

## Exercise ability after Mustard's operation

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### Abstract

Twenty children who were well six to 12 years after undergoing Mustard's operation for transposition of the great arteries were studied. Each child performed a graded maximal treadmill test with measurements of gas exchange and oxygen saturation, and had electrocardiography carried out. Nineteen were also catheterised, and oxygen consumption was measured so that pulmonary and systemic flow could be calculated. Compared with 20 age and size matched controls, seven of the patients had normal exercise tolerance (as judged by a maximal oxygen consumption of greater than 40 ml/kg/min), 10 showed a moderate reduction (30-39 ml/kg/min), and three were more seriously limited. None of the patients with normal exercise tolerance had obstruction of venous return but six of those with mild impairment of exercise ability had partial or complete obstruction of one or both of the vena cavae. More severe limitation was associated with pulmonary vascular disease and fixed ventricular outflow tract obstruction.

Formal exercise testing of apparently well children who have undergone Mustard's operation identifies those with haemodynamic abnormalities that may require intervention.

Mustard's operation has for many years been a recognised treatment for transposition of the great arteries.<sup>1-3</sup> More recently the development of the 'arterial switch' operation has focused interest on which method is likely to produce the best long term results.<sup>4</sup> The early mortality and medium term survival of children who have undergone the Mustard's procedure at this hospital have been reported previously.<sup>5</sup> The present report forms part of a detailed study of a group of patients who seem to have excellent results. Our clinical impression is that many children reviewed as outpatients are remarkably well, and we considered that it was important both for the individual child and for planning future surgical strategies to ascertain whether this was indeed the case.

Exercise performance was assessed in each child using a graded treadmill test continued to exhaustion, with continuous measurement of gas exchange, oxygen saturation, and heart rate.

Previous studies have reported restriction of exercise ability,<sup>6</sup> poor ventricular function,<sup>7-10</sup> and a high incidence of arrhythmias and sinus node dysfunction<sup>11-13</sup> in some patients. In addition problems in constructing the baffle may result in reduced systemic or pulmonary venous

return.<sup>14-16</sup> To assess the importance of these changes in the limitation of exercise ability, cardiac catheterisation with biplane right ventriculography and measurement of cardiac output was carried out during the same admission. Aspects of lung function including spirometry, plethysmography, and carbon monoxide transfer factor were also measured.

### Patients and methods

Twenty children (18 boys and two girls) aged from 6 to 14 years were studied between November 1985 and February 1987, an average of nine years (range 6-12) after they had undergone Mustard's operation. They were recruited consecutively from the outpatient department when they attended for routine follow up if they were symptom free, of suitable age, and were living a normal, active, school life.

Two had previously had symptomatic rhythm disturbances (treated in one by pacing and in the other by disopyramide) but both these children had been stable for at least three years. The group was taken from some 105 surviving children who underwent the Mustard's procedure for simple transposition of the great arteries at this hospital during the period 1974-85.<sup>5</sup> Balloon atrial septostomy had been carried out in all patients at a mean age of 12 days, and Mustard's operation followed at six weeks to 22 months (mean 10 months). The atrial baffle, constructed according to the design of Quaegebeur and Brom, was made of Teflon 00951/USCI, dura mater, or pericardium.<sup>17</sup> The mean period of follow up was nine years (range 5.7-12.1).

The tests were completed in three days, except in two patients who were recalled for cardiac catheterisation a few weeks later, and in one in whom it was deferred because his blood contained hepatitis antigen.

Informed consent was obtained from the parents, and the children agreed to take part. At the time of the study, with increasing awareness of late complications after Mustard's operation and the risk of sudden death in an apparently well child, it was felt to be in the best interests of the children to obtain as much information as possible about them. Cardiac catheterisation was therefore normal clinical practice in our unit.

