

## Development and Animal Study of a Pediatric Ventricular Assist Device

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*We have developed a pneumatic type ventricular assist device (VAD) for pediatric use and implanted it in six mongrel dogs to study its efficacy and to identify any problems. The diaphragm-type blood pump has a stroke volume of 34 cc. The ventricle of the blood pump was made from polyurethane to enhance antithrombogenesis. The pump was implanted between the left atrium and the descending thoracic aorta and it functioned in a fill-to-empty control mode. The average pump flow rate was 0.41 L/min when the pump rate was 60 bpm. The duration of support ranged from 1 to 26 hours. The hemodynamic effects of the VAD on the heart failure model were monitored. An increase in pump flow rate was indicated in such a deteriorated cardiac function. The most frequent complication was bleeding. The main causes of death were heart failure and respiratory failure. Studies to date suggest that, with further refinement, a more reliable VAD with clinical applications could be developed.*

**Key Words:** Ventricular assist device, animal study, thrombosis

The main purposes for temporary use of a ventricular assist device (VAD) are to maintain normal circulation irrespective of the severity of heart failure and to restore the failing heart by gradually decreasing the bypass flow as the heart recovers (Oaks *et al.* 1991). As well, an increasing number of potential transplant recipients have undergone mechanical circulatory support as a bridge to cardiac transplantation. The scarcity of donor hearts complicates the management of patients with end-stage heart failure who are suitable candidates for transplantation.

Current intraaortic balloon pump and venoarterial bypass are not always efficient and safe because the

former is too large for children and the latter tends to be accompanied by complications (Sabiston and Spenser, 1990). The advent of the VAD was expected to treat pediatric patients after cardiac surgery with profound heart failure refractory to drug therapy. After the first pioneering animal study with blood pumps by Akutsu and Kolff (1958) and the first clinical attempt by Cooley *et al.* (1969), continued research with animal implantation has led to improved design techniques, material selection, and reliability of mechanical components (Pierce *et al.* 1981; Farrar *et al.* 1990; McCarthy *et al.* 1991). Currently, two types of driving system, the pneumatic and electric type VAD, have been used clinically. In the pneumatic type, the action of the blood pump is powered by compressed air while in the electric type, the blood pump is driven by an electromagnetic field or by an electric motor. Commercial manufacture of pediatric VADs (Toyobo, Japan; BerlinHeart, Germany, etc.) has been of the pneumatic type because the electric type blood pump has a limitation in size reduction.

In response to the demand for such a device, we

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developed the pneumatic and diaphragm-type VAD (Kim *et al.* 1993). We selected the pneumatic type because it is more economic to develop and has fewer risks in clinical situations. We tested it *in vitro* and obtained satisfactory results.

This report describes the evaluation of a pediatric VAD under development. The application procedures and physiological performance of the pediatric VAD have been studied in the hope of treating patients effectively and safely because the functional characteristics of pediatric patients are more complex than adults.

