THE RESPONSE TO EXERCISE

OF CHILDREN WITH CONGENITAL HEART DISEASE

A thesis submitted by

Mervyn Richard Hamilton Taylor
M.A., M.D., M.R.C.P.I., M.R.C.P.(Lond.)., D.C.H.,

for the degree of Doctor of Philosophy

at the University of London

October 1972

CONTENTS

CONTENTS

Dedication 6

Notes 7

Acknowledgements 8

Abstract 9

General Summary 11

SECTION I

Introduction 25

SECTION II

Abbreviations 32

Methods and Materials 35

Outline of the Exercise Test 39

Source of Normal Values 45

Children Studied 45

Spirometry 45

Peak Expiratory Flow Rate 46

Maximum Voluntary Ventilation 46

Body Surface Area 46

Blood Samples 46

Blood Gas Electrodes 49

pH Electrode 51

The Gasmeter and Tissot Spirometer 52

Tap, Valve and Rebreathing Circuit 52

Breathing Circuit Resistances 53

Oxygen and Carbon Dioxide Meters 53

Mixed Venous PCO_2 54

Collision Broadening Effect 55

Recorder 56

The Bicycle Ergometer 56

Electrocardiograph 61

Cardiac Catheterisation 61

SECTION III

Normal Values 65

Introduction 67

Statistics 68

Spirometry and PEFR 70

Maximum Voluntary Ventilation 70

Comparison of 1969 and 1971 Results 70

Maximum work load 73

Heart Rate 74

Ventilation 78

Cardiac Output 80

Stroke Volume 84

Cardiac Output Based on Ear Blood Samples 87

Cardiac Output at Rest 88

Venous Admixture 89

Blood Gases, pH and Oxygen Saturation at Rest and on Exercise 92

Physiological Dead Space 93

SECTION IV

Cyanotic Congential Heart Disease 102

(1) The Ventilatory Response to Hypoxic Exercise 103

Introduction 103

Materials and Methods 104

Results 110

Discussion 114

Summary 117

(2) Oxygen Consumption During Hypoxic Exercise 118

Introduction 121

Materials and Methods 121

Results 130

Discussion 131

Summary 136

(3) Fallot's Tetralogy: The Response to Exercise Before and After Total Surgical Correction 137

Introduction 138

Materials and Methods 140

Results 144

Discussion 158

Summary 165

SECTION V

Acyanotic Congenital Heart Disease 168

(1) Congential Heart Block 169

Introduction 170

Materials and Methods 172

Results 178

Discussion 189

Summary 195

(2) Aortic Stenosis 196

Introduction 198

Materials and Methods 198

Results 202

Discussion 221

Summary 226

(3) Pulmonary Stenosis 227

Introduction 229

Materials and Methods 229

Results 229

Discussion 240

Summary 243

SECTION VI

Appendix 245

Tables of Individual Results .. .. .. } 246 - 267

Equations .. .. }

Bibliography 268

DEDICATION

This thesis is about children with congenital heart disease. Some of them are dead now, and most of these died during or shortly after an attempt to give them an easier, longer life. Some of those still surviving have little apparent disability, some are greatly disabled and could scarcely ride the bicycle when they came to the laboratory. Among the severely disabled children who will not survive a normal lifespan were some of the most helpful, cheerful, and co-operative children I have met; others, of course, were tearful and withdrawn. All of the children had anxious parents. The rest of this thesis is made of numbers and figures, there are no personalities in it, but behind it are the sick children and their parents to whom this work is dedicated in the hope that it may help to increase the understanding of what happens in congenital heart disease.

NOTES

1. None of the patients studied were taking cardioactive drugs at the time of study.

2. Tables with the suffix 'A' will be found in the appendix.

3. The paper on congenital heart block which was to have been appended to this thesis has been omitted. Instead the data from the paper, with some additional data, has been incorporated into the sub-section on congenital heart block.

ACKNOWLEDGEMENTS

The work for this thesis was carried out between February 1970 and February 1972. It would have not been possible but for the help of many people. The research was supported for the first few months by the Brompton Research Fund and for the remainder of the time by the Eden Fellowship in Paediatrics.

Dr. Simon Godfrey was my supervisor and a continual source of ideas and argument. The frequency with which his name appears in the references indicates how much this work is based on research that he has done in the past. Dr. M. Joseph, Dr. M. Honey, Mr. O. Tubbs, Mr. M. Paneth and Mr. D. Ross allowed me to study patients under their care. Miss S. Anderson and Dr. M. Silverman provided technical assistance, informed comment and sarcastic wit. Dr. Rajamma Matthew gave advice on cardiological matters. For further technical assistance I am grateful to Miss J. Woodley-Page, Miss H. Dean, Miss G. Earl, Miss T. Andrea, Miss A. Turner and Mr. E. Ziedford

Mr. J. Greenway at the Imperial College Computer Centre gave assistance with computer programming and day-to-day running of programmes. Mr. A. Nunn of the Medical Research Council Tuberculosis Research Unit gave advice on statistical matters.

