Haemodilution and total body perfusion

DOUGLAS COHEN, GRAHAM FISK, D. C. GENGOS,
AND BARBARA BATES¹

From the Adolph Basser Institute of Cardiology, The Royal Alexandra Hospital for Children, Sydney, Australia

During the last 10 years the technique of cardiopulmonary by-pass has been developed to enable intracardiac surgery to be carried out in a deliberate and unhurried manner for the correction of a variety of congenital and acquired cardiac defects. Though it is realized that there are certain dangers inherent in perfusion itself, accumulated laboratory and clinical experience has gradually reduced these to an acceptable minimum. During the past few years we have seen a progressive simplification of the apparatus used for total body perfusion in an attempt to make the whole procedure less elaborate and time-consuming and, if necessary, suitable for use at relatively short notice.

One of the problems that has had to be overcome to enable this aim to be achieved has been a reduction in the amount of fresh heparinized blood originally required for the priming of the apparatus. Initially, heparinized blood freshly collected on the morning of operation was used. Because of the difficulties and delays that occurred, blood was collected on the afternoon preceding surgery and was stored overnight at a temperature of 4° C. This has not apparently produced any adverse effects. Some centres were using older blood collected in Edglucate solution and reconstituted immediately before use, also apparently without ill-effects.

More recently, varying degrees of haemodilution have been used for cardiopulmonary by-pass (Greer, Carey, and Zuhdi, 1962; Cooley, Beall, and Grondin, 1962; DeWall, Lillehei, and Sellers, 1962). Some units use no blood at all for priming, and others reduce the amount.

A variety of clear perfusates have been employed, such as 5% glucose in distilled water, with or without the addition of low molecular weight dextran, and N/4 glucose saline with serum albumin added (Long, Sanchez, Varco, and Lillehei, 1961). Although some centres have continued to use a normothermic perfusion, the majority rely upon some degree of hypothermia.

¹ Supported by a grant from the National Heart Foundation.

Haemodilution has been developed for two reasons. First, the large amount of homologous blood required to prime the heart-lung machine was often expensive and difficult to obtain, especially at short notice. Secondly, a number of adverse physiological changes have been attributed to the use of large amounts of homologous blood (Gadbois, Slonim, and Litwak, 1962). As experience with haemodilution has been accumulated, it appears that there are certain other advantages in its use. Evidence suggests that the reduction in blood viscosity, which is achieved by haemodilution, results in a better perfusion at a capillary level. There is also less tendency to sludging of the red cells when the circulation is slowed or arrested for any reason. Proponents of this technique maintain that the post-operative course of these patients is smoother and that their renal function is better. Using less homologous blood reduces blood damage during perfusion and the risk of homologous serum jaundice.

Haemodilution has been employed at the Royal Alexandra Hospital for Children since January 1963 in our last 50 perfusions. We feel that haemodilution has improved the standard of perfusion. The purpose of this preliminary report is to present the results in the first 10 uncomplicated cases of septal defects perfused with diluted blood, compared with 10 similar cases in our initial series in which fresh whole blood was used for priming the heart-lung machine. These 10 cases were prepared as a pilot study before continuing to use haemodilution. Initially, it was our practice to prime the heart-lung machine with whole blood freshly collected on the morning of operation. In the middle of 1962 we began to use blood collected on the previous afternoon, since this was already accepted practice in many overseas centres. This was not associated with any apparent adverse effects and was a more convenient arrangement both for the Red Cross Blood Transfusion Service and for ourselves. Since the beginning of 1963 we have continued to use blood collected the afternoon before and

stored overnight at 4° C., but this has been diluted as set out below.