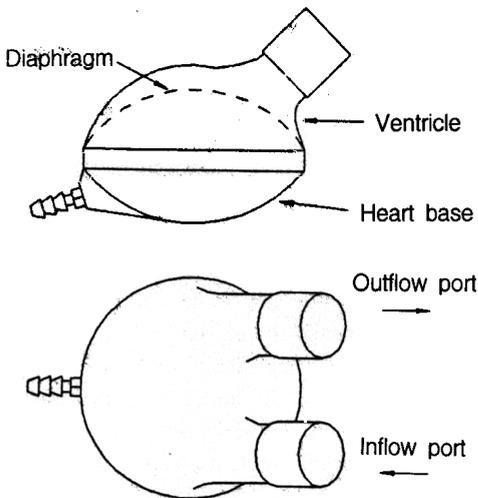


Fig. 1. Schematic view of the blood pump

## MATERIALS AND METHODS

### Description of devices

The pneumatic VAD consists of a blood pump and pneumatic control driver. The blood pump consists of an extremely smooth and seam-free polyurethane diaphragm and ventricle which is enclosed in a rigid epoxy pump base (Fig. 1 and Fig. 2). The diaphragm and ventricle were made by a dip-coating technique with segmented polyurethane (Pellethane<sup>R</sup>, Dow Chemical, Midland, Michigan, U.S.A.). Fig. 3 shows the stainless-steel molds used to make the diaphragm and blood pump for this experiment. Two 23 mm inlet and outlet mechanical valves (Carbomedics, Austin, Texas, U.S.A.) provide unidirectional flow. The blood pump has a stroke volume of 34 ml and is capable of pumping 3.5 L/min with an inlet

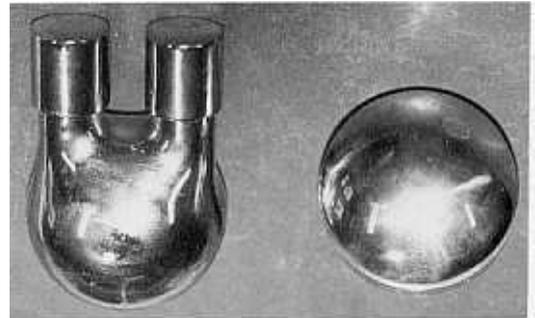


Fig. 3. Metal mould of the diaphragm and ventricle

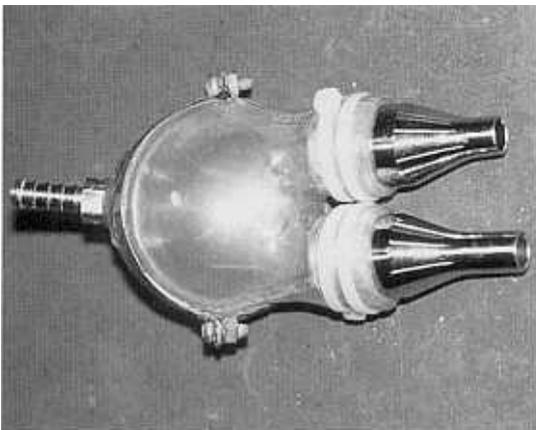


Fig. 2. Pediatric blood pump of the VAD.

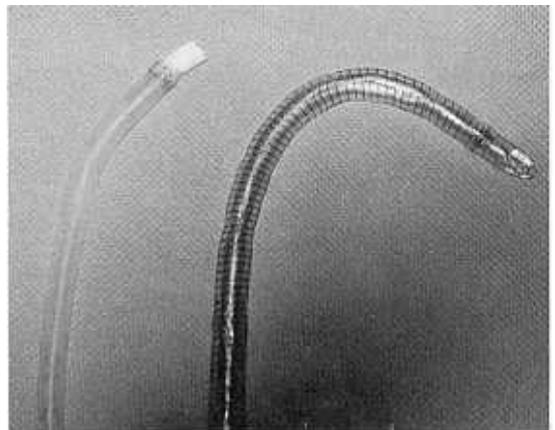


Fig. 4. Conduits used in the VAD animal experiment

pressure of 10 mmHg and an outlet pressure of 120 mmHg (mean). The atrial cannula is a 28F tube (Stockert-Shiley, Irvine, California, U.S.A.) and the aortic cannula is made from 6.4 mm polyethylene tube (Fig. 4). A Dacron graft was made at the end of the polyethylene tube with a polyurethane solution, permitting a standard vascular anastomosis to the aorta. The inner surface of each cannula was coated with polyurethane to reduce blood coagulation.

