

# Prolonged partial left heart bypass in sheep: successful use of a new type of pump

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A method of partial left heart bypass is described. A non-pulsatile atraumatic pump capable of handling 2 to 4 litres of blood a minute has been developed and tested. It lends itself to easy adjustment to meet changes in left atrial and systemic pressures and can function for many hours without adjustment. Partial left heart bypass for 24 hours was carried out on sheep. No damage to the blood resulted from its use and air embolism was completely excluded. Initial difficulties associated with 24 hours' anaesthesia were solved by maintaining the animal erect in a cage. In the last series of experiments only one out of 11 sheep had an unexplained death that could have been associated with bypass. The equipment appears to be suitable for clinical trial.

Total cardiopulmonary bypass since the initial pioneer work by Stokes and Gibbon (1950) has evolved as a safe and acceptable procedure for periods of several hours. Attempts materially to prolong this period have so far not proved successful (Fisher and Smyth, 1959; Salisbury, Cross, Rieben, and Lewin, 1960; Connolly, Kountz, and Boyd, 1962; Liotta *et al.*, 1963; Ekeström, Hill and Rådegran, 1964).

Relief of the failing heart by partial bypass or cardiac assistance has been investigated (Spencer, Eiseman, Trinkle, and Rossi, 1965; Galletti, Hopf, and Brecher, 1960) and, in particular, assistance for the left ventricle appears to be clinically demanded. Methods of assistance have included counter pulsation (Clauss *et al.*, 1961), implantable artificial hearts (Kaufman *et al.*, 1968), and indwelling aortic balloons (Brown, Goldfarb, Topaz, and Gott, 1967). Partial bypass of the left heart avoids the use of an oxygenator with its potential damage to the blood (Tooley, Finley, and Gardner, 1961), and direct pumping of oxygenated blood from the left atrium to a systemic vessel presents clear advantages (Dennis, Hall, Moreno, and Senning, 1962b).

We considered that left heart bypass by a suitable method would have a clinical application in the following conditions:

1. acute pulmonary oedema from left heart cause, for example, mitral stenosis in pregnancy ;

2. cardiac infarction with low output syndrome ;  
3. acute mitral incompetence due to spontaneous rupture of a chorda or surgical trauma ;  
4. low output syndrome after technically successful valve surgery.

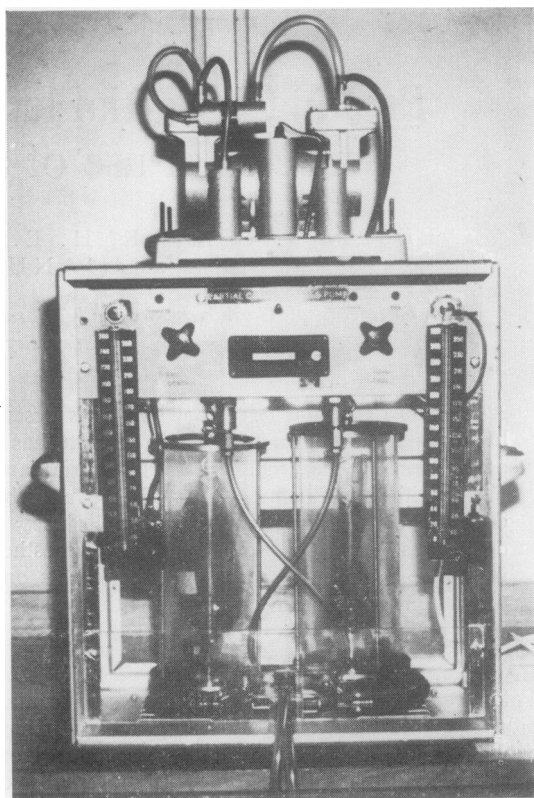
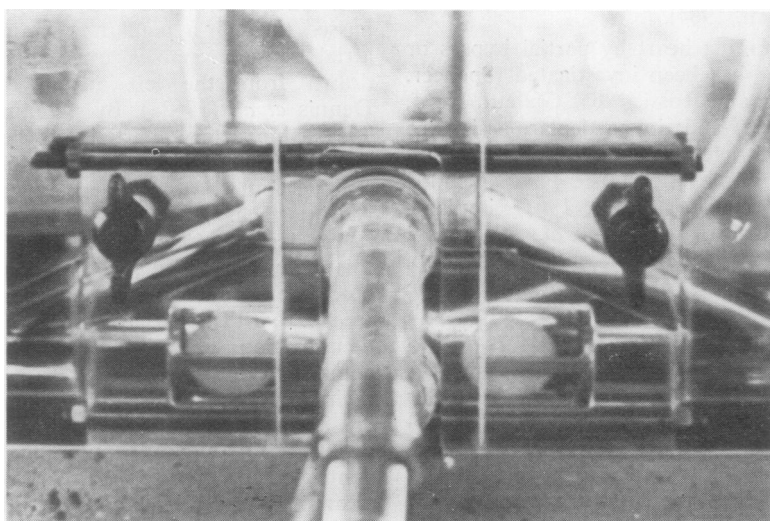
Partial bypass of the left heart clearly is only possible if the right ventricle and lungs can function effectively. The use of a metal cannula passed through a jugular vein and traversing the atrial septum enables oxygenated blood to be drawn from the left atrium as described by Dennis *et al.* (1962a). By pumping this blood to a systemic artery, partial left heart bypass can be established without the need for a thoracotomy and without the use of an oxygenator or blood gas interface.

