
Nutritional Considerations in Treating Anemia

Chris D. Meletis, N.D.

Anemia is not a disease per se but rather a symptom that arises from either a reduction in the number of red blood cells (RBCs) or the quantity of hemoglobin in the blood. Even the slightest sign of anemia represents an imbalance in the body that is worthy of clinical investigation. Only an in-depth review and methodical elimination of possible etiologies allows for an accurate and reliable diagnosis that measures the severity of the anemia.

Healthy RBCs have an average survival period of 120 days, thus, during each day, roughly 1 percent of a patient's RBCs must be replaced. However, during the rare occasion of complete cessation of RBC production, a 10 percent decrease in RBC count might be noted per week. If RBC counts drop more rapidly than 10 percent per week then destructive processes, such as hemolysis, must be considered. The causes of anemia can be broken down into three basic categories: Blood loss, decreased production of RBCs, or increased destruction of RBCs.

Differentiating Types of Anemia

Types of anemia are based primarily on the morphology of the RBCs, such as size and color. The following indices are used to identify types of anemias: mean corpuscular volume, the average volume of red blood cells; mean corpuscular hemoglobin, the average amount of hemoglobin per RBC; and mean corpuscular hemoglobin concentration, the average concentration of

hemoglobin per RBC. For a list of the better-known anemia types, consult the box entitled Some Common Types of Anemia.

Common Presenting Symptoms

Often, the most prominent symptoms that could lead a clinician to diagnose and treat an underlying anemia are among the same symptoms that, all too often, are associated with the condition that caused the anemia in the first place. Some of the most typical symptoms of anemia are listed in the box entitled Anemia-Related Symptoms.

Nutritional Considerations

There are numerous vitamins and minerals that are critical for hematopoiesis. Yet, the true key to addressing anemia, as with any condition, is not only to correct the symptom but to determine the cause, treat it, and establish true sustained healing. Nourishing the body and supporting specific individualized nutritional needs are the keys to both reversing the symptom of imbalance called anemia and supporting a foundation of optimal health.

Copper

It is well documented that rapidly growing infants and patients on total parenteral nutrition without copper supplementation develop anemia and neutropenia.¹ Copper deficiency can lead to iron-deficiency anemia, because of the effect of copper deficiency on ceruloplasmin. Hence, supplementation with copper can reverse the cause of some types of anemia.²

Folic Acid

Folate deficiency is well established as a principal cause of megaloblastic anemia, which is corrected with supplementation. The essential role folic acid plays in supporting the replication and replenishment of dividing tissues makes it a critical foundational nutrient for the treatment of many forms of anemia, including sickle-cell and aplastic anemia.^{3,4}

Hydrochloric Acid

Treating underlying achlorhydria/hypochlorhydria can help to correct both iron- and vitamin B₁₂-deficiency anemia, that commonly arise from decreased stomach acid. Iron absorption is largely dependent upon having sufficient hydrochloric acid (HCl). Studies have shown that achlorhydric patients, when given supplements with HCl, absorbed iron significantly better than they had prior to treatment.^{5,6} Equally relevant is the relationship between lowered stomach acid quantity and diminished vitamin B₁₂ assimilation. Treatment with betaine HCl can help to ensure that patients who are suffering from diminished stomach acidity do not develop anemia.

An additional reason for supplementation is that there is growing evidence that lowered stomach acid has been hypothesized to lead to imbalanced intestinal bacteria, predisposing individuals to nutritional deficiencies and malabsorption of nutrients. This can result in decreased bacterial vitamin synthesis and infection with opportunistic microorganisms, compromising overall health further.^{7,8}

Megaloblastic anemia improved upon administration of 20 mg of thiamine and recurred upon cessation of treatment.