The blood pump is connected to a pneumatic drive console (Fig. 5) to provide positive pressure during VAD ejection and negative pressure during VAD filling. During the filling phase, the pressure-driving flow in the VAD is assisted by a  $-10$  to  $-50$  mmHg vacuum set on the drive console. The drive pressure during ejection is usually set to at least 200 mmHg to entirely empty the VAD. The pneumatic driver uses pneumatic logic components for controlling the diastolic interval and the duration of each systolic pressure stage. The pneumatic logic elements perform essentially the same functions as digital electric logic. A single chip microcomputer is interfaced with the pneumatic system via solid-state pressure transducers and it displays the driving parameters (heart rate, as well as diastolic and systolic duration). The VAD is operated under a fill-to-empty asynchronous mode which provides a simple but effective method of responding to the flow demands of the body. When the VAD is operating in the fill-to-empty mode, the pump rate multiplied by the stroke volume equals VAD flow.



Fig. 5. Pneumatic control driver

## Animal experiment

Six mongrel dogs weighing 12~18 kg were used for the animal study. The animals were intubated after pentobarbital sodium (700 mg/kg) was administered intramuscularly. Anesthesia was maintained with intermittent injection of pentobarbital sodium. A semi-sterile technique was enforced throughout the operation. A thoracotomy was performed through the left fifth intercostal space. The internal arterial thoracic pressure, left atrial pressure and ECG were monitored. After administration of heparin (200 mg/kg), the blood pump was implanted between the left atrium and the descending aorta. The aortic cannula was anastomosed to the proximal portion of the descending thoracic aorta. A Prolene (5/0) suture was used for the anastomosis. During the procedure, a clamp was partially placed on the aorta to maintain the renal and abdominal blood flow. The curved atrial cannula was inserted into the left atrium. The atrial cuff was used to secure insertion of the cannula. Fig. 6 shows the cannulae after connection. The pump was placed extracorporeally on the chest wall. After confirming the connection of the VAD, the pneumatic control driver started pumping, with special attention paid that the pump was running in a fill-to-empty mode. The aortic root flow and the bypass flow were measured by an ultrasonic blood flow meter (Transonic systems, Ithaca, New York, U.S.A.). Postoperatively, anticoagulation was maintained with heparin (0.1 mg/kg/min). The animals were put to death after the assist pump function ceased.

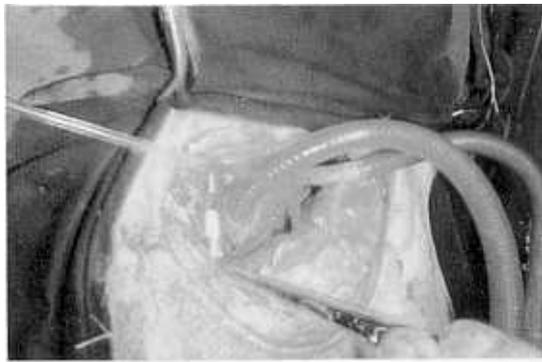


Fig. 6. The inflow and outflow cannulae connected to the heart and aorta

or after we found evidence of a nonremediable illness. Necropsy, pump disassembly, and inspection were performed for each animal.

## RESULTS

In this experiment pediatric VADs were applied to 6 animals. Table 1 lists the weight, pump output, survival, and cause of death for each animal. The body weight of animals was between 12 and 18 kg. The VADs were implanted without difficulty and the perioperative hemodynamic parameters were satisfactory. The average cardiac output was 2.1 L/min before the VAD implantation. The pump output of the VADs varied from 0.21 to 0.55 L/min. The average pump output was 0.41 L/min when the pump rate was maintained at 60 bpm. The pump output was generally low right after starting the VAD and

then it became normal within two hours. With VAD assistance, the animals recovered well from anesthesia and experienced few complications in the course of their VAD connection. Fig. 7 shows a dog in which a VAD was implanted. The first animal had a pump failure after air entered the device through dehiscence between the diaphragm and the ventricle. It was replaced immediately by a new one. A metal ring was added to tighten the connection between the upper ventricle and the pump base to prevent another failure. The second animal survived more than 24 hours. Thrombi were identified at the diaphragm junction and valve junction in the pump despite anticoagulation with heparin. The third animal died of cardiac arrest after massive bleeding because the Dacron graft became detached from the polyethylene tube in the aortic cannula. The graft and tube were then sutured to confirm the connection after it was attached with polyurethane solution. After about six hours the fourth and fifth animals died of excessive intraoperative bleeding which occurred at the suture site of the aorta. The sixth animal could not be weaned from the ventilator because its pulmonary function deteriorated 10 hours post-operatively without demonstrating any improvement in cardiac function.

