mg/week × 4), together with prednisone as part of first-line treatment. It is especially encouraging that this approach seems to reduce the rate of relapse, a common occurrence in AIHA.

For patients who do relapse or are refractory to medical treatment, additional therapeutic strategies are now available. Splenectomy does not cure the disease, but it can produce significant benefit by removing a major site of hemolysis, thus improving the anemia and/or reducing the need for other therapies (e.g., the dose of prednisone); of course, splenectomy is not free of risk, as it entails increased risk of sepsis and of thrombosis. The response rate to splenectomy and to rituximab are similar. Since the introduction of rituximab, azathioprine, cyclophosphamide, cyclosporine, mycophenolate and intravenous immunoglobulin have become second- or third-line agents. In very rare severe refractory cases, one may have to consider a high dose of cyclophosphamide (50 mg/kg/d for 4 days) followed by a myelo-stimulating agent to support bone marrow or the anti-CD52 agent, alemtuzumab. When severe anemia is associated with reticulocytopenia, the use of erythropoietin may help to reduce or avoid the requirement for transfusion of red cells.

PAROXYSMAL COLD HEMOGLOBINURIA (PCH) PCH is a rare form of AIHA occurring mostly in children, usually triggered by a viral infection, usually self-limited, and characterized by the so-called Donath-Landsteiner antibody. In vitro, this antibody has unique serologic features; it has usually anti-P specificity and it binds to red cells only at a low temperature (optimally at 4°C), but when the temperature is shifted to 37°C, lysis of red cells takes place in the presence of complement. Consequently, in vivo there is intravascular hemolysis, resulting in hemoglobinuria. Clinically the differential diagnosis must include other causes of hemoglobinuria (Table 100-6), but the presence of the Donath-Landsteiner antibody will prove PCH. Active supportive treatment, including blood transfusion, may be needed to control the anemia; subsequently, recovery is the rule.

COLD AGGLUTININ DISEASE This designation indicates the other main type of AIHA, which has quite different features when compared with