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Guidance for the Clinician in Rendering Pediatric Care

Clinical Report—Diagnosis and Prevention of Iron Deficiency and Iron-Deficiency Anemia in Infants and Young Children (0–3 Years of Age)

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KEY WORDS
iron deficiency, iron-deficiency anemia, iron intake, infants, toddlers, breastfeeding, formula

ABBREVIATIONS
ID—iron deficiency
IDA—iron-deficiency anemia
Hb—hemoglobin
SF—serum ferritin
IOM—Institute of Medicine
WIC—Special Supplemental Program for Women, Infants, and Children
CHr—reticulocyte hemoglobin
TfR1—transferrin receptor 1
CRP—C-reactive protein
AAP—American Academy of Pediatrics

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The guidance in this report does not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate.

www.pediatrics.org/cgi/doi/10.1542/peds.2010-2576

doi:10.1542/peds.2010-2576

All clinical reports from the American Academy of Pediatrics automatically expire 5 years after publication unless reaffirmed,revised, or retired at or before that time.

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

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abstract

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This clinical report covers diagnosis and prevention of iron deficiency and iron-deficiency anemia in infants (both breastfed and formula fed) and toddlers from birth through 3 years of age. Results of recent basic research support the concerns that iron-deficiency anemia and iron deficiency without anemia during infancy and childhood can have long-lasting detrimental effects on neurodevelopment. Therefore, pediatricians and other health care providers should strive to eliminate iron deficiency and iron-deficiency anemia. Appropriate iron intakes for infants and toddlers as well as methods for screening for iron deficiency and iron-deficiency anemia are presented. *Pediatrics* 2010;126: 000

INTRODUCTION

Iron deficiency (ID) and iron-deficiency anemia (IDA) continue to be of worldwide concern. Among children in the developing world, iron is the most common single-nutrient deficiency.[1] In industrialized nations, despite a demonstrable decline in prevalence,[2] IDA remains a common cause of anemia in young children. However, even more important than anemia itself is the indication that the more common ID without anemia may also adversely affect long-term neurodevelopment and behavior and that some of these effects may be irreversible.[3,4] Because of the implications for pediatric health care providers and their patients, this report reviews and summarizes this information.

This clinical report is a revision and extension of a previous policy statement published in 1999,[5] which addressed iron fortification of formulas. This report covers diagnosis and prevention of ID and IDA in infants (both breastfed and formula fed) and toddlers aged 1 through 3 years.

DEFINITIONS

Anemia: A hemoglobin (Hb) concentration 2 SDs below the mean Hb concentration for a normal population of the same gender and age range, as defined by the World Health Organization, the United Nations Children's Fund, and United Nations University.[6] On the basis of the 1999–2002 US National Health and Nutrition Examination Survey, anemia is defined as a Hb concentration of less than 11.0 g/dL for both male and female children aged 12 through 35 months.[7,8] For certain populations (ie, people living at high altitudes), adjustment of these values may be necessary.

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Iron sufficiency: A state in which there is sufficient iron to maintain normal physiologic functions.

Iron deficiency: A state in which there is insufficient iron to maintain normal physiologic functions. ID results from inadequate iron absorption to accommodate an increase in requirements attributable to growth or resulting from a long-term negative iron balance. Either of these situations leads to a decrease in iron stores as measured by serum ferritin (SF) concentrations or bone marrow iron content. ID may or may not be accompanied by IDA.

Iron-deficiency anemia: An anemia (as defined above) that results from ID.

Iron overload: The accumulation of excess iron in body tissues. Iron overload usually occurs as a result of a genetic predisposition to absorb and store iron in excess amounts, the most common form of which is hereditary hemochromatosis. Iron overload can also occur as a complication of other hematologic disorders that result in chronic transfusion therapy, repeated injections of parenteral iron, or excessive iron ingestion.

Recommended dietary allowance for iron: The average daily dietary intake that is sufficient to meet the nutrient requirements of nearly all individuals (97%–98%) of a given age and gender.

Adequate intake for iron: This term is used when there is not enough information to establish a recommended dietary allowance for a population (eg, term infants, 0–6 months of age). The adequate intake is based on the estimated average nutrient intake by a group (or groups) of healthy individuals.

IRON REQUIREMENTS FOR INFANTS (UP TO 12 COMPLETED MONTHS OF AGE)

Eighty percent of the iron present in a newborn term infant is accreted during the third trimester of pregnancy. Infants born prematurely miss this rapid accretion and are deficient in total body iron. A number of maternal conditions, such as anemia, maternal hypertension with intrauterine growth restriction, or diabetes during pregnancy, can also result in low fetal iron stores in both term and preterm infants.

Preterm Infants

The deficit of total body iron in preterm infants increases with decreasing gestational age. It is worsened by the rapid postnatal growth that many infants experience and by frequent phlebotomies without adequate blood replacement. On the other hand, sick preterm infants who receive multiple transfusions are at risk of iron overload. The use of recombinant human erythropoietin to prevent transfusion therapy in preterm infants will further deplete iron stores if additional supplemental iron is not provided. The highly variable iron status of preterm infants, along with their risks for ID as well as toxicity, precludes determining the exact requirement, but it can be estimated to be between 2 and 4 mg/kg per day when given orally.[9]

Term Infants (Birth Through 12 Completed Months of Age)

The Institute of Medicine (IOM)[10] used the average iron content of human milk to determine the adequate intake of 0.27 mg/day for term infants from birth through 6 months' completed age. The average iron content of human milk was determined to be 0.35 mg/L, and the average milk intake of an exclusively breastfed infant was determined to be 0.78 L/day. Multiplying these 2 numbers determined the adequate intake of 0.27 mg/day for term infants from birth through 6 months of age in the IOM report. The IOM further reasoned that there should be a direct correlation between infant size and human milk ingestion; therefore, no correction need be made for infant weight. It should be pointed out, however, that although bigger infants may ingest more milk, there is a large variation in iron concentration of human milk, and there is no guarantee that the iron content of the maternal milk matches the needs of the infant for iron.

For infants from 7 to 12 months' completed age, the recommended dietary allowance for iron, according to the IOM, is 11 mg/day, which was determined by using a factorial approach. The amount of iron lost, primarily from sloughed epithelial cells from skin and the intestinal and urinary tracts, was added to the amounts of iron required for increased blood volume, increased tissue mass, and storage iron during this period of life. It was noted that the iron needs of infants do not suddenly jump from 0.27 to 11 mg/day at 6 months of age; this disjuncture is the result of the use of very different methods of determining these values. However, it is clear that healthy, term newborn infants require very little iron early in life compared with the significant amounts of iron required after 6 months of age.

IRON REQUIREMENTS FOR TODDLERS (1–3 YEARS OF AGE)

Using a similar factorial approach as described for infants 7 to 12 months' completed age, the IOM determined that the recommended dietary allowance for iron for children from 1 through 3 years of age is 7 mg/day.[9]

PREVALENCE OF ID AND IDA

There are currently no national statistics for the prevalence of ID and IDA in infants before 12 months' completed age. Hay et al[11] reported on a cohort of 284 term Norwegian infants. Using the definitions provided by Dallman[12] in an IOM report, the prevalence of ID at 6

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months of age was 4% and increased to 12% at 12 months of age.