Anemia-Related Symptoms

- Lack of energy
- Overall fatigue
- More easily induced fatigue
- Irritability
- Vertigo
- Headaches
- Tinnitus
- Spots before eyes
- Amenorrhea
- Shortness of breath
- Increased pulse
- Swelling of ankles
- Drowsiness
- Heart failure
- Shock
- Pale palms
- Pale fingernail beds
- Pale conjunctiva

Some Common Types of Anemia

- Achrestic
- Aplastic
- Autoimmune hemolytic
- Cooley's deficiency
- Drug induced anemia
- Erythroblastic
- Hemolytic
- Hypochromic
- Hypoplastic
- Lederer's
- Macrocytic
- Mediterranean
- Megaloblastic
- Microcytic
- Myelopathic
- Normochromic
- Normocytic
- Nutritional
- Pernicious
- Sickle cell
- Sideroblastic spur cell thalassemia

Iron

Iron deficiency is the most common nutritional deficiency in the United States and, thus, not surprisingly, is the most common form of anemia seen in clinical practice. The single best common laboratory test for the diagnosis of iron deficiency is serum ferritin.^{9,10}

It is estimated that some degree of iron deficiency is present in 35–60 percent of healthy young women. The other groups at highest risk of becoming deficient in iron are children under 2, pregnant women, teenage girls, and elderly people.

Deficiency is frequently associated with chronic disease, blood loss, malnutrition, and malabsorption of nutrients. While discussing the role of iron in the treatment of anemia with patients, the practitioner must be sure that patients are aware of the two forms of iron: heme and nonheme. Heme iron, the most efficiently absorbed dietary iron, is found in animal products and is bound to hemoglobin and myoglobin. Nonheme iron, found in plant sources, is relatively poorly absorbed.

Gastrointestinal (GI) conditions, including hypochlorhydria, celiac disease, Crohn's disease, and ulcerative colitis all contribute directly or indirectly to iron-deficiency anemia. Other conditions, such as pernicious anemia, sickle-cell anemia, and generalized nutritional deficiencies can exacerbate an underlying anemia.^{11–13}

An example of a related nutritional deficiency that can affect iron absorption and utilization is a study that was done on vitamin A. When administered alone to subjects in one study, both iron and vitamin A each produced meaningful changes in hematocrit, hemoglobin, percent of transferrin saturation, and RBC

count. Yet, when these two nutrients were given simultaneously to the patients, hematopoietic responsiveness was enhanced further.¹⁴

Pantothenic Acid

A case study of a middle-age female presenting with weight loss, lethargy, incontinence, anorexia, and hypochromic anemia associated with increased bone-marrow iron storage that had not responded previously to treatment demonstrated great improvement with the administration of pantothenic acid 50–200 mg intramuscularly daily.¹⁵ Although pantothenic acid is not well known for its role in hematopoiesis, such cases demonstrate, quite well, the need to maintain the balance of B vitamins when administering supplements as opposed to offering isolated vitamins.

Riboflavin

Riboflavin deficiency can lead to normochromic, normocytic anemia and responds to riboflavin supplementation. In a small study, men that were induced, via dietary restriction, to become riboflavin deficient all developed reversible anemia.¹⁶ What is more, another study, researchers noted that that 90 percent of vitamin E-deficient patients with sickle-cell anemia were also riboflavin deficient.¹⁷ Riboflavin supplementation has also been shown to improve both total iron-binding capacity and serum ferritin levels significantly.¹⁸

Thiamine

Two case reports have revealed the usefulness of thiamine supplementation in patients with anemia. One case involved megaloblastic anemia that did not respond to either folic acid or to vitamin B₁₂, yet improved upon administration of 20 mg of

Subclinical vitamin A deficiency may be an important consideration when treating anemic patients with poor nutritional status or malabsorption of nutrients.

thiamine and recurred upon cessation of treatment.¹⁹ In another case, an infant who presented with diabetes, anemia, cardiac and neurologic disturbance, and normal transketolase improved when given 100 mg of thiamine; the patient's symptoms reappeared when treatment was discontinued.²⁰

Vitamin A

In addition to the successful treatment of anemia with the concomitant use of vitamin A and iron, this vitamin appears to have additional positive effects on correcting anemia.