The clinical history was supplemented by a parental questionnaire about exercise ability (table 1). This was designed at this hospital after a pilot project in which we analysed the habitual exercise tolerance of a number of children with various types of congenital heart disease and

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widely differing abilities. It was given to the mother when the child was admitted, and a researcher worker was available to answer queries.

Each child was weighed, measured, and examined, and had chest radiography, electrocardiography, and echocardiography performed; most also had a 24 hour recording of the electrocardiograph.

#### EXERCISE TESTING

Each child performed graded maximal exercise on a treadmill using the progressive treadmill test described by Bruce *et al.*<sup>18</sup> A full 12 lead electrocardiogram was recorded every three minutes, with a short trace for the rate every minute (Cambridge model 3044B). An Ohmeda oximeter was attached to the ear and the saturation read at one minute intervals. Fractional concentrations of all the expired gases were measured by respiratory mass spectrometry, enabling minute ventilation, oxygen consumption, and carbon dioxide production to be calculated every half minute, using the argon dilution method described by Davies and Denison.<sup>19</sup> After a series of measurements at rest, each child walked, and then ran, on the treadmill following the Bruce *et al.* protocol, using three minute stages with a progressive increase in both speed and inclination. The children were encouraged to continue until they could run no more. During the recovery phase, heart rate and oxygen saturation were noted each minute until the resting levels had been regained. The tests were done in an air conditioned room (ambient temperature 20–22° C) during the morning at least an hour after a normal breakfast.

A control group of 28 normal school children with no evidence of past or current cardiac or respiratory disease performed the same exercise protocol. From these a subgroup of 20 was selected, matched for height and weight, and as nearly as possible for age and sex.

#### CARDIAC CATHETERISATION

Each child was catheterised under ethomidate anaesthesia with the ventilation monitored by measurements of end tidal gases. With the patients breathing air and then oxygen, continuous calculations of respiratory gas exchange were made.<sup>19 20</sup> Systemic and pulmonary blood flows were calculated from the measured oxygen consumption and the oxygen content of the blood calculated using the direct Fick principle. Right and left ventriculography was carried out after the measurements were complete. In those patients with evidence of vena caval obstruction, balloon dilatation was attempted and the pressure measurements repeated.

#### CALCULATION AND ANALYSIS OF THE EXERCISE DATA

Minute ventilation ( $\dot{V}_E$ ), oxygen consumption ( $\dot{V}O_2$ ), and carbon dioxide production ( $\dot{V}CO_2$ ) were calculated for each 30 second period dur-

ing rest and exercise. Ventilation was expressed in l/min at body temperature, water vapour, and prevailing atmospheric pressure.  $\dot{V}O_2$  and  $\dot{V}CO_2$  were corrected for temperature, pressure, and saturation, and quoted in ml/kg/min at standard temperature and pressure (dry).

The achievement of each child was analysed first in terms of his peak level of oxygen consumption, carbon dioxide production, and the respiratory ratio ( $r = \dot{V}CO_2 : \dot{V}O_2$ ). The length of time that he ran, and the heart rate and minute ventilation just before stopping, were also compared in the two groups.

To study the responses of heart rate and ventilation during submaximal exercise the data were analysed in the following ways:

(1) The pulse rate and minute ventilation at an oxygen consumption of half the predicted maximum for weight was calculated from the graphs of pulse rate and  $\dot{V}_E$  against  $\dot{V}O_2$ . Predicted maximal  $\dot{V}O_2$  was derived from the normal values collected by Godfrey (54 ml/kg/min for boys, and 45 ml/kg/min for girls).<sup>21</sup>

(2) The ventilatory anaerobic threshold was calculated from the plot of  $\dot{V}_E$  against  $\dot{V}O_2$  as described by Wasserman and Whipp.<sup>22</sup> The threshold is the point at which  $\dot{V}_E$  begins to rise more steeply than  $\dot{V}O_2$ , and was determined by drawing the regression line through the first half of the data points and observing where the graph began to diverge from that line. This point is considered to be an indirect indicator of the onset of detectable metabolic acidosis, provided that pain or anxiety have not caused hyperventilation. That possibility is excluded by showing that  $\dot{V}_E : \dot{V}CO_2$  does not increase at the same point.

