

Cardiac Assist Devices



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The Surgical Research Laboratory at Sinai Hospital of Detroit has as its primary goal the development of mechanical and biological technics for augmenting or replacing the function of a damaged heart. Scientific contributions from our group include the development of a cardiac pacemaker, a method for electronic control of bladder evacuation, technics for chronic stimulation of nerves, and a method for relieving paralytic ileus. Our dominant interest, though, is in developing methods to overcome circulatory failure.

In 1951, some observations made by my brother and me in experimental investigations performed at Western Reserve University, in Cleveland, Ohio, became the basis of later research. We had found that retarding of the arterial pressure pulse offered a means of increasing perfusion of the coronary arteries. In those experiments, the peak pressure in the central part of the aorta occurred during the diastolic phase of the cardiac cycle. This observation suggested to us the feasibility of augmenting coronary flow and reducing left ventricular work by mechanical means.

In 1955, at Maimonides Hospital in Brooklyn, New York, some of the ramifications of this concept were explored. In devising a means for assisting the chronically failing heart, it was found that the left hemidiaphragm, mobilized and wrapped around the distal segment of the thoracic aorta and stimulated to contract during diastole, could propel blood to the periphery. Although the system worked, it did not take over enough of the work load of the left ventricle to provide effective cardiac assistance.

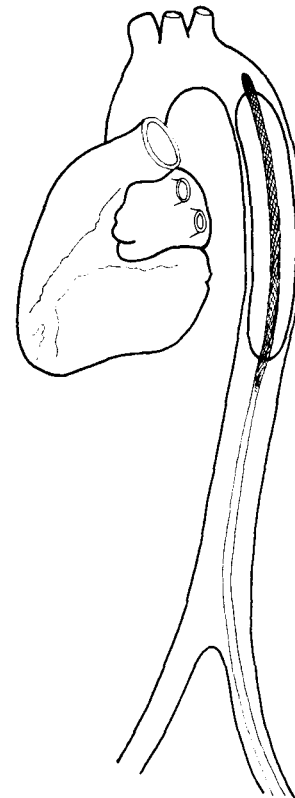
Permanent Ventricular Assistance

We then sought to improve the hemodynamic results by using a prosthesis. Aided by some of the research associates in the laboratory—among them Y. Nose', F. Gradel, P.-A. Chaptal, and T. Akutsu—we studied a series of mechanical systems for augmenting diastolic pressure. A flexible rubber bag inside a rigid housing was implanted in the aorta, and could be compressed by pressurized air so as to divert blood into the coronary and systemic circulation. Working with the Avco Corporation, we found that a U-shaped device implanted across the aortic arch offered the best combination of hemodynamic results and freedom from clot formation. In this configuration the prosthesis consisted of a flexible silicone-rubber inner chamber encased in a rigid fiber glass housing. An air tube connected the space between the outer shell and the silicone-rubber bag to an external control unit. Dacron cuffs were joined to each end of the inner chamber, for connecting the device to the proximal and distal segments of the aorta. The external control unit was adjusted to admit gas to the space between the outer housing and the inner chamber at a predetermined interval after the R wave of the electrocardiogram. After an additional preset interval, the gas was exhausted to the atmosphere.

Laboratory studies confirmed the hemodynamic effectiveness and safety of this mechanical auxiliary ventricle. In typical experiments in dogs with induced heart failure, the auxiliary ventricle reduced the left ventricular work and pressure by averages of 47% and 40%, respectively, while systolic ejection time decreased by an average of 24 m/sec. Aortic flow was increased by 50 to 54%, left ventricular end diastolic pressure returned to normal, and arterial peak pressure during diastole exceeded the natural systolic peak.

Chronic studies demonstrated that the device remained free of clots for as long as 14 months. Tissues surrounding the implanted unit were free of adverse reactions. In collaboration with engineers of the Avco Corporation, we designed an improved external control unit for the system that tests indicated to be highly reliable.

Considering the system as it had been developed to this point, we believed that a limited clinical investigation next was appropriate. Accordingly, two clinical trials of the system were made in 1966. The first patient, a 33-year-old with alcoholic myocarditis and hepatic cirrhosis, had a three-year history of chronic left ventricular failure that had become intractable. The patient withstood well the implantation of the auxiliary ventricle, and when the device was functioning, it supported the blood pressure at reasonable levels and reduced the left ventricular end diastolic pressure. About eight hours after completion of the operation, progressive tachycardia developed which we were not able to control. Hypotension with low cardiac output ensued, and the patient died some 24 hours postoperatively.



