MASTER

ERDA ARTIFICIAL HEART PROGRAM WORKSHOP

Final Report
for Period September 1, 1975-August 31, 1976

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August 1976

Prepared for

THE U.S. ENERGY RESEARCH AND DEVELOPMENT ADMINISTRATION
UNDER CONTRACT NO. E(11-1)-2815-1

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ABSTRACT

The major conclusions of the ERDA Artificial Heart Program Workshop are that the concept of a biologically compatible mechanical device which can totally replace the heart is sound, that such a device is needed as an alternative to cardiac transplantation and that its development is a realistic goal.

The major recommendation of the committee is that an ERDA program with primary orientation toward development of a total heart replacement should continue, with assured funding about 50% higher than at present, for a minimum of 3 additional years at which time another major review should take place.

To achieve better management of the program it is recommended that the present contract effort be reorganized under one prime contractor with responsibility for development and demonstration of the ERDA artificial heart system.

The formation of a joint artificial heart advisory committee to improve coordination between ERDA and NHLI is also recommended.

The committee suggests future policies and directions which it believes will lead to more effective use of funds available for specific aspects of the program. These include the nuclear heat source, engine, blood pump, biomaterials and overall system reliability.

Possible future goals for the program are also proposed.

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INTRODUCTION

NEED FOR THE PROGRAM

The magnitude of problems associated with heart disease is almost inestimable. Cardiovascular diseases claim more American lives than all other causes of death combined and cost the nation an estimated \$22.7 billion annually. In addition to lost income and expenditures for medical care, 52 million man-days of production are lost each year, and this figure does not include the hidden costs of losses of management skills, production know-how, personnel training and development, and labor turnover, which are difficult to determine.

Of the more than one million deaths from diseases of the heart and great vessels in 1973, over 680,000 resulted from heart attacks. More than 13,000 patients died of rheumatic heart disease and almost 7,000 from congenital heart disease. Between 350,000 and 400,000 people in the United States die of chronically symptomatic heart disease each year, and between 100,000 and 165,000 are under the age of 65.

The past 25 years have produced much new scientific understanding of the pathogenesis and abnormal physiology of heart diseases, yet the process of atherosclerosis and other processes leading to cardiac debility are still far from being understood. The possibility of effectively preventing development of heart disease is at least a generation away. Therefore, the great number of patients afflicted with coronary artery disease, rheumatic heart disease, heart disease of unknown cause (cardiomyopathies), and congenital heart disease require new efforts to prevent death and improve their quality of life.

During the past two decades considerable scientific progress has been made in treatment of patients with near-terminal heart disease. Advances, including the development of greatly improved diuretics, new drugs for control of arrhythmias, aortocoronary vein bypass graft surgery, valve replacement, definitive operations for congenital heart disease, temporary and permanent pacemakers, and the ability to remove large portions of the heart, such as ventricular aneurysms, all improve the overall heart function.

Unfortunately, despite these great advances there remain patients for whom conventional surgical approaches are of essentially no value. Three methods to treat these patients have been investigated. First, cardiac transplantation is feasible in a small number of patients. Second, a partial mechanical heart or auxiliary ventricle has been effective in experimental animals and in a limited number of patients thus far. Third, a totally implantable pump to replace the function of the heart has been tested in several animal species with several months of survival occurring after implantation. Immunology, cardiovascular medicine, surgery, biomaterials technology and power supply technology have progressed to the point where it is now feasible to consider total replacement of the human heart.

Cardiac Transplantation Replacement of diseased hearts with donor hearts transplanted orthotopically is now feasible without major problems of surgical technique. The major problems which limit the use of orthotopic cardiac transplantation are first, the lack of adequate donors; second, the inability to control rejection and infection, for which a major break-

through would appear to be required; and third, the unsettled state of moral and ethical questions relating to societal acceptance of cardiac transplantation. Major progress in transplantation biology in the near future would undoubtedly permit widespread application of cardiac transplantation. However, even if such progress is achieved, there are not likely to be enough donor hearts to replace diseased hearts within the United States.

Total Artificial Heart and Heart Assist Devices During the past decade, several types of artificial pumps to replace or to assist the failing heart have been developed and tested in animals. Complex problems that seem to have been at least partially solved include those of power supply, engine, pump, and control system of acceptable durability and reliability. Survival for as long as three months has been reported in animals with total cardiac pumps. Biomaterials and blood interfaces, with their associated problems of flex life, heat dissipation, and reactions with blood remain significant factors limiting long-term successful use of an artificial heart in animals. Considering these limitations, development of a total artificial heart for implantation in man will probably require a number of years.

When a left ventricular assist device (for example, one of those developed in programs that paralleled the artificial heart effort) is used the natural heart remains in situ. If appropriate, the artificial support system can be removed and the natural heart can then support the circulation. Implantation of the total artificial heart, in contrast, requires excision

of the natural heart and the option of return to the status quo ante is not available. This consideration may discourage clinical adoption of the total artificial heart.

While it is not possible to determine the exact number of cardiac patients who might be candidates for heart replacement, the great majority of people under the age of 65 with heart disease is not afflicted by severe organ deterioration due to diabetes, lung diseases, neoplastic disease, or renal diseases. Consequently a large percentage of those who now die would not present contraindications to utilization of an artificial heart or heart assist device.

If one limits the potential candidates for heart replacement to those who are destined to die imminently ("terminal heart disease"), they would number between 12,000 and 32,000 per year, according to an NHLI estimate. If one assumes that implantation of an artificial heart would eliminate major disability, another large group of patients, perhaps as many as 100,000 to 150,000, would be potential candidates for an artificial heart or a partial mechanical heart.