The length of time any pump can be used in this way is limited by the damage caused to blood constituents, particularly haemolysis, interference with the clotting mechanism, and denaturation of protein. Peristaltic pumps in common use for cardiac bypass work, whatever their individual design, traumatize blood by crushing or shear forces and are therefore inappropriate for long-term pumping. A double-acting ventricle type pump having a low repetition rate allows very gentle blood handling, continuous blood flow, and mechanical simplicity.

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## THE PUMP

The pump (Fig. 1) consists of two 1-litre flexible PVC bags each suspended within a rigid airtight cylindrical chamber. The bags are connected by short lengths of tubing to a valve block (Fig. 2) containing non-return ball valves. To the same valve block are connected a venous line from the left atrial cannula and the arterial return line to the femoral artery. The circuit is shown diagrammatically in Figure 3 (a, b). The two cylinders containing the PVC bags are suspended each from a spring balance which detects whether the bag is full or empty, and from these a signal is transmitted to solenoid valves. By means of these valves positive air pressure is applied to one cylindrical chamber and negative air pressure to the other so that the bag which has just emptied is then subjected to negative pressure in the range 40–50 mmHg and, conversely, the bag which has just filled is subjected to a positive pressure of 100–125 mmHg. Both positive and negative pressures are adjustable to suit the needs of the individual case. The positive air pressure forces blood out of the full bag through the valve block into the femoral artery cannula, thus supplying the aorta with a steady flow of blood, and at the same time the negative air pressure sucks blood out of the atrial cannula into the other bag. When the arterial bag becomes empty

