elevated RDW and, thus, may complicate the diagnosis. Historical features and laboratory assessments that may distinguish these conditions from IDA are presented in Table 3. Alpha thalassemia trait may be detected in the newborn period by the presence of Hb Bart's on the newborn screen, if a high enough amount is present, and/or by Hb analysis. Outside the newborn period, confirmation of the diagnosis can only be made by globin sequencing. Such testing is generally expensive and has limited impact on the patient's clinical course; some families may request it for genetic counseling purposes. In contrast, beta thalassemia trait can be diagnosed by Hb analysis after 6 months of age by demonstrating an elevated percentage of Hb A2. Because presence of ID confounds results of Hb electrophoresis testing (falsely normalizing the Hb A2) in children for whom both diagnoses are being considered (based on family history or low SF), treatment of IDA should be undertaken first and results assessed prior to definitive testing.

Iron Studies

A number of iron laboratory measures are available. Although no single test is 100% definitive in diagnosing ID, this section reviews the indications, limitations, and interpretations of these measures (Table 4).[45] SF concentration is considered the best indirect estimate of total body iron stores. A low SF is diagnostic of ID. There is wide variability in reported normal values for SF. Longstanding SF thresholds for diagnosed ID (10 to 12 ng/mL) were based on very small sample size studies.[41,46] A 2017 study in 1200 children found that SF levels of 17.9 to 23.7 ng/dL corresponded to higher Hb values and may be more physiologically relevant values compared with existing norms.[41] Similar results were found on an analysis of data from the National Health and Nutrition Examination Surveys.[47] The 2020 World Health Organization "Guideline on Use of Ferritin Concentrations to Assess Iron Status in Individuals and Populations" recommends a threshold of <12 ng/mL for young children and <15 ng/mL for children 5 years and older.[48] New guidance from the American Society of Hematology suggests an SF≤20 ng/mL for young children and SF≤30 ng/mL for all menstruating individuals.[49] On the basis of this guidance, available data, and clinical expertise, the AAP therefore recommends that an SF level of ≤20 ng/mL indicates ID for young and school-aged children; an SF level of ≤30 ng/mL indicates ID for adolescents and all menstruating individuals.

In most otherwise healthy children without evidence of acute infection or chronic disease, SF is an accurate marker of iron status, and a low SF is always diagnostic for ID

TABLE 4. Indications for and Interpretation of Available Iron Parameters

Parameter	Indication	Interpretation
Serum ferritin, ng/mL	Indirect estimate of storage iron Considered best peripheral measure of total body iron status	Low ferritin is diagnostic for iron deficiency Inflammation causes elevation of ferritin, as it is an acute phase reactant
Serum iron, mg/dL	Measure of circulating iron Ideally assessed when fasting	Typically low in iron deficiency May be elevated if measured after iron absorption
Transferrin or total iron binding capacity (TIBC), μg/dL	Measure of available iron transport protein Ideally assessed when fasting	Typically elevated in iron deficiency May be low in states of inflammation or protein-loss
Transferrin saturation (TSAT), %	Calculated measure of circulating iron and iron transporter (iron/TIBC)	Low in states of inflammation/iron-restricted erythropoiesis, as well as iron deficiency
Soluble transferrin receptor (sTfR1), nmol/L	Measure of erythropoietic activity Relatively unaffected by inflammation compared to other iron parameters Not reliable iron measure in persons with hemolytic anemia	Elevated in states of iron deficiency, even in people with concomitant inflammation More specific when interpreted with ferritin (sTfR1-ferritin index >2 consistent with ID)
Reticulocyte hemoglobin content or equivalent (CHr or RET-He), pg	Measure of hemoglobin within reticulocytes First peripheral blood marker that becomes low in iron deficiency	Improves rapidly with initiation of iron therapy Also low in patients with thalassemia trait
Hepcidin, ng/mL	Elevated in people with genetically confirmed IRIDA May assist in determining response to oral iron therapy; currently limited availability	Low in iron deficiency Elevated in states of inflammation

Abbreviation: IRIDA, iron-refractory iron deficiency anemia.

(Table 4). In patients with acute or chronic inflammation by clinical history or physical examination, it is important to note that SF is an acute phase reactant and may be falsely elevated or normalized with concurrent inflammation, even at low levels, or in patients with tissue injury.[50] In an ill child or in the setting of inflammation, an elevated C-reactive protein would indicate that the SF level should not be considered a reliable measure for iron deficiency (ie, may be falsely normalized). In a clinically well child, concurrent measurement of C-reactive protein is unnecessary.

Serum iron is most accurate when performed on fasting individuals. In nonfasting individuals, values can be variable and even "elevated" as a reflection of recent intestinal iron absorption from either food or medications. Serum transferrin concentration and total iron binding capacity (TIBC) are typically both increased in ID. Occasionally, states of inflammation or protein loss can reduce both of these iron parameters, resulting in falsely normal or reduced values, even in the setting of ID.[51] A fasting transferrin saturation (TSAT), calculated as the serum iron divided by the TIBC (expressed as a percent), is more useful than interpretation of the serum iron or TIBC individually.

In children with chronic inflammatory conditions with risk factors for ID, assessment of the soluble transferrin receptor (sTfR) test may be performed. In contrast to other iron parameters, sTfR measures a circulating protein derived from cleavage of the membrane transferrin receptor on erythroid precursor cells within the marrow, is less affected by inflammation than SF. It is inversely proportional to tissue iron availability and generally increased in patients with ID. Thus, it is helpful in identifying ID in people with concurrent inflammation. The sTfR-ferritin index (sTfR/$\log_{10}$ferritin) can further assist in distinguishing IDA from anemia of chronic inflammation. In patients with ID, the sTfR-ferritin index is elevated (>2).[52,53] Patients with anemia of chronic inflammation without concomitant ID are likely to have a sTfR-ferritin index <1. The test was recommended in the 2010 AAP clinical report,[2] but its limitations include lack of widespread availability and lack of published norms in healthy children. Utilization of hepcidin levels to distinguish between these conditions may prove beneficial in the future but is not currently recommended.

Additional Laboratory Assessments

The reticulocyte Hb content or equivalent (reported as CHr or Ret-He) are 2 similar measures of Hb in new red blood cells having just entered the circulation. Reticulocyte Hb content declines prior to the onset of anemia and conversely one of the initial hematologic parameters, along with the reticulocyte count, that rises shortly after initiation of iron therapy.[54] Where available, this laboratory test may be reported with a reticulocyte count, and if drawn at the time of a CBC may facilitate the diagnosis of IDA. CHr and Retic-He values are also reduced in thalassemia trait and other hemoglobinopathies, although typically to a greater extent compared with those patients with IDA alone. An elevated free erythrocyte protoporphyrin (FEP) was previously used as a screening measure for ID. It is also elevated in lead toxicity and is no longer widely utilized for ID screening. Serum

hepcidin, the iron regulatory hormone, is typically low in patients with ID but not yet widely available as a laboratory test.