I am grateful to Mr. P. Bishop and his staff in the Institute Library, Miss J. Scott-Elliot and Miss Pegus and their staff in the Marsden Hospital Medical Illustration Department and to Mrs. D. Peacock who turned her hand from reports on research for Guinness to medical research, and typed this thesis.

ABSTRACT

This thesis is based on a study of the cardio-respiratory response to exercise of normal children and children with congenital heart disease.

A. Normal Children

Values were obtained for

1. heart rate
2. minute ventilation
3. cardiac output
4. venous admixture

on exercise.

B. Cyanotic congenital heart disease.

1. Children who became hypoxic hyperventilated on exercise. The degree of hyperventilation was proportional to the fall in arterial oxygen saturation.

2. Children who became hypoxia on exercise had a lower oxygen consumption than normal children but a normal carbon dioxide production.

3. Children with Fallot's tetralogy were studied before and after total surgical correction. The maximum work load completed by the two groups did not differ significantly nor did the pulmonary blood flow on exercise. A large proportion of the 'totally corrected' group still had right to left shunts on exercise.

C. Acyanotic congenital heart disease.

1. Congenital heart block

The atrial rate increased normally with work; the ventricular rate increased more slowly. Patients who reached a normal maximum work load had a low cardiac output on exercise. Patients who failed to reach a normal maximum work load had a normal cardiac output.

2. Aortic Stenosis

The mean maximum work load completed by these children was significantly lower than normal. Caridac output and stroke volume were low on exercise. Minute ventilation was normal. The change in cardiac output (and also stroke volume) between work loads was related to the severity of the aortic stenosis.

3. Pulmonary stenosis

The mean maximum work load completed by these children did not differ significantly from normal. Minute ventilation on exercise was normal in contrast to a report of increased minute ventilation on exercise in adults with pulmonary stenosis. Heart rate, cardiac output and stroke volume were all significantly lower than normal on exercise.

GENERAL SUMMARY

GENERAL SUMMARY

This thesis reports the results of exercise studies in normal children, children with aortic stenosis, pulmonary stenosis, congenital heart block, Fallot's tetralogy and totally corrected Fallot's tetralogy. There is little information available regarding the cardiopulmonary response to exercise in children with congenital heart disease, and much of the data is therefore new. The changes which occur in each form of heart disease have been recorded but the reason for these changes is not always clear and further research will be required to determine why these variations from the normal occur.

Most exercise tests on children with congenital heart disease have involved very small numbers of children. The controls have usually been few or adult or children with mild degrees of heart disease. The concept of cardiac index unfortunately haunts the literature. The resting systemic cardiac output/body surface area regression line does not pass through zero (Cayler et al 1963). On exercise in the present study it did not pass through zero either. It is therefore illogical to use the cardiac index to compare the results of different patients although it may be 'good enough' for clinical purposes at rest. In the present study the number of controls exceeds the number of patients and the same methods and equipment were used for the normal and abnormal subjects.

Normal Values

The re-study of 27 normal children has provided that is probably the first longitudinal study of the cardio-respiratory response to exercise. It confirmed the regression equations of Godfrey et al (1971). It appears that the increments for height given in their equations adequately describe the changes in maximum working capacity, cardiac output, stroke volume and heart rate which occur with growth. The increase in physiological dead space with increasing weight also agreed with that of Godfrey et al (1971) although the intercept was lower.

The normal values provided for venous admixture, cardiac output and stroke volume based on arterialised ear blood samples provide standards with which to compare results from children who cannot be assumed to have a normal dead space or who have heart or lung disease causing a right to left shunt.

Between the ages of 9 and 16 years boys increase in height by approximately 39 cm. and girls by 32 cm. The boys' weight goes up by about 30 kg. and the girls' by 27 kg. over the same period (Tanner 1958). During this time there will be a mean yearly increase of cardio-respiratory parameters of the following amounts:-

	Boys	Girls	
Dead space	5.6 ml.	5.1 ml.	At rest (Plus an increment for tidal volume)
Heart rate	-6.6 beats/min.	-5.8 beats/min.	On exercise, dependent on $\log_{10} \dot{V}O_2$
Minute ventilation	.8 l./min.	1.0 l./min.	On exercise
Cardiac output	0.14 l./min.	0.11 l./min.	On exercise
Stroke volume	4 ml.	3.8 ml.	On exercise
Maximum work load	16 watts	11 watts	

The longitudinal study has shown that these values will hold good over a period of two years and with such a base of normal values it should now be possible to make a longitudinal study of the changes brought about by heart and lung disease. The natural history of these diseases could then be expressed in terms of their functional effect as measured by exercise testing and not only as reported by the parents. It should also be possible to provide some information for the surgeons so that they may know how good or bad the functional results of operation have been.

Maximum Working Capacity

Maximum working capacity in normal children is higher in boys than in girls and increases with increasing height. The maximum working capacity of children with aortic stenosis, Fallot's tetralogy and surgically corrected Fallot's tetralogy was significantly lower than normal.

In children with pulmonary stenosis the maximum working capacity was lower than normal but not significantly so. In both the aortic stenosis and pulmonary stenosis groups some of the children exceeded the expected maximum work load. In the Fallot's tetralogy and corrected Fallot's tetralogy groups none did so.