(3) There are many reasons for thinking that metabolism at cellular level alters gradually, and that to seek a single point at which the change takes place can only give an artificial value. Buller and Poole-Wilson therefore treated the graph of  $\dot{V}O_2/\dot{V}CO_2$  as a curve and fitted to it a polynomial equation of the form  $y = ax - bx^2$ .<sup>23</sup> In this model  $y$  would reach a peak (and subsequently decline) when  $x = a/2b$  and  $y = a^2/4b$ . This peak they called the 'extrapolated maximal oxygen consumption'. They showed that in adults it was little more than the actual maximal oxygen consumption achieved, and that it was not dependent on effort. This method was applied to each child's data (fig 1).

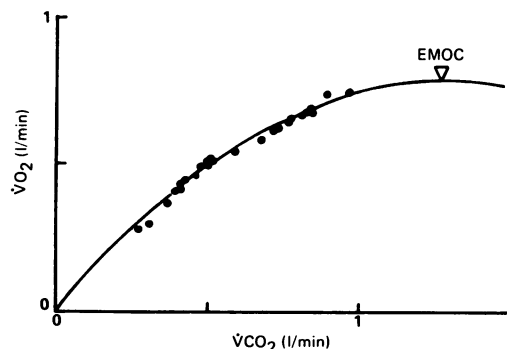


Figure 1 An individual child's data showing the plot of  $\dot{V}O_2$  against  $\dot{V}CO_2$  and the curve  $y = ax - bx^2$  fitted to it, using multiple regression. The curve is extrapolated to its theoretical maximum (EMOC).

Table 1 Questionnaire for parents: Please mark the box on each line that best describes your child during the past six months

	0	1	2	3	4	5
<b>School:</b>	None	Half time or less	Part time or special school	Full time limited sport	Full sport	Competitive sport
<b>Walking on the flat:</b>	Breathless at rest	A few yards	30-50 Yards slowly	100-400 Yards, slowly	Two miles, steadily	Two miles, briskly
<b>Stairs:</b>	Never tries	One flight difficult	Two flights difficult	Two flights all right	Normal	Can run up four flights
<b>Running:</b>	Never tries	Few paces only	20 Yards gently	100 Yards jogging	Normal speed, 100 yards	Normal speed, 400 yards
<b>Tiredness:</b>	Always tired	Tired every day	Often tired	Sometimes tired	Normal	Very energetic

Maximum score 25.

The differences between the children who had undergone Mustard's operation and the normal controls were examined using Student's *t* test for the group as a whole, and where appropriate the paired *t* test. Regression lines for each child's data were drawn using the method of least squares.

### Results

The 18 boys had a mean age of 10 years (range 6-13) and two girls were 7 and 8 years old. All the children had classical transposition and none had had a ventricular septal defect large enough to require closure at the time of operation. One boy had had moderately raised pulmonary artery pressure at the time of his Mustard's operation when 11 months old (47/25, mean 32, mm Hg).

All the children were white, and the heights and weights of all but one were distributed normally across the centiles. The one exception lay substantially below the third centile for height and weight, and had done so since infancy.

All the patients presented as clinically well, leading a normal life and at school full time. Most of the children took part in normal sport at school, three of them playing in teams. Replies to the exercise questionnaire (table 1) suggested that almost all could walk two miles gently, manage two flights of stairs, and run 100 yards. Scores for patients ranged from 18-21 compared with 22-25 for the normal subjects.

All the children looked well, except one who looked slightly desaturated (confirmed by a resting oxygen saturation by ear oximetry of 86%). The liver was palpable below the costal margin in each of four boys, and slightly raised jugular venous pressure was found in three. The second heart sound was generally single and loud.

The chest radiographs showed clear lung fields with heart sizes and pulmonary vascular markings that were either normal or minimally increased.

