THE USE OF HEPARINIZED BLOOD IN OPEN-HEART SURGERY

A REVIEW OF 250 CASES

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INTRODUCTION

Extracorporeal circulation with a heart-lung apparatus was pioneered using fresh heparinized blood, after Sköld[1] first recommended heparin as an anticoagulant for blood transfusion in 1936. As early as 1937, Gibbon[2] described the use of cat's heparinized blood in his experimental work with a heart-lung machine; he achieved the first clinically successful intracardiac operation with extracorporeal circulation and heparinized blood in 1952.

Cookson *et al.*[3] referred to the toxic effects of citrated blood and suggested that heparin would be a better anticoagulant for donor blood intended for cardiac surgery. Reports describing the suitability of freshly drawn heparinized blood for extracorporeal circulation soon became available.[4-6] However, when this surgery became routine in the larger centres, the increasing demand for open-cardiac corrections — sometimes several in one day — soon emphasized that the use of fresh heparinized blood is not altogether ideal.

The difficulties in collecting fresh blood have been reported from different countries,[4,7-12] and are related mainly to organizational problems in handling a relatively large number of donors and their blood in a special way.

Several alternatives to the use of freshly-drawn heparinized blood have been developed, and have been evaluated by laboratory tests as well as during clinical trials. Reports are available on the use of conventional pump-oxygenators primed with heparinized blood between 12 and 13 hours old, containing glucose as additive;[4,9,13] Edglugate-Mg stored blood;[8,14,15] and acid-citrate-dextrose (ACD) stored blood, converted for perfusion by the addition of heparin and calcium gluconate.[16,17] Pump-oxygenators of reduced capacity have been primed with (*a*) saline and the patient's heparinized blood;[18] (*b*) 5% dextrose and water;[19,20] or (*c*) low-molecular-weight dextran, with or without stored heparinized blood.[21]

In view of the choice of techniques for priming machines and perfusing patients, we consider it necessary to assess our results and to compare them — as far as such comparisons are valid — with those reported from other centres. This is particularly necessary in view of the fact that every perfusion in this centre has been managed with freshly-drawn heparinized blood, a practical procedure, but undoubtedly one requiring considerable effort on the part of the blood-collecting organization. Persistence with the present programme requires justification.

MATERIAL AND METHODS

The first 250 patients operated upon using total cardiopulmonary bypass at the University of Cape Town Teaching Hospitals by one of us (C.N.B.) form the basis of this study; the blood-transfusion programme for open-cardiac surgery in this area started with this series. In 246 patients intracardiac surgical procedures were undertaken with perfusion. In the remaining 4, aneurysms of the ascending aorta or arch of the thoracic aorta were resected using extracorporeal circulation. Ten of the operations were considered to be emergency procedures (Table I). The operations were performed between July 1958 and June 1962, and the ages of the patients varied between 2 weeks and 59 years.

All patients subjected to surgical treatment were investigated at the Cardiac Clinic, Groote Schuur Hospital, the indication for operation being a condition which could be improved by surgical treatment. Details of the pre-operative diagnosis and surgical techniques, and follow-up results for some of the patients in this series have been published.[22-34]

A De Wall/Lillehei helix reservoir bubble oxygenator with sigmamotor pumps was employed for all perfusions (Fig. 1). The conduct of perfusions in the early cases was based on experience gained at the University of Minnesota Hospitals, Minneapolis, Minn., USA, although certain alterations were incorporated later, based on changing concepts, clinical experience, laboratory data and reports by other workers.

The oxygenator was primed with heparinized blood drawn on the morning of surgery. The first 84 perfusions were performed at normal body temperature with flows of between 2·1 and 2·4 litres/sq. metre of body surface/minute. In the next 50 perfusions, profound hypothermia was used with extracorporeal circulation for the more complex lesions, but normothermic perfusions were still employed in uncomplicated cases. In the latter half of the series either moderate or profound hypothermia was used with extracorporeal circulation in all cases.[35,36] Potassium arrest was induced in 25 normothermic perfusions.