The prevalence of ID and IDA among toddlers (1–3 years of age) in the United States is listed in Table 1 and was derived from National Health and Nutrition Examination Survey data collected between 1999 and 2002.[7,8] The overall prevalence of anemia and possibly ID and IDA in infants and toddlers has declined since the 1970s.[2] Although there is no direct proof, this decline has been attributed to use of iron-fortified formulas and iron-fortified infant foods provided by the Special Supplemental Program for Women, Infants, and Children (WIC) in the early 1970s and the decrease in use of whole cow milk for infants.[8] Still, ID remains relatively common and occurs in 6.6% to 15.2% of toddlers, depending on ethnicity and socioeconomic status. The prevalence of IDA is 0.9% to 4.4%, again depending on race/ethnicity and socioeconomic status,[7,8] but only accounts for approximately 40% of the anemia in toddlers (Table 1). These numbers are comparable to data collected in other industrialized countries.[13,14]

Related to the problem of ID/IDA is the interaction of iron and lead. Results of both animal and human studies have confirmed that IDA increases intestinal lead absorption.[15–17] A reasonably well-established epidemiologic association has been made between IDA and increased lead concentrations.[18] Thus, primary prevention of IDA could also serve as primary prevention of lead poisoning. This possibility is all the more attractive, because lead has been reported to induce neurotoxicity at even very low blood concentrations.[19,20] In addition, preexisting IDA decreases the efficiency of lead chelation therapy, and iron supplementation corrects this effect. In contrast, iron supplementation in a child with IDA who also has lead poisoning without chelation therapy seems to increase blood lead concentrations and decrease basal lead excretion.[21,22] The effect of iron supplementation on blood lead concentrations in iron-replete children with or without lead poisoning is not known. Thus, in theory, selective rather than universal iron supplementation would be more likely to reduce lead poisoning and its potential harmful effects on these children.

TABLE 1 ID, IDA, and Anemia in the 1999–2002 National Health and Nutrition Examination Survey,[7] Children 12 to 35 Months of Age

Population Sampled (No.)	Proportion of US Toddler Population, % (SE)[a]	ID, % (SE)	IDA, % (SE)	All Anemia, % (SE)
General US population (672)		9.2 (1.3)	2.1 (0.6)	5.1 (0.8)
Above poverty line (355)[b]	66.4 (2.9)	8.9 (1.7)	2.2 (0.8)[c]	4.6 (1.1)
Below poverty line (268)[b]	33.6 (2.9)	8.6 (1.6)	2.3 (1.2)[c]	6.2 (1.3)
Enrolled in WIC (360)[d]	44.4 (3.2)	10.7 (2.1)	3.1 (1.2)[c]	6.6 (1.4)
Non-Hispanic white (196)	58.0 (3.8)	7.3 (1.9)	2.0 (0.8)[c]	4.6 (1.2)
Non-Hispanic black (173)	14.1 (2.1)	6.6 (1.8)	1.6 (0.9)[c]	8.3 (1.9)
Mexican American (231)	15.0 (2.2)	13.9 (3.1)	0.9 (0.7)[c]	3.2 (1.2)[c]
Other ethnicity (72)	13.0 (2.7)	15.2 (4.7)[c]	4.4 (2.7)[c]	5.5 (2.7)[c]

Shown are the unweighted number and weighted percentage and SEs for all children with complete data for Hb, SF, transferrin saturation, and zinc protoporphyrin. Anemia was defined as a Hb concentration of <11.0 g/dL; ID[7] was defined as an abnormal value for at least 2 of 3 indicators: SF (abnormal cutoff: <10 μg/dL), zinc protoporphyrin (>1.42 μmol/L red blood cells), and transferrin saturation ($<10\%$); and IDA was defined as anemia plus ID.

[a] Proportion of row descriptor of all children in analytic sample ($N = 672$).

[b] Children with income data ($N = 623$).

[c] Estimate is statistically unreliable. Relative SE (SE of estimate/estimate $\times$ 100) $\geq 30\%$.

[d] Any member of household who received benefits from WIC in the previous 12 months: children with food-security data ($N = 668$).

ID AND NEURODEVELOPMENT

The possible relationship between ID/IDA and later neurobehavioral development in children is the subject of many reports.[3,23–31] Results of a preponderance of studies have demonstrated an association between IDA in infancy and later cognitive deficits. Lozoff et al[3,25] have reported detecting cognitive deficits 1 to 2 decades after the iron-deficient insult during infancy. However, it has been difficult to establish a causal relationship because of the many confounding variables and the difficulty in designing and executing the large, randomized controlled trials necessary to distinguish small potential differences. The authors of a Cochrane Database systematic review, in which the question of whether treatment of IDA improved psychomotor development was examined, stated that there was inconclusive but plausible evidence (only 2 randomized controlled trials) demonstrating improvement if the treatment extended for more than 30 days.[27] McCann and Ames[28] recently reviewed the evidence of a causal relationship between ID/IDA and deficits in cognitive and behavioral function. They concluded that for IDA, there is at least some support for causality, but because specificity for both cause and effect have not been established unequivocally, it is premature to conclude the existence of a causal relationship between IDA and cognitive and behavioral performance. For ID, some evidence of causality exists, but it is less than that for IDA.[28]

It is known that iron is essential for normal neurodevelopment in a number of animal models. ID affects neuronal energy metabolism, the metabolism of neurotransmitters, myelination, and memory function. These observations would explain the behavioral findings in human infants that have been associated with ID.[29–31] Therefore, taking into account that iron is the world's most common

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single-nutrient deficiency, it is important to minimize IDA and ID among infants and toddlers, even if an unequivocal relationship between IDA and ID and neurodevelopmental outcomes has yet to be established.

DIAGNOSIS

Iron status is a continuum. At one end of the spectrum is IDA, and at the other end is iron overload. ID and IDA are attributable to an imbalance between iron needs and available iron that results in a deficiency of mobilizable iron stores and is accompanied by changes in laboratory measurements that include Hb concentration, mean corpuscular Hb concentration, mean corpuscular volume, reticulocyte Hb concentration (abbreviated in the literature as CHr) content, total iron-binding capacity, transferrin saturation, zinc protoporphyrin, SF concentration, and serum transferrin receptor 1 (TfR1) concentration. Measurements that are used to describe iron status are listed in Table 2.