The resting electrocardiograms had axes between +120 and +190 with the expected right ventricular dominance and hypertrophy in 17 children, but evidence of biventricular hypertrophy in three. At rest the electrocardiograms showed junctional rhythm with inverted p waves in aVF in 11 children, and marked sinus bradycardia (38 and 42 bpm) in two. One child was paced. Of the five in normal sinus rhythm, the 24 hour tape showed episodes of junctional rhythm in two. Four with evidence of sinus node dysfunction at rest also had ventricular ectopic beats on the tape.

Haemoglobin concentrations ranged from 122-162 g/l, mean 138 g/l. All three children with an increased haemoglobin concentration (greater than 150 g/l) showed mild resting desaturation, both on ear oximetry and during catheterisation.

Mean values for the whole group of patients for lung volumes and carbon monoxide transfer were within the normal range, though in two children vital capacity was reduced to 60% of the predicted value.

### EXERCISE TESTS: MAXIMAL PERFORMANCE

Figure 2 shows the highest values for heart rate, oxygen consumption, minute ventilation, and respiratory ratio, which were measured just before the end of exercise. Most of the patients developed at least as high a respiratory ratio as their controls and in only one can poor effort explain the reduced performance. One patient developed ventricular bigemini at a heart rate of 145 bpm and her test was stopped by the obser-

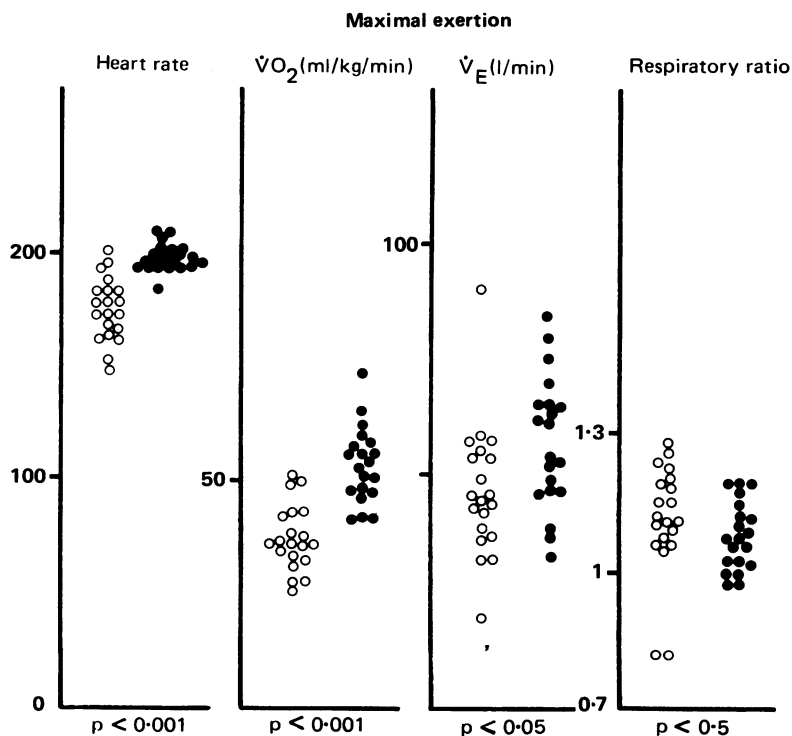
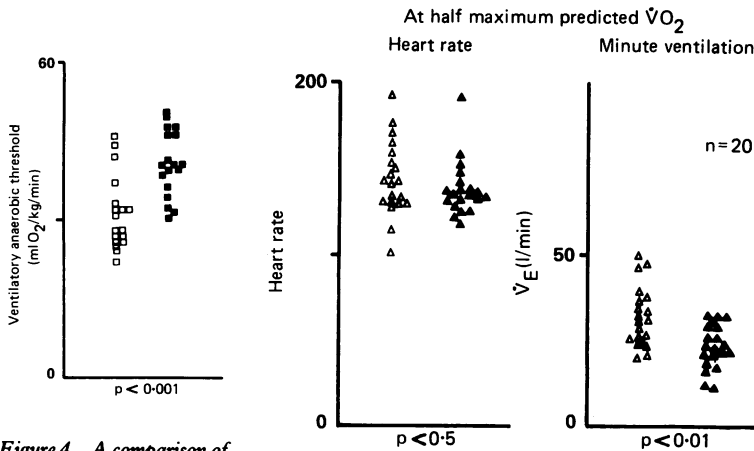


