Functional status of patients with large ventricular septal defect and pulmonary vascular disease 6 to 16 years after surgical closure of their defect in childhood

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We have reviewed 27 patients now 6 to 16 years after closure of a ventricular septal defect at 3 to 12 years of age associated with pulmonary hypertension with a view to assessing their quality of life, respiratory function, and exercise performance.

All the patients led normal unrestricted lives. Their subjective lack of symptoms was, in general, confirmed by the results obtained from assessment of lung function tests and two-stage exercise testing in 19 volunteers. Abnormal ventilation in relation to work load was noted in 5 patients and a slightly low exercise cardiac output in 6.

Although the patients led normal lives and had a satisfactory response to exercise, measurement of pulmonary artery pressure showed striking pulmonary hypertension on effort.

Despite the satisfactory progress of these patients their more long-term future must be one of conjecture and their residual pulmonary hypertension, indicative of residual pulmonary obstruction, must lend weight to arguments for earlier closure of ventricular septal defect before 1 to 2 years of age when changes in the pulmonary vascular bed may be reversed after closure of the defect.

The first successful closures of ventricular septal defect were reported in 1955 (Lillehei *et al.*, 1955; Kirklin *et al.*, 1955) and so the early childhood survivors are now young adults. Without closure of their large ventricular septal defects many of these patients could have developed progressive pulmonary vascular obstruction leading to reversal of shunt and the Eisenmenger syndrome. The object of the present study is to evaluate the quality of life of long-term survivors of surgical closure of large ventricular septal defects with preoperative pulmonary hypertension and to assess their capacity for effort by formal exercise tests and resting and exercise haemodynamics. This study is essentially an extension of a previous clinical and haemodynamic study conducted 1 to 8 years after surgical correction (Hallidie-Smith *et al.*, 1969).

Patients

We were able to follow up 27 patients, 25 of whom had been included in the previous study (Hallidie-

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Smith *et al.*, 1969), now 6 to 16 years after operation. Before operation these 25 patients all had systolic pressures in the pulmonary artery at or within 15 mmHg of that in the systemic arteries; all had a pulmonary arteriolar resistance of 8 units or above but all had clinical, radiological, and haemodynamic evidence of a pulmonary blood flow in excess of systemic. The other 2 patients who were studied (cases 14 and 15—Table 1), 6 and 8 years after operation, respectively, had systolic pulmonary arterial pressures at systemic level but low pulmonary resistances and pulmonary/systemic flow ratios of 4:1 and 5:1, respectively.

Methods

Twenty-one patients were interviewed and examined and a further 6 patients were contacted by letter. Each patient available for examination was weighed and measured and the values expressed as expected centiles of normal (Tanner, 1958). Each was questioned about his or her symptomatology, occupation, and leisure activities.

Table 1 Clinical and haemodynamic data (19 patients)