In a child with ID, as the Hb concentration falls 2 SDs below the mean for age and gender, IDA is present, by definition; for infants at 12 months of age, this is 11.0 mg/dL.[7,8] When IDA accounted for most cases of anemia in children, "anemia" and "IDA" were roughly synonymous, and a simple measurement of Hb concentration was sufficient to make a presumptive diagnosis of anemia attributable to ID. Particularly in industrialized nations, the prevalence of ID and IDA has decreased, and other causes of anemia, such as hemolytic anemias, anemia of chronic disease, and anemia attributable to other nutrient deficiencies, have become proportionately more common.[32]

TABLE 2 Spectrum of Iron Status

Parameter	ID Without Anemia	IDA	Iron Overload
SF[a]	↓	↓ ↓	↑
Transferrin saturation	↓	↓	↑ ↑
TfR1	↑ ↑	↑ ↑ ↑	↓
CHr	↓	↓	Normal
Hb	Normal	↓	Normal
Mean corpuscular volume	Normal	↓	Normal

[a] Confounded by the presence of inflammation. If SF is normal or increased and the CRP level is normal, then there is no ID. If SF is decreased, then ID is present regardless of the measure of CRP. If SF is normal or increased and the CRP level is increased, then the presence of ID cannot be determined.

Modified from American Academy of Pediatrics, Committee on Nutrition. Iron deficiency. In: Kleinman RE, ed. *Pediatric Nutrition Handbook*. 5th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2004:304.

No single measurement is currently available that will characterize the iron status of a child. The limitations of using Hb concentration as a measure of iron status are its lack of specificity and sensitivity. Factors that limit erythropoiesis or result in chronic hemolysis, such as genetic disorders and chronic infections, may result in low Hb concentrations. Vitamin B_{12} or folate deficiency, although uncommon in the pediatric population, also can result in a low Hb concentration. The lack of sensitivity is largely attributable to the marked overlap in Hb concentrations between populations with iron sufficiency and those with ID.[33] Thus, to identify ID or IDA, Hb concentration must be combined with other measurements of iron status. Once the diagnosis of IDA has been established, however, following Hb concentration is a good measure of response to treatment.

In establishing the definitive iron status of an individual, it is desirable to use the fewest tests that will accurately reflect iron status. Any battery of tests must include Hb concentration, because it determines the adequacy of the circulating red cell mass and whether anemia is present. One or more tests must be added to the determination of Hb concentration if ID or IDA is to be diagnosed. The 3 parameters that provide discriminatory information about iron status are SF, CHr, and TfR1 concentrations.

SF is a sensitive parameter for the assessment of iron stores in healthy subjects[34–36]; 1 μg/L of SF corresponds to 8 to 10 mg of available storage iron.[34,37,38] Measurement of SF concentration is widely used in clinical practice and readily available. Cook et al[36] selected an SF concentration below 12 μg/L as diagnostic for ID after a comprehensive population survey in the United States. Thus, a cutoff value of 12 μg/L has been widely used for adults and denotes depletion of iron stores. In children, a cutoff value of 10 μg/L has been suggested.[39] Because SF is an acute-phase reactant, concentrations of SF may be elevated in the presence of chronic inflammation, infection, malignancy, or liver disease, and a simultaneous measurement of C-reactive protein (CRP) is required to rule out inflammation. Although Brugnara et al[40] found SF concentration to be less accurate than either the CHr or TfR1 concentration in establishing iron status of children, combining SF concentration with a determination of CRP is currently more readily available to assess iron stores and is a reliable screening test as long as the CRP level is not elevated[41] (Table 2).

CHr and TfR1 concentrations are not affected by inflammation (infection), malignancy, or anemia of chronic disease and, thus, would be preferable as biomarkers for iron status. Only the CHr assay is currently available for use in children. The CHr content assay has been validated in children, and standard values have been determined.[40,42] The CHr assay provides a measure of iron available to cells recently released from the bone marrow. CHr content can be measured by flow cytometry, and 2 of the 4 automated hematology analyzers commonly used in the United States have the capability to measure CHr.[43] A low CHr concentra-

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tion has been shown to be the strongest predictor of ID in children[40,42,43] and shows much promise for the diagnosis of ID when the assay becomes more widely available.

TfR1 is a measure of iron status, detecting ID at the cellular level. TfR1 is found on cell membranes and facilitates transfer of iron into the cell. When the iron supply is inadequate, there is an upregulation of TfR1 to enable the cell to compete more effectively for iron, and subsequently, more circulating TfR1 is found in serum. An increase in serum TfR1 concentrations is seen in patients with ID or IDA, although it does not increase in serum until iron stores are completely exhausted in adults.[44–46] However, the TfR1 assay is not widely available, and standard values for infants and children have yet to be established.

Thus, to establish a diagnosis of IDA, the following sets of tests can be used at the present time (when coupled with determination of a Hb concentration of <11 g/dL): (1) SF and CRP measurements or (2) CHr measurement. For diagnosing ID without anemia, measure either (1) SF and CRP or (2) CHr.

Another approach to making the diagnosis of IDA in a clinically stable child with mild anemia (Hb concentration between 10 and 11 g/dL) is to monitor the response to iron supplementation, especially if a dietary history indicates that the diet is likely to be iron deficient. An increase in Hb concentration of 1 g/dL after 1 month of therapeutic supplementation has been used to signify the presence of IDA. This approach requires that iron supplementation be adequate, iron be adequately absorbed, and patient compliance with adequate follow-up can be ensured. However, because only 40% of the cases of anemia identified at 12 months of age will be secondary to IDA (Table 1), strong consideration should be given to establishing a diagnosis of IDA by using the screening tests described previously.

PREVENTION OF ID AND IDA

Preterm Infants

The preterm infant (<37 weeks' gestation) who is fed human milk should receive a supplement of elemental iron at 2 mg/kg per day starting by 1 month of age and extending through 12 months of age.[47] This can be provided as medicinal iron or in iron-fortified complementary foods. Preterm infants fed a standard preterm infant formula (14.6 mg of iron per L) or a standard term infant formula (12.0 mg of iron per L) will receive approximately 1.8 to 2.2 mg/kg per day of iron, assuming a formula intake of 150 mL/kg per day. Despite the use of iron-containing formulas, 14% of preterm infants develop ID between 4 and 8 months of age.[48] Thus, some formula-fed preterm infants may need an additional iron supplement,[47] although there is not enough evidence to make this a general recommendation at this time. Exceptions to this iron-supplementation practice in preterm infants would be infants who received multiple transfusions during hospitalization, who might not need any iron supplementation.

