

Special Article—

**ORTHOTOPIC CARDIAC PROSTHESIS: PRELIMINARY
EXPERIMENTS IN ANIMALS WITH
BIVENTRICULAR ARTIFICIAL HEART***

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The high incidence and fatality rates of heart disease, and our lack of
knowledge of its cause and prevention, point up the need for a mechanical
substitute to maintain circulation in patients with irreversible cardiac fail-
ure. More than a decade ago, one of us (M.E.D.) first became interested in
the development of an artificial heart. The first implantation of an artificial
ventricle in a human being took place in July, 1963, under the senior auth-
or's direction.⁷ Recognizing the need for collaboration of biologic and phy-
sical scientists to design a mechanical substitute for the natural heart, he
enlisted the aid of engineering scientists to assist in this project. Since 1964,
the artificial heart research teams of Baylor College of Medicine and Rice
University have collaborated in a formal research program for development
of a mechanical device to replace the human heart.

Initially, attention was focused on total cardiac replacement,^{5,11} but a
number of problems not immediately soluble and the fact that many cardiac
patients need only temporary cardiac support during the critical recuperative
period after cardiac damage redirected our attention to development of
a pump for support of the failing left ventricle.^{6,10} This research resulted in
the left ventricular bypass pump, which proved safe and effective in tests on
a large series of animals.^{7,10} In 1966, its clinical effectiveness was demon-
strated in a series of patients critically ill with heart failure,^{2,3} and success
with this device prompted resumption of our work in development of a
pump for total cardiac replacement. The left ventricular bypass pump and
our previous use of the biventricular bypass led us to consider design of a
biventricular pump for human orthotopic implantation.

With the first human cardiac transplantation late in 1967, the need for
development of an artificial heart, at least for temporary use, became more
urgent,¹ and we therefore began concentrating on development of a biven-
tricular artificial heart. By September, 1968, the design of such a heart had
been completed (Fig. 1).

MATERIALS AND METHODS

A pneumatically controlled, biventricular cardiac prosthesis was de-

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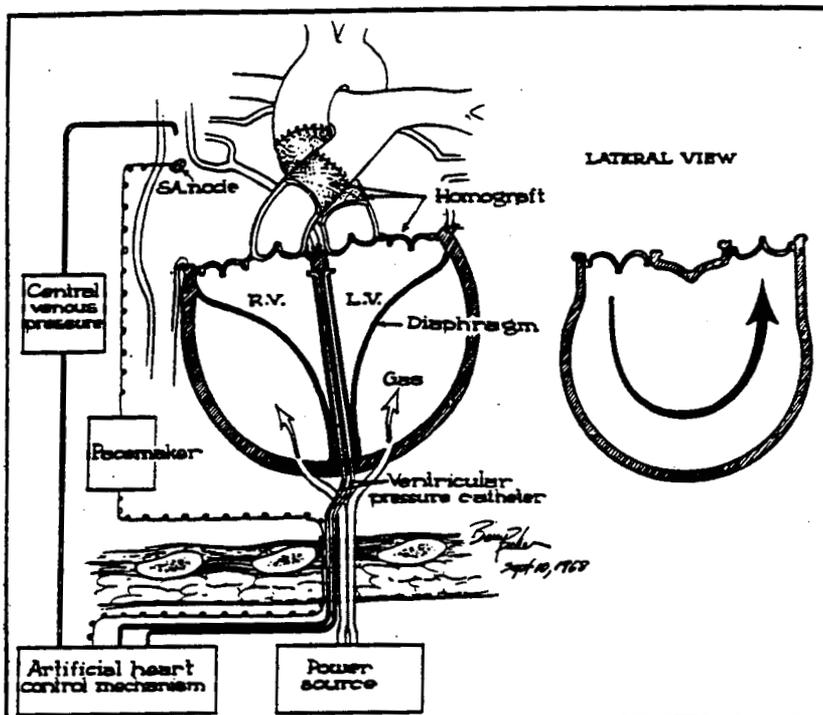


Figure 1a. Schematic drawing (Sept. 10, 1968) showing design of bivalent artificial heart in which homograft valves were to be used.

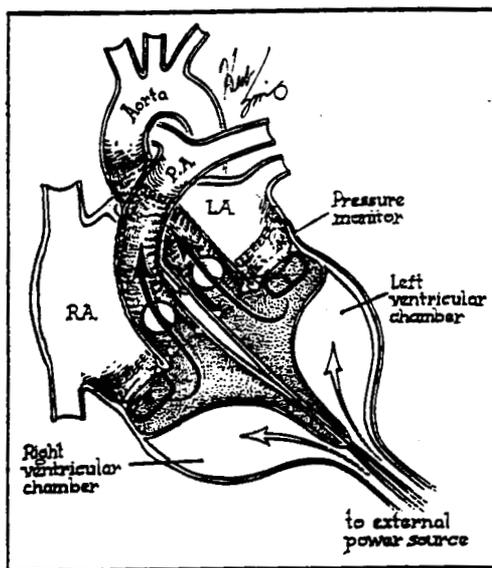


Figure 1b. Schematic drawing showing later design of bivalent pump in which prosthetic valves were to be used.

