A New Era of Iron Deficiency:

Updates to screening, diagnosis, and treatment of iron deficiency with and without anemia in children

Amanda Jacobson-Kelly, MD, MSc
Associate Professor of Pediatrics
Division of Pediatric Hematology/Oncology
Partners for Kids Webinar
October 14, 2026

Nationwide Children's
When your child needs a hospital, everything matters.

Objectives

- Describe the diagnosis of iron deficiency (ID) with and without anemia, including updated diagnostic criteria and clinical practice guidelines (AAP and ASH)
- Recognize the nonhematologic manifestations and associated conditions of ID
- Discuss treatment strategies and when to refer to hematology for further management

No disclosures

The Burden of Iron Deficiency



- The most common nutritional deficiency and most common cause of anemia in the world
- Affects approximately 1 in 3 people, 2.3 billion people worldwide
- One of the few nutritional deficiencies that remains significantly prevalent in industrialized countries
- Up to 70% of cases among high-risk populations are missed due to limited screening and variability in diagnostic reference ranges

Iron Deficiency in the US

Using physiologically-based ferritin thresholds

- Most common in young children and females of reproductive age
- 30% of toddlers 1-2 years have ID
- 15-20% of children under 5 years have ID
- > 40% of menstruating individuals have ID
- 45% of pregnant women, regardless of trimester
- Nearly 70% of pregnant women in the 3rd trimester

NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.

(Gupta, Perrine et al. 2016)
(Benson, Lo et al. 2025)
(Hamarsha, Kawtharany et al. 2025)
(Jefferds, Mei et al. 2022)
(Mei, Addo et al. 2024)
(Addo, Jefferds et al. 2026)

Understanding iron studies

- **Serum iron**: circulating iron bound to transferrin in the blood
  - Highly susceptible to recent dietary intake→ ID can be present despite elevated level
  - Should be drawn in a fasting state (including fasting from multivitamin/iron supplements)



- **Ferritin**: indirect biomarker of stored iron in the body
  - Can rise significantly with inflammation or infection → ID can be present despite elevated level
  - Low ferritin is *always* indicative of ID

- **Transferrin**: primary iron transport protein
  - Rises with ID but can be decreased with inflammation → ID can be present even if normal/low

