New Hearts for Old: The Mechanical Option

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GIBBON, working at Jefferson Medical College in Philadelphia, developed the heart-lung machine and achieved the first successful clinical use in 1953. In less than fifty years, heart surgery has evolved to a point at which the cardiac surgeon can repair a large variety of congenital lesions, and where a series of spare parts is available, including artificial blood vessels, valves, and pacemakers for treatment of a variety of forms of heart disease. Risks of open heart surgery have progressively diminished from over 50 percent to less than 5 percent for valvular surgery and to less than one percent for coronary artery bypass grafting. The last barrier to be overcome in the goal to have effective therapy for all forms of heart disease is represented by the patient who has significant (i.e., greater than 50 percent) heart muscle damage, generally as a result of one or more heart attacks, or of a poorly understood condition in which normal heart muscle is rendered non-functional or is replaced by non-contractile fibrous tissue. For a small number of these patients, heart transplantation has provided a near-miraculous solution, but most patients remain inadequately treated. This manuscript describes the problem of end-stage congestive heart failure and the efforts of engineers and physicians to develop effective heart assist pumps and what will surely be the first artificial organ to be used in man—the artificial heart.

End-Stage Congestive Heart Failure

Most organs of the body have considerable redundancy. Thus, one lung can be removed with little functional loss to the patient and, currently, a relative or friend may donate a kidney to a loved one while still retaining normal renal function. Similarly, the heart has consider-

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able reserve. Fifty percent of the left ventricular muscle can be damaged with the patient having a comfortable existence. However, further loss of muscle function has progressive consequences and results in the condition referred to as congestive heart failure (CHF). Elevation in left atrial pressure results in lung congestion and resultant shortness of breath. Compromised forward flow of blood by the damaged pump results in fatigue and, depending on the degree of muscle damage, inability to perform activities of daily life. Poor kidney perfusion and triggering of neuro-hormonal activity results in reduced urine output, lower extremity edema, and further build-up of fluid in the lungs. The ejection fraction of the left ventricle, normally 60 to 70 percent, is reduced, at times, to as low as 10 percent. The forward flow of blood, normally $2.4 \text{ l/min/m}^2$, is reduced to half of that value, or less. Such patients are uncomfortable, and basically lead a bed and chair existence.

Fortunately, a variety of medications is available to ameliorate some symptoms of CHF. Thus, medications are available to improve remaining muscle function, including digitalis and beta-blockers. Diuretics improve the ability of the kidneys to remove excess water and salt. Vasodilators reduce the arterial blood pressure and improve left ventricular function. The degree to which these medications work depends on the severity of muscle cell derangement. Mild cell derangement can certainly be improved with medication, although no drug therapy will be effective when the myocyte has died and been replaced by a non-contractile fibrocyte. The condition of CHF is generally a progressive one, characterized by gradual loss of responsiveness to medications with the need to increase dosage. As a result, undesirable side effects appear. The patient becomes dependent on a rigid time schedule for medications. Indiscretion in diet (excessive salt or water intake), errors in dosing, and inadvertent stopping of medication all result in exacerbation of symptoms, physician visits, and costly hospitalization.

Improved health care and increased longevity have been a wonderful part of the twentieth century. However, this benefit coincidentally resulted in a significant increase in the number of patients with CHF. Older patients have a higher incidence of congestive heart failure. Moreover, patients who have undergone life-saving open-heart surgery often have residual heart disease and are candidates for CHF.

Congestive heart failure is among the most common Diagnostic Related Groups (DRG's) reported for hospital admissions. The cost of the initial hospitalization, which includes multiple tests and consultation with a variety of physicians, and generally includes cardiac catheterization as well as stabilization of the patient on a medical regimen, can easily amount to $25,000 (in year-2000 dollars). There are additional hospitalizations for tests and procedures; up to ten per year...
would not be uncommon, with costs averaging $10,000 per admission.\(^2\) The need for pacemaker implantation and use of the implanted defibrillator become increasingly common, and further add to the cost. The annual cost to our health system for care of patients with CHF is the largest for any disease. It currently exceeds six billion dollars annually, far more than cancer-related costs.\(^3\) It is important to note that, while the patient’s symptoms may be improved, the underlying problem is not well understood, and where myocytes are no longer present, the problem is really beyond the help of medication. Accordingly, the relentless progression of disease and increase in symptoms remain unabated. Severity of CHF is graded according to the New York Heart Association classification. Class 3 patients, unable to work, have an annual mortality of 10 percent, while class 4 patients, symptomatic at rest, have an annual mortality as high as 80 percent.\(^2\) Thus, in spite of expert, state-of-the-art care, the outlook of patients with severe CHF is dismal.