TABLE I. ANALYSIS OF EMERGENCY OPERATIONS PERFORMED ON ACUTELY DISABLED PATIENTS

Case no.	*Age*	*Lesion*	*Surgical procedure*	*Outcome*
87	9 months	Cor triloculare	Not rectifiable	Died in theatre
90	1 year	Tetralogy of Fallot	Complete repair	Died in theatre
107	14 days	Ebstein's anomaly	Not rectifiable	Died in theatre
132	5 years	Tetralogy of Fallot	Complete repair	Survived
153	45 years	Ruptured aneurysm of ascending thoracic aorta	Excision and graft	Died on 10th day
176	3 months	Pulmonary stenosis and patent foramen ovale	Relief and repair	Died in theatre
184	9 months	Persistent truncus arteriosus	Not rectifiable	Died in theatre
220	1½ years	Tetralogy of Fallot	Complete repair	Survived
236	1 year	Tetralogy of Fallot	Complete repair	Survived
250	34 years	Ruptured aneurysm of ascending thoracic aorta	Excision and graft	Survived

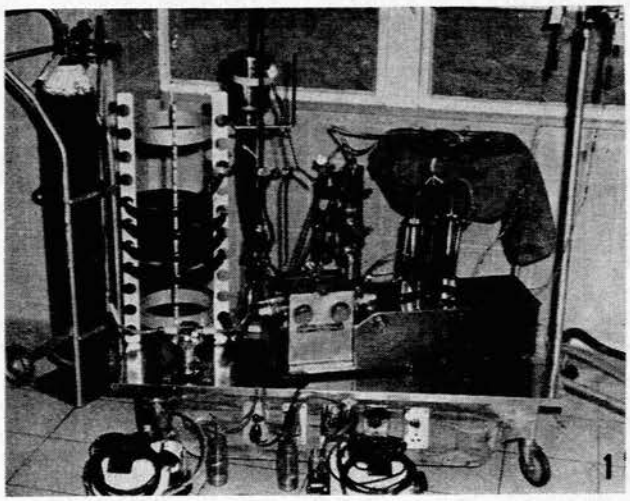

Fig. 1. The de Wall/Lillehei helix reservoir bubble oxygenator with sigmamotor pumps and Benington heat exchangers, used for extra-corporeal circulation with hypothermia in all patients in the latter half of the series.

Heparin was administered intravenously to the patients immediately before cannulation in a dose of 2 mg./kg. body weight in the first 56 patients. The dosage was changed to 90 mg./sq. metre body surface area thereafter. At the conclusion of bypass, the heparin was neutralized by the intravenous administration of protamine in a dose of 1·5 : 1 of heparin in the first 12 perfusions, and then by the use of intravenous polybrene in a dose of 1·25 : 1 of heparin.

The record of each case in this series has been carefully reviewed. Necropsy was performed in all patients who died, and postoperative complications were studied to determine whether the use of heparinized blood could have contributed to them.

BLOOD TRANSFUSION PROCEDURE

1. *Donors*

All blood is provided by voluntary, unpaid donors through the Western Province Blood Transfusion Service, an association constituted and controlled by the donors and staffed by its own medical and other personnel. Women with children, and persons previously transfused are acceptable as donors, while a history of hepatitis or malaria, or the presence of active disease, are grounds for exclusion.

In the first 150 cases, the required number of donors, augmented by 3 or 4, made a preliminary visit to the transfusion clinic 3 days before operation and a specimen was collected for a cross-match test. For the later operations, the required and the spare donors attended the clinic only on the morning of operation. An extra 1 - 2 units of heparinized blood over and above the minimum required for priming may be collected, particularly for more complex procedures; this blood is often added to the machine during long perfusions. Up to 2 operations in 1 day and 5 in 1 week have been undertaken in this fashion without instances of undue delay or confusion.

2. *Blood-group and Cross-match Tests*

Some days before operation, or in an emergency some hours before, a sample of approximately 20 ml. of the patient's blood is examined as follows:

(*a*) The ABO group is determined by tests against known cells and serum; A_2 and A_2B bloods are examined for anti-A_1.

(*b*) The blood is grouped for the Rh factor D (Rh_o).

(*c*) The serum is screen-tested for irregular antibodies against a representative panel of 8 different group-O blood cells containing all the major antigens. Frozen stocks of these test cells are kept. Tests are done variously, some in saline, others in albumin or by anti-human globulin (AHG), and tests at 4°C., room temperature and 37°C. are used.

(*d*) Auto-agglutinin controls with patient's cells and serum are done at 4°C., 22°C. and 37°C. in saline and by AHG test.

(*e*) As the results become available they are recorded on a blackboard in the laboratory, under the name of the patient and the date of operation; also listed are the amounts of heparinized and of ACD blood required and the date on which it was ordered.

The patient's blood group and the required number of units of heparinized and ACD blood are made known to the blood transfusion service as early as possible. Homologous ABO and Rh blood is used, group A_2 being ordered only when patients of this sub-group possess anti-A_1 agglutinins active at 20°C.

The only instance of postponement of operation owing to delay in finding donors for homologous blood occurred when 2 out of the 3 patients belonging to group A_2B, with moderately strong anti-A_1 agglutinins, were scheduled for operation in the same week. For emergency surgery or late substitution of patients, blood was sometimes ordered the day before or very occasionally on the day of operation.