PRINCIPLES OF ID AND IDA MANAGEMENT

Education or Addressing the Underlying Etiology

For young children 12 months and older with nutritional IDA, specific dietary counseling includes limitation of milk intake (both cow milk and plant-based milk alternatives) to <24 ounces per day, and for infants and children >6 months of age, accompanied by an increase in iron-rich table foods as developmentally appropriate and based on the family's preference (ie, sources of heme iron such as fish, poultry, red meat, and liver and/or nonheme iron such as beans, lentils, tofu, spinach, nuts, and iron-enriched and fortified cereals and breads).[2,16] Transitioning the child to a regular or "sippy" cup in lieu of the bottle often facilitates reduction of milk intake. It is advisable to counsel parents about the difficulty in reducing milk consumption because of the potential for tantrums and initial lack of interest in other foods. Parents can be reassured that decreasing milk intake will result in the child trying and consuming more foods, including those with iron.

In children and adolescents with chronic blood loss as the primary etiology of ID and IDA, identification and correction of the etiology, when possible, ensures sustained recovery from anemia following institution of iron therapy. Adolescents with excessive menstrual blood loss should be assessed by their pediatrician and/or a subspecialist in adolescent medicine or pediatric gynecology to determine an underlying etiology, including assessment for an inherited bleeding disorder. Hormonal therapies and/or anti-fibrinolytic therapy reduce menstrual blood loss.[55] Children with gastrointestinal (GI) bleeding causing ID, suspected *Helicobacter pylori* infection, iron malabsorption related to duodenal disease (ie, celiac disease or inflammatory bowel disease), or surgery (ie, short bowel syndrome or bariatric surgery) should undergo appropriate evaluation and treatment of the underlying cause, which may include referral to a gastroenterology subspecialist.

Therapeutic Iron Preparations

Addressing the underlying etiology is necessary for correction of ID and IDA but not sufficient, and iron therapy is indicated even in mild anemia or ID without anemia. Myriad oral iron preparations exist in liquid, tablet, and capsule forms (additional information on available iron preparations can be found in the iron chapter of *Pediatric Nutrition,* 9th ed[16]). Oral iron is considered a dietary supplement, not a drug. Therefore, the Food and Drug Administration (FDA) does not have the authority to review iron products for safety and effectiveness before marketing. Thus, some iron supplements available "over the counter" lack the pharmacokinetic and efficacy testing required for drugs designed for treatment of specific conditions. Prescription coverage for iron supplements by public and private insurance is also variable. Advocacy efforts are needed to allow for all children to have access to such supplements, if indicated.

Many children tolerate oral iron supplementation with minimal to no negative effects. However, common adverse effects of oral iron include poor taste, nausea or abdominal pain, diarrhea, and constipation. Transient discoloration of the teeth may occur with liquid iron preparations. Families should also be informed about darkening of the stool while taking oral iron. Less frequent dosing (see Therapeutic Dosing Schedule and Administration) may mitigate some adverse effects.

One group of available iron products that has been used for decades with established efficacy are iron salts. The iron within iron salts is in the ferrous (+2) form, and includes ferrous sulfate, ferrous fumarate, ferrous gluconate, and others. Ferrous sulfate is the least costly, most commonly available, and most studied of all oral iron preparations. Iron polysaccharide complexes also have demonstrated efficacy in the treatment of IDA. Their better taste may be more palatable to children who refuse other forms of liquid iron because of taste. However, cost may be prohibitive for some formulations. Further, most iron polysaccharide preparations contain iron in the ferric (3+) form, which can result in less absorption and decreased efficacy compared with iron salts in the ferrous (2+) form.[56–58] A recent randomized clinical trial in young children with nutritional IDA demonstrated that ferrous sulfate, likely because of enhanced absorption, was superior to an iron polysaccharide complex in increasing Hb.[59] Therefore, ferrous sulfate is recommended for initial treatment of IDA.

Therapeutic Dosing Schedule and Administration

Infants and Children (Early and Middle Childhood)

Textbook recommendations for daily oral iron dosing have varied widely from 3 to 6 mg/kg of elemental iron divided into 2 or 3 doses throughout the day. Despite a lack of clinical trials comparing various iron dosing strategies in children, adult studies have demonstrated equivalence or superiority of low-dose oral iron therapy over previously recommended higher doses.[60] In children, one clinical trial involving 80 children with moderate to severe nutritional IDA (median Hb, 7.8 g/dL) demonstrated improvement with 3 mg/kg of elemental iron administered just once daily at bedtime as either ferrous sulfate or iron polysaccharide complex drops.[59] Accordingly, oral iron dosed at 3 mg/kg of elemental iron once daily as ferrous sulfate either on an empty stomach or with water is recommended for the initial treatment of young children. A clinical trial in which adults with IDA were randomly assigned to receive oral iron therapy alone vs oral iron with vitamin C supplementation

demonstrated no difference in hematologic response.[61] Thus, vitamin C-containing juices may be given with oral iron but are not necessary. The majority of iron absorption occurs via the duodenum. Children receiving enteral feeds via a nasogastric (NG) tube or gastrostomy tube (G-tube) may receive iron supplementation via NG or G-tube with minimal impact on absorption. Children receiving enteral feeds primarily via a jejunostomy tube (J-tube), however, may have limited response to oral iron administered via the J-tube, and intravenous iron therapy should be considered.

Adolescents

Limited data also exist regarding optimal iron dosing in adolescents who require iron therapy. Adult dosing recommendations vary considerably from 65 to 130 mg of elemental iron 1 to 3 times daily. However, trials involving adults with IDA have demonstrated that lower and less frequent oral iron dosing is as effective but with fewer adverse effects and improved adherence.[60] In addition, a study in women with ID but without anemia that evaluated the effects of iron dosing on hepcidin levels (the key iron regulatory hormone[62]) and subsequent iron absorption found that the fractional absorption of oral iron is maximized when it is administered just once daily or every other day when compared with the conventional approach of dividing the dose to 2 or 3 times daily.[63,64] Additional studies in adult women with ID but without anemia evaluated iron supplementation administered once vs twice daily and found no significant differences in either fractional or total iron absorption between the groups.[65] These studies have not yet been replicated in pediatric and adolescent patients. However, on the basis of these studies, it appears that 1 tablet of ferrous sulfate (65 mg elemental iron) once daily should suffice for most adolescents with IDA in whom the ability to successfully take the medication and control of the primary etiology are ensured.

Administration

Oral iron is best administered on an empty stomach or with water. Oral iron may also be taken with juice, although a recent trial in adults assessing impact of vitamin C with oral iron demonstrated no additional benefit.[61] Dairy, coffee, and tea products should be avoided concomitantly as the presence of calcium or tannins will reduce absorption of iron, as will many solid foods "competing" with iron for intestinal absorption.[13,66] Because most iron absorption occurs in the duodenum, enteric-coated or slow-release iron tablets are less effective.

FOLLOW-UP: MILD TO MODERATE, UNCOMPLICATED IDA

Uncomplicated IDA characterizes children and adolescents who are both clinically stable and who have a typical underlying etiology for their IDA by clinical history (eg, excessive milk intake in toddlers or heavy menstrual bleeding in adolescents). Mild and moderate IDA are defined here as patients with confirmed IDA whose Hb is ≥9 g/dL and Hb 7 to 9 g/dL, respectively. In these children, evaluating response to therapy is necessary to promote both treatment efficacy and correction of the underlying etiology.