In summary, it appears a highly desirable goal at this time to develop a pump not damaging to human tissue which could substitute for, or aid the function of, the heart. The partial assist device and the total artificial heart are not mutually exclusive. Each is a desirable goal, and an assist device which proves successful will probably aid in the introduction of a total artificial heart substitute. Many of the medical and biological problems which will occur with the substitution of a pump for the heart now appear soluble. Either device should have a power

source adequate to function for a number of years and should be of an implantable size. The system must be highly reliable and produce a cardiac output large enough to permit adequate physiologic function.

This report is intended to review the accomplishments of the ERDA Artificial Heart Program and to suggest future policies and directions which the review committee believes will lead to the realization of a total artificial heart.

PROGRAM HISTORY

In 1966 the Atomic Energy Commission (AEC) and the National Heart and Lung Institute (NHLI) jointly funded four study contracts to evaluate the feasibility of a radioisotope-powered artificial heart. The contractors were Aerojet-General Corporation, Donald W. Douglas Laboratories, Thermo Electron Corporation, and Westinghouse Astronuclear Laboratory (WANL). In 1967, NHLI awarded contracts to Aerojet-General, Douglas and Thermo Electron to develop hardware. Contractors continue to be supported by NHLI to develop energy sources for radioisotope-powered heart assist devices. In 1968, AEC initiated a program at Los Alamos Scientific Laboratory (LASL) for the development of plutonium-238 fuel. Studies were also started at Pacific Northwest Laboratory (PNL) to determine the potential radiation effects upon a recipient of a radioisotope-powered heart device. In early 1969, a contract was awarded to Hittman Associates, Inc., to develop radioisotope heat source subsystems suitable for use in implantable heart assist devices and consisting of a radioisotope capsule, thermal energy storage material, thermal insulation, and a heat

exchanger to be mated with a thermal converter. Two heat source subsystems were built and evaluated, one for use with a Rankin cycle power converter and the other for use with a Stirling cycle power converter. About this time, studies of radiation effects were initiated at Cornell University using radiation-equivalent sources in Labrador Retrievers. In 1970 a study was initiated at PNL to determine the dose to bystanders and to the population at large which would result from widespread utilization of radioisotope-powered artificial heart devices.

In 1971, the AEC initiated a three-phase effort to develop a prototype radioisotope-powered artificial heart. The objective of the Phase I study was to select from the many alternatives a concept of thermal energy conversion having the greatest potential of leading to a practicable, fully implantable, system which could operate reliably for ten years. A Stirling cycle converter with a mechanical blood pump drive was selected for Phase II, a bench model demonstration. The objective of the Phase III effort, which was initiated in 1973, was to advance the Stirling converter technology toward a fully implantable system which can be used extensively in animal testing and eventually can qualify for clinical use. In support of the engineering effort started in 1971, contracts were awarded to the University of Utah for bioengineering investigations, to the Cleveland Clinic for study of the optimal size and shape of a device to replace the human heart, and to the University of Utah and the University of Washington for biomaterials studies.

The AEC effort, which has been in existence for over a decade, has now been organized as the ERDA Artificial Heart Program and is a responsibility of the biomedical and environmental division of ERDA. It is the sole U.S. effort exclusively directed toward a total artificial heart as a primary goal. Since 1967 NHLI has also sponsored development of artificial hearts using nuclear power sources. The committee sees merit in the parallel programs at NHLI and at ERDA.

PRESENT STATUS OF THE ERDA PROGRAM

Following completion in 1971 of preliminary studies begun in 1966, an active research and development program was started. Four major goals have been met.

1. An isotopic heat source using Pu-238 has been developed which provides power adequate to meet design requirements; animal studies show that it imposes tolerable radiation and thermal burdens on the recipient.
2. An implantable Stirling engine has been developed to convert the thermal energy of the isotopic source to the mechanical energy needed to drive a heart pump. The flexible shaft drive needed to transfer the mechanical energy from the engine to the blood pumping unit is being developed.
3. A blood pump consisting of two diaphragms and a scotch yoke and pusher-plate unit has been designed and built. This pump has furnished complete support to calves for periods up to 21 days.

4. Each of the above goals has been reached without exceeding the constraints required to achieve a workable overall system. The pump is designed to fit into the space occupied by the natural heart, and the power package is to be implanted in space available in the abdomen.

CRITIQUE

NUCLEAR HEAT SOURCE PROGRAM

The successful development of a nuclear-powered artificial heart will not be complete without public acceptance of the safety of the nuclear heat source. Thus the qualification of the heat source must be assigned the highest priority in the total plan. Plutonium-238 provides the thermal energy to drive the Stirling engine of the artificial heart. Plutonium heat sources have been used for over a decade to provide thermal energy for power devices in the space program, and have also been used to provide the thermal energy required in nuclear pacemakers. Thus the use of a plutonium heat source does not require new technology but builds upon a well-established technological base.

The artificial heart heat source, 2.5 cm in diameter and 4.6 cm long, contains sufficient plutonium dioxide to produce 33.1 watts of thermal energy and weighs 282 g. No other technology is known which can provide so much thermal energy in so small a package for so long a period of time. Foremost among design constraints is that of providing complete isotope containment, not only during long-term exposure to its operating environment but also during potential accidents which could occur during,

or at the end of, the proposed minimum ten-year life of the artificial heart. Since they had been considered by past review groups, the design and testing of the heat source were not extensively examined during this review. Nevertheless, the stringent safety requirements and extensive testing which accompanied the development of the heat source should be noted. The nuclear safety criteria established for the capsule included the ability of the heat source to survive an impact simulating that of an airplane crash, a train collision, a bullet impact, a fire, and a crushing blow (of the power of a multi-ton load). The heat source met all of these criteria except that of bullet impact; it survived the impact of a 45-caliber bullet at point-blank range but failed some 30-06 rifle bullet tests. The capsule has been licensed for laboratory testing.