The ACD blood, for use before or after perfusion, is collected from the extra donors not required for heparinized blood, or is provided from relatively fresh blood-bank stock. Some of this blood is cross-matched on the day before operation.

The heparinized blood is delivered to the hospital laboratory immediately after collection, by which time the anaesthetic has been commenced in the operating theatre. During the ensuing 60 - 75 minutes a single technician undertakes a cross-match test, as follows:

(*a*) The cells of individual donors are matched against the patient's serum (*i*) in saline, with and without bromelin, at room temperature; and (*ii*) by AHG test after water-bath incubation at 37°C. for half-an-hour in pre-warmed tubes.

(*b*) Each donor's (*i*) ABO group, and (*ii*) Rh group for the factor D (Rh_o), are checked.

(*c*) Each donor's serum is tested against 2 representative cell pools (*i*) at 22°C. by bromelin, and (*ii*) by AHG test after 30 minutes' incubation at 37°C. as above.

Occasionally this programme of tests is modified, for instance when a small patient with a very high haematocrit provides only a limited amount of serum.

On completion of the laboratory tests the blood is taken to the operating theatre, where the thoracotomy is usually well under way.

To avoid any possibility of confusion on days when more than 1 operation is scheduled, the needs for the first are completed in the donor clinic before the donors for the subsequent operation are received. The same procedure is followed with the specimens in the laboratory.

RESULTS

1. *Laboratory Reactions of the Patients' Blood*

Out of 250 patients, one was found to have an immune antibody (anti-E or Hr") of undoubted clinical significance which made it obligatory to find special donors; this patient has been operated on twice, once in this series. Three others belonged to group A_2B with anti-A_1 agglutinins active at 20°C.; it was thought best to use only group A_2B blood for them. Ninety-two patients, many of them non-European, possessed cold agglutinins with or without blood-group specificity; of this group the serum of 4 patients showed a non-specific agglutination in the temperature range 20 - 22°C. and moderate hypothermia only was induced. Another patient, urgently in need of surgery for which hypothermia was indicated, possessed a cold agglutinin of high titre (over 1 in 100 at 4°C.) and strongly active at 28°C. This posed a nice problem in judgment until the large dose of antibiotic (given for the syphilis which underlay his aneurysm of the ascending aorta) also rapidly reduced the strength and thermal amplitude of the cold agglutinin. This temporarily

left unresolved a point at issue between the dictates of cardiac surgery and blood-group serology. Finally, in 6 instances a weak or doubtful reaction in the cross-match test, usually by bromelin test at room temperature, led to a single pint of blood not being released immediately for perfusion.

2. *Laboratory Reactions of the Donors' Blood*

Altogether 2,620 bottles of heparinized blood from many hundreds of donors were used. In 4 instances donors having a first antibody screen-test shortly before the operation were totally excluded because of the presence of specific antibodies. These were a strong anti-Kell, 2 moderately strong anti-D (anti-Rh_0) and a low-temperature anti-Le^a antibody. The would-be donor with the anti-Le^a antibody was detected on 2 widely separated occasions.

More recently, donors are being called for open-heart surgery only after 3 routine donations, thus ensuring that repeated previous tests for specific antibodies and syphilis have been negative.

On 4 other occasions donor blood was excluded from extracorporeal circulation because it contained a non-specific cold agglutinin active at room temperature in the presence of bromelin.

All specimens and blood bottles were stored for at least 24 hours after perfusion. In instances when the patient's clinical condition in the post-perfusion period was not clearly understood, or when jaundice or renal symptoms were noted, the whole procedure for testing the patient's and donors' blood was repeated in a more leisurely fashion. At no time did the results between the two series of tests differ.

ANALYSIS OF RESULTS

It is probably unwise to attempt to evaluate the adequacy of any single aspect of a complex surgical technique from the analysis of the results of a series of operations. However, the chain is as strong as its weakest link and it is probably fair to assume that, if the results are good, all facets of the technique must be sound.

1. *Mortality*

Some clinical data and results of the 250 cases in this series are given in Table II. There were 32 hospital deaths in the series (a mortality of 13·6%). In 6 patients a second operation with cardiopulmonary bypass was necessary (Table III) giving a total of 256 perfusions and thus a mortality of 12·5% of all perfusions.

2. *Analysis of Causes of Death (Table IV)*

(*a*) *Anatomically inoperable conditions.* Four of the deaths (cases 17, 87, 107 and 184) are classified as arising from conditions which were not rectifiable. In these cases the pre-operative diagnosis was incorrect and at surgery it was found that anatomical correction was not possible; all these deaths occurred during surgery.