In children with aortic stenosis, Fallot's tetralogy and corrected Fallot's tetralogy the maximum working capacity was compared with the parents assessment of the child's exercise tolerance. It was found that the group of children assessed as having mild exercise intolerance included children whose maximum working capacity ranged from 35% to 96% of the expected maximum. Parents cannct help but be emotionally affected by knowing that their child has congenital heart disease and this colours their assessment of the child's exercise capabilities, yet their assessment is often taken into account in deciding the timing of surgery for the children.

Minute Ventilation

In children with cyanotic congenital heart disease it was found that on exercise their minute ventilation was greater than normal and their oxygen consumption was less than normal. The child with the greatest increase in minute ventilation had a ventilation of 298% of the expected minute ventilation. The increase in minute ventilation in these children was related to their change

in arterial oxygen saturation. Three children with a long history of cyanosis from early life, low arterial oxygen saturations at rest in air, and haemoglobin concentrations of greater than 16 grams/100 ml. did not increase their minute ventilation as much as the other children, although measurement of their maximum voluntary ventilation had shown that they were capable of doing so. At rest it has been shown that patients with cyanotic congenital heart disease have a diminished ventilatory response to hypoxia (Sorensen and Severinghaus 1968, Byrne-Quinn et al 1972) and this diminished response has also been shown in subjects living for many years at high altitude (Weil et al 1970). It has been suggested that a diminished response to hypoxia only develops after about 10 years residence at high altitude (Weil et al 1970) but of the children who had a diminished response to hypoxia on exercise in this study two were under the age of 7 years and one was 10½ years of age. The longest any one of them had been cyanosed was 3½ years. It seems that a diminished response to hypoxia on exercise in congenital heart disease may be apparant at an earlier age than in normal subjects exposed to the hypoxia of high altitude. It must however be remembered that the altitude studies were performed at rest.

Patients with heart DISEASE OFTEN COMPLAIN THAT they become 'breathless' on exercise. It is however, important to distinguish between dyspnoea which is a

sensation and hyperventilation which is an abnormal increase in ventilation. In this study only the cyanosed children were found to hyperventilate during steady state exercise. The patients with aortic stenosis and pulmonary stenosis did not hyperventilate during steady state exercise. In adults with pulmonary stenosis hyperventilation has been found during steady state exercise and was related to the increase in mean right atrial pressure (Gazetapolous et al 1966). It may be that an increase in mean right atrial pressure and hyperventilation on exercise only occur in long standing pulmonary stenosis and so will only be found in adults.

Oxygen Consumption

A reduction in oxygen consumption during exercise was found in children who became hypoxic on exercise. The oxygen consumption fell below the normal for a given work load in proportion to the fall in arterial oxygen saturation. The children with acyanotic heart disease did not have a reduction in oxygen consumption on exercise. No technical cause was found for this phenomenon. Children with cyanotic congenital heart disease have been reported to have a lower than normal oxygen consumption during treadmill exercise although it was possible that the work load had been reduced by the children holding onto the treadmill bars (Cassells and Morse 1962).

Changes in lactate as calculated from base excess changes, did not differ significantly from normal in the children with a reduced oxygen consumption, nor was their carbon dioxide production increased. It is suggested that the reduction in oxygen consumption may be due to shunting of blood away from organs not directly concerned with performing external work.

A complete absence of oxygen consumption has been reported in babies with cyanotic congenital heart disease during 'cyanotic spells' (Kinnaird 1971). New-born sheep have the ability to reduce their oxygen consumption in response to hypoxia but this ability is lost soon after birth (~~Moss~~ CROSS et al 1959). An ability to reduce oxygen consumption in response to hypoxia would obviously increase a baby's chances of surviving a difficult delivery and it may be thatchildren with cyanotic congenital heart disease retain this ability while normal children do not.

Heart Rate

Heart rate on exercise at any given work load decreases with increasing height and is related to the logarithm of the oxygen consumption, so that the heart rates of children of different heights differ more at high than at low work loads. Girls have a higher heart rate than boys at any given work load. The children with aortic stenosis had a lower than normal heart rate at low levels of work but a higher than normal heart rate

at high levels of work. The children with pulmonary stenosis had a low heart rate at both the lower and higher work loads but the heart rates were closer to normal at the higher work loads. Children with Fallot's tetralogy had heart rates that were higher than normal on exercise. The children who had undergone total surgical correction had heart rates within the normal range but also had prolongation of their intraventricular conduction times as shown by abnormally long QRS complexes. It is difficult to see why an obstruction at one point in the circulation should produce one pattern of heart rate changes and an obstruction at another point produce a different pattern. The increase in heart rate on exercise in a group of children with cyanotic congenital heart disease (mainly Fallot's tetralogy) has been reported previously. (Cassels and Morse 1962).