Term, Breastfed Infants

Infants who are born at term usually have sufficient iron stores until 4 to 6 months of age.[49] Infants born at term have high Hb concentration and high blood volume in proportion to body weight. They experience a physiologic decline in both blood volume and Hb concentration during the first several months of life. These facts have led to the supposition that breastfed infants need very little iron. It is assumed that the small amount of iron in human milk is sufficient for the exclusively breastfed infant. The World Health Organization recommends exclusive breastfeeding for 6 months, and the American Academy of Pediatrics (AAP) has recommended exclusive breastfeeding for a minimum of 4 months but preferably for 6 months. Exclusive breastfeeding for more than 6 months has been associated with increased risk of IDA at 9 months of age.[49,50] Recommendations for exclusive breastfeeding for 6 months do not take into account infants who are born with lower-than-usual iron stores (low birth weight infants, infants of diabetic mothers), a condition that also has been linked to lower SF concentrations at 9 months of age.[51] In a double-blind study, Friel et al[52] demonstrated that exclusively breastfed infants supplemented with iron between 1 and 6 months of age had higher Hb concentration and higher mean corpuscular volume at 6 months of age than did their unsupplemented peers. Supplementation also resulted in better visual acuity and higher Bayley Psychomotor Developmental Indices at 13 months. Thus, it is recommended that exclusively breastfed term infants receive an iron supplementation of 1 mg/kg per day, starting at 4 months of age and continued until appropriate iron-containing complementary foods have been introduced (Tables 3 and 4). For partially breastfed infants, the proportion of human milk versus formula is uncertain; therefore, beginning at 4 months of age, infants who receive more than one-half of their daily feedings as human milk and who are not receiving iron-containing complementary foods should also receive 1 mg/kg per day of supplemental iron.

Term, Formula-Fed Infants

For the term, formula-fed infant, the level of iron fortification of formula to prevent ID remains controversial.[53,54] For more than 25 years, 12 mg of iron per L has been the level of fortification in standard term infant formulas in the United States, consistent with

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guidelines of WIC for iron-fortified formula (at least 10 mg/L), thus creating a natural experiment. The level of 12 mg/L was determined by calculating the total iron needs of the child from 0 to 12 months of age, assuming average birth weight and average weight gain during the first year. The calculation also assumed that formula was the only source of iron during this period. Others have recommended lower amounts of iron in infant formula,[55] and there have been studies to examine iron-fortification levels of less than 12 mg/L.[56–61] However, it is the conclusion of the AAP that infant formula that contains 12 mg of elemental iron per L is safe for its intended use. Although there has been some concern about linear growth in iron-replete infants given medicinal iron,[62] no published studies have convincingly documented decreased linear growth in iron-replete infants receiving formulas containing high amounts of iron. Evidence is also insufficient to associate formulas that contain 12 mg of iron per L with gastrointestinal symptoms. At least 4 studies have shown no adverse effects.[63–66] Reports have conflicted on whether iron fortification is associated with increased risk of infection. Decreased incidence, increased incidence, and no change in number of infections have all been reported.[67,68] The authors of a recent systematic review concluded that "iron supplementation has no apparent harmful effect on the overall incidence of infectious illnesses in children, though it slightly increases the risk of developing diarrhoea."[69] Finally, when examining specifically infants given formula with 12 mg of iron per L, Singhal et al[70] were "unable to identify adverse health effects in older infants and toddlers consuming a high iron-containing formula." They found no difference between controls and the treatment group in incidence of infection, gastrointestinal problems, or general morbidity.

TABLE 3 Foods to Increase Iron Intake and Iron Absorption

	Elemental Iron, mg
Commercial baby food,[a] heme iron	
Meat	
Baby food, lamb, junior, 1 jar (2.5 oz)	1.2
Baby food, chicken, strained, 1 jar (2.5 oz)	1.0
Baby food, lamb, strained, 1 jar (2.5 oz)	0.8
Baby food, beef, junior, 1 jar (2.5 oz)	0.7
Baby food, beef, strained, 1 jar (2.5 oz)	0.7
Baby food, chicken, junior, 1 jar (2.5 oz)	0.7
Baby food, pork, strained, 1 jar (2.5 oz)	0.7
Baby food, ham, strained, 1 jar (2.5 oz)	0.7
Baby food, ham, junior, 1 jar (2.5 oz)	0.7
Baby food, turkey, strained, 1 jar (2.5 oz)	0.5
Baby food, veal, strained, 1 jar (2.5 oz)	0.5
Commercial baby food,[a] nonheme iron	
Vegetables	
Baby food, green beans, junior, 1 jar (6 oz)	1.8
Baby food, peas, strained, 1 jar (3.4 oz)	0.9
Baby food, green beans, strained, 1 jar (4 oz)	0.8
Baby food, spinach, creamed, strained, 1 jar (4 oz)	0.7
Baby food, sweet potatoes, junior (6 oz)	0.7
Cereals	
Baby food, brown rice cereal, dry, instant, 1 tbsp	1.8
Baby food, oatmeal cereal, dry, 1 tbsp	1.6
Baby food, rice cereal, dry, 1 tbsp	1.2
Baby food, barley cereal, dry, 1 tbsp	1.1
Table food, heme iron	
Clams, canned, drained solids, 3 oz	23.8
Chicken liver, cooked, simmered, 3 oz	9.9
Oysters, Eastern canned, 3 oz	5.7
Beef liver, cooked, braised, 3 oz	5.6
Shrimp, cooked moist heat, 3 oz	2.6
Beef, composite of trimmed cuts, lean only, all grades, cooked, 3 oz	2.5
Sardines, Atlantic, canned in oil, drained solids with bone, 3 oz	2.5
Turkey, all classes, dark meat, roasted, 3 oz	2.0
Lamb, domestic, composite of trimmed retail cuts, separable lean only, choice, cooked, 3 oz	1.7
Fish, tuna, light, canned in water, drained solids, 3 oz	1.3
Chicken, broiler or fryer, dark meat, roasted, 3 oz	1.1
Turkey, all classes, light meat, roasted, 3 oz	1.1
Veal, composite of trimmed cuts, lean only, cooked, 3 oz	1.0
Chicken, broiler or fryer, breast, roasted, 3 oz	0.9
Pork, composite of trimmed cuts (leg, loin, shoulder), lean only, cooked, 3 oz	0.9
Fish, salmon, pink, cooked, 3 oz	0.8
Table food, nonheme iron	
Oatmeal, instant, fortified, cooked, 1 cup	14.0
Blackstrap molasses,[b] 2 tbsp	7.4
Tofu, raw, regular, ½ cup	6.7
Wheat germ, toasted, ½ cup	5.1
Ready-to-eat cereal, fortified at different levels, 1 cup	~4.5 to 18
Soybeans, mature seeds, cooked, boiled, ½ cup	4.4
Apricots, dehydrated (low-moisture), uncooked, ½ cup	3.8
Sunflower seeds, dried, ½ cup	3.7
Lentils, mature seeds, cooked, ½ cup	3.3
Spinach, cooked, boiled, drained, ½ cup	3.2
Chickpeas, mature seeds, cooked, ½ cup	2.4
Prunes, dehydrated (low-moisture), uncooked, ½ cup	2.3
Lima beans, large, mature seeds, cooked, ½ cup	2.2
Navy beans, mature seeds, cooked, ½ cup	2.2
Kidney beans, all types, mature seeds, cooked, ½ cup	2.0
Molasses, 2 tbsp	1.9
Pinto beans, mature seeds, cooked, ½ cup	1.8
Raisins, seedless, packed, ½ cup	1.6

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TABLE 3 Continued

	Elemental Iron, mg
Prunes, dehydrated (low moisture), stewed, ½ cup	1.6
Prune juice, canned, 4 fl oz	1.5
Green peas, cooked, boiled, drain, ½ cup	1.2
Enriched white rice, long-grain, regular, cooked, ½ cup	1.0
Whole egg, cooked (fried or poached), 1 large egg	0.9
Enriched spaghetti, cooked, ½ cup	0.9
White bread, commercially prepared, 1 slice	0.9
Whole-wheat bread, commercially prepared, 1 slice	0.7
Spaghetti or macaroni, whole wheat, cooked, ½ cup	0.7
Peanut butter, smooth style, 2 tbsp	0.6
Brown rice, medium-grain, cooked, ½ cup	0.5

Note that all figures are rounded.

