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Acute renal failure complicating cardiopulmonary bypass surgery

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SUMMARY Acute renal failure developed in 24 (5.3%) of 456 children undergoing cardiopulmonary bypass surgery during a 2-year period. It was more common in younger children, in those with complex cardiac lesions, and in those with long overall bypass times. Fourteen (58%) recovered renal function; renal failure was responsible for death in only two. Early vigorous peritoneal dialysis is advocated after cardiopulmonary bypass surgery if there is oliguria (≤ 1.0 ml urine/kg per hour) resistant to volume repletion, dopamine infusion and diuretics, intractable fluid overload, or hyperkalaemia.

Acute renal failure (ARF) has long been known as an important complication of cardiopulmonary bypass surgery (CPBS) and carries a poor prognosis.¹ The incidence of postoperative ARF differs in reported series, being influenced by the criteria used for its definition and the patient population studied, as well as by intrinsic variation. Chesney *et al.*² observed ARF in 20 (8.1%) of 248 infants undergoing cardiac surgery: 6 were dialysed and 13 (65%) died. Bhat *et al.*³ studied 490 adults undergoing open heart surgery and identified 21 (4.3%) in whom the plasma creatinine concentration exceeded 5 mg/100 ml (440 μ mol/l); 11 were dialysed and 14 (67%) died.

We have formed the impression that ARF remains a major problem after CPBS in children; perhaps advances in surgical technique have resulted in complex operations being performed on sick infants hitherto deemed inoperable. We therefore embarked on a prospective study of the incidence of ARF in children undergoing CPBS in order to investigate the factors which predispose to ARF and its outcome with treatment.

Patients and methods

Four hundred and fifty-six children underwent CPBS in the thoracic unit of The Hospital for Sick Children in 1978-79. The unit is a national and international referral centre for children with congenital heart disease and therefore receives a high proportion of complex cases.

CPBS was carried out under hypothermia using core cooling; surface cooling was also used in some

sick infants. The pump was primed with citrate-phosphate-dextrose anticoagulated whole blood and Hartmann's solution to give a haematocrit on bypass of about 0.3. Flow rates of 2.4 l/m² surface area were used with periods of reduced flow and circulatory arrest as appropriate for the surgery undertaken. All children had urinary catheters *in situ* during surgery and during at least the first postoperative day. Gentamicin (2 mg/kg 8 hourly) was given prophylactically for 5 days to nearly every infant and to older children if surface prosthetic material had been used, unless renal impairment supervened. Frusemide (0.5-5 mg/kg intravenously) was administered only if a diuretic was clinically indicated.

We have not attempted to distinguish between oliguria arising from poor renal perfusion and established acute tubular necrosis; in this complex clinical state in which diuretics have been administered and many other factors are operative, such distinction is often difficult and is of little practical importance as the outcome is determined by the inability of the kidney to fulfil its excretory role whatever the underlying pathogenesis. In this study all children who developed oliguria (the production of ≤ 1.0 ml urine/kg per hour averaged over 4 hours) resistant to volume repletion, dopamine infusion, and diuretics (frusemide 5 mg/kg intravenously), or hyperkalaemia (plasma potassium > 6.0 mmol/l), or increasing uraemia (urea > 40 mmol/l) were defined as having ARF and were dialysed.

Peritoneal dialysis was performed using standard paediatric dialysis catheters and commercially

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Arrhythmia and late mortality after Mustard and Senning operation for transposition of the great arteries

An eight-year prospective study

Arrhythmia and late sudden death are recognized complications of intraatrial repair of transposition of the great arteries. We performed a prospective study over 8 years in 100 consecutive hospital survivors who underwent Mustard (46 patients) or Senning (54 patients) operations between 1978 and 1982. Arrhythmia was analyzed by preoperative, postoperative, and serial follow-up Holter monitoring and standard electrocardiograms and was related to clinical outcome. Before repair, all patients were in sinus rhythm with a low incidence of arrhythmia. After repair, there was a gradual decrease in stable sinus rhythm during follow-up so that at a mean of 7 years after operation only 56% of patients having the Senning operation and 66% having the Mustard, with simple transposition, were in stable sinus rhythm on Holter monitoring. There was no significant difference between the two operations. Eleven patients (five after Senning [two simple, three complex], six after Mustard [five simple, one complex]) died during follow-up, four suddenly (two after Senning, two after Mustard). However, loss of sinus rhythm or the presence of arrhythmia on standard electrocardiograms or Holter recordings did not identify patients at risk for increased morbidity or mortality. Thus, even with current surgical techniques, gradual loss of sinus rhythm occurred after both Mustard and Senning operations. Because late death could not be predicted by electrocardiographic analysis, an alternative approach involving detailed hemodynamic and electrophysiologic measurements may be required to identify high-risk patients.

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A number of surgical options are now available for the treatment of children with transposition of the great arteries. Physiologic repair, involving redirection of the systemic and pulmonary venous return within the atria, by either the Mustard or Senning operation, has been the most widely performed operation.^{1,2} However, despite excellent short-term results, late complications including loss of sinus rhythm and arrhythmia have been

reported.³⁻⁷ Concern about the long-term outcome has been used as an argument in favor of anatomic repair by the arterial switch procedure.⁸ The data available on the prevalence of arrhythmia after intraatrial repair is largely retrospective and derived either from small groups of patients or from data pooled from multiple centers.^{4,7,9,10} The data apply almost exclusively to the Mustard procedure, and little information has been reported for the more recently revived Senning operation.¹¹ Interpretation of the highly variable findings of such studies is complicated by the heterogeneous nature of both the patients and surgical techniques used. In addition, many studies have not investigated the possibility that arrhythmia may have been present before operation, either as a result of atrial septostomy or septectomy or as an inherent part of the disorder itself.¹²

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Table I. Clinical characteristics

	Mustard (n = 46)		Senning (n = 54)	
	Simple	Complex	Simple	Complex
n	30	16	44	10
Boys	14	10	31	7
Girls	16	6	13	3
BAS	28	12	40	8
BH	4	4	2	0
Other previous operation				
PDA		1	2	1
PAB		4	1	
COA		1		
RBT		1		
Age range at diagnosis (mo)	1-34	3-183	2-33	3-51
Median (mo)	10	8	9	9

BAS, Balloon atrial septostomy; BH, Blalock-Hanlon; CoA, coarctation; PAB, pulmonary artery band; PDA, patent ductus arteriosus; RBT, right Blalock-Taussig shunt.

We have, therefore, performed a prospective study of arrhythmia in consecutive patients with transposition undergoing intraatrial repair at a single institution with current surgical techniques. Our aims were to determine the long-term effects on the cardiac rhythm of both the Mustard and Senning operations by means of serial electrocardiograms and Holter monitoring, to examine whether postoperative arrhythmia was related to late morbidity and mortality and whether a group of patients at higher risk for late sudden death could be identified by this approach.

Methods

Patients (Table I). The study group consisted of 100 consecutive hospital survivors of intraatrial repair of transposition of the great arteries, operated on at The Hospital for Sick Children, Great Ormond Street, between August 1978 and March 1982. They included patients with simple and complex transposition. All operations were performed by the same two surgeons, with one surgeon performing only Mustard operations and one only Senning operations. Patients were allocated to one or the other operation on the basis of the day they were first seen by the surgeon, without clinical selection, and the two operative series were performed concurrently throughout the study. Baseline clinical data collected included sex, type of transposition, date of birth, date of operation, previous palliative procedures, date of last follow-up, outcome (alive or dead), clinical symptoms, medications, and mode of death.

Protocol. Cardiac rhythm was analyzed from 12-lead electrocardiograms and Holter recordings. All patients underwent 24-hour Holter monitoring during the week before operation and 2 weeks after operation. Further follow-up recordings were obtained in all patients at The Hospital for Sick Children or at other centers with this facility at least 1 year after operation (66 patients). Recordings were repeated at 3-year intervals when possible, and no clinical criteria were applied in selecting patients for electrocardiographic monitoring. Oxford Medilog cassette recorders (Oxford Medical Inc.,

Clearwater, Fla.) with two leads (CM₁ and CM₅) were used, and tapes were analyzed visually with an Oxford Medilog playback unit. The cardiac rhythm, maximum and minimum heart rates (over 1-minute periods), longest R-R interval, and the presence of any arrhythmia or conduction defect were noted. These included junctional rhythm, supraventricular and ventricular premature beats, supraventricular tachycardia, atrial fibrillation, atrial flutter, and ventricular tachycardia. Ventricular arrhythmia was classified with a modification of the Lown criteria previously reported, with frequent (>30 per hour) or complex (multiform, couplets) premature beats considered significant.¹³ For analysis of 24-hour recordings, tapes were classified as indicating stable sinus rhythm if sinus rhythm persisted for >90% of the 24-hour period, intermittent sinus and junctional rhythm when junctional escape rhythm was present for 10% to 50% of the recording, and junctional rhythm if this was present for >50% of the 24-hour period.