(*b*) *Unrelated deaths.* Three deaths were from causes unrelated to cardiac surgery or total body perfusion. Case 104 died as a result of coronary thrombosis and myocardial infarction, confirmed at necropsy, on the 8th post-operative day. Case 142 died 12 hours after surgery from

TABLE II. ANALYSIS OF MATERIAL AND RESULTS

Classification by anatomical diagnosis	*No. of patients*	*Survived*	*Average age (years)*	*Average perfusion time (minutes)*	*Average units of blood*
Interatrial septal defect (ostium secundum)	34	34	19	33	10·6
Interatrial septal defect with anomalous pulmonary venous return	4	4	17	61	7·25
Interatrial septal defect with other associated conditions	8	8	29	50	10·7
Interventricular septal defect	21	19	11	60	9·3
Interventricular septal defect with other associated conditions	19	16	15	81	9·8
Pulmonary stenosis	13	13	11	41	9·0
Pulmonary stenosis with atrial septal defect (cyanotic)	6	5	14	71	8·5
Pulmonary stenosis with other associated conditions	8	7	12	63	9·0
Tetralogy of Fallot	59	52	10	98	9·0
Endocardial cushion defect	17	15	14	86	9·7
Mitral valve disease	20	20	29	95	11·8
Aortic valve disease (congenital)	4	4	13	51	8·0
Aortic valve disease (acquired)	9	4	38	76	13·0
Aortic valve disease (acquired—with associated conditions)	1	0	12	—	12·0
Mixed multiple valvular lesions	8	4	27	118	12·0
Miscellaneous (congenital)	7	3	3	105	6·0
Miscellaneous (acquired)	12	10	33	81	13·0
Total	250	218			

TABLE III. PATIENTS REQUIRING A SECOND OPEN-HEART OPERATION, AND THE RESULTS

Case no.	*Lesion*	*First operation*	*Second operation performed for*	*Outcome*
85	Tetralogy of Fallot	Complete repair	Persistent VSD	Survived
128	Mitral valve disease	Annuloplasty	Persistent MI	Survived
144	Tetralogy of Fallot	Complete repair	Persistent VSD	Survived
205	Mixed valvular lesions	Cardiotomy and inspection	Persistent MI	Died
213	Endocardial cushion defect	Complete repair	Persistent MI and VSD	Survived
235	Tetralogy of Fallot	Complete repair	Persistent VSD	Survived

VSD=ventricular septal defect, MI=mitral incompetence.