[a] Baby food values are generally based on generic jar, not branded jar; 3 oz of table-food meat = 85 g; a 2.5-oz jar of baby food = 71 g (an infant would not be expected to eat 3 oz [approximately the size of a deck of cards] of pureed table meat at a meal).

[b] Source of iron value was obtained from a manufacturer of this type of molasses.

Source of iron values in foods: US Department of Agriculture, Agricultural Research Service. USDA National Nutrient Database for Standard Reference, Release 20: Nutrient Data Laboratory home page. Available at: www.ars.usda.gov/ba/bhnrc/ndl.

TABLE 4 Selected Good Vitamin C Sources to Increase Iron Absorption

Fruits	Vegetables
Citrus fruits (eg, orange, tangerine, grapefruit)	Green, red, and yellow peppers
Pineapples	Broccoli
Fruit juices enriched with vitamin C	Tomatoes
Strawberries	Cabbages
Cantaloupe	Potatoes
Kiwifruit	Leafy green vegetables
Raspberries	Cauliflower

Toddlers (1–3 Years of Age)

The iron requirement for toddlers is 7 mg/day. Ideally, the iron requirements of toddlers would be met and ID/IDA would be prevented with naturally iron-rich foods rather than iron supplementation. These foods include those with heme sources of iron (ie, red meat) and nonheme sources of iron (ie, legumes, iron-fortified cereals) (Table 3). Foods that contain vitamin C (ascorbic acid), such as orange juice, aid in iron absorption and are listed in Table 4. Foods that contain phytates (found in soy) reduce iron absorption. Through public education and altering feeding practices, the amount of iron available to older infants and toddlers via a normal diet could be maximized (Table 3).

In developing countries, iron requirements of older infants and toddlers have been met by iron fortification of various foods, including corn flour,[71] soy sauce,[72] fish sauce,[73] and rice.[74] However, there are many technical and practical barriers to a successful fortification program for toddlers. Not the least of these barriers is the determination of which foods to fortify with iron. In the United States, fortification of infant formula and infant cereal has been credited with the decline in IDA. However, toddlers in the United States typically do not eat enough of any other food to serve as a vehicle for iron fortification. Universal food fortification for all ages is problematic, given the possible adverse effects of iron in certain subsets of older children and adults.

As an alternative for toddlers who do not eat adequate amounts of iron-containing food (Table 3), iron supplements are available in the form of iron sulfate drops and chewable iron tablets or as a component of either liquid or chewable multivitamins. Iron sprinkles with or without additional zinc are available in Canada. Barriers to adequate iron supplementation are (1) lack of education for care providers and patients, (2) poor compliance made worse by the perception of adverse effects, including nausea, vomiting, constipation, stomach upset, and teeth staining, (3) cost, (4) current federal supplemental nutrition programs not providing iron supplements, and (5) risk of iron overload.

Screening for ID and IDA

The AAP has concluded that universal screening for anemia should be performed with determination of Hb concentration at approximately 1 year of age. Universal screening would also include an assessment of risk factors associated with ID/IDA: history of prematurity or low birth weight; exposure to lead; exclusive breastfeeding beyond 4 months of age without supplemental iron; and weaning to whole milk or complementary foods that do not include iron-fortified cereals or foods naturally rich in iron (Table 3). Additional risk factors include the feeding problems, poor growth, and inadequate nutrition typically seen in infants with special health care needs as well as low socioeconomic status, especially children of Mexican American descent, as identified in the recent National Health and Nutrition Examination Survey[8,75] (Table 1). Selective screening can be performed at any age when these risk factors for ID and IDA have been identified, including risk of inadequate iron intake according to dietary history.

It has been acknowledged that screening for anemia with a Hb determination neither identifies children with ID nor specifically identifies those with IDA.[76] In the United States, 60% of anemia is not attributable to ID, and most tod-

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dlers with ID do not have anemia (Table 2). It is also known that there is poor follow-up testing and poor documentation of improved Hb concentrations. In 1 study, 14% of the children had a positive screening result for anemia. However, only 18.3% of these children with a positive screening result had follow-up testing performed, and of that group, only 11.6% had documented correction of low Hb levels.[77] Therefore, for infants identified with a Hb concentration of less than 11.0 mg/dL or identified with significant risk of ID or IDA as described previously, SF and CRP or CHr levels in addition to Hb concentration should be measured to increase the sensitivity and specificity of the diagnosis. In addition, the AAP, the World Health Organization, and the European Society for Pediatric Gastroenterology, Hepatology and Nutrition also support the use of the measurement of TfR1 as a screening test once the method has been validated and normal values for infants and toddlers have been established.

Another step to improve the current screening system is to use technology-based reminders for screening and follow-up of infants and toddlers with a diagnosis of ID/IDA. Reminders could be incorporated into electronic health records, and there should be documentation that Hb concentrations have returned to the normal range. The efficacy of any program for minimizing ID and IDA should be tracked scientifically and evaluated through well-planned surveillance programs.

SUMMARY

Given that iron is the world's most common single-nutrient deficiency and there is some evidence of adverse effects of both ID and IDA on cognitive and behavioral development, it is important to minimize ID and IDA in infants and toddlers without waiting for unequivocal evidence. Controversies remain regarding the timing and methods used for screening for ID/IDA as well as regarding the use of iron supplements to prevent ID/IDA. Although further study is required to generate higher levels of evidence to settle these controversies, the currently available evidence supports the following recommendations.