One-Month Follow-Up

Once treated with oral iron, clinicians should reevaluate patients 1 month later with a CBC and reticulocyte count to assess treatment response. An increment in the reticulocyte count occurs 5 to 7 days after initiation of iron therapy followed by normalization. For mild anemia, the normal Hb for age is expected within 4 weeks of therapeutic iron therapy. In children with moderate anemia, an increment in the Hb of at least 2 g/dL above the baseline level is expected within 4 weeks. A suboptimal response is defined as either failure to normalize Hb when IDA is mild or having a <2 g/dL increase in Hb in those with moderate to severe IDA. These patients require reassessment of the underlying etiology and iron dosing (amount, preparation, frequency, and success or challenges in medication administration). Children whose Hb has normalized should continue on the same therapeutic dose for a total of 3 months to ensure repletion of iron stores.

Three-Month Follow-Up

All children with IDA receiving therapeutic iron whose diet has improved and/or have had their abnormal blood loss corrected should achieve a normal Hb within 3 months regardless of the severity of anemia at diagnosis. However, some such children and adolescents continue to have ID secondary to continued dietary inadequacies, ongoing external blood loss (most commonly from heavy menses or GI bleeding), barriers to taking iron therapy, or malabsorption of iron. Therefore, SF should be assessed again to determine the need for ongoing iron therapy. Patients with SF≤20 ng/mL or ≤30 ng/mL (based on the diagnostic threshold for their age group and menstruating status) should continue iron supplementation for an additional 3 months and be reassessed for ongoing ID and IDA clinical risk factors.[41,47] A slightly higher SF threshold is recommended for cessation of therapy to minimize the risk of recurrent ID.

Small case series report improvement in symptoms associated with ID, such as pica, fatigue, restless legs, and sleep or behavioral disturbance when iron supplementation is continued until an SF of >50 ng/mL is achieved.[28] Specific recommendations regarding such practice are outside the scope of this report.

TREATMENT OF SEVERE OR REFRACTORY IDA

Severe IDA

Severe IDA in both young children and adolescents is defined as confirmed IDA and a Hb <7 g/dL. Yet, some such children and adolescents with IDA may have few or no symptoms despite their very low Hb values. Children with severe IDA but no evidence of hemodynamic instability (eg, tachycardia, respiratory distress) or acute or ongoing blood loss can be followed closely (see below) as outpatients when reliable follow-up can be assured. In such cases, clinicians should identify and correct the underlying etiology, and promptly initiate oral iron therapy. Close follow-up within 7 to 10 days with laboratory testing (CBC and reticulocyte count) is necessary to re-assess the child and ensure an initial hematologic response. Reassessment should occur again at the 1- and 3-month time points with CBC and reticulocyte count, as well as iron studies (SF) at 3 months, to facilitate full IDA recovery and correction of the underlying etiology.

Children and adolescents with severe IDA who are clinically unstable at presentation (eg, with concurrent viral or respiratory illness, poor oral intake, evidence of heart failure, uncontrolled blood loss, etc) should receive red blood cell transfusion and close monitoring. Barriers to accessing medical care, which limits communication and follow-up (within 7 to 10 days) may also necessitate blood transfusion. Administer packed red blood cell transfusions slowly and in small aliquots to prevent heart failure from volume overload such as two or three 5-mL/kg volume transfusions over 3 hours, each with cardiopulmonary assessment in between. The goal of transfusion is to stabilize the child so the goal of a posttransfusion Hb of 7 to 9 g/dL is typically sufficient. Although post-transfusion testing is not necessary, it can be performed within 1 hour of transfusion completion. Such children receiving transfusions should receive the same diagnostic evaluation and treatment as those with severe, stable anemia. Because the iron in the transfused cells is not readily available for erythropoiesis, children requiring transfusion should also receive a 3-month treatment course of iron therapy to ensure repletion of iron stores. Transfused children should also follow-up at 1 week, 1 month, and 3 months with CBC and reticulocyte count at each visit, as well as iron studies (SF) at 3 months, to confirm full IDA recovery and facilitate correction of the underlying etiology.

Refractory, Persistent, or Recurrent IDA

Common Causes

"Refractory" or "persistent" IDA is defined as continued anemia after greater than 3 months of iron supplementation or recurrence (1 or more episodes of anemia following documentation of previous IDA resolution) within a 2-year period. Its management should include (1) confirmation of the IDA diagnosis; (2) review of previous iron treatment (formulation, dosing, route of administration, and duration) and concurrent medications that may affect absorption (eg, antacids); (3) estimated success in taking medication[67]; and (4) reevaluation of the underlying etiology of IDA (eg, low-iron diet, malabsorption, and/or ongoing blood loss).[18]

Differential Diagnoses

Causes of microcytic anemia other than ID include thalassemia syndromes and rare conditions such as congenital or acquired sideroblastic anemia.[18] Such conditions warrant referral to a hematology subspecialist. Sources of blood loss aside from the most common GI and gynecologic sites should also be considered. Rarely, IDA may be the presenting manifestation in patients with idiopathic pulmonary hemosiderosis characterized by recurrent or persistent respiratory symptoms and prominent lung infiltrates in the absence of other risk factors. Occult urinary blood loss is another rare cause of IDA in children. Endurance athletes performing high levels of physical activity can develop ID resulting from microscopic gastrointestinal or occult urinary blood or Hb loss (eg, march hemoglobinuria or footstrike hemolysis).[68] Lead toxicity alone does not result in microcytic anemia. Rather, it likely occurs at higher rates in iron deficient children due to more avid lead absorption in such patients. This enhanced absorption, when coupled with symptoms of pica and increased consumption of nonfood items, increases the risk of lead toxicity.

Anemia of Chronic Inflammation and Iron-Refractory IDA

Children may have persistent microcytic anemia attributable to iron-restricted erythropoiesis resulting from the sequestration of iron in the reticuloendothelial system as well as blockade of intestinal iron absorption related to elevated hepcidin (eg, anemia of chronic inflammation). Acquired elevated hepcidin,[69] most commonly attributable to conditions such as inflammatory bowel disease, rheumatologic disorders, and chronic kidney disease, often results in this type of anemia. In contrast, a rare inherited disorder, iron-refractory IDA (IRIDA) is an autosomal-recessive condition resulting from mutations in the TMPRSS6 gene that lead to increased hepcidin production and persistent microcytic anemia from infancy that is poorly responsive to both oral and intravenous (IV) iron therapy.[70,71]

CONSIDERATIONS FOR INTRAVENOUS IRON THERAPY

IV iron therapy is now far safer than it was several decades ago and has been widely accepted for use in children and adults.[72] Although the efficacy and safety data of IV iron in children are limited to case series,[73–76] diverse groups of young patients with IDA have benefitted from its use.[77] Table 5 lists the circumstances for which IV iron therapy may be considered in children. The most frequent indication is a poor response to oral iron treatment because of