Case No.	Sex	Age (y)	Age at operation (y)	Occupation	Physical recreations	Centile Ht	Wt	Resting last recorded PAP (Systolic/diastolic) (mmHg)	Supine exercise (mmHg) (Systolic/diastolic mean)				Heart rate/min	
									PAP Rest	Ex	BAP Rest	Ex	Rest	Ex
1	M	14	6	School	Numerous	50	75	65/45	80/35	115/65	145/75	150/85	80	106
2	M	16	8	Farmer	Football, cycling	10	15	60/25	90/40	160/55	140/70	180/90	90	154
3	M	26	10	Motor mechanic	Climbing	10	5	55/25	60/30	80/40	160/80	180/105	78	120
4	M	18	7	Farmer	Football, cricket, cycling	50	50	50/15	45/15	75/40	125/70	135/75	64	120
5	M	20	6	Chef	Cycling	3	3	40/18	45/15	85/25	130/80	155/80	85	110
6	M	22	8	Church organ builder	Cycling, football	25	25	50/20	60/35	115/55	120/80	130/90	72	130
7	M	24	10	Commercial traveller	Running, weight lifting	90	97	80/20	75/20	160/70	130/75	160/100	54	112
8	M	28	12	French horn player	Cricket, cycling	10	90	60/20	40/25	100/40	110/75	180/110	84	126
9	M	21	5	Clerical worker	Football	10	10	25/12						
10	M	23	10	Builders' labourer	Football	50	50	45/15						
11	M	24	8	Policeman	Numerous	97	97	30/15						
12	F	12	13	School	Numerous	97	75	45/15	75/30	115/40	125/75	130/85	72	124
13	F	14	6	School	Top class athlete and swimmer	50	25	45/15	80/40	110/60	130/80	140/90	90	120
14	F	14	8	School	Numerous	10	3	35/12	48/20	70/35	120/80	155/80	84	122
15	F	15	8	School	Numerous	3	10	40/12	45/15	70/25	145/80	155/80	84	108
16	F	16	5	School	Tennis	50	90	45/15	65/45	100/50	100/60	140/80	86	130
17	F	23	11	University student	Tennis, hockey	50	50	55/25	80/30	120/45	140/75	120/80	84	132
18	F	26	12	Factory worker	Dancing	3	50	35/12	40/15	70/25	140/65	150/75	74	118
19	F	16	4	School	Dancing, tennis	25	10	35/10						

PAP, pulmonary arterial pressure; BAP, brachial arterial pressure.

LUNG FUNCTION TESTS (19 patients)

Forced expiratory volume in one second (FEV₁) and vital capacity (VC) were measured on a dry spirometer. Total lung capacity (TLC) was measured using constant volume plethysmography (Dubois *et al.*, 1956). The carbon monoxide transfer factor (TLCO) was measured by the single breath method (Ogilvie *et al.*, 1957). A bronchodilator (isoprenaline 100 µg) was given to assess reversibility of airways obstruction if present.

EXERCISE TESTS

Nineteen patients volunteered for two-stage exercise tests. These were performed on a constant work-rate bicycle ergometer (Elema-Schönander) at a room temperature of 19 to 22°C. The stage I, or increasing work load, test was carried out with the patients performing upright bicycle ergometry starting at zero load and increasing by 100 kpm/minute. The test was stopped in 5 patients at 85 per

cent of their predicted maximum heart rate (Astrand 1960) and continued until the patient could not continue in the other 14. Inspired ventilation was measured on a dry gas meter (Parkinson Cassu C.D.). Mixed expired concentrations of carbon dioxide (CO₂) and oxygen (O₂) were estimated (accuracy ±0.05%) on a URAS capnograph and Servomex OA 137 oxygen analyser. The analysers were calibrated with a range of previously determined CO₂/O₂ gas mixtures. These values were continuously monitored on a Mingograph 81 recorder and total ventilation (VE), oxygen intake (VO₂), and carbon dioxide output (VCO₂) were calculated. Throughout the test an electrocardiogram was simultaneously monitored on the recorder and oscilloscope screen from which the heart rate was measured. There was a period of 30 to 40 minutes' rest before the second stage.

The stage II, or steady state, exercise test was carried out in 18 patients at two-thirds of the pre-

viously determined maximum working capacity. Throughout exercise ventilation, electrocardiogram and expired O_2 and CO_2 were displayed on the Mingograph recorder as before. When steady state was reached—usually at about 4 minutes—the cardiac output was estimated using the indirect CO_2 Fick equation. Arterialised ear lobe blood was taken at rest and on exercise (after 4 to 5 minutes) for the determination of $PaCO_2$, PaO_2 , and lactate (Hohorst, 1957). In 6 patients the blood samples were inadequate and corrected end-tidal CO_2 (Jones *et al.*, 1967) was used as an estimation of arterial CO_2 . Mixed venous CO_2 ($PvCO_2$) was then determined by the plateau CO_2 rebreathing technique without correction for the downstream effect (Jones *et al.*, 1967). If the plateau was unsatisfactory an extrapolate of $PvCO_2$ was derived (Denison *et al.*, 1969).