FIG. 1. *The low trauma pump.*FIG. 2. *The valve block.*

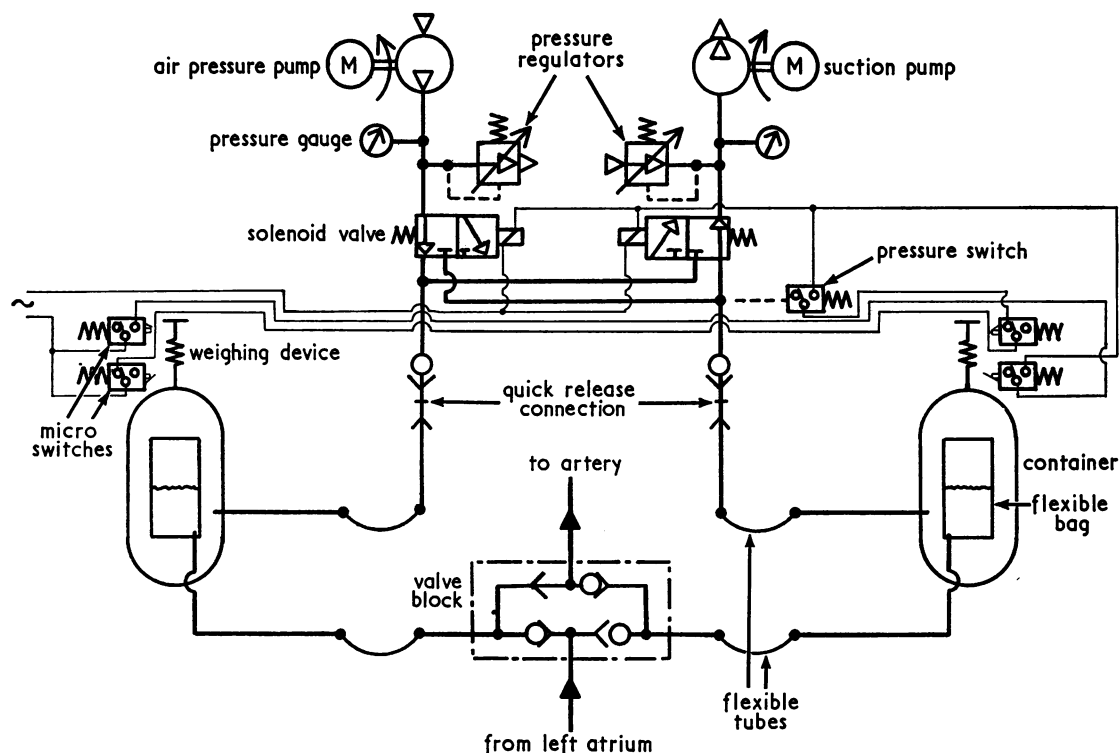


FIG. 3(a). Pneumatic, electrical, and hydraulic circuit diagram.

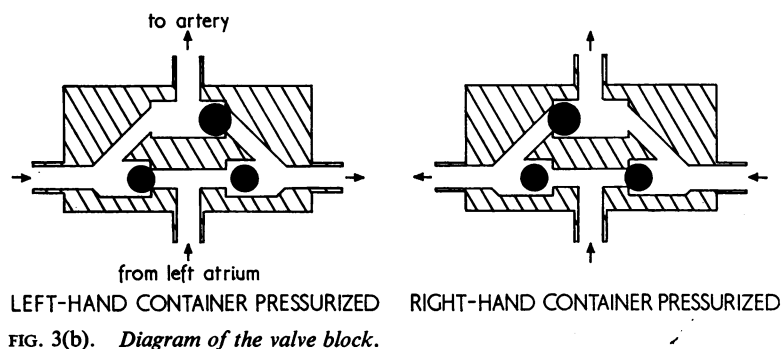


FIG. 3(b). Diagram of the valve block.

and the venous bag becomes full, the appropriate signals from the balances very rapidly reverse the action of the solenoid valves and flow then proceeds almost uninterruptedly with the function of the bags reversed. Pressures are adjusted so that the emptying of one bag takes the same time as the filling of the other. In practice, conditions of flow remained stable for many hours at a time. The machine is primed with 1,500 ml of isotonic fluid. The flow rate depends on the

size of the cannula used and the configuration of the left atrium. During experimental use the pump was run at 2–4 litres/minute.

The advantages of the pump are:

1. Blood is handled very gently and the amount of trauma caused is minimal.
2. Because soft silicone rubber balls are used in the valve block, no leakage occurs from one bag to the other.

3. The blood-handling parts can be injection moulded and are cheap, disposable, and sterilized by gamma ray.

4. The blood-handling parts and the cylinders are transparent and any air bubbles can easily be seen.

5. The valve balls move only once for each litre of flow. Since the ball valve principle is extensively used in prosthetic replacements of heart valves, movement at this rate cannot cause significant damage.

6. The output flow is smooth and the delivery pressure pre-set as required. This enables the lines to artery and atrium of the patient to be cross-clamped if required and this immediately arrests the machine without any damage.

7. The pump will run for long periods without attention or supervision. Our present pump has been used for 700 hours and pumped nearly 100,000 litres of blood without requiring any repair.

8. The pump has an air-trapping ability. Any bubbles accumulate at the apex of the plastic bag. There is otherwise no blood-gas interface.