Cardiac Output

At rest the cardiac output was low in congenital heart block and aortic stenosis but not in pulmonary stenosis. On exercise the cardiac output was low in aortic stenosis and pulmonary stenosis. The patients with congenital heart block fell into two groups, those with a low cardiac output on exercise and those with a normal cardiac output on exercise. The congenital heart block patients with a normal cardiac output on exercise had a lower than normal maximum working capacity, while those with a low cardiac

output on exercise had a normal maximum working capacity. It appears that an ability to tolerate a low cardiac output and the consequently large arterio-venous oxygen difference is necessary to attain a normal maximum working capacity. Patients who cannot compromise and maintain a normal cardiac output do not reach a normal maximum work load. The maximum work load of the children with pulmonary stenosis was not significantly lower than normal. The maximum work load of the children with aortic stenosis was significantly lower than normal but three children with severe stenosis still exceeded their expected maximum work load. It appears that children can compensate, to a certain extent, for the limitations imposed by aortic or pulmonary stenosis or congenital heart block but the degree to which the compensation is successful varies from individual to individual. It has been shown that the low cardiac output found in pulmonary stenosis may persist after the stenosis has been relieved by surgery and it has been suggested that this is due to tissues having become adapted to working with a wide arterio-venous oxygen difference (Jonsson and Lee 1968).

Stroke Volume

Stroke volume on exercise was increased in congenital heart block. This provides some compensation for the slow ventricular rate. In aortic stenosis and pulmonary stenosis the stroke volume on exercise was lower than normal and in aortic stenosis the difference between the observed and expected change in stroke volume was

related to the degree of aortic stenosis, but this relationship was not found in pulmonary stenosis. It is suggested that the relationship between the aortic valve gradient and stroke volume changes might be used to follow the progress of children with aortic stenosis and enable an assessment of changes in the severity of the stenosis to be made without subjecting the child to repeated cardiac catheterisation. This could be an important aspect in the management of aortic stenosis as this condition increases in severity with increasing age (Cohen et al 1968).

Fallot's Tetralogy

Children with Fallot's tetralogy had a lower than normal maximum working capacity, an increased minute ventilation and heart rate, an increased systemic blood flow and a decreased pulmonary blood flow. At rest eight out of nine of the children had an abnormal degree of right to left shunting. On exercise the shunt became progressively greater as the work load increased.

'Totally Corrected' Fallot's Tetralogy

On exercise the maximum working capacity and pulmonary blood flow of the children who had had total correct of Fallot's tetralogy was not significantly higher than that of the pre-operative children. Their systemic blood flow was lower than normal and the right to left shunt was lower than in the pre-operative children although on exercise seven of the eleven 'totally corrected' children still had right to left shunts.

Heart rate on exercise was lower than in the pre-operative group. It is not possible to say whether the reduction in heart rate was a response to the alteration in haemodynamics and the increase in arterial oxygen saturation or to damage to the heart during surgery, as the majority of the patients had prolonged QRS complexes on their electrocardiographs.

Minute ventilation on exercise was lower than in the pre-operative group but was still greater than normal probably due to the persistance of right to left shunts in some of the patients.

On exercise the main 'benefits' produced by total surgical correction were a reduction in minute ventilation, a reduction in right to left shunting with a consequent reduction in hypoxia, anda reduction in systemic blood flow. The maximum working capacity of the post-operative children was higher than that of the pre-operative children, though not significantly so, and it still remained lower than normal. The post-operative children were improved as compared with the pre-operative ones but the response to exercise was not normal. This is in contrast to the reports of some workers (Gotsman 1966, Bristow et al 1970, Haider 1971). In the majority of patients the operation of 'total surgical correction' of Fallot's tetralogy was certainly not 'total'.

Exercise studies of children with congenital heart disease provide a view of the functional effect of congenital heart disease which is not obtained from resting studies or from a history of exercise tolerance. Longitudinal studies of congenital heart disease by exercise studies are possible and should be of value in clinical management.

SECTION I

INTRODUCTION

INTRODUCTION

Congenital heart disease is a common disability which is gradually being mitigated by advances in surgery. Routine cardiac catheterisation has helped to define the anatomical abnormalities and resting haemodynamics and so guide the course of palliative and corrective surgery. However, little is known of the functional effects of congenital heart disease.

It is a general principle that to test the function of a system it should be stressed and the results studied. Engineers studying a machine built to perform work do not just examine it at a slow tick over; they stress it in a way which simulates, as closely as possible, the extremes of its usual working conditions. In contrast to this the assessment of the congenitally defective heart is made at rest. The clinical examination is made, the chest x-ray taken, and the electrocardiograph recorded, at rest. Cardiac catheterisation in children is normally performed under heavy sedation or a general anaesthetic. Information about a child's response to exercise is normally obtained by asking the mother, who cannot help but give an emotionally biased reply. Despite this the mother's reply is often taken into account when making major decisions such as whether or not to subject the child to surgery.

In general, studies of haemodynamics in congenital heart disease in young children have only been made at rest on the catheter table. In a few cases studies have been made in older children during low levels of exercise but

the normal controls have usually been adults (Gotsman 1966) or children with mild degrees of congenital heart disease (Keyler et al 1963). These studies have usually been performed during supine bicycle exercise, a form of work which is most unlikely to be encountered in daily life. Supine exercise has been chosen because cardiac output can be measured relatively easily during cardiac catheterisation and this is normally performed with the patient lying flat.