CARDIAC CATHETERISATION

Fifteen patients agreed to have cardiac catheterisation performed with the object of measuring the pulmonary artery pressure at rest and during exercise in the supine position. The patients had already experienced at least one previous postoperative catheterisation so it was already known that 4 had a small residual ventricular septal defect. In 3 patients there was a significant step up in oxygen saturation and the ratio of pulmonary to systemic flow was 1.5:1 or less (cases 5, 6 and 8). The remaining defect could be detected only by green dye dilution technique (case 13).

Catheters were introduced percutaneously into a median cubital vein and brachial artery. The venous catheter was advanced to the pulmonary artery so that resting pulmonary arterial and brachial arterial pressures could be recorded and blood samples for oxygen saturation obtained. The zero level for the pressure measurements was the mid chest. The patients were then exercised supine for 3 minutes using alternate leg raising, the ankles being placed in wide slings with counterbalanced weights run over pulleys. The phasic pulmonary arterial and brachial arterial pressures were recorded throughout the exercise and the mean pressures each minute. Oxygen saturations were estimated at rest and immediately before the end of the exercise.

In 8 patients the arterial catheter was advanced into the left ventricle and after a 10-minute rest period the exercise test was repeated and left ventricular end-diastolic pressure recorded and left ventricular stroke work calculated at rest and after 3 minutes of exercise. Cardiac output was measured at rest and exercise by the indocyanine green dye dilution technique.

The day-to-day occupation of French horn playing

of one patient (case 8) was simulated by blowing in the supine position with simultaneous recording of pulmonary arterial and brachial arterial pressures.

Six patients volunteered to exercise in the upright position on the bicycle ergometer with pulmonary and brachial arterial lines in position. They performed an increasing work load test, starting at zero load and increasing by 100 kpm each minute until their known maximum work load was reached. Measurements of pulmonary and brachial arterial pressures were made at rest, at minute intervals, and at maximum work load with the measurement made from the xiphisternum.

Results

Twenty-one patients were interviewed and examined and a further 6 patients were contacted by letter. All except 1 patient said that they were symptom free with normal exercise tolerance. The exception (case 16) was overweight but said she lacked energy and could not sustain a prolonged game of tennis. There were 14 male and 13 female patients. Ten were still attending school and one was a university student. Of the 15 who had left school, one (mentally retarded) is at a training centre, one young woman had married and had one healthy normal baby, and the others were all in full-time employment, 6 involving heavy manual work. Four of the male patients had married and had children. All the patients remarked that they felt completely unrestricted both at work and in their leisure time and the young men seemed to participate more than the average in active sports of many varieties. Before operation all the patients were under weight (many less than 3rd centile), and short in stature (many less than 10th centile). All improved after closure of the ventricular septal defect and 2 young men are above 90th centile for height (cases 7 and 11). The individual clinical and haemodynamic findings in 19 patients who volunteered for tests of lung function are detailed in Table 1.

LUNG FUNCTION TESTS (Table 2)

Lung function tests were normal for the group as a whole but 2 showed mild restrictive ventilatory defects (cases 2 and 12). The former patient also had a low total lung capacity, residual volume, and transfer factor. The latter had a normal transfer factor but total lung capacity was not measured. Two others (cases 10 and 16) had mild airways obstruction not reversed by bronchodilator and case 16 also had a reduced transfer factor. Neither gave a history of asthma and both were non-smokers.