TABLE 5. Potential Indications for IV Iron Therapy	
Treatment Failure	**Persistent or Refractory Anemia Despite ≥3 mos of Oral Iron Supplementation**
Incorrect/inadequate dosing or formulation	Insufficient iron provided to correct underlying anemia
Improper iron administration or discontinuation	Poor absorption attributable to concomitant products that inhibit iron absorption (ie, calcium, tannins, antacids); iron discontinued prior to repletion of iron stores
Barriers to taking medications	Side effects including poor taste, abdominal pain, and constipation may affect consistent use of oral iron
Barriers to accessing medical care	Barriers to addressing underlying etiology or follow-up to document resolution
Losses	Oral iron repletion is possible but difficult because of ongoing blood loss or inability to address underlying etiology, leading to recurrence
Gastrointestinal losses	Various gastrointestinal conditions; hereditary hemorrhagic telangiectasia
Menstrual losses	Failure to initiate hormonal therapy or subsequent barriers to taking or discontinuation of such therapy
Anatomic	
History of intestinal surgery	History of necrotizing enterocolitis, intestinal surgery (short bowel syndrome), or history of bariatric surgery
Duodenal pathology	Celiac disease, inflammatory bowel disease
Excess Hepcidin	Limited iron absorption and lack of accessibility to iron stored in macrophages due to elevation in hepcidin
Inflammatory conditions	Inflammatory bowel disease; rheumatologic conditions; epidermolysis bullosa
IRIDA (rare)	No response to oral iron therapy; limited response to IV iron therapy
Abbreviation: IRIDA, iron-refractory iron deficiency anemia.	

barriers to taking the medication, particularly in adolescents, and in children whose families have barriers to accessing medical care. Children and adolescents with elevated hepcidin levels as a result of chronic inflammatory conditions (eg, inflammatory bowel disease,[78] rheumatologic conditions, epidermolysis bullosa,[79] chronic infection, heart failure[80–84]) have limited intestinal absorption of oral iron. Such patients may benefit greatly from IV iron therapy, which obviates the need for intestinal absorption. Children and adolescents with intestinal malabsorption attributable to villous blunting, injury, or reduced surface area (eg, celiac disease, inflammatory bowel disease, short bowel syndrome, and other forms of intestinal failure) may also benefit from IV iron.[85]

Important Considerations

Most children or adolescents in whom IV iron therapy is being considered should be referred to a pediatric specialty center with experience in parenteral iron administration when available. Despite improved safety profiles of parenteral iron, appropriate monitoring is necessary with medical staff prepared to appropriately address and treat rare serious adverse effects.

Available IV Formulations

All current IV iron formulations available in the United States share the common structure of a carbohydrate shell containing an iron core (Table 6). The shell stabilizes the iron and limits its release into the plasma. The formulations differ by the size of the iron core, identity, and density of the carbohydrate shell, maximum dose, and cost. Six IV iron preparations are currently available in the United States: iron sucrose, ferric gluconate, low molecular weight iron dextran, ferumoxytol, ferric carboxymaltose, and ferric derisomaltose. FDA-approved indications as well as dosing and administration guidelines vary substantially by formulation. Although each agent lists a maximum dosage in the package insert, administering a total dose of iron (ie, the total amount of iron required to correct the patient's iron deficit, which can be derived from patient's body weight, current Hb, and target Hb via the Ganzoni formula[18]) in a single outpatient infusion is possible using low molecular weight iron dextran, ferumoxytol, ferric carboxymaltose, and/or ferric derisomaltose.

Risks and Benefits of IV Therapy

The safety profile of IV iron preparations is greatly improved when compared with agents used several decades ago.[86,87] Two IV iron preparations, low-molecular weight iron dextran and ferumoxytol, carry a black box warning for the most serious adverse effect of hypersensitivity/anaphylaxis reactions.[87] Low-molecular weight iron dextran requires a test dose prior to full dose infusion. However, most of the adverse effects observed are transient and include nausea, vomiting, abdominal pain, headache, flushing, pruritus, and urticaria. Ferric carboxymaltose

TABLE 6. Intravenous Iron Formulations Available in the United States

Generic Name	Ferric Gluconate	Iron Sucrose	LMW Iron Dextran	Ferumoxytol	Ferric Carboxymaltose	Ferric Derisomaltose
FDA indication	CKD on dialysis + ESAs	CKD	Oral iron administration is unsatisfactory or impossible	CKD	Intolerance or unsatisfactory response to oral iron; NDDCKD	Intolerance or unsatisfactory response to oral iron; NDDCKD
FDA approved (pediatrics)	Yes, >6 y	Yes, >2 y	Yes, >4 mos	No	Yes, >1 y	No
Test dose	No	No	Yes	No	No	No
Black box	No	No	Yes	Yes	No	No
Maximum FDA-approved single infusion dose	125 mg	Initial: 100 mg Maintenance: 300 mg	<5 kg: 25 mg 5–10 kg: 50 mg >10 kg: 100 mg	510 mg	15 mg/kg or 750 mg	20 mg/kg or 1000 mg
Infusion time (minutes)	60 min	Diluted: 30–90 min Undiluted: 5 min	60 min	15–60 min	Diluted: ≥15 min Undiluted: slow IV push no faster than 100 mg/min	≥20 min

Abbreviations: FDA, US Food and Drug Administration; CKD, chronic kidney disease; ESAs, erythropoietin-stimulating agents; NDDCKD, nondialysis-dependent chronic kidney disease

results in hypophosphatemia in a subset of treated patients.[88] Data in children have found that effects are typically transient and asymptomatic.[89] Extravasation of any IV iron preparation, although typically painless, can result in iron staining of the skin, which can be long lasting with limited treatment options. Prevention efforts aimed at ensuring adequate venous access, potentially avoiding major joints, and close monitoring as well as appropriate flushing post-infusion may mitigate this risk. Relative benefits of IV iron therapy include the avoidance of major barriers to taking medication related to taste and GI side effects and duration of oral iron treatment.

Cost Considerations

IV iron is more costly than oral iron preparations. Direct costs to patients and families vary greatly depending on insurance coverage as well as indication. In addition to the drug cost, consider ancillary infusion charges, particularly if multiple infusions are required to correct the total iron deficit. However, in children whose anemia is persistent when oral iron is ineffective or not tolerated, successful treatment with IV iron reduces the need for ongoing follow-up visits and laboratory assessments.

Importance of Follow-Up

Children treated with IV iron therapy should be followed 4 to 6 weeks after iron infusion(s) to verify a complete and sustained response to therapy and adequate assessment of the etiology of IDA to prevent or monitor for recurrence. Children with chronic inflammatory conditions or ongoing blood loss may benefit from follow-up with a hematology subspecialist every 3 to 6 months, depending on the underlying etiology. Additional IV iron therapy may be indicated, as guided by CBC and iron parameters, rather than being continued indefinitely.

SUMMARY

Although ID and IDA can occur at any age, it is most common in young children and menstruating adolescents. IDA is associated with impaired neurocognitive development, which may be mitigated by iron therapy. In adolescents with ID, iron supplementation has improved verbal learning, concentration, and memory. Screening at risk children and adolescents should occur at the ages at which they are most likely to become iron deficient. The diagnostic evaluation should focus on well-established clinical risk factors and informative, widely available laboratory tests. Specific iron replacement management strategies for children with IDA are provided in this clinical report. The recommendations below are made by expert consensus upon thoughtful consideration of published IDA literature. A list of all actionable items by topic and target population within this clinical report may be found in the Supplemental Material.