Twelve-lead electrocardiograms were obtained annually at each follow-up visit. If any rhythm other than sinus rhythm was found on any recording, the patient was classified as having lost sinus rhythm from the date of the last electrocardiogram in sinus rhythm. This classification was then not altered even by return of normal sinus rhythm in all subsequent electrocardiograms. Follow-up information was obtained on the symptomatic status of patients either by personal interview or by contact with the local hospital physician.

Operative technique. The operative technique was standard during the study period. Both the Mustard and Senning operations were performed with hypothermic cardiopulmonary bypass (20° to 25° C) with aortic and bicaval cannulation. The surgeons took care to avoid damage to the sinus node, sinus node artery, and atrioventricular node, by staying away from the site of the sinus node, either high on the superior vena cava or on the tip of the right atrial appendage, when cannulating the superior vena cava. Excessive resection in the superior part of the interatrial septum was avoided. Intraatrial manipulation was also minimized. The operations were performed with aortic cross-clamping and cardioplegia with St. Thomas' Hospital solution¹⁴ injected every 30 minutes into the root of the aorta and recovered from the coronary

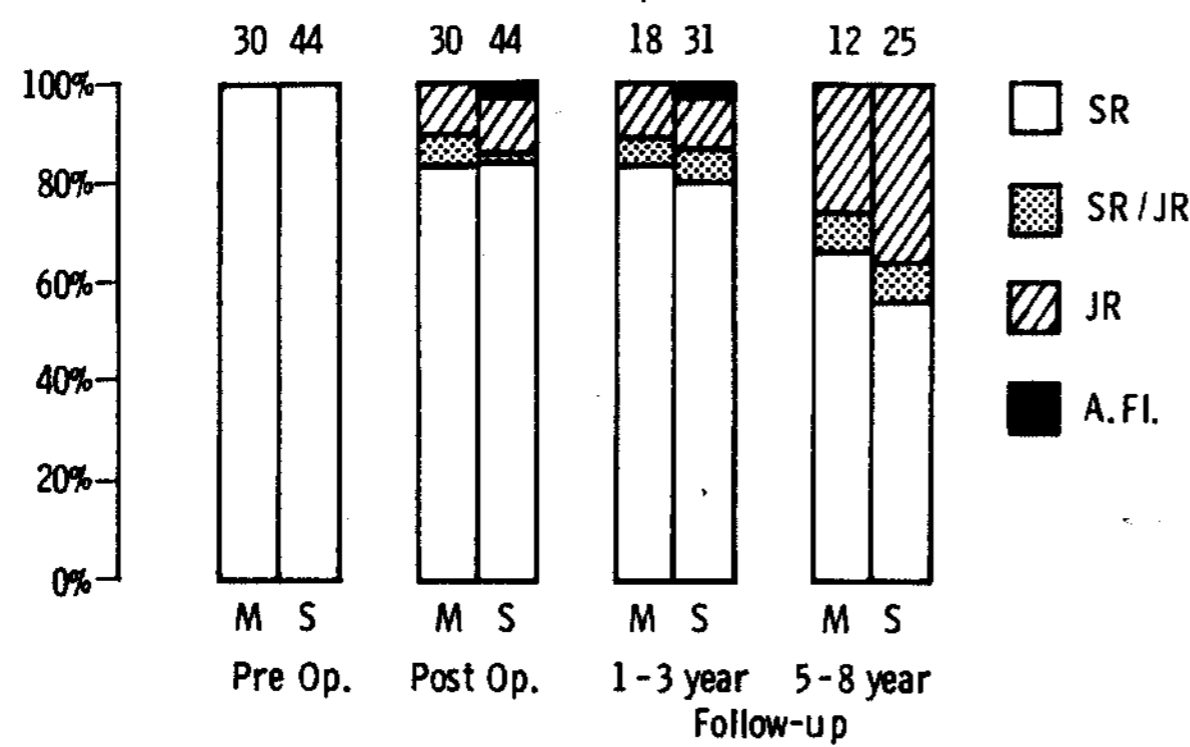


Fig. 1. Cardiac rhythm on serial 24-hour Holter monitoring after Mustard (*M*) and Senning (*S*) operation for simple transposition. There was a significant decrease in stable sinus rhythm at late follow-up. *A.F.I.*, Atrial flutter; *JR*, junctional rhythm; *SR*, sinus rhythm.

sinus. A trouser-shaped pericardial patch was used throughout the Mustard series.¹⁵ If a ventricular septal defect was present, it was closed through the tricuspid valve. Other technical details of the Mustard and Senning operations, as performed in our unit, have been described elsewhere.^{16,17}

Statistics. Survival and maintenance of sinus rhythm on serial electrocardiograms were analyzed by Kaplan-Meier estimates with intergroup comparisons by the log rank test. The effect of loss of sinus rhythm on survival was tested by Cox regression with loss of sinus rhythm as a time-dependent covariate. Comparison of continuous variables reflecting clinical characteristics between the Mustard and Senning groups was performed with unpaired Student's *t* tests. Inpatient comparison of continuous variables was done by paired *t* tests. Two-tailed tests were used throughout and the null hypothesis was rejected at a probability of <0.05.

Results

Patient characteristics (Table I). Of the 100 consecutive patients, 74 had simple transposition and underwent either a Senning (44 patients) or a Mustard operation (30 patients). In eight, this operation was accompanied by ligation of a small persistent ductus arteriosus. The remaining patients had intraatrial repair together with additional closure of a ventricular septal defect (10 Mustard operations, five Senning), relief of left ventricular outflow tract obstruction with a left ventricle-to-pulmonary artery conduit (one Mustard, one Senning), or a palliative operation for established pulmonary vascular disease (five Mustard, four Senning). The median age at repair was not significantly different for the two operations (1 to 34 months, median 10 months, for simple Mustard procedures; 2 to 33 months, median 9 months, for simple Senning procedures). Likewise there was no significant difference between the age at operation for the complex groups.

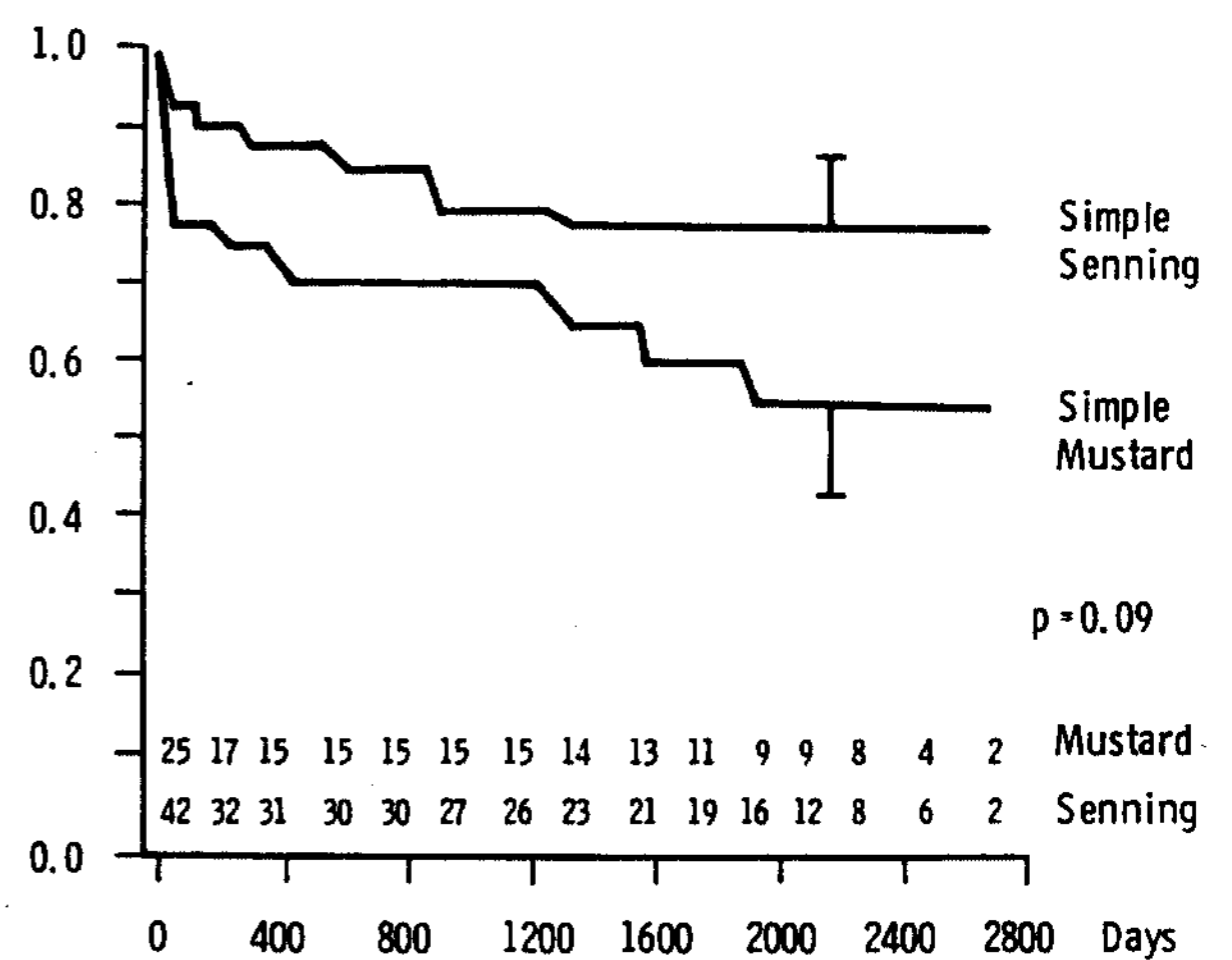


Fig. 2. Maintenance of stable sinus rhythm on serial electrocardiograms in survivors after Mustard and Senning operations for simple transposition. Vertical axis shows proportion of survivors maintaining sinus rhythm (see text for definition).