1. Term, healthy infants have sufficient iron for at least the first 4 months of life. Human milk contains very little iron. Exclusively breastfed infants are at increasing risk of ID after 4 completed months of age. Therefore, at 4 months of age, breastfed infants should be supplemented with 1 mg/kg per day of oral iron beginning at 4 months of age until appropriate iron-containing complementary foods (including iron-fortified cereals) are introduced in the diet (see Table 3). For partially breastfed infants, the proportion of human milk versus formula is uncertain; therefore, beginning at 4 months of age, partially breastfed infants (more than half of their daily feedings as human milk) who are not receiving iron-containing complementary foods should also receive 1 mg/kg per day of supplemental iron.
2. For formula-fed infants, the iron needs for the first 12 months of life can be met by a standard infant formula (iron content: 12 mg/dL) and the introduction of iron-containing complementary foods after 4 to 6 months of age, including iron-fortified cereals (Table 3). Whole milk should not be used before 12 completed months of age.
3. The iron intake between 6 and 12 months of age should be 11 mg/day. When infants are given complementary foods, red meat and vegetables with higher iron content should be introduced early (Table 3). To augment the iron supply, liquid iron supplements are appropriate if iron needs are not being met by the intake of formula and complementary foods.
4. Toddlers 1 through 3 years of age should have an iron intake of 7 mg/day. This would be best delivered by eating red meats, cereals fortified with iron, vegetables that contain iron, and fruits with vitamin C, which augments the absorption of iron (Tables 3 and 4). For toddlers not receiving this iron intake, liquid supplements are suitable for children 12 through 36 months of age, and chewable multivitamins can be used for children 3 years and older.
5. All preterm infants should have an iron intake of at least 2 mg/kg per day through 12 months of age, which is the amount of iron supplied by iron-fortified formulas. Preterm infants fed human milk should receive an iron supplement of 2 mg/kg per day by 1 month of age, and this should be continued until the infant is weaned to iron-fortified formula or begins eating complementary foods that supply the 2 mg/kg of iron. An exception to this practice would include infants who have received an iron load from multiple transfusions of packed red blood cells.
6. Universal screening for anemia should be performed at approximately 12 months of age with determination of Hb concentration and an assessment of risk factors associated with ID/IDA. These risk factors would include low socioeconomic status (especially children of Mexican American descent [Table 1]), a history of prematurity or low birth weight, exposure to lead, exclusive breastfeeding beyond 4 months of age without supplemental iron, and weaning to whole milk or complementary foods that do not include iron-fortified cereals or

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foods naturally rich in iron (Table 3). Additional risk factors are the feeding problems, poor growth, and inadequate nutrition typically seen in infants with special health care needs. For infants and toddlers (1–3 years of age), additional screening can be performed at any time if there is a risk of ID/IDA, including inadequate dietary iron intake.

7. If the Hb level is less than 11.0 mg/dL at 12 months of age, then further evaluation for IDA is required to establish it as a cause of anemia. If there is a high risk of dietary ID as described in point 6 above, then further testing for ID should be performed, given the potential adverse effects on neurodevelopmental outcomes. Additional screening tests for ID or IDA should include measurement of:
   - SF and CRP levels; or
   - CHr concentration.
8. If a child has mild anemia (Hb level of 10–11 mg/dL) and can be closely monitored, an alternative method of diagnosis would be to document a 1 g/dL increase in plasma Hb concentration after 1 month of appropriate iron-replacement therapy, especially if the history indicates that the diet is likely to be iron deficient.
9. Use of the TfR1 assay as screening for ID is promising, and the AAP supports the development of TfR1 standards for use of this assay in infants and children.
10. If IDA (or any anemia) or ID has been confirmed by history and laboratory evidence, a means of carefully tracking and following infants and toddlers with a diagnosis of ID/IDA should be implemented. Electronic health records could be used not only to generate reminder messages to screen for IDA and ID at 12 months of age but also to document that IDA and ID have been adequately treated once diagnosed.

ADDENDUM

Development of This Report

This report was written by the primary authors after extensive review of the literature using PubMed, previous AAP reports, Cochrane reviews, and reports from other groups.[1,6,7,48,77]

The report was also submitted to the following sections and committees of the AAP that were asked to comment on the manuscript: Committee on Fetus and Newborn (COFN); Committee on Practice and Ambulatory Medicine (COPAM); Committee on Psychosocial Aspects of Child and Family Health (COPACFH); Section on Administration and Practice Management (SOAPM); Section on Developmental and Behavioral Pediatrics (SODBP); Section on Gastroenterology, Hepatology, and Nutrition (SOGHN); Section on Hematology and Oncology (SOHO); and Section on Breast Feeding (SOBr).

Additional comments were sought from the Centers for Disease Control and Prevention (CDC), the Department of Agriculture (WIC), the National Institutes of Health (NIH), and the Food and Drug Administration (FDA), because these governmental agencies were involved in the development of the statement and will necessarily deal with its impact. As it was developed it was extensively reviewed and revised by members of the AAP Committee on Nutrition, who unanimously approved this clinical report. It is openly acknowledged that where the highest levels of evidence are absent, the opinions and suggestions of members of the Committee on Nutrition as well as other groups consulted for this statement were taken into consideration in developing this clinical report.

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REFERENCES

1. United Nations Administrative Committee on Coordination/Sub-Committee on Nutrition and International Food Policy Research Institute. *Fourth Report of the World Nutrition Situation.* Geneva, Switzerland: United Nations Administrative Committee on Coordination/Sub-Committee on Nutrition; 2000
2. Sherry B, Mei Z, Yip R. Continuation of the decline in prevalence of anemia in low-income infants and children in five states. *Pediatrics.* 2001;107(4):677–682
3. Lozoff B, Jimenez E, Smith JB. Double burden of iron deficiency in infancy and low socioeconomic status: a longitudinal analysis of cognitive test scores to age 19 years. *Arch Pediatr Adolesc Med.* 2006;160(11):1108–1113
4. Bruner AB, Joffe A, Duggan AK, Casella JF, Brandt J. Randomized study of cognitive effects of iron supplementation in nonanemic iron-deficient adolescent girls. *Lancet.* 1996;348(9033):992–996
5. American Academy of Pediatrics, Committee on Nutrition. Iron fortification of infant formulas. *Pediatrics.* 1999;104(1 pt 1):119–123