TABLE IV. ANALYSIS OF ALL DEATHS IN 256 OPERATIONS WITH EXTRACORPOREAL CIRCULATION

Death no.	*Case no.*	*Lesion*	*Age*	*Duration of perfusion (mins.)*	*Time of death after operation*	*Cause of death*	*Classification of death*
1	5	VSD+AI+PDA	13 yrs.	55	12 hours	Persistent AI	Surgical failure
2	16	ECD + VSD	15 yrs.	93	36 hours	Cardiac failure with pulmonary oedema	Surgical failure
3	17	AS + ASD + PVS	12 yrs.	135	In theatre	Myocardial failure	Not rectifiable
4	23	PIS + TI	12 yrs.	69	24 hours	Cardiac failure with pulmonary oedema	Surgical failure
5	32	Calcific AS	36 yrs.	31	In theatre	Persistent AI	Surgical failure
6	35	Tetralogy of Fallot	26 yrs.	83	24 hours	Hypovolaemic perfusion	Perfusion death
7	58	AI + MI + TI	32 yrs.	85	In theatre	Myocardial failure	Surgical failure
8	72	Tetralogy of Fallot	4 yrs.	87	6 hours	Complete heart block	Surgical failure
9	78	Calcific AS + AI	56 yrs.	100	In theatre	Persistent AI	Surgical failure
10	79	VSD	3 yrs.	60	3 hours	Respiratory failure	Perfusion death
11	84	VSD + AI	56 yrs.	192	In theatre	Persistent AI	Surgical failure
12	86	Tetralogy of Fallot	40 yrs.	176	2 hours	Persistent VSD	Surgical failure
13	87	Cor triloculare	9 mths.	114	In theatre	Not rectifiable	Not rectifiable
14	90	Tetralogy of Fallot	1 yr.	58	In theatre	Persistent RV stenosis	Surgical failure
15	100	Tetralogy of Fallot	8 yrs.	214	3 hours	Hypoplastic PA	Surgical failure
16	104	VSD + PS	30 yrs.	130	8 days	Myocardial infarct (necropsy)	Unrelated death
17	106	VSD	4 yrs.	173	8 days	Cardiac air tamponade	Surgical failure
18	107	Ebstein's anomaly	2 weeks	61	In theatre	Not rectifiable	Not rectifiable
19	112	Transposition	3 mths.	73	4 hours	Cardiac failure	Surgical failure
20	131	Calcific AS	32 yrs.	118	2 days	Persistent AI	Surgical failure
21	140	Tetralogy of Fallot	16 yrs.	196	3 months	Jaundice, renal tubular necrosis, congestive cardiac failure	Surgical failure
22	142	Tetralogy of Fallot	2½ yrs.	108	12 hours	Digitalis intoxication	Unrelated death
23	153	Ruptured thoracic aortic aneurysm	45 yrs.	219	10 days	Anoxic brain damage	Perfusion death
24	176	PS + patent foramen ovale	3 mths.	130	In theatre	Cardiac failure—emergency operation	Surgical failure
25	183	Aortic + subvalvular stenosis + AI	29 yrs.	300	In theatre	Persistent AI	Surgical failure
26	184	Persistent truncus arteriosus	9 mths.	170	In theatre	Cardiac failure — emergency operation	Not rectifiable
27	187	AI + MI	12 yrs.	235	In theatre	Persistent AI	Surgical failure
28	205	3rd op. for calcific MS + TI	43 yrs.	162	Half-an-hour	Cardiac failure	Surgical failure
29	215	Syphilitic AI	48 yrs.	189	4 days	Mesenteric infarct	Unrelated death
30	218	ECD + VSD	3 yrs.	149	24 hours	Persistent pulmonary hypertension	Surgical failure
31	247	Mitral, aortic, and tricuspid stenosis and incompetence	14 yrs.	209	In theatre	Myocardial failure	Surgical failure
32	248	Aneurysm of ascending thoracic aorta and arch	45 yrs.	350	In theatre	Persistent AI	Surgical failure

VSD = ventricular septal defect, AI = aortic incompetence, PDA = patent ductus arteriosus, ECD = endocardial cushion defect, AS = aortic stenosis, ASD = atrial septal defect, PVS = pulmonary valvular stenosis, PIS = pulmonary infundibular stenosis, TI = tricuspid incompetence, MI = mitral incompetence, MS = mitral stenosis, RV = right ventricular, PA = pulmonary artery, PS = pulmonary stenosis.

digitalis intoxication. Case 215 died on the 4th post-operative day from a superior mesenteric artery thrombosis and infarction of the bowel, confirmed at necropsy.

(*c*) *Perfusion deaths.* Kirklin *et al.* in 1957[37] defined a perfusion death as one related to the perfusion itself or any part of the surgical, anaesthetic or supportive management necessitated by the use of the pump oxygenator. In this series only 3 deaths can be classified under this heading. Case 35 became hypovolaemic during perfusion; this occurred early in the series, before it was recognized that after perfusion in a case of tetralogy of Fallot blood-volume restoration should be judged on venous pressure rather than on body weight. Case 79 died suddenly 3 hours after perfusion; necropsy did not reveal the cause of death, which can be classified in the group described by Kirklin *et al.*[37] as an 'acute syndrome of apparently sudden death'. Case 153 died as a result of cerebral damage from anoxic periods during the bypass. There were no deaths from haemorrhage, pulmonary complications or infection in this series.

(*d*) *Surgical deaths.* A surgical death occurs when the surgeon has failed to correct the haemodynamics to a state compatible with life after surgical intervention. Under this heading we have placed 22 cases. Of these, 10 died during surgery, 8 within 24 hours of the completion of the operation and 4 after 24 hours.

It is interesting to note that 8 of the surgical deaths were associated with persistent aortic incompetence. There were 7 patients with complete heart block and this complication resulted in only one hospital death. Six patients in whom surgical correction was not adequate survived long enough to make a second operation possible (Table III) and only one failed to survive the second operation.

3. *Analysis of Morbidity*

(*a*) *Haemorrhage.* Adequate perfusion must not cause destruction of blood elements resulting in uncontrolled bleeding in the postoperative period. Of the 236 patients who survived for any length of time after perfusion, there was excessive bleeding in 10 (4%). These were all re-explored and the bleeding found to be from an artery, e.g. a branch of a coronary artery, the internal mammary artery or intercostal arteries. Without exception, ligation of the bleeding points stopped further haemorrhage. Calculation of the postoperative drainage in the last 75 patients surviving surgery showed that drainage amounted to approximately 10 ml. per kg. body weight in the first 24 hours after bypass.