The age range, however, was greater than that for simple repair, the patients with ventricular septal defect being operated on at a younger age and those with pulmonary vascular disease at an older age. Balloon atrial septostomy had been performed as part of the initial management in 88% of patients and 10% had undergone Blalock-Hanlon atrial septectomy.

Preoperative recordings. All 100 patients were in sinus rhythm and none were receiving antiarrhythmic medication apart from digoxin (six patients). The incidence of arrhythmia was low in all groups. Five patients had sinus pauses of 1 to 1.3 seconds. Four patients had infrequent (<30 per hour) uniform ventricular premature beats, and two patients, both with pulmonary vascular disease, had higher grade ventricular arrhythmia consisting of frequent multiform premature beats and ventricular tachycardia (four beats) in one and a single run of ventricular tachycardia (five beats) in the other. Seven patients had occasional atrial premature beats (<30 in any hour), and one patient had a short run of atrial fibrillation. Intermittent junctional escape rhythm was found in five patients at a rate >60 per minute, and one patient had first degree atrioventricular block. There was no significant difference in the maximum and minimum heart rates or in arrhythmia between patients undergoing Mustard and Senning operations or between patients with simple and complex transposition (minimum heart rate during 24 hours: simple Senning group 60 to 140 beats/min [median 102], simple Mustard 60 to 150 [median 100], complex Senning 75 to 144 [median 108], and complex Mustard 60 to 127 [median

Table II. "Active" arrhythmia during postoperative 24-hour Holter monitoring

	Simple Mustard (n = 30)		Simple Senning (n = 44)		Complex Mustard (n = 16)		Complex Senning (n = 10)	
	No.	%	No.	%	No.	%	No.	%
R-R intervals 1 to 1.4 sec	3	10	5	11	2	12	2	20
SVT	1	3	1	2	0	0	1	0
AF/AFl	0	0	2	4	0	0	0	0
APCs (>30/hr)	2	7	2	4	2	12	1	10
VPCs (infrequent, uniform)	6	20	3	7	1	6	3	30
VT	0	0	0	0	1	6	0	0

AF/AFl, Atrial fibrillation/flutter; APCs, atrial premature contractions; SVT, supraventricular tachycardia; VPCs, ventricular premature contractions; VT, ventricular tachycardia.

Table III. "Active" arrhythmia during follow-up 24-hour Holter monitoring for simple transposition

	Age 1-3 yr				Age 5-8 yr			
	Mustard (n = 18)		Senning (n = 31)		Mustard (n = 12)		Senning (n = 25)	
	No.	%	No.	%	No.	%	No.	%
SVT	3	16	0	0	2	17	3	12
AF/AFl	0	0	0	0	0	0	0	0
APCs (>30/hr)	1	5	2	6	0	0	0	0
VA	0	0	0	0	1	8	0	0

AF/AFl, Atrial fibrillation/flutter; APCs, atrial premature contractions; SVT, supraventricular tachycardia; VA, ventricular arrhythmia.

110]) ($p = \text{NS}^*$). Maximum heart rates were as follows: simple Senning group 125 to 200 beats/min (median 157), simple Mustard 110 to 200 (median 166), complex Senning 120 to 220 (median 155), and complex Mustard 120 to 210 (median 160) ($p = \text{NS}$).

Postoperative recordings. Overall, 84 (84%) of the patients were in sinus rhythm on the postoperative 24-hour recordings. The remainder had either sinus rhythm with intermittent junctional escape or established junctional rhythm with a lowest heart rate of 55 beats/min. There was no significant difference in basic cardiac rhythm between the Mustard and Senning groups with simple transposition of the great arteries: In the simple Mustard procedure group, 25 patients had sinus rhythm (83%), two had sinus rhythm with intermittent junctional rhythm (7%), and three had junctional rhythm (10%); in the simple Senning procedure group, 38 had sinus rhythm (84%), one had sinus rhythm with intermittent junctional rhythm (2%), five had junctional rhythm (12%), and one had atrial flutter (2%) (Fig. 1). Likewise there was no significant difference in basic cardiac rhythm between patients with

simple and complex transposition: In the complex Mustard procedure group, 13 patients had sinus rhythm (81%), one had sinus rhythm with intermittent junctional rhythm (6%), and two had junctional rhythm (13%); in the complex Senning procedure group, seven patients had sinus rhythm (70%), one had sinus rhythm with intermittent junctional rhythm (10%), and two had junctional rhythm (20%). The incidence of "active" arrhythmia during the postoperative 24-hour recordings is shown in Table II. Overall, 12 patients had longest individual R-R intervals of 1 to 1.4 seconds ending with either a sinus or junctional escape beat. Infrequent uniform ventricular premature beats were found in 13 patients, and one patient with pulmonary vascular disease had a short (six-beat) run of ventricular tachycardia after a palliative Mustard operation. Supraventricular premature beats were found in 34 patients, but only seven had >30 beats in any hour. The incidence of supraventricular tachyarrhythmias was also low, with paroxysmal supraventricular tachycardia in three patients and atrial flutter in two. One patient had transient complete atrioventricular block (40 beats/min) and another had transient 2:1 block after a Mustard operation together with closure of a ventricular

*NS = Not significant.

defect. There was no significant difference in the incidence of any active arrhythmia apart from ventricular tachycardia between the simple and complex transposition groups or between patients having the Mustard or Senning operation. Three patients had ventricular tachycardia on Holter monitoring (two before and one after operation). All were in the group with established pulmonary vascular disease who underwent palliative Mustard or Senning procedures (33% incidence).

Follow-up

Simple transposition. Actuarial analysis of sinus rhythm on serial electrocardiograms is shown in Fig. 2. Stable sinus rhythm was present in 89% of patients after Senning and 78% after Mustard operations for simple transposition at 1 year. This had fallen to 78% and 65%, respectively, at 5 years after repair. The difference between the two operations did not reach statistical significance ($p = 0.09$).

Serial 24-hour Holter monitoring also revealed a decrease in sinus rhythm during follow-up (Fig. 1). Recordings 1 to 3 years after operation (49 patients) revealed sinus rhythm in 80% of patients with simple transposition after the Senning operation and 83% of patients after the Mustard operation ($p = \text{NS}$). The remaining patients had either intermittent sinus and junctional escape rhythm or established junctional rhythm. At 5 to 8 (mean 7) years after operation only 56% of the patients in the Senning group and 66% of those in the Mustard group had stable sinus rhythm. The minimum heart rate during the 24-hour period was significantly lower at 5 to 8 years than during the early postoperative monitoring period (45 to 120, median 82 beats/min, at 1 to 3 years versus 30 to 75, median 52 beats/min, at 5 to 8 years after operation: $p < 0.05$). However, there was no difference between the Mustard and Senning groups. Minimum heart rates below 40 beats/min were found in six of the 37 patients (16%) during the last postoperative monitoring period, but no heart rates below 30 beats/min were found. The incidence of active arrhythmias during follow-up remained low (Table III). Only three patients showed paroxysmal supraventricular tachycardia and three showed frequent atrial premature beats after 1 to 3 years of follow-up. No significant increase in arrhythmia was noted at 5 to 8 years compared with that found at early follow-up monitoring.