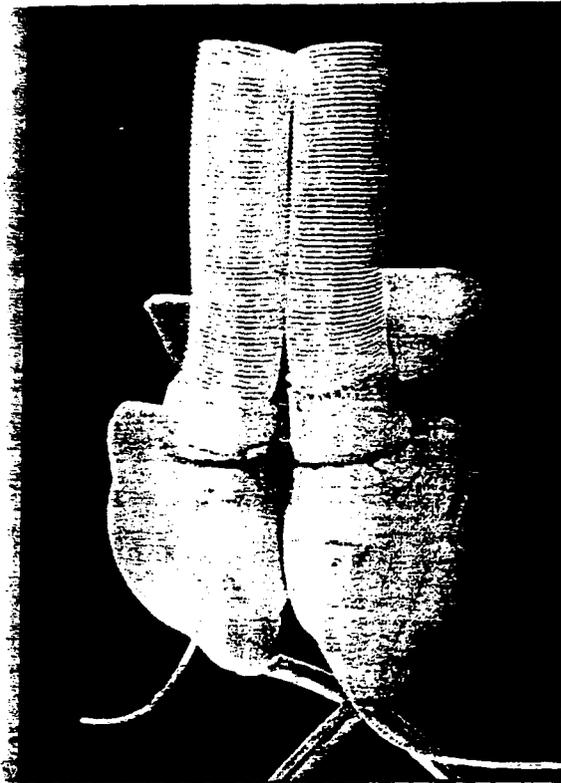


Figure 2a. Photograph of biventricular artificial heart. Anterior view.

signed as a direct outgrowth of the single ventricle pump, and in September, 1968, the experimental model was ready to be fabricated for study, in animals, of the control mechanism required for maintaining proper balance of both pulmonary and systemic circulation and adequate cardiac output and perfusion during total mechanical replacement of the heart. For this purpose, particular attention was directed toward left atrial pressure, as a result of previous experience with the left ventricular bypass procedure.^{2,3} In addition, other hemodynamic phenomena were measured, including particularly cardiac output with use of an electromagnetic flowmeter, right atrial pressure, and systemic arterial pressure.

Description of Biventricular Artificial Heart

Pump Unit.—The right and left ventricles of this biventricular heart model, which is a diaphragm design, are fabricated of impervious Dacron embedded in Silastic[®]** (Figs. 2 and 3). Each of the two separate units contains a valve between the atrioventricular chamber and the outflow chamber (Fig. 3). Silastic tubing connected to each ventricle and brought through

** Dow-Corning Corporation, Midland, Michigan.

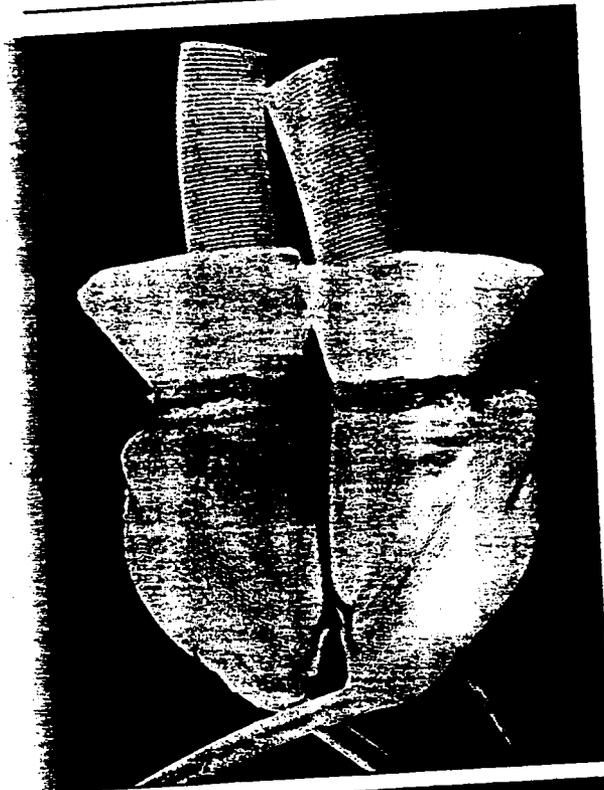


Figure 2b. Photograph of biventricular artificial heart. Posterior view.

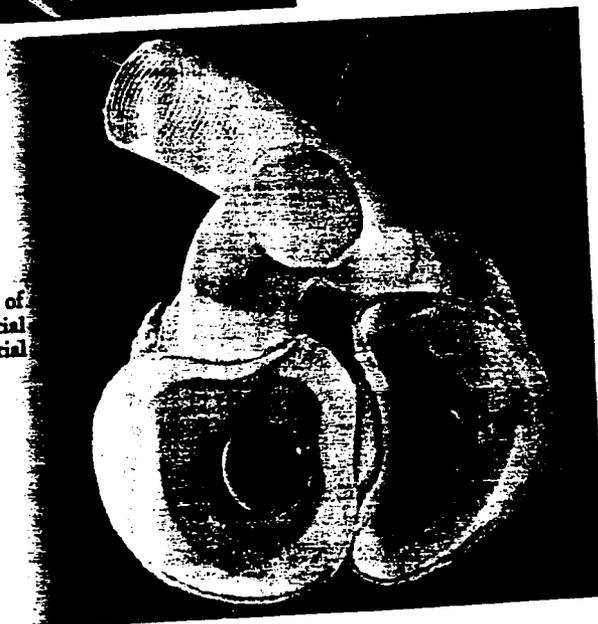


Figure 2c. Photograph of the biventricular artificial heart, showing the atrial cuffs.



