Children's Hospital of Richmond at VCU

Anemia

Fast facts

- Anemia affects 1.62 billion people worldwide. According to the WHO, worldwide prevalence is highest among preschool aged children (47%). Prevalence among school aged children worldwide is estimated at 25%.
- Iron deficiency anemia is the most common type of anemia, estimated to make up about 50% of cases.

Background

Anemia refers to a hemoglobin (Hgb) that is lower than normal for age and leads to decreased ability to deliver adequate oxygen to the body. Anemia in pediatrics is generally defined as a hemoglobin or hematocrit level lower than the age-adjusted reference range for healthy children. This leads to diminished oxygen-carrying capacity that does not optimally meet the metabolic demands of the body. Long-standing anemia can lead to problems with growth and development. There are many causes of anemia, and these causes vary based age at presentation, family history, socioeconomic factors, medications, genetics, diet, and comorbidities. In neonates and young infants, immune hemolytic disease, infection, and hereditary disorders are most common causes, while in older children, acquired causes related to diet or blood loss are more likely. The most common cause of anemia worldwide is iron deficiency.

Assessment:

Risk factors and clinical history should be assessed as appropriate on routine visits.

- Clinical history:
  - Signs/symptoms of anemia
  - Any bleeding history
  - Diet and growth history
- Family history:
  - Ethnicity, any other family members with anemia
- Medications that may contribute to anemia

Labs will inform management/treatment. If anemia is suspected based on assessment/risk factors or Hgb <10 on 12 month screen, obtain CBC with differential, reticulocyte count, iron studies including total iron, ferritin, and transferrin. If macrocytic, get B12 and folate levels.

Of note, if there is concern for abnormal newborn screen, please call CHoR 1PAL line for a doc to doc consult with CHoR Hematology.

Management/Treatment in the PCP office:

If Red Flags present, consider ED:

- Hgb <5 g/dL (indicates need for blood transfusion)
- Concern for severe symptoms of anemia (hypoxia, dyspnea on exertion, syncopal episodes)
- Abnormalities in all 3 cell lines

Refer to CHoR Hematology urgently (visit within 24-28 hours) or consider ED if:

- More than one cell line abnormality (i.e. neutropenia or thrombocytopenia in addition to anemia) Note: thrombocytosis is common in iron deficiency anemia

If Hgb is below lower limit for age (see table in algorithm), microcytic anemia (MCV < 80) and no other cell lines involved, treatment for suspected iron deficiency anemia can begin in the PCP office.

- If there is additional concern for failure to thrive, pica, or tachycardia syncopal episodes which may indicate severe or long-standing anemia, consider non-urgent referral to CHoR Pediatric Hematology in addition to beginning steps below.

1. Obtain baseline iron studies (as above, CBC, retic, total iron, ferritin, and transferrin)
2. Iron supplementation: 3 mg/kg/day of elemental iron given once daily (ferrous sulfate or iron polysaccharide if better tolerated)
3. Increase dietary intake of iron: provide hand-out on iron rich foods

4. If >12 months of age, decrease cow's milk intake to <18 oz (2 cups) per day.
5. Advise taking iron with vitamin C and to avoid milk within 2 hours of taking supplement to optimize absorption
6. Recheck labs after 1 month of adherence to iron supplementation. If there is a significant increase in reticulocytes or increase in hemoglobin by at least 1 g/dL, recheck CBC and iron studies after 3 months. Iron can be discontinued when ferritin is normalized (generally after 3-6 months).

If no increase in hemoglobin or reticulocytes after 1 month on consistent iron supplementation, non-urgent referral to CHoR Hematology with the following:

- Send iron studies (ferritin, transferrin, iron) before starting treatment and after 1 month of treatment.
  A. Assess for any symptoms of malabsorption, i.e. blood in stools, poor growth, or diarrhea. Consider need for Pediatric Gastroenterology referral as well.
  B. Ensure patients are compliant with medications – prescription has been picked up, being taken as instructed, milk intake has decreased, etc.
- If applicable, also send any abnormal hemoglobin variants on newborn screen.

References:

1. de Benoist B et al., eds. Worldwide prevalence of anaemia 1993-2005. WHO Global Database on Anaemia Geneva, World Health Organization, 2008.
2. Shuoyan Ning, Michelle P. Zeller; Management of iron deficiency. Hematology Am Soc Hematol Educ Program 2019; 2019 (1): 315–322. doi: https://doi.org/10.1182/hematology.2019000034
3. Short MW, Domagalski JE. Iron deficiency anemia: evaluation and management. Am Fam Physician. 2013 Jan 15;87(2):98-104. PMID: 23317073.
4. Powers JM, Buchanan GR. Diagnosis and management of iron deficiency anemia. Hematol Oncol Clin North Am. 2014 Aug;28(4):729-45, vi-vii. doi: 10.1016/j.hoc.2014.04.007. Epub 2014 Jun 2. PMID: 25064710.
5. Powers JM, Buchanan GR, Adix L, Zhang S, Gao A, McCavit TL. Effect of Low-Dose Ferrous Sulfate vs Iron Polysaccharide Complex on Hemoglobin Concentration in Young Children With Nutritional Iron-Deficiency Anemia: A Randomized Clinical Trial. JAMA. 2017 Jun 13;317(22):2297-2304. doi: 10.1001/jama.2017.6846. PMID: 28609534; PMCID: PMC5815003.