A major milestone in the development of a nuclear-powered artificial heart will be the licensing of the device by the appropriate nuclear regulatory agency. Much of the data required for such licensing is being developed in the heat source program, but the responsibility of assuring that all the required data are obtained is not clearly defined. To date, there has not been a thorough safety analysis for the artificial heart which defines accident probabilities, source terms, consequences, etc. Such an analysis might reveal potential problems and would indicate whether additional data were required. The review should assess consequences of population exposure resulting from the projected use of the device. It should include a thorough examination of all aspects of the system.

Supporting expertise should be provided as required. The current LASL program is inadequate, both in scope and in emphasis, to serve this function.

Alternative Energy Sources

The potential toxicity of plutonium-238 and its high cost have encouraged an extensive search for alternative energy sources for implantable devices. The committee recommends that this search continue. It is not impossible that a rechargeable storage device that would allow the patient the same mobility (and freedom from external accessories) between charges as the plutonium source might be developed.

Two storage systems which in principle offer the prospect of sufficiently long life and ease of percutaneous recharging have been proposed but appear to lack merit. The first, thermal energy storage, would be compatible with the present Stirling engine. The present engine would require, for 24 hours storage at 33 watts thermal, 792 watt hours at temperatures greater than 800 °C. A lithium fluoride (LiF) storage system (with which Philips has experience) that can store roughly 300 watt hours/kg would require 2.64 kg LiF, or approximately the mass of the entire present engine and heat source. (The specific gravity of LiF is 1.8, so that the system would be larger as well as heavier than the present design.) There are hydrides that offer up to 1290 watt hours/kg, so that 24-hour storage with an approximate increase of 25 percent in weight and volume over the present system is said to be possible. However, apart from increased mass of the implantable component the thermal energy storage approach suffers from other serious technical limitations. On balance, this approach is likely to be exceedingly impractical and is not recommended.

The second form of storage, the flywheel, offers storage capacities up to 200 watt hours/kg with a specific gravity of 2. Since the flywheel would couple directly to the pump with a transmission loss of less than 50 percent, storage of approximately 240 watt hours would be required. Thus the power supply would weigh approximately 1 to 2 kg and would occupy 1/2 to 1 L. There are substantial transmission and suspension problems associated with the flywheel option: for the immediate future, a combination of a heat source (or thermal storage capability) and the heat engine appears most practicable.

In summary, to accomplish the awesome task of supplying 33 watts, roughly a third of the normal metabolic rate, around the clock, there are at present two options: (1) a nuclear source or (2) a constantly (or frequently) attended external source. The latter is clearly unrealistic for a practical, widely used system. The committee believes that the advantages of the plutonium-238 source outweigh the risks and that plutonium-238 should be pursued as the energy source of choice.

Specific Recommendations for the Heat Source Program

The heat source program has made significant contributions to the total heart program. However, to assure that the complete program can be advanced as rapidly as the technology permits, and at a minimum cost, it is important that the component programs clearly define milestones, interfaces, priorities and responsibilities. The following specific recommendations are offered:

1. Designate a single point of responsibility for the qualification and licensing of the system, and clarify responsibilities of participating laboratories and development groups to one another.
2. Initiate a dialog with the Nuclear Regulatory Commission about licensing procedures and data requirements.
3. Develop an overall plan to license the artificial heart.
4. Prepare a safety analysis report covering all aspects of the system.
5. Initiate configuration control management procedures on the heat source as soon as practicable.
6. Reorient the Los Alamos program by (a) increasing emphasis on compatibility testing; (b) increasing emphasis in support of safety testing relevant to licensing requirements; (c) decreasing emphasis on fuel development and electrorefining processes.
7. Continue the Battelle Pacific Northwest Laboratories program on "population radiation exposure" and "recipient radiation exposure from circulatory support systems."
8. Consider a parallel approach in which, on one path, all activities directly relating to the development, qualification and licensing of the nuclear-powered artificial heart, except the LASL program,

are placed under a single systems contractor and in which, on a second path, the long-range research and development required for the next generation of the devices is conducted by designated contractors who report not to the systems contractor, but to the program office. These activities should include a limited but finite program to maintain awareness and development that could lead to a workable non-nuclear heat source.

ENGINE

The development of the Philips Stirling engine with mechanical drive suitable for powering the artificial heart was begun in 1971. A bench model completed in 1973 had 12 percent engine efficiency and 87 percent drive efficiency; with an input of 38 watts thermal it delivered 4 watts to the pump diaphragms.

The implantable version of the bench model (IVBM) presently being tested delivers 4.3 watts to the diaphragms with an input of 33 watts thermal. The dimensions are 22 x 9 x 10 cms., the weight, 2.8 kg., and the specific gravity, 2.3.

The experience gained at Philips in designing the latter system has led to the design of the Mark I prototype, which Philips and Westinghouse propose to build. The major improvement in performance is to be achieved by shortening the stroke, and thus reducing the inevitable thermal losses associated with the displacer piston. In addition, the Mark I would be smaller and lighter than its predecessor. The ultra-thin wall displacer

piston represents an imaginative approach to the problem of thermal losses along the displacer. However, because of the metallurgical and structural characteristics of the material from which the piston is fabricated, concerns were expressed about its durability, and these concerns should be considered.