Figure 2 The maximal values for oxygen consumption, heart rate, minute ventilation, and respiratory ratio achieved by 20 children who had undergone the Mustard's operation (open circles) and by 20 age and size matched controls (closed circles). The significance of differences was analysed with Student's *t* test.

**Table 2** Peak exercise performances of those 18 children who had had Mustard's operations and who completed satisfactory exercise tests compared with their normal matched controls

	Patients	Controls	p Value
Male:female ratio	17:1	15:3	
Mean age (years)	9.8	9.5	>0.5
Mean height (cm)	136	137	>0.5
Mean weight (kg)	30	31	>0.5
Maximal heart rate	175	195	<0.001
Peak $\dot{V}O_2$ (ml/kg/min)	38	52	<0.001
Peak $\dot{V}_E$ (l/min)	49	57	<0.1
Maximal r value	1.15	1.08	0.01
Minutes run	12.1	17.6	<0.001



**Figure 4** A comparison of the ventilatory anaerobic threshold in 18 patients (open squares) and 18 controls (closed squares). The significance of differences was analysed with the paired t test.

**Figure 3** The heart rate and minute ventilation at an oxygen consumption corresponding to half the maximal predicted  $\dot{V}O_2$  for weight, in 20 children who had undergone the Mustard's operation (open triangles) and 20 controls (closed triangles). The significance of differences was analysed with the paired t test.

ver after eight minutes. These two patients were therefore excluded from the analysis of maximal performance (table 2). The 18 children who were able to complete satisfactory tests compare closely with the controls in average age, height, and weight, but there are significant differences in the mean times run on the treadmill, the peak oxygen consumption achieved, and the heart rates at the end of exercise.

Most children established sinus rhythm soon after starting exercise, even when they had been in junctional rhythm at rest. In the child who had a pacemaker an endogenous atrial node took over shortly after the beginning of exercise.

Six patients had resting ear oximeter readings of 95% or less, confirmed in the five who were catheterised by a mean oxygen pressure in air of 8 kPa. Ten children desaturated during exercise by at least 5%.

**SUBMAXIMAL EXERCISE**

Figure 3 shows the heart rates and ventilation measurements during submaximal exercise when the  $\dot{V}O_2$  reached half the predicted maximum. There is no difference between the patients and their controls in the heart rate, but at that level of exercise there is a significant difference in minute ventilation (paired t test,  $p < 0.01$ ).

No ventilatory anaerobic threshold could be detected in one patient and one control child. Thus 18 pairs of results are compared in fig 4, and there is a significant difference between them, with a lower threshold in the patient group (paired t test  $p < 0.001$ ).