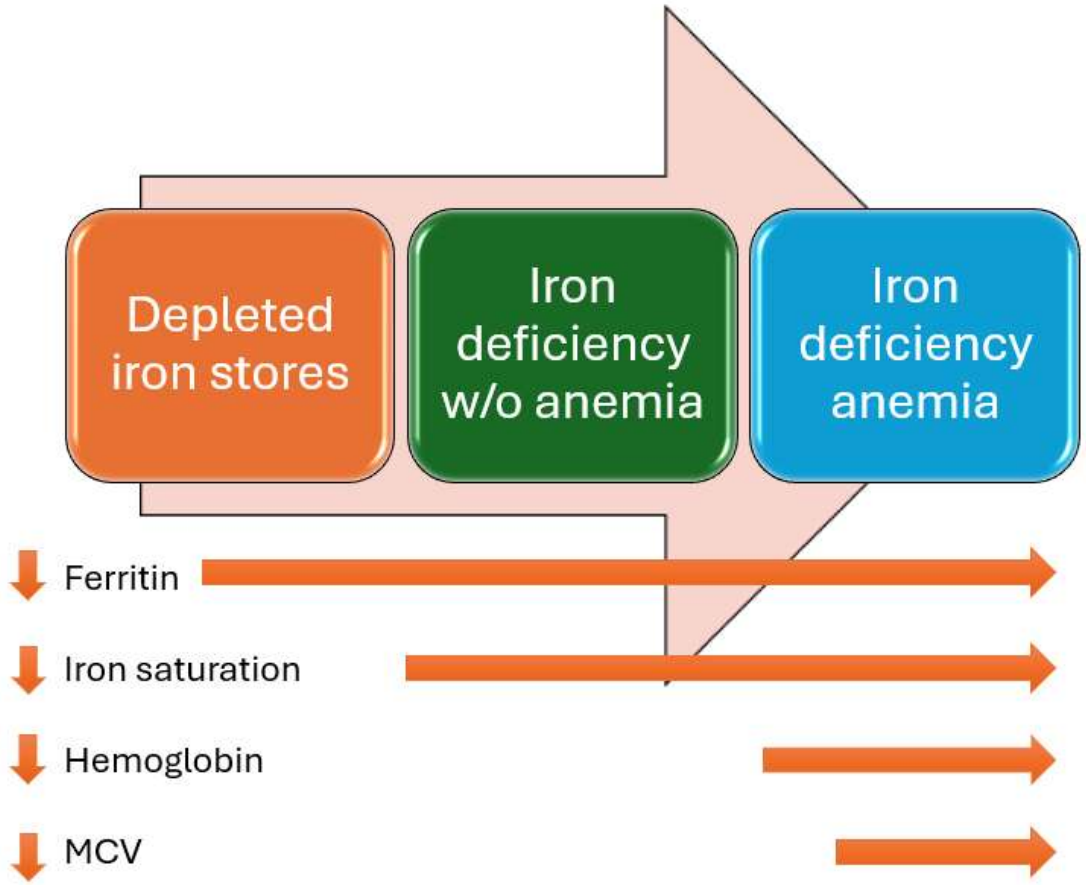
Understanding iron studies



- **Total iron binding capacity (TIBC):** indicative of blood's capacity to bind transferrin
  - Rises with ID but can be decreased with inflammation → ID can be present even if normal/low

- **Transferrin Saturation (TSAT) (aka Iron Saturation):** Calculation based on serum iron and TIBC (iron ÷ TIBC)
  - Low TSAT is indicative of ID
  - Should be drawn in a fasting state (including fasting from multivitamin/iron supplements) as the test is susceptible to recent dietary intake
  - If TIBC is decreased due to inflammation, TSAT may be normal or elevated

- **Soluble Transferrin Receptor (sTfR):** can help distinguish true ID from anemia of chronic disease
  - Serum value increases with ID and is usually unaffected by inflammatory states
  - Reference intervals not well establish in children


Depleted iron stores
Iron deficiency w/o anemia
Iron deficiency anemia
Ferritin
Iron saturation
Hemoglobin
MCV

CLINICAL REPORT Guidance for the Clinician in Rendering Pediatric Care

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

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

Jacquelyn M. Powers, MD, FAAP,[1] Matthew M. Heeney, MD, FAAP,[2] Jeffrey Hord, MD, FAAP,[3] Christoph U. Lehmann, MD, FAAP,[4] Steven A. Abrams, MD, FAAP,[5] George R. Buchanan, MD, FAAP,[6] and the AAP Section on Hematology-Oncology; AAP Committee on Nutrition; and AMERICAN SOCIETY OF PEDIATRIC HEMATOLOGY-ONCOLOGY

NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.

Definitions of iron deficiency

- Old definition (WHO):
  - Serum ferritin < 12-15 mcg/L (ng/dL) in apparently healthy individuals
  - Serum ferritin < 30-70 mcg/L in individuals with infection or inflammation

- **New definition (ASH/AAP):**
  - **Serum ferritin ≤ 20 mcg/L (ng/dL) in children 10 years and younger**
  - **Serum ferritin ≤ 30 mcg/L in children 11 years and older**
  - **Serum ferritin ≤ 30 mcg/L in adults (excluding pregnant and menstruating)**
    - **Serum ferritin ≤ 50 mcg/L if symptoms or ongoing risk factors of ID are present**
  - **Serum ferritin ≤ 30 mcg/L in menstruating individuals**
    - **Serum ferritin ≤ 50 mcg/L if HMB, additional risk factors, or symptoms of ID are present**
  - **Serum ferritin ≤ 30 mcg/L in pregnant individuals**
    - **Serum ferritin ≤ 50 mcg/L if anemia, additional risk factors, or symptoms of ID are present**
  - **Serum ferritin ≤ 100 mcg/L or TSAT (iron sat) ≤ 20% in patients with inflammation**

WHO. 2020
Powers, Heeney et al. Pediatrics 2026
Powers et al. Blood Advances 2026

The Many Roles of Iron



- Essential for production of RBCs
- 75% of total body iron is bound in heme proteins (hemoglobin and myoglobin)



- Required for dopamine synthesis
- Critical for myelin synthesis and monoamine metabolism



- Cofactor for enzymes in the mitochondrial electron transport chain



- Myocardium is particularly at risk when ID is present due to its high energy demands



- Crucial for immune cell growth, differentiation, and certain cell-mediated immunity



- Essential cofactor for enzyme-driven aerobic metabolism



- Absorption occurs primarily in the duodenum
- Homeostasis is primarily regulated by hepcidin

NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.