(*b*) *Infection.* There were 14 patients with superficial wound infection, 4 with deep infection of the wound and 2 with bacterial endocarditis. No deaths occurred as a result of infection.

(*c*) *Pulmonary complications.* Apart from pulmonary oedema following cardiac failure as a result of inadequate surgical correction of the lesion, there were no major pulmonary complications.

Pleural effusion, mild tracheo-bronchitis, and small areas of atelectasis were occasionally encountered and always responded to treatment. Tracheostomy was resorted to in 7 patients — in 1 patient for oedema of the glottis, probably as a result of trauma from the endotracheal tube; in 2 infants for the easy removal of tenacious bronchial secretions; while in the remaining 4 mechanical assistance of respiration was deemed necessary. One patient died as a result of the tracheostomy in that, on the ninth postoperative day, when the tracheostomy tube was already removed, a fistula developed between the tracheal wound and the median sternotomy and acted as a one-way valve. The patient developed air tamponade.

(*d*) *Jaundice.* Serum-bilirubin estimations were not performed as a routine. Clinically, mild jaundice was present in 6 patients after surgery and lasted only a few days. One patient developed jaundice as a result of congestive cardiac failure a month after surgery and died from liver and cardiac failure. In a careful follow-up there have been no cases of serum hepatitis.

(*e*) *Renal tubular necrosis.* Kidney damage in this series, as marked by oliguria and a rise in the blood-urea level, was seen in 6 patients, an incidence of just over 2·5% (Table V). This responded well to medical treatment and, although 2 patients in this group died, death could not be attributed to the renal lesion. In these cases the patients' and donors' blood was re-investigated for evidence of incompatibility, but in none was there any evidence to suggest that this was the cause of the renal damage.

(*f*) *Cardiac failure.* Severe heart failure was seen only in patients in whom the lesion had not been adequately corrected. Right heart failure was frequently encountered in patients who had had a right ventriculotomy, especially in the tetralogy of Fallot malformation, where pulmonary incompetence results from the insertion of an outflow-tract patch across the pulmonary-valve ring. All but one responded to medical treatment; in the exception (a patient with severe tetralogy of Fallot with gross right heart failure before surgery) the failure persisted after complete correction of the defects.

(*g*) *Pyrexia of unknown origin after cardiopulmonary bypass.*[38] Fever starting or continuing after the initial reactionary temperature response to surgical trauma has subsided, was seen in 63 cases in this series. The rise in temperature usually starts on the 5th - 8th postoperative day, 2 - 3 days after the fever response to surgical trauma has subsided. However, it may occur later in the con-

TABLE V. LENGTH OF PERFUSION AND RESULTS IN PATIENTS WHO DEVELOPED RENAL DAMAGE.

No.	*Age group*	*Perfusion no.*	*Duration of perfusion (minutes)*	*Outcome*
1	4–15 years	182	138	Recovered
2	4–15 years	138	118	Recovered
3	Over 15 years	93	90	Recovered
4	Over 15 years	104	130	Died 8th day—myocardial infarct
5	Over 15 years	114	120	Recovered
6	Over 15 years	140	196	Died 3 months later—cardiac failure

valescence, especially on the 12th - 14th days, when the patient becomes more active, and often occurs as late as a month or more after surgery. The fever is usually unassociated with a corresponding rise in pulse rate or an increase in the white-cell count. Minimal symptoms and signs accompany this syndrome. In some patients there is evidence of pericardial inflammation and in some signs of pleural inflammation. Although more common in patients with rheumatic heart disease, this syndrome may be encountered after any bypass. The aetiology is not quite clear, but is probably non-bacterial inflammation of the myocardium, pericardium or pleura, following trauma to these structures.

DISCUSSION

This series of 256 perfusions was associated with a hospital mortality of 12·5%. However, if the deaths due to unrelated causes and those due to anatomically inoperable conditions are excluded, the mortality is less than 10%. Mortality figures for a mixed series of cases, although unselected, may be misleading, since they will depend on the number of patients included who are suffering from relatively simple defects with an inherent low operative mortality. It is thus necessary to study the results of various groups of operations. The analysis of the selected groups in this series (Table II) shows:

1. *Interatrial septal defects.* In a series of 46 ostium secundum and sinus venosus defects there was no death.[39]

2. *Tetralogy of Fallot.* In 59 patients suffering from this malformation the mortality was under 12%.[31] There were no deaths among the last 32 patients in this group.

