S-20200016
Management of Nutritional Iron Deficiency Anemia in the Emergency Department
TXCH Best Current Practice Standard

Scope:

The target population for this protocol is children age 9 months to 5 years who are presenting to the TCH Emergency Department (ED) and are diagnosed with nutritional iron deficiency anemia (IDA) based on history, physical exam, and laboratory results. Children with a history of an underlying bleeding disorder and/or previous treatment with intravenous (IV) iron therapy are excluded.

Definitions:

AAP	American Academy of Pediatrics
ASH	American Society of Hematology
ASPHO	American Society of Pediatric Hematology/Oncology
CBC	complete blood count
CHF	congestive heart failure
CPG	Clinical Practice Guideline
CRP	C-reactive protein
CSVT	cerebral sinovenous thrombosis
CXR	chest x-ray
DAT	direct antiglobulin test
EBOC	Evidence-Based Outcomes Center
ECG	electrocardiogram
ED	emergency department
FCM	ferric carboxymaltose
Hb	hemoglobin
H/H	hemoglobin/hematocrit
IDA	iron deficiency anemia
IV	intravenous
LDH	lactate dehydrogenase
PCP	primary care provider
pRBC	packed red blood cell
PRN	as needed (*pro re nata*)
ROS	review of systems
URI	upper respiratory infection
WCC	well-child check

Background:

The goal of this Practice Standard is to improve and standardize the management of nutritional iron deficiency anemia (IDA) in young children presenting to the ED. IDA is a significant hematologic condition worldwide.[1] In the U.S., iron deficiency has a prevalence of 7-8% amongst toddlers; 2-3% progress to IDA. The primary etiology is nutritional due to either excessive milk intake or prolonged breastfeeding without sufficient iron supplementation. IDA is often under-recognized until the anemia becomes severe (Hb <5 g/dL).[2] Serious complications of untreated and/or severe IDA include impaired neurocognitive function,[3-4] thrombosis or stroke,[5] CHF, and even death. Many patients with moderate to severe IDA are referred to the ED for initial evaluation and management by their PCP, and thus, the ED is an ideal clinical location to implement a protocol to optimize IDA management in such patients.[6] Evidence-based guidelines for the approach to IDA are lacking, leading to significant variability in management.

Based on current ASH and ASPHO Choosing Wisely recommendations, transfusion of pRBCs for children with asymptomatic IDA should be avoided when there is no evidence of hemodynamic instability or active bleeding.[7] However, the literature to support this recommendation comes from two Canadian IDA guidelines,[8-9] one of which excludes children under 5 years of age.[8] The other broadly reviews the diagnosis and treatment of IDA across all age groups, and is targeted at primary care providers. Unfortunately, no other data or expert consensus was utilized for this recommendation, and there is no consensus on how to define "asymptomatic" and "hemodynamically stable" in a young patient population. A **new** joint clinical report on the treatment of IDA across the pediatric lifespan from the AAP and ASPHO is currently in development. This Practice Standard is aligned with this new effort.

Overall, this Practice Standard aims to provide institutional-wide guidance on the most updated recommendations regarding evaluation for nutritional IDA; oral iron medication and dosing; [10] IV iron administration;[11-15] best practices for pRBC transfusion;[9,16-17] as well as disposition and follow-up.

Recommendations for Evaluation and Treatment:

Please refer to the algorithm (**Appendix 1**) for a step-wise approach to evaluation and management in these patients, as detailed below.

History:

A careful and documented history should include:

1. The referral route for the patient (e.g., ED or PCP) and mention of whether previous lab assessments suggestive of IDA were performed and available (i.e., during routine CBC screening at a WCC)
2. Review of previous lab results, if available
3. Information about the presence or absence of symptoms of anemia: pallor, fatigue/exercise intolerance, decreased energy/activity levels, dizziness/orthostasis, dyspnea/tachypnea, pica
4. Diet history: average daily intake of cow's milk in ounces/day, intake of iron-rich foods, breastfeeding (including maternal diet), history of iron supplementation
5. A thorough ROS ensuring that other causes of anemia are considered:
    a. IDA due to blood loss (bloody stools, prolonged epistaxis (>10 min));
    b. hemolytic anemia (jaundice, dark urine);
    c. malignancy (weight loss, bone pain, unexplained fevers, lymphadenopathy, petechiae);
    d. viral myelosuppression (fever, sore throat, URI symptoms);
    e. stroke/CSVT (lethargy, vomiting, seizures, altered mental status, focal weakness);
    f. CHF (respiratory distress)
6. All other pertinent medical history as per standard medical practice