BALLOON PUMP IN DESCENDING AORTA

The second patient was a 63-year-old woman also in left ventricular failure, with a history of three myocardial infarctions, diabetes mellitus, peripheral diabetic neuropathy, Kimmelstiel-Wilson syndrome, and chronic pyelonephritis. At the conclusion of the implantation, the device immediately was of hemodynamic benefit.

In the days that followed, the patient did relatively well—she sat up, ate her meals, and visited with her family. The auxiliary ventricle was used only intermittently during this period, so that the heart would not become wholly dependent on the mechanical device. Several episodes of acute pulmonary edema developed when the system was not in use, but these were always resolved with resumption of pumping. Then, suddenly on the twelfth day, the patient died from a cerebrovascular accident. Postmortem examination disclosed a thrombus that had formed inside the prosthesis.

The experience with these two patients appeared to establish that permanent ventricular assistance is clinically feasible. A deviation from the experimental procedure, partial clamping rather than transection of the aorta between the limbs of the unit, had been necessary in the second patient, and possibly accounted for the clotting problem. Nevertheless, it was thought that renewed laboratory work on the system was desirable before resuming clinical trial.

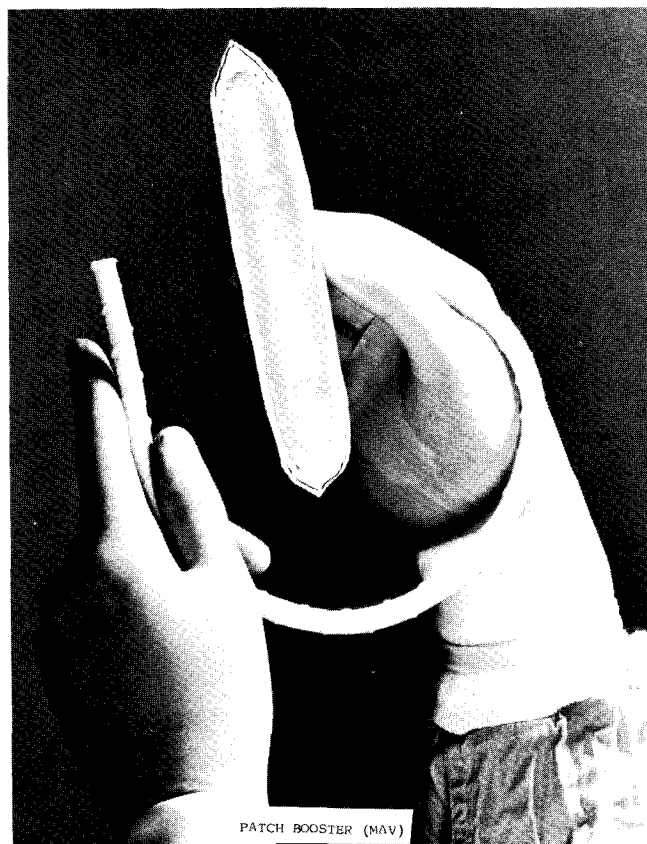
Phase-Shift Balloon Pumping

Soon after the clinical experiences with the mechanical auxiliary ventricle, we focused efforts on another technic of assisted circulation—intraaortic phase-shift balloon pumping. Our modification of a concept described by Mouloupoulos, Topaz, and Kolff included a flexible, cigar-shaped polyurethane balloon or pumping chamber, mounted on an intraarterial catheter, and an extra-corporeal control unit. The balloon, which has a displacement volume of about 33 cc, is threaded through a femoral arteriotomy into the thoracic aorta of the subject. The pumping chamber is inflated with helium during cardiac diastole, and is exhausted to the atmosphere at the end of diastole, providing diastolic augmentation, just as the auxiliary ventricle does.

Our initial experimental results with balloon pumping that was performed in collaboration with research associate W. Schilt, and bioengineer P. Freed, demonstrated dramatic hemodynamic effectiveness of the method. In dogs in experimental cardiogenic shock, the mechanical assistance increased left ventricular and central aortic pressures approximately 13%, and femoral arterial pressure about 14%, above shock levels. In other experiments in dogs in which the coronary artery was ligated, pumping reduced left ventricular end diastolic pressure from 11 mm Hg to nearly control levels, and shortened the duration of systole by 80 m/sec.

