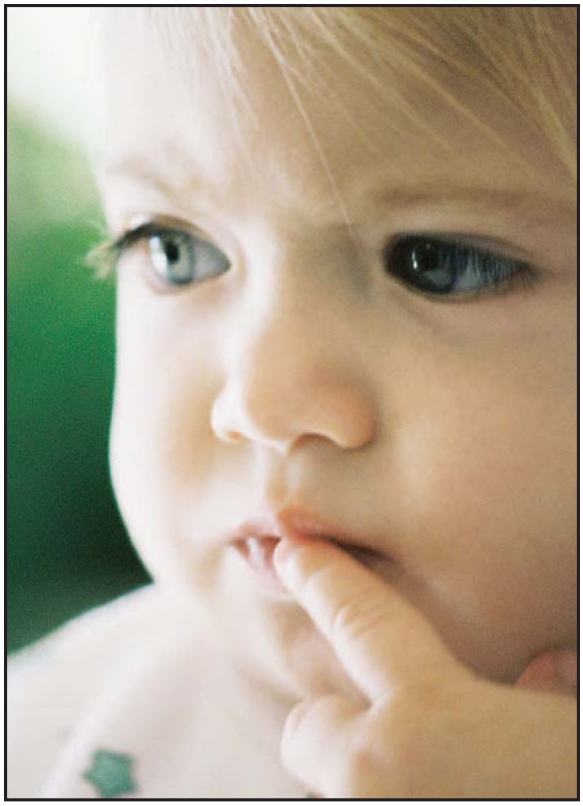
How Do I Spot Anemia in



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In this article:

Anemia is defined as a reduction in red cell mass, or blood hemoglobin concentration more than two standard deviations below the mean for the normal population. By this definition, some overlap between normal and abnormal values is to be expected with the result that 2.5 % of the normal population would be classified as anemic, while some anemic individuals would be placed in the normal range. Individual measurement of hemoglobin should therefore be interpreted taking into consideration the age, sex, previous values in the same patient, and other determinants of oxygen delivery to tissues (*e.g.,* cyanotic heart disease, chronic respiratory insufficiency or mutant hemoglobin with high affinity for oxygen). Anemias can be classified according to the primary pathophysiologic mechanisms or on the basis of red cell size and morphology. The two major pathophysiologic mechanisms underlying anemias are:

- Defective red cell production in which the rate of red cell production is reduced or disorders of

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Katie's case

Katie, 19-months-old, presented with a month's history of diarrhea and vomiting. The diarrhea was five to six times a day with no mucus or blood. She had been in very good health before the onset of her symptoms. She was born vaginally at term with a birth weight of 3.6 kg. She had normal growth and developmental milestones, and had completed all immunizations appropriate for her age. She was described as being a "fussy eater."

Further inquiry revealed that Katie consumed 40-50 oz of cow's milk daily.

Examination revealed a very pale and lethargic girl with no jaundice. Vital signs were:

- Heart rate 130/min
- Respiratory rate 22/min
- Blood pressure 94/60 mm Hg
- Oxygen saturation 95-99% in room air
- A grade 2/6 systolic murmur was audible
- Respiratory, abdominal and central nervous system examination were unremarkable

Investigations

- Hemoglobin (Hb) 39 g/L
- White blood cell 15.2 x 10^9/L (N 8.5, L 5.3)
- Platelets 283 x 10^9/L
- Mean cell volume 46.1 fL
- Mean corpuscular hemoglobin (MCH) 12.7 pg
- Red blood cell distribution width (RDW) 29.0
- Reticulocytes 19 (Normal 10-86 X 10^9/L)
- Ferritin < 1 mg/L
- Lytes & LFT, normal
- Albumin 27 g/L
- Antitransglutaminase imunoglobulin A, normal
- Stool virology and bacteriology, normal

Katie was started on iron replacement therapy (5 mg elemental/kg/day) and was not transfused blood. Nutritional counselling was given. Cow's milk consumption was drastically reduced and iron-rich food was introduced. Ten days after iron therapy, complete blood count showed hemoglobin 62 g/L, mean cell volume 50.5 fl, MCH 16.1 pg, RDW 39.6, Retic 367. Further improvement and eventual normalization of Hb was achieved and iron replacement was discontinued after six months.

