Drugs at a Glance: Immunosuppressants (*continued*)

Generic/Trade Name	Indications for Use	Contraindications	Routes and Dosage Ranges
Muromonab-CD3 (Orthoclone OKT3)	Treatment of renal cardiac and hepatic transplant rejection	Allergy to muromonab-CD3 Signs of fluid overload (eg, heart failure, weight gain during week before starting drug therapy) Cautious use during pregnancy	IV 5 mg bolus injection once daily for 10–14 d
Mycophenolate mefetil (CellCept)	Prevent renal cardiac and hepatic transplant rejection	Hypersensitivity to the drug or any component of the product	*Renal transplantation:* PO, IV 1 g twice daily *Cardiac and hepatic transplantation:* PO, IV 1.5 g twice daily
Sirolimus (Rapamune)	Prevent renal transplant rejection	Hypersensitivity to any component of the drug formulation	*Adults:* PO 6 mg as soon after transplantation as possible, then 2 mg daily *Children >13 y:* PO 3 mg/m^2 as loading dose, then 1 mg/m^2 daily.
Tacrolimus (Prograf)	Prevent liver, kidney, and heart transplant rejection	Hypersensitivity to the drug or the castor oil used in the IV formulation	*Adults:* IV infusion, 25–50 mcg/kg/d, starting no sooner than 6 h after transplantation, until the patient can tolerate oral administration, usually 2–3 d PO 150–200 mcg/kg/d, in two divided doses q12h, with the first dose 8–12 h after stopping the IV infusion *Children:* IV 50–100 mcg/kg/d PO 200–300 mcg/kg/d

of B lymphocytes to produce autoantibodies that produce inflammation and tissue damage.

In addition to the factors that activate an immune response, there are also factors that prevent the immune system from "turning off" the abnormal immune or inflammatory process. One of these factors may be a deficient number of suppressor T cells. At present, it is unclear whether suppressor T cells are a separate group or a subpopulation of helper or cytotoxic T cells with suppressive functions.

TISSUE AND ORGAN TRANSPLANTATION

Tissue and organ transplantation usually involves replacing diseased host tissue with healthy donor tissue. The goal of such treatment is to save or enhance the quality of the host's life. Skin and renal grafts are commonly and successfully performed; heart, liver, lung, pancreas, and bone marrow transplantations are increasing. Although numerous factors affect graft survival, including the degree of matching between donor tissues and recipient tissues, drug-induced immunosuppression is a major part of transplantation technology. The goal is to provide adequate, but not excessive, immunosuppression. If immunosuppression is inadequate, graft rejection reactions occur with solid organ transplantation, and graft-versus-host disease (GVHD) occurs with bone marrow transplantation. If immunosuppression is excessive, the client develops serious infections and other adverse effects because the drug actions that slow the proliferation of activated lymphocytes also affect any rapidly dividing nonimmune cells (eg, epithelial cells of the gastrointestinal [GI] tract and hematopoietic stem cells of the bone marrow). Serious complications can occur.

Rejection Reactions With Solid Organ Transplantation and Host-Versus-Graft Disease

A rejection reaction occurs when the host's immune system is stimulated to destroy the transplanted organ. The immune cells of the transplant recipient attach to the donor cells of the transplanted organ and react against the antigens of the donor organ. The rejection process involves T and B lymphocytes, antibodies, multiple cytokines, and inflammatory mediators. In general, T cell activation and proliferation are more important in the rejection reaction than B cell activation and formation of antibodies. Cytotoxic and helper T cells are activated; activated helper T cells stimulate B cells to produce antibodies and lead to a delayed hypersensitivity reaction. The initial target of the recipient antibodies is the blood vessels of the transplanted organ. The antibodies can injure the transplanted organ by activating complement, producing antigen–antibody complexes, or causing antibody-mediated tissue breakdown. This reaction can destroy the solid organ graft within 2 weeks,