Table 2 Lung function results

Case No.	FEV ₁ (s)	VC	FEV ₁ s VC (per cent)	TLC	TLCO
1	2.40	3.00	80	4.25	21.8
2	2.45	2.80	88	3.60	21.7
3	3.85	4.05	95	—	—
4	3.80	4.90	78	6.85	32.5
5	2.80	3.50	80	5.60	35.6
6	4.20	5.35	79	6.10	35.9
7	4.50	5.40	83	—	—
8	3.10	3.70	85	5.30	26.9
9	3.70	4.20	88	6.30	28.7
10	3.10	4.50	69	6.10	33.1
11	4.60	5.20	88	6.81	35.2
12	1.85	2.25	82	—	17.2
13	2.10	2.50	84	3.30	18.2
14	—	—	—	—	14.7
15	2.60	2.80	93	4.10	14.3
16	2.05	3.05	67	3.90	19.2
17	3.10	3.90	79	5.00	20.6
18	2.00	2.20	91	3.90	18.0
19	2.30	2.40	96	3.40	20.1
Mean ± SD	3.00 ± 0.42	3.65 ± 0.47	84 ± 7	4.93 ± 0.74	24.4 ± 3.2
% Predicted mean ± SD	85.4 ± 14	90.2 ± 13		93.8 ± 15	86.9 ± 1.3
Norman range* % Predicted	80–120	80–120	> 75	80–120	> 75

FEV₁s forced expiratory volume in 1 second—litres/second; VC, vital capacity—litres; TLC, total lung capacity—litres; TLCO, carbon monoxide transfer factor—ml/mmHg per min.

*Normal data (Cotes, 1968).

INCREASING WORK LOAD TESTS (Table 3)

The increasing work load tests carried out on 11 male and 8 female patients showed a low maximum work load for the group as a whole. However, 5 patients were stopped when they reached 85 per cent of predicted maximum heart rate for normal subjects (Astrand, 1960). One male patient (case 2) stopped at 60 per cent of predicted maximum work load. The female patients were less enthusiastic than the males and averaged only 63 per cent of predicted maximum work load. Five stopped because of aching legs at a time when both heart rate and ventilation were quite appropriate for the work load reached. Two female patients (cases 13 and 16) had grossly abnormal ventilation for the work load reached and stopped because of breathlessness; case 16 was subsequently unable to complete the steady state exercise test. The results of these 2 female patients and 1 male patient (case 2) are the only definitely abnormal exercise responses.

STEADY STATE EXERCISE TEST (Table 4)

The cardiac and metabolic response to steady state exercise test was normal for the group. At rest blood gases and lactate were normal in all except case 13 who had a low PaCO₂. The cardiac output was calculated to be normal at rest in all patients but since the indirect Fick method can be variable at rest, these data are omitted.

The cardiac output during submaximal steady

state exercise (Fig. 1) was within normal limits in 12 patients and below normal in 6 (cases 2, 5, 7, 9, 13, and 15). Three patients (cases 3, 8, and 13) had a high venous admixture ratio. Arterial oxygen tension was low in 5 (cases 3, 5, 7, 8, and 13) and blood lactate was marginally high in case 5.

Table 3 Increasing work load test

Case No.	Sex	Maximum work load (W max) kpm/min	W max observed/expected %	Heart rate at W max beats/min	Ventilation at W max l/min
1	M	700	70	170	40.6
2	M	600	60	182	33.3
3	M	800	73	170	—
4*	M	1000	83	164	54.2
5	M	900	86	153	59.5
6*	M	800	67	175	56.8
7	M	1100	85	182	106.0
8	M	800	73	173	67.9
9*	M	900	82	186	58.7
10*	M	800	67	169	56.0
11*	M	1100	85	164	63.7
12	F	500	63	166	32.8
13	F	500	63	179	50.2
14	F	400	57	175	22.0
15	F	700	100	179	53.2
16	F	400	44	170	52.4
17	F	600	67	169	59.0
18	F	400	57	108	19.8
19	F	500	63	155	32.0
Mean ± SD		711 23	71 13	168 17	51 20

*Exercise stopped at 85 per cent predicted maximum heart rate (Astrand, 1960). Predicted values from Godfrey *et al.* (1971b).

CARDIAC CATHETERISATION

The last known resting pulmonary arterial pressures before the present study are shown in Table 1, and the resting and exercise pulmonary and brachial arterial phasic and mean pressures and heart rates

recorded during this study are also shown. Serial resting pulmonary arterial pressures of the 15 patients currently studied are shown in Fig. 2 and supine resting and exercise pulmonary artery pressure (after 3 minutes of alternate leg raising) are shown in Fig. 3 (15 patients).