**Cardiac Transplantation**

The outlook for patients with CHF brightened in 1967 when a relatively unknown surgeon, Christiaan Barnard, M.D., successfully transplanted a human heart from a brain-dead donor into a patient with end-stage CHF at the Groote Schuur Hospital in Cape Town, South Africa.\(^4\) Within a short time, surgeons around the world readily repeated this experiment. However, the immunologic problems were poorly understood, and rejection resulted in frequent complications and early deaths. By the late 1970s, Cyclosporin A became available, and dramatic improvement resulted. Soon, a national system for fair donor heart allocation was established, following that of the renal transplant program. Every attempt was made to increase the availability of donor hearts. As the results of cardiac transplantation were analyzed, certain contraindications became apparent. Immunosuppression in insulin-requiring diabetics, intercurrent infections, pulmonary consolidation, and other factors resulted in complications, poor results, and loss of the scarce donor hearts. Rigid criteria are now assiduously followed to insure good results. Currently, for a select group of CHF patients, cardiac transplantation offers safe and effective treatment with an 85 percent one-year survival and a 77 percent three-year survival.\(^5\) Unfortunately, however, the only source of donor hearts is the brain-dead donor, most commonly resulting from a motor vehicle accident. The number of donor hearts available in the United States for the past five years has been 2,300 annually, an order of magnitude less than that needed.\(^6\) The number of patients on the national list await-
ing a donor heart on any day is twice the yearly availability! Moreover, many patients with end-stage CHF have contraindications to immunosuppression, so that, while they would benefit from heart replacement, they cannot be listed for a donor heart. Thus, what appeared to be an effective treatment for patients with CHF, is helpful on a statistical basis to less than 10 percent of those patients affected. Other forms of treatment are desperately needed.

**What Alternatives Are Available to Heart Transplantation?**

The effort to understand and develop improved treatment options for patients with CHF has never been greater. It involves physicians and research scientists worldwide. The effort ranges broadly from understanding normal myocardial cell metabolism to developing improved drug regimens. However, certain generalizations can be made regarding improved drug therapy. The seemingly inexorable progression of congestive heart failure and the past history of drugs that improve myocardial performance lead to the conclusions that new, more effective drugs will, most likely, have to be administered by the continuous intravenous route, and that improved myocardial function is likely to be transient, lasting only weeks to months. Furthermore, in many patients with CHF, the muscle cells are virtually gone, replaced by fibrocytes and/or scar. In such patients, drugs effecting myocyte performance will have little, if any, salutary effect.

Many patients with CHF have enlarged hearts, so-called dilated cardiomyopathy. In such patients, the myocardium is exposed to high wall tension (overstretched). Favorable reports appeared in the literature following surgical procedures in which a wedge of left ventricular myocardium was excised and the ventricle sutured together in a smaller configuration. What appeared to be too good to be true probably was, and the procedure has now fallen into question. A related procedure in which the heart is restrained within a mesh jacket has been described and is now undergoing clinical trial. While negative comments may be premature, the degree of tightening of the jacket may be critical, and the degree of improvement is likely to be marginal, not sustained.

Efforts have been made to bring new muscle to aid the failing left ventricle. Cardiomyoplasty is a technique whereby a skeletal muscle, such as the latissimus dorsi or pectoralis major, is first conditioned through pacing to convert the muscle type to one capable of continuous cycling (fast twitch fibers become slow twitch type). Then one end of the vascularized muscle is passed into the chest and wrapped around
the enlarged, failing heart. Pacing the muscle synchronously with the heart completes the procedure. Extensive laboratory experiments yielded favorable results and led to clinical trials. Unfortunately, these trials have proven disappointing, with significant operative risk and minimal, if any, improvement in cardiac function.\(^{10}\) Indeed, the suggestion has been made that any improvement in cardiac function may result from the reduction in cardiac size and jacketing effect of the muscle wrap. Another attempt to bring additional muscle into the left ventricle has been proposed, in which myocardial cells are cultured and injected directly into the damaged myocardium.\(^{11}\) While early studies are encouraging, considerable additional research will be needed before such a procedure could be expected to reverse the course of a patient with end-stage CHF.

A non-invasive technique to improve myocardial function is currently being evaluated both in the laboratory and in clinical studies. Biventricular pacing has been shown to increase the effectiveness of myocardial contraction and to improve cardiac output.\(^{12}\) Clinical studies underway will provide answers to important questions, including (1) What is the degree of improvement in cardiac function? (2) Will the improvement be sustained for months? Years? and (3) What are the appropriate indications for biventricular pacing? Again, this advance depends on the existing myocardial cells. Any degradation in myocyte performance will be followed by decreased effectiveness of biventricular pacing.

