

50,000 to 70,000 patients by 1990 at a cost of \$1.7 billion (64). According to Barnes (9), the National Dialysis Registry estimates an annual mortality rate of only 10.8 percent for patients on dialysis during the first 4 years of care. Since the highest mortality rate occurs in the first year, this estimate is in marked contrast to the estimate of a 20-percent annual mortality rate of the Office of the Actuary of the SSA noted above.

A number of problems have occurred with regard to cost estimates for the ESRD program. Both Barnes (9) and Rettig (64) address them thoroughly. We summarize the most important points below.

- There has been persistent underestimation of total costs.
- The early hope of increased success with cadaveric transplantation has not been realized.
- The increased problem of poor quality of life for patients and the small proportion rehabilitated was not anticipated. \*
- Cost-reducing innovations in therapy through R&D have not occurred.
- Prospects for disease prevention seem remote.
- The least expensive mode of treatment, home dialysis, is not being used as exten-

\*Quality of life parameters are discussed below in another part of this case study.

sively as expected. Some of this problem is the result of taking marginal patients such as the elderly and diabetics, as well as the result of economic disincentives for home dialysis by patients and physician providers.

The artificial heart program has received more Federal research money than the hemodialysis program did at equivalent stages of development. Early meetings of the American Society for Artificial Internal Organs saw development of an artificial heart as much more complex than that of an artificial kidney, because a permanent, complete artificial heart must constantly perform the full and precise function of the human heart, whereas a kidney can function part time and at a comparatively low capacity.

Anderton, et al. (4) have concluded that there is no positive economic benefit for the treatment of renal failure. In paying for such treatment, society is tacitly agreeing to pay for the intangible" benefits of avoidance of pain, discomfort, grief, and premature loss of human life. For the artificial heart program, the dialysis experience indicates that the allocation of scarce medical resources for the saving or prolonging of lives deserves thoughtful deliberation.

"In economics, "intangibles" are those *costs* and benefits that cannot be quantified or priced.

## ESTIMATES OF THE POTENTIAL SUCCESS OF THE ARTIFICIAL HEART

### LVAD Research and Clinical Trials

Since its inception, the artificial heart program has advocated simultaneous research on both permanent heart replacement and temporary LVADs. Because of the obstacles encountered in developing a totally implantable artificial heart, however, the development of the LVAD now takes priority. NHLBI funding since 1974 has been largely concentrated on the development of LVAD control systems, pump design, biomaterials, and beginning in 1975, clinical trials.

The goals of the LVAD program center at present on developing a long-term (2- to 5-year) implantable LVAD capable of taking over the pumping function of the weakened left ventricle of the heart and enabling its eventual recovery. The development of a long-term assist device will draw heavily on current experience with the temporary (2-week) LVAD. Many models of the temporary LVAD currently exist; these have been funded largely through NHLBI,<sup>2</sup> but partly

<sup>2</sup>See Report of Cardiology Advisory Committee, *Journal of Artificial Internal Organs (JAIO)*, November 1977, for summary of NHLBI devices.

through independent corporate investment (e.g., by Medtronic and Arco Medical Products). Because of the recent emphasis on developing a long-term implantable LVAD, explicit funding of total artificial heart development has been much less extensive; in 1978, NHLBI had only four total artificial heart contracts, totaling \$1 million.

In 1974, NHLBI convened a workshop to consider the desirability and feasibility of conducting LVAD clinical trials. Ruth Hegyeli and Michael Machesko, 1974 workshop participants, reviewed *in vitro* and animal data on the Thermoelectron LVAD (TECO models VII and X) used by John Norman of the Texas Heart Institute and William Bernhard of Boston Children's Hospital (34). They concluded that clinical trials would be in order once biomaterials suitable for short-term use were developed, adequate provisions were made to protect patient/subject rights, and criteria were established for patient selection.

After meeting these criteria, Norman and Bernhard received funding from NHLBI for clinical trials of the short-term (2-week) LVAD. Both the Texas Heart Institute and Boston Children's Hospital trials used the same patient selection protocol, which sets forth a number of conditions to be met by potential LVAD recipients. Only patients unable to resume cardiac function at the conclusion of cardiac pulmonary bypass were included. A total of 38 implants (23 Texas, 15 Boston) were performed in this program (58). Three patients were alive at this writing (May 1980), 25, 24, and 18 months after surgery; one patient survived 7 months. Of the last 14 implants, 8 were successfully supported for more than 40 hours (77). \*

In addition to the NHLBI clinical trial contract program, several other clinical trials of different LVAD models have taken place.\*\* William Pierce, of Pennsylvania State University, has used a smooth-surfaced, polyurethane-coated pump in approximately nine patients and re-

ported the first long-term survivor (57). Limited clinical use of other LVADs in at least 11 patients has been reported, with 2 long-term survivors (57). The extent of use of commercially developed pumps (e.g., Arco, Arothane) in therapeutic settings is unknown, because data from these implants are not formally reported.