3. *Interventricular septal defects.* Only patients with large ventricular septal defects were operated upon, since we believe that small defects may close spontaneously.[40,41] Of the 40 patients with ventricular septal defects, in 21, in whom the septal defect was the only lesion, there were 2 deaths (a mortality of 10%), and in the remaining 19, who had associated defects such as pulmonary stenosis, aortic incompetence and atrial septal defects, there were 3 deaths (a mortality of 16%).

4. *Pulmonary stenosis.* In 13 patients with pure pulmonary stenosis there was no mortality. In those with associated atrial septal defects (trilogy) there was only 1 death in an infant 3 months old (Table I). In 8 patients in whom the pulmonary stenosis was associated with other defects, such as aortic stenosis, tricuspid incompetence and aortic incompetence, there was 1 death.

5. *Endocardial cushion defects.* There were 2 deaths in 17 patients suffering from this malformation. Both occurred in the group with a functioning ventricular septal defect.[26]

6. *Acquired valve disease.* There was no hospital death in 20 patients operated on for mitral incompetence. In acquired aortic valve disease and in multiple valvular lesions, the mortality was 55%. The high mortality in the latter group is due to surgical failures but, since the development of prosthetic valves, results have been greatly improved.[34]

Comparison with Other Series

A limited number of reports provide mortality figures for an unselected mixed series of congenital and acquired heart lesions. The mortality figures available for reasonably large mixed series vary from 15 to 24%.[17,42-44] Of interest are the mortality figures quoted in studies undertaken to evaluate perfusion techniques in which the nature of the priming fluid of the pump oxygenator is known. Thus, when fresh and overnight stored heparinized blood was used, the mortality was 13·8%;[13] Edglugate-Mg blood, 23%[15] and 28%;[8] dextrose-water, 14%;[45] and, using saline as priming fluid in a highly selected group of 25 patients, 8%.[18]

The acceptable mortality for a particular operation is also difficult to establish. For the first-stage correction of tetralogy of Fallot, mortality figures of between 15 and 20% have been reported.[46] The mortality for the closure of ventricular septal defects depends on whether the defect is associated with increased pulmonary resistance or other anomalies; an acceptable mortality for all cases is in the neighbourhood of 10%.[47]

The correction of relatively simple defects, such as ostium secundum and isolated pulmonary stenosis, should not carry a mortality of more than 1 - 2%.[37]

Although the comparison of mortality figures and morbidity for a whole series or for a particular operation is difficult, it still appears to be the only way to evaluate a technique. Mortality in this series, whether taken as a whole or for a particular group, is gratifyingly low and the postoperative courses of the patients were fairly uncomplicated. It is thus fair to conclude that the use of fresh heparinized blood for priming the pump oxygenator gives excellent results.

The 3 perfusion deaths (1·2%) were discussed (Table IV); none of these can be attributed to the use of freshly-drawn heparinized blood, nor can the postoperative complications be associated with this aspect of the technique.

Length of Perfusion

The longest perfusion followed by survival was 154 minutes, although a hospital death (from unrelieved cardiac disability) followed 3 months after a 196-minute perfusion. A patient operated on after this series was ended survived a 270-minute perfusion without apparent ill-effect. Longer perfusions in this series were associated with patients who did not survive (Table IV). However, continuation of perfusion may be resuscitative and long duration in itself may be the result of surgical and cardiac failure in the operating theatre and thus not of significance in causing such deaths.

Renal Complications

Our experience with post-perfusion renal complications is different to that recently reported by Doberneck *et al.*[48] Of their 1,000 extracorporeal perfusions, 3% were followed by acute renal failure; there was no correlation with length of perfusion or age group. More than half their patients developing renal failure had been perfused for less than 60 minutes. The occurrence of low urinary output with a rise in blood-urea and serum-potassium levels was clearly associated with preceding arrhythmia or other cause of low cardiac output. Of their 30 patients with renal complications, the mortality was 87%, and clinically there was an unusually rapid onset of high levels of blood urea and serum potassium. The possibility is mentioned that the biochemical disturbance may be related either to the trans-

fusion of stored bank blood containing free potassium and non-viable cells, or to absorption of breakdown products of blood free in the chest.

The duration of perfusion in the patients in our series who developed renal tubular necrosis (2·5% — Table V) was invariably longer than the average for their age group; with a single exception, perfusion lasted longer than 100 minutes in all. Compared with the report of Doberneck *et al.*,[48] a relatively smaller risk of morbidity, without mortality, arises after perfusion with fresh heparinized blood in the volumes used, and then only if perfusion is continued for more than 100 minutes. This is more particularly so in the older age group (over 15 years).

The occurrence of post-perfusion jaundice (1·7%) was also related to longer perfusions and likewise carried no mortality in this series.