Effective xenotransplantation would eliminate the long wait for a donor heart. Suitable-size hearts may come from sheep, calves, or small ponies. Suture techniques are well worked out. Unfortunately, at the present time our immune suppression techniques are insufficiently developed to permit animal to human organ transplant. Furthermore, the profound reduction required in recipient immune response results in high risk of virulent infections and in a significant risk of cancer induction. Nevertheless, replacement of the diseased human heart by xenografting would represent a major step toward treatment of a significant number of patients with CHF, and will follow as a direct result of the progressive understanding of the immune system and its interrelation with malignancy.

**Ventricular Assist Devices**

Patients awaiting heart transplant often deteriorate during the months required to gain seniority on the waiting list; 20 percent die before a suitable donor heart can be identified. Implantable blood pumps have been developed that can support the failing ventricle for weeks to
months while a donor heart is identified. These pumps take oxygenated blood from the heart and pump the blood into the arterial system. These pumps are capable of handling the full output of the left ventricle (six to eight liters per minute) and reducing the back pressure on the lungs. Remarkably, transplant candidates with a ventricular assist pump are suddenly relieved of shortness of breath and have considerably more stamina, often more than they have had in years; they feel better. As a result of their effectiveness in temporarily supporting the transplant candidate, these pumps are now being considered as permanent devices for treatment of patients with end-stage CHF.

The most widely used ventricular assist device (VAD) is the Heartmate pulsatile assist pump. This device employs a diaphragm-type pump and is unique in having a blood-contacting surface consisting of a textured moving diaphragm and a sintered titanium-bead stationary surface to reduce the risk of thromboembolism. Glutaraldehyde preserved tissue inlet and outlet valves are employed. The system incorporates a compact brushless DC motor and a face cam to actuate the diaphragm. The device removes blood from the left ventricular apex and infuses it into the ascending aorta. It is positioned in the upper abdominal cavity. A wire and an adjacent tube pass through the skin to power the motor and to provide for the displacement of gas as the pump fills. The patient carries a battery pack. A drug such as aspirin that decreases platelet adhesiveness is employed to minimize thromboembolic complications. Several patients have now lived for nearly two years with this VAD in place. Following the encouraging results obtained with this pump in more than two thousand “bridging” applications and with the few “outliers” who have not received donor hearts, a major study, “REMATCH,” is being conducted to compare the effectiveness of this device with optimal medical therapy as a treatment for CHF.

The Novacor assist pump is a smooth-surface sac-type pump also employing tissue inlet and outlet valves. In an effort to minimize sac strain, the sac is activated on both sides by cantilevered pusher plates. A rotary solenoid is used to move the opposite end of the opposing cantilevers. Again, the device pumps blood from the left ventricle to the aorta and is positioned in the left upper quadrant of the abdomen. Both electrical and pneumatic conduits pass through the skin. Extensive bench testing showed the system to have a high degree of mechanical reliability. Anticoagulation with warfarin sodium is required to minimize thromboembolic complications. Effectiveness has been shown in more than a thousand patient applications in “bridging” to transplantation. Again, a few “outliers” have had the device function for more than two years with good relief of symptoms.
The Arrow Lionheart is a completely implantable left ventricle to aorta pulsatile assist pump. Bjork-Shiley tilting disk inlet and outlet valves are used. The blood pump sac is smooth, seamfree polyurethane, and the pump is positioned in the upper abdomen. To eliminate disfigurement and the ever-present risk of infection from having wires and a tube cross the skin, this system is fully implantable. Electrical energy (fifteen to twenty watts) is transmitted across the skin using inductive coupling techniques. The gas volume displacement problem is handled by using a pliable compliance chamber positioned between the left lung and the chest wall, eliminating the need for the tube to cross the wall. The system, as designed, should considerably reduce the risk of infection present at any skin-prosthetic material junction. This system was designed for “permanent” use and not for the “bridge” application. Thirty clinical applications have been reported, with the longest being about two years.

Clinical use of left ventricular assist pumps for the treatment of end-stage congestive heart failure shows great promise. The natural heart
remains in place to provide a “back-up” in the event the system malfunctions. Components are modular and can be replaced as the need arises. The effectiveness of this form of therapy will require five years to determine. If the technique is as effective as it now appears in relieving symptoms, and the longevity of the device is two years or more, the proposed device cost of $100,000 per unit will be in line with the monies currently required for treatment of the CHF patient, but with considerable relief of symptoms and a probable increased survival.