There are considerable reservations regarding the seal separating the crankcase from the working gas. At present a "roll-sock" design, discussed below, is used. Philips is considering the possibility of using ferromagnetic fluid seals. The present lack of knowledge about instabilities in ferromagnetic fluid systems makes these seem a choice of uncertain merit. The reservations concerning the roll-sock seal expressed at a site visit are summarized below:

The Philips design uses two rolling diaphragms to separate the argon working fluid from the crankcase lubricant. To achieve long life, a proper flex pattern of the diaphragms must be maintained and they must be absolutely free of debris. Philips has made significant and noteworthy progress over the years in the development of these roll-sock seals, one of the key factors in its achievement of such excellent efficiencies and performance in Stirling engine applications. While these seals achieved a long operational life in bench tests, their performance in an engine which will be subjected to a closed in vivo environment must still be demonstrated. The key concern of the reviewers is the proposed five- to ten-year unattended life. One can intuitively

assume that argon, the working fluid within the engine, will permeate the roll-sock seals and be absorbed into the crankcase lubricant.

Since engine performance is very sensitive to changes in the working fluid, it is feared that with time, performance will degrade significantly in a closed environment. It is therefore recommended that both Westinghouse and Philips attack the problem of permeation through the seals to determine whether the desired long life is achievable or whether makeup provisions must be incorporated in the design.

The Westinghouse contribution to the engine has been primarily the development of insulation for the hot finger. The overall objective of this task is to advance the multi-foil insulation technology currently being used by Westinghouse to protect its thermal engine system. The specific objectives during the proposed period are to develop a reliable, long-life, static multi-foil insulation package, a vacuum scram system, and thermal insulation coverings for heat transmission components. A key portion of the proposed Westinghouse multi-foil insulation research and development activities will be devoted to the evaluation of outgassing characteristics of hot finger, insulation, and spacer materials. In addition, Westinghouse plans to determine the permeability of various materials and to evaluate candidate materials for possible incorporation into the insulation system. Westinghouse also has plans to evaluate its multi-foil insulation packages; to optimize insulation, weight, volume, performance, and cost by testing and evaluating alternative designs and materials; and to develop thermal insulation and application

techniques for heat transmission components in order to provide acceptable tissue interface temperatures and heat fluxes with a minimal increase in weight and volume.

The site visit team found that Westinghouse has made considerable progress in the research and development associated with multi-foil insulation packages. The reviewers believe that the scientific approach proposed by Westinghouse is appropriate and should result in the development of insulation packages which fulfill the objectives of performance and size reduction. The outgassing studies were felt to be particularly important and should increase the chances of reaching such objectives. Studies of "getter" materials were also judged appropriate because an appropriate gettering system must be developed to establish a positive long-life static vacuum insulation package. Research on insulation to protect tissue from the warm outer casing has consisted of performance tests on wetted commercially available foam insulation. This work is far inferior to the excellent multi-foil high temperature insulation work.

Engine to Pump Coupling

Various approaches to development of a flexible transmission connecting the engine to the blood pumps have been investigated. These include flexible shafts with solid or wound wire cores, bellows, and universal joints. Of these, the wound wire core was chosen as the best approach. Life testing has been performed using pulsatile torque with a 6-inch radius of curvature (30°) applied to the shaft. Tests to date include

80 days at the expected maximum torque (24 inch-ounce) and 150 additional days at 3 times expected torque. There was some doubt that a shaft flexible enough for human comfort can be developed to last the 5-10 years desired. Because the flexible shaft is crucial to the present design the committee believes that alternative concepts should be encouraged by issuing RFPs for short studies which would serve to demonstrate which ideas are most promising.

Specific Recommendations for the Engine and Coupling Programs

1. Because the engine development program has progressed to the point where design performance over a time period that is a substantial fraction of the target operating time of 10 years is to be evaluated, much greater emphasis should now be placed on reliability analysis and identification of the life-limiting aspects of the design, with particular emphasis on (1) the engine's displacer piston (2) the engine's seals, and (3) the flexible coupling.
2. Excellent progress in vacuum insulation should be consolidated by a more careful analysis of lifetime requirements including, as discussed in the foregoing text, long-term outgassing characteristics, and adequate "getters."
3. A more sophisticated analytical approach should be taken to the design of insulation placed between the casing and tissue.

4. Flexible coupling designs currently under development suggest continuing uncertainties with this aspect of the mechanical system. It is suggested that additional effort, possibly using additional contractors and substantially different approaches, be expended.

BLOOD PUMP

The blood pump proper of the ERDA artificial heart consists of a pair of elastomeric sacs ("ventricles"), each with a blood inlet and blood outlet, and both usually equipped with prosthetic heart valves. The ventricles are alternately compressed by pusher cups and are thus different from sac systems in which compression is effected pneumatically or hydraulically. To adjust for inevitable mismatch between flows of the two ventricles, their filling has been made to depend upon inlet pressure, a feature that requires each ventricle to be suspended in a highly compliant medium. Ventricle design, fabrication, and evaluation have been the responsibility of contractees at the University of Utah. Problems surrounding ventricle development include basic performance as a pump; control, especially the maintenance of a compliant ambient; thromboresistance; fatigue resistance; and achievement of efficiency such that the system provides sufficient fluid energy from the power delivered by the drive system. These problems are the most difficult in the entire project to separate and to treat rationally. Their successful solution appears to require intensive interaction among surgeons, biological scientists, and engineers, and is highly dependent upon improvements in biomaterials. Progress toward solution of each of these problems is considered below.