Those who have conducted LVAD clinical trials believe they have obtained much valuable information that will contribute to the successful development and use of future long-term devices. Such information includes confirmation of the hypothesis that temporarily taking over the left ventricle pumping function can, in some patients, lead to partial recovery of the depressed ventricle and the observation that right heart function is not always necessary during LVAD implantation (52).

Major problems in device design and function still exist, however. A primary challenge is the development of biomaterials that do not encourage thrombogenesis (formation of blood clots) and do not decompose over long-term use. Another challenge is the development of a portable, reliable energy source. Current prototypes using electric batteries have both mechanical and operational liabilities; Pu-238-powered fuel cells provide a compact energy source but pose severe problems due to health risks from radiation.\*\*\*

NHLBI has given top priority to further research in the areas of biomaterials and energy sources (16). A special biomaterials task force issued recommendations in 1977 calling for the exploration of the comparative viability of rough and smooth surfaces, the development of operational and quantitative definitions of blood compatibility, theories that correlate blood compatibility with physiochemical characteristics of biomaterials, and adequate test and evaluation methods. There has been progress in these areas, and advances will increase as NHLBI grants for basic research in biomaterials expand. Because of the magnitude of the technical problems that must be solved in order to develop a long-term (2-year) LVAD, estimates for commencement of clinical trials of the long-

\*A summary of the clinical trial program is currently being developed by NHLBI.

\*\*For example, see articles in the 1978 issue of JAIO devoted exclusively to LVADS.

\*\*\*The problems of a nuclear-powered heart are discussed below in a separate section of this case study.

term LVAD range from 3 to 6 years. Industry representatives (Thermoelectron and Aerojet General) note that even the 6-year estimate may be overly optimistic if the level of Federal funding does not increase.

Another factor complicating long-term device development is the diversity of existing LVAD programs and the difficulty of coordinating research or clinical trial results. Although data from NHLBI-sponsored LVAD programs have been difficult to compile, the existence of privately funded programs makes comprehensive data collection and coordinated research efforts even more difficult.

The experience of clinical trials of short-term LVADs appears to be of only limited use in projecting the potential success of permanent devices, in part because the research protocols restricted potential recipients to very ill patients who are likely to die regardless of the form of treatment. Because the devices are implanted temporarily, only short-term mechanical performance and negative side effects can be observed; medium- and long-term device performance and side effects cannot be evaluated. Since most patients die on the operating table from other causes, even potential complications due to the short-term device cannot usually be identified.

### Instrument Reliability

Instrument reliability is of utmost importance in the effort to achieve a clinically successful totally implantable artificial heart. With the patient's natural heart removed, sudden instrument failure would lead to the patient's death within minutes unless corrected. Reliability is different from durability. The durability of the individual components of a device can be bench tested and predicted with some confidence (e.g., materials that will flex with every stroke of the heart pump can be tested for the enormous number of such flexions to which the materials will be subjected over the anticipated instrument life). The reliability of the assembled components under the conditions of use cannot be predicted from bench tests alone, and testing has not yet been done in animals. Testing, when

begun, will have to extend for at least as long a period of time as the required life of the device and, perhaps, twice as long. \* Thus, if the target is for a 5-year device, it will be necessary to wait for 5 to 10 years before reliability can be established. " Further, since the concept of reliability is a statistical one, large numbers of trials may need to be carried out.

Experience with other medical devices offers some basis for expectation and for concern. The cardiac pacemaker, an enormously less complex instrument, has presented a series of serious difficulties which, after nearly 20 years of clinical use, have only now been resolved with reasonable success. These include lead breaks, battery failure, runaway pacemakers, electromagnetic interference, and errors in manufacture as well as errors and complications in clinical application. \*\*\* The cardiac pacemaker is a simple, primarily electrical device with a low energy requirement. The artificial heart is a complex electromechanical device which has high energy and mechanical requirements. Although pacemaker failure is a serious complication, the patient often survives long enough for replacement. Failure of the artificial heart, however, would in almost all imaginable circumstances lead rapidly to death.

Our consultants express confidence that an appropriate energy source (e.g., battery) with 5 to 7 years predictable life is currently feasible. No such assurances have been offered for the mechanical components or for the artificial heart system as a whole. Opinions have been offered that a system life as short as 60 days or as long as a year may be encountered. Contributing to the uncertainty is the existence of a number of identifiable problems that have yet to be resolved.

● Accelerated aging at increased temperatures can be used to shorten the period of testing of implantable electronic devices but would not be appropriate under the hemodynamic conditions of the artificial heart. A method to shorten the test period for the artificial heart is urgently needed but cannot be counted on.

\*\*In discussing this section, Kolff and others have pointed out that a device of even as little as 1-year reliability would be welcomed by many patients and physicians.

\*\*\*See app. A by Dr. Thomas Preston for a summary of the introduction of the pacemaker and difficulties encountered; see also testimony of Sidney M. Wolfe and Anita Johnson on medical device legislation before the House Subcommittee on Health, July 28, 1975 and Oct. 23, 1973.