GUIDANCE FOR PEDIATRICIANS

1. Exclusively breastfed term infants should receive iron supplementation (1 mg/kg/d) by 4 months of age. Alternatively, some caregivers may wish to wait until 6 months of age when complementary foods containing iron are introduced. Preterm infants (less than 37 weeks' gestational age at birth) receiving full enteral feeds should begin iron fortification or supplementation by 2 weeks of life to ensure iron intake of 2 to 3 mg/kg/d. Children >6 months up to 5 years of age should receive sufficient quantities of iron-rich foods. Cow milk or milk alternatives, including plant-based milk, (in lieu of

human milk or formula) should not be offered to any infant prior to 12 months of age. Children >1 year should drink less than 24 ounces per day of milk (cow milk and/or plant-based milk alternatives). School-aged children and adolescents should be encouraged to consume a variety of iron-rich foods.

2. Laboratory screening for ID and IDA, consisting of a CBC and SF, should occur in all infants and young children. Screening should occur at the time point at which the child is most at risk for ID, on the basis of the child's primary source of nutrition during the first year of life.
   a. In infants whose primary source of nutrition is human milk, screening is recommended at 9 to 12 months of age.
   b. In infants whose primary source of nutrition is iron-fortified formula, screening is recommended at 15 to 18 months of age after transition to cow milk (or plant-based milk alternatives).
   c. If a CBC and SF cannot be obtained, at a minimum, Hb should be assessed.
   d. Children with ongoing risk factors, specifically excessive milk intake and/or inadequate intake of iron-containing complementary foods, should be rescreened for IDA at each subsequent well-child assessment until 4 years of age.
3. Universal laboratory screening for ID and IDA with a CBC and SF should be performed in all adolescents who are at least 1 year postmenarche but no later than 14 years of age. Screening thereafter should be performed in menstruating adolescents with clinical risk factors of excessive menstrual blood loss or low-iron diet.
4. For the majority of affected children and adolescents, a positive clinical history of IDA risk factors combined with a microcytic anemia confirms its diagnosis.
   a. SF≤20 ng/mL is consistent with ID in young and school-aged children.
   b. SF≤30 ng/mL is consistent with ID in adolescent and menstruating individuals.
   c. When combined with anemia, a low SF is consistent with IDA.
5. Treatment for children with IDA includes identifying and addressing the underlying etiology (ie, dietary changes, control of blood loss) as well as initiation of iron replacement therapy. In young children, initial therapy should consist of ferrous sulfate, 3 mg/kg elemental iron, administered once daily. In adolescents, initial therapy should consist of ferrous sulfate, 65 mg elemental iron, administered once daily.
6. Children with severe IDA (Hb <7 g/dL) who are clinically stable and in whom reliable follow-up can be ensured may receive oral iron therapy with close outpatient follow-up at 7 to 10 days, in addition to 1- and 3-month follow-up visits. Children who are clinically unstable with severe IDA should receive a blood transfusion administered slowly in small aliquots as well as the same diagnostic workup, iron therapy (for a minimum 3 months), and follow-up as those children not requiring transfusion.
7. All children with IDA should have, at minimum, follow-up visits at 1 and 3 months after initiation of therapy. In children with mild IDA, defined as Hb ≥9 g/dL, an appropriate response to therapy consists of normalization of the Hb at the 1-month follow-up visit. In children with moderate (Hb ≥7 to <9 g/dL) or severe IDA (Hb <7 g/dL), an adequate response to therapy consists of Hb increment of at least 2 g/dL at the 1-month follow-up. In such patients, oral iron therapy should be continued at the same therapeutic dosing for a minimum of 3 months. Patients with SF<20 ng/mL at the 3-month follow-up should continue iron supplementation for an additional 3 months.
8. In children with persistent microcytic anemia or recurrent IDA, the provider should: (1) confirm the diagnosis; (2) review the prior iron therapy; (3) assess success or barriers to taking medication; and (4) reevaluate the underlying etiology. IV iron therapy may be considered for children with inadequate response to oral iron therapy or in conditions impairing iron absorption, including chronic inflammatory disorders. Children in whom IV iron therapy is being considered should be referred to a pediatric specialty center with experience in parenteral iron administration, when available.

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ABBREVIATIONS

AAP: American Academy of Pediatrics
ACOG: American College of Obstetrics and Gynecology
CBC: complete blood cell count
CHr, Ret-He: reticulocyte hemoglobin content/equivalent
FDA: Food and Drug Administration
GI: gastrointestinal
Hb: hemoglobin
ID: iron deficiency
IDA: iron deficiency anemia
IRIDA: iron refractory iron deficiency anemia
IV: intravenous
MCV: mean corpuscular volume
RDW: red blood cell distribution width
SF: serum ferritin; sTfR1, serum/soluble transferrin receptor 1
TSAT: transferrin saturation