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6. World Health Organization. *Iron Deficiency Anemia: Assessment, Prevention, and Control—A Guide for Program Managers*. Geneva, Switzerland: World Health Organization; 2001. WHO/NHD/01.3
7. Centers for Disease Control and Prevention, National Center for Health Statistics. National Health and Nutrition Examination Survey. Available at: www.cdc.gov/nchs/nhanes.htm. Accessed September 29, 2008
8. Cusick SE, Mei Z, Freedman DS, et al. Unexplained decline in the prevalence of anemia among US children and women between 1988–1994 and 1999–2002. *Am J Clin Nutr*. 2008;88:1611–1617
9. Rao R, Georgieff MK. Microminerals. In: Tsang RC, Uauy R, Koletzko R, Zlotikin SH, eds. *Nutrition of the Preterm Infant. Scientific Basis and Practical Guidelines*. Cincinnati, OH: Digital Educational Publishing Inc; 2005:277–310
10. Institute of Medicine. *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*. Washington, DC: National Academies Press; 2003
11. Hay G, Sandstad B, Whitelaw A, Borchlohnsen B. Iron status in a group of Norwegian children aged 6–24 months. *Acta Paediatr*. 2004;93(5):592–598
12. Dallman PR. Iron deficiency anemia: a synthesis of current scientific knowledge and U.S. recommendations for prevention and treatment. In: Earl R, Woteki CE, eds. *Iron Deficiency Anemia: Recommended Guidelines for Prevention, Detection and Management Among U.S. Children and Women of Childbearing Age*. Washington, DC: National Academies Press; 1993:41–97
13. Gregory JR, Collins DL, Davies PSW, Hughes JM, Clarke PC. *National Diet and Nutrition Survey: Children Aged 1½ to 4½ Years: Volume 1—Report of the Diet and Nutrition Survey*. London, England: Her Majesty's Stationery Office; 1995
14. Male C, Persson LA, Freeman V, Guerra A, van't Hof MA, Haschke F; Euro-Growth Iron Study Group. Prevalence of iron deficiency in 12-mo-old infants from 11 European areas and influence of dietary factors on iron status (Euro-Growth study). *Acta Paediatr*. 2001;90(5):492–498
15. Six KM, Goyer RA. The influence of iron deficiency on tissue content and toxicity of ingested lead in rats. *J Lab Clin Med*. 1972; 79(1):128–136
16. Barton JC, Conrad ME, Nuby S, Harrison L. Effects of iron in the absorption and retention of lead. *J Lab Clin Med*. 1978;92(4): 536–547
17. Watson WS, Morrison J, Bethel MI, et al. Food iron and lead absorption in humans. *Am J Clin Nutr*. 1986;44(2):248–256
18. Wright DO, Shannon MW, Wright RJ, Hu H. Association between iron deficiency and low-level lead poisoning in an urban primary care clinic. *Am J Public Health*. 1999; 89(7):1049–1053
19. Canfield RL, Henderson CR Jr, Cory-Slechta DA, Cox C, Jusko TA, Lanphear PB. Intellectual impairment in children with blood lead concentration below 10 microg per deciliter. *N Engl J Med*. 2003;348(16):1517–1526
20. Finkelstein Y, Markowitz ME, Rosen JF. Low-level lead-induced neurotoxicity in children: an update on central nervous system effects. *Brain Res Brain Res Rev*. 1998;27(2): 168–176
21. Angle CR, Stelmak KL, McIntyre MS. Lead and iron deficiency. In: Hemphill DD, ed. *Trace Substances in Environmental Health. Vol IV*. Columbia, MO: University of Missouri; 1975: 367–386
22. Ruff RA, Markowitz ME, Bijur PE, Rosen JF. Relationship among blood lead levels, iron deficiency and cognitive development in two year old children. *Environ Health Perspect*. 1996;104(2):180–185
23. Idjradinata P, Pollitt E. Reversal of developmental delays in iron-deficient anemic infants treated with iron. *Lancet*. 1993; 341(8836):1–4
24. Lozoff B, Jimenez E, Wolf AW. Long-term developmental outcome of infants with iron deficiency. *N Engl J Med*. 1991;325(10): 687–694
25. Lozoff B, Jimenez E, Hagen J, Mollen E, Wolf AW. Poorer behavioral and developmental outcome more than 10 years after treatment for iron deficiency in infancy. *Pediatrics*. 2000;105(4). Available at: www.pediatrics.org/cgi/content/full/105/4/e51
26. Lozoff B, De Andraca I, Castillo M, Smith JB, Walter T, Pino P. Behavioral and developmental effects of preventing iron-deficiency anemia in healthy full-term infants [published correction appears in *Pediatrics*. 2004;113(6):1853]. *Pediatrics*. 2003;112(4): 846–854
27. Logan S, Martins S, Gilbert R. Iron therapy for improving psychomotor development and cognitive function in children under the age of three with iron deficiency anemia. *Cochrane Database Syst Rev*. 2001;(2): CD001444
28. 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
29. Georgieff MK. The role of iron in neurodevelopment: fetal iron deficiency and the developing hippocampus. *Biochem Soc Trans*. 2008;36(pt 6):1267–1271
30. Carlson ES, Tkac I, Magid R, et al. Iron is essential for neuron development and memory function in mouse hippocampus. *J Nutr*. 2009;139(4):672–679
31. Tran PV, Fretham SJ, Carlson ES, Georgieff MK. Long-term reduction of hippocampal brain-derived neurotrophic factor activity after fetal-neonatal iron deficiency in adult rats. *Pediatr Res*. 2009;65(5):493–498
32. Yip R, Binkin NJ, Fleshood L, Trowbridge FL. Declining prevalence of anemia among low-income children in the United States. *JAMA*. 1987;258(12):1619–1623
33. Garby L, Irnell L, Werner I. Iron deficiency in women of fertile age in a Swedish community: II. Efficiency of several laboratory tests to predict the response to iron supplementation. *Acta Med Scand*. 1969; 185(1–2):107–111
34. Jacobs A, Miller F, Worwood M, Beamish MR, Wardrop CA. Ferritin in the serum of normal subjects and patients with iron deficiency and iron overload. *Br Med J*. 1972;4(5834): 206–208
35. Walters GO, Miller FM, Worwood M. Serum ferritin concentration and iron stores in normal subjects. *J Clin Pathol*. 1973;26(10): 770–772
36. Cook JD, Lipschitz DA, Miles LE, Finch CA. Serum ferritin as a measure of iron stores in normal subjects. *Am J Clin Nutr*. 1974; 27(7):681–687
37. Birgegård G, Högman C, Killander A, Levander H, Simonsson B, Wide L. Serum ferritin and erythrocyte 2,3-DPG during quantitated phlebotomy and iron treatment. *Scand J Haematol*. 1977;19(4):327
38. Jacob RA, Sandstead HH, Klevay LM, Johnson LK. Utility of serum ferritin as a measure of iron deficiency in normal males undergoing repetitive phlebotomy. *Blood*. 1980;56(5):786–791
39. Dallman PR, Siimes MA, Stekel A. Iron deficiency in infancy and childhood. *Am J Clin Nutr*. 1980;33(1):86–118
40. Brugnara C, Zurakowski D, DiCanzio J, Boyd T, Platt O. Reticulocyte hemoglobin content to diagnose iron deficiency in children. *JAMA*. 1999;281(23):2225–2230
41. World Health Organization. Assessing the iron status of populations: report of a Joint World Health Organization/Centers for Disease Control and Prevention technical consultation on the assessment of iron status at the population level. Geneva, Switzerland; April 6–8, 2004. Available at: http://

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whqlibdoc.who.int/publications/2004/9241593156_eng.pdf. Accessed September 29, 2008

