Transplant Roundup

The State of Artificial Heart Therapy

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The 1960s, a decade of striking change in the culture of the United States, also featured advances in the field of cardiac surgery: the first successful heart transplantation, the development of left ventricular assist devices (LVADs), and implantation of the first total artificial heart (TAH). Heart disease remains the leading cause of death worldwide; in the U.S., the prevalence of heart failure (HF) is now 6.5 million.[1]

Heart transplantation is the surgical treatment of choice for most patients with end-stage HF; however, the number of available donor hearts remains inadequate to meet the demand. According to Organ Procurement and Transplantation Network data collected in May 2018, the heart transplantation rate has increased by 47% in the past 10 years; however, even though 3,244 such procedures were performed in the U.S. during 2017, 4,021 additional patients remained on the waiting list. Another confounding statistic shows the underutilization of available donor organs: in 2017, of 14,000 potential donor hearts, only about 4,000 were used. Perhaps the most important contributing factor is the large number of centers approved to perform heart transplantation (n=147); most of these performed 10 or fewer transplantations in 2017, and 17 performed 2 or fewer. The logistics necessary for the equitable distribution of hearts may contribute to this underutilization.

Consequent to the endemic shortage of donor hearts, mechanical circulatory support (MCS) emerged as a means of providing short- and long-term hemodynamic support—including that from LVADs and TAHs—to patients with advanced HF. Ever since Dr. Denton Cooley implanted the first TAH at our institution in 1969, investigators worldwide have sought to develop and improve upon MCS technology.[2] Limitations of total heart replacement have included both the size of the TAH and its durability of only 1.5 to 2 years. Therefore, funding has instead been dedicated to developing LVADs, which can improve the hemodynamic performance of a failing heart but do not re-create the physiology of the normal heart.[3]

Initial LVADs were pulsatile and were intended to replicate the function of the native heart. The National Institutes of Health's goal for the initial request for proposals was a 2-year pump. This was achieved by both the Novacor® Left Ventricular Assist System (World Heart Corporation) and the Thoracic Cardiovascular Institute's pump. However, these pumps had limited durability and were large, which restricted their practical application to bridging patients to transplantation when heart transplantation was reintroduced in the early 1980s. Ultimately, their use served only to increase the number of patients on the transplant waiting list.

The clinical need to deal with these crucial limitations stimulated our development of continuous-flow LVADs. This technology alters normal physiology by producing a constant flow that decreases the systolic pressure in HF patients and converts the diastolic flow from passive to active, thereby achieving a constant arterial pressure.

The 2 devices that became the basis of the first clinical applications of continuous-flow LVAD technology were the Hemopump® (not commercially produced) and the Jarvik 2000® (Jarvik Heart, Inc.) (Fig. 1). The initial in vivo research and clinical use of these devices began at the Texas Heart Institute. The barriers to the use of continuous-flow pumps included the necessity of a bearing in the axial-flow implantable pumps then available for use. It was thought that a bearing without lubrication was impossible; and, because the bearing had to be in the bloodstream, this was a major obstacle to treating patients. In addition, the high pump speeds (>2,500 rpm) thought necessary to produce adequate flow were considered to be prohibitively risky in terms of the potential for blood damage.

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Research began in our laboratories in 1985 to confront these problems. The pump-speed barrier was overcome by the development of the Hemopump by Dr. Richard Wampler, working with the Nimbus Corporation. This pump afforded short-term clinical benefit and caused no blood damage even at speeds of 25,000 rpm. This technology was first used clinically at our institution in April 1988. Dr. Robert Jarvik perfected the use of blood-washed bearings after more than 5 years of research in our laboratories. This was the first use of nonlubricated, blood-washed bearings in a long-term implantable MCS device. This pump, the Jarvik 2000®, was first implanted at our institution in April 2000.

A long-term implantable continuous-flow LVAD, the HeartMate II™ Left Ventricular Assist System (Abbott Laboratories), has been in use for more than 14 years. Unlike the pulsatile pumps—the durability of which is limited because of membrane disruption—continuous-flow pumps have not been operated to mechanical failure. Thus, continuous-flow LVADs are capable of supporting patients for up to 10 years. The HeartMate II has been implanted in more than 25,000 patients worldwide, with excellent long-term outcomes. The U.S. Food and Drug Administration (FDA) has approved this pump for both destination therapy and bridging to transplantation.