Figure 2d. Photograph of biventricular artificial heart, showing attachments to calf's aorta and pulmonary artery, as observed at postmortem examination.

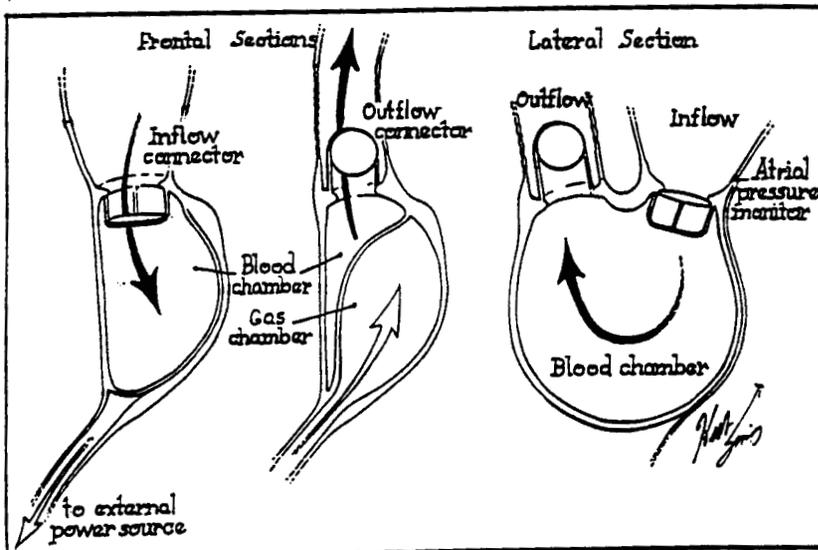


Figure 3. Drawing showing design of ventricle and outflow connector with mobile diaphragm separating gas chambers.

an intercostal space provides a pathway for pulsing the diaphragm by attachment to the two external pneumatic power units. A separate pressure line attached to the left atrial chamber permits continuous monitoring of atrial pressure (Fig. 3). A whirling motion of the blood during diastole, produced by the positions of the inflow and outflow connectors, assures a constant flux in the region of the apex.²⁴

Previous tests of paracorporeal bypass systems in animals and *in vitro* flow studies showed that potential stagnation of blood is reduced by the large radius of the apex of the pump, which is determined by the diameter of the round diaphragm.²⁴ In previous experiments in which fabric-lined pumps were implanted in dogs, we observed formation of thin neo-endocardium in the vicinity of the apex of the pumps.^{12,18}

Special Dacron reticular fabric† is used to line the pump chamber, as well as the inflow and outflow tracts, to enhance formation of an autologous blood interface. Experience with long-term implants of Dacron arterial grafts had shown that an internal lining readily develops that simulates normal arterial intima histologically and functionally⁸. This experience led, in 1963, to studies of the possible value of such a lining in blood pumps. Initially, a loose knitted Dacron fabric was used to line a tubular diaphragm pump. The Dacron was backed with Silastic because the pump had to be impervious to the activating gas pressures. Later, warp-knitted Dacron velour was found to be preferable⁹⁻¹³. The thin, flexible, cuff-shaped inflow tracts are made of impervious Dacron felt and Silastic adhesive. Woven DeBakey arterial grafts‡ (25 mm) are attached to the infundibular-shaped outflow tracts for suturing to the pulmonary artery and ascending aorta.

The individual components of the pump unit—body, dome, and diaphragm—are constructed separately, and the two ventricles of the pump are then bound together with Dacron‡ embedded in Silastic, whereas the diaphragm is made of No. 372, 0.030 Silastic pressed into reticular Dacron to give a total thickness of about 0.045 inch. Molding of this diaphragm in a systolic position (reverse type), rather than the usual diastolic position, reduces stretching of the Silastic at the flexion area when the pneumatic chamber is under pressure.

For maximal durability, the diaphragm must be as thin as possible, to reduce compression and tension of the material. This requirement is complicated by the necessity for material of sufficient strength to withstand the tension exerted on it during normal use.

The durability of the diaphragm depends on other criteria as well, such as a large radius of curvature in the region of flexion, which can be achieved by use of fairly large radius shoulders to capture the diaphragm and limit its excursion. In addition, a fairly uniform thickness of the diaphragm will help eliminate concentration of stress.

† Prepared by Professor Thomas Edman, Philadelphia College of Textiles and Sciences, Philadelphia, Pennsylvania.

‡ U. S. Catheter & Instrument Corporation, Glens Falls, New York.

The diaphragm is attached to the pump unit by a modified "O" ring, which is molded into the rim of the diaphragm and which not only anchors the diaphragm but also seals the halves of the pump.

Three sizes of pumps were fabricated for use in calves weighing 150 to 250 pounds: one with a stroke volume of about 55 ml, one with a stroke volume of about 85 ml, and one with a stroke volume of 95 ml. The systolic residual volume of each is about 40 per cent of the stroke volume.