Table 1. Results of the animal experiment for the VAD

No.	Weight (kg)	Pump output (L/min)	Survival (hours)	Cause of death
1	12	0.42	5	blood pump leakage
2	14	0.55	25	bleeding
3	18	0.21		cannula disruption, arrest
4	15	0.44	6	bleeding
5	13	0.46	6	bleeding
6	16	0.37	19	respiratory failure

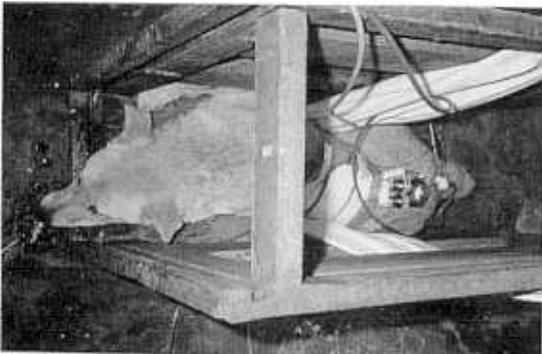


Fig. 7. An animal in which the VAD was implanted.

## DISCUSSION

Our experience with the VAD demonstrated that the device can be implanted with relative ease into animals and that it can provide adequate cardiac output. The pneumatic drive system functioned very well, and the device operated up to 24 hours in vivo without signs of device-related failure. The 34 ml VAD produced physiological cardiac outputs that ranged between 0.21 and 0.55 L/min at a heart rate between 50 and 80 bpm. The potential problem for thrombus formation remains, particularly at the diaphragm junction and valve junctions. Improvements in valve port and ventricle design of the blood pump are required to reduce thrombotic complications. The VAD functioned well in a fill-to-empty mode. This mode was effective in terms of preventing static areas and decreasing the tendency for thrombosis, as well as providing maximum flow to the animal.

Complications related to bleeding were associated with improper management of cannulae. A metal ring attachment to the blood pump and suturing confirmation in the aortic cannula may prevent subsequent failure during future experiments. This experiment has shown that anticoagulation is necessary and that the blood pump should be made extremely carefully to avoid the risk of clot formation, pump failure and embolus. Bleeding was a significant problem in 3 of the 6 animals. The size of the animals was relatively too small to withstand excessive bleeding and to overcome long-term cardiac surgery. To evaluate the hemodynamic effects of VAD on profound heart failure, ligation of the visible left anterior descending coronary artery feeding the left ventricle was performed. An increase in pump output was indicated in such a deteriorated cardiac function. It demonstrated that the left ventricular function of the model was profoundly depressed to the degree that it was neither possible to sustain circulation nor to have spontaneous recovery without the VAD. Further study will be necessary to improve thrombogenicity of the device, and to reduce bleeding before and after the device is implanted. Improvements in the perioperative management of animals will increase postoperative survival and will make it compatible to the survival rate of those receiving commercially-made VAD.

Although we experienced a high number of perioperative problems after implanting the VADs, the results of our experiment were quite encouraging. The VAD in this study has provided an effective means for bridging to cardiac transplantation, particularly in the current setting of donor limitation and the need for prolonged circulatory support. It adequately restored physiologic hemodynamics and assisted normal cardiac function. The pneumatic driver

ran the VAD stably to pump enough blood to the animal. This promising result should lead to further improvements and the eventual development of this VAD for clinical use. This information may also prove to be helpful in the development of permanent assist systems. Continued animal and bench studies will provide additional data on host compatibility and reliability.

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