Basic Performance as a Pump A system with adequate basic pumping performance has been demonstrated. Ventricles that act in coordination with artificial heart valves, or more recently and with greater efficiency using natural heart valves left in situ, have functioned satisfactorily. How broadly useful the latter approach will be in a clinical setting remains to be established.

Control Control has not been a problem with these devices, but the relatively short-term tests conducted so far do not constitute an adequate evaluation, and known tendencies for scar tissue to form on implanted materials suggest that this problem may be very serious in longer-term applications. Further effort in design, materials selection, and testing is required.

Thromboresistance While the extent to which this problem has been solved for heart prostheses has been the subject of some controversy in the scientific community, the committee is convinced that greater resistance to thrombosis and embolism is required for adequate long-term performance. Thromboresistance is achieved through a combination of the flow pattern (which is in turn dependent upon ventricle geometry during the pumping cycle) and the material. Very significant effects may occur at the valves as well as within the ventricles. These factors are poorly understood both in general and in the particular situation under consideration here. No effort has been made to visualize flow or to calculate local fluid stresses in ERDA ventricle designs, although

such a study is possible and appropriate. Efforts have been made to analyze deposition of blood constituents on ventricles obtained at autopsy, and some information believed relevant to thromboresistance is available for the three materials from which ERDA ventricles have been fabricated (silicone rubber, "Avcothane," and "Biomer" segmented polyurethane). The choice of ventricle material appears never to have been a carefully constructed decision by top managers of the program.

Fatigue Resistance Tests of fatigue resistance have recently begun at Utah. Committee reviewers felt, however, that the test program as presently planned will be of limited utility because (1) the actual stress distribution in a working ventricle, although easily measurable, has never been obtained or estimated; (2) the in vivo environment (blood components on one side, oil on the other) may not be adequately simulated; and, (3) those planning and conducting the tests may not have adequate knowledge of, or ability effectively to apply, theory pertinent to fatigue testing of elastomeric materials.

Efficiency Achievement of design levels of efficiency of conversion of mechanical to fluid energy is important to stabilization of other factors in system design. Further effort is required to establish (1) peak energy levels required; (2) the practicality of using autologous valves in situ rather than less efficient prosthetic valves; and (3) the role of valve, ventricle, and valve-ventricle interactions in determining efficiency.

Alternative pumps Aside from the ventricle mechanically driven by pusher plates other blood pump designs should be considered. Centrifugal pumps of several designs are being explored as left ventricular assist devices (LVAD) with the capacity to pump the entire output of the left ventricle. Pumps intended for left ventricular assistance, as described by Bernhard and Norman, have blood interface surfaces specifically designed to encourage the laying down of a tenacious, thin, flexible blood coagulum which appears to be stable in the hydrodynamic designs described by these authors. They are presently being installed between the apex of the left ventricle and the descending aorta. Two such pumps might well be used as a left and right ventricular bypass for a total artificial heart. In such a circuit the pump could be closely coupled to the Stirling engine (indeed, of all the implantable nuclear engines under development, only the Philips-Stirling engine, with its mechanical output, is capable of powering the centrifugal pump.) The use of a centrifugal pump would likely circumvent several of the problems that may limit the lifetime of the present ERDA artificial heart:

1. Close coupling would eliminate the need for the flexible shaft.
2. The pump, made of rigid materials, eliminates the flexing ventricle membrane and its associated longevity problem, as well as the need for a compliant outer membrane.

3. Control is simple: experience indicates that aortic pressure is a function of rotor speed; at fixed rotor speed aortic pressure can be maintained constant over a wide range of flow rates.
4. Power requirements are estimated at 3 to 4 watts mechanical.
5. The outlet scroll of the pump offers a convenient heat rejection region, with local heat transfer coefficients of $2 \text{ watts/cm}^2 \text{ } ^\circ\text{C}$.

These ventricles are presently designed to be pneumatically or hydraulically driven. Whether these designs could be adapted for coupling to the ERDA plutonium-powered driving system is a question that would have to be carefully explored. The present designs, however, do have the advantage of a significant positive testing history; they have functioned continuously in calves for as long as nine months. Similar designs are presently undergoing tests in a limited clinical trial that calls for temporary use (for up to 2 weeks) in patients.

As a matter of good management these and other alternatives should be periodically reviewed. To give the program a variety of choices, the committee recommends an RFP for short studies of any alternative concepts.

Specific Recommendations for the Blood Pump Program

1. Rational mechanical design of ventricles should be commenced to permit specification of the resting shapes, wall thicknesses, and mechanical properties that will lead to a desired shape-time relationship over the cardiac cycle.
2. Analysis of flow patterns and ventricle-valve interactions should be commenced to clarify and accelerate progress in understanding what ventricle shape-time relationships and valve choices lead to improvements in efficiency and suppression of thrombus formation.
3. Long-term maintenance of the autoregulatory feature of ERDA ventricles depends upon sustained compliance of the outer shell of the ventricle which, in turn, requires that the shell remain free of adhesions. Specific tests to verify that this requirement can be met are recommended.
4. A more consistent and sustained program of testing blood-wetted surfaces of ventricles for thromboresistance is recommended. Tests selected should permit comparison of materials already selected for this service with other biomaterials, including those under development with NHLI sponsorship.
5. A carefully analyzed program for accelerated fatigue testing of ventricle materials in contact with fluids similar physically,

chemically, and biologically to those expected in use (e.g. blood and oil) should be commenced.