Exercise studies in children present many problems. The main one is co-operation. Adults will usually co-operate dispite discomfort but few children will do this, as it is usually impossible to explain the procedures adequately in terms that a child can understand. For this reason studies in children have largely been limited to those which do not involve invasive techniques and so assessments have mainly been concerned with maximum working capacity, minute ventilation and heart rate. Yet it is important to know what haemodynamic changes occur during exercise, for this is the state in which children spend most of their waking day. However, results from abnormal children are worthless unless they can be compared with those from normal children, and any set of normal data must take into account the changes due to growth and sex.

At present, not only are we largely ignorant of what happens during exercise in congenital heart disease, but we are also largely ignorant of the effects of surgery on the response to exercise in these same conditions. An entirely new type

of human is alive today with a heart that has been stopped, opened, rearranged and restarted, but apart from measurements made at rest and such crude indices as maximum working capacity, heart failure, cyanosis and mortality we have little idea of the functional effects of surgery in these people. The techniques of exercise testing have gradually become more refined and exercise testing has been used to investigate pathological as well as physiological changes. The application of these techniques to children has been infrequent mainly due to the invasive methods required to measure cardiac output.

Robinson in 1938, showed that younger subjects could reach higher maximal heart rates and oxygen uptakes in relation to body weight than could older subjects. Astrand (1952) measured the maximum working capacity in 227 subjects aged 4 to 33 years. These tests, involving measurement of heart rate, ventilation and maximum working capacity have been applied to children with heart disease (Cassels and Morse 1962, Duffie and Adams 1963, Goldberg et al 1969) but measurements of cardiac output during exercise were not made by these workers. Cardiac output during supine leg exercise was measured in children with congenital heart disease by Cayler et al (1963). Unfortunately they gave no measurement of the work performed by the children or of the oxygen consumption during exercise. Cardiac output on exercise was given as 'cardiac index', (i.e. cardiac output per square metre body surface area). This is equivalent to relating the cardiac output on <u>exercise</u> to the oxygen consumption at <u>rest</u> so the results as published are of little value.

In 1966, Gadhoke and Jones reported values for cardiac output during exercise in 40 normal boys aged 9½ to 14 years and in 1971 Godfrey et al published values for cardiac output on exercise in 117 normal boys and girls aged 6 to 16 years.

These last two studies showed that the indirect (CO_2) Fick technique could be used to measure cardiac output in children. As estimates of mixed venous carbon dioxide are obtained by a rebreathing technique the method is acceptable even to small children. These studies provided normal values with which to compare haemodynamic data from children with congenital heart disease. The object of the studies described in this thesis was to discover what changes congenital heart disease had induced in a child's response to exercise, to make an objective assessment of exercise tolerance, and to see whether the response to exercise gave any indication of the severity of the disease.

SECTION II

ABBREVIATIONS

ABBREVIATIONS

B.E.	=	base excess
B.S.A.	=	body surface area
B.T.P.S.	=	body temperature and pressure saturated with water vapour
cm	=	contimetres
C_2	=	carbon dioxide
FEV.	=	forced expiratory volume in one second
FVC	=	forced vital capacity
Hb	=	haemoglobin concentration in grams/100 ml.
hr.	=	hours
H.R.	=	heart rate in beats/min.
Ht.	=	height
kg.	=	kilograms
l.	=	litres
ml.	=	mililitres
mm.Hg.	=	milimetres of mercury
MVV	=	maximum voluntry ventilation
n	=	number of subjects
N.S.	=	p value greater than 0.05
O_2	=	oxygen
p	=	significance level
$PaCO_2$	=	partial pressure of CO_2 in arterial blo mm.Hg.)
PaO_2	=	partial pressure of O_2 in arterial blo mm.Hg.)
$PECO_2$	=	partial pressure of CO_2 in mixed expired air (mm.Hg.)
P_{Bar}	=	Barometric pressure (mm.Hg.)
PEFR	=	Peak expiratory flow rate
$P_{ET}CO_2$	=	partial pressure of CO_2 (mm.Hg.) in end tidal air

$P\bar{v}CO_2$ = partial pressure of CO_2 in mixed venous blood (mm.Hg.)

$\dot{Q}$ = cardiac output in litres/min.

$\dot{Q}ear$ = cardiac output (l/min.) based on corrected ear blood PCO_2 values

$\dot{Q}$ ET = cardiac output (l/min.) based on PCO_2 in end tidal air.

$\dot{Q}p$ = pulmonary blood flow (l/min.)

$\dot{Q}s$ = systemic blood flow (l/min.)

$\dot{Q}$ VD = cardiac output (l/min.) based on assumed normal dead space calculated from the equation of Godfrey et al (1971)

r = correlation coefficient

sec. = seconds

S.D. = standard deviation

S.E. = standard error of the mean

S.E.Y. = standard error of the estimate of Y

S.T.P.D. = standard temperature and pressure of dry gas

SV_{ear} = stroke volume (ml.) based on $\dot{Q}ear$

SV_{VD} = stroke volume (ml.) based on $\dot{Q}$ VD

T = temperature

$\dot{V}$.E. = expired minute ventilation in litres B.T.P.S.