Complex transposition. Follow-up 24-hour electrocardiogram recordings were available for only two of 10 patients after complex Senning operation and seven of 16 patients after complex Mustard operation. Of patients in the Mustard group, four were in stable sinus rhythm, two had sinus rhythm with intermittent junc-

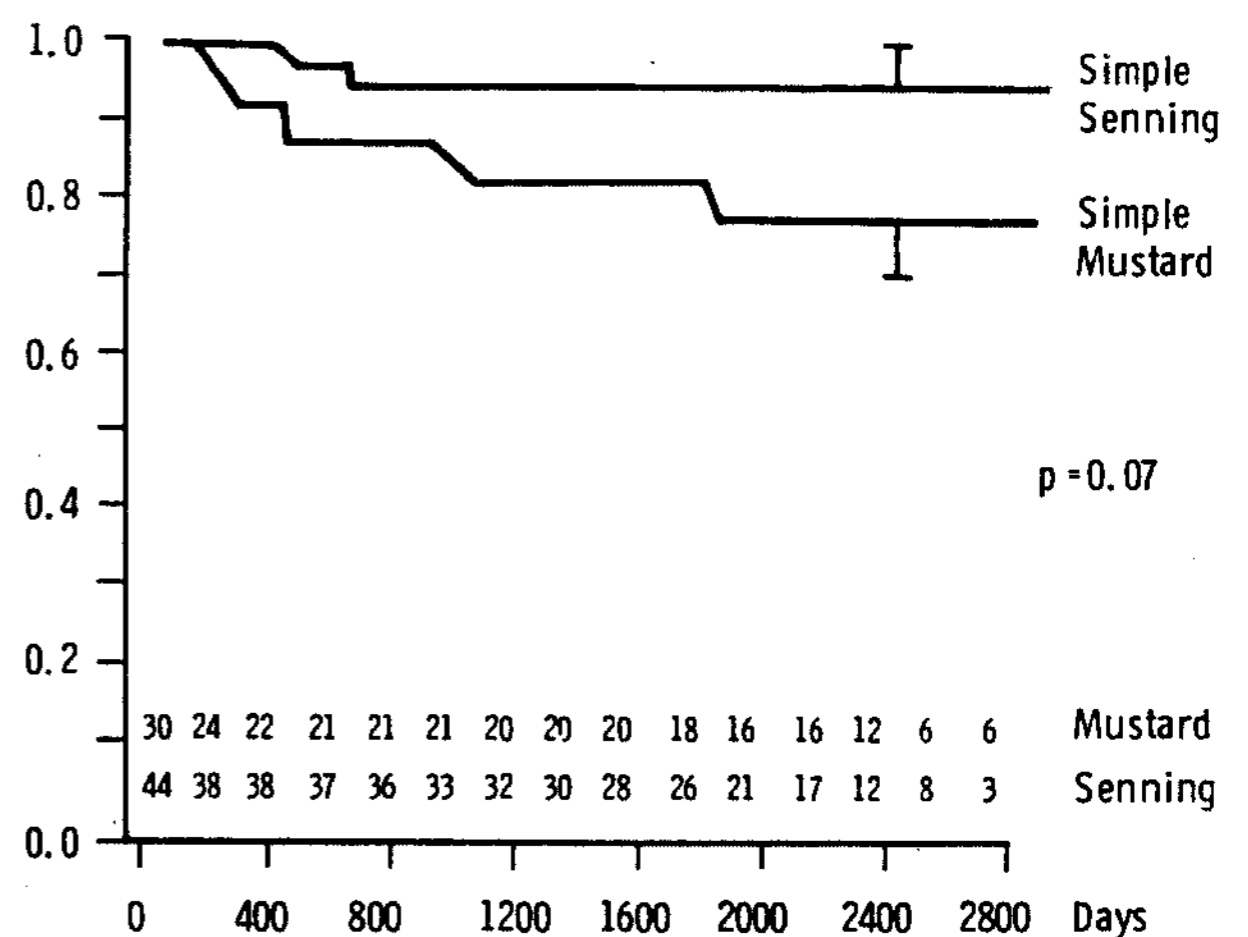


Fig. 3. Life table for survival after Senning and Mustard operations for simple transposition.

tional rhythm, and one had atrial flutter. Both patients in the complex Senning group had stable sinus rhythm. The incidence of active arrhythmia was low: One patient had paroxysmal supraventricular tachycardia, and one had frequent (>30 in any hour) atrial premature beats.

Outcome

Simple transposition. Actuarial survival rates for the simple Mustard and Senning groups are shown in Fig. 3. The survival rates at 1 year were 100% for simple Senning and 94% for simple Mustard procedures, at 5 years 95% for Senning and 84% for Mustard procedures, and at 7 years 95% for Senning and 80% for Mustard procedures ($p = 0.07$).

Complex transposition. In the smaller, more heterogeneous group of patients with complex transposition, the survival rate at 1 year was 88% for complex Senning and 94% for complex Mustard operations. At 5 years, the survival rate was better after the Mustard than the Senning operation (94% versus 70%, $p = 0.02$).

Late deaths. Eleven patients died during follow-up, five after the Senning operation (two simple, three complex) and six after the Mustard (five simple, one complex) (Table IV). Late mortality after simple Mustard repair included two patients who died after a repeat Mustard operation for attempted relief of pulmonary venous pathway obstruction (patients 4 and 5, Table IV) and one who died suddenly 18 months after a revision of a Mustard procedure for systemic venous pathway obstruction (patient 2, Table IV). One patient died in congestive cardiac failure three months after a Mustard operation with a ventricular septal defect closure (patient 6, Table IV). In the Senning group, one patient

Table IV. Clinical and electrocardiographic details of 11 patients who died during follow-up

No.	Operation	Diagnosis	Interval after operation to death (mo)	Interval after Holter to death (mo)	Holter monitoring			Clinical
					Preop.	Postop.	F-U	
1	Mustard	TGA	11	—	SR	SR	—	Died in bed
2	Mustard × 2 (SVO)	TGA	18	1	SR, VPCs	SR, VPCs, APCs	SR, VPCs, APCs	Sudden death in swimming pool
3	Mustard	TGA	10	—	SR	SR	—	<i>Salmonella</i> enteritis
4	Mustard × 3 (PVO)	TGA	1 After second repeat operation	1	SR	SR	SR	Postoperative
5	Mustard × 2 (PVO)	TGA	After repeat operation	1 wk	SR	SR	SR	Operative
6	Mustard/VSD	TGA/VSD	3	—	SR	SR	—	Congestive cardiac failure
7	Senning	TGA	16	1	SR	SR, APCs	SR/JR	Sudden death
8	Senning	TGA	22	7	SR	SR	SR	Sudden death: chest pain the day before death
9	Senning/VSD	TGA/PVD	15	4	SR	SR	SR	RV failure
10	Palliative Senning	TGA/PVD	1	—	SR	SR/JR	—	Early death
11	Senning/LV- PA conduit	TGA/LVOTO	5	—	SR, APCs ($<30/hr$)	SR, APCs ($>30/hr$)	—	Unknown

TGA, Transposition of the great arteries; APCs, atrial premature contractions; F-U, follow-up; JR, junctional rhythm; LVOTO, left ventricular outflow tract obstruction; PVD, pulmonary vascular disease; PVO, pulmonary vascular obstruction; SR, sinus rhythm; VPCs, ventricular premature contractions; VSD, ventricular septal defect; SVO, systemic venous obstruction; LV-PA, left ventricular-pulmonary artery.

with pulmonary vascular disease died in a chronic low output state (one month after a palliative operation (patient 10, Table IV), and one patient with a left ventricle-pulmonary artery conduit for severe left ventricular outflow tract obstruction died abroad in unknown circumstances (patient 11, Table IV). A further patient died in congestive cardiac failure 15 months after the Senning operation and ventricular septal defect closure (patient 9, Table IV). Of the 11 patients who died late, six had significant hemodynamic abnormalities (patients 2, 4, 5, 6, 9, and 10), and one patient died of a noncardiac cause (patient 3).

A total of four patients died suddenly, two after Mustard operations (patient 1 and 2) and two after Senning (patients 7 and 8), 11 to 22 months after operation. All were in sinus rhythm at hospital discharge and at last electrocardiogram (rate 80 to 95 beats/min). Holter monitoring during follow-up revealed only intermittent junctional rhythm in one patient and supraventricular and ventricular premature beats in the patient who had undergone Mustard revision 18 months previously.

Only one survivor after the Senning operation for simple transposition had symptoms of arrhythmia.

These symptoms coincided with a supraventricular tachycardia of 300 beats/min detected at emergency admission to the hospital. This patient subsequently required a permanent pacemaker (inserted 7 years after operation) and antiarrhythmic therapy with digoxin and propranolol. No other patients have received pacemakers.

Survival together with maintenance of stable sinus rhythm was significantly better after the Senning than after the Mustard operation for simple transposition ($p = 0.03$) because of the lower incidence of late deaths that were due to hemodynamic complications after the Senning operation (Fig. 4).