Postoperative Haemorrhage

All postoperative haemorrhage has been surgical. Re-intervention for ligature, usually of a single artery, has always been successful in dealing with this complication, the occurrence of which was independent of the length of perfusion. Even lengthy perfusions did not produce any systemic bleeding tendency. The average postoperative drainage from the chest was approximately 10 ml./kg./24 hours, which is equivalent to results obtained using ACD blood, and less than half the bleeding associated with the heparinized blood, between 12 and 18 hours old, used in the same study.[14] An average drainage of 25 ml./kg./24 hours for both stored and fresh heparinized blood has been recorded elsewhere.[7]

CONCLUSION

We conclude that the use of fresh heparinized blood in priming and extracorporeal circulation is justified by results and is suitable for all patients with cardiac defects requiring surgery. It meets the needs of the poor risk cases, i.e. the very young and the older patients. The two extremes in the ratio of flow rate to body weight occur at infancy and adulthood among candidates for heart surgery,[15] and it is common experience that mortality rates are higher in patients outside childhood and adolescence. It is generally agreed that, even in machines designed to dispense with a blood prime, some donor blood is always required for infants in view of the small blood volume of the patient.[18] Because of the poor buffering potential of the small extracellular spaces at this age, fresh heparinized blood is advisable.[49] Its use in all cases allows a single proficient procedure for collection, handling and testing, which has proved suitable for emergency operations and is acceptable by good laboratory standards, to become routine.

In our practice, the possibility of incompatibility being detected on the morning of operation or even during thoracotomy is prevented by thorough tests, done previously, which exclude or identify significant blood-group antibodies in the patient. In the same way, all donors are screened at an early stage, i.e. at the time of enrolment, and then again on the occasion of each donation. This eliminates time-consuming inter-donor cross-match tests. The practice of calling and bleeding an extra donor or two for the day of operation precludes a last-minute shortage of heparinized blood, and at the same time ensures that a doubtful compatibility test or donor screen test, which occasionally excludes a unit of blood, does not inconvenience the surgical team. Repeated at greater leisure, doubtful tests are usually negative. An additional unit or two of fresh blood may thus become available during the later stage of longer perfusions.

It is still not certain at what level cold agglutinins in the patient or donors become significant with the use of hypothermia. In this series, occurrences of cold agglutinins of a high titre or wide thermal amplitude, reaching 12 to 22°C., have been brought to the prior attention of the surgeons and the degree of hypothermia is adjusted accordingly.

With the cooperation of self-reliant and enthusiastic donors, all the requirements of a programme which relies on fresh blood may be met. This surgical centre receives its cardiac patients from a very large area and depends for donation of fresh blood on a community (300,000 total population) which does not possess any particular advantages. On the contrary, the non-European section of the population does not donate blood freely or consistently. About one-third of the patients in this series were from the Coloured population group. With voluntary unpaid blood donation, the cost of cardiac surgery based on perfusion is kept to a minimum.

SUMMARY

1. A variety of anticoagulant-preservative solutions are available for the collection of donor blood intended for extracorporeal circulation; recently, pump oxygenators have been primed with the patient's own blood or with substitutes for blood. Fresh heparinized blood is, by common consent, the best priming fluid, but organizational problems in donor bleeding and laboratory management of pretransfusion blood-grouping tests have persuaded many centres to adopt other programmes for handling blood.

2. In this centre, freshly drawn heparinized blood has been used exclusively for all patients assisted by extracorporeal circulation. An account is given of the blood transfusion aspect, the blood grouping methods, and the laboratory results obtained in the extracorporeal programme of 250 patients who had a total of 256 perfusions.

3. The surgical aspects of a personal series consisting of the first 250 mixed cases of intracardiac surgery are discussed. The 32 hospital deaths are analysed in detail. The overall mortality was found to be 13·6% and, following a classification of the patients by anatomical diagnosis, the following mortality was obtained: interatrial septal defect — nil; tetralogy of Fallot — less than 12%; interventricular septal defect, uncomplicated — less than 10%; interventricular septal defect with associated conditions — 16%; pulmonary stenosis, pure — nil; pulmonary stenosis with associated conditions — 2 deaths in 14; endocardial cushion defect — 2 deaths in 17; mitral incompetence — nil; acquired aortic valve disease and multiple valvular lesions — 55%. The post-perfusion complications, with particular reference to renal tubular necrosis, are considered.

4. The surgical results obtained in this study are compared with those reported from some other centres. Mortality in this series is gratifyingly low and the post-operative courses were fairly uncomplicated.

5. It is concluded that the use of fresh heparinized blood in priming an extracorporeal circulation is justified by the results.

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