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REFERENCES

1. Georgieff MK. Iron assessment to protect the developing brain. *Am J Clin Nutr*. 2017;106(suppl 6):1588S–1593S. PubMed doi: 10.3945/ajcn.117.155846
2. Baker RD, Greer FR; Committee on Nutrition American Academy of Pediatrics. Diagnosis and prevention of iron deficiency and iron-deficiency anemia in infants and young children (0–3 years of age). *Pediatrics*. 2010;126(5):1040–1050. PubMed doi: 10.1542/peds.2010-2576
3. Gupta PM, Hamner HC, Suchdev PS, Flores-Ayala R, Mei Z. Iron status of toddlers, nonpregnant females, and pregnant females in the United States. *Am J Clin Nutr*. 2017;106(suppl 6):1640S–1646S. PubMed doi: 10.3945/ajcn.117.155978
4. Gupta PM, Perrine CG, Mei Z, Scanlon KS. Iron, Anemia, and Iron Deficiency Anemia among Young Children in the United States. *Nutrients*. 2016;8(6):330. PubMed doi: 10.3390/nu8060330
5. Gessner BD. Geographic and racial patterns of anemia prevalence among low-income Alaskan children and pregnant or postpartum women limit potential etiologies. *J Pediatr Gastroenterol Nutr*. 2009;48(4):475–481. PubMed doi: 10.1097/MPG.0b013e3181888fac
6. Powers JM, Stanek JR, Srivaths L, Haamid FW, O'Brien SH. Hematologic considerations and management of adolescent girls with heavy menstrual mleeding and anemia in U.S. children's hospitals. *J Pediatr Adolesc Gynecol*. 2018;31(5):446–450. PubMed doi: 10.1016/j.jpag.2018.06.008
7. American Academy of Pediatrics. Delayed umbilical cord clamping after birth. *Pediatrics*. 2017;139(6):e20170957. PubMed doi: 10.1542/peds.2017-0957
8. McDonald SJ, Middleton P, Dowswell T, Morris PS. Effect of timing of umbilical cord clamping of term infants on maternal and neonatal outcomes. *Evid Based Child Health*. 2014;9(2):303–397. PubMed doi: 10.1002/ebch.1971
9. Qasem WA, Friel JK. An Overview of Iron in Term Breast-Fed Infants. *Clin Med Insights Pediatr*. 2015;9:79–84. PubMed doi: 10.4137/CMPed.S26572
10. Obbagy JE, English LK, Psota TL, et al. Complementary feeding and micronutrient status: a systematic review. *Am J Clin Nutr*. 2019;109(suppl 7):852S–871S. PubMed doi: 10.1093/ajcn/nqy266
11. Dogan E, Yilmaz G, Caylan N, Turgut M, Gokcay G, Oguz MM. Baby-led complementary feeding: Randomized controlled study. *Pediatrics international: official journal of the Japan Pediatric Society*. Dec 2018;60(12):1073–1080. PubMed doi: 10.1111/ped.13671
12. Domellöf M, Braegger C, Campoy C, et al; ESPGHAN Committee on Nutrition. Iron requirements of infants and toddlers. *J Pediatr Gastroenterol Nutr*. 2014;58(1):119–129. PubMed doi: 10.1097/MPG.0000000000000206
13. Iron. *Food and nutrition board of the Institute of Medicine: Dietary reference intakes for vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc*. National Academy Press; 2000:311.
14. Das JK, Salam RA, Mahmood SB, et al. Food fortification with multiple micronutrients: impact on health outcomes in general population. *Cochrane Database Syst Rev*. 2019;12(12):CD011400. PubMed doi: 10.1002/14651858.CD011400.pub2
15. Suchdev PS, Jefferds MED, Ota E, da Silva Lopes K, De-Regil LM. Home fortification of foods with multiple micronutrient powders for health and nutrition in children under two years of age. *Cochrane Database Syst Rev*. 2020;2(2):CD008959. PubMed doi: 10.1002/14651858.CD008959.pub3
16. Iron. In: Greer FR, Abrams SA, eds. *Pediatric Nutrition*. 9th ed. American Academy of Pediatrics; 2024:559–590.
17. Algarín C, Peirano P, Garrido M, Pizarro F, Lozoff B. Iron deficiency anemia in infancy: long-lasting effects on auditory and visual system functioning. *Pediatr Res*. 2003;53(2):217–223. PubMed doi: 10.1203/01.PDR.0000047657.23156.55
18. Powers JM, Buchanan GR. Diagnosis and management of iron deficiency anemia. *Hematol Oncol Clin North Am*. Aug 2014;28(4):729–45, vi-vii. PubMed doi: 10.1016/j.hoc.2014.04.007
19. Lozoff B, Beard J, Connor J, Barbara F, Georgieff M, Schallert T. Long-lasting neural and behavioral effects of iron deficiency in infancy. *Nutr Rev*. 2006;64(5 Pt 2):S34–S43. PubMed doi: 10.1301/nr.2006.may.S34-S43
20. Kemper AR, Fan T, Grossman DC, Phipps MG. Gaps in evidence regarding iron deficiency anemia in pregnant women and young children: summary of US Preventive Services Task Force recommendations. *Am J Clin Nutr*. 2017;106(suppl 6):1555S–1558S. PubMed doi: 10.3945/ajcn.117.155788
21. Bruner AB, Joffe A, Duggan AK, Casella JF, Brandt J. Randomised study of cognitive effects of iron supplementation in non-anaemic iron-deficient adolescent girls. *Lancet*. 1996;348(9033):992–996. PubMed doi: 10.1016/S0140-6736(96)02341-0
22. McCann JC, Ames BN. An overview of evidence for a causal relation between iron deficiency during development and deficits in cognitive or behavioral function. *Am J Clin Nutr*. 2007;85(4):931–945. PubMed doi: 10.1093/ajcn/85.4.931
23. Lozoff B, Smith JB, Kaciroti N, Clark KM, Guevara S, Jimenez E. Functional significance of early-life iron deficiency: outcomes at 25 years. *J Pediatr*. 2013;163(5):1260–1266. PubMed doi: 10.1016/j.jpeds.2013.05.015
24. Halterman JS, Kaczorowski JM, Aligne CA, Auinger P, Szilagyi PG. Iron deficiency and cognitive achievement among school-aged children and adolescents in the United States. *Pediatrics*. 2001;107(6):1381–1386. PubMed doi: 10.1542/peds.107.6.1381
25. Zhu YI, Haas JD. Iron depletion without anemia and physical performance in young women. *Am J Clin Nutr*. 1997;66(2):334–341. PubMed doi: 10.1093/ajcn/66.2.334
26. Sharma R, Stanek JR, Koch TL, Grooms L, O'Brien SH. Intravenous iron therapy in non-anemic iron-deficient menstruating adolescent females with fatigue. *Am J Hematol*. 2016;91(10):973–977. PubMed doi: 10.1002/ajh.24461
27. Konofal E, Lecendreux M, Deron J, et al. Effects of iron supplementation on attention deficit hyperactivity disorder in children. *Pediatr Neurol*. 2008;38(1):20–26. PubMed doi: 10.1016/j.pediatrneurol.2007.08.014

28. Dye TJ, Jain SV, Simakajornboon N. Outcomes of long-term iron supplementation in pediatric restless legs syndrome/periodic limb movement disorder (RLS/PLMD). *Sleep Med.* 2017;32:213–219. PubMed doi: 10.1016/j.sleep.2016.01.008

29. Recommendations for Preventive Pediatric Health Care. *Bright Futures/American Academy of Pediatrics.* 2017;

30. Roess AA, Jacquier EF, Catellier DJ, et al. Food Consumption Patterns of Infants and Toddlers: Findings from the Feeding Infants and Toddlers Study (FITS) 2016. *J Nutr.* 2018;148(suppl 3):1525S–1535S. PubMed doi: 10.1093/jn/nxy171

31. Brotanek JM, Halterman JS, Auinger P, Flores G, Weitzman M. Iron deficiency, prolonged bottle-feeding, and racial/ethnic disparities in young children. *Arch Pediatr Adolesc Med.* 2005;159(11):1038–1042. PubMed doi: 10.1001/archpedi.159.11.1038

32. Brotanek JM, Gosz J, Weitzman M, Flores G. Iron deficiency in early childhood in the United States: risk factors and racial/ethnic disparities. *Pediatrics.* 2007;120(3):568–575. PubMed doi: 10.1542/peds.2007-0572

33. Baggett HC, Parkinson AJ, Muth PT, Gold BD, Gessner BD. Endemic iron deficiency associated with Helicobacter pylori infection among school-aged children in Alaska. *Pediatrics.* 2006;117(3):e396–e404. PubMed doi: 10.1542/peds.2005-1129

34. Centers for Disease Control and Prevention (CDC). Iron deficiency anemia in Alaska native children-Hooper Bay, Alaska, 1999. *MMWR Morb Mortal Wkly Rep.* 1999;48(32):714–716. PubMed

35. Sekhar DL, Murray-Kolb LE, Kunselman AR, Weisman CS, Paul IM. Association between menarche and iron deficiency in non-anemic young women. *PLoS One.* 2017;12(5):e0177183. PubMed doi: 10.1371/journal.pone.0177183

36. Sekhar DL, Murray-Kolb LE, Schaefer EW, Paul IM. Risk-Based Questionnaires Fail to Detect Adolescent Iron Deficiency and Anemia. *J Pediatr.* 2017;187:194–199.e1. PubMed doi: 10.1016/j.jpeds.2017.04.007

37. Cooke AG, McCavit TL, Buchanan GR, Powers JM. Iron deficiency anemia in adolescents who present with heavy menstrual bleeding. *J Pediatr Adolesc Gynecol.* 2017;30(2):247–250. PubMed doi: 10.1016/j.jpag.2016.10.010

38. Sekhar DL, Murray-Kolb LE, Kunselman AR, Paul IM. Identifying factors predicting iron deficiency in United States adolescent females using the ferritin and the body iron models. *Clin Nutr ESPEN.* 2015;10(3):e118–e123. PubMed doi: 10.1016/j.clnesp.2015.03.001

39. *Recommendations to Prevent and Control Iron Deficiency in the United States.* Vol. 47. 1998:1–29. MMWR Recomm Rep.