Although the balloon pump was not quite so effective as the mechanical auxiliary ventricle, it was quite adequate for circulatory support and it offered the advantage of being a rapidly applied, essentially non-surgical technic. The system, therefore, seemed particularly suitable for patients in acute left ventricular failure, as the pumping could be promptly instituted at the bedside of the patient. In May of 1967 we thought that the technic was ready for clinical evaluation. The initial trials were scheduled to take place in patients in cardiogenic shock, secondary to acute myocardial infarction, who had failed to respond to conventional medical therapy and whose prognosis was considered hopeless by the attending physicians.

The first patient to undergo balloon pumping came to us on June 30, 1967. She was a 45-year-old woman with diabetes mellitus and a five-year history of angina pectoris and dyspnea on exertion, and was admitted to the hospital because of an acute infarct. Congestive failure and shock were present. Her skin was ashen, cold, and clammy; blood pressure and pulse were unobtainable; respirations were labored; and the neck veins markedly distended. The initial central venous pressure was 14 cm H₂O. Moist inspiratory rales were heard in the midscapular region. The electrocardiogram was interpreted as showing an acute myocardial infarct on the posterior wall.



Despite vigorous medical treatment, the patient's condition progressively deteriorated, and five hours after admission to the hospital she was still in shock and was anuric despite the infusion of 9 ampules of Levarterenol in 500 ml of 5% dextrose solution. When her condition deteriorated to the point that the prognosis seemed hopeless, intraaortic balloon pumping was started.

The patient's improvement was dramatic. During pumping, systolic and diastolic pressures improved, and urine output was restored, and increased to an average of 40 ml per hour. After intermittent pumping over a seven-hour period, the patient was hemodynamically stable, cyanosis was alleviated, and her skin was warm, dry, and pink.

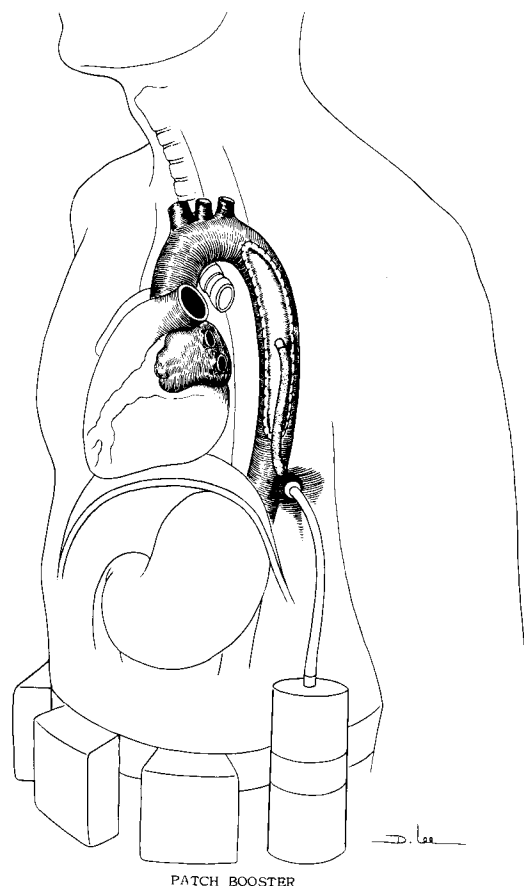
The patient recovered from the infarct, but approximately 19 months after the balloon pumping she died of causes not related to the procedure.

In the three and one-half years since this initial clinical trial, my associates, including Dr. J. Krakauer, Dr. A. Aris, Dr. G. Hines, Dr. C. Titone, Dr. S. Phillips, Dr. D. Jaron, and Mr. P. Freed, and I have treated an additional 29 patients. The results, briefly, have been as follows. Of the total of 30 patients, 20 went into shock relatively soon after development of infarcts—within less than 30 hours. During intraaortic balloon pumping, shock was reversed in 18 patients, or 90% of this group. Fifteen of the patients, or 75%, regained circulatory stabilization and pumping was terminated. Of those patients, 9—45%—went on to recover from the infarcts and were discharged from the hospital.

Of the 10 patients in whom the infarct-shock interval exceeded 30 hours, seven came out of shock during mechanically assisted circulation. Only four patients regained hemodynamic stability, and none survived to be discharged from the hospital. Nevertheless, it was our impression that the circulatory assist procedure improved hemodynamic parameters and prolonged survival, an observation of significance if the diagnosis is correct that such patients, because of the extent of the myocardial damage, require some type of cardiac replacement.

