CLINIC GUIDELINE

Outpatient evaluation and management of iron deficiency anemia (IDA) in children ≤ 5 years old

Children's MINNESOTA

Aim: to standardize the treatment of nutritional iron deficiencyanemia in children

EXCLUSION GUIDELINES:
- Concern for alternative etiology of anemia (note 6) including, but not limited to: signs of blood loss or hemolysis, 2 or more cytopenias, macrocytic anemia
- Hemodynamic instability or ill appearance

Does the patient have:
- symptoms/signs of anemia (e.g. fatigue, irritability, shortness of breath) OR
- nutritional concerns OR
- due for routine hemoglobin screening?

Yes → **Further workup indicated**
- Perform detailed H&P (Note 1)
- Obtain hemoglobin (Hgb)

What is the hemoglobin level (if <11)? (Note 2). If Hgb ≥11, patient is off guideline.

No → No further IDA workup indicated. **Off guideline.**

Hgb 10-11 g/dL Mild anemia

Is history consistent with IDA (note 3)?
- No → No further IDA workup indicated. **Off guideline.**
- Yes → Start **oral iron** 2-4 mg/kg (elemental dosing) Qday, provide **education** (note 4)

- Recheck Hgb in 1 month
- Increase of 1 g/dL confirms IDA
- After Hgb normalizes, treat with iron for additional 3 months to replete stores remove trigger for <10

Hgb <10:

Obtain CBC, ferritin, ±iron panel, reticulocyte count (Notes 1 & 2) to assess for IDA (Note 3)

Is Hgb < 6 g/dL or are there concerning symptoms (Note 5)**?**
- Yes → Refer to ED or arrange direct admission (call 866-755-2121) if reassuring vitals within 24 hours
- No → **Moderate anemia Hgb 6 - 10 g/dL** → Start **oral iron** 2-4 mg/kg (elemental dosing) QD, provide **education** (note 4)

Recheck Hgb and retic in 1-2 weeks.
Is Hgb stable/slightly improved (0.5-1 g/dL higher) and retic increasing?
- Yes →
  - Continue iron suContinue iron and recheck CBC and ferritin **every 1-2 months** until Hgb normalizes and ferritin >20 (usually 3-6 months).
  - pplementation
- No →
  - Assess compliance with dietary recs and iron supplement (note 7)
  - Consider further work-up: ED referral, GI consult (if GI symptoms) and/or Hematology consult (note 6)

Alternative forms of iron (see note 7):
- **You and Yours:** tasteless powder
- **Celebrate:** chewable tabs, better taste, contains Vitamin C.
- **Novaferrum:** better tasting liquid, gentle on the stomach.
- **Iron Gummies:** palatable, low iron content
- **Proferrin:** less GI upset, improved correction of iron deficiency.

Most are available over the counter, **dose based on elemental iron.*

ED GUIDELINE

ED evaluation and management of iron deficiency anemia (IDA) in children ≤ 5 years old

Children's MINNESOTA

Aim: to standardize the treatment of iron deficiency anemia related to nutritional concerns

EXCLUSION GUIDELINES:
- Concern for alternative etiology of anemia (note 6) including, but not limited to: signs of blood loss or hemolysis, 2 or more cytopenias, macrocytic anemia
- Hemodynamic instability or ill appearance

Concern for Iron Deficiency Anemia in patient, e.g. nutritional concerns or symptoms/signs of anemia (e.g. pallor, fatigue, irritability, shortness of breath) (notes 1-3)

→ **Obtain laboratory evaluation**
- CBC with diff
- Type and screen
- Reticulocyte count
- Ferritin
- +/- Iron panel

→ Is hemoglobin <11?