#### LEFT ATRIAL CANNULA

In designing the left atrial cannula, we tried to calculate the lumen that would be required to give the type of flow that we were envisaging. Under the normal gravity conditions of flow as seen in the conventional heart/lung bypass machines, a lumen of 4.5 mm would be adequate to give a flow of 2 litres/minute. In practice, the greater suction pressure used in our machine enables considerably higher flows to be obtained. The limiting factor with this method is the rate of flow through the left atrial catheter. The shape and size of the left atrial cannula were determined by taking latex casts of the veins and right atrium of the sheep at necropsy and from measurements of these a catheter was finally designed (Fig. 4). It was made of 7.5 mm diameter stainless steel tube, polished inside and out, 30 cm long and

with a lumen of 4.8 mm. The atrial end was slightly rounded and four holes, each of 3.5 mm diameter, were drilled round its circumference 3 mm from the end. The cannula was bent in two places at right angles to each other. The first bend was through an angle of 55°, 3 cm from the distal end, and the second was through an angle of 14°, 3 cm from the first bend. A 2 mm high crescent-shaped protrusion was placed 1.25 cm from the end on the inside of the bend to form a ridge which would rest against the atrial wall and prevent the cannula from slipping back from the left atrium into the right atrium. A further stainless steel tube, 15 cm long, of 12.5 mm diameter with a 9.5 mm diameter lumen, was attached to the cannula to form a handle, and a pointer indicated the direction of the bend in the cannula. This cannula is a modification of the original one described by Dennis *et al.* (1962b). Our cannula, however, did not use a cutting edge for perforating the septum.

#### EXPERIMENTAL WORK

The pump was initially tested by priming with litres of stored citrated human blood and pumping it in a closed circuit for 24 hours at a flow rate of 2 litres/minute. At the end of this period no increased haemolysis was detected and although the same volume of blood had traversed the circuit approximately 1,500 times, the platelet count was reduced insignificantly and the blood clotted readily as soon as the citrate was neutralized with calcium.

The machine was then used to shunt blood from the venous to the arterial side of a sheep without traversing the sheep's lungs. This was only done on a short-term basis because of the cyanosis produced but we could not demonstrate any damage to the blood. We then used this pump with left atrial cannulation of the sheep via the jugular vein. No difficulty was experienced in passing a metal cannula of an external diameter of 7.5 mm or a balloon-ended plastic catheter of similar size into the left atrium via the fossa ovalis. At first this was done under x-ray screening control, but with practice it became possible accurately to pass the metal catheter or the plastic catheter stretched over an introducer without radiographic help.



FIG. 4. The left atrial cannula.



Under halothane anaesthesia adult sheep (weight 60–90 kg) were subjected to left atrial cannulation under sterile conditions. At the same time a peripheral artery was cannulated and a catheter was passed from a peripheral vein into the superior vena cava. Heparin was administered in an initial dose of 3 mg/kg and additional dosage of 1.5 mg/kg given hourly thereafter. A large vessel—either the femoral artery or the carotid artery—was cannulated and the left atrial and arterial cannulae were connected to the pump, which was primed with 750 ml of 5% dextrose solution and 750 ml of Hartman's solution. Blood samples were taken at intervals to estimate pH,  $PCO_2$ ,  $PO_2$ , and electrolyte levels. In the later experiments blood was examined at intervals for haemolysis, packed cell volume, platelets, and fibrinogen level.

**INITIAL ACUTE EXPERIMENTS** These were undertaken to evolve a suitable method of maintaining the cannulated sheep. Although bypass for 24 hours or even 36 hours was possible, the sheep, anaesthetized and lying on its side, never survived to recovery. We found that anaesthesia without bypass also led to the death of those sheep when they were kept on one side.

The plastic catheter, held in the left atrium by its balloon, was next used and the sheep was allowed to recover consciousness during bypass, but it proved impossible adequately to restrain the animal in these circumstances. Finally, the metal cannula was passed in sheep which remained anaesthetized but were supported by a framework in normal squatting position. With this last method two series of experiments were carried out.

**SURVIVAL EXPERIMENTS** Two groups of sheep were used.

**Group I (4 sheep)** All the sheep were maintained on a ventilator and the carotid artery was used for the arterial return. All survived 24 hours of bypass but one died during decannulation and the others at 25 and 12 hours after the end of bypass. In all there were signs of cerebral damage associated with the use of a cannula in the carotid artery.