Discussion

The incidence of late complications after intraatrial repair of transposition of the great arteries is now of crucial importance because of the introduction of the alternative arterial switch operation.⁸ Despite the low immediate risk and excellent shortterm results, intra-atrial repair may not remain the operation of choice if serious late complications prove to be common and unavoidable. Numerous retrospective series have shown a loss of stable sinus rhythm late after repair.^{3-5, 7, 9, 10}

Electrophysiologic studies have demonstrated that damage to the sinoatrial node or its blood supply is likely to be responsible,^{18,19} and modifications of surgical technique have been made in an attempt to prevent this complication.^{16,17,20}

Retrospective series that include patients operated on over a long period of time and multicenter studies (in which operative technique is likely to vary) cannot answer the question of whether such modifications actually result in preservation of sinus node function. Furthermore, before a postoperative arrhythmia can be attributed to the operation itself, it is necessary to demonstrate that it was not present preoperatively. Our results do not support the earlier suggestion that significant arrhythmias are already present before interatrial repair.¹² By criteria established in studies with Holter monitoring in normal subjects, the incidence of preoperative arrhythmia was negligible and all patients were in sinus rhythm.²¹ No preoperative factors could, therefore, be established as predisposing to arrhythmia. The incidence of postoperative loss of sinus rhythm in previous publications varies greatly, which reflects significant differences in study populations and methods of detection. Our findings in patients operated on over a more recent, short study period show better preservation of sinus rhythm than in earlier reports.¹⁰ Nevertheless, even with current surgical techniques, a proportion of patients lose sinus rhythm in the postoperative period, and there is a further gradual fall-off over a follow-up of up to 8 years. In our series the probability of being alive and in sinus rhythm after Mustard operation was virtually identical to that reported by Kirklin and Barratt-Boyes.²² Although there was a trend on serial, conventional electrocardiograms toward better maintenance of sinus rhythm after the Senning operation than the Mustard, this difference did not reach statistical significance and was not supported by the results of repeated follow-up Holter monitoring. It is likely, therefore, that electrophysiologic abnormalities of the sinus node or atria are an inevitable consequence of the extensive intraatrial procedures involved in both operations.

Interest in late loss of sinus rhythm and arrhythmia stems from the possible association with late sudden death. Sudden death occurred in four of our patients, a similar incidence to that noted in earlier series.²² There was no association between late death and loss of sinus rhythm or bradycardia on either routine electrocardiograms or Holter recordings. Indeed, significant bradycardias, in either sinus or junctional rhythm, did not occur and only one patient required insertion of a pacemaker for bradycardia as a result of antiarrhythmic medications prescribed for symptomatic supraventricu-

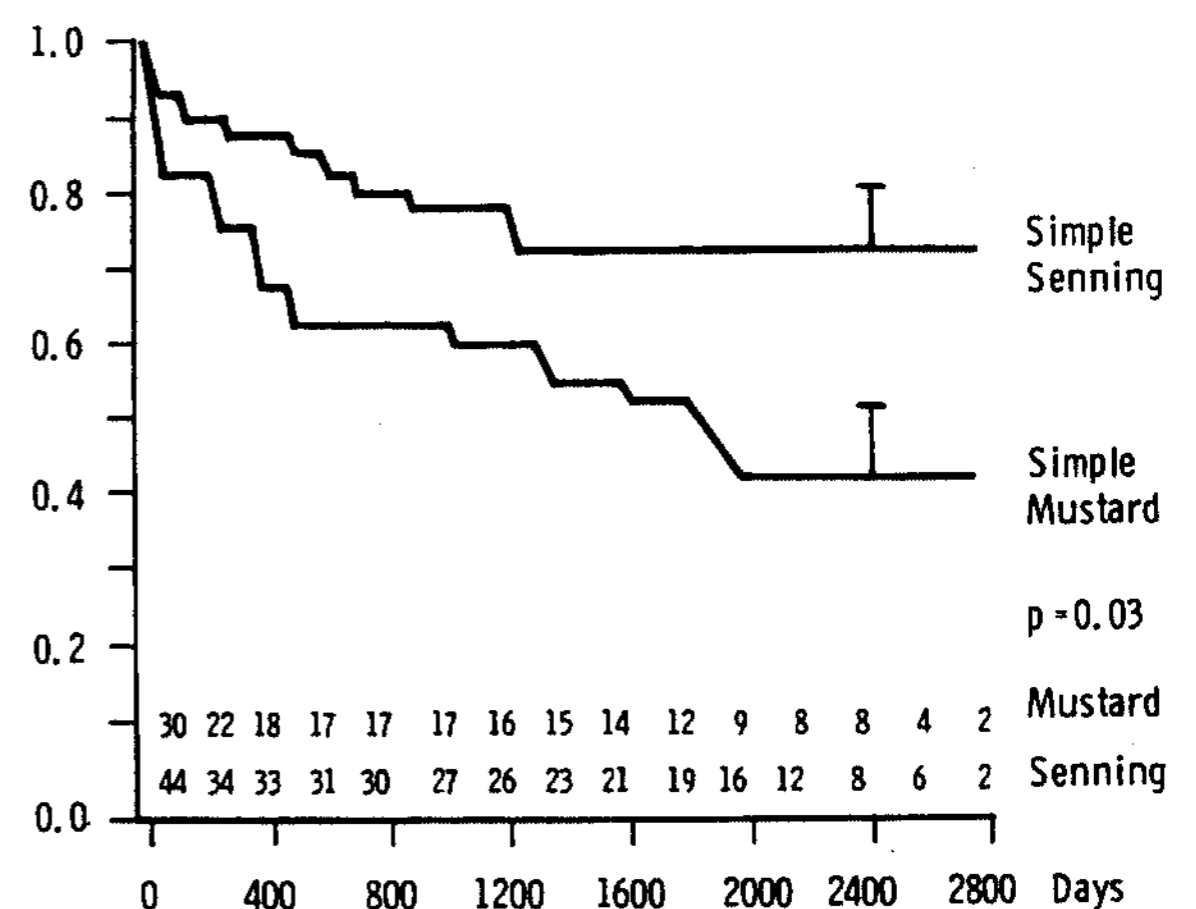


Fig. 4. Survival with stable sinus rhythm after Senning and Mustard operations for simple transposition.

lar tachycardia. Others have been more liberal in the use of pacemakers after Mustard repair. In a multicenter study from eight institutions, 39 of 372 patients received permanent pacemakers, more than half within the year after the Mustard operation.⁷ This did not appear to reduce the risk of sudden death, and two patients with normally functioning pacemakers subsequently died. The dissociation between loss of sinus rhythm and sudden death argues against a primary bradycardia as the mechanism for sudden death and, therefore, against the use of prophylactic pacing for patients without symptoms.

Postoperative Holter monitoring does reveal additional "active" arrhythmias compared with routine electrocardiograms, but in our series the incidence was low and not significantly different for the two operations. There was no difference in the results of early and late follow-up monitoring, and no association was found between supraventricular tachyarrhythmias and loss of sinus rhythm or, as has been suggested, between the presence of arrhythmia on Holter monitoring and late death. Because others have found that long-term antiarrhythmic treatment did not affect the risk of sudden death, the use of antiarrhythmic prophylaxis in patients without symptoms is not clearly indicated.⁷

This study indicates that progressive loss of sinus rhythm occurs after intraatrial repair of transposition by both Mustard and Senning operations despite modifications to surgical technique over the years. Although this fact was disquieting, we were unable to demonstrate that the loss was associated with either an increase in tachyarrhythmia or increased morbidity and mortality. Thus, at present, it should not be viewed as a powerful reason for abandoning intraatrial repair. Serial Holter

monitoring as performed in this study demonstrated few active arrhythmias and did not identify patients who subsequently died suddenly. This may be because asymptomatic arrhythmia was missed between sampling periods or, alternatively, the arrhythmias responsible for sudden death may not be preceded by arrhythmia detectable by any monitoring strategy. Because few of the rhythm disturbances documented would be expected to be life-threatening in patients with otherwise normal hearts, a more comprehensive evaluation with assessment of the hemodynamic response to different physiologic states²³ rather than a simple electrophysiologic approach may be necessary to improve understanding of the basis for late death in this condition.

