Tired Blood

Anemia, which afflicts millions, can have many different causes.

Anemia is a generic term for a range of blood disorders in which the blood is deficient in red blood cells (RBCs), hemoglobin, or total volume, and it ranges from acute and problematic to chronic and life-threatening. It is perhaps no surprise that rosy cheeks and the flush of good health are associated with wellness, while an ashen complexion is often one of the first signs of ill health. Paleness, of course, can have many causes, but a lack of RBCs, which transport oxygen-bearing hemoglobin in the body, is often the reason for a pasty face. There are many reasons why numbers of healthy RBCs might fall, but fewer RBCs means less vital oxygen reaching the tissues and organs, and a range of symptoms can then ensue.

According to the U.S. Centers for Disease Control and Prevention (CDC, www.cdc.gov), anemia affects approximately 3.4 million Americans of all ages and from all walks of life. Those over 65, people undergoing surgery, or those suffering from certain other diseases are at higher risk.

The early signs of anemia can often be confused with the symptoms of many other disorders, sometimes resulting in inappropriate treatment. Some signs of anemia are pale skin with a lack of “pinkness” in the lips, gums, eyelids, nails, and palms; extreme tiredness; weakness; shortness of breath; lack of concentration and confusion; dizziness; fainting; tachycardia (rapid heart rate); chills; and depression. This is not an exhaustive list of anemia’s effects. There are many other symptoms associated with specific forms of anemia.

B₁₂ and Iron Deficiency

So-called pernicious anemia is caused by a deficiency in vitamin B₁₂ and/or folic acid. These vitamins, along with iron, are essential ingredients in the manufacture of RBCs from bone marrow stem cells. B₁₂ is the precursor molecular ring system used to create the iron-bearing heme group in the hemoglobin molecule. B₁₂ deficiency causes a range of symptoms, including a reduced sense of taste, altered or reduced sense of touch, inability to feel vibrations (caused by neuronal damage), psychological symptoms, pain in the legs, muscle spasms, shortness of breath, palpitations, and angina.

It is all too easy to succumb to pernicious anemia through an inadequate diet. B₁₂, like iron, is obtained from red meat, dairy products, and fish. Vegans and vegetarians may need to consider supplements and alternative sources of the vitamin. Others may develop pernicious anemia because their intestines are unable to absorb enough of the necessary nutrients.

Iron deficiency anemia is frequent in women during pregnancy, after childbirth, and in cases of menorrhagia. Childhood and pubertal growth spurts can also lead to iron deficiency simply because supply does not meet the—literally—growing demands. Moreover, premature infants can suffer anemia because iron storage is not complete until the final stages of gestation.

Insufficient oxygen reaching the heart and other organs puts them under stress. To compensate for the lower oxygen content of the blood, the heart has to work harder to boost the supply of blood reaching the various tissues. Tachycardia and left ventricular hypertrophy are serious complications of long-term anemia.

An anemic condition is often the result of suffering from a different medical problem. A wide range of illnesses put people at increased risk of developing anemia. Chronic kidney disease, diabetes, cancer, heart disease, chronic inflammatory conditions such as rheumatoid arthritis, inflammatory bowel disease, gluten intolerance (which lowers iron absorption), Crohn’s disease, and HIV/AIDS can all result in anemia. The underlying problem is often simply that the disease interferes with hemoglobin formation. Anemia caused by chronic disease is the second most common form of the disorder. The most common form of anemia is simply blood loss.

Aplastic Anemia

Aplastic anemia is another insidious form of anemia. It is an idiopathic disorder, although it is also associated with myelodysplasia. Again, the common feature is a failure to manufacture RBCs. Aplasia, as it is also known, is rare, with just 5–10 cases per million per year in the developed world. Exposure to volatile aromatic solvents including toluene, pesticides like DDT and lindane, trinitrotoluene, wood preservatives such as pentachlorophenol, and distillates of petroleum are known causes of aplasia. Some drugs, especially those structurally related to benzene, such as chlo-
ramphenicol and phenylbutazone, are also known to cause aplasia. These two drugs are rarely used in industrialized nations but are inexpensive and still commonly prescribed in the developing world. Other pharmaceuticals associated with a moderate risk of aplastic anemia are arthritis drugs such as gold salts and penicillamine, epilepsy treatments such as carbamazepine and phenytoin, and the diuretic acetazolamide. These compounds are still used frequently in the developed world. Medical practitioners are advised to be alert to signs of aplasia in patients taking these medications.