- No → No further IDA workup indicated. **Off guideline.**
- Yes → Does patient have severe symptoms (e.g. Dyspnea or hypoxia) or hemodynamic instability?
  - Yes → Consider admission to PICU and blood transfusion*
  - No → Does patient have:
    - Hemoglobin ≤ 6 or
    - Concerning symptoms (note 5) or
    - A barrier to taking oral iron or
    - Failed outpatient management?
      - Yes → Admit to hospitalist service
      - No →
        - Start oral iron 2-4 mg/kg (elemental dosing) Qday
        - Provide education (note 4)
        - Give first iron dose in ED

→ **Discharge to home & follow-up with PCP**
- F/u in 1-2 weeks with repeat CBC and retic
- Then, recheck CBC and ferritin every 1-2 months until Hgb normalizes and ferritin >20 (usually 3-6 months).

Alternative forms of iron (see note 7):
- **You and Yours:** tasteless powder
- **Celebrate:** chewable tabs, better taste, contains Vitamin C.
- **Novaferrum:** better tasting liquid, gentle on the stomach.
- **Iron Gummies:** palatable, low iron content
- **Proferrin:** less GI upset, improved correction of iron deficiency.

Most are available over the counter,* ***dose based on elemental iron.*

INPATIENT GUIDELINE

Inpatient evaluation and management of iron deficiency anemia (IDA) in children ≤ 5 years old

Children's MINNESOTA

Aim: to standardize the treatment of iron deficiency anemia related to nutritional concerns for children

Admission criteria (any of the following):
- Hemoglobin (Hgb) < 6 or
- Symptomatic anemia (note 5) or
- Barriers to outpatient iron therapy or follow-up

→ Severe symptoms (e.g. dyspnea, hypoxia) or hemodynamic instability?

Yes → Consider transfer to PICU and urgent blood transfusion *

No ↓

EXCLUSION GUIDELINES:
- Concern for alternative etiology of anemia (note 6) including, but not limited to: signs of blood loss or hemolysis, 2 or more cytopenias, macrocytic anemia
- Hemodynamic instability or ill appearance

Work-Up:
- See note 1 for key elements of H+P and lab considerations
- Obtain initial labs: CBC, reticulocyte count, iron panel, ferritin, and Type and Screen, ensure lead testing recently completed
- If concerns for alternative diagnosis (note 6), consider directed labs and consultation.

Inpatient Management of IDA:
- Nutrition consult and/or provide dietary iron education (Patient Handout)
- Diet orders: **Milk free diet**, no bottles in room (if applicable)
- IV Iron:
  - Iron sucrose (Venofer) 5 mg/kg x 1 dose (max 300 mg) (Note 8)
  - For patients at high risk for persistent IDA (e.g. autism, prior oral iron failure), discuss with Hematology re: additional outpatient IV iron and/or inpatient iron dextran
- Blood transfusion parameters:
  - If Hgb is <4, patient symptomatic, or Hgb <5 with barriers to follow up, give blood transfusion.*
  - If transfusing, still give IV iron
- Recheck hemoglobin and retic at least once prior to discharge.
- Consider hematology consult if labs or history are not consistent with IDA (see note 3 and 6).

*__Blood transfusions__ should be given in 5 ml/kg aliquots run over 2 hours. Each aliquot should increase Hgb by 1 g/dL to achieve goal ~6.
- Recheck Hgb >= 30 min after 2nd aliquot. Consider lasix for signs of fluid overload.
- Contact blood bank to hold additional aliquots to minimize donor exposures (Mpls 5-6824, StP 6-6558).

Alternative forms of iron (see note 7):
- **You and Yours:** tasteless powder
- **Celebrate:** chewable tabs, better taste, contains Vitamin C.
- **Novaferrum:** better tasting liquid, gentle on the stomach.
- **Iron Gummies:** palatable, low iron content
- **Proferrin:** less GI upset, improved correction of iron deficiency.