6. The recently developed procedure for increasing ventricle efficiency by using cardiac valves left in situ should be analyzed for its applicability to the human population likely to need cardiac replacement. It is recommended that studies of valves be continued using methods more extensive than evaluation of their performance when juxtaposed to natural hearts.
7. Studies of alternative concepts of pump design, including but not limited to those discussed in the foregoing text, are recommended.

BIOMATERIALS

At present one contractor is studying the formation of hydrogels on various substrate polymers as a means of improving blood compatibility. Grafting monomers are hydroxyethyl methacrylate (HEMA), acrylamide (AA), corresponding acids, vinylpyrrolidone, and appropriate cross-linking agents. The hydrogels are produced by irradiation of mixtures of these materials layered onto silicone rubber, polyurethane, polyethylene, and Dacron (as fabric).

The research has shown that, generally, polyacrylamide hydrogels have better thromboresistance than do the HEMA's in in vivo evaluations. In ex vivo evaluations, however, the AA hydrogels reduced the platelet half-life more than did the HEMA hydrogel despite the lower platelet adsorption on AA surfaces. In view of this observation, attention has been turned to acid-containing (e.g., acrylic acid) copolymer hydrogels,

with promising results. Hydrogels are also under investigation as surfaces to enhance cell adhesion for tissue implants. All of these surfaces have been evaluated in vitro at the University of Washington and in vivo at Pacific Northwest Laboratory.

This contract is the sole effort in the ERDA program to develop improved surfaces. The quality of the work is high, and it is of definite scientific interest. Progress is also being made in developing new methods to evaluate the blood compatibility of candidate materials. notably, by measurement of the effect of surfaces on platelet lifetime.

Despite the quality of the research, the committee feels that the probability that this limited effort will produce improved materials for an artificial heart is too small to warrant its continuation after a reasonable period of decreasing effort (about one year). The rationale for this conclusion is that the total of all investigations of hydrogels in this and other laboratories has not produced materials of significant promise and that multiple projects encompassing several phases of biomaterials development are now being pursued here and in other countries.

It is believed that the major contribution that the ERDA program can make in the area of biomaterials is in development of techniques to predict the service life of candidate polymers for the artificial heart. To develop such methods will require detailed consideration of the cyclic stresses and strains occurring in the ventricles and domes of artificial

hearts. These stresses have not been determined, and the committee recommends that this be done as a step not only toward development of an accelerated test method but also toward optimizing the pump design with regard to polymer properties and blood flow.

Because of intensive current research by other agencies in the development of biomaterials and methods of evaluation of blood compatibility, it is recommended that ERDA not fund additional work in these two areas. Rather, full advantage should be taken of past and current research on biomaterials and blood compatibility.

Specific Recommendations for the Biomaterials Program

1. The materials development program at the University of Washington concerned with synthesis and evaluation of hydrogel materials should be terminated within approximately one year. With one exception (see 2 below), other programs involving materials synthesis and development of new evaluation methods should not be undertaken unless they are addressed to a specific need of the ERDA program that is not common to other applications for materials that are required to be blood-compatible.
2. A program for accelerated testing of the fatigue resistance of ventricle materials over extended time periods and in contact with appropriate materials is recommended. The program should take cognizance of the stresses anticipated in the ventricle and the best available theory for predicting the fatigue resistance of elastomers.

3. Arrangements should be made for biomaterials used in this program to be tested by contractors of the NHLI biomaterials program. Whenever possible such tests should be on surfaces fabricated in the same manner as the blood surfaces of ventricles.
4. Post-mortem examination of biomaterials used in test ventricles should continue.
5. Selection of biomaterials used in ventricles should be made at the program level upon recommendation of the concerned contractors.

SYSTEM RELIABILITY

The utilization of an artificial heart will require public acceptance of its long-term reliability. It is clear that the reliability of the artificial heart at a significantly high confidence level cannot be demonstrated by full-scale life test data alone since many such tests would be required. The reliability of components and subsystems will have to be demonstrated with extensive reliance on analyses and accelerated testing. Further, this reliability can be demonstrated only if the designer considers in the early phase of the design the testing that each component must undergo to achieve the required reliability of the total device. Fortunately, proved techniques exist which allow the designer to identify critical areas of the design in the early stages so as to permit extensive testing.

The artificial heart program has utilized a generally accepted reliability methodology. However, uncertainties in the data used for the reliability analyses lead one to question the final results. In addition, it is unclear that a concerted effort exists to develop data which are required for a sophisticated reliability analysis.

Specific Recommendation Concerning System Reliability

Additional emphasis should be placed on reliability engineering, and a program should be developed to evaluate quantitatively the reliability of the total artificial heart system.

PROGRAM MANAGEMENT

This program has a principal and particular goal as well as clear subsidiary goals. We have argued elsewhere that these goals have great social value and are in fact attainable. However, the project is complex and, as with all complex projects concerned with the development of medical devices, requires the coordinated efforts of a wide range of professional and technical disciplines. The following paragraphs summarize the committee's deliberations concerning program management and develop its recommendations for future project management.

No single contractor in the present program possesses both adequate engineering and adequate biomedical skill. Communication between the principal biomedical contractor (University of Utah) and the principal engineering contractor (WANL) was found by the committee to be deficient.