Exam:

A careful and documented physical exam should include:

1. Vital signs including blood pressure, heart rate, respiratory rate, temperature, oxygen saturation, height, weight. Note: Mild tachycardia may be commonly seen in IDA
2. Review of a growth chart to assess trend for poor growth, if multiple time points available
3. Documentation of presence and/or absence of: pallor, jaundice, respiratory distress, cardiac murmur or gallop, abdominal organomegaly, lymphadenopathy, petechiae/purpura, distal extremity perfusion, mental status, focal neurological deficits

Evaluations:

A focused approach to laboratory evaluation should include:

- CBC with differential, reticulocyte count
- Iron panel (serum ferritin, serum iron, total iron binding capacity [TIBC], transferrin saturation)
- As per standard ED management, children presenting with abnormal labs/severe anemia should also have ABO/Rh type and antibody screen, chem 10

*The following labs/tests are NOT typically needed:

- Labs: peripheral blood smear, liver panel, bilirubin, coagulation markers, DAT, CRP, LDH, uric acid, hemoglobin profile/electrophoresis, lead level, folate level, vitamin B12 level

- Imaging: No routine imaging or diagnostic studies (e.g. CXR, EKG) are needed for patients treated for IDA in the ED, unless complications of severe IDA are suspected (CHF, stroke)

General approach to management (refer to **Appendix 1** for management algorithm)**:**

- Confirm expected findings of nutritional IDA on history, exam and laboratory investigations.
- Assess for findings suggestive of other anemia causes/complications, especially if anemia is severe
- Apply Hb-based risk stratification to determine appropriate therapy and disposition
- Initiation of risk-stratified therapy, with appropriate monitoring if required.
- Disposition: Either discharge home with appropriate education and hematology follow-up or transfer to appropriate inpatient care team(s).

Treatment Plan:

Required observations prior to treatment (all should be available based on initial labs drawn):

- CBC, reticulocyte count, and iron panel: all patients for diagnostic evaluation (as above).
- Phosphorus level^: Patients receiving IV iron.
- ABO/Rh type and antibody screen: Patients receiving pRBC transfusion.

^Vitamin D 25 OH level should be sent as "ADD ON" for patients receiving IV iron, though not required prior to treatment.

Treatment selection and administration guidelines based on risk stratification and in consultation with Hematology. Risk stratification is based primarily on degree of anemia (i.e. hemoglobin value). Therapy decisions should be determined by the Algorithm in **Appendix 1**.

- Low Risk (Hb >7 g/dL)
- Intermediate Risk (Hb 5-6.9 g/dL)
- High Risk (Hb 3-4.9 g/dL)
- Very High Risk (Hb <3 g/dL)

Low- or Intermediate-risk patients selected for **oral iron therapy**:

- Medication: Ferrous sulfate or Fer-in-sol liquid
- Dose: 3 mg/kg/day of elemental iron, administered once daily
- Rounding to nearest 0.5 mL as needed is reasonable for ease of administration.
- Provide prescription for one month with two refills (Total duration: 3 months).

Low- or Intermediate-risk patients selected for **IV iron therapy**:

- Medication: Ferric carboxymaltose (FCM), **diluted form (3 mg/mL)**, given over 30 minutes
- Dose: 15 mg/kg as a one-time dose
- Use Epic **FCM Order Smartset** – all nursing communication and medication orders included.

High- and very-high-risk patients selected for **pRBC transfusion:**

- Obtain matched pRBC product per Blood Bank preparation.
- Give 5 mL/kg volume over 3-4 hours, initiate in ED if blood available
- Multiple transfusions as needed, to be determined by severity of anemia.
- Oxygen therapy via low-flow nasal cannula PRN to keep oxygen saturation >95%

Lab monitoring:
For patients receiving multiple pRBC transfusions:

- Check H/H after second transfusion.
- Repeat transfusions to goal Hb >6 g/dL.
- Further lab monitoring per inpatient admitting/consult team(s).