**TABLE I**  
GROUP II: WEIGHT OF SHEEP 60–90 kg

Sheep No.	Duration of Bypass (hr)	Average Flow Rate (l/min)	Result
20	22	2.0	Survived
21	24	1.0	Survived
22	24	2.4	Survived
23	24	2.2	Survived
24	15	2.3	Died on bypass
25	24	2.1	Survived
26	24	2.4	Survived
27	24	2.8	Died decannulating
28	21	2.1	Survived
29	24	2.5	Survived
30	24	2.0	Survived

**Group II (11 sheep)** These were treated as group I but the femoral artery was used for the arterial return. Great care was taken to replace only the fluid lost as saliva and urine to avoid overhydration. The results are shown in Table I.

## RESULTS

Nine of the 11 sheep survived 24 hours of bypass. One death was due to technical difficulties in decannulation, and necropsy of the other (which died on bypass) revealed almost total destruction of the liver by parasites. Of the nine survivors, six were sacrificed at intervals after surviving two weeks. Of the remaining three, one died on the first postoperative day as a result of an erroneous overdose of intravenous potassium; one died from a faulty ligature on the femoral artery that became displaced on the first postoperative day, and there was one death on the first postoperative day of unexplained origin, presumably due to an arrhythmia. This was the only death in group II that could in any way have been attributed to the method of bypass. Excessive bleeding did not occur after bypass in any case. In the sacrificed animals progressive healing of the puncture in the atrial septum was noted. At three months healing was virtually complete.

In some of the experiments simultaneous pressures were measured in the left ventricle and in the aorta. Figure 5, taken from one of these experiments, shows a fall in left ventricular pressure compared with aortic pressure during a period of total left heart bypass and a return of left ventricular function within one heart-beat of the abrupt cessation of bypass.

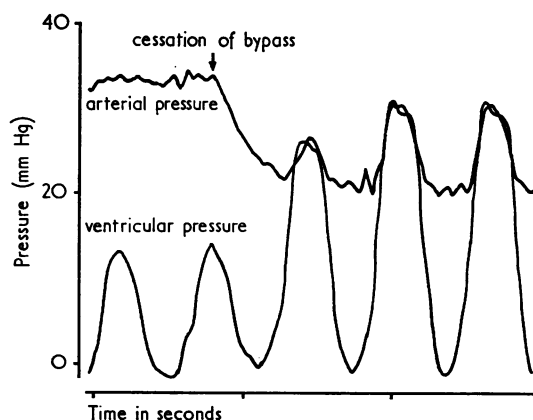


FIG. 5. Aortic and left ventricular pressures on cessation of total left heart bypass.

**HAEMATOLOGICAL INVESTIGATIONS** Examination of the blood was carried out incompletely during the earlier experiments while techniques were still changing. Full haematological investigation was completed on the last 14 sheep.

Samples of blood were obtained:

1. before bypass for:
  - (a) cross matching
  - (b) monitoring the experiment
2. during bypass (in some experiments the parameters were measured one hour after the commencement of the bypass but, as this appeared to yield little further information, it was abandoned);
3. after bypass:
  - (a) for the purpose of monitoring
  - (b) for heparin titration.

No incompatibility was ever demonstrated between donor and recipient blood before bypass. Fourteen experiments were monitored in respect of:

1. haemolysis
2. platelet destruction
3. defibrination.

1. The haemoglobin PCV and plasma haemoglobin were determined before and after bypass. The sheep used were somewhat anaemic. Their haemoglobin varied from 3.3 g/100 ml to 12.8 g/100 ml with a mean of 8.4 g/100 ml before bypass (normal 10.8 g/100 ml, Hackett, Gaylor, and Bustad, 1957). After bypass the haemoglobin ranged from 7.8 to 10.5 g/100 ml, an average of 8.3 g/100 ml. Similarly, little change occurred in the PCV. Plasma haemoglobin was measured by the method of Crosby and Furth (1956). Before bypass it ranged from 0 to 14 mg/100 ml with a mean of 3.2 mg/100 ml. After bypass the mean value was 3.0 mg/100 ml if the two samples showing 128 and 110 mg/100 ml are excluded. Both samples were from sheep that survived well, but the time of termination of the experiments was such that there was a long delay in despatching the samples to the laboratory and they were damaged in transit.