Successes with continuous-flow LVADs have encouraged the development of single-rotor devices that can replace the systemic and pulmonary flows previously provided by the native heart. A 3rd-generation centrifugal-flow LVAD, the HeartWare™ HVAD (Medtronic Inc.), has a smaller, more flexible driveline and does not need a pump pocket. The HeartMate 3™ Left Ventricular Assist System (Abbott) is a completely bearingless pump that is now in widespread clinical use.[4] Both devices have been approved by the FDA. Overall, the technology is progressing toward smaller size and eradication of drivelines (Fig. 2). Transcutaneous powering of devices was demonstrated in pulsatile pumps in the 1980s and 1990s, and its application to continuous-flow pumps should soon become a clinical reality. In addition, we hope to apply continuous-flow technology (currently experimental) to total heart replacement in the near future.

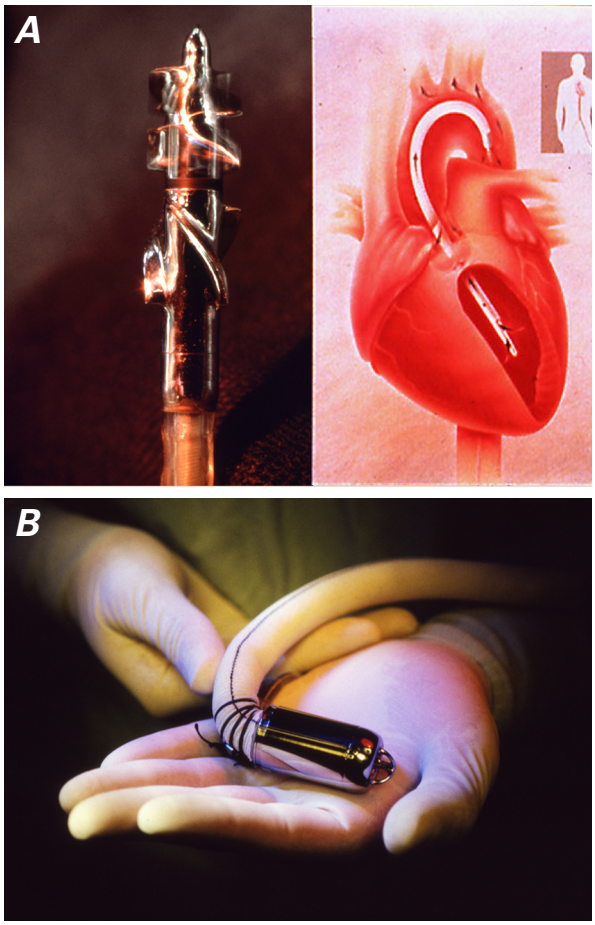

Fig. 1 *Photographs show **A**) the Hemopump (with illustration of placement in the left ventricle), development begun in 1988; and **B**) the Jarvik 2000, development begun in 1986.*

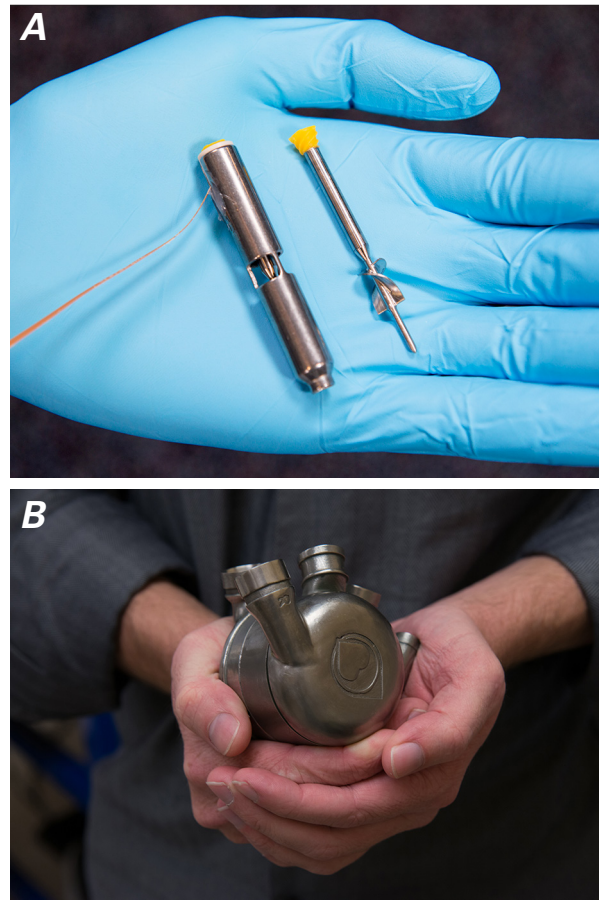

Fig. 2 *Photographs show products under development at the Texas Heart Institute: **A**) an intra-aortic pump for minimally invasive placement, and **B**) the BiVACOR total artificial heart.*

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