The Artificial Heart

The promise of left ventricular assist devices for treatment of end-stage congestive heart failure is great. Several expert panels have concluded that ten thousand patients or more annually may be candidates for this form of therapy. However, there are potential problems that must be considered. Left ventricular assistance relies on a normally functioning right ventricle. The output of the left ventricle can only match that of the right ventricle. Any derangement of natural right ventricular function will limit the effectiveness of an implanted LVAD. Accordingly, patients with derangement of both right and left ventricles will not benefit from an implanted LVAD. Moreover, patients who have serious arrhythmias in addition to congestive heart failure may require near toxic doses of antiarrhythmic drugs, not an ideal situation. Other problems that may limit the usefulness of the implanted LVAD have become apparent to surgeons experienced in cardiac transplantation. The appearance of the excised heart, particularly the left ventricle, may reveal areas of thrombus, calcific debris, or aneurysms, all of which may serve as a future source of emboli and debilitating strokes if the heart is allowed to remain in place.

At least 20 percent of patients with end-stage congestive heart failure who are candidates for a mechanical device may be best served by excising the heart and implanting a heart replacement device using surgical techniques similar to those of cardiac transplantation. Accordingly, patients with biventricular failure, extensive scarring of the left ventricle, previously placed prosthetic heart valves, or aortic regurgitation will have the natural heart excised and an electrically powered mechanical heart positioned in the pericardial sac within the chest.

While the electric heart has not yet been applied to humans, air powered pumps were employed in the mid-1980s as a permanent heart substitute by DeVries and his colleagues. These implants followed encouraging calf implant studies using the Jarvik 70 heart, air powered from a large external air compressor with the pneumatic energy crossing the chest wall in twelve-mm diameter tubes. While several patients
did live more than one year, the significant incidence of strokes, the risk of infection attendant with the transdermal tube passage, and the limitation in life style caused by the bulky external compressors led to a reconsideration of this technology.

Two electric hearts having significantly different technical aspects are vying for clinical application. The Abiocor device is an electrohydraulic heart. The left and right ventricles are each polyurethane sacs with integral polyurethane leaflet-type inlet and outlet valves. Positioned between the two pumping ventricles is a miniature brushless DC motor-driven pump that pressurizes a silicone working fluid. A separately powered hydraulic spool valve shuttles fluid to compress first one pumping sac and then the alternate sac. An implanted control system and sufficient lithium ion battery power to provide thirty minutes of internal power complete the hardware. Power for long-term use is provided by inductive coupling. Accordingly, no break in the skin is required for function of the device. By carrying portable batteries in a shoulder holster or briefcase, the patient will be fully mobile.

The prosthetic heart, developed by the research team at The Pennsylvania State University, is an electromechanical unit. Again, the

![Diagram of implanted components of the Penn State artificial heart](image)
activation unit is positioned between two polyurethane blood sacs. This unit consists of a brushless DC motor, a roller screw, and pusher plates positioned at both ends of the roller screw threaded shaft. The motor turns the roller screw nut, driving the pusher plate toward and compressing one sac. The motor then counter-rotates, resulting in compression of the other sac. Conventional Bjork-Shiley tilting disc cardiac valves are employed. As in the Abiocor heart, an implanted battery and control system and an inductive coupling power transfer system are used. Both hearts are undergoing mock circulatory loop durability tests and both are being evaluated in the calf animal model. It is important that the units are quiet and the calves with implanted hearts really appear to be normal, with good appetites and normal growth curves. As a result of calf growth, the output of the hearts is only sufficient to support the circulation for a period of months; longer studies must rely on the durability test data. The current research effort should result in hearts that will have initial clinical application within the next twenty-four months.

**THE FUTURE**

A tremendous effort is being expended to improve the outlook of the patient with end-stage heart disease. It does appear that only so much
can be done to rejuvenate a seriously damaged heart. The unqualified success of cardiac transplantation has led to a conclusion that heart replacement therapy must now be made available to a much broader group of patients. The decade of the 1990s has seen compact, safe blood pumps come into their own. The decade of the 2000s will be remembered, in part, for the use of permanent heart assist pumps and mechanical hearts, available as “shelf items” in hospitals, that will begin to solve the twenty-year shortage of donor hearts. As experience is gained in the use of these devices in the clinical setting, improvements will be made in design, function, and implantation techniques. Smaller size, less weight, and fewer components will be the result of advances in material science, mechanics, motor design, electronics, and other fields. Nevertheless, evidence suggests that even with our best efforts, we will continue to be in awe of the superb design and engineering of the human heart for many years to come.

**Addendum**

Since the preparation of this manuscript, Abiomed, Inc. has obtained permission from the Food and Drug Administration to initiate clinical trials using the AbioCor heart. Five implants have now been performed. One patient was recently discharged from the hospital to home seven months following implantation of the prosthetic heart.

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