THE ABC'S OF ANEMIA
by Sue Herms

The simplest definition of anemia is a condition that occurs when you don’t have enough healthy red blood cells (also called erythrocytes or red corpuscles). Anemia is not a disease in and of itself but is rather a sign of an underlying disease process.

Red blood cells (RBCs) are the transporters of oxygen and carbon dioxide to and from your lungs and your tissues. They are made in the bone marrow through a series of complicated steps requiring several nutrients and interaction with a hormone called erythropoietin produced by the kidneys, which monitor the oxygen level in the body. As RBCs mature, they are released into the bloodstream. The part of each RBC that binds to oxygen and carbon dioxide is the red-pigmented protein called hemoglobin. One of the interesting things about red blood cells is that mature cells no longer have a nucleus or many other typical cell structures and cannot reproduce themselves. Basically, they are not much more than a container for hemoglobin. They last for about 120 days in the circulation and constantly need to be replaced because of the wear and tear they go through while traveling throughout the body.

The general symptoms of anemia may range from very mild to severe. Commonly, affected people complain of weakness or fatigue, dizziness, cold hands and feet, headache, poor mental concentration, and shortness of breath. Pale skin, lips, gums, and nail beds can indicate more severe anemia. Very severe anemia can lead to palpitations, sweatiness, and heart failure. Some types of anemia also have their own fairly specific symptoms, which can be helpful in the diagnosis.

The starting point for the diagnosis of anemia is usually the Complete Blood Count (CBC), and the tests that the physician examines are red blood cell count, hemoglobin, and hematocrit. Normal ranges for these values vary somewhat by age and gender: normal RBC count is approximately 4-6 million cells per cubic millimeter, normal hemoglobin is generally 12-18 grams per deciliter, and normal hematocrit is usually 35-45%. Instruments also measure the size of the RBCs (the mean corpuscular volume or MCV), which can be an important tool in distinguishing among the causes of anemia, since some anemias will cause RBCs to be either smaller or larger than normal. An experienced medical technologist or pathologist can look at red blood cells under a microscope and see clues that point to a particular cause – in addition to size variations, certain kinds of anemia will result in changes to the shape or intensity of color of the RBCs. Another measurement that can be helpful is the reticulocyte count. Reticulocytes are immature RBCs that are released into the bloodstream; a certain amount is normal in order to maintain a steady RBC turnover, but large numbers of reticulocytes may indicate that the bone marrow is attempting to replace excessive losses of RBCs.

Additional tests are usually required to establish a firm reason for the anemia. It is important for patients to have these additional workups rather than assume the cause of the problem. Occasionally, there may be more than one reason for anemia; for instance, a poor diet can cause one to be anemic due to several dietary deficiencies. Also, one should not take dietary supplements without establishing that they are necessary or beneficial since overdosing of some supplements can create problems.

Because of the complex process involved in the development and maintenance of the proper amount of RBCs in our bodies, a problem in any part of this process can lead to anemia. Believe it or not, there are more than 400 different anemias. A description of every anemia is beyond the scope of this article, but this discussion will include some of the most common ones and/or the ones most closely associated with diseases such as
Anemia can be classified into four broad categories: anemia due to excessive blood loss, inefficient or faulty hemoglobin or red blood cell production, anemia of chronic disease, and anemia due to excessive destruction of red blood cells.

**Anemia Due to Excessive Blood Loss**

Anemia through excessive blood loss can occur in many different ways. Obviously, an acute hemorrhage can cause anemia, but chronic blood loss is an often-overlooked reason because it can be difficult to detect. Chronic blood loss can occur because of bleeding ulcers, hemorrhoids, colon cancer, parasitic infestation, menstruation, pregnancy, or the use of nonsteroidal anti-inflammatory drugs (NSAIDS), just to name a few of the most common examples. A physician who suspects anemia from chronic bleeding might test for occult blood or parasites in the stool or perform endoscopy, colonoscopy, X-rays, CT scans, etc., to look for the sources of the bleeding.

**Anemia Due to Inefficient or Faulty Hemoglobin or Red Blood Cell Production**

Inefficient or faulty red blood cell production can be due to many different factors. The most common cause, and the one that we are probably most familiar with, is iron deficiency. Iron is a key component of hemoglobin, so if you don’t consume enough in your diet, you will be anemic. After absorption into the bloodstream, the iron is transported by a carrier protein called transferrin to the bone marrow where it is incorporated into the red blood cells. Excess iron is stored as ferritin and hemosiderin in the liver, spleen, and other places. Therefore, if your doctor suspects that you have an iron deficiency, he will do tests to measure the amount of iron in your system, both circulating and stored, by tests called serum ferritin, serum iron, serum transferrin, and total iron binding capacity. Obviously, the treatment for iron deficiency anemia is to increase your iron intake.