PERFUSION TECHNIQUE

Perfusion was carried out with the Ebsray R.A.H.C. heart-lung machine (Cohen, Hercus, and Ebsary, 1960). The pump was of the rotary type with spring-loaded rollers, just occlusive to 300 mm. of mercury. A rotating disc oxygenator was used, a 15-in. oxygenator being employed for estimated flow rates up to 2 litres per minute and a 21-in. oxygenator for estimated flows in excess of this. Blood was returned to the machine from the right atrium by gravity drainage, the venous reservoir being 10 in. lower than the right atrium. A clamp on the venous line was adjusted to maintain the venous pressure at the pre-perfusion level. Blood was returned to the body via the external iliac artery; the largest sized cannula that would fit into the artery was used. No silicone or anti-foaming agent was used in any part of the equipment. The machine was primed with heparinized blood collected on the afternoon before surgery. Blood was collected into 500-ml. glass bottles containing 2,500 units of heparin. The bottles were then stored at 4°C. until the morning of operation. When the 15-in. oxygenator was used, the machine was primed with 1,500 ml. of heparinized blood, 1,000 ml. of N/4 glucose saline, and 200 ml. of 25% serum albumin. When the 21-in. oxygenator was used, an additional 500 ml. of blood was used. The body temperature was reduced to 25–30°C. during perfusion, and the patient was rewarmed to 36°C. before the by-pass was discontinued. Intravenous heparin was given in a dosage of 3 mg./kg.

The patients were perfused at an estimated flow rate of 2.4 l./m.² of body surface/min. No citrated blood was used until after the termination of by-pass; any replacement needed before or during perfusion was effected from the machine. At the end of perfusion the patient was transfused from the machine until the heart was well filled, there was a satisfactory peripheral pulse and arterial blood-pressure, and venous pressure was approximately 20 mm. of mercury. Further small transfusions were given from the machine during closure of the chest to replace any continuing losses. After removal of the arterial cannula, heparin was neutralized with polybrene in a dosage of 1.5 mg. of polybrene per mg. of heparin.

BIOCHEMICAL ESTIMATIONS

Blood pH, PCO₂, base excess, and standard bicarbonate were measured using the E.I.L.-Robertson micro PCO₂ system (Robinson and Utting, 1961) attached to an E.I.L. model 33B pH meter, according to the method of Astrup (1956), and using the nomogram of Siggaard Andersen and Engel (1960). Oxygen

saturation and haemoglobin were determined colorimetrically with a Unicam SP 600 spectrophotometer. Estimations were carried out on the arterial blood before by-pass, on a sample from the machine-priming mixture before by-pass, at 15-minute intervals during the by-pass procedure, and on a venous sample obtained two to three hours after the patient had been returned to the recovery ward. Further post-operative sampling was only undertaken if indicated by the patient's condition. Complete clotting studies were carried out pre-operatively and were normal in every case. These included the kaolin clotting time, bleeding time, clot retraction, prothrombin index, and prothrombin activity. The clotting times were measured in plain glass test tubes, according to the method described by Lee White, 10 minutes after the administration of polybrene.

In addition to the above biochemical estimations, we measured the blood lost at operation and on the first three post-operative days, and the urinary output on the day of operation and on the first and second post-operative days.

DISCUSSION

The first 10 patients with septal defects submitted to by-pass using the haemodilution technique were compared with 10 patients with septal defects selected from the previous group, in whom fresh whole blood collected on the morning of operation had been used and who had had an uninterrupted post-operative course free from complications and with complete recovery. The 'diluted' group consisted of five patients with secundum atrial septal defects and five with ventricular septal defects. The 'undiluted' group contained six patients with atrial septal defects, three with ventricular septal defects, and one patient with an atrial septal defect and a ventricular septal defect. The age, weight, perfusion time, and surface area of the patients in each group are set out in Table I. It can be seen that the patients in the diluted group were slightly younger but that the perfusion time is comparable in each series. A comparison of the acid-base balance of the two groups is rather difficult, as the pH was the only result obtained from the first group of patients and the state of the acid-base equilibrium cannot be accurately deduced from this figure alone. However, studying the three-hour post-operative pHs from each group, it seems probable that there was a significantly greater degree of post-operative acidosis in the undiluted group with a mean arterial pH of 7.24 compared with a mean venous pH of 7.26 in the diluted group. In the second group, where complete results were obtained, it can be seen that immediately before perfusion

TABLE I

COMPARISON OF 10 PATIENTS SUBMITTED TO BY-PASS USING THE HAEMODILUTION TECHNIQUE WITH 10 PATIENTS RECEIVING FRESH WHOLE BLOOD

	Perfusate	
	Blood, N/4 Saline, and Albumin	Fresh Whole Blood
Age (yr.)		
Average	6	9
Range	3-9	4-12
Weight (kg.)		
Average	19.32	27.4
Range	13.00-26.25	16.5-44.5
Surface area (m. ²)		
Average	0.74	0.94
Range	0.56-0.94	0.71-1.32
Perfusion time (min.)		
Average	30	37
Range	15-50	13-51

there was generally no metabolic imbalance (base excess of -1 mEq/l.) but a mild respiratory alkalosis (PCO_2 of 26 mm. Hg).

