The Coombs test, established as a clinical tool in 1945 by R.R. Coombs, usually is ordered when hemolytic anemia is suspected or if a transfusion reaction has occurred. An overview of the etiologies of these two conditions will increase oncology nurses’ understanding of what is measured with a Coombs test and increase the understandings of why a Coombs test is ordered, what diagnosis is suspected, and what patient populations are at highest risk for transfusion reactions.

Hemolytic anemia is characterized by lysis of patients’ red blood cells (see Figure 1). Hereditary hemolytic anemias involve cell membrane defects related to abnormalities in the production of certain proteins or enzymes, such as in the case of patients with hereditary spherocytosis or lupus. Acquired hemolytic anemias are disorders that occur when antibodies either develop or are introduced by transfusion against patients’ red blood cells. These antibodies attach to the red blood cells and cause hemolysis, an abnormality that is detected with a Coombs test. The cause of the formation of these antibodies often is unidentifiable. If this is the case, the hemolytic anemia is termed idiopathic. Several other laboratory tests are included in the diagnostic workup of hemolytic anemia in addition to the Coombs test (see Table 1).

Antibodies occasionally are formed in reactions to drugs such as penicillin, methyldopa, or fludarabine (Hoffbrand, Pettit, & Moss, 2001). In these cases, the drug is interacting with red blood cell membranes either directly or with the involvement of a complement or a drug-protein-antibody complex. Withdrawal of the causative agent leads to resolution of the hemolytic anemia. In other occasions, antibodies are formed in response to an autoimmune disease, such as lupus, or in the presence of advanced cancer, such as lymphoma.

Even more rarely, primary red cell aplasia may occur with lymphoma. Although not specific to hemolysis, anemia of chronic disease is common in malignant conditions with an apparent pathogenesis related to decreased release of iron from macrophages. This results in a decrease in erythroblasts, reduced red blood cell lifespan, and inadequate responses to erythropoietin. Other contributing factors to anemia for patients with cancer are well known, including marrow infiltration by disease, cancer treatment modalities that suppress marrow function, inadequate nutrient intake (particularly iron and vitamin C necessary for red blood cell formation). All of these may lead to the patient eventually requiring a red blood cell transfusion.

The Coombs test is helpful in detecting the antibodies that are coating the transfused red blood cells and, therefore, helpful in confirming suspected transfusion reactions. The Coombs test does not have a range; it is read as either positive if antibodies are found or negative if no antibodies are detected. If no agglutination is detected, the test is read as negative (Pagana & Pagana, 2006).

### Direct Coombs Test

Two types of Coombs tests are available, direct and indirect. The direct Coombs test demonstrates whether the patient’s red blood cells have been attacked by antibodies in the blood. To perform this test, a solution called Coombs serum is mixed with the patient’s red blood cells. Coombs serum is a solution that contains antibodies to human globulin. If the red blood cells have antibodies on them, then agglutination or clumping occurs; the greater the number of antibodies, the more agglutination. Levels are read on a scale from trace (very little antibodies) to +4 (the highest level of antibodies). If agglutination does not occur, the test is read as negative.