Low plasma levels of vitamin A have been associated with lowered hemoglobin levels.²¹

In a study of 8 men that became vitamin A-deficient, as a result of a restricted diet, serum hemoglobin levels fell prior to detectable serum vitamin A-deficiency values or loss of night vision. This suggests that subclinical vitamin A deficiency may be an important consideration when treating anemic patients with poor nutritional status or malabsorption of nutrients.²²

Vitamin B₆

Pyridoxine-dependent microcytic anemia can arise even with apparent adequate dietary intake and serum levels of the vitamin.²³ In addition, there have also been cases of folic acid- and pyridoxine-resistant sideroblastic anemia that responded to parenteral pyridoxal phosphate. The pyridoxal phosphate was given for 8–10 days at a dosage of 25–50 mg, 4 times per day. The success of the parenteral method of delivery compared to oral administration suggests that defective phosphorylation may be preventing pyridoxine from being ultimately converted to pyridoxal phosphate.²⁴

Nutritional Supplementation Guideline	
Natural medicine	Possible dosage ^a
Aqueous liver extract	500 mg, 1–3 times per day
Copper	1–3 mg per day
Folic acid	800 mcg, 1–3 times per day
Betaine hydrochloric acid	520 mg with meals, as tolerated
Iron (succinate)	15–30 mg, 2 times per day
Pantothenic acid	500 mg, 3 times per day
Riboflavin	20–50 mg, 2 times per day
Thiamine	50 mg, 2 times per day
Vitamin C	500 mg, 2–3 times per day
Vitamin E (d-alpha-tocopherol)	400 IU, ^b 2 times per day
Zinc	15–30 mg, 1–2 times per day

^aIndividualized dosing according to a patient's weight, age, gastrointestinal assimilation must be considered to achieve optimal results; ^bIU, international units.

In one study, vitamin B₆ therapy proved to be helpful to patients with sickle-cell anemia at a level of 50 mg, 2 times per day, this treatment increased the subjects' hemoglobin and lessened their crises.²⁵ Clinically, administration of 100 mg per day of this vitamin has also proven to be helpful in cases of anemia that had not responded to iron administration alone.

Vitamin B₁₂

Supplementation with vitamin B₁₂, along with folic acid, is one of the best-known treatments for resolving megaloblastic anemia, as well as pernicious anemia, specifically. Vitamin B₁₂ is commonly used in conjunction with folic acid to offer more comprehensive and thorough treatment. Although folic acid can help to resolve megaloblastic anemia independently, folic acid cannot address potential underlying neurologic degener-

ative changes that require vitamin B₁₂ augmentation. Thus, folic acid is traditionally not given without cobalamin.

Vitamin C

Vitamin C plays several critical roles in the maintenance of proper hematopoiesis. This vitamin enhances the absorption of nonheme iron. It has also been observed, in at least one study, to increase hemoglobin and hematocrit levels when administered at 50–100 mg per day for 8 weeks. Upon completion of the trial, these indices returned to their starting baselines within 10 weeks.²⁶ Ascorbic acid may also play a role in protecting against the oxidation of tetrahydrofolate, allowing it to stay metabolically active and available. Interestingly, specific forms of anemia, such as heterozygous beta-thalassemia, have shown a mild lowering of platelet vitamin C level,

Up to 69 percent of patients with sickle-cell anemia were vitamin E deficient.

suggesting a yet poorly defined role of ascorbic acid in the maintenance of RBCs.²⁷

Vitamin E

Supplementation with vitamin E has been demonstrated to help patients with various types of anemias, ranging from Mediterranean-type glucose-6-phosphate dehydrogenase deficiency,²⁸ beta-thalassemia,²⁷ and sickle-cell anemia,¹⁷ to cystic fibrosis-associated anemia.

When patients with sickle-cell anemia were given between 450 and 800 international units of vitamin E per day for at least 6 months, there was an observed decrease in the percentage of irreversibly sickled cells. This is not surprising, because it had been shown in one study that up to 69 percent of patients with this disorder were vitamin E deficient. What is more, it is also well known that vitamin E is a potent stabilizer of cell membranes.