$\dot{V}CO_2$ = carbon dioxide production in ml./min. at S.T.P.D.

VD = Physiological dead space in ml. B.T.P.S.

VD_A = Anatomical dead space in ml. B.T.P.S.

VD_{ET} = Physiological dead space (ml. B.T.P.S. estimated from end tidal PCO_2 values

VD_{ear} = Physiological dead space (ml. B.T.P.S.) estimated from corrected ear blood values of PCO_2

$\dot{V}O_2$ = Oxygen consumption (in ml./min. S.T.P.D. unless stated otherwise)

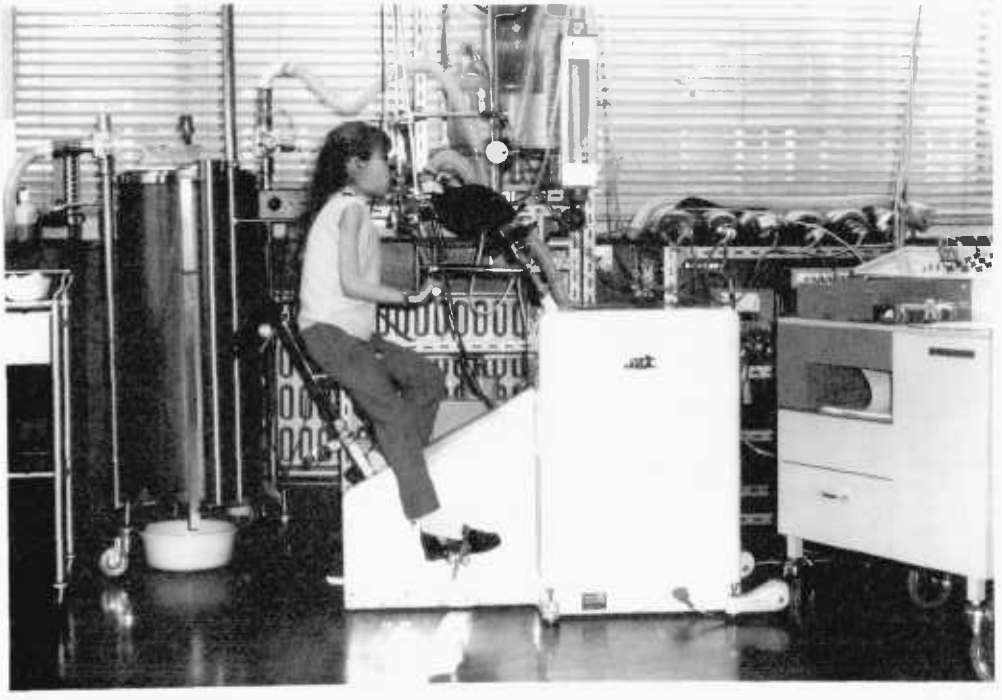
VT = Tidal volume in ml. B.T.P.S.

W	=	Watts
$W_{max.}$	=	Maximum work load completed in the progressive exercise test.
$\frac{1}{3}$ W.max.	=	one-third of W max.
$^{2}/_{3}$ W.max.	=	two-thirds of W max.
wt.	=	weight
yr.	=	years
%	=	percent
*	=	p value equal to or less than 0.05 but greater than 0.001
**	=	p value equal to or less than 0.01 but greater than 0.001
***	=	p value 0.001 or less
$\triangle$	=	Change between two values