(Benson, Lo et al. 2025)
(Andrews 1998)
(Musallam and Taher 2018)

What is hepcidin?



- A peptide hormone that regulates intestinal absorption and transport of iron
- An acute phase reactant (like ferritin)
- Low hepcidin → increased iron absorption
- High hepcidin → decreased iron absorption
- Expression is affected by inflammation (↑↑↑), low iron stores (↓↓), normal iron stores (↑), recent iron ingestion (↑)

Common Questions

- What value is considered a low ferritin?
- When should I screen for ID and what are the new AAP recommendations?
- What are other symptoms of iron deficiency outside of anemia?
- What ferritin value is adequate for athletes? For patients with restless leg syndrome?
- How long do I try iron before I refer to hematology?
- How do I overcome the challenges of compliance?
- What multivitamin with iron should I recommend?
- When should I give a blood transfusion for iron deficiency?

UPDATED AAP Recommendations on Screening for Iron Deficiency



- Screening should include a **CBC** and a **serum ferritin**
- Infants/toddlers
  - Primarily *breastfed* infants should be screened between 9 and 12 months
  - Primarily *formula* fed infants should be screened between 15 and 18 months
- All menstruating adolescents should be screened at least 1 year post-menarche but no later than 14 years of age

AAP



Serum ferritin ≤ 20 mcg/L (ng/dL) in children 10 years and younger

Serum ferritin ≤ 30 mcg/L in children 11 years and older

REVIEW ARTICLE | SEPTEMBER 16, 2026

American Society of Hematology 2026 guidelines for diagnosis of iron deficiency

Jacquelyn M Powers ✉, Ming Yeong Lim, Maureen O. Achebe, Imo J Akpan, Michael Auerbach, Megan C Brown, Maria Paula Cardenas, Caroline Cromwell, Thomas G. DeLoughery, Robert E. Fleming, Martina Fraga, George Goshua, Paula D. James, Adam K Lewkowitz, Jori Ellen May, Grace Nnadozie, Frances Ogunnaya, Guillermo J. Ruiz-Arguelles, Michelle Sholzberg, Layla Van Doren, Angela C. Weyand, Michelle Paula Zeller, Muayad Azzam, Ali Choaib, Qais Hamarsha, Hassan Kawtharany, Jana Khawandi, Reem A. Mustafa

Caveats, exceptions, special populations: *Presence of SYMPTOMS is key*

Serum ferritin ≤ 30 mcg/L in adults (excluding pregnant and menstruating)

- **Serum ferritin ≤ 50 mcg/L if symptoms or ongoing risk factors of ID are present**

Serum ferritin ≤ 30 mcg/L in menstruating individuals

- **Serum ferritin ≤ 50 mcg/L if HMB, additional risk factors, or symptoms of ID are present**

Serum ferritin ≤ 100 mcg/L or TSAT (iron sat) ≤ 20% in patients with inflammation

- **TSAT should be done fasting for best accuracy**

Risk factors for iron deficiency



Infants

- Maternal ID
- Perinatal hemorrhagic events
- PREMATURITY
- EBF w/o iron supplement after 4 months
- Low iron formula
- Early introduction of cow's milk
- Use of EPO
- Short gut/TPN dependence



Toddlers/School age

- Excessive cow's milk
- Occult blood loss from
- Insufficient iron rich foods
- Obesity
- Malabsorption (celiac disease, H pylori)
- Short gut/TPN dependence
- Chronic blood loss (IBD, gastritis)
- Chronic illness



Adolescents

- Obesity
- Rapid growth
- Elite athletes
- Heavy menstrual bleeding
- Vegetarian or vegan diet
- Eating disorders/low body weight
- Chronic illness
- Malabsorption (celiac disease, H pylori)
- Chronic blood loss (IBD, gastritis)
- Blood donors

Prevention of Iron Deficiency

- It all starts with mom, ideally, mom should be iron replete BEFORE conception
- Delayed cord clamping
- Routine supplementation of pre-term infants (2-3 mg/kg/day of elemental iron)
- Breastfed infants should receive iron supplementation (1 mg/kg/day of elemental iron) by 4-6 months of age
- Avoid cow's milk before 12 months of age