To calculate the 'extrapolated maximal

**Table 3** Details of 20 patients who had undergone Mustard's operations

Age (years)	Maximal $\dot{V}O_2$ (ml/kg/min)	Maximal heart rate	Desaturation at rest (<10 kPa in air and <50 kPa in 100% oxygen)	Desaturation on exercise (by ear oximeter)	Baffle leak	Superior or inferior vena caval obstruction	Poor right ventricular function (ejection fraction <50%)	Other
<b>Group 1: normal maximal oxygen uptake (&gt;40 ml/kg/min)</b>								
13	57	180	No	No	No	No	Yes	No
11	50	170	No	No	No	No	Yes	Left ventricular outflow tract obstruction
9	49	190	No	No	No	No	No	No
10	43	170	No	>10%	Yes	No	No	No
13	42	165	Yes	No	No	No	No	No
9	41	180	No	>10%	No	No	No	No
9	40	175	No	No	Yes	No	No	No
<b>Group 2: maximal oxygen uptake (30-39 ml/kg/min)</b>								
12	39	150	No	>10%	Yes	Superior (complete)	Yes	No
7	39	192	No	No	No	Inferior	No	Balloon dilatation during catheterisation
10	36	168	No	>10%	No	Both	No	Balloon dilatation during catheterisation
11	36	170	No	5-10%	Yes	Inferior	No	Balloon dilatation during catheterisation
9	36	175	No	5-10%	No	No	Yes	No
10	35	180	No	>10%	No	No catheter	No catheter	No catheter
11	35	180	Yes	No	Yes	Inferior (complete)	Yes	No
13	33	160	No	5-10%	No	Inferior	No	Balloon dilatation during catheterisation
6	32	160	No	No	No	No	No	Paced
10	32	174	No	5-10%	Yes	No	No	No
<b>Group 3: maximal oxygen uptake (&lt;30 ml/kg/min)</b>								
9*	28	145	Yes	No	No	No	Yes	No
7	28	175	Yes	5-10%	No	No	Yes	Pulmonary vascular disease
12	26	199	No	No	Yes	No	No	Left ventricular outflow obstruction

\*Child taking disopyramide developed bigemini.

oxygen consumption', the curve  $y=ax-bx^2$  was fitted to the graph  $\dot{V}O_2/\dot{V}CO_2$  for each patient and control using multiple regression. The mean value for the patients was 63% of that for the controls, but the actual peak  $\dot{V}O_2$  achieved was considerably less than the extrapolated maximum in both groups (71% in controls and 79% in patients). This contrasts with reported findings in adults in whom the achieved level was at least 95% of that extrapolated.<sup>23</sup> Taken together, these three ways of analysing information during exercise—not just at the end—show that anaerobic metabolism begins at a lower level of exercise in the patients than in their matched controls.

#### EXERCISE ABILITY IN RELATION TO HAEMODYNAMIC FINDINGS

Seven patients had peak oxygen consumptions in the normal range (that is,  $>40$  ml/kg/min), 10 had mild reduction in exercise ability (30–39 ml/kg/min), and three were more severely restricted ( $<30$  ml/kg/min). Comparison of parents' responses to the questionnaire (table 1) showed almost no difference between the three groups, the range of scores being 19–21 in group 1, 18–21 in group 2, and 18–20 in group 3.

Table 3 summarises the characteristics of the three groups, and their main findings at cardiac catheterisation. The detailed haemodynamic data are being published elsewhere.<sup>24</sup> Only one child in the group with normal exercise tolerance had an appreciable haemodynamic abnormality; this was a variable gradient of 70 mm Hg across the left ventricular outflow tract apparently caused by a leaflet of the mitral valve, and unlikely to be amenable to treatment.

In the group of patients with moderate restriction of exercise, however, six of nine had partial or complete obstruction of either the inferior or superior vena cava, or both. In four of these six the obstruction was successfully relieved during cardiac catheterisation by balloon dilatation.<sup>24 25</sup> The three children with more severe restriction of maximal performance had pulmonary vascular disease (mean pulmonary artery pressure 86 mmHg), severe fixed left ventricular outflow tract obstruction, and ventricular bigemini, respectively.

The presence of an actual or potential leak through the baffle was shown by the course of the catheter or by saturation data in seven patients; this did not seem to affect exercise ability.

#### Discussion

All the patients studied were considered by themselves and their families to have normal exercise ability on initial questioning in the clinic, though a later questionnaire revealed a slight reduction in regular activity. The selection of well children was deliberate: these are children for whom we are particularly anxious to secure a good future, and in whom the early detection of problems may be most valuable. The group represented more than half of those operated on who were symptom free, of school age, and still attending follow up at this hospi-

tal. There was an obvious predominance of boys in the study. This reflected the fact that only a quarter of all the Mustard's operations had been in girls, and also an element of chance in that we recruited all suitable subjects as they presented to the outpatient clinic.