We have resumed clinical studies of intraaortic balloon pumping here at Sinai, with the investigative collaboration of Doctors Rubenfire, Noe, Cascade, Kobernick, Mandell, Whitty, and others. We are continuing to utilize the technic in patients in pharmacologically refractory cardiogenic shock. In addition, preparations are being made to evaluate the prophylactic benefits of the technic in uncomplicated myocardial infarction. Consideration is also being given to the use of balloon pumping in patients in septic shock. To obtain definitive data on the effect of intraaortic balloon pumping on survival of subjects in cardiogenic shock, and also to accelerate acquisition of information on the hemodynamic and metabolic actions of pumping, the Sinai Hospital of Detroit research group is participating in a cooperative study of this modality with investigators from nine other medical centers: Albany Medical Center (Albany, New York), Baylor College of Medicine (Texas Medical Center, Houston, Texas), Peter Bent Brigham Hospital (Boston, Massachusetts), Cedars-Sinai Medical Center (Los Angeles, California), The New York Hospital-Cornell Medical Center (New York, New York), Downstate Medical Center (Brooklyn, New York), Duke University Medical Center (Durham, North Carolina), St. Vincent's Hospital and Medical Center of New York (New York, New York), Barnes Hospital, Washington University School of Medicine (St. Louis, Missouri). All ten centers will follow the same data forms and all data will be coordinated at St. Vincent's Hospital and Medical Center of New York.

Experimental studies are also in progress here. For example, a series of investigations is being performed under the direction of Doctor Jaron to determine all the conditions that are necessary for maximal effectiveness of phase-shift balloon pumping. In an earlier portion of this work it was shown that the phasing of an in-series assist device is a determinant of its hemodynamic effectiveness: maximal hemodynamic benefits were seen when the ventricular afterload phase angle was approximately 180° . These findings are expected to have application in work now being done with the goal of optimizing the assist operation. These and related studies are being pursued with the aid of the recently installed computer made possible by a gift from the Gulton Foundation and a loan from the Sinai Hospital Educational Corporation.



ORTHOTOPIC CARDIAC TRANSPLANTATION

In addition to mechanical approaches to cardiac assistance, our research group is interested in a biological approach, cardiac transplantation. Our work in this area began in 1963, stimulated by the reports of Lower and Shumway, who developed a technic for orthotopic allotransplantation and made a number of contributions to the study of the physiology of the transplanted heart. We were particularly interested in transplantation as a treatment for certain congenital cardiac anomalies, for it seemed clear that a prosthesis the capacity of which would grow with the infant or child would have advantages over one that periodically had to be replaced. Accordingly, a surgical technic utilizing circulatory arrest and profound hypothermia was developed. Over the course of several years, Doctors Y. Kondo, G. Dureau, G. Khalil, Y. Koga, and S. Yagi helped to refine this method in several hundred experiments in puppies. We also studied several methods of preserving cadaver hearts, and performed transplantation in adult dogs during cardiopulmonary bypass.

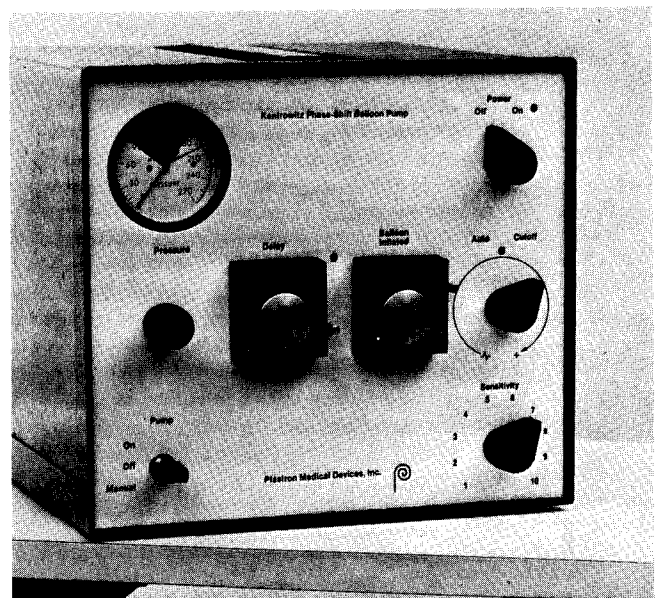
In brief, this experimental work supported several conclusions: (1) An excised donor heart can almost invariably be resuscitated. (2) The risk of transplantation for the recipient can be kept at reasonable levels when a meticulous technic is followed. (3) The rejection reaction can be controlled with drugs in animals reasonably well matched to their grafts. (4) The transplanted heart, although denervated for at least the first 6 to 12 postoperative months, can maintain adequate circulation. (5) The excised cadaver can be resuscitated, its viability maintained, and its condition assessed by means of isolated normothermic coronary perfusion.