Power Unit.—The external energizing unit is connected to the intrapericardial pumps by Silastic tubing (5 mm internal diameter) covered with special Dacron. In our previous laboratory and clinical use of the left ventricular bypass pumps, we observed that attachment of surrounding tissue takes place in percutaneous leads covered with Dacron and that later fibrocytes become embedded in this lining to eliminate sinus tract formation.

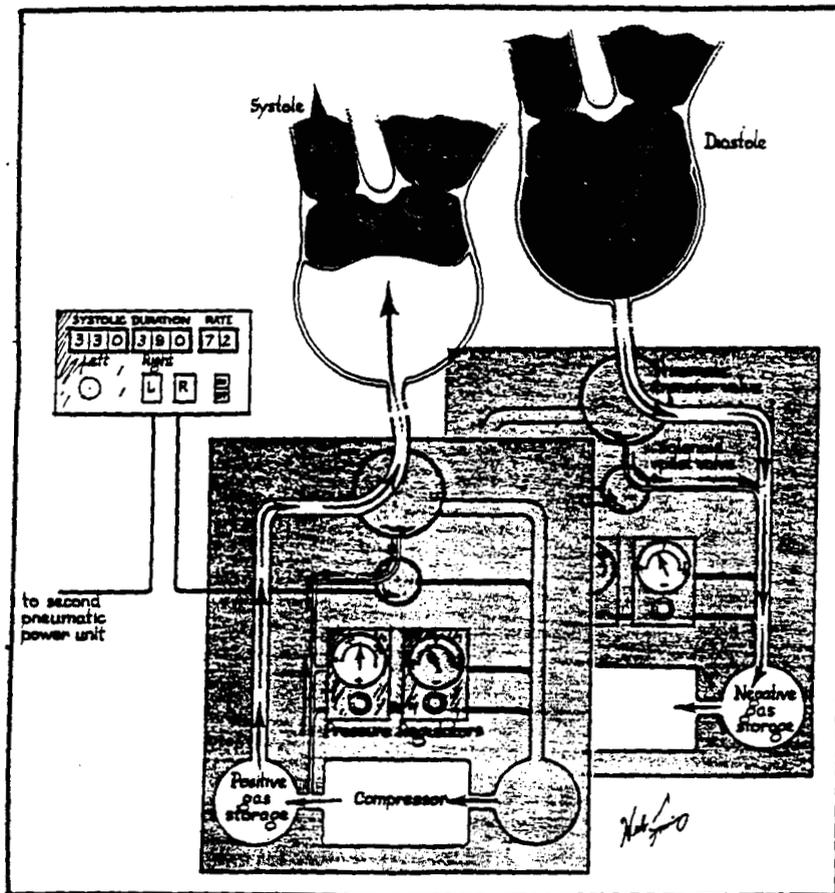


Figure 4. Drawing of dual ventricle power unit and subsystems.

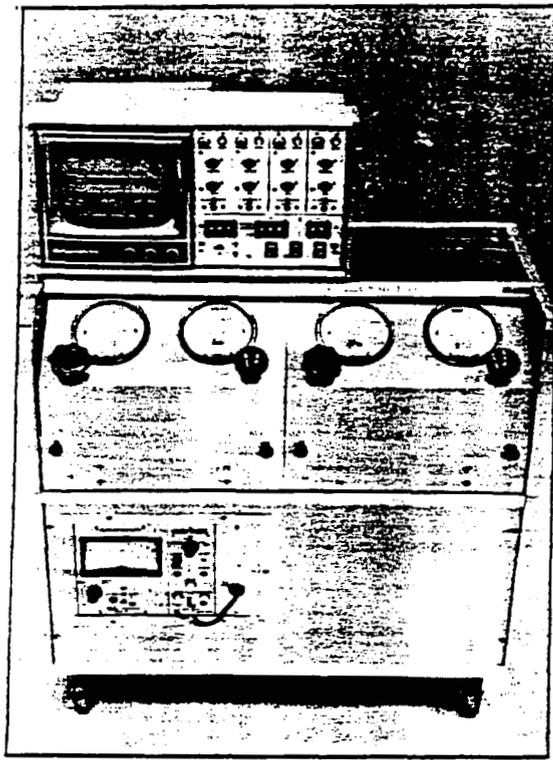


Figure 5. Photograph of the dual ventricle power unit for the biventricular artificial heart.

The dual ventricle power unit (Figs. 4 and 5) has two major subsystems: the pneumatic pressure sources (Fig. 6) and the monitor and control unit (Fig. 7). The two pneumatic power units, each with a motor-driven pump, generate the pressure and vacuum necessary for pulsing the prosthesis. Each of the pneumatic pressure sources consists of a compressor, a pressure (ejection pressure) regulator, a vacuum (filling vacuum) regulator, a pressure gauge, a vacuum gauge, a three-way solenoid pilot valve, and a pneumatic transfer valve. In operation, the ejection pressure and the filling vacuum are connected alternately to the output line by the pneumatic transfer valve. The transfer valve is controlled in the monitor and control unit. The magnitudes of the pressure and vacuum are set manually with the two regulators and are monitored on the precision gauges. Pressure (0–250 mm Hg) and vacuum (0–50 mm Hg) can be adjusted instantaneously by the regulators. A 1/3 hp motor powers the pump in each unit, which requires about 345 va at 115 v 60 hz. The transmitting gas is carbon dioxide. Pulse rate and systolic duration are controlled in the pulse unit, which also provides for synchronization of the two pneumatic sources.