Table 4 Results of stage 2: steady state exercise test

Case No.	Oxygen intake (l/min)	Arterial PO ₂ (mmHg)	Arterial PaCO ₂ (mmHg)	Lactate (mEq/l)	Cardiac output (l/min)	Venous admixture (Qs/Qt) (%)	Heart rate (beats/min)	Stroke volume (ml/min)
1	1.08	92	35	2.6	8.0	2.4	143	53
2	1.26	86	37	2.7	7.7	2.7	152	51
3	1.44	68	32	3.2	10.5	7.2	180	58
4	1.57	88	40	1.1	10.7	2.4	123	87
5	1.69	75	29	6.0	8.8	4.1	152	57
6	1.46	87	34	2.7	11.0	3.4	142	78
7	2.05	75	28	—	12.3	5.0	170	72
8	1.41	72	31	3.8	11.8	6.8	141	84
9	1.48	100	36	2.0	8.7	0.5	155	56
10	1.37	95	41	—	10.3	1.9	149	69
11	1.60	103	39	1.5	13.5	0.3	129	104
12	0.92	105	39	1.9	7.1	—	135	53
13	1.15	56	30	5.1	6.7	11.3	165	41
14	0.71	—	42	—	5.8	—	169	34
15	1.06	102	32	4.3	6.9	1.0	138	50
17	1.31	99	27	2.7	9.6	2.0	139	69
18	0.77	103	37	1.5	7.0	0.2	91	80
19	0.99	98	35	2.0	7.4	1.4	134	55
Summarised data								
Mean ±SD	1.30 ±0.34	88 ±15	35 5	2.8 ±1.4	9.1 ±2.2	3.4 ±3.1	144 ±23	64 ±12
Per cent of predicted normal value								
Mean ±SD	—	—	—	—	80 ±11	—	95 ±16	85 ±18
Normal range	—	> 85	—	2.0–5.5	80–120	1.0–4.4	80–120	80–120

Normal values taken from Spiro (1975). Qs/Qt, volume of right to left shunts as percentage of systemic cardiac output.

Fig. 1 Cardiac output during steady state exercise related to oxygen consumption. Normal value lines from Godfrey et al. (1971a).

Fig. 2 Serial resting systolic pulmonary arterial pressures (15 patients).

Resting pulmonary arterial pressure (Fig. 4)

Of the 15 patients under discussion who volunteered for supine exercise recording of their pulmonary arterial pressure none could be considered to have a normal pulmonary arterial pressure (systolic pressure of 30 mmHg or less at rest). Values of 70 mmHg or more (systolic) were recorded in 8 patients. The serial recordings of pulmonary arterial pressure suggested that pulmonary hypertension might be progressive in 4 patients and in no patient could it be regarded as becoming less severe.

Supine exercise

The supine measurements of pulmonary and brachial arterial pressures and heart rate at rest and on effort are set out in Table 1, and the pulmonary arterial systolic pressures are shown in Fig. 3. It

Fig. 3 Pulmonary artery systolic pressure at rest and on completion of 3 minutes of supine leg raising (15 patients).

should be emphasised that the exercise called for only brief effort; this was not standardised and some patients put in much greater physical work than others who had to be much encouraged. In 5 patients the exercise pulmonary arterial pressure rose to close approximation with systemic (cases 2, 6, 7, 12, 13, and 17) and in all except 3 patients (cases 3, 14, and 15) the rise of systolic pulmonary arterial pressure was 30 mmHg or more.

Upright exercise (Table 5 and Fig. 4)

The upright maximum work load test with pulmonary artery and brachial artery lines *in situ* was completed by all 6 volunteers whose maximum work load was already known. In 3 patients the pulmonary arterial systolic pressure was within 30 mmHg of the systemic arterial systolic pressure at maximum work load (cases 1, 6, and 12).

Left ventricular function (Fig. 5)

Left ventricular stroke work was calculated in the 8 patients in whom left ventricular pressures were recorded at rest and after 3 minutes leg exercise.

Fig. 4 Increasing work load test pulmonary artery systolic pressure (6 patients).

