decision to pursue retransplantation in an individual patient difficult and ethically complex.

Malignancy An increased incidence of malignancy is a well-recognized sequela of any program of chronic immunosuppression, and organ transplantation is no exception. Lymphoproliferative disorders are among the most frequent posttransplantation complications and, in most cases, seem to be driven by Epstein-Barr virus. Effective therapy includes reduction of immunosuppression (a clear "double-edged sword" in the setting of a life-sustaining organ), administration of antiviral agents, and traditional chemo- and radiotherapy. Most recently, specific antilymphocyte (CD20) therapy has shown great promise. Cutaneous malignancies (both basal cell and squamous cell carcinomas) also occur with increased frequency among transplant recipients and can follow aggressive courses. The role of decreasing immunosuppression in the treatment of these cancers is far less clear.

Infections The use of currently available nonspecific immunosuppressive modalities to prevent allograft rejection naturally results in increased susceptibility to infectious complications in transplant recipients. Although the incidence has decreased since the introduction of cyclosporine, infections with unusual and opportunistic organisms are still the major cause of death during the first postoperative year and remain a threat to the chronically immunosuppressed patient throughout life. Effective therapy depends on careful surveillance for early signs and symptoms of opportunistic infection, an extremely aggressive approach to obtaining a specific diagnosis, and expertise in recognizing the more common clinical presentations of infections caused by CMV, *Aspergillus*, and other opportunistic agents.

PROLONGED ASSISTED CIRCULATION

The modern era of mechanical circulatory support can be traced back to 1953, when cardiopulmonary bypass was first used in a clinical setting and ushered in the possibility of brief periods of circulatory support to permit open-heart surgery. Subsequently, a variety of extracorporeal pumps to provide circulatory support for brief periods have been developed. The use of a mechanical device to support the circulation for more than a few hours initially progressed slowly, with the implantation of a total artificial heart in 1969 in Texas by Cooley. This patient survived for 60 h until a donor organ became available, at which point he underwent transplantation. Unfortunately, the patient died of pulmonary complications after transplantation. The entire field of mechanical replacement of the heart then took a decade-long hiatus until the 1980s, when total artificial hearts were reintroduced with much publicity; however, they failed to produce the hoped-for treatment of end-stage heart disease. Starting in the 1970s, in parallel with the development of the total artificial heart, intense research had addressed the development of ventricular assist devices, which provide mechanical assistance for (rather than replacing) the failing ventricle.

Although conceived of initially as alternatives to biologic replacement of the heart, LVADs were introduced—and are still employed primarily—as temporary "bridges" to heart transplantation in candidates in whom medical therapy begins to fail before a donor heart becomes available. Several devices are approved by the U.S. Food and Drug Administration (FDA) and are in widespread use (see later). Those that are implantable within the body are compatible with hospital discharge and offer the patient a chance for life at home during a wait for a donor heart. However successful such "bridging" is for the individual patient, it does nothing to alleviate the scarcity of donor hearts; the ultimate goal in the field remains that of providing a reasonable alternative to biologic replacement of the heart—one that is widely and easily available and cost-effective.

CURRENT INDICATIONS AND APPLICATIONS OF VENTRICULAR ASSIST DEVICES

Currently, there are two major indications for ventricular assistance. First, patients at risk of imminent death from cardiogenic shock are eligible for mechanical support. These patients are generally managed with temporary cardiac assist devices. Second, if patients have a left ventricular ejection fraction <25% or a peak VO_2 <14 mL/kg per min or are dependent on inotropic therapy or support with intra-aortic balloon counterpulsation, they may be eligible for mechanical support. If they are eligible for heart transplantation, the mechanical circulatory assistance is termed the "bridge to transplantation." By contrast, if the patient has a contraindication to heart transplantation, the use of the device is deemed to constitute "destination" left ventricular assistance therapy.

BASIC CONCEPTS

Pulsatile vs. Nonpulsatile Devices *Pulsatile* devices are ventricular assist devices whose mechanism of action mandates the alternating filling and emptying of a volume chamber within the device that mimics the mechanism of action of the natural heart. *Nonpulsatile* devices have a mechanism of action that results in continuous blood flow through the device, eliminating the need for pulsatility. The pulsatile devices are larger, bulkier, and associated with greater energy requirements and higher rates of complications than the nonpulsatile devices. However, pulsatile devices provide greater degrees of support and may even be capable of replacing the function of the heart entirely in the form of a total artificial heart. Because of the bulkiness of these devices, many patients are too small to be supported with intracorporeal pulsatile pumps. However, paracorporeal versions are available. These devices are versatile and can be used for right, left, or biventricular assistance/replacement.

Continuous-flow (nonpulsatile) devices are further categorized on the basis of impeller design and mechanism. The older designs have tended to be axial-flow pumps, which operate on the Archimedes screw principle. These devices have an impeller that is in line with the direction of blood flow, and the inlet direction of blood is the same as the outlet direction. Continuous-flow devices have been dependent on the presence of blood-washed bearings within the pump housing and may be associated with an increased risk of blood and platelet activation. The newer devices are centrifugal in design; the blood flow takes a 90° turn between the inlet section of the pump and the outlet section. Another major difference in the newer devices is the absence of blood-washed bearings (with most devices having magnetically levitated impellers). This design allows the construction of smaller pumps with less blood-element activation than the axial-flow designs.

Available Devices In the United States, there are currently four FDA-approved devices that are used as bridges to transplantation in adults. Of these four devices, one is also approved for use as destination therapy or as long-term mechanical support of the heart. A number of other devices are approved only for short-term support in post–cardiac surgery shock or in cardiogenic shock secondary to acute myocardial infarction or fulminant myocarditis; these will not be considered here. So far, no long-term device is totally implantable, and, because of the need for transcutaneous connections, all share a common problem with infectious complications. Likewise, all share some tendency to thromboembolic complications and are subject to the possibility of mechanical failure common to any machine.

The total artificial heart (TAH) (Syncardia, Tucson, AZ) is a pneumatic, biventricular, orthotopically implanted ventricular assist device with an externalized driveline connecting it to its console. The TAH is currently the only FDA-approved device for use in patients who have severe biventricular failure.

The Thoratec LVAD (Thoratec Corp., Pleasanton, CA) is an extracorporeal pump that takes blood from a large cannula placed in the left ventricular apex and propels it forward through an outflow cannula inserted into the ascending aorta. The extracorporeal nature of this pump allows its use in small adults for whom intracorporeal pumps would be too large. This device provides not only left but also right ventricular assistance and can be utilized for biventricular support within the same patient (BiVentricular Assist Device).

The HeartMate II LVAD (Thoratec) similarly uses a drainage cannula in the left ventricular apex to drain blood into a small chamber, where the blood is driven by an electrically powered motor that spins a rotor, accelerating blood outflow into the ascending aorta (Fig. 281-2). This device is currently the only FDA-approved axial-flow pump that can be used both as a bridge to transplantation and as destination therapy.