Zinc

Prior to administering zinc, obtaining an accurate measure of a patient's zinc level is crucial. When zinc is given at high dosage levels, such as 100 mg or more per day for a few months, a copper deficiency can arise. This deficiency, in turn, causes sideroblastic anemia accompanied by findings of hypocupremia, leukopenia, and neutropenia.²⁹

That being said, zinc has proven to be helpful in the treatment of anemia, with a particularly large amount of positive research having been done on sickle-cell anemia.

Zinc should be considered as a possible therapy in patients who are suffering from vitamin E deficiency, because approximately 10 percent of such patients will also be zinc deficient.¹⁷ Zinc deficiency has also been found in patients with homozygous sickle-cell anemia. In one study of 30 patients with sickle-cell anemia, their

serum zinc levels were low and their membrane stability was reduced. Zinc supplementation at a dosage of 200 mg of zinc sulfate, 3 times per day, for 4 months improved both the zinc status and membrane stability of the patients.³⁰

Other Considerations Contributing to Anemia

Other factors that may contribute to anemia in patients include ingestion of certain substances and physical problems.

Aluminum

RBC production has been observed to be lowered in patients with elevated serum aluminum levels. This is a relatively common finding among patients who experience chronic renal failure on hemodialysis.^{31,32} The effects of elevated aluminum levels, in the general population, especially elderly people, in the face of growing evidence of a link between aluminum and Alzheimer's disease, have yet to be examined fully. Thus, elevated serum levels of aluminum may be worth clinical consideration in cases of persistent or unresponsive unexplained anemia.

Gastritis

The association of atrophic gastritis, its resulting hypochlorhydria or achlorhydria, and pernicious anemia are well known. In a study conducted in Italy, 37.5 percent of patients with gastritis had macrocytic anemia and 19.5 percent had microcytic anemia. The patients with microcytic anemia were, on average, 20 years younger than those with macrocytic anemia. Not surprisingly, the majority of the patients with the microcytic form of anemia were premenopausal females. Of great clinical significance is that 61 percent of the patients that had microcytic anemia also had *Helicobacter pylori*. This study offers the suggestion that clinicians who must deal with

unexplained microcytic anemia might consider determining fasting gastrin levels and performing gastric mucosal biopsies.³³

Lead

Although we do not think of lead poisoning as being as prevalent as it was in the previous couple of decades, this problem still is a vital issue, especially among certain socioeconomically underserved populations. Yet, the potential for seeing a case of full-fledged lead poisoning in any population was well illustrated in a case of 24-year-old woman that worked as an administrative employee. This woman drank out of a Greek ceramic cup, which proved to be the source of her lead exposure. She presented with colicky abdominal pain, constipation, breathing-related chest pain, a cough, and blood streaked sputum. Laboratory tests showed microcytic anemia, mild leukocytosis, and anisocytosis. Upon treatment with 2,3-dimercapto-1-propanesulphonic acid, her symptoms disappeared.³⁴

Milk

It is now a generally accepted fact that overconsumption of milk by infants can lead to iron-deficiency anemia. This results from GI bleeding induced by the milk. It has been estimated that 50 percent of iron-deficiency anemia in infants results from milk-induced bleeding. An occult blood test can serve as one of many screening measures, in addition to a complete blood cell count when this is clinically indicated.³⁵ It is worth considering whether milk-induced bleeding is completely outgrown or if it may remain as an underlying predisposition. Clinically speaking, if an infant has a tendency towards otitis media, this may also be a good indication that avoidance of milk could be a worthwhile approach, because a sensitivity to milk and a tendency to milk reactivity may be present.

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Summary

When treating patients with anemia, the conventional nutritional treatments have been iron, vitamin B₁₂, and folic acid. However, as a review of the research literature shows, a patient's overall nutritional status may often play an equally critical role in correcting anemia. Because anemia is merely a symptom of a greater underlying imbalance present in the body, elimination of the laboratory signs of anemia and lessening of its symptoms is often not enough. Clinically, the root cause must be fully investigated and treated, which supports the use of a broad and comprehensive nutritional approach to correct the anemia and nourish the body. □

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Chris D. Meletis, N.D., serves as the dean of clinical affairs/chief medical officer, National College of Naturopathic Medicine, Portland, Oregon.

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