Table 5 Bicycle progressive work load test in 6 patients

Case No.	Rest PA (mmHg)	BA (mmHg)	HR/min	At 400 kpm PA (mmHg)	BA (mmHg)	HR/min	Max work load PA (mmHg)	BA (mmHg)	HR/min
1	84/45	158/100	84	118/60	148/100	130	130/75	150/110	190
3	55/32	102/60	90	95/55	100/80	135	100/60	150/85	180
5	45/15	130/80	92	80/30	160/90	142	100/40	160/105	196
6	66/35	105/60	70	90/45	120/80	115	120/80	130/85	194
8	60/25	120/80	88	88/40	130/80	122	105/45	155/100	196
12	65/30	134/84	98	105/70	140/90	160	120/80	145/90	180

PA, pulmonary arterial pressure; BA, brachial arterial pressure; HR, heart rate per minute.

Fig. 5 Left ventricular function at rest and during supine exercise in patients with repaired ventricular septal defect. Solid symbols: at rest; open symbols: during exercise.

Left ventricular end-diastolic pressure was normal at rest in 5 of them and slightly raised in 3 (cases 1, 2, and 12), but on effort it rose to 20 to 30 mmHg in 5 of the 8 patients. Those patients with mild resting pulmonary hypertension were able to increase their left ventricular stroke work while maintaining a normal left ventricular filling pressure while those with more severe pulmonary hypertension had an abnormal rise in left ventricular filling pressure with either a small increase or fall in left ventricular stroke work, suggesting impaired left ventricular function.

Haemodynamics in simulated work

We were anxious to record haemodynamic events during the day-to-day life of our patients. One of them (case 8), a professional French horn player, volunteered to simulate blowing his instrument while on the catheter table with pulmonary arterial and brachial arterial pressures recorded simultaneously. We recorded a pulmonary arterial pressure varying between 70/20 and 100/75 mmHg during this manoeuvre with simultaneous corresponding brachial arterial pressure of 120/80 and 160/105 mmHg, respectively.

Discussion

There are few reports of the effects of a ventricular septal defect or pulmonary hypertension on lung function. Kimball and McIlroy (1966) described restrictive ventilation defects with high residual volumes in 3 patients with ventricular septal

defects. McIlroy and Apthorp (1958) considered the effects of isolated pulmonary hypertension on lung function to be negligible, though a low carbon monoxide transfer factor possibly secondary to abnormal pulmonary vasculature has been occasionally described (Turino *et al.*, 1959).

In the present study 2 patients had restrictive ventilatory defects, 1 with a low transfer factor, possibly relating to pulmonary hypertension. Two other patients had mild irreversible airways obstruction which may have been the result of their previous recurrent chest infections in infancy. In the 4 patients with abnormalities of lung function the ventilation reached during exercise was below the calculated voluntary minute ventilation (as assessed by $FEV_1 \times 35$), suggesting that impaired lung function played no part in reducing maximum working capacity.

The majority of our patients have been shown to exercise normally but some have a low cardiac output on exercise which supports the findings of Maron *et al.* (1973) and Lueker *et al.* (1969), who exercised patients after closure of a ventricular septal defect in the upright and supine positions, respectively. Johnson (1962) and Jonsson and Lee (1968) showed that patients who had had a pulmonary valvotomy for pulmonary valve stenosis may also have a low cardiac output on exercise. The latter suggested that the peripheral circulation might be adapted to extract and use oxygen to a greater degree than normally and that persistence of this adaptive mechanism after operation might result in a lesser rise in cardiac output than is normally expected on effort. However, impairment of left or right ventricular function, or both, cannot be excluded and it could also be suggested that abnormal pulmonary vascular activity might limit cardiac output (Lueker *et al.*, 1969). However, in our series the finding of a low cardiac output on effort was not confined to those with severe pulmonary hypertension. Impaired left ventricular function has also been suspected in patients after closure of ventricular septal defect by finding raised left atrial pressures on exercise (Hallidie-Smith *et al.*, 1969; Maron *et al.*, 1973). More recently, Graham (1974) noted a decreased left ventricular ejection fraction in a similar group of patients. A decrease in left ventricular end-diastolic volume was also noted before operation, raising the question as to whether left ventricular function is ever normal in a patient with a large ventricular septal defect. Graham suggests that the decrease in ejection fraction may become apparent after operation because of the decreased after-load after closure of the ventricular septal defect. Our own findings are limited and relate only to postoperative studies but

suggest that there may be impairment of left ventricular function on effort, most obvious in those patients with the more severe residual pulmonary hypertension.