For patients receiving oral or IV iron therapy and discharged by ED:
Labs to be assessed again at Hematology follow-up visit and are beyond the scope of this protocol.

Dosing Modifications and Anticipated Toxicities

No anticipated dosing modifications given that treatment in ED should be an isolated encounter. Potential adverse effects for medications are detailed below (*Sources: TCH Formulary/ Lexicomp® ; TXCH IDA CPG*).

Oral iron therapy

- Adverse effects: Abdominal pain, nausea, vomiting, constipation, diarrhea, dark stools.
- Accidental overdose/poisoning – All families should be advised to store iron medications in a safe space, away from the reach of children.

Intravenous ferric carboxymaltose
**NOTE: Vital signs/monitoring must be assessed at baseline prior to infusion and 5 minutes after infusion initiation. Any evidence of adverse reaction must result in immediate termination of infusion, assessment by a provider, and additional interventions as needed.*

- Adverse effects:
  - Allergic reactions: mild (urticarial); moderate (dyspnea without wheezing); anaphylaxis-like reaction (flushing, hypertension, hypotension; transient)
  - Other adverse effects: nausea, vomiting, dizziness, headache
  - Skin extravasation at infusion site with persistent discoloration
  - Hypophosphatemia (<2 mg/dL; transient)
  - Paresthesia at infusion site
- Management of adverse effects:
  - Urticaria: diphenhydramine; IV steroids
  - Anaphylaxis: epinephrine, normal saline, IV steroids, diphenhydramine
  - Nausea/vomiting: anti-emetic medication(s), +/- normal saline
  - Paresthesia at infusion site: application of warm pack
  - Skin extravasation: stop infusion and evaluate level of injury to determine next steps

Supportive Care Recommendations:

Educational instructions and detailed counseling should be provided to families regarding dietary and behavioral modifications that will help ensure resolution of IDA. Such directions should include:

- Limit patient's intake of cow's milk to <16 ounces/day.
- Eliminate using a milk bottle at night and/or before bedtime.
- Encourage age-appropriate introduction and/or increased intake of iron-rich foods, such as red meats, eggs, beans, nuts, lentils, cereal, green leafy vegetables, dried fruits. *See Handouts.*
- Give oral iron medication with foods/drinks rich in vitamin C (i.e., citrus juice) and not milk.

Additional recommendations regarding dietary modifications can be found in the existing: **Iron Deficiency Anemia Clinical Practice Guideline**. Sample handouts listed below.

HealthyChildren.org (AAP): https://www.healthychildren.org/English/health-issues/conditions/chronic/Pages/Anemia-and-Your-Child.aspx

Centers for Disease Control and Prevention: https://www.cdc.gov/nutrition/infantandtoddlernutrition/vitamins-minerals/iron.html