The monitor and control unit consists of a display oscilloscope, four

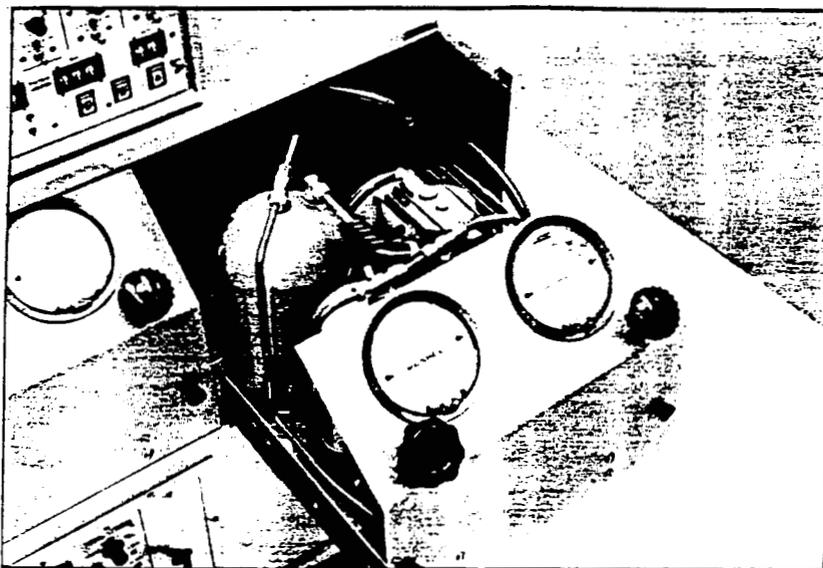


Figure 6. Photograph of one of the two pneumatic pressure sources for the dual ventricle power unit.

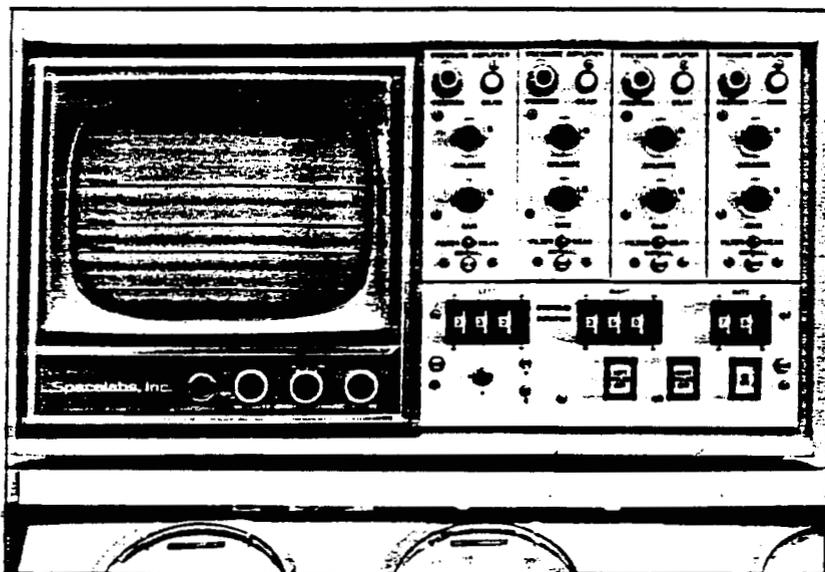


Figure 7. Photograph of monitor and control unit of the dual ventricle power unit.

pressure preamplifiers, and the pulse unit. The basic oscilloscope was modified from a commercial unit. The pressure amplifier and pulse unit were designed at Rice University. The pulse timer unit, consisting of electronic rate and duration circuits, controls the solenoid valve which applies pressure and vacuum, alternately, to the prosthesis. The pulse unit incorporates a relaxation oscillator (rate), adjustable over a range of 20 to 120 pulses per minute, and two monostable multivibrators (right and left systolic duration), adjustable over a range of 100 to 900 milliseconds. The two timers are identical, and one power unit can be triggered or synchronized from the other, an essential feature for a biventricular artificial heart, since the rate and time sequence on both sides must be the same. Direct reading thumb-wheel switches are used to set rate and duration. The pulse unit also contains the main power controls for the system.