Assessment:
All patients screened at 12 months.
Risk factors and clinical history assessed as appropriate on routine visits

If concern for abnormal newborn screen, doc to doc consult with CHoR Hematology

Risk factors for anemia:
- Family history of anemia
- Ethnicity- African ancestry in sickle cell disease; Mediterranean, Asian, or African ancestry in thalassemia; Sephardic Jewish, Filipino, Greek, Sardinian, or Kurdish ancestry in G6PD deficiency
- Bleeding history (ie blood in stools, heavy period)
- Recent illness or chronic illness
- Vegan diet or other restrictive diet
- Toddlers and children with milk intake >24 oz a day
- Currently taking medications which can cause anemia (ie sulfa drugs, nitrofurantoin)

Clinical signs/symptoms of anemia:
- Fatigue
- Lightheadedness
- Exercise intolerance
- Syncopal episodes
- Palpitations
- Pallor
- Pica

Suspect possible anemia based on risk factors, symptoms or Hgb/Hct flagging low on screening lab?

No → Assess at future visits as appropriate

Yes → Labs
- CBC with differential
- Reticulocyte count
- Iron studies including total iron, ferritin, and transferrin
- *If macrocytic, get B12 and folate levels*

Are Red Flags Present?
Hgb <5 g/dL (indicates need for blood transfusion)
Concern for severe symptoms of anemia (hypoxia, dyspnea on exertion, syncopal episodes)
Abnormalities in all 3 cell lines

Yes → Consider ED

No → Is Hgb below the lower limit of normal for age? *(See table page 2)*

No → Continue to screen for signs/symptoms as appropriate on follow-up visits

Yes →
- Increase dietary intake of iron- educate on iron rich foods
- Children >1 year should drink no more than 18oz (~2 cups) cow's milk per day.
- Iron Supplementation: 3mg/kg/day of elemental iron given once daily – Max dose of 200mg elemental iron
- Take iron with vitamin C and avoid milk within 2 hours of taking supplement to maximize absorption
- Adherence to iron supplementation can be an issue, collaborate with families to ensure adherence

Recheck labs (CBC and reticulocytes) after one month on consistent iron supplementation

PO Iron Formulations:
Ferrous Sulfate - 325mg contains 62mg elemental iron
Iron Polysaccharide - 150mg contains 150mg elemental iron

Yes → Are there other cell line abnormalities besides Hgb?

Yes → Consider ED or refer to CHoR Hematology for urgent visit (within 24-48 hours)

No → Upon recheck after 1 month of adherence to iron supplementation, is there an increase in reticulocytes or or hemoglobin by 1g/dL

No → Refer to CHoR Hematology

Yes → Recheck CBC and iron studies after 3 months. Can discontinue iron when ferritin normalized – generally after 3-6months

For doc to doc consult with a CHoR Heme-Onc doc or to schedule an urgent visit call CHoR's 1PAL line 804-628-1PAL (1725)

First Approved May 2022, Created by CHoR division of Heme-Onc, with input from Virginia Children's Care Network Community PCPs

TABLE A1.8 Red Cell Values at Various Ages: Mean and Lower Limit of Normal (22 SD)[a]

	Hemoglobin (g/dl)		Hematocrit (%)		Red cell count (10^{12}/l)		MCV (fl)		MCH (pg)		MCHC (g/dl)		Reticulocytes	
Age	Mean	22 SD	Mean	22 SD	Mean	22 SD	Mean	22 SD	Mean	22 SD	Mean	22 SD	Mean	22 SD
Birth (cord blood)	16.5	13.5	51	42	4.7	3.9	108	98	34	31	33	30	3.2	1.8
1–3 days (capillary)	18.5	14.5	56	45	5.3	4.0	108	95	34	31	33	29	3.0	1.5
1 week	17.5	13.5	54	42	5.1	3.9	107	88	34	28	33	28	0.5	0.1
2 weeks	16.5	12.5	51	39	4.9	3.6	105	86	34	28	33	28	0.5	0.2
1 month	14.0	10.0	43	31	4.2	3.0	104	85	34	28	33	29	0.8	0.4
2 months	11.5	9.0	35	28	3.8	2.7	96	77	30	26	33	29	1.6	0.9
3–6 months	11.5	9.5	35	29	3.8	3.1	91	74	30	25	33	30	0.7	0.4
0.5–2 years	12.0	10.5	36	33	4.5	3.7	78	70	27	23	33	30	1.0	0.2
2–6 years	12.5	11.5	37	34	4.6	3.9	81	75	27	24	34	31	1.0	0.2
6–12 years	13.5	11.5	40	35	4.6	4.0	86	77	29	25	34	31	1.0	0.2
12–18 Years														
Female	14.0	12.0	41	36	4.6	4.1	90	78	30	25	34	31	1.0	0.2
Male	14.5	13.0	43	37	4.9	4.5	88	78	30	25	34	31	1.0	0.2
18–49 Years														
Female	14.0	12.0	41	36	4.6	4.0	90	80	30	26	34	31	1.0	0.2
Male	15.5	13.5	47	41	5.2	4.5	90	80	30	26	34	31	1.0	0.2

[a]*These data have been compiled from several sources. Emphasis is given to studies employing electronic counters and to the selection of populations that are likely to exclude individuals with iron deficiency. The mean ± 2 SD can be expected to include 95% of the observations in a normal population.*
From Dallman, P.R., 1997. Blood and blood-forming tissue. In: Rudolph, A. (Ed.), Pediatrics, sixteenth ed. Appleton-Cernuary-Croles, Norwalk, CT, with permission.

From Lanzkowsky's Manual of Pediatric Hematology and Oncology. 6th Ed.