40. White KC. Anemia is a poor predictor of iron deficiency among toddlers in the United States: for heme the bell tolls. *Pediatrics.* 2005;115(2):315–320. PubMed doi: 10.1542/peds.2004-1488

41. Abdullah K, Birken CS, Maguire JL, et al. Re-evaluation of serum ferritin cut-off values for the diagnosis of iron deficiency in children aged 12–36 months. *J Pediatr.* 2017;188:287–290. PubMed doi: 10.1016/j.jpeds.2017.03.028

42. Staffa SJ, Joerger JD, Henry E, Christensen RD, Brugnara C, Zurakowski D. Pediatric hematology normal ranges derived from pediatric primary care patients. *Am J Hematol.* 2020;95(10):E255–E257. PubMed doi: 10.1002/ajh.25904

43. del Giudice EM, Santoro N, Amato A, et al. Hepcidin in obese children as a potential mediator of the association between obesity and iron deficiency. *J Clin Endocrinol Metab.* 2009;94(12):5102–5107. PubMed doi: 10.1210/jc.2009-1361

44. Nead KG, Halterman JS, Kaczorowski JM, Auinger P, Weitzman M. Overweight children and adolescents: a risk group for iron deficiency. *Pediatrics.* 2004;114(1):104–108. PubMed doi: 10.1542/peds.114.1.104

45. Lynch S, Pfeiffer CM, Georgieff MK, et al. Biomarkers of Nutrition for Development (BOND)-Iron Review. *J Nutr.* 2018;148(suppl 1):1001S–1067S. PubMed doi: 10.1093/jn/nxx036

46. Powers JM, Buchanan GR. Potential for Improved Screening, Diagnosis, and Treatment for Iron Deficiency and Iron Deficiency Anemia in Young Children. *J Pediatr.* 2017;188:8–10. PubMed doi: 10.1016/j.jpeds.2017.04.069

47. Mei Z, Addo OY, Jefferds ME, Sharma AJ, Flores-Ayala RC, Brittenham GM. Physiologically based serum ferritin thresholds for iron deficiency in children and non-pregnant women: a US National Health and Nutrition Examination Surveys (NHANES) serial cross-sectional study. *Lancet Haematol.* 2021;8(8):e572–e582. PubMed doi: 10.1016/S2352-3026(21)00168-X

48. *WHO guideline on use of ferritin concentrations to assess iron status in individuals and populations.* Wolrd Health Organization; 2020.

49. Special Interest Session for ASH Clinical Practice Guidelines on Diagnosis of Iron Deficiency with and without Anemia presented at: 2025 *American Hematology Society Annual Meeting*; Orlando, FL.

50. Suchdev PS, Williams AM, Mei Z, et al. Assessment of iron status in settings of inflammation: challenges and potential approaches. *Am J Clin Nutr.* 2017;106(suppl 6):1626S–1633S. PubMed doi: 10.3945/ajcn.117.155937

51. Powers JM, Buchanan GR. Disorders of Iron Metabolism: New Diagnostic and Treatment Approaches to Iron Deficiency. *Hematol Oncol Clin North Am.* 2019;33(3):393–408. PubMed doi: 10.1016/j.hoc.2019.01.006

52. Skikne BS, Punnonen K, Caldron PH, et al. Improved differential diagnosis of anemia of chronic disease and iron deficiency anemia: a prospective multicenter evaluation of soluble transferrin receptor and the sTfR/log ferritin index. *Am J Hematol.* 2011;86(11):923–927. PubMed doi: 10.1002/ajh.22108

53. Infusino I, Braga F, Dolci A, Panteghini M. Soluble transferrin receptor (sTfR) and sTfR/log ferritin index for the diagnosis of iron-deficiency anemia. A meta-analysis. *Am J Clin Pathol.* 2012;138(5):642–649. PubMed doi: 10.1309/AJCP16NTXZLZFAIB

54. Brugnara C, Laufer MR, Friedman AJ, Bridges K, Platt O. Reticulocyte hemoglobin content (CHr): early indicator of iron deficiency and response to therapy. *Blood.* 1994;83(10):3100–3101. PubMed doi: 10.1182/blood.V83.10.3100.3100

55. Haamid F, Sass AE, Dietrich JE. Heavy Menstrual Bleeding in Adolescents. *J Pediatr Adolesc Gynecol.* 2017;30(3):335–340. PubMed doi: 10.1016/j.jpag.2017.01.002

56. Moore CV, Arrowsmith WR, Welch J, Minnich V. Studies in iron transportation and metabolism. Observations on the absorption of iron from the gastro-intestinal tract. *J Clin Invest.* 1939;18(5): 553–580. PubMed doi: 10.1172/JCI101069

57. Moore CV, Dubach R, Minnich V, Roberts HK. Absorption of ferrous and ferric radioactive iron by human subjects and by dogs. *J Clin Invest.* 1944;23(5):755–767. PubMed doi: 10.1172/JCI101548

58. Diamond LK, Naiman JL, Allen DM, Oski FA. The treatment of iron-deficiency anemia–palatable but ineffective iron medication. *Pediatrics.* 1963;31(6):1041–1044. PubMed doi: 10.1542/peds.31.6.1041

59. Powers JM, Buchanan GR, Adix L, Zhang S, Gao A, McCavit TL. Effect of Low-Dose Ferrous Sulfate vs Iron Polysaccharide Complex on Hemoglobin Concentration in Young Children With Nutritional Iron-Deficiency Anemia: A Randomized Clinical Trial. *JAMA.* 2017; 317(22):2297–2304. PubMed doi: 10.1001/jama.2017.6846

60. Rimon E, Kagansky N, Kagansky M, et al. Are we giving too much iron? Low-dose iron therapy is effective in octogenarians. *Am J Med.* Oct 2005;118(10):1142–7. PubMed doi: S0002-9343(05)00210-X [pii] 10.1016/j.amjmed.2005.01.065

61. Li N, Zhao G, Wu W, et al. The Efficacy and Safety of Vitamin C for Iron Supplementation in Adult Patients With Iron Deficiency Anemia: A Randomized Clinical Trial. *JAMA Netw Open.* 2020;3(11): e2023644. PubMed doi: 10.1001/jamanetworkopen.2020.23644

62. Girelli D, Nemeth E, Swinkels DW. Hepcidin in the diagnosis of iron disorders. *Blood.* 2016;127(23):2809–2813. PubMed doi: 10.1182/blood-2015-12-639112

63. Moretti D, Goede JS, Zeder C, et al. Oral iron supplements increase hepcidin and decrease iron absorption from daily or twice-daily doses in iron-depleted young women. *Blood.* 2015;126(17):1981–1989. PubMed doi: 10.1182/blood-2015-05-642223