Technic of Implantation

The operative technic of orthotopic cardiac replacement with the biventricular pump is similar to that used for allotransplantation of the human heart (Fig. 8). The heart is excised, a posterior cuff of the left and

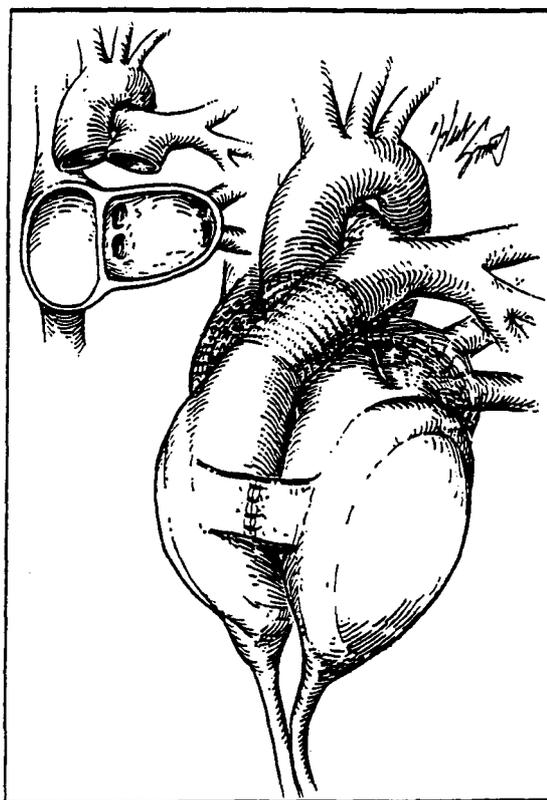


Figure 8. Drawing showing operative technic of implantation of the orthotopic cardiac prosthesis, which is similar to that used for allotransplantation of human heart.

right atria, atrial septum, ascending aorta, and main pulmonary artery of the biologic heart being left in the recipient. The prosthetic heart is attached to the recipient by a continuous suture, beginning with the atria and proceeding around the septum. The aorta and pulmonary artery are joined to the outflow connector from the left and right ventricles, respectively. Air is evacuated from the chambers, and the pumps are energized. This experimental model provides an opportunity to test certain variables of control, including flow, rate, ventricular ejection, atrial pressure, and ventricular pressure.

Animal Experiments

On January 30, 1969, calf experiments with this biventricular pump were begun, to determine the technical feasibility of replacing the heart with this device, to modify the design for proper technical and anatomic application in animals, and to study certain physiologic criteria that might be used in the proper control of the driving mechanism of the pump.

RESULTS

The first four calves in which the pump was implanted died on the operating table because of various technical problems (Table 1). Most important among these was the difficulty encountered in suture anastomosis of the atrial flange, with leakage of blood and air and consequent air embolism. As a result of this experience, the design of the pump was modified to permit better attachment of the device. Thus, in the first animal experiment, incorporation of the two ventricles in a single case caused extreme difficulty in the suture anastomosis of the atrial flange.

TABLE 1.—Results of Implantation of Biventricular Artificial Heart Pump in Seven Calves

(*Department of Surgery, Baylor College of Medicine*)

| CALF NO. | DATE OF IMPLANTATION | DURATION OF EXPERIMENT | FATE OF CALF |
|----------|----------------------|------------------------|---|
| 4578 | 1/30/69 | 59 min | Died on table; technical difficulties. |
| 4576 | 2/3/69 | 67 min | Died on table; technical difficulties. |
| 4582 | 2/13/69 | 47 min | Died on table; technical difficulties. |
| 4583 | 2/20/69 | 50 min | Died on table; rupture of pump diaphragm. |
| 4584 | 2/24/69 | 12.5 hrs | Some reflex movement, but calf unable to stand. Rupture of pump diaphragm. Renal failure; no urinary output during last 8 hrs. |
| 4587 | 3/17/69 | 8 hrs, 25 min | Some reflex movement, but calf unable to stand. Renal failure; no urinary flow. Calf intubated and on resuscitator. Increasing anoxia. |
| 4596 | 3/20/69 | 44 hrs | No reflex movement. No urinary output. Calf virtually cadaver from time of implantation. Calf heparinized and given artificial respiration. |

This procedure was therefore modified by fabrication of the biventricular pump as two separate units, to permit separate attachment of the atrial flanges of the two ventricles to the interatrial septum and the left and right residual atrial walls; after completion of the suture anastomosis of the pulmonary artery and aorta, the two halves of the pump were firmly bonded together by a Dacron attachment. Further modifications in the design and construction of the atrial flange were also made to facilitate suture anastomosis of the atrial walls. These modifications proved to be successful, and in the next three calves, technical application of the pump was satisfactory, but the device did not maintain adequate viability of vital organs in any of these calves.

The fifth calf, which died 12.5 hours after implantation from rupture of the pump diaphragm, showed some reflex movement on stimulation, including spontaneous respiration, but was unable to stand and had progressive renal failure after the first four hours. Despite these observations of inadequate functional viability of vital organs, hemodynamic evidence of pump function in this animal was encouraging. The pressure in the left ventricular pump was maintained at about 150 to 160 mm Hg systolic, and little or no vacuum was required. The systolic duration was 250 milliseconds. The right ventricular pump was energized with a systolic pressure of about 50 mm Hg, and a diastolic pressure of -2 to 4 mm Hg, and the systolic duration was 350 milliseconds. The systolic arterial pressure ranged from 120 to 150 mm Hg, and the diastolic values from 50 to 70 mm Hg. The right atrial pressure was maintained within the range of 4 to 15 cm H₂O, and the left atrial pressure from 3 to 10 mm Hg (Fig. 9). Moreover, for the relatively