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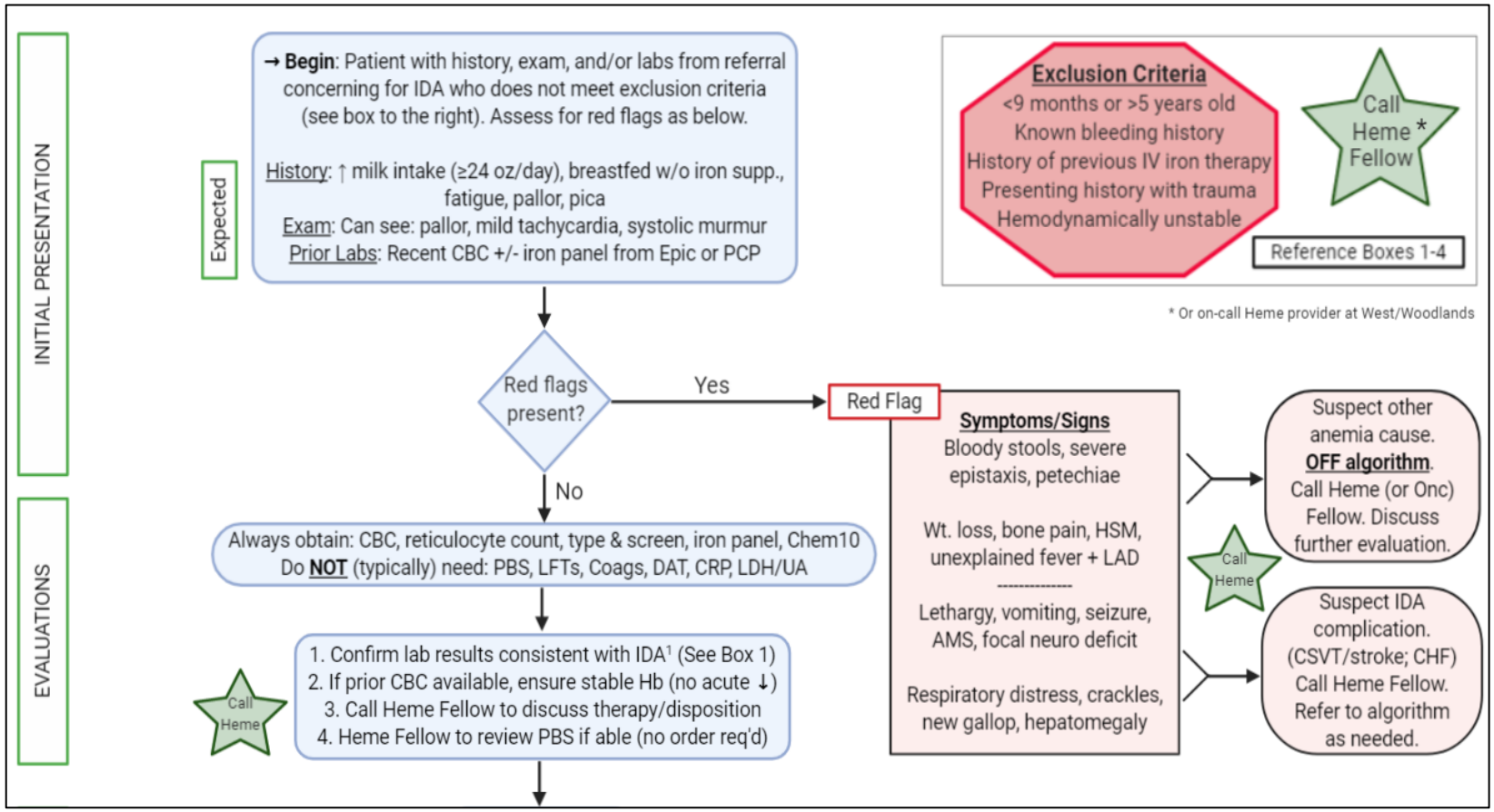
Date of Approval: 09/21/2022

Revision History:

Date	Revision Number	Revision

Appendix 1: ED Algorithm for Nutritional Iron Deficiency Anemia in Children <5 years old