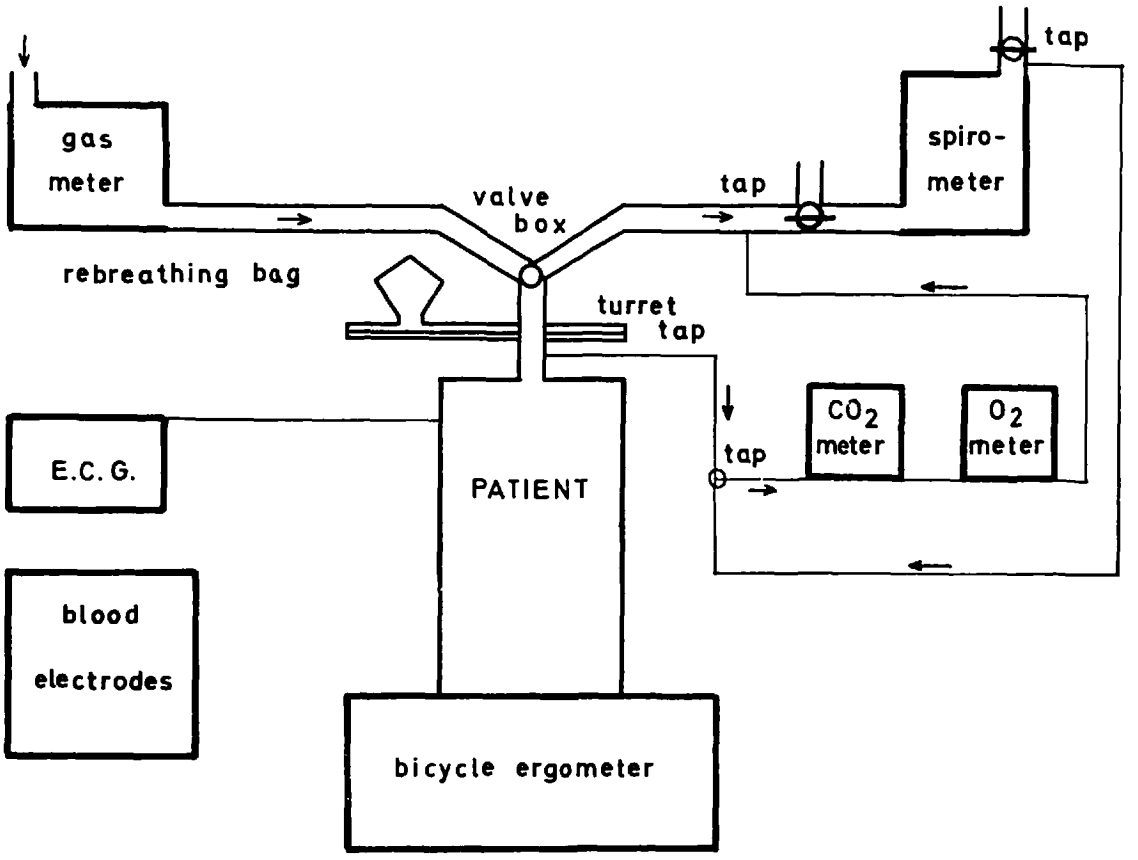
METHODS AND MATERIALS

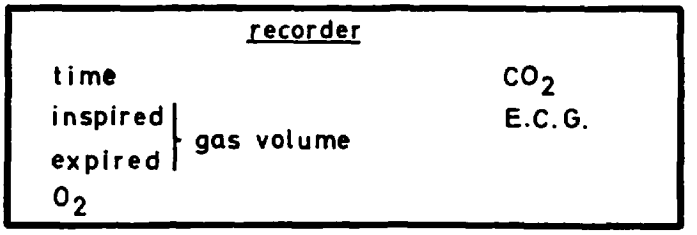
FIGURE II - 1

A child seated on the bicycle ergometer.



TAYLOR 1972





THE EXERCISE TEST CIRCUIT

MATERIALS AND METHODS

Outline of the Exercise Test

The basic method used in the investigation of these patients was the exercise test as described by Godfrey et al (1971). The calculation were made using the computer programme described by Godfrey (1970). The exercise was performed in the upright position on an electrically braked bicycle ergometer (Lode). The tests were divided into two parts. The first part was the progressive exercise test in which measurements of heart rate and minute ventilation were made at rest and then at progressively higher levels of work up to the maximum that the child could attain. Each work load was performed for one minute and the work loads were increased in regular increments depending on the size of the child.

Size	Increment
Less than 120 cm.	10 watts
120 - 150 cm.	15 watts
Greater than 150 cm.	20 watts

In a few children who were likely to have severe exercise intolerance the work was increased in smaller steps. Obviously the assessment of whether a child is really trying hard is almost entirely subjective, although the minute ventilation rate and heart rate do give some indication as to how severely the child is being stressed.

Godfrey et al (1971) found the heart rate at the maximum work load to be 195 beats/min. (SD13) in boys and 196 (SD13) in girls.

The main value of the progressive exercise test was to act as a 'sighting shot' to estimate the maximum work which the child could complete. This was then used as a guide for the second part of the exercise test, the steady state test.

The steady state test was performed at least half an hour after the progressive test. Measurements were made at rest and at one and two thirds of the maximum work load completed in the progressive test. Expired air was flushed through a Tissot spirometer and analysed continuously for O_2 and CO_2. When the heart rate, minute ventilation and expired gas concentration had all become steady (usually after 2 - 3½ minutes depending on the size of the child) a collection of expired air was made in the spirometer andthe CO_2 analyser was switched to measure end tidal PCO_2. Blood samples were taken from an ear lobe as described by Godfrey et al (1971a) and the blood analysed for pH, PCO_2 and PO_2 usingthe Eschwieiler micro electrode system. After at least 15 litres of expired air had been stored or the collection had lasted for more than one minute the collection of expired air was stopped. An electrocardiograph (ECG) trace is taken at normal ECG speed (25 mm./sec.) andthe patient was then switched into a rebreathing bag at the end of an expiration. The bag contained a CO_2 in oyxgen mixture appropriate to the expected mixed venous PCO_2 ($P\bar{v}CO_2$). If a plateau or gently

sloping CO_2 trace (measured from a sampling line at the mouth) was not obtained within 10 seconds rebreathing was abandoned for at least thirty seconds. Another attempt was then made. After rebreathing was complete the expired air in the spirometer was analysed for CO_2 and O_2 and the patient started the next work load.