Anthony's case

Anthony, 4, presented with pain in his left foot and swelling of the left wrist. Six weeks earlier, he had fallen on his arm and sustained a fracture of the left radius, requiring a plaster cast.

Orthopedic assessment of the tender foot had queried the diagnosis of osteomyelitis based on X-ray findings.

Bone and white cell scans were normal, while examination revealed a tender left ankle and no palpable adenopathy or abdominal organomegaly.

Investigations

- Hemoglobin 101 g/L
- White blood cell 5.3 x 10^9/L (N 1.2, L 4.0)
- Platelets 306 x 10^9/L
- Mean cell volume 73.4 fl
- Mean corpuscular hemoglobin 24.7 pg
- Blood film – atypical/immature lymphocytes
- Lytes and LFT-normal
- LDH 366 ANA-negative RF < 11 IU/l
- ESR 33 Ferritin 112 mg/L

Bone marrow aspirate showed almost total infiltration with lymphoblasts, immunophenotyping in keeping with B-precursor lymphoblasts and normal cerebrospinal fluid.

Chemotherapy for acute lymphoblastic leukemia (ALL) was commenced.

erythrocyte maturation and ineffective erythropoiesis.

- Excessive destruction or loss of red cells through hemolysis or bleeding.

Distinction between these mechanisms can generally be made on the basis of the reticulocyte count. The reticulocyte count is increased in hemolytic anemias, but not in anemias resulting from defective red cell production.

Use of automated blood cell counters permits ready-measurement of red cell size and a diagnostically useful classification based on whether the red cells are microcytic, normocytic or macrocytic (Table 1).

Anemia in Kids

What's the significance of Katie's case?

Katie's case illustrates how profoundly severe nutritional iron deficiency can be even in children from high-income families. Severe iron deficiency in this toddler was never a diagnostic problem. The ingestion of excessive amounts of cow's milk in infancy is commonly associated with occult blood loss from the gastrointestinal tract, compounding the low iron content and poor availability of the iron in cow's milk. The result could be profound anemia in a supposedly "thriving" child. The recommendations of The Canadian Pediatric Society for the prevention of iron deficiency include:

- Breast-feeding, or use of iron-fortified infant formula for six months;
- Weaning to iron-fortified cereals and other iron-rich foods by the age of six months;
- Avoidance of cow's milk, until an adequate amount of solid food containing iron and vitamin C if included in the diet, preferably at nine to 12 months;
- Children over one should be given iron-containing foods, such as meats, legumes, fruits and iron-fortified infant or toddler cereals.

What's the significance of Anthony's case?

Anthony presents with mild anemia without obvious white cell or platelet abnormalities. However, the findings of ankle tenderness on examination together with abnormalities on peripheral blood film were pointers to further investigation.

The diagnosis of acute lymphoblastic leukemia (ALL) was easily made by examination of the bone marrow. The examination of the peripheral blood smear is the single most useful procedure in the initial assessment of a child with anemia. It certainly was the main reason for this boy's referral to a pediatric hematologist. Bone pain and tenderness are well-recognized manifestations of acute leukemia in childhood.

As illustrated by this case, not uncommonly, the rheumatologist or orthopedic surgeon is the first specialist to see the patient.