In support of our patients' lack of symptoms we have the objective evidence of their varied employments, their sporting activities, sometimes keenly competitive, of their normal respiratory function tests and the normal exercise performance of the majority. These findings contrast with the conspicuously abnormal measurements of pulmonary arterial pressure recorded in the majority of patients at rest and in all patients on effort including the 2 patients in whom pulmonary vascular disease was not detected before operation. Some of our patients must be subjected to severe pulmonary hypertension during the course of their day-to-day activities as shown by our French horn player (case 8) whose increase in pulmonary arterial pressure could not be explained on the basis of a raised intrathoracic pressure or normal Valsalva response (Lee *et al.*, 1954). Our overall findings of pulmonary hypertension suggest that preoperative changes in the pulmonary vascular bed have failed to resolve to a greater or lesser extent. Thus, even those patients with a normal or nearly normal resting pulmonary arterial pressure may show a pronounced increase in pulmonary arterial pressure on effort because of limitation of the pulmonary vascular bed, perhaps related to lack of elasticity of small pulmonary vessels or fixed pulmonary vasoconstriction.

Serial records of pulmonary arterial pressure in our patients now 6 to 16 years after closure of their ventricular septal defects have not suggested any remission of pulmonary hypertension though in 10 of the 15 patients there is no evidence of progression. However, in 5 patients there is some increase in pulmonary arterial pressure and Weidman and DuShane (1974) noted a progressive increase in pulmonary vascular resistance in 4 of 12 comparable patients.

It was recognised that all except 2 of our patients had developed pulmonary vascular disease before closure of their defect; but the 2 in whom it was not recognised (cases 14 and 15), nevertheless, had been shown to have exercise pulmonary hypertension, suggesting that they already had some reduction of their pulmonary vascular bed by obstructive disease before operation. Thus, it seems that pulmonary vascular disease may already be established by early childhood in any patient with a large ventricular septal defect. This may not completely regress after operation and indeed may progress. Vogel *et al.* (1974) have shown the importance of the vasoconstrictive element and it seems likely that those individuals whose pul-

monary blood flow was appreciably increased by vasodilators when investigated before operation may have the best chance of good long-term results. However, the most important long-term prognostic factor may be the age at which the ventricular septal defect is closed. Our patients were all over 2 years of age at the time of closure of their defect but recent advances in surgical and cardiopulmonary bypass techniques have made closure of ventricular septal defects in infants over 6 months of age a safe procedure (Weidman and DuShane, 1974). The Eisenmenger syndrome is rare below the age of 2 years and it has been shown that pulmonary arterial intimal changes are rare in the first year of life (Hislop *et al.*, 1975), and in infancy failure of the pulmonary vascular resistance to fall may not necessarily imply a poor long-term prognosis (Wagenvoort and Wagenvoort, 1974). Thus it seems advisable to recommend closure of a large ventricular septal defect with pulmonary hypertension well before the age of 2 years to ensure a satisfactory long-term result and the results of the present series should act as impetus to early surgical correction. The life expectancy and prognosis of our patients must remain in doubt, perhaps on the continued ability of the right ventricle to sustain the severe pulmonary hypertension which has challenged it from birth, on adequate left ventricular function and on factors which determine the progressive nature of pulmonary vascular obliterative changes. Thus far, however, the quality of life for these young men and women has been very good and certainly superior to that expected of comparable patients with ventricular septal defects and pulmonary vascular disease treated medically.

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