At the end of perfusion there was a significant metabolic acidosis (base excess of -8 mEq/l.) plus a respiratory alkalosis (PCO_2 of 19 mm. Hg) resulting in a normal pH (7.43). Post-operatively, there was a mild metabolic acidosis (base excess -5 mEq/l.) with normal respiratory figures (PCO_2 of 49 mm. Hg). The full results can be seen in Table II. It will be noted that the post-operative results in the diluted group were obtained from central venous blood. There are errors in this technique due to the greater buffering power of oxyhaemoglobin. It was found that unless the blood was grossly desaturated the errors were slight and apply only to the buffer base and PCO_2 figures. Haemodilution did not

TABLE II
BIOCHEMICAL STUDIES

	Perfusate			
	Blood, N/4 Saline, and Albumin		Fresh Whole Blood	
	Mean	Range	Mean	Range
<i>Before by-pass—Arterial sample</i>				
pH	7.50	7.42-7.57	7.44	7.32-7.56
PCO_2 (mm. Hg)	26	19-38		
Base excess (mEq/l.)	-1	+2 to -5		
Standard bicarbonate (mEq/l.)	23	21-25		
<i>End of by-pass—Machine sample (arterial)</i>				
pH	7.43	7.38-7.50	7.37	7.26-7.48
PCO_2 (mm. Hg)	19	16-22		
Base excess (mEq/l.)	-8	-3 to -12		
Standard bicarbonate (mEq/l.)	17	15-21		
<i>Three hours post-operatively</i>				
	<i>Venous Sample</i>		<i>Arterial Sample</i>	
pH	7.26	7.20-7.34	7.24	7.19-7.30
PCO_2 (mm. Hg)	49	43-55		
Base excess (mEq/l.)	-5	-2 to -8		
Standard bicarbonate (mEq/l.)	20	18-22		

affect the ability of the Ebsray R.A.H.C. heart-lung machine to produce a satisfactory oxygen saturation at all times (Table III). Subsequent to this series, the oxygen flow through the heart-lung machine has been reduced progressively from 6 litres per minute to as low as 1.5 litres per minute, as it was found that this lessened the

TABLE III
OXYGEN SATURATION WITH A PERFUSATE OF BLOOD, N/4 SALINE, AND ALBUMIN

	Machine Sample O_2 Saturation (%)
<i>Before by-pass</i>	
Average	97.6
Range	94.2-99.5
<i>At end of by-pass</i>	
Average	98.2
Range	95.2-100.5

degree of respiratory alkalosis during perfusion. Oxygenation of the blood appears to be adequate at this low flow rate, and the PCO_2 figure could be maintained within the normal range. Higher flow rates caused a washing out of CO_2 from the blood in the machine. The clotting studies do not suggest interference with blood coagulation, the mean figure being in the normal range (Table IV). Table V shows the operative and post-operative blood loss in the two groups and indicates that haemodilution was not associated with an increased tendency to bleeding either during or

TABLE IV
CLOTTING TIMES

Mean Clotting Time (min.)	Perfusate	
	Blood, N/4 Saline, and Albumin	Fresh Whole Blood
Average	9	7
Range	7-12	5-10

TABLE V
BLOOD LOSS

Blood Loss (ml.)	Perfusate	
	Blood, N/4 Saline, and Albumin	Fresh Whole Blood
<i>At operation</i>		
Average	265	340
Range	56-500	48-1,100
<i>24 Hours Post-op.</i>		
Average	222	226
Range	59-413	66-420
<i>24 to 48 Hours Post-op.</i>		
Average	63	132
Range	0-150	30-380
<i>48 to 72 Hours Post-op.</i>		
Average	19	29
Range	0-74	0-77