Cow's milk and iron deficiency

- AAP recommends <24 ounces of cow's milk per day
- Excessive consumption leads to ID due to:
  - Low concentration and low bioavailability of iron in cow's milk
  - Calcium and proteins in dairy inhibit iron absorption
  - Fills toddler up, less iron rich food intake
  - Occult gastrointestinal blood loss



(1998 CDC MMWR)
(Agostoni and Turck 2011)

Cow's milk and iron deficiency

- Intestinal blood loss is much higher in infants who are introduced to cow's milk when < 1 year of age
  - increases incidence of occult blood + stools in 30% of infants 5-6 months compared to breast milk and formula
- Severe IDA from excessive milk intake can lead to protein losing enteropathy
- Bottle feeding beyond infancy can further increase risk



(Ziegler, Fomon et al. 1990)
(Brotanek, Halterman et al. 2005)

Iron deficiency and obesity

- Obese children and adolescents are at higher risk for ID and should be screened
- Etiology is not completely clear but likely related to poor quality diet, inflammation, and ↑ iron needs
- Both boys and girls are at risk, but risk is 3 times higher in girls
- Ferritin may not always be reliable

(Nead, Halterman et al. 2004)
(Pinhas-Hamiel, Newfield et al. 2003)
(Benson, Lo et al. 2025)





Non-hematologic Manifestations of Iron Deficiency

Common symptoms of ID

Fatigue	Hair loss	Muscle weakness	Exercise/effort intolerance
Difficulty concentrating	Restless legs, sleep disturbances	Learning difficulties	Headaches
	Depression, mood changes	Pica	

Iron deficiency and neurodevelopment

- IDA in young children has been associated with impaired cognitive development
  - Worse with chronic or severe IDA
- Higher serum ferritin associated with higher cognitive function
- Associated with poorer object permanence and memory in infants
- Neurodevelopmental changes may persist after IDA is corrected

(Halterman, Kaczorowski et al. 2001)
(Parkin, Koroshegyi et al. 2020)
(Carter, Jacobson et al. 2010)
(Walter, De Andraca et al. 1989)
(Walter 2003)

Iron deficiency and athletes

- ID impairs exercise capacity
- Iron supplementation can significantly improve performance in non-anemic athletes with ID
- Female athletes at much higher risk due to menstrual blood loss/increased iron needs as compared to males



Definition for ID in athletes:
<30-50 mcg/L for females
<40-50 mcg/L for males

NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.

(Rowland, Deisroth et al. 1988)
(Powers and O'Brien 2019)
(Powers. 2024)

Iron deficiency and athletes

- Oral iron is inefficient for repletion of iron stores in patients with increased iron needs
- Elite athletes have ↑ iron needs
  - loss of iron in sweat
  - increased O2 demand → increased RBC production
  - foot strike hemolysis
  - microscopic GI losses
- Athletes can have higher levels of hepcidin
- Iron replacement therapy does NOT benefit patients without ID (not a doping agent)

(Powers and O'Brien 2019)
(McClung 2012)
(Powers 2024)
(Pedlar, Brugnara et al. 2018)
(Clenin, Cordes et al. 2015)
(Burden, Pollock et al. 2015)

Iron deficiency and breath holding spells

- Involuntary reaction (consisting of apnea and cyanosis or pallor) to frustration, reprimand, or mild injury
- Iron supplementation has been shown to decrease frequency and severity of spells
- Iron supplementation may be helpful even if not anemic and iron replete



(Leung, Leung et al. 2019)
(Jain, Omanakuttan et al. 2017)
(Gurbuz, Perk et al. 2019)

NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.