The precise line along which responsibility divides was not clear, and to the extent that it was determinable, was not altogether rationally fixed. Communication between these contractors was substantial as a result of effort from both sides, but large areas of information needed to produce desired results were not adequately developed. For example, as noted in earlier parts of this report Utah has evidenced neither the interest nor the competence to analyze stresses and flow patterns in the elastomer ventricle. The committee judges such analysis to be valuable to the program, particularly in improving reliability of the device. Similar analyses are performed on all mechanical elements under control of the engineering contractors. To take another example: the flexible shaft drive under development at WANL is being tested at a 15° deflection, but no careful, documented evaluation of the actual angles of deflection required for use with humans has been performed. Thus important biological information is lacking in the design of a critical test being performed by an engineering contractor. Many similar examples could be cited.

Specific Recommendation on Program Management

The committee believes that greater effort to actively manage this program is urgently necessary. It strongly recommends that the present contract effort be reorganized under one prime contractor with responsibility for development and demonstration of the ERDA artificial heart system. It also recommends that an ERDA program office be established with not less than three professional persons engaged full-time in monitoring and directing the contract effort. At least one of these professionals

should have competence in biology and medicine. The committee foresees, in addition to the primary contract effort, both a research effort directed by the program office whose goal is understanding of fundamental processes, incomplete understanding of which limits development options and forces undesirable compromises between performance and reliability, and a series of investigations designed to explore specific alternatives to the current design concept assigned to the prime contractor. Several particular projects of this sort have been discussed elsewhere in this report.

**ADDITIONAL POSSIBLE GOALS FOR THE ERDA ARTIFICIAL HEART PROGRAM :
ASSIST DEVICES OTHER THAN THE TOTAL ARTIFICIAL HEART**

It is not too early to consider possible "spin-offs" from the total artificial heart program. One obvious application of the new technology under development in this program is to devices which assist, rather than totally replace, the failing heart.

The development of a number of cardiac assist devices is far advanced, in some cases several years ahead of the artificial heart. The intra-aortic balloon pump and the dynamic aortic patch (both counterpulsating devices that alternately remove volume from the aorta in systole and return it in diastole) have functioned without complications in humans for well in excess of 30 days. Pumps placed in parallel with the left ventricle, including the left atrium to aorta bypass, and the abdominal left ventricular assist device (ALVAD) have also been implanted in humans. In contrast to a replacement device, the biomaterials problem for an

assist device may be greatly simplified because the device itself is so much simpler. Further, reliability and longevity tests are available for several assist devices over long periods of time.

It should be noted that patients who might benefit from improvement in assist device technology would probably not be those who need short-term assistance (e.g., those with low cardiac output immediately following cardiac surgery). For them, external power sources and/or driving mechanisms will continue to prove satisfactory for periods of up to several weeks. There is, however, a large number of persons with marked cardiac disability who are not in that desperate situation in which only cardiac replacement can sustain meaningful life. Cardiologists currently have available only limited approaches to alleviating such disability, and corrective surgery is often impossible.

In all candor we must recognize that the first widespread trials and, we hope, acceptance of artificial devices to aid cardiac function are much more likely to occur in cases where the heart need not be removed, and therefore, where device malfunction might not be catastrophic. For patients less than terminally ill, physicians as well as patients will initially be more likely to accept heart assist devices rather than heart replacement, and a great deal of scientific information about, and popular support for, artificial devices, both of incalculable eventual benefit to the total artificial heart program, are likely to result. The number of

patients who might benefit from an assist device rather than from cardiac replacement is large, if the presumptions are accepted that an assist device would be simpler and probably safer and thus that eligible patients need be less seriously disabled.

There are, of course, dangers in this line of reasoning. The engineering problems in interfacing portions of the artificial heart system--presumably the heat source, engine, and in some cases the transmission apparatus--to any given assist device not originally a part of the development program are formidable. The current tightly disciplined program directed toward a single goal, the total artificial heart, might be jeopardized by efforts directed toward interfacing with many different assist devices. Diversion of resources from the parent artificial heart program would be unfortunate and must be avoided.

Finally, the benefits and risks of long-term cardiac assistance (as opposed to replacement) need more study. It is possible that assist devices may be unequal to the task of maintaining meaningful life over any reasonable time period, and thus premature reliance on assist devices might raise false hopes, subject patients to surgery and expense for little reason, and waste developmental time, money, and effort that would otherwise have gone to the total artificial heart program.

Specific Recommendation Concerning Additional Goals

On balance, the committee believes that it would be worthwhile to study the possibility of applying portions of the artificial heart technology

to other cardiac assist devices in advanced stages of development. Any such work should be in addition to, not a diversion from, resources allocated to the artificial heart program. Since NHLI is devoting considerable resources to development of assist devices, the ERDA effort should continue to be directed primarily toward the total artificial heart.

OVERALL RECOMMENDATIONS

A careful and extensive review of the ERDA artificial heart effort over the past few years reveals a record of genuine accomplishment. It is the only program dedicated to such a goal and we strongly urge its continuation. Although the engineering problems are far from completely solved, clear and steady progress has been made in reducing their number.

The review group unanimously believed that it was of the utmost importance that some reasonable continuity of funding for this effort be guaranteed. The on-again, off-again nature of the funding in the recent past has been detrimental. It has eroded the eagerness and enthusiasm of the groups involved, encouraged the drifting away of talent from the program, and discouraged the recruitment of other talented workers because of the unnecessary insecurity associated with the effort. The group was firmly convinced that continuous funding for a period of 3 to 5 years would bring the program close enough to achievement of crucial goals that a review at that time would clearly show the value of further efforts. If intermediate goals of exploring the usefulness of the already developed technology of the ERDA power drive system with assist devices are to

be met, increased funding will be necessary. It was clearly the feeling of the review group that such programs should be implemented with increased funding and not at the expense of the total artificial heart program as originally envisaged. To support the new efforts described herein funding would probably have to be increased approximately 50 percent above the present level.