Aplastic anemia is associated with bone marrow failure and is usually accompanied by failure to produce other blood components, such as white blood cells and platelets. The symptoms common to most anemias are seen—tiredness, weakness, and breathlessness—but a low white cell count (neutropenia) is also often observed, causing fever, sore throat, and shivering. A low platelet count (thrombocytopenia) will lead to bruising and bleeding, mouth ulcers, and hemorrhages in the eyes.

**Sickle-Cell Anemia**

Sickle-cell anemia is an inherited form of anemia. It is a chronic illness, and until recently was a significant cause of childhood deaths in some ethnic groups. It leads to periodic episodes of pain caused by defective hemoglobin, which forms numerous rodlike aggregates on releasing its oxygen. This causes the otherwise smooth and supple RBCs to become stiff and deform into the sickle shape characteristic of the disease. Unlike their lithe counterparts, sickled RBCs cause blockages in capillaries, starving organs of oxygen.

Sickled RBCs are also short-lived, lasting just 10–20 days, whereas a healthy RBC will function for 120 days. The sickled RBCs are not replaced quickly enough, so sufferers are chronically short of RBCs and hence are not replaced quickly enough, so sufferers are chronically short of RBCs and hence present the common symptoms of anemia. Although there is no unique pattern of symptoms, pain, tissue damage, and life-threatening conditions are common. One such disorder is “acute chest syndrome”, in which sickled RBCs are trapped in the lungs, which may lead to a type of pneumonia. Sickle-cell sufferers are also prone to swelling of the hands and feet, eye problems, jaundice, and delayed growth and puberty. They are frequently more susceptible to infection because of spleen damage caused by lack of blood supply to this organ.

Strokes are often seen in childhood because of blocked blood vessels in the brain.

Sickle-cell anemia is caused by an error in a gene. Parents who carry one copy of the faulty gene will not have symptoms, but statistically, if both parents carry a copy, then one in four of their children will carry two copies and present the disease. Evidence accumulated in the 1970s showed that carriers of the so-called genetic error are less prone to malaria than those without, hinting at a possible adaptive origin to the error. This is perhaps no consolation to the millions of sufferers in the African-American community, but it does present a dilemma to medical researchers who might seek to eradicate the error from the human genome to preclude the appearance of sickle-cell anemia.

There is no easy cure for the disorder, but there are therapies. Analgesics for pain and blood transfusions limit many of the symptoms, and regular antibiotics in childhood can stave off pneumococcal infections. Improved management of the disease has led to a reduction in the number of childhood strokes.

**Thalassemia**

Like sickle-cell anemia, the thalassemia group of disorders is a genetic anemia that seems to have originated as an adaptation against the malaria parasite. Carriers of the gene responsible for the disorder have a reduced risk of contracting malaria. However, those who carry two copies of the error are prone to the unpleasant and life-threatening symptoms of thalassemia. The disorder affects the alpha-hemoglobin chain genes or the beta-hemoglobin, but clinical descriptions of the disorder often clash with the subsequently revealed molecular and genetic basis of the various forms of the disease. This has led to a degree of confusion in the literature. Nevertheless, as with sickle-cell anemia, misshapen RBCs are present in the alpha form. In an effort to overcome the body’s deficit of healthy RBCs, the bone marrow production line is accelerated, leading to bone deformities. An enlarged spleen and associated energy loss are also seen in alpha-thalassemia.

Thalassemia affects populations of Mediterranean, Middle Eastern, and Asian Indian origin, and in its most insidious form—beta-thalassemia major—requires repeated and frequent blood transfusions to fend off death. Inevitably, iron overload is a complication of this therapy, and although chelating drugs are available, sufferers in the developing world lucky enough to receive transfusions often suffer the fatal consequences of iron overload because the drugs to prevent iron toxicity are not available to them.

It is possible to cure both sickle-cell anemia and thalassemia through bone-marrow transplant. In children with either disorder who have a fully matched sibling, a transplant before chronic organ damage occurs is the treatment of choice. Expense and human leukocyte antigen matching are the limiting factors.

**Management Is Key**

The treatment for anemia varies greatly depending on the origin of the problem. Changing one’s diet, taking nutritional supplements, or using medication are perhaps the most obvious. In anemia associated with chronic disease, treating the underlying disease is the primary approach. Disease management, however, is often the only possibility for those suffering from the debilitating effects of thalassemia and sickle-cell anemia.

**Further Reading**


Aplastic Anemia and MDS International Foundation; www.aplastic.org.

Sickle cell anemia; http://sickle.bwh.harvard.edu/menu_sickle.html.

Thalassemia Group of Disorders; http://sickle.bwh.harvard.edu/menu_thal.html.

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