Iron deficiency and RLS/PLMD



- Restless leg syndrome (RLS) and periodic limb movement disorder (PLMD) are closely related disorders that are relatively common in pediatrics (2-4%)
- Cause a substantial impact on sleep
- Iron deficiency is implicated in the pathogenesis of RLS/PLMD among other causes (including genetic causes)

Iron deficiency and RLS/PLMD

- Iron is important for dopamine production, myelin synthesis, synaptic density
- Likely involved in norepi and serotonin synthesis
- Multiple pediatric trials have supported iron supplementation in the treatment of RLS/PLMD
- Trial of iron supplementation recommended for any child with RLS/PLMD and ferritin less than 50-75 mcg/L

(Allen 2004)
(Burhans, Dailey et al. 2005)
(Allen, Picchietti et al. 2018)
(Silber, Becker et al. 2013)
(Dye, Jain et al. 2017)
(Winkleman et al. 2025)

Achieving ferritin > 50-75 mcg/L

- Can challenging to do with oral iron alone
  - Once iron stores are replenished, hepcidin will limit subsequent iron absorption
  - Many patients have a “set point” of optimal ferritin that is lower than 50 mcg/L
- Symptomatic children RLS with *sub-optimal* ferritin and inadequate response to oral iron may benefit from IV iron
- Prior to referral for IV iron, an evaluation by sleep medicine is recommended if concerns are for poor sleep/RLS
  - Not all restless sleep is RLS/PLMD

Grim, Lee et al. 2013
2025 American Academy of Sleep Medicine Guidelines

Treatment of Iron Deficiency





ASH Iron Deficiency Treatment Guidelines

- Draft of Iron deficiency treatment guidelines is available for public comment currently
- https://www.hematology.org/-/media/hematology/files/clinicians/guidelines/ash-draft-recommendations-for-treatment-of-iron-deficiency-and-iron-deficiency-anemia.pdf
- Publication date summer 2027

Pediatric patients (<18 years of age)

Recommendation 2: The American Society of Hematology Guideline Panel *suggests either* oral iron *or* IV iron for the treatment of iron deficiency anemia in children (conditional recommendation, very low certainty evidence ⊕◯◯◯).

Remarks:

- For children in whom either treatment is reasonable, shared decision-making should consider the expected speed of response, route of administration, treatment duration, need for IV access and infusion visits, potential adverse effects, available IV iron formulations, out-of-pocket expenses to the patient/caregiver, and patient and caregiver preferences.
- Oral iron therapy may be preferred due to the ability to administer at home, lower initial out-of-pocket expenses and resources required, as well as the avoidance of IV access.
- IV iron is preferred in children with severe anemia, upcoming surgery, or other conditions requiring rapid improvement in hemoglobin concentration.
- IV iron is preferred when oral iron cannot be taken or adequately absorbed, such as in children with significant oral aversion, intestinal failure conditions (i.e. short bowel syndrome), inflammation, or other conditions that impair enteral iron absorption as well as for children who do not improve with oral iron due to poor palatability, gastrointestinal intolerance, non-adherence, or have an inadequate erythropoietic response.

DRAFT

Question: Should alternate day iron vs. once daily iron be used for children with confirmed iron deficiency anemia?

Recommendation 3: The American Society of Hematology Guideline Panel *suggests* oral iron administration *either* once daily *or* every other day for the treatment of iron deficiency anemia in children. (conditional recommendation, very low certainty evidence ⊕◯◯◯).

Remarks:

- The choice regarding the dosing schedule and frequency of iron therapy should consider the severity of anemia, anticipated adherence, gastrointestinal adverse effects, and patient and/or caregiver preference through shared decision-making.
- Daily therapy may be preferred when a more rapid erythropoietic response is desired (i.e. in moderate to severe anemia) or when a consistent routine is likely to improve adherence.
- Every other day dosing may be preferred for pediatric patients with mild anemia or iron deficiency without anemia, those who experience gastrointestinal intolerance with daily therapy, or for whom a less frequent schedule is more acceptable.
- For children who cannot tolerate oral iron therapy, cannot absorb oral iron, or in whom there is active inflammation, see Recommendation 2 re: oral versus IV iron therapy.

Good Practice Statement: For young children receiving oral iron therapy, an oral iron salt (ferrous sulfate) at a dose of 3 mg/kg/dose elemental iron is appropriate. For adolescents, standard adult oral iron dosing is appropriate.

DRAFT

Menstruating individuals

Question: Should IV iron vs. Oral iron be used for menstruating individuals with iron deficiency with or without anemia?

Recommendation 4: The American Society of Hematology Guideline Panel *suggests* IV iron rather than oral iron for the treatment of iron deficiency with or without anemia in menstruating individuals (conditional recommendation, low certainty of evidence ⊕⊕◯◯).

Remark: Individuals with heavy menstrual bleeding should undergo gynecologic investigation and management of menstrual blood loss. If not regulated, improvement in hemoglobin concentration and iron stores will be limited.