There are other nutrients that can affect red blood cell production, and these include primarily Vitamin B12 and folate. Megaloblastic anemia is caused by a deficiency of B12, folate, or both. A subtype of megaloblastic anemia, called pernicious anemia, occurs primarily from the lack of intrinsic factor, which is produced in the stomach and is required for absorption of B12 from food. Patients with pernicious anemia may have additional symptoms of peripheral neuropathy, balance problems, and a very red, smooth, swollen tongue. Levels of B12, folate, and intrinsic factor can be tested. If diet is the problem, then one needs to increase the intake of the particular nutrient involved; if it is an absorption problem, then regular injections of B12 may be necessary.

Sideroblastic anemia is a disorder in which the body has adequate iron but is unable to incorporate it into the hemoglobin. The iron accumulates in the RBCs and gives the inside of the immature cells a characteristic appearance, which can be viewed by special staining under a microscope. These immature RBCs develop poorly and anemia is the consequence. Sideroblastic anemia may be inherited or may be acquired due to nutritional imbalances or prolonged exposures to toxins such as alcohol, lead, or drugs. Iron overload accompanies sideroblastic anemia because iron accumulates in the tissues rather than being used in the synthesis of hemoglobin. Repeated blood transfusions to relieve the resulting anemia will contribute significantly to the iron burden and may require chelation therapy to reduce the iron.

There are several genetic conditions affecting the formation of the red cell or of the hemoglobin protein. Probably the one most familiar to us is sickle cell anemia. In this case, a genetic defect in the hemoglobin causes the red blood cells to assume a crescent or sickle shape instead of the normal round shape. These red blood cells break down rapidly, so that sufficient oxygen does not get to the body’s tissues, and the red blood cells can get stuck in the tiny blood vessels, causing pain and tissue damage. Thalassemia, another genetic defect, occurs when the protein chains that make up hemoglobin are produced at a decreased rate. Hemoglobin
electrophoresis is a useful test for diagnosing these hereditary hemoglobin disorders. Other acquired or genetic defects in the RBC membrane can cause changes in the shape or size of the cell that lead to a shorter span of life in the circulation. Some diseases, called porphyrias, result from problems in the various enzyme pathways involved in production of the hemoglobin protein.

Aplastic anemia occurs when there is a marked reduction or absence of the stem cells that produce the blood-forming cells. This can be an inherited condition or can be acquired as a result of exposure to radiation, toxins (such as lead), certain medications, chemotherapies, or infections. Bone marrow biopsies are useful in diagnosing aplastic anemia, and therapy might include bone marrow transplantation.

**Anemia of Chronic Disease**

Many long-term medical conditions can cause anemia. One that we are all aware of is cancer, particularly the blood cancers such as leukemia or lymphoma. Anemia can be one of the earliest indicators of blood cancer and frequently initiates the process leading to the cancer diagnosis. In this situation, the tumor cells increase and crowd the normal blood-forming cells in the marrow so that they cannot adequately supply the body’s need for RBCs. Some cancers may produce chemokines, or substances that may interfere with the normal mechanisms for blood cell formation. Chronic kidney disease can lead to anemia because the kidneys cannot produce enough erythropoietin to stimulate adequate red blood cell production. In these cases, transfusions or administration of erythropoietin agents such as Procrit or Aranesp may help with red blood cell production. Obviously, improvement of the underlying conditions with appropriate treatments can improve production as well.

**Anemia Due to Excessive Destruction of Red Blood Cells**

When red blood cells break down normally, most are removed by macrophages, particularly macrophages in the spleen. The iron in the hemoglobin protein is recycled to the bone marrow, the amino acids are returned to the liver, and another portion of the original hemoglobin protein is converted to bilirubin and transported to the liver, where it is further broken down and small amounts are excreted in the stool and the urine. Excessive destruction of red blood cells in the spleen, sometimes resulting from an enlarged spleen, will result in more bilirubin, possibly causing jaundice (yellowing) of the skin and eyes. Occasionally, removal of the spleen (splenectomy) may help to alleviate this problem.

When red blood cells are fragile and cannot withstand the stress of the circulatory system, they may rupture prematurely, causing hemolytic anemia. Some conditions causing hemolytic anemia are inherited. Others can be acquired as a result of certain infections, medications, or autoimmune diseases. In rare cases of WM, the cancerous B-cells produce an IgM protein which initiates an antibody attack on the body’s own red blood cells at cold temperatures, causing them to break down. This condition is called cold agglutinin disease or cold hemolytic anemia. If this occurs in the bloodstream, large amounts of hemoglobin are released into the blood rather than going through the destruction process in the spleen and liver. Some of this hemoglobin may be recycled, but it may also overwhelm the body’s usual mechanisms and be excreted by the kidneys, resulting in pink or red urine (hemoglobinuria). Hemolytic anemias can be treated with steroids, immunosuppressant drugs, or gamma globulin to help suppress the immune system’s attack on the red blood cells.

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