The first clinical application of the technic was to be undertaken in the late spring of 1966, on behalf of an infant with pulmonary atresia and patent ductus arteriosus, ventricular and atrial septal defects, and corrected transposition. The potential donor was an anencephalic infant who died on June 30. Our efforts to resuscitate and perfuse the donor heart were unsuccessful, and transplantation was not attempted.

Subsequently, we performed transplantation in an infant diagnosed as having tricuspid atresia with atrial communication. The donor was again an anencephalic baby. The operation was successful, and for the first several postoperative hours the recipient infant responded satisfactorily. Then progressive metabolic and respiratory acidosis rapidly developed, and therapeutic efforts were unavailing. Autopsy disclosed an Ebstein's anomaly in the recipient's own heart, with almost complete obstruction of the right ventricular outflow tract.

Early in January 1968, transplantation was accomplished in a 57-year-old man with severe coronary artery disease, severe ventricular myocardial failure, and moderate pulmonary hypertension. Despite continual medical therapy he was dyspneic at complete bed rest and in severe heart failure. The donor organ was taken from a 29-year-old woman who died as a result of an intracranial catastrophe. Her heart was perfused at 28° C during preparations for cardiopulmonary bypass. At the conclusion of the implantation, signs of heart failure appeared each time that bypass flow was reduced, until for a brief time the heart was able to support the circulation unaided. Because failure then recurred, it was decided to support the heart with phase-shift balloon pumping. Despite this support, the patient died 10-½ hours after the operation.

Although our early clinical trials have not demonstrated the expected potential of the procedure, our laboratory experience has yielded two long-term canine survivors of heart transplantation. The one dog, now 46 months posttransplantation, has, so far as we know, survived longer than any other similarly treated mammal. Postoperatively, this dog grew normally and was in good health until approximately nine months ago, when heart failure developed. The other dog has had a cardiac allograft for some 29 months. Atrio-ventricular block developed soon after the operation and persisted. Several rejection crises occurred and unremitting heart failure developed during the last year. Despite the extremely precarious condition of these animals, Doctors Rubenfire and Cascade were able to perform cardiac catheterization and angiocardiographic studies, the results of which are important in the overall assessment of the courses of the dogs.



PROGRESS OF THE AUXILIARY VENTRICLE: THE DYNAMIC AORTIC PATCH

In the course of further work on the U-shaped mechanical auxiliary ventricle, it occurred to us that one solution to the problem of developing a permanently implanted prosthesis with minimally thrombogenic effects would be a permanent phase-shift balloon pump. Accordingly, while further trials of the U-shaped system are planned, we have developed the dynamic aortic patch as an experimental configuration of the prosthesis.

The patch consists of a cigar-shaped silicone-rubber pumping chamber of approximately 15-ml displacement volume for canine experiments, an air tube emerging from one surface, and prosthetic material covering both surfaces of the pumping chamber. The device is implanted by incising the descending thoracic aorta from the origin of the left subclavian artery to the diaphragm and suturing the covering material to the incision. In effect, the prosthesis is sutured into the wall of the aorta in essentially the same location as the phase-shift balloon pump. Adjustment of inflation and deflation of CO₂ is similar to that for the balloon pump. Preliminary experiments indicated that the hemodynamic effects obtained with the patch closely parallel those due to balloon pumping. The patch thus represents an approach in which a small measure of hemodynamic effectiveness is sacrificed for the potential advantage of freedom from clot formation because the intravascular physiology is minimally modified.

Most of the experimental work with this prosthesis has been directed toward evaluating various materials for the blood interface. Long-term results, obtained with an electronegative material, evaluated by Doctors Kobernick and Mandell, have been particularly encouraging. A portable driving unit for the system has been developed and is now being refined. Such a system may be of sufficient benefit to the patient with severe, chronic, left ventricular heart failure so that he will be able to return to a normal, productive existence.

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