Oral iron Replacement

Ferrous sulfate (tried and true):

- 3 mg/kg/day of ***elemental*** iron PO q day for toddlers/children for at least 3 months
- One 325 mg tablet (65 mg elemental iron) once daily for adolescents (or every other day/MWF) for at least 3 months
- Never dose more than once daily

- Take with Vit C/juice to enhance absorption
- SE's: GI intolerance, dark stools, stained teeth, it tastes (and smells) TERRIBLE (like penny water)

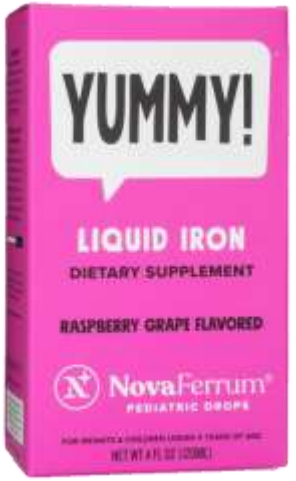
(Stoffel, Cercamondi et al. 2017)
(Powers et al, 2026)

Oral iron replacement

- Avoid taking with ***cow's milk***, tannates (tea), phosphate rich brans, and phylates (plant fiber)
- Avoid taking around the same time as PPIs or other antacids
- GI SE's are typically dose-dependent

What if the kid won't take it

- Mix with syrup, apple sauce, juice
- Try lowest dose (3 mg/kg once daily)
- Can try other formulations
  - **Iron complex polysaccharide**
    - Dosed as elemental iron already (no conversion needed)
    - Not quite as effective as ferrous sulfate
  - Ferrous fumerate, ferrous gluconate (iron salts are MORE effective)





NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.

(Stoffel, Cercamondi et al. 2017)
(Powers, Buchanan et al. 2017)