REFERENCES

1. Mustard WT. Successful two-stage correction of transposition of the great vessels. *Surgery* 1964;55:469.
2. Senning A. Surgical correction of transposition of the great vessels. *Surgery* 1959;45:966.
3. El-Said GM, Rosenberg HS, Mullins CE, Hallman GL, Cooley DA, McNamara DG. Dysrhythmias after Mustard's operation for transposition of the great arteries. *Am J Cardiol* 1972;30:526.
4. Lewis AB, Lindesmith GG, Takahshi M, et al. Cardiac rhythm following the Mustard procedure for transposition of the great vessels. *J THORAC CARDIOVASC SURG* 1977;73:919.
5. Trusler GA, Williams WG, Szukawa T, Olley PM. Current results with the Mustard operation in isolated transposition of the great arteries. *J THORAC CARDIOVASC SURG* 1980;80:381.
6. Mazzei EA, Mulder DG. Superior vena cava syndrome following complete correction (Mustard repair) of transposition of the great vessels. *Ann Thorac Surg* 1971;11:243.
7. Flinn CJ, Wolff GS, Dick M, et al. Cardiac rhythm after the Mustard operation for complete transposition of the great arteries. *N Engl J Med* 1984;310:1635.
8. Jatene AD, Fontes VF, Paulista PP, et al. Successful anatomic correction of transposition of the great vessels: a preliminary report. *Arq Bras Cardiol* 1975;28:461.
9. Clarkson PM, Barratt-Boyes BG, Neutze JM. Late dysrhythmias and disturbances of conduction following Mustard operation for complete transposition of the great arteries. *Circulation* 1976;53:519.
10. Hayes CJ, Gersony WM. Arrhythmias after the Mustard operation for transposition of the great arteries: a long-term study. *J Am Coll Cardiol* 1986;7:133.
11. Byrum CJ, Bove EL, Sondheimer HM, Kavey R-EW, Blackman MS. Hemodynamic and electrophysiologic results of the Senning procedure for transposition of the great arteries. *Am J Cardiol* 1986;58:138.
12. Southall DP, Keeton BR, Leanage R, et al. Cardiac rhythm and conduction before and after Mustard's operation for complete transposition of the great arteries. *Br Heart J* 1980;32:21.
13. Deanfield JE, McKenna WJ, Presbitero P, England D, Graham GR, Hallidie-Smith K. Ventricular arrhythmia in unrepaired and repaired tetralogy of Fallot: relation to age, timing of repair, and haemodynamic status. *Br Heart J* 1984;52:77.
14. Braimbridge M, Chayen J, Bitensky L, Hearse D, Jynge P, Canković-Darracott S. Cold cardioplegia or continuous coronary perfusion? *J THORAC CARDIOVASC SURG* 1974;74:900.
15. Quaegebeur JM, Brom AG. The trouser-shaped baffle for use in the Mustard operation. *Ann Thorac Surg* 1978;25:240.
16. Stark J. Concordant transposition—Mustard operation. In: Stark J, de Leval M, eds. *Surgery for congenital heart defects*. London: Grune & Stratton, 1983:331.
17. Pacifico A. Concordant transposition—Senning operation. In: Stark J, de Leval M, eds. *Surgery for congenital heart defects*. London: Grune & Stratton, 1983:345.
18. El-Said GM, Gillette PC, Mullins CE, Nihill MR, McNamara DG. Significance of pacemaker recovery time after the Mustard operation for transposition of the great arteries. *Am J Cardiol* 1976;38:488.
19. Gillette PC, El-Said GM, Sivarajan N, Mullins CE, Williams RL, McNamara DG. Electrophysiologic abnormalities after Mustard's operation for transposition of the great arteries. *Br Heart J* 1974;36:186.
20. Ullal RR, Anerson RH, Lincoln C. Mustard's operation modified to avoid dysrhythmias and pulmonary and systemic venous obstruction. *J THORAC CARDIOVASC SURG* 1979;78:431.
21. Southall DP, Johnston F, Shinebourne EA, Johnston PGB. 24-hour electrocardiographic study of heart rate and rhythm patterns in population of healthy children. *Br Heart J* 1981;45:281.
22. Kirklin JW, Barratt-Boyes BG. *Cardiac surgery*. New York: John Wiley, 1986.
23. Griffin M, Cartwright T, Choi J, Deanfield JE. Determinants of cardiac reserve following intra-atrial repair of transposition of the great arteries [Abstract]. *Circulation* 1987;76 (Pt 2):IV 289.

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Incidence of neurological complications of surgery for congenital heart disease

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Abstract

A total of 523 cardiac surgical discharge summaries were searched for recorded evidence of adverse neurological events occurring between operation and time of discharge. Neurological events were recorded in 31 and included one or more of seizure disorder (n=16), pyramidal signs (n=11), extrapyramidal signs (n=8), coma (n=6), and neuro-ophthalmic deficits (n=6).

There were significantly more adverse neurological events after repairs for arch anomalies (16.6% of cases). There was also an association with the length of cardiopulmonary bypass and a period of low perfusion pressure either intraoperatively or postoperatively.

Of the 19 out of 23 survivors in whom long term outcome data were available, four were normal and six had persisting neurological problems directly related to the perioperative period. In a further nine of the 19 survivors, established preoperative neurodevelopmental abnormality probably contributed to their present neurological status, in addition to perioperative events.

In view of the way these data were collected, this study must represent the minimum incidence of neurological events in children undergoing cardiac surgery.

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Keywords: congenital heart disease, heart surgery, brain.

The mortality associated with the surgical repair of congenital heart defects has fallen dramatically in the last 25 years and is now less than 10% in most major units.¹ As mortality has fallen, concern has been raised that an underlying neurological morbidity has been exposed.² The incidence of this neurological morbidity in children is not known, yet this information is essential for the planning of relevant prospective studies into underlying pathophysiology in the population at risk.

Relatively simple cardiac surgery may be carried out using a closed heart approach. For more complex procedures, the heart must be opened and cardiopulmonary bypass used. During bypass, venous blood is drained from the right side of the heart, via a cannula to a pump system. The blood is then oxygenated, cooled, and pumped back to the left side of the

heart via an aortic cannula. For most bypass procedures, the aorta is also clamped proximal to this cannula. In some complex surgical procedures, complete circulatory arrest may be required for a period of time. For this the patient is profoundly cooled (<20°C) and the pump is stopped altogether.³

Previous studies in both adults and children have investigated the effect of these various bypass techniques on cerebral haemodynamics and some have looked at the relationship with subsequent neurological outcome.^{4,5} There are, however, very few data that define the overall morbidity or relate it to any particular diagnosis or surgical procedure.

The present study is a retrospective review of a consecutive series of patients undergoing cardiac surgery, at the Hospital for Sick Children, Great Ormond Street. The purpose of the study was to establish the frequency of immediate neurological events after cardiac surgery in this unit and to examine some of the factors associated with this morbidity.

Methods

Five hundred and twenty three surgical discharge summaries, created during a one year period, November 1990–October 1991, were searched for evidence of adverse neurological events occurring between operation and time of discharge. By consulting the register of admissions, we determined that this accounted for 96% of all patients undergoing cardiac surgery at the Hospital for Sick Children during the one year time period chosen. The summaries are written around the time of discharge by the cardiac surgical senior registrar by extraction from the patient's notes. The information obtained was supplemented by the perfusion records, the operation notes, and the hospital records.

Patients were initially grouped by cardiac diagnosis based on the *International Classification of Diseases*, ninth revision (ICD9), since the UK government currently requires returns of data in this form. We then regrouped them in order to reflect the underlying pathology more closely. Complex diagnoses were reviewed by an independent consultant paediatric cardiologist. The final cardiac diagnostic groups were defined as follows:

- Transposition of the great arteries (TGA) (all sorts of transposition, simple TGA, 'corrected' TGA, TGA and ventricular septal defect, double outlet right ventricle);
- Right ventricular outflow tract obstruction (tetralogy of Fallot or nearly Fallot's –

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for example, double outlet right ventricle, subaortic ventricular septal defect, and pulmonary valve stenosis or atresia);

- Left to right shunts (ventricular septal defect, atrial septal defect, atrioventricular septal defect, patent ductus arteriosus);
- Coarctation of the aorta (all arch anomalies including interrupted aortic arch)*;
- Left sided valve lesions (aortic valve disease, mitral valve disease);
- Complex conditions (including truncus arteriosus, univentricular heart, and complex combinations of the above).

Any insult to the central or peripheral nervous system, was recorded as an adverse neurological event. Neurological events were grouped as follows:

- Pyramidal signs (hemiparesis, quadripare-
sis);
- Extrapyrmidal signs (dystonia, chorea);
- Coma (including fluctuating levels of con-
sciousness);
- Neuro-ophthalmic defects (gaze palsies,
visual field defects);
- Miscellaneous disorders including
Horner's syndrome secondary to brachial
plexus injury, vocal cord palsy, isolated bul-
bar palsy, and transient ischaemic episode.

Important variables of the surgery or post-operative period were noted, for example:

- Length of cardiopulmonary bypass;
- Periods of low perfusion pressure;
- Prolonged ventilation on the intensive
care unit (>48 hours).

Intraoperatively, if the perfusion charts contained at least two consecutive entries of mean arterial pressure (MAP) below 40 mm Hg a record was made, although the frequency of recording of entries onto the perfusion charts was not known. Forty mm Hg was chosen arbitrarily as a cut off point for perfusion pressure. This value was chosen because in a previous study, carried out by this group, loss of cerebrovascular reactivity to carbon dioxide was found during cardiopulmonary bypass in children when the MAP fell below this level, suggesting that compensatory vasodilatation may not occur below this point.⁶ Further studies of non-traumatic coma in children have shown poor outcome when mean cerebral perfusion pressure (CPP) fell below 40 mm Hg, irrespective of age (CPP=MAP-intracranial pressure).^{7,8}

Postoperatively, a record was made if the notes had emphasised that there had been difficulty maintaining the child's perfusion pressure despite inotropic support. The numerical value was not known for these cases.

The families and general practitioners of those patients known to be alive were surveyed in order to establish the long term effect of any neurological event. Where possible, further information was obtained from copies of neurological and developmental examinations carried out by local paediatricians or paediatric neurologists.