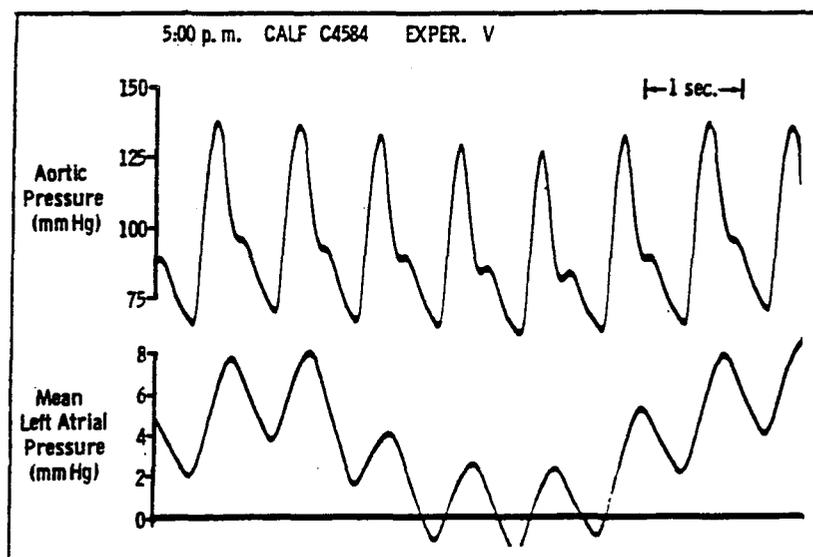


Figure 9. Pressure tracings made in calf experiment with biventricular pump.

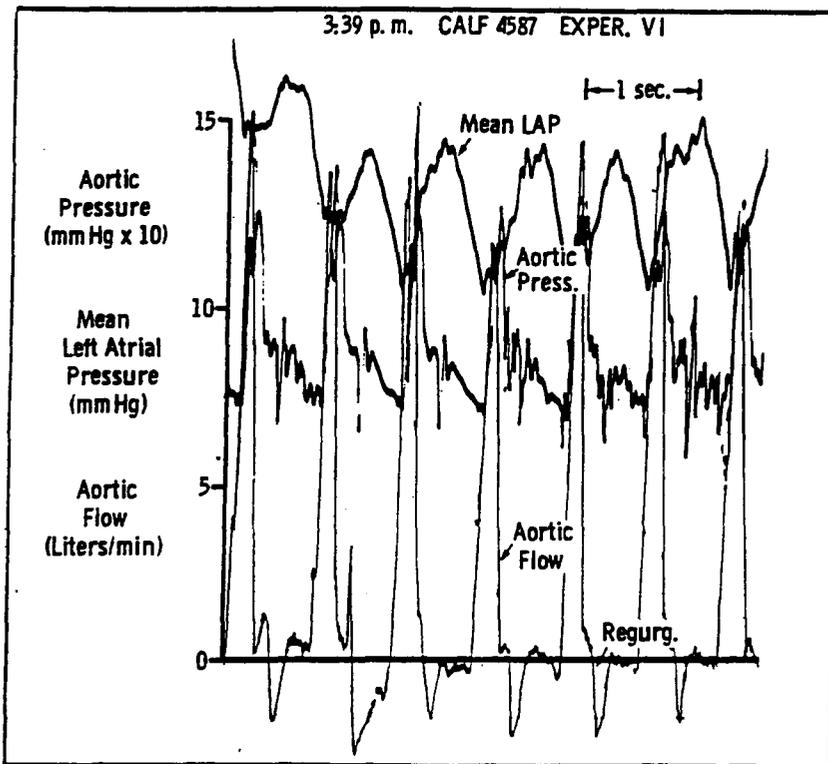


Figure 10. Pressure tracings made in calf experiment with biventricular pump, showing aortic regurgitation.

short duration of this experiment, serial blood gas determinations reflected satisfactory blood oxygenation while the calf was connected to the respirator, and the pO_2 values fell significantly only when the respirator was disconnected.

The sixth calf survived about 8.5 hours; it showed only some reflex movement, was unable to stand, and had complete renal failure. Although the pressures in both the left and right atria, as well as the systemic arterial pressure, were maintained within relatively satisfactory levels (Fig. 10), there was progressive hypoxia and eventual anoxia, with pO_2 values dropping to 38 despite use of the respirator with 100 per cent oxygen. The estimated output of the pump was about 3 liters per minute. These findings suggest that this pump was too small for the calf, and the result was a low output syndrome with high peripheral resistance. In addition, valvular insufficiency was observed.