Blood films were examined before and after bypass and showed little evidence of red cell destruction.

2. Platelet counts before bypass showed a range of 60,000 to 510,000/mm<sup>3</sup> with a mean of 236,000/mm<sup>3</sup>. After bypass the range was from 60,000 to 600,000/mm<sup>3</sup> with a mean of 213,000/mm<sup>3</sup>. In only one case was there gross platelet reduction after 24 hours' bypass, and this was accompanied by defibrination.

3. Chemical estimation of fibrinogen was carried out by the method of Parfentjev, Johnson, and Clifton (1953) and fibrinogen titre with and without epsilon aminocaproic acid (Sharp, Howie, Biggs, and Methuen, 1958). Fibrinogen before bypass ranged from 120 to 400 mg/100 ml (mean 233 mg/100 ml). After bypass the range was 70 to 380 mg/100 ml (mean 232 mg/100 ml). The prothrombin and kaolin cephalin times showed no significant change during bypass.

In only one case was there gross defibrination (accompanied by the reduction of platelets described above), and this was associated with the inclusion of a filter in the left atrial cannula line for the whole of the 24 hours bypass period. The fibrinogen level fell from 300 to 50 mg/100 ml and active fibrinolysis was demonstrated. A filter was never again used for periods longer than the first five minutes of bypass, its object being to trap any pieces of dislodged atrial septum.

The results shown in Table II appear to indicate that there was little significant damage to the blood of sheep following 24 hours of bypass using this pump.

TABLE II  
HAEMATOLOGY—14 SHEEP—24 HOURS' BYPASS  
Average of Group

	Before Bypass	After Bypass
Haemoglobin	8.4 g %	8.3 g %
Plasma haemoglobin (Crosby and Furth, 1956)	3.2 mg %	3.0 mg % (2 excluded)
Platelets	236,000/mm <sup>3</sup>	213,000/mm <sup>3</sup> (1 excluded)
Fibrinogen (Parfentjev <i>et al.</i> , 1953)	233 mg %	232 mg % (1 excluded)

## DISCUSSION

The experimental results obtained with this machine, whilst not excluding any blood damage, do demonstrate that the damage to blood constituents is within the limits with which the animal can cope. Clinically, one could anticipate that subtotal bypass by this method for at least 24 hours is not in itself harmful. The toxic effects produced in blood by conventional heart/lung machines, as demonstrated by Tooley *et al.* (1961), did not occur.

If, however, this method is to be used clinically there must be grounds for believing that it will aid survival in the conditions postulated in the introduction to this paper. In a large number of publications the notion that partial bypass of

the left ventricle is likely to reduce left ventricular work has been challenged (Small, 1967). If work of the ventricle is related to the tension time index almost entirely, there can be no reduction in cardiac work without a lowering of systemic pressure (Yates, 1967).

In the course of several hundred total bypass procedures for cardiac surgery we have deliberately lowered the systemic blood pressure by vasodilatation whilst maintaining flow with the heart/lung machine. This has resulted in excellent perfusion of all the tissues including the kidneys (Kane, 1968). Patients with cardiogenic shock exhibit a state of peripheral vasoconstriction that maintains systemic pressure. The vasoconstriction is also responsible for the metabolic acidosis that results from tissue anoxia. No attempt at vasodilatation could be considered since, at the low cardiac output available from the injured ventricle, better peripheral perfusion could only be at the expense of the blood supply to the brain and heart. The first benefit to the patient on the left heart bypass would be the possibility of lowering the systemic blood pressure, thus decreasing ventricular work, improving tissue perfusion, and eliminating metabolic acidosis. At the same time the suction of blood from the left atrium would relieve lung congestion and oedema, thus improving oxygenation. The retrograde steady flow from the machine into the femoral artery may also aid coronary filling in the diastole.

It remains to be seen whether all these factors would be sufficient to effect survival in the categories of patients discussed. Since, however, in patients admitted to hospital whose cardiogenic shock from infarct persists over 24 hours the mortality is in excess of 90% (Epstein and Relman, 1949; Griffith *et al.*, 1954), there seems to be ample justification for a clinical trial of a machine such as we have described.

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