64. Schrier SL. So you know how to treat iron deficiency anemia. *Blood.* 2015;126(17):1971. PubMed doi: 10.1182/blood-2015-09-666511

65. Stoffel NU, Cercamondi CI, Brittenham G, et al. Iron absorption from oral iron supplements given on consecutive versus alternate days and as single morning doses versus twice-daily split dosing in iron-depleted women: two open-label, randomised controlled trials. *Lancet Haematol.* 2017;4(11):e524–e533. PubMed doi: 10.1016/S2352-3026(17)30182-5

66. Siegenberg D, Baynes RD, Bothwell TH, et al. Ascorbic acid prevents the dose-dependent inhibitory effects of polyphenols and phytates on nonheme-iron absorption. *Am J Clin Nutr.* 1991;53(2): 537–541. PubMed doi: 10.1093/ajcn/53.2.537

67. Powers JM, Daniel CL, McCavit TL, Buchanan GR. Deficiencies in the management of iron deficiency anemia during childhood. *Pediatr Blood Cancer.* 2016;63(4):743–745. PubMed doi: 10.1002/pbc.25861

68. Powers JM, O'Brien SH. How I approach iron deficiency with and without anemia. *Pediatr Blood Cancer.* 2019;66(3):e27544. PubMed doi: 10.1002/pbc.27544

69. Camaschella C. Iron-deficiency anemia. *N Engl J Med.* 2015; 372(19):1832–1843. PubMed doi: 10.1056/NEJMra1401038

70. Buchanan GR, Sheehan RG. Malabsorption and defective utilization of iron in three siblings. *J Pediatr.* 1981;98(5):723–728. PubMed doi: 10.1016/S0022-3476(81)80831-1

71. Heeney MM, Finberg KE. Iron-refractory iron deficiency anemia (IRIDA). *Hematol Oncol Clin North Am.* 2014;28(4):637–652, v. PubMed doi: 10.1016/j.hoc.2014.04.009

72. Avni T, Bieber A, Grossman A, Green H, Leibovici L, Gafter-Gvili A. The safety of intravenous iron preparations: systematic review and meta-analysis. *Mayo Clin Proc.* 2015;90(1):12–23. PubMed doi: 10.1016/j.mayocp.2014.10.007

73. Crary SE, Hall K, Buchanan GR. Intravenous iron sucrose for children with iron deficiency failing to respond to oral iron therapy. *Pediatr Blood Cancer.* 2011;56(4):615–619. PubMed doi: 10.1002/pbc.22930

74. Plummer ES, Crary SE, McCavit TL, Buchanan GR. Intravenous low molecular weight iron dextran in children with iron deficiency anemia unresponsive to oral iron. *Pediatr Blood Cancer.* 2013; 60(11):1747–1752. PubMed doi: 10.1002/pbc.24676

75. Powers JM, Shamoun M, McCavit TL, Adix L, Buchanan GR. Intravenous Ferric Carboxymaltose in Children with Iron Deficiency Anemia Who Respond Poorly to Oral Iron. *J Pediatr.* 2016;180:212–216. PubMed doi: 10.1016/j.jpeds.2016.09.053

76. Hassan N, Boville B, Reischmann D, Ndika A, Sterken D, Kovey K. Intravenous Ferumoxytol in Pediatric Patients With Iron Deficiency Anemia. *Ann Pharmacother.* 2017;51(7):548–554. PubMed doi: 10.1177/1060028017699429

77. Mantadakis E. Advances in Pediatric Intravenous Iron Therapy. *Pediatr Blood Cancer.* 2016;63(1):11–16. PubMed doi: 10.1002/pbc.25752

78. Laass MW, Straub S, Chainey S, Virgin G, Cushway T. Effectiveness and safety of ferric carboxymaltose treatment in children and adolescents with inflammatory bowel disease and other gastrointestinal diseases. *BMC Gastroenterol.* 2014;14(1):184. PubMed doi: 10.1186/1471-230X-14-184

79. Hubbard L, Haynes L, Sklar M, Martinez AE, Mellerio JE. The challenges of meeting nutritional requirements in children and adults with epidermolysis bullosa: proceedings of a multidisciplinary team study day. *Clin Exp Dermatol.* 2011;36(6):579–583. PubMed doi: 10.1111/j.1365-2230.2011.04091.x

80. Puri K, Jeewa A, Adachi I, et al. Prevalence of Anemia and Iron Deficiency in Pediatric Patients on Ventricular Assist Devices. *ASAIO J.* 2018;64(6):795–801. PubMed doi: 10.1097/MAT.0000000000000725

81. Goldberg JF, Shah MD, Kantor PF, et al. Prevalence and Severity of Anemia in Children Hospitalized with Acute Heart Failure. *Congenit Heart Dis.* 2016;11(6):622–629. PubMed doi: 10.1111/chd.12355

82. Lewis GD, Malhotra R, Hernandez AF, et al; NHLBI Heart Failure Clinical Research Network. Effect of Oral Iron Repletion on Exercise Capacity in Patients With Heart Failure With Reduced Ejection Fraction and Iron Deficiency: The IRONOUT HF Randomized

Clinical Trial. *JAMA*. 2017;317(19):1958–1966. PubMed doi: 10.1001/jama.2017.5427

83. Anker SD, Comin Colet J, Filippatos G, et al; FAIR-HF Trial Investigators. Ferric carboxymaltose in patients with heart failure and iron deficiency. *N Engl J Med*. 2009;361(25):2436–2448. PubMed doi: 10.1056/NEJMoa0908355
84. Puri K, Price JF, Spinner JA, et al. Iron Deficiency Is Associated with Adverse Outcomes in Pediatric Heart Failure. *J Pediatr*. 2020;216:58–66.e1. PubMed doi: 10.1016/j.jpeds.2019.08.060
85. Ubesie AC, Kocoshis SA, Mezoff AG, Henderson CJ, Helmrath MA, Cole CR. Multiple micronutrient deficiencies among patients with intestinal failure during and after transition to enteral nutrition. *J Pediatr*. 2013;163(6):1692–1696. PubMed doi: 10.1016/j.jpeds.2013.07.015
86. Bircher AJ, Auerbach M. Hypersensitivity from intravenous iron products. *Immunology and allergy clinics of North America*. 2014;34(3):707–23, x-xi. PubMed doi: 10.1016/j.iac.2014.04.013
87. Rampton D, Folkersen J, Fishbane S, et al. Hypersensitivity reactions to intravenous iron: guidance for risk minimization and management. *Haematologica*. 2014;99(11):1671–1676. PubMed doi: 10.3324/haematol.2014.111492
88. Wolf M, Rubin J, Achebe M, et al. Effects of Iron Isomaltoside vs Ferric Carboxymaltose on Hypophosphatemia in Iron-Deficiency Anemia: Two Randomized Clinical Trials. *JAMA*. 2020;323(5):432–443. PubMed doi: 10.1001/jama.2019.22450
89. Kirk SE, Scheurer ME, Bernhardt MB, Mahoney DH, Powers JM. Phosphorus levels in children treated with intravenous ferric carboxymaltose. *Am J Hematol*. 2021;96(6):E215–E218. PubMed doi: 10.1002/ajh.26165