TABLE VI
URINARY OUTPUT

Urinary Output (ml.)	Perfusate	
	Blood, N/4 Saline, and Albumin	Fresh Whole Blood
Day of operation		
Average	550	703
Range	114-929	528-972
First day post-op.		
Average	651	751
Range	360-990	330-1,340
Second day post-op.		
Average	511	740
Range	90-1,026	160-1,350

after operation. The urinary output is shown in Table VI, and, making allowance for the age difference between the two groups, the figures are comparable and indicate that haemodilution does not impose an excessive water load on these children.

Haemodilution figures are available for the diluted perfusate at the end of by-pass and three hours post-operatively and show, as one would expect, some reduction in the haemoglobin of the perfusate which, however, has returned to normal figures three hours post-operatively (Table VII).

These comparative studies and our subsequent experience in a further 40 cases have indicated that there are no deleterious effects associated

TABLE VII
HAEMOGLOBIN VALUES WITH A PERFUSATE OF
BLOOD, N/4 SALINE, AND ALBUMIN

Sample	Haemoglobin (g./100 ml.)
Patient before by-pass	
Average ..	13.7
Range ..	12.9-15.8
Machine before perfusion	
Average ..	8.6
Range ..	6.8-10.3
Machine at end of perfusion	
Average ..	9.9
Range ..	8.7-11.1
Patient 3 hr. post-op.	
Average ..	11.6
Range ..	10.7-12.5
Patient 24 hr. post-op.	
Average ..	15.2
Range ..	13.0-17.3

with this degree of haemodilution, and that there may be real advantages. The fact that blood is collected on the afternoon before surgery and that relatively small quantities are required has eliminated some of the problems associated with whole body perfusion and has helped to bring it more into line with other major procedures.

SUMMARY

A technique of whole body perfusion with haemodilution is described using the Ebsray R.A.H.C. heart-lung machine.

The results obtained in the first 10 patients are compared with those of a similar group of patients in whom fresh whole blood was used as the perfusate.

This study was made possible by a grant supplied by the National Heart Foundation to provide biochemical assistance.

REFERENCES

- Astrup, P. (1956). A simple electrometric technique for the determination of carbon dioxide tension in blood and plasma, total content of carbon dioxide in plasma, and bicarbonate content in "separated plasma" at a fixed carbon dioxide tension (40 mm Hg). *Scand. J. clin. Lab. Invest.*, **8**, 33.
- Cohen, D. H., Hercus, V. M., and Ebsary, V. R. (1960). The Royal Alexandra Hospital for Children heart-lung machine. *Med. J. Aust.*, **2**, 734.
- Cooley, D. A., Beall, A. C., and Grondin, P. (1962). Open-heart operations with disposable oxygenators, 5 per cent dextrose prime and normothermia. *Surgery*, **52**, 713.
- DeWall, R. A., Lillehei, R. C., and Sellers, R. D. (1962). Hemodilution perfusions for open-heart surgery. *New Engl. J. Med.*, **266**, 1078.
- Gadbois, H. L., Slonim, R., and Litwak, R. S. (1962). Homologous blood syndrome: I. Preliminary observations on its relationship to clinical cardiopulmonary bypass. *Ann. Surg.*, **156**, 793.
- Greer, A. E., Carey, J. M., and Zuhdi, N. (1962). Hemodilution: principle of hypothermia perfusion. A concept obviating blood priming. *J. thorac. Surg.*, **43**, 640.
- Long, D. M., Sanchez, L., Varco, R. L., and Lillehei, C. W. (1961). The use of low molecular weight dextran and serum albumin plasma expanders in extracorporeal circulation. *Surgery*, **50**, 12.
- Robinson, J. S., and Utting, J. E. (1961). A simple interpolation method for the estimation of PCO₂ in whole blood. *Brit. J. Anaesth.*, **33**, 327.
- Siggaard Andersen, O., and Engel, K. (1960). A new acid-base nomogram. An improved method for the calculation of the relevant blood acid-base data. *Scand. J. clin. Lab. Invest.*, **12**, 177.