STATISTICS

Differences between proportions were assessed for a priori significance by constructing $2 \times k$ tables and using the χ^2 statistic; if significant, differences between groups were then assessed by constructing 2×2 tables with the χ^2 statistic and Fisher's exact test as appropriate. Patients were grouped according to immediate outcome and differences in perioperative factors were determined by analysis of variance and a posterior significance testing using a modified t test (adjusting p values by the Bonferoni method).

Results

There was no significant difference in mean age between those children who were subsequently normal and those who had some form of adverse neurological event (35 months *v* 30 months; not significant). However, the mean age of patients who subsequently died was significantly younger (35 months *v* 12 months; $p < 0.05$).

Death rates and adverse neurological events for children with different cardiac pathologies were compared (table 1). Only those patients with the various forms of transposition of the great arteries had a significantly higher incidence of death ($p < 0.05$).^{**} 16.6% of patients within the broad classification of arch anomalies were found to have had a neurological event that was significantly greater than in those patients with other cardiac diagnoses ($p < 0.01$).

Of the 31 patients with adverse neurological events, 16 had seizures, 11 pyramidal signs, eight extrapyramidal signs, six neuro-ophthalmic deficits, six were unconscious, and there were a further four miscellaneous events. Seizures were therefore apparent in more than 50% of cases and pyramidal signs in more than a third. Twenty patients had abnormal electroencephalograms (EEGs) out of a total of 24 patients who had EEGs performed.

Of the 523 operations, 411 involved cardiopulmonary bypass, 97 used a closed heart approach, and in 15 patients (14 normal, one died) the records were not available. There was no difference in the proportion with events who had undergone open heart surgery using cardiopulmonary bypass or a closed heart approach (6.1% and 6.2% respectively). Patients with adverse neurological events had a significantly longer mean cardiopulmonary

*Note: In our view the ICD9 term 'coarctation of aorta' is misleading, since it implies uniformity of diagnosis. Henceforth, this group will therefore be referred to as arch anomalies.

**This high mortality reflects a localised period of poor results before changing surgical technique for simple transposition.⁹

Table 1 Outcome of patients undergoing cardiac surgery by diagnosis

Diagnostic group	Total No of patients	No of deaths	Deaths (%)	No of adverse neurological events	Adverse neurological events (%)
TGA	52	10	19.2*	2	3.8
Right ventricular outflow tract obstruction	134	7	5.2	11	8.2
Left to right shunts	209	8	3.8	6	2.9
Arch anomalies	36	3	8.3	6	16.6**
Left sided valve lesions	25	2	8.0	2	11
Complex	67	7	10.4	4	5.9
Total	523	37	7.1	31	5.9

* $p < 0.05$; ** $p < 0.01$.

bypass time than normal survivors (113 v 93 minutes; $p < 0.05$), as did patients who subsequently died (199 v 93 minutes; $p < 0.001$). There was no significant difference in mean aortic cross clamp time between normal survivors and those with adverse neurological events (48 v 54 minutes; not significant). However, the aortic cross clamp time in patients who subsequently died was significantly longer (48 v 79 minutes;

Table 2 Adverse neurological events, investigations and long term outcome

Diagnostic group (cardiac diagnosis)	Patient No	Age	Previous history	Cardiac operation (previous operations)	Adverse neurological events and investigations	Long term outcome	Months after surgery
RVOTO (pulmonary atresia, VSD)	5	66 m	Normal	Total correction of pulmonary atresia closure VSD (bilateral MBTS)	Encephalopathy, mild chorea, bulbar signs	Poor coordination, chorea, speech regression, obsessive behaviour, short attention span	1
						General improvement but still with chorea, short attention span, immature behaviour	21
RVOTO (TOF)	8	58 m	Down's syndrome	Left MBTS	Right hemiparesis; atrial clot on echocardiography	Global developmental delay	30
RVOTO (TOF)	10	22 m	Normal	Emergency repair of TOF (right MBTS)	Right homonymous hemianopia, left convergent squint	Left convergent squint, partially sighted	24
RVOTO (pulmonary atresia, IVS)	18	1 d	Normal	Right MBTS	Generalised seizures, pyramidal signs, poor vision; EEG: burst suppression discharges right > left, computed tomogram: bilateral parietal infarcts	Motor delay, poor vision	3
						Mild right hemiparesis, improved visual function	12
						'Functioning at prelinguistic level'	15
RVOTO (TOF)	20	5 m	Normal	Repair TOF	Variable tone, involuntary movements left leg; EEG: slow activity right > left	Febrile and afebrile seizures	24
RVOTO (TOF)	27	12 m	Down's syndrome	Repair TOF	Seizures: generalised, EEG: spike left anterior hemisphere	Learning difficulties, language delay	24
Left-right shunt (VSD)	12	10 m	Premature birth (29/40), developmental delay	Patch closure VSD	Dystonic movements	Normal	24
Left-right shunt, (VSD x 2, small right ventricle)	14	26 m	Normal	Repair VSD (repair VSD)	Seizures, coma (decerebrate posture), extrapyramidal signs, pyramidal signs, right visual field defect; EEG: excess slow waves right > left no discharges, computed tomogram: cerebral atrophy, subcortical, calcification, left subdural	Global developmental delay; functioning at 24 months (at 44 months), tremor of hands, impaired vision 6/24 right = left	18
Left-right shunt (VSD)	16	43 m	Down's syndrome	Patch closure VSD	Abnormal movements, not fixing or following	Global developmental delay	24
Left-right shunt (AVSD)	24	2 m	Down's syndrome	Two patch repair of AVSD	Focal seizures left; EEG: severe bilateral multifocal discharges	Microcephaly, floppy, global development delay	18
Left-right shunt (VSD)	29	5 m	DiGeorge syndrome: previous seizures associated with hypocalcaemia, developmental delay	Closure VSD	Seizures; EEG: multifocal discharges, computed tomogram: hypoxic ischaemic changes	Motor disorder, visual problems, learning difficulties, language delay, seizures	18
Arch anomalies (recoarctation)	13	4 m	Premature birth (27/40), bilateral ankle clonus, right porencephaly	Repair recoarctation on bypass (repair coarctation)	Focal seizures: right; EEG: multifocal discharges left	No seizures, left sided hypertonia, visual impairment	12
Arch anomalies (simple coarctation)	15	21 m	Floppy, pyramidal signs, hearing loss	End to end anastomosis not on bypass	Seizures: generalised; EEG: normal	Motor delay, hand regarding	3
Arch anomalies (hypoplastic arch and aortic coarctation)	17	25 d	Normal	Repair hypoplastic arch and aortic coarctation on bypass	Seizures, fluctuating level of consciousness; EEG: discharges around vertex with associated tongue and mouth movements	Normal	12
Arch anomalies (simple coarctation)	19	1 m	Normal	End to end anastomosis not on bypass	Seizures; EEG: low amplitude activity discharges right > left	Normal	12
Arch anomalies (IAA, VSD)	21	6 d	Respiratory arrest and period of hypotension at home (partial DiGeorge syndrome)	Reconstruction of aortic arch on bypass	Focal seizures right and left; EEG: multifocal discharges right > left poor activity in between	Squint, microcephaly, development delay	7 8 12
Arch anomalies (IAA, VSD)	23	9 d	Cardiac arrest, seizures	Repair IAA, closure VSD	Right focal seizures, dystonic posturing to pain; EEG: low amplitude both hemispheres, bitemporal discharges.	Right hemiplegia, global developmental delay	12
Left sided valve lesion (localised supra-ventricular aortic stenosis)	22	168 m	Normal	Supravalvular aortoplasty	Horner's syndrome, brachial plexus injury	Normal	12
Complex (truncus arteriosus interrupted pulmonary arteries)	6	52 m	Normal	Truncal valve replacement, revision of homograft (anastomosis left pulmonary artery to right pulmonary artery, conduit right ventricle to pulmonary artery, patch closure right ventricle)	Seizures, coma, pyramidal signs; EEG: generalised slow activity	Speech delay	24

AVSD=atrioventricular septal defect, IAA=interrupted aortic arch, IVS=intact ventricular septum, MBTS=modified Blalock-Taussig shunt, RVOTO=right ventricular outflow tract obstruction, TOF=tetralogy of Fallot, VSD=ventricular septal defect; d=days of age, m=months of age.

$p < 0.001$). One hundred and six patients in our study had circulatory arrest during cardiopulmonary bypass and although this period of time for the patients with adverse neurological events was longer (mean 44 minutes) compared with normal survivors (mean 25 minutes) and those who died (mean 27 minutes), this was not statistically significant.

Postoperatively, significantly more patients with adverse neurological events were ventilated for over 48 hours ($p < 0.05$) and they had more periods of low MAP ($p < 0.05$).

Overall, of the 31 patients with adverse neurological events, 16 (52%) had had a period of low MAP either intraoperatively or postoperatively, compared with 75 (17%) of the subsequently normal patients ($p < 0.001$). In addition, of the children with right ventricular outflow tract obstruction (the diagnosis in over one third of all patients with adverse neurological events), seven (64%) had a period of low MAP and this compares with 25 (22%) of the subsequently normal patients with this diagnosis ($p < 0.01$). For those patients with adverse neurological events and arch anomaly as their diagnosis, four (66%) had experienced a period of low MAP and this compares with only one (4%) of patients in the arch anomaly group who were subsequently normal ($p < 0.01$).

