Nutritional Influences on Illness
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Nutritional Imbalances in Anemia

When laboratory testing reveals anemia, the clinician needs to investigate whether nutritional imbalance is an underlying cause. Nutrient deficiencies are found in a large variety of anemias, while excessive iron is characteristic of beta-thalassemia major (Figure 1). We will review how various nutrients influence the development of the anemias.

VITAMINS

Vitamin A
Anemia gradually develops several months after starting a diet deficient in vitamin A. Serum hemoglobin begins to decline well before the loss of night vision or the development of "deficient" serum levels of the vitamin. The anemia, which is due to impaired hemoglobin synthesis, is reversible with supplementation. Vitamin A may also be deficient in sickle cell anemia.

Vitamin B Complex
Folic acid deficiency is a well-known cause of megaloblastic (enlarged red cell) anemia. Folate deficiency may also occur in sickle cell anemia, a hereditary hemolytic anemia in which the presence of an abnormal hemoglobin results in distorted, sickle-shaped erythrocytes. The deficiency responds to folate supplementation. Moreover, folate deficiency may also promote aplastic anemia and red cell aplasia; both anemias respond to supplementation.

When pantothenic acid is deficient, supplementation can be helpful in alleviating anemia. Riboflavin deficiency can cause a normochromic, normocytic anemia and reticulocytopenia that responds to supplementation. Riboflavin deficiency also may be associated with sickle cell anemia, usually in conjunction with other deficiencies. Thiamine deficiency may be associated with a megaloblastic anemia which, in turn, may respond to supplementation.

Vitamin B6 deficiency may be associated not only with a megaloblastic anemia, but also with a microcytic (miniaturized red cell) anemia; both respond to supplementation. When the vitamin is deficient, sickle cell anemia may also show a response to vitamin supplements. Furthermore, if a sideroblastic anemia is unresponsive to pyridoxine, supplementation with pyridoxal-5'-phosphate may be effective, as the anemia may be due to defective phosphorylation of pyridoxine to its active form.

Vitamin B12 deficiency is well-known to cause pernicious anemia, a megaloblastic anemia in which the red blood cells are abnormally formed, and supplementation may be able to reverse the neurological damage. Moreover, a B12 deficiency may be associated with sickle cell anemia whose symptoms may respond to intramuscular supplementation.

Vitamin C
Vitamin C deficiency is occasionally associated with a normochromic, normocytic, or else a macrocytic, anemia. Vitamin C enhances non-heme iron absorption, which may stimulate hematopoiesis (red blood cell production) and aid in the prevention and treatment of iron-deficiency anemia.
**MINERALS**

Copper

If pharmacologic doses of zinc (100-300 mg daily) are given for several months, a severe copper deficiency may develop, causing a sideroblastic anemia as well as leukopenia and neutropenia.\(^{26}\) (A sideroblastic anemia is marked by large numbers of ringed sideroblasts in the bone marrow, ineffective production of red blood cells, hypochromic erythrocytes in the peripheral blood, and, usually, increased levels of tissue iron.)

Because of its effects on ceruloplasmin (a copper-binding glycoprotein), copper deficiency may also cause an iron deficiency anemia due to impaired iron absorption and reduced heme synthesis while iron accumulates in storage tissues. Also, sickle cell anemia may be associated with reduced serum copper levels.\(^{27}\)

Iron

Iron deficiency is likely to be the most frequent cause of anemia and responds well to iron supplementation.\(^{28}\) In addition, iron is often deficient in pernicious anemia\(^{29}\) as well as in sickle cell anemia.\(^{5}\) By contrast, beta-thalassemia major (Cooley's anemia), an inherited microcytic anemia, may be associated with iron overload, and levels of ferritin (an iron-storage protein) may be positively correlated with lipid peroxidation product concentrations in this disorder.\(^{10}\) Thus, when treating a microcytic anemia, iron supplementation is contraindicated unless iron is found to be deficient.

Magnesium

Magnesium nutriture may be reduced in a number of anemias, including beta-thalassemia,\(^{31}\) sickle cell anemia,\(^{27}\) and sideropenic anemia.\(^{32}\) In the case of beta-thalassemia, dietary magnesium supplementation has been shown to improve some of the characteristic cellular function abnormalities.\(^{33}\) As for sickle cell anemia, magnesium depletion appears to be at least partly due to excessive urinary excretion.\(^{34}\) Supplementation may increase the absolute reticulocyte count and the number of immature reticulocytes, while reducing the number of dense sickle erythrocytes.\(^{35}\)

Zinc

Plasma levels of zinc may be low in sickle cell anemia;\(^{27}\) this may be corrected by supplementation.\(^{3}\) Also, in beta-thalassemia, chronic hemolysis causing excessive zinc loss in the urine may result in a zinc deficiency.\(^{36}\)

**Notes**
