Therapeutic Management

The objectives of treatment are based on the recognition that the underlying disease process is failure of the bone marrow to carry out its hematopoietic functions. Therefore, therapy is directed at restoring function to the marrow and involves two main approaches: (1) immunosuppressive therapy (IST) to remove the presumed immunologic functions that prolong aplasia or (2) replacement of the bone marrow through transplantation. Bone marrow transplantation is the treatment of choice for severe AA when a suitable donor exists (see later in chapter).

Antilymphocyte globulin (ALG) or **antithymocyte globulin (ATG)** is the principal drug treatment used for AA. The rationale for using ATG is based on the theory that AA may be a result of autoimmunity. IST is a combination of ATG and cyclosporine that suppress T cell–dependent autoimmune responses by recognizing human lymphocyte cell surface antigen and decreasing the lymphocytes without causing bone marrow suppression (Peinemann and Labeit, 2014). Cyclosporine is administered orally for several weeks to months. ATG usually is administrated intravenously over 12 to 16 hours for 4 days after a test dose to check for hypersensitivity. Response to IST is typically delayed and responses generally do not start before 3 to 4 months (Samarasinghe and Webb, 2012). An IST course may be repeated, depending on the reduction in circulating lymphocytes and the patient's response. Because of the hypersensitivity response associated with ATG (i.e., fever, chills, myalgias), methylprednisolone is given intravenously to prevent these side effects. Growth factors, given parenterally, may be used to prevent neutropenic infection and enhance bone marrow production (Passweg and Marsh, 2010). Androgens may be used with ATG to stimulate erythropoiesis if the AA is unresponsive to initial therapies.

HSCT should be considered early in the course of the disease if a compatible donor can be found. Transplantation is more successful when performed before multiple transfusions have sensitized the child to leukocyte and **human leukocyte antigens (HLAs)**. HSCT is associated with an approximately 90% survival rate in patients who receive a bone marrow transplant from an HLA-identical sibling (Hord, 2011; Scheinberg, 2012).