18 mg elemental iron per tab



30-60 mg elemental iron per tab





7-9 mg elemental iron per tab

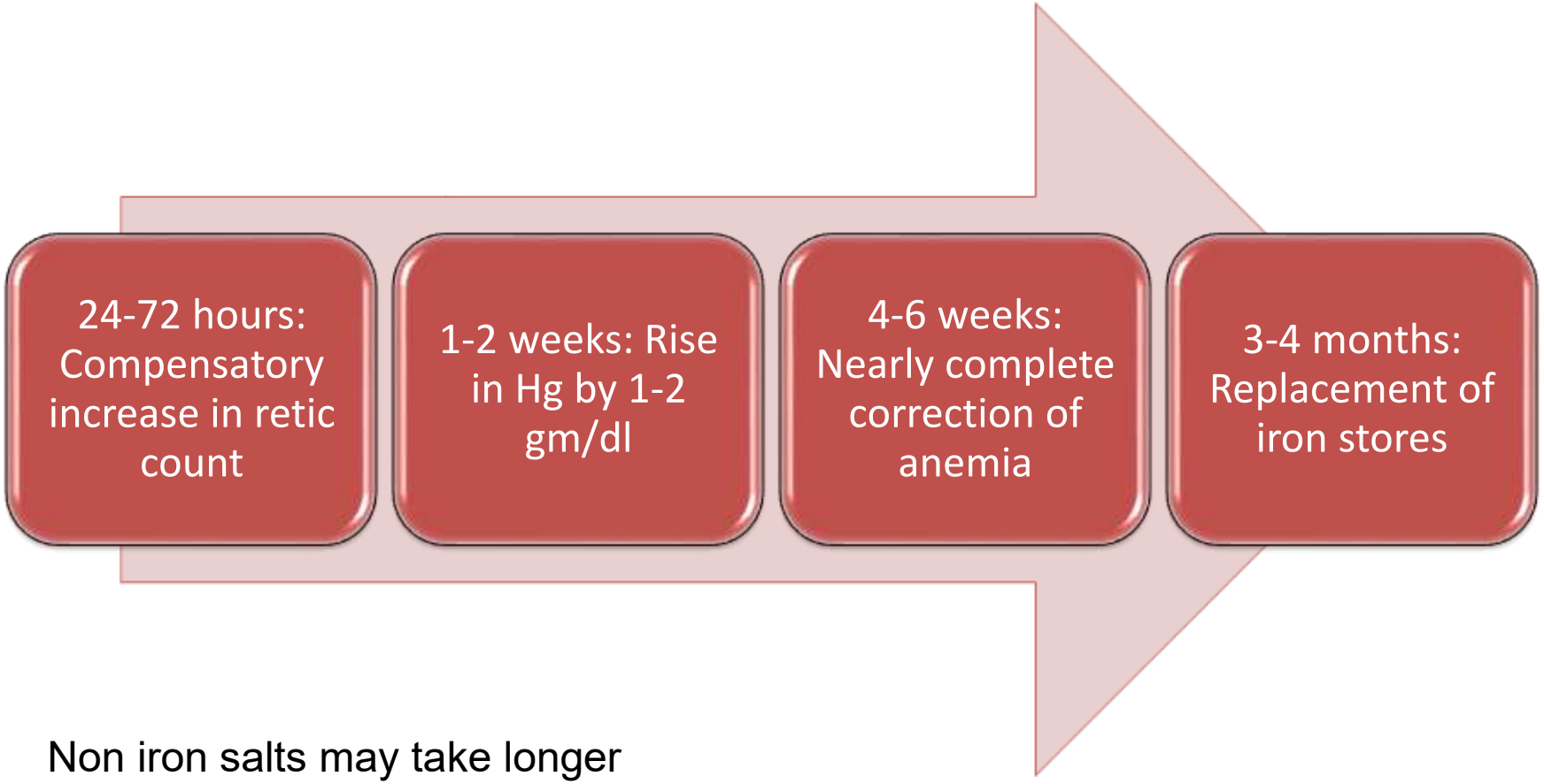






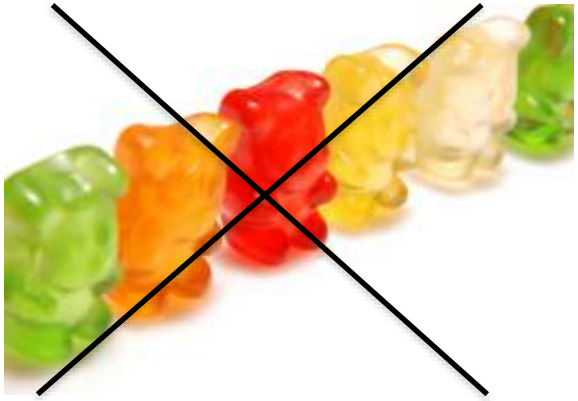
NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.

Expected response to oral iron replacement in IDA



Non iron salts may take longer

Multivitamins, etc



- AVOID GUMMY vitamins
  - they don't contain much iron
- I usually recommend Flintstone's chewable or similar (18 mg of elemental iron)
- Avoid taking with cow's milk and other inhibitors of iron absorption

Dietary Iron

- Heme iron (iron from meat) is better absorbed (20-30% vs 10% absorption) than non-heme iron (iron from vegetables)

- Non-heme iron must be reduced from its ferric to ferrous form to be transported