On formal testing seven did indeed perform just as well as their controls, and 10 did slightly less well. Three were clearly so limited that one would expect their lifestyle to be affected and yet their parents seemed satisfied. Our results suggest that parents of a child who has had major cardiac surgery are pleased with the result even when it falls short of normality and do not, unless specifically asked, draw attention to moderate exercise limitation. Moreover it is not possible to discriminate the more able children from the rest on the basis of the parents' assessment.

Even though most of the patients had some evidence of sinus node dysfunction at rest, they generally established and maintained sinus rhythm during exercise. The heart rate responses at half the predicted maximum work rate were the same as in the controls.

Desaturation during exercise is likely to be the result of a combination of factors including an increase in the gradients through the baffle as systemic venous return increases, encouraging right to left shunting through any potential leak.

Both the increased ventilatory response at half the maximal predicted  $\dot{V}O_2$  (fig 3) and the lower ventilatory anaerobic threshold (fig 4) show that carbon dioxide production increases in relation to oxygen consumption at a lower work rate in patients than in controls. This suggests a relative reduction in muscle perfusion and cardiac output which, if not the result of a diminished chronotropic response, must reflect a smaller stroke volume.

The validity of the concept of the ventilatory anaerobic threshold as the point at which anaerobic metabolism is detected has been fiercely debated.<sup>26 27</sup> Anaerobic metabolism is associated with the production of lactate, but this occurs at different work levels in different muscles and the blood concentrations of lactate are determined by rates of removal as well as production. In addition at any level of exercise there will be some muscles that are better perfused than others. To expect to define a single point where the pattern of metabolism changes therefore is patently a simplification. Nevertheless it is known that endurance exercise ability can be well predicted from the ventilatory anaerobic threshold, and it therefore seems to have empirical justification.<sup>26</sup>

Buller and Poole-Wilson described the method of fitting the curve  $y=ax-bx^2$  to the graph of  $\dot{V}O_2/\dot{V}CO_2$ , because a continuous and progressive change is more probable than an abrupt alteration in metabolism. In this study the fit was good (mean  $r=0.96$ ) and there was a clear difference between patients and controls, reflecting an earlier divergence from a linear relationship in the patients, but the difference between the actual and predicted maximum values was far greater than that found by Buller and Poole-Wilson in adults.<sup>23</sup>

The analysis of data at the end of maximal exercise that has been satisfactorily performed enables separation of the normal from the abnormal. It is data collected during submaximal exercise, however, that show that the abnormality lies in the shifts in metabolism not in the heart rate response.

In summary, we have shown that the moderate restriction of exercise is caused by patients not being able to continue with full aerobic exercise as long as normal children, and this leads to earlier fatigue. Their impressive determination to try is shown by the high respiratory ratios achieved (table 2).

Those children who had normal exercise tests, with one exception, had satisfactory results on cardiac catheterisation, whereas the incidence of partial obstruction of systemic venous return was high in the group with moderate restriction of exercise. This group may require relief of obstruction by surgery or by balloon dilatation.<sup>24 25</sup> Those with severely impaired exercise ability will have important (although previously unsuspected) haemodynamic abnormalities.

As a result of this study and the increasing sophistication of echocardiographic equipment it is now our policy to do formal exercise tests and echocardiography with Doppler studies on all children five to 10 years after they have undergone Mustard's operation. If either test suggests the possibility of partial obstruction of systemic venous return we then recommend cardiac catheterisation and balloon dilatation.

We thank Dr Brodie Knight for permission to use data on the exercise tests of a number of normal children. We are also grateful to Mr D Cramer and the technical staff of the department of clinical physiology for their help with the exercise tests.

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