Most are available over the counter,* ***dose based on elemental iron.*

Discharge Criteria:
- Hgb stable or improving, ideally with increasing reticulocyte count.
- No severe symptoms of anemia (note 5) and stable vitals
- Patient is tolerating oral iron (see note 7 for troubleshooting)
- Dietary education completed including **milk-free diet** (note 4)
- Appropriate follow-up arranged

→

Discharge Recommendations:
Medications:
- Ferrous sulfate 2-4 mg/kg (elemental dosing) QD or palatable alternative
- Miralax prn for iron-associated constipation

PCP f/u in 1-2 weeks with repeat CBC and retic
- Recheck CBC and ferritin every 1-2 months until Hgb normalizes and ferritin > 20 (usually 3-6 months).
- Consider dentistry referral (if prolonged bottle use)
- Consider OT or Feeding Clinic referral if patient has barriers to dietary modifications

CLINICAL GUIDELINE

Iron deficiency anemia (IDA) in children ≤ 5 years old: Notes

Children's MINNESOTA

Aim: to standardize the treatment of iron deficiency anemia related to nutritional concerns for children ≤ 5 years old.

Note 1: Work- Up

- History should include:
  - Dietary intake with focus on milk consumption (>16 oz/day is concerning), bottle-feeding habits, and intake of iron-rich foods (e.g. animal meat). In infants <1 year old, iron-rich solids (e.g. iron-fortified infant cereal, meats) should be introduced by 6 mo
  - Pica or lead exposure (e.g. home painted prior to 1978)
  - Newborn screen results (specifically regarding thalassemias) can be confirmed by the Minnesota Department of Health (1-800-664-7772).
  - Bleeding symptoms, chronic abdominal pain, chronic diarrhea, or hematochezia (e.g. suggesting either IBD or malabsorption)
  - Family history with focus on anemias, blood transfusions, bleeding disorders or autoimmune disease (e.g. Inflammatory Bowel Disease)
- Physical exam should include: Review of growth chart. Evaluation for spleen or liver enlargement, lymphadenopathy, joint swelling, jaundice, or dysmorphology, which may suggest an etiology other than IDA.
- Additional screening tests for ID or IDA: Ferritin, CRP, reticulocyte count +/- iron panel. **Ferritin** is the single best test for assessing iron stores. Goal ferritin >20 ng/dL.
- Hemoglobin electrophoresis (e.g. testing for beta thalassemia and other variants) can be inaccurate if patient has a co-existent iron-deficiency anemia. Hemoglobin electrophoresis should only be sent after any iron deficiency has been repleted and at least 3-6 months after any blood transfusion.

Note 2: Definition of Anemia.

For children 6 mo - 5 yrs old, anemia is defined as a hgb <11 g/dL. Iron deficiency due to inadequate dietary intake is the most common cause of anemia in children.

Note 3: Findings supportive of iron deficiency

- Low MCV
- Mentzer index (MCV/RBC): Mentzer index >13 is consistent with iron-deficiency (Mentzer Index < 13: thalassemia may be more likely). Note a patient can have both IDA and thalassemia/thalassemia trait.
- Low ferritin (<12 mcg/L) is diagnostic for iron deficiency. **However, ferritin is an acute phase reactant and may be falsely elevated if the patient is inflamed
- Low iron saturation
- Low reticulocyte count for degree of anemia
- Low CHr (Reticulocyte hemoglobin content)
- Typical diet: high in milk (>16 oz), picky eating, low in animal meat
- Increase in hemoglobin with trial of iron is a way to treat and retrospectively diagnose mildly anemic patients

Note 4: Patient Education Patient Handout

- Encourage **no milk** if excessive milk consumption led to severe IDA requiring admission. Otherwise, limit cow milk consumption to ≤16 oz per day.
- Increase iron in diet: many cereals have iron fortification. Animal meat (the darker the better) is the most easily absorbed. Legumes and beans have high iron, however non-heme iron is not absorbed as well as heme iron
- Iron should be given on an empty stomach with water or juice (Vitamin C increases absorption). Do not give with dairy (calcium inhibits absorption)
- Iron supplements should be kept out of reach of young children. If there is any concern for an overdose or accidental ingestion, the child should be immediately evaluated in the ED.
- Complications of iron deficiency include anemia, impaired brain development (e.g. decreased IQ), decreased exercise capacity, pica, impaired leukocyte and lymphocyte function