42. Ullrich C, Wu A, Armsby C, et al. Screening healthy infants for iron deficiency using reticulocyte hemoglobin content. *JAMA*. 2005; 294(8):924–930
43. Brugnara C, Schiller B, Moran J. Reticulocyte hemoglobin equivalent (Ret He) and assessment of iron-deficient states. *Clin Lab Haematol*. 2006;28(5):303–308
44. Skikne BS, Flowers CH, Cook JD. Serum transferrin receptor: a quantitative measure of tissue iron deficiency. *Blood*. 1990; 75(9):1870–1876
45. Ferguson BJ, Skikne BS, Simpson KM, Baynes RD, Cook JD. Serum transferrin receptor distinguishes the anemia of chronic disease from iron deficiency anemia. *J Lab Clin Med*. 1992;119(4):385–390
46. Worwood M. Serum transferrin receptor assays and their application. *Ann Clin Biochem*. 2002;39(pt 3):221–230
47. American Academy of Pediatrics, Committee on Nutrition. Nutritional needs of the premature infant. In: Kleinman RE, ed. *Pediatric Nutrition Handbook*. 6th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2008:79–112
48. Griffin IJ, Cooke RJ, Reid MM, McCormick KP, Smith JS. Iron nutritional status in preterm infants fed formulas fortified with iron. *Arch Dis Child Fetal Neonatal Ed*. 1999;81(1): F45–F49
49. Dallman PR. Nutritional anemias in childhood: iron, folate and vitamin B_{12}. In: Suskind RM, Lewinter-Suskind L, eds. *Textbook of Pediatric Nutrition. 2nd ed*. New York, NY: Raven Press; 1993:91–105
50. Meinzen-Derr JK, Guerrero ML, Altaye M, Ortega-Gallegos H, Ruiz-Palacios GM, Morrow AL. Risk of infant anemia is associated with exclusive breast-feeding and maternal anemia in a Mexican cohort. *J Nutr*. 2006; 136(2):452–458
51. Georgieff MK, Wewerke SW, Nelson CA, deRegnier RA. Iron status at 9 months of infants with low iron stores at birth. *J Pediatr*. 2002;141(3):405–409
52. Friel JK, Aziz K, Andrews WL, Harding SV, Courage ML, Adams RJ. A double-masked, randomized control trial of iron supplementation in early infancy in healthy term breast-fed infants. *J Pediatr*. 2003;143(5): 582–586
53. Lönnerdal B. Effects of milk and milk components on calcium, magnesium and trace element absorption during infancy. *Physiol Rev*. 1997;77(3):643–669
54. Pizarro F, Yip R, Dallman PR, Olivares M, Hertrampf E, Walter T. Iron status with different infant feeding regimens: relevance to screening and prevention of iron deficiency. *J Pediatr*. 1991;118(5):687–692
55. Agostoni C, Domellof M. Infant formulae: from ESPGAN recommendations towards ESPGHAN-coordinated global standards. *J Pediatr Gastroenterol Nutr*. 2005;41(5): 580–583
56. Walter T, Pino P, Pizarro F, Lozoff B. Prevention of iron-deficiency anemia: comparison of high- and low-iron formulas in term healthy infants after six months of life. *J Pediatr*. 1998;132(4):635–640
57. Haschke F, Vanura H, Male C, et al. Iron nutrition and growth of breast- and formula-fed infants during the first 9 months of life. *J Pediatr Gastroenterol Nutr*. 1993;16(2): 151–156
58. Haschke F, Ziegler EE, Edwards BB, Fomon SJ. Effect of iron fortification of infant formula on trace mineral absorption. *J Pediatr Gastroenterol Nutr*. 1986;5(5):768–773
59. Hernell O, Lönnerdal B. Iron requirements and prevalence of iron deficiency in term infants during the first six months of life. In: Hallberg L, Asp NG, eds. *Nutrition in Health and Disease*. London, England: John Libbey & Co Ltd; 1996
60. Lönnerdal B, Hernell O. Iron, zinc, copper and selenium status of breast-fed infants and infants fed trace element fortified milk-based infant formula. *Acta Paediatr*. 1994; 83(4):367–733
61. Dewey KG, Domellof M, Cohen RJ, Landa Rivera R, Hornell O, Lönnerdal B. Iron supplementation effects growth and morbidity of breast-fed infants: results of a randomized trial in Sweden and Honduras. *J Nutr*. 2002;132(11):3249–3255
62. Iannotti LL, Tielsch JM, Black MM, Black RE. Iron supplementation in early childhood: health benefits and risks. *Am J Clin Nutr*. 2006;84(6):1261–1276
63. Oski FA. Iron-fortified formulas and gastrointestinal symptoms in infants: a controlled study. *Pediatrics*. 1980;66(2):168–170
64. Nelson SE, Ziegler EE, Copeland AM, Edwards BB, Fomon SJ. Lack of adverse reactions to iron-fortified formula. *Pediatrics*. 1988;81(3):360–364
65. Bradley CK, Hillman L, Sherman AR, Leedy D, Cordano A. Evaluation of two iron-fortified, milk-based formulas during infancy. *Pediatrics*. 1993;91(5):908–914
66. Hyams JS, Treem WR, Etienne NL, et al. Effect of infant formula on stool characteristics of young infants. *Pediatrics*. 1995;95(1):50–54
67. Murray MJ, Murray AB, Murray MB, Murray CJ. The adverse effect of iron repletion on the course of certain infections. *Br Med J*. 1978;2(6145):1113–1115
68. Baqui AH, Zaman K, Persson LA, et al. Simultaneous weekly supplementation of iron and zinc is associated with lower morbidity due to diarrhea and acute lower respiratory infection in Bangladeshi infants. *J Nutr*. 2003;133(12):4150–4157
69. Gera T, Sachdev HP. Effect of iron supplementation on incidence of infectious illness in children: systematic review. *BMJ*. 2002; 325(7373):1142
70. Singhal A, Morley R, Abbott R, Fairweather-Tait S, Stephenson T, Lucas A. Clinical safety of iron-fortified formulas. *Pediatrics*. 2000; 105(3). Available at: www.pediatrics.org/cgi/content/full/105/3/e38
71. Layrisse M, García-Casal MN, Méndez-Castellano H, et al. Impact of fortification of flours with iron to reduce the prevalence of anemia and iron deficiency among schoolchildren in Caracas, Venezuela: a follow-up. *Food Nutr Bull*. 2002;23(4):384–389
72. Chen J, Zhao X, Zhang X, et al. Studies on the effectiveness of NaFeEDTA-fortified soy sauce in controlling iron deficiency: a population-based intervention trial *Food Nutr Bull*. 2005;26(2):177–186; discussion 187–189
73. Ho M. NaFeEDTA-fortified fish sauce: the cure to iron deficiency anemia in Vietnam? *Nutr Noteworthy*. 2005;7:11
74. Haas JD, Beard JL, Murray-Kolb LE, del Mundo AM, Felix A, Gregorio GB. Iron-biofortified rice improves the iron stores of nonanemic Filipino women. *J Nutr*. 2005; 135(12):2823–2830
75. Centers for Disease Control and Prevention. Iron deficiency: United States, 1999–2000. *MMWR Morb Mortal Wkly Rep*. 2002;51(40): 897–899
76. 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
77. Biondich PG, Downs SM, Carroll AE, et al. Shortcomings in infant iron deficiency screening methods. *Pediatrics*. 2006; 117(2):290–294

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Robert D. Baker, Frank R. Greer and THE COMMITTEE ON NUTRITION

Pediatrics originally published online October 5, 2010;

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Pediatrics originally published online October 5, 2010;

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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