Of the 31 patients with adverse neurological events, three died during the reported admission and five died at a later date. Four patients were lost to further follow up, three of these cases living abroad. The long term outcome of the remaining 19 patients together with their specific adverse neurological event, relevant investigations, and duration of follow up is shown in table 2. In essence, patient numbers 8, 12, 13, 15, 16, 17, 19, 22, and 27 probably recovered from their perioperative insult whereas patient numbers 5, 6, 10, 14, 18, 20, 21, 23, 24, and 29, had evidence of long term sequelae.

Discussion

We have found that one in every 20 children undergoing cardiac surgery at this institution, during a one year time period, had an adverse neurological event in the immediate postoperative period. From the retrospective way in which our data were collected this must represent a minimum incidence, as it is likely that only the more severe or unusual neurological events would have been documented in the cardiac surgical discharge summaries, our initial source of reference. A recent survey seeking opinions from both paediatric neurologists and cardiac surgeons, reported a prevalence of neurological morbidity ranging from 2% to 25% (mean 8%) at six major paediatric cardiac surgery programmes in North America.¹⁰ No published first hand data are available against which to compare our results, although in a similar retrospective study of neurological morbidity in survivors of paediatric cardiac surgery in the Northern region of England an incidence of 15% was

found (A G Stuart *et al*, paper presented at the British Paediatric Meeting in York, April 1989).

Two mechanisms of neurological injury associated with cardiopulmonary bypass are postulated; microembolism (of air or particulate matter) and ischaemia, but their relative importance remains controversial.¹¹ This was *not* a study of underlying aetiology, but we did have some evidence that a period of low perfusion pressure either intraoperatively or postoperatively was present in more patients who had an adverse neurological event than in those who were subsequently normal. Future prospective studies, investigating the influence of both intraoperative and postoperative perfusion pressure on subsequent neurological morbidity may help to determine the strength of this relationship.

Pre-existing neurological abnormalities in children before their cardiac surgery have been previously documented. In one study, preoperative neurological abnormalities were present clinically in 15 of 21 (71%) patients before their corrective surgery.¹² From this present study, 13 of the 31 children (42%) with a subsequent adverse neurological event, had either a pre-existing neurological abnormality, for example, Down's syndrome, CHARGE association, or had experienced an event preoperatively that could have accounted for some of their abnormal postoperative neurology. Necropsy studies have confirmed central nervous system malformations in patients with congenital heart disease, specifically in those patients with TGA (2-5%), Fallot's tetralogy (5-10%), coarctation of the aorta (4-9%), truncus arteriosus (4-10%), and hypoplastic left heart syndrome (2-10%).^{13 14} These pre-existing abnormalities may in some way predispose towards further neurological injury during surgery.

The ICD9 system of classification cannot adequately account for the variety of congenital cardiac lesions or distinguish the differing effects on outcome of the precise nature of the lesion, for example between a simple TGA and a more complex TGA with additional intracardiac pathology or between a simple coarctation of the aorta and an interrupted aortic arch. It was for this reason that the regrouping was performed in an attempt to at least reflect the functional effect of the cardiac conditions encountered. Nevertheless, an interesting finding from this study was that the highest frequency of adverse neurological events was in the cardiac diagnostic group of arch anomaly. This group includes those patients who had simple coarctation, interrupted aortic arch, or hypoplastic arch.

These more severe forms of coarctation, often result in a preoperatively sick, acidotic and hypotensive infant, who may then undergo a technically complex repair (with, for example, in a hypoplastic arch clamping of the left carotid artery) and therefore it would not be surprising to isolate this group as potentially at high risk for neurological sequelae. As can be seen from the table of long term outcome, two of these patients had 'simple' coarctations

and were repaired via a closed heart approach; all six had seizures as their adverse neurological event. A possible explanation for the high incidence of adverse neurological events among the arch anomalies is that embolism of air or particulate matter may result from manipulation of the arch. Also in simple coarctations repaired without the use of cardiopulmonary bypass, heparin is not administered which may also increase the risk from emboli. Our results also suggest that a period of low perfusion pressure may be a contributing factor in this group. One could also speculate that a pre-existing midline brain abnormality, such as focal cortical dysplasia, could be associated with this midline arch defect and this could predispose to seizures. Certainly further research targeting this particular diagnostic group is warranted.

The most frequently noted adverse neurological event throughout the whole group was seizures, documented in 16 patients. This results in an overall frequency of 3.1% of cases undergoing surgery. The reported incidence of postoperative seizures varies between 4% and 10%, however, this quoted figure is for specific surgical procedures, for example, profound hypothermia and circulatory arrest rather than an overall frequency covering various forms of surgery.¹²⁻¹⁵ Only one child (number 29), with seizures as his postoperative adverse neurological event, continued with seizures on a long term basis (and this particular child had seizures associated with hypocalcaemia before his cardiac surgery). The rarity of long term seizures is consistent with the reported natural history of fits associated with cardiac surgery,¹⁵ but a follow up study, for example, of young adults, would be needed to exclude the possibility of epilepsy as an outcome.

In summary, of our 19 children with adverse neurological events in the immediate postoperative period for whom some long term follow up data are available, nine probably recovered from their perioperative insult, of whom only three had been normal preoperatively. Ten patients remained with long term neurological sequelae, all of these had substantial perioperative adverse neurological events. In four of these, it is difficult to determine the relative contribution of immediate preoperative from intraoperative/postoperative

insults. The remaining six had been completely normal preoperatively and their subsequent sequelae must be directly related to the period surrounding their cardiac surgery.

This represents a significant proportion of children and families whose lives may well have been impaired, despite correction of their cardiac abnormality. It must also represent a significant cost in terms of long term provision of both medical and rehabilitation services. Further research to limit the development of this neurological damage must continue to be actively supported.

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- 1 Lansing AM, Giradat RE, Masri Z. Mortality in pediatric cardiac surgery: review of a seven year experience with 944 operations. *J Ky Med Assoc* 1984; 82: 273-7.
- 2 Ferry PC. Neurologic sequelae of cardiac surgery in children. *Am J Dis Child* 1987; 141: 309-12.
- 3 Elliott MJ. Perfusion for pediatric open heart surgery. *Semin Thorac Cardiovasc Surg* 1990; 2: 332-40.
- 4 Kirklin JK, Westaby S, Blackstone EH, Kirklin JW, Chenoweth DE, Pacifico AD. Complement and the damaging effects of cardiopulmonary bypass. *J Thorac Cardiovasc Surg* 1983; 86: 845-57.
- 5 Newburger JW, Jonas RA, Wernovsky G, et al. A comparison of the perioperative neurologic effects of hypothermic circulatory arrest versus low-flow cardiopulmonary bypass in infant heart surgery. *N Engl J Med* 1993; 329: 1057-64.
- 6 Fallon P, Roberts I, Kirkham FJ, et al. Cerebral hemodynamics during cardiopulmonary bypass in children using near-infrared spectroscopy. *Ann Thorac Surg* 1993; 56: 1473-7.
- 7 Tasker RC, Matthew DJ, Helms P, Dinwiddie R. Monitoring in non-traumatic coma. Part 1: invasive intracranial measurement. *Arch Dis Child* 1988; 63: 888-94.
- 8 Kirkham FJ. ICP and CBF in non-traumatic coma in childhood. In: Minns RA, ed. *Problems of ICP in childhood*. (Clinics in developmental medicine No 113/114.) Mac Keith Press, 1991: 283-348.
- 9 De Leval MR, François K, Bull C, Brawn W, Spiegelhalter D. Analysis of a cluster of surgical failures. Application to a series of neonatal arterial switch operations. *J Thorac Cardiovasc Surg* 1994; 107: 914-24.
- 10 Ferry PC. Neurologic sequelae of open heart surgery in children. *Am J Dis Child* 1990; 144: 369-73.
- 11 Taylor KM. Brain damage during cardiac surgery. *Current Opinion in Cardiology* 1986; 1: 697-701.
- 12 Brunberg JA, Reilly EL, Doty DB. Central nervous system consequences in infants of cardiac surgery using deep hypothermia and circulatory arrest. *Circulation* 1974; 50 (suppl 2): 60-6.
- 13 Glauser TA, Rorke LB, Weinburg PM, Clancy RR. Congenital brain anomalies associated with the hypoplastic left heart syndrome. *Pediatrics* 1990; 85: 984-90.
- 14 Okada R, Johnson D, Lev M. Extracardial malformations associated with congenital heart disease. *Archives of Pathology* 1968; 85: 649-57.
- 15 Ehyai A, Fenichel GM, Bender HW. Incidence and prognosis of seizures in infants after cardiac surgery with profound hypothermia and circulatory arrest. *JAMA* 1984; 252: 3165-7.