The last calf in the series showed no evidence of viability from the time the artificial heart was implanted until the experiment was discontinued 44 hours later. The animal was essentially a cadaver, in which the device con-

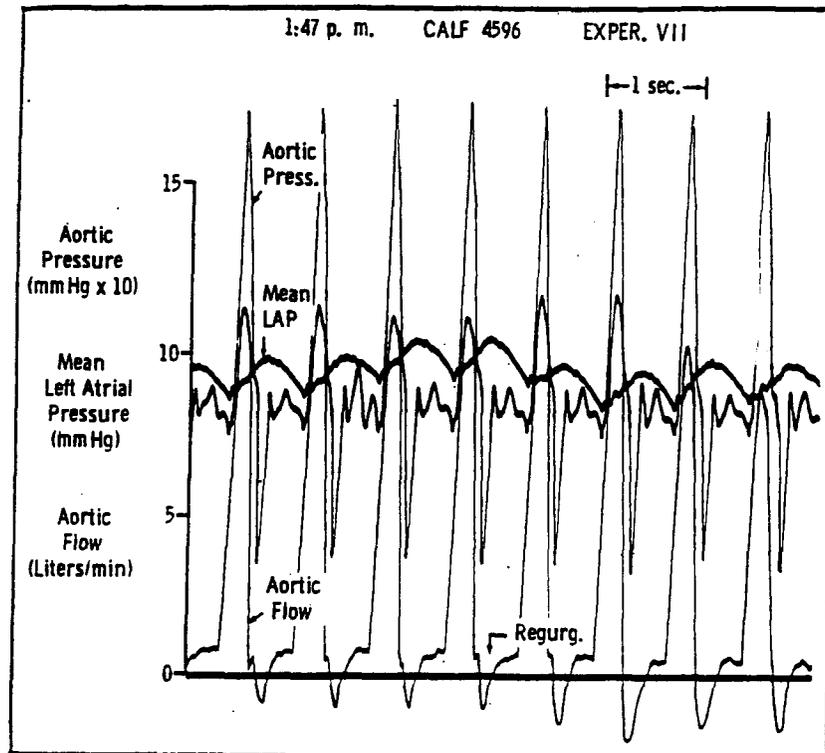


Figure 11. Pressure tracings made in calf experiment with biventricular pump, showing aortic regurgitation.

tinued to pump blood that was anticoagulated by heparin to prolong the testing of the integrity and function of the pump and energizing mechanism. It was possible to maintain reasonably satisfactory systemic arterial pressure, as well as mean left atrial pressure, and satisfactory flow rates, but again valvular insufficiency was observed (Fig. 11).

DISCUSSION

Results of these preliminary experiments suggest that a biventricular pump of this design can be developed to duplicate the function of the two ventricles of the heart, but much work needs to be done before it will be possible to obtain proper control of the mechanism for adequate perfusion and viability of vital organs. Although two calves survived a short time, functional viability was inadequate, and modifications are needed to permit more adequate peripheral perfusion. Further study must therefore be directed toward achieving adequate outflow to sustain functional viability of the organism.

Homograft and heterograft valves (calf and pig), used in the pumps implanted in the first three calves, proved impractical. Because they were difficult to attach and did not provide the proper valvular function, use of

prosthetic valves was resumed. Valving of artificial cardiac prosthetic devices has received considerable attention in our laboratory, but the ideal valve for this purpose has not yet been found.¹⁴ Satisfactory valvular function has, however, been possible with a number of valves, including those used in clinical practice at this time. Wada-Cutter valves were used in the biventricular pump in the last four calf experiments in this series, but these were not entirely satisfactory, as indicated by some evidence of insufficiency (Figs. 10 and 11). Accordingly, other types of valves are now being tested, along with modifications in the pump design for their proper incorporation. Still another feature of the pump design and fabrication that requires further attention is the diaphragm, since rupture of the diaphragm occurred in two of the calves and some evidence of a defect in the attachment was found in another.

Although it was possible to obtain satisfactory pulse wave forms and even adequate arterial pressure levels with maintenance of reasonable normal left and right atrial pressures in a few of the calves for brief periods, these parameters did not provide adequate indices of maintenance of satisfactory circulation and peripheral perfusion. Further studies directed toward this purpose are therefore indicated.

A major obstacle to successful development of a total artificial heart for permanent implantation is the blood interface.⁴ The present experiments have provided no solution to this problem. None of the calves survived long enough to make worthwhile any studies of the potential traumatic effect of the pump on the blood elements. The autologous surface that results from deposits of fibrin on the Dacron lining used in the present biventricular pump model, as observed in previous experiments in animals, was satisfactory for some weeks, although not permanently.^{10,12,13} Earlier experimental and clinical experience with this type of pump, lined with Dacron similar to that of the left ventricular bypass pump, has provided evidence of relatively slight damaging effect on the blood and thromboembolic complications, certainly within tolerable limits, but there is considerable difference in the total pumping effect of the two devices. Because the present experiments were of brief duration, we do not know how long changes in the blood would remain within tolerable limits. If we can prolong the survival time of the animals in current experiments, we shall be able to evaluate better the changes related to blood trauma. The critical importance of such studies is recognized, and will be included in future experiments.

The blood interface problem, then, remains to be solved before total cardiac replacement with an artificial heart can be considered applicable for clinical purposes. Indeed, as may be observed from these preliminary experiments, there remain a number of technical and functional problems with the type of biventricular pump described here that require further experimentation and resolution.

CONCLUSIONS

Preliminary experiments with a pneumatically controlled biventricular

artificial heart for orthotopic implantation in seven calves have been useful in pointing out certain technical and physiologic problems that need to be solved before a satisfactory total mechanical replacement for the human heart can be developed. Human experimentation must await unequivocal evidence of the safety and effectiveness of such a device in animals.

ACKNOWLEDGMENT

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