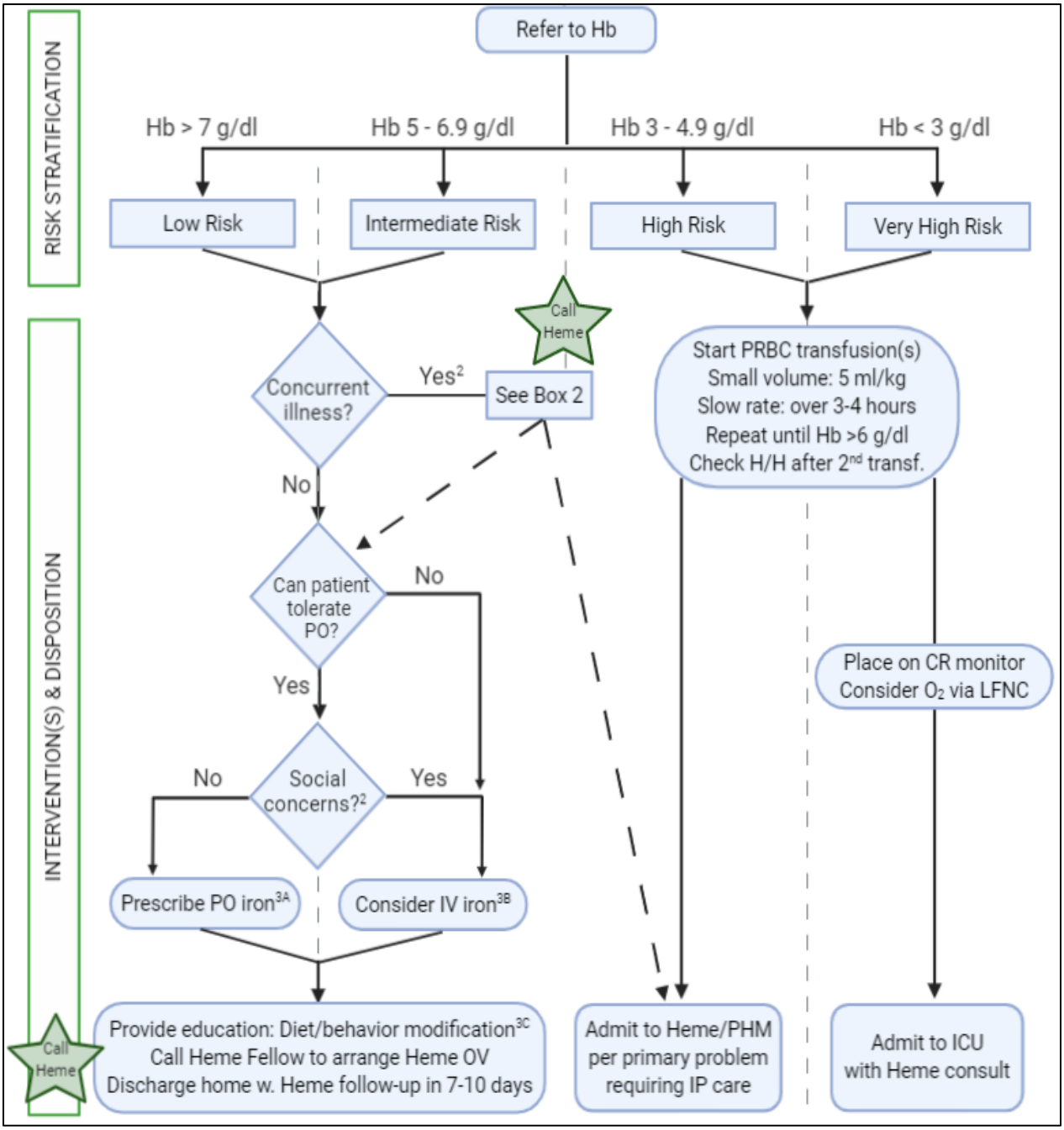


Proceed to Part 2 of Algorithm on next page.

These practice standards are intended for use by professional health care providers. These standards do not constitute advice concerning an individual's medical care and treatment.

Approved by PSC on	09/21/2020	Next Review Date	09/21/2022

Part 2 of Algorithm



References for Algorithm

1. IDA Lab Findings
Low: Hb, MCV, +/- retic
High: RDW, Plt, TIBC
(Mentzer index: **not** reliable)
Ferritin: <15 ng/ml
Transferrin Sat: <15%

2. Discharge/Social Concerns
*Call Heme Fellow to discuss:
-Potential evaluation for multifactorial anemia
-Illness features/VS precluding discharge home
-Acute inflammatory state precluding IV iron
-If admission: Heme vs PHM
*Social concerns: per provider discretion
(i.e., family distance from TCH, concern for suboptimal compliance, etc.)

3. Detailed Therapy Recommendations
A: Oral iron:
Ferrous sulfate or Fer-in-sol liquid,
3 mg/kg of *elemental* iron
dosed *once* daily (not BID/TID)

B: IV iron:
Add-on vit D 25-OH screening lab
Ferric carboxymaltose (FCM) 15 mg/kg x1
Use FCM Order Set to ↓ extravasation risk

C. Family education:
-Limit milk intake to ≤16 oz/day
-Introduce iron-rich foods as able
(meats, eggs, beans, nuts, cereal, etc.)
-Eliminate bottle at night/before bedtime
-Give PO iron w. juice (not milk/formula)
-Give IDA informational handout

4. Abbreviations
AMS = altered mental status; CHF = congestive heart failure; CR = cardiorespiratory; CSVT = cerebral sinovenous thrombosis; Hb = hemoglobin; HSM = hepatosplenomegaly; IDA = iron deficiency anemia; IP = inpatient; LAD = lymphadenopathy; LFNC = low-flow nasal cannula; NS = normal saline; OV = outpatient/office visit; PBS = peripheral blood smear; PRBC = packed red blood cells; supp. = supplement; w/o = without; wt. = weight