CLINICAL FOCUS

Disorders of the Blood

ERYTHROCYTOSIS

Erythrocytosis (ĕ-rith′rō-sī-tō′sis) is an overabundance of red blood cells, resulting in increased blood viscosity, reduced flow rates, and, if severe, plugging of the capillaries. **Relative erythrocytosis** results from decreased plasma volume, such as that caused by dehydration, diuretics, and burns. **Primary erythrocytosis,** often called **polycythemia vera** (pol′ē-sī-thē′mē-ă ve′ra), is a stem cell defect of unknown cause that results in the overproduction of red blood cells, granulocytes, and platelets. Erythropoietin levels are low and the spleen can be enlarged. **Secondary erythrocytosis (polycythemia)** results from a decreased oxygen supply, such as that which occurs at high altitudes, in chronic obstructive pulmonary disease, and in congestive heart failure. The resulting decrease in oxygen delivery to the kidneys stimulates erythropoietin secretion and causes an increase in red blood cell production. In primary and secondary erythrocytosis, the increased number of red blood cells increases blood viscosity and blood volume. There can be clogging of capillaries and the development of hypertension.

ANEMIA

Anemia (ă-nē′mē-ă) is a deficiency of hemoglobin in the blood. It can result from a decrease in the number of red blood cells, a decrease in the amount of hemoglobin in each red blood cell, or both. The decreased hemoglobin reduces the blood's ability to transport oxygen. Anemic patients suffer from a lack of energy and feel excessively tired and listless. They can appear pale and quickly become short of breath with only slight exertion.

One general cause of anemia is nutritional deficiency. **Iron-deficiency anemia** results from a deficient intake or absorption of iron or from excessive iron loss. Consequently, not enough hemoglobin is produced, and the red blood cells are smaller than normal (microcytic). **Folate deficiency** can also cause anemia. An inadequate amount of folate in the diet is the usual cause of folate deficiency, with the disorder developing most often in the poor, in pregnant women, and in chronic alcoholics. Because folate helps in the synthesis of DNA, folate deficiency results in fewer cell divisions. There is decreased red blood cell production, but the cells grow larger than normal (macrocytic). Another type of nutritional anemia is **pernicious** (per-nish′ŭs) **anemia,** which is caused by inadequate amounts of vitamin B_{12}. A 2- to 3-year supply of vitamin B_{12} can be stored in the liver. Because vitamin B_{12} is important for folate synthesis, inadequate amounts of vitamin B_{12} causes a secondary folate deficiency. Thus, a deficiency of vitamin B_{12} also causes the decreased production of red blood cells that are larger than normal. Although inadequate levels of vitamin B_{12} in the diet can cause pernicious anemia, the usual cause is insufficient absorption of the vitamin. Normally, the stomach produces intrinsic factor, a protein that binds to vitamin B_{12}. The combined molecules pass into the small intestine, where intrinsic factor facilitates the absorption of the vitamin. Without adequate levels of intrinsic factor, insufficient vitamin B_{12} is absorbed, and pernicious anemia develops. Present evidence suggests that the inability to produce intrinsic factor is due to an autoimmune disease in which the body's immune system damages the cells in the stomach that produce intrinsic factor.

Another general cause of anemia is the loss or destruction of red blood cells. **Hemorrhagic** (hem-ŏ-raj′ik) **anemia** results from a loss of blood, such as can result from trauma, ulcers, or excessive menstrual bleeding. Chronic blood loss, in which small amounts of blood are lost over time, can result in iron-deficiency anemia. **Hemolytic** (hē-mŏ-lit′ik) **anemia** is a disorder in which red blood cells rupture or are destroyed at an excessive rate. It can be caused by inherited defects. For example, hereditary spherocytosis (sfēr′ŏ-sī-tō′sis) results from a mutation of a gene on chromosome 14 that codes for a cytoskeleton protein called spectrin (spek′-trin). Spectrin normally stabilizes the plasma membrane, but when defective, red blood cells assume a spherical shape and rupture easily. Many kinds of hemolytic anemia result from unusual damage to the red blood cells by drugs, snake venom, artificial heart valves, autoimmune disease, or hemolytic disease of the newborn.

Aplastic anemia is caused by an inability of the red bone marrow to produce red blood cells and often white blood cells and platelets. It is usually acquired as a result of damage to stem cells in the red marrow by chemicals (e.g., benzene), drugs (e.g., certain antibiotics and sedatives), or radiation. Aplastic anemia is usually associated with an inability to produce granulocytes and platelets.

Some anemias result from inadequate or defective hemoglobin production. **Thalassemia** (thal-ă-sē′mē-ă) is an autosomal-recessive hereditary disease found predominantly in people of Mediterranean, Asian, and African ancestry. It is caused by insufficient production of the alpha or beta globin in hemoglobin (see figure 19.4). The gene for alpha globin is on chromosome 16 and the gene for beta globin is on chromosome 11. Depending on the mutation of these genes, the effects of thalassemia can vary from minor changes to hemoglobin to severe or fatal anemia.