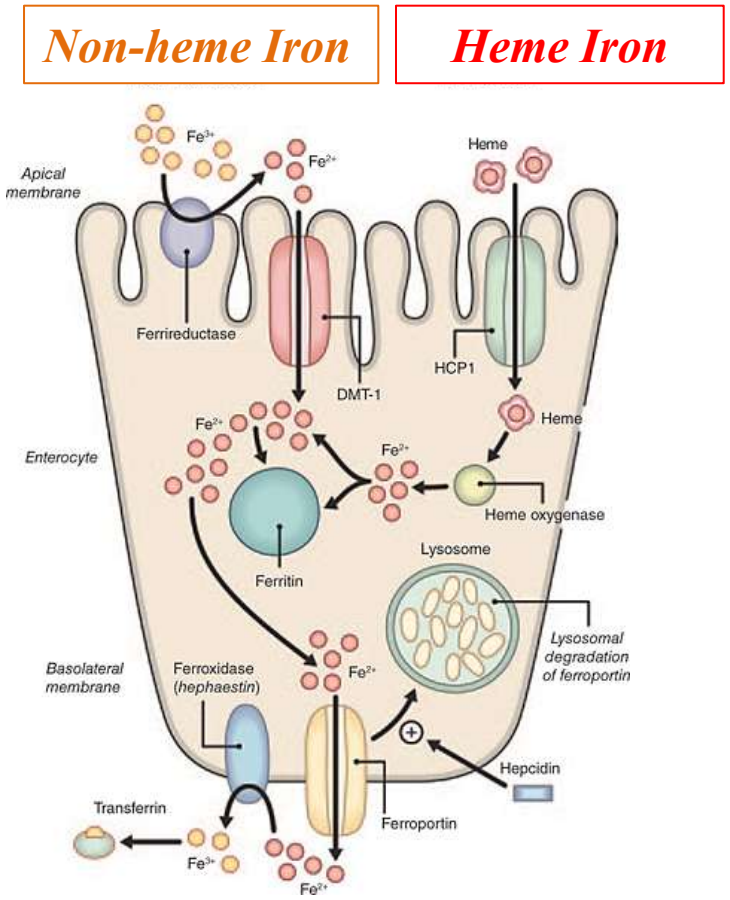


Figure adapted from: Rizvi S et al. Am J Gastroenterol 2011; 106:1872–1879

NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.

Intravenous Iron

- Indications: inadequate response or poor tolerance to oral iron, chronic kidney disease, non-adherence to oral iron despite appropriate education and support
- Pros: It works; Cons: It's expensive
- It is safe
  - (adverse reaction in < 1%, anaphylaxis very rare)
- Requires hematology referral

Intravenous Iron (approved in pediatrics)

Generic Name	Ferric gluconate	Iron sucrose	Low Molecular Weight Iron Dextran	Ferric Carboxymaltose
Trade Name	Ferrlecit	Venofer	INFeD	Injectafer
FDA Indication (Adult)	Patients with chronic kidney disease on dialysis + erythropoiesis-stimulating agents	Patients with chronic kidney disease	Patients in whom oral iron administration is unsatisfactory or impossible	Patients with intolerance or unsatisfactory response to oral iron; non-dialysis dependent chronic kidney disease
FDA Approved (Pediatric)	Yes, >6 years	Yes, >2 years	Yes, >4 months	Yes, >1 year
Pediatric Dosing per Infusion (Max)	1.5 mg/kg (125 mg)	5-7 mg/kg (300 mg)	Calculate deficit (100 mg)*	15 mg/kg (750 mg)
Infusion Time	60 minutes	2-5 minutes	60 minutes	15-60 minutes
Test Dose Required	No	No	Yes (10-25 mg)	No
Black Box Warning	No	No	Yes	No
Iron Concentration	12.5 mg/mL	20 mg/mL	50 mg/mL	50 mg/mL

*Iron dextran is routinely given up to 1000 mg (100 mg is max FDA approved dose)



Ferric carboxymaltose and treatment-emergent hypophosphatemia

- Occurs in up to 70% of adults, often transient and asymptomatic, but can be severe and persistent
- Less common in children (15%), we use it often at NCH
- Mechanism: renal wasting regulated by the phosphoturic hormone fibroblast growth factor 23 (FGF23)
- Phosphorus monitoring is advised, especially with repeat doses
- Generally avoided in children and adults needing chronic IV iron therapy

Doren and Auerbach. 2023.
Kirk, Mahoney et al. 2019.

When to refer to hematology

- Failure/intolerance to oral iron
- ID or IDA with heavy menstrual bleeding (reasonable to try oral iron first if not anemic)
- Severe symptoms and need for rapid replacement
- Feel free to call PCTC to ask or reach out via email: Amanda.Jacobson-Kelly@nationwidechildrens.org

When to transfuse for IDA

- Transfusion is appropriate for otherwise healthy children with severe IDA AND debilitating symptoms, active bleeding, or hemodynamic instability
- Otherwise, transfusions should typically be avoided
- If needed, transfusion should be done in small aliquots and with caution to avoid fluid overload and heart failure



Summary

- The diagnosis and treatment of ID can be nuanced; always obtain a ferritin
- ID can cause many symptoms even if anemia is not present
- Pay attention to iron dosing; multivitamins w/iron generally do not have enough iron to correct ID, especially IDA
- IV iron is a safe option and can be used for patients who have failed/intolerant of oral iron

Summary

- Iron deficiency is MUCH more common than we previously thought

Acknowledgements

Mentors: Sarah O'Brien and Jacquelyn Powers

American Society of Hematology Iron Deficiency Diagnosis and Treatment Guideline Panel

Patients and families