The management of nutritional iron deficiency is best done in the context of general practice without the need for referral to a hematologist. Nutritional counselling provides the long-term solution following the initiation of iron replacement therapy. Iron replacement should continue for about three to six months to ensure adequate replenishment of iron stores. Prolonged treatment should be avoided, especially in patients with improved intake of dietary iron. It cannot be over-emphasized that, except in extreme circumstances where urgent improvement of anemia is desirable (*e.g.,* prior to major emergency surgery or impending heart failure), red cell transfusions are not indicated. Besides, overzealous transfusions in some children could precipitate overt heart failure. Response to oral iron therapy occurs quickly enough to make exposure to blood products an unnecessary risk. The most common cause of non-response to iron therapy is lack of compliance. The differential diagnosis or coexistence of thalassemia trait (alpha and beta) should always be considered. Hemoglobin electrophoresis with quantification of Hb A2 will be helpful in beta thalassemia minor. Diagnosis of alpha thalassemia may be made by assessing red cell H-inclusions (supravital staining), but often requires molecular testing. The anemia of chronic disorders and sideroblastic anemias are usually associated with normal or elevated serum ferritin levels.

When should I refer?

Physicians in family practice not uncommonly encounter difficulty in deciding whether or not a child with anemia should be referred to a specialist. The two case scenarios indicate that although the severity of the anemia is an impor-

Table 1

Classification of anemia

Microcytic anemias
- Iron deficiency
- Thalassemia syndromes
- Anemia of chronic disease
- Sideroblastic anemias
- Chronic lead poisoning

Macrocytic anemias

1. With megaloblastic bone marrow
- Vitamin B_{12} deficiency
- Folic acid deficiency
- Orotic aciduria

2. Without megaloblastic bone marrow
- Hypothyroidism
- Liver disease
- Bone marrow infiltration
- Aplastic anemia
- Diamond-Blackfan syndrome
- Dyserythropoietic anemias

Normocytic anemias

1. Hemolytic anemias
   - Congenital hemolytic anemias
     - Disorders of red cell membrane
     - Red cell enzyme defects
     - Hemoglobin mutants
   - Acquired hemolytic anemias
     - Immune-mediated
     - Acute infections
     - Microangiopathic hemolytic anemias
2. Acute blood loss
3. Anemia of chronic disease
4. Leukemia and bone marrow infiltration
5. Chronic renal failure
6. Hypersplenism

Anemia in Kids

tant determinant of such referral, it should not be considered in isolation. Katie had severe anemia (hemoglobin of 39 g/L), but with an easily treatable cause: iron supplementation and dietary advice. By contrast, Anthony's case, despite a near normal hemoglobin concentration, nevertheless needed urgent testing to reveal the diagnosis of ALL.

The initial investigation of anemia should include hemoglobin, red cell indices, reticulocyte count, white blood cell count, platelet count, and peripheral blood film examination. The results of these investigations together with the findings of history and physical examination will form the basis for other laboratory procedures. These include serum ferritin, bilirubin and haptoglobin, supravital staining of red cells, direct and indirect Coombs' test, screening for G6PD deficiency, Hb electrophoresis, serum vitamin B12, red cell folate, and examination of bone marrow. CME

Take-home message

Some important factors or points to consider in making a decision to refer a child include the following:

- Associated leucopenia or leucocytosis
- Associated thrombocytopenia
- Abnormal peripheral blood film report
- Significant reticulocytosis or reticulocytopenia
- Presence of hepatomegaly, splenomegaly or significant lymphadenopathy
- Macrocytic anemias
- Microcytic anemia unresponsive to iron therapy (compliance confirmed)
- Associated symptoms and signs (*e.g.,* diarrhea, jaundice and dysmorphism)
- Children with nutritional iron deficiency need nutritional advice, not a hematologist
- If in doubt, always remember that a hematologist is just a phone call away.

Suggested Readings

1. Nathan DG, Oski FA: Hematology of Infancy and Childhood. Fourth Edition. Saunders, Philadelphia, 1993, p 346-53.
2. Lilleyman JS, Hann IM: Pediatric Hematology. Second Edition. Churchill Livingstone, Edinburgh, 1992, p 201-04.
3. Nutrition Committee, Canadian Paediatric Society: Meeting the iron needs of infants and young children: an update. Can Med Assoc J 1991; 144(11):1451-54.

Net readings

1. http://www.vh.org/pediatric/patient/pediatrics/cqqa/anemia.html
2. http://www.diagnostico.com/Pediatrics/Common/Anemia.stm