VON WILLEBRAND DISEASE

Von Willebrand disease is an autosomal-dominant hereditary disorder caused by a mutation of the von Willebrand factor gene on chromosome 12. It is the most common inherited bleeding disorder, occurring as frequently as in 1 in 1000 individuals. Von Willebrand factor (vWF) helps platelets stick to collagen (platelet adhesion) and is the plasma carrier for factor VIII (see "Coagulation," p. 664 and table 19.3). One treatment for von Willebrand disease involves injections of vWF or concentrates of factor VIII to which vWF is attached. Another therapeutic approach is to administer a drug that increases vWF levels in the blood.

HEMOPHILIA

Hemophilia (hē-mŏ-fil′ē-ă) is a genetic disorder in which clotting is abnormal or absent. It is most often found in people from northern Europe and their descendants. Because hemophilia is most often an X-linked trait (see chapter 3), it occurs almost exclusively

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in males. **Hemophilia A** (classic hemophilia) results from a deficiency of plasma coagulation factor VIII, and **hemophilia B** is caused by a deficiency of plasma factor IX. Hemophilia A occurs in approximately 1 in 10,000 male births, and hemophilia B occurs in approximately 1 in 100,000 male births. Treatment of hemophilia involves injection of the missing clotting factor.

DISSEMINATED INTRAVASCULAR COAGULATION

Disseminated intravascular coagulation (DIC) is a complex disorder involving clotting throughout the vascular system followed by bleeding. Normally, excessive clotting is prevented by anticoagulants. DIC can develop when these control mechanisms are overwhelmed. Many conditions can cause DIC by overstimulating blood clotting. Examples include massive tissue damage, such as burns, and the alteration of the lining of blood vessels caused by infections or snake bites. If DIC occurs slowly, the predominant effect is thrombosis and the blockage of blood vessels. If DIC occurs rapidly, massive clot formation occurs, quickly using up available blood clotting factors and platelets. The result is continual bleeding around wounds, intravenous lines, and catheters, as well as internal bleeding. The best therapy for DIC is to treat the condition that is causing it.

THROMBOCYTOPENIA

Thrombocytopenia (throm′bō-sī-tō-pē′nē-ă) is a condition in which the number of platelets is greatly reduced, resulting in chronic bleeding through small vessels and capillaries. Thrombocytopenia has several causes, including increased platelet destruction, caused by autoimmune disease (see chapter 22) or infections, and decreased platelet production, resulting from pernicious anemia, drug therapy, radiation therapy, or leukemias. Hereditary thrombocytopenia can be X-linked or autosomal-dominant (chromosome 10).

LEUKEMIA

The **leukemias** are cancers of the red bone marrow in which abnormal production of one or more of the white blood cell types occur. Because these cells are usually immature or abnormal and lack their normal immunologic functions, patients are very susceptible to infections. The excess production of white blood cells in the red marrow can also interfere with red blood cell and platelet formation and thus lead to anemia and bleeding.

INFECTIOUS DISEASES OF THE BLOOD

Microorganisms do not normally survive in the blood. Blood can transport microorganisms, however, and they can multiply in the blood. Microorganisms can enter the body and be transported by the blood to the tissues they infect. For example, the poliomyelitis virus enters through the gastrointestinal tract and is carried to nervous tissue. After microorganisms are established at a site of infection, some can enter the blood. They can then be transported to other locations in the body, multiply within the blood, or be eliminated by the body's immune system.

Septicemia (sep-ti-sē′mē-ă), or blood poisoning, is the spread of microorganisms and their toxins by the blood. Often, septicemia results from the introduction of microorganisms by a medical procedure, such as the insertion of an intravenous tube into a blood vessel. The release of toxins by microorganisms can cause septic shock, which is a decrease in blood pressure that can result in death.

In a few diseases, microorganisms actually multiply within blood cells. **Malaria** (mă-lar′ē-ă) is caused by a protozoan (*Plasmodium*) that is introduced into the blood by the bite of the *Anopheles* mosquito. Part of the development of the protozoan occurs inside red blood cells. The symptoms of chills and fever in malaria are produced by toxins released when the protozoan causes the red blood cells to rupture. **Infectious mononucleosis** (mon′ō-noo-klē-ō′sis) is caused by a virus (Epstein-Barr virus) that infects lymphocytes (B cells). The virus alters the lymphocytes, and the immune system attacks and destroys the lymphocytes. The immune system response is believed to produce the symptoms of fever, sore throat, and swollen lymph nodes. **Acquired immunodeficiency syndrome (AIDS)** is caused by the human immunodeficiency virus (HIV), which infects lymphocytes and suppresses the immune system (see chapter 22).

The presence of microorganisms in the blood is a concern with blood transfusions, because it is possible to infect the blood recipient. Blood is routinely tested, especially for AIDS and hepatitis, in an effort to eliminate this risk. One cause of **hepatitis** (hep-ă-tī′tis) is an infection of the liver caused by viruses (see chapter 24). After recovering, hepatitis victims can become virus carriers. Although they show no signs of the disease, they release the virus into their blood or bile. To prevent the infection of others, anyone who has had hepatitis is asked not to donate blood products.