The necessity for improved coordination between ERDA and NHLI cannot be overemphasized. Even though there is communication between the two programs, it appears to be very informal, and in many instances, findings in one program do not reach the other program for one or two years because of administrative difficulties. The review committee therefore recommends the formation of an NHLI-ERDA joint artificial heart advisory committee which could identify areas where interagency cooperation would be fruitful. For example, NHLI might well benefit from the ERDA expertise in the physical sciences just as ERDA might well find the NHLI experience in the biological and medical sciences of considerable help.

However, it is also recommended that the programs be independently managed so that neither is dependent for its basic success upon the success of the other. The committee feels that a major advantage of the ERDA program is the long experience of ERDA staff with product-oriented contract research with a strong physical science component, and that this experience is important in assuring successful completion of a project of this nature.

The technical and engineering capabilities of ERDA should be available to other governmental programs and more use should be made of them.

Representatives of the ERDA artificial heart program would undoubtedly lend strength to conferences at which information and technical details are exchanged, and should be invited to participate, for instance, in collaborative efforts involving Soviet and European artificial heart programs.

Finally, the review committee believes that the major obstacle to further progress in the program is the physical limitations of the Utah animal testing group. Under the dynamic leadership of Dr. Willem Kolff, this group has done an outstanding job. Its efforts were carefully studied by a site review group which visited Salt Lake City on February 5 and 6, 1976. The site reviewer's report clearly demonstrates the confidence that the reviewers had in the Salt Lake City effort. Nevertheless, the animal testing facility remains one of the weak spots of the program because of its limited capacity to perform the number of detailed tests required to set and reset the blood pump specifications. It was the unanimous feeling of the review group that there be no decrease in the effort at the Salt Lake City testing area, but that the development of a second testing group of high caliber be encouraged at some other site. Since animal testing of the implanted blood pump remains the final common path to the achievement of this goal, it seems that some duplication of effort in this area is highly desirable. There are several groups throughout the country which could be encouraged to take part in the ERDA artificial heart effort.

Respectfully submitted,

Adrian Kantrowitz, M.D.,
Committee Chairman

SUMMARY

The major conclusions of the ERDA Artificial Heart Program Workshop are that the concept of a biologically compatible mechanical device which can totally replace the heart is sound, that such a device is needed for many patients as an alternative to cardiac transplantation and that its development is a realistic goal.

The committee has made recommendations which it believes will lead to more effective use of funds available. The major recommendation is that an ERDA program with primary orientation toward development of a total heart replacement should continue, with assured funding about 50% higher than at present, for a minimum of 3 additional years at which time another major review should take place. This recommendation is made in full cognizance of: (1) a related program in the National Institutes of Health, (2) some doubts about the social acceptance of the nuclear heat source on which this device depends, (3) some uncertainty that present engineering concepts can be fully realized, (4) continuing discussion about the medical need for a total artificial heart, and (5) competition of other worthy projects for these funds. The full report addresses these points.

The committee recommends that improved coordination between ERDA and NHLI be achieved by the formation of a joint artificial heart advisory committee. However, it also recommends that the programs be independently managed so that neither will be dependent upon the other for its ultimate success.

It was the unanimous feeling of the review group that the capacity for animal testing should be expanded by the establishment of a second testing facility at a site other than Salt Lake City.

Specific comments about various aspects of the program are summarized as follows:

Nuclear Heat Source: The advantages of the plutonium-238 heat source are thought to outweigh the risks associated with its use, and this is the energy source of present choice. The committee is of the opinion that the qualification and licensing of the energy source can be advanced by making fundamental changes in organization which are specified in the body of the report.

Engine: The work on the engine by Philips and on the foil insulation by Westinghouse is judged to be good, but certain potential difficulties should receive more attention. It is recommended that requests for proposals be issued for further study of the engine to pump coupling.

Blood pump: The mechanical performance of the pump now being tested is believed to be adequate but its performance as part of a living system has not been adequately assessed. Further major efforts in design, materials selection, and testing are required to produce a pump suitable for long-term use. It is recommended that requests for proposals be issued for short studies of alternative concepts which might broaden the variety of pump choices available.

Biomaterials: While the quality of ERDA sponsored research on biomaterials has been quite high, the scope of the effort has been very limited and its continuation is thought to be unjustified. The committee recommends that in the future the ERDA program focus its efforts on development of techniques to predict the service life of candidate materials developed elsewhere.

System Reliability: It is believed that the artificial heart program has utilized a generally accepted reliability methodology, but it is recommended that increased emphasis be placed on reliability engineering and that a concerted effort be made to develop data required for a sophisticated reliability analysis.

Program Management: The committee believes that better management of the program is imperative and that, to establish better liaison between its biological and engineering aspects, the present contract effort should be reorganized under one prime contractor with responsibility for development and demonstration of the ERDA artificial heart system. It also recommends that an ERDA program office be established with not less than three professional persons engaged full-time in monitoring and direction of the contract effort. At least one of these professionals should have competence in biology and medicine. It also recommends that research and the evaluation of alternative concepts be managed by the program office so as not to broaden or confuse the mission of the prime contractor mentioned above.

Additional Goals: The committee feels that it would be worthwhile to study the possibility of applying portions of the artificial heart technology to other cardiac assist devices in advanced stages of development. Any such work should be an addition to, not a diversion from, resources allocated to the artificial heart program.