Iron Deficiency Anemia Education Video Series link and QR code

- https://www.youtube.com/playlist?list=PLsRN8YNulFf4TT-QqUie41loIJSOs2aeJ

CLINICAL GUIDELINE

Iron deficiency anemia (IDA) in children ≤ 5 years old: Notes

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Note 5: Concerning symptoms/signs of anemia that would warrant admission include (but are not limited to): orthostasis, lethargy, dyspnea, persistent tachycardia, or hypotension

Note 6: Red Flags that warrant Hematology consultation and/or further work-up include (but are not limited to):

- Patient not responding to iron therapy as expected (and compliance is confirmed)
- Rapid drop in hemoglobin (i.e. concerning for active bleeding or hemolysis)
- Symptoms such as bleeding, fever, chronic diarrhea, chronic abdominal pain, joint pains
- Signs such as weight loss or growth faltering, diffuse lymphadenopathy, jaundice, hepatosplenomegaly
- Family history of anemia in a child or thalassemia
- History of pica or lead exposure
- Family reports a "normal" diet rich in iron
- Labs such as: normal ferritin (in the absence of acute inflammation), normocytic or macrocytic anemia, Mentzer index <13 (see note 1), or labs suggesting hemolysis (e.g. elevated indirect bilirubin)
    - If anemia persists after ferritin has normalized, a hemoglobinopathy (most commonly a trait form) should be considered and hemoglobin electrophoresis and/or hematology referral is appropriate.
- Thrombocytopenia, leukopenia and/or neutropenia in addition to the anemia:
    - **If well appearance and counts mildly depressed:** leukemia outpatient screening may be appropriate including peripheral smear review by a pathologist, CBC with differential, reticulocyte count, CMP, uric acid, phosphorus, LDH, and coagulation screening (PT, PTT, fibrinogen) if bruising.
    - **If ill-appearing or counts are severely low:** referral to emergency department where Hematology/Oncology will be consulted

Note 7: Iron Administration Troubleshooting

- Consistent iron supplementation, along with any necessary dietary changes, should improve Hgb by 2 g/dL/month and ferritin should normalize (>20 ng/dL) within 3-6 months of anemia resolution.
- Failure to respond to iron supplementation is most often due to poor compliance. Strategies to improve compliance and efficacy include:
    - Assess for side effects. Consider Miralax prn for constipation.
    - Assess for optimal administration (e.g. give medication with water or juice, not with milk products, and separate 2+ hours from H2 blockers)
    - **Consider switching to another form of iron to improve compliance.** Be aware that most insurances will not cover these and some pharmacies do not carry them. Purchase OTC or online. **Dose based on elemental iron**. Alternative iron formulations may cause less GI upset than traditional iron salts (ferrous sulfate).
        - **You+Yours tasteless** iron for kids can be purchased over the counter
        - **Celebrate** tabs are flavorful iron tablets. Contains ferrous fumarate and Vitamin C to enhance absorption.
        - **Novaferrum** is a better tasting liquid. It contains polysaccharide-iron complex that can be gentler on the stomach.
        - Though **gummy iron supplements** are palatable, the iron content may be quite low, so be sure dosing is adequate (i.e. may require multiple gummies/day)
        - Heme-iron formulations, such as **Proferrin**, may cause less GI upset and provide more significant correction of iron deficiency than iron salts. Proferrin ES can be purchased over the counter (Amazon) and Proferrin Forte can occasionally be processed through insurance.

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Note 8: IV Iron

- IV Venofer generally *cannot completely correct an iron deficiency in a single dose*, but can be used to jump-start iron repletion, and then must be followed by (1) oral iron supplementation (usually 3-6 mo) and (2) dietary modifications
- IV Iron Dextran may be considered for a patient with ongoing bleeding (i.e. off-pathway) or for patients unable to take enteral iron who cannot receive future IV Venofer or simply need more repletion, e.g. live far away, autism concerns with high risk of recurrence
- When transfusing blood, IV iron is recommended after completion of the transfusion to provide additional iron for hematopoiesis.
- Refer to Iron Infusion Reaction Clinical Practice Guideline if any symptoms during iron infusion.

References

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