The object of many of the manouvers in the steady state test was to obtain enough information to allow the cardiac output to be calculated by following CO_2 transport and applying the Fick principle. The movement of the Tissot spirometer was recorded and so the volume of gas in it was known, as was the time over which this volume was collected. The CO_2 concentration in this expired air was known and so the carbon dioxide production per minute could be calculated. The Patient's haemoglobin (Hb) concentration, pH, $PaCO_2$, PaO_2 and the $P\bar{v}\ CO_2$ had been measured and by applying the CO_2 dissociation curve (Godfrey 1971) the carbon dioxide content difference between arterial and venous blood could be calculated. Then by the Fick principle:-

$$\dot{Q} = \frac{\dot{V}\ CO_2}{\bar{v} - a\ CO_2 \text{ difference}}$$

Where $\dot{Q}$ = cardiac output

$\dot{V}CO_2$ = carbon dioxide production

$\bar{v} - a\ CO_2$ difference = mixed venous minus arterial content difference

The reproducibility of this method of measuring cardiac output has been investigated by Ziedifard et al (1972) using the same equipment and methods as were used in the present study. The author was one of the normal subjects in the study. Ziedifard et al (1972) used an assumed value for dead space (calculated from the equation of Godfrey et al 1971) in their calculation of cardiac output. Each subject was studied on several occasions and a coefficient of variation calculated for each subject at each level of work. The highest and lowest values obtained are given below as are the highest and lowest values for the mean oxygen consumption at each work load:-

Work (watts)	Mean VO_2	Coefficient of Variation (%)
Rest	193-341	6.6-30.2
35	727-863	6.6-9.0
50	965-1106	2.9-10.1
70	1199-1224	3.5-5.0
100	1572-1646	4.0-7.7
150	2120 ~~212~~-2363	2.5-9.9

At rest the coefficient of variation varied widely from subject to subject but on exercise the variation between subjects was less and the values obtained compare favourably with those of the direct CO_2 Fick and dye dilution methods of estimating cardiac output (Ziedifard et al 1972).

Two alternative estimates of arterial PCO_2 ($PaCO_2$) can be used, the end tidal PCO_2 and that derived from an assumed normal dead space. The use of these estimates allows cardiac output to be measured without taking blood samples but assumed values must also be used for haemoglobin, arterial pH, base excess and PaO_2 or arterial oxygen saturation.

The end tidal estimate suffers from the disadvantage of being higher than the $PaCO_2$ measured directly from arterial blood samples during exercise (Jones 1966).

The use of an assumed normal dead space allows the $PaCO_2$ to be estimated from the adaption of the Boher equation:-

$$\frac{VD}{Vt} = \frac{PaCO_2 - PECO_2}{PaCO_2}$$

Where VD = the physiological dead space plus equipment dead space

Vt = the tidal volume

$PaCO_2$ = arterial PCO_2

$PECO_2$ = PCO_2 of expired air

Wood et al (1971) have shown that the dead space of normal children varies quite widely, and so this method gives a reasonable, but not an accurate estimate of $PaCO_2$. However, quite wide variation in estimates of dead space has little effect on the estimate of cardiac output because of the slope of the cardiac output PCO_2 curve (Godfrey 1971). Wide variations in base excess also have little effect on the cardiac output estimate (Godfrey 1971).

The following measurements are made during the exercise test:-

The Progressive Exercise Test

Measurement	Derived Values
Continuous ECG trace	Heart rate & ECG pattern
Continuous inspired ventilation trace	Inspired minute ventilation Frequency of breathing Tidal volume

The Steady State Exercise Test

Measurements as for progressive test plus:-

Measurement	Derived Values
Expired air { Volume; O_2; CO_2 } content	O_2 consumption CO_2 production Cardiac output Stroke volume Minute ventilation Frequency of breathing Tidal volume Dead space
Electrocardiograph	Heart rate ECG pattern Stroke volume
End tidal CO_2 concentration	End tidal PCO_2
Mixed venous CO_2 concentration	$P\bar{v}CO_2$ cardiac output

Ear blood pH	Arterial pH
PCO_2	$PaCO_2$
PO_2	PaO_2
Hb	Haemoglobin
	Base excess
	Arterial oxygen saturation
	Cardiac output
	Right to left shunt
	Physiological dead space
	Alveolar-arterial oxygen gradient

NORMAL VALUES

The normal values used for comparison with the present studies are either those reported by Godfrey et al (1971) or form part of this thesis.

CHILDREN STUDIED

Twenty-eight normal children were examined in the present study, all of them had been studied by Godfrey et al (1971) two years previously. They attended local schools.

The patients with heart disease attended the Brompton, Guy's or Hillingdon Hospitals. Details of the individual patients are given at the start of the appropriate sections.

METHODS

Spirometry

Forced expired volume in one second (FEV_1) and forced vital capacity (FVC) were measured before exercise using a light weight, balanced, wet spirometer (P.K. Morgan).

The best of three attempts was recorded. A nose clip was not used.

Peak Expiratory Flow Rate

Peak expiratory flow rate (PEFR) was measured using Wright peak flow meters (~~Arined~~ AIRMED). Two models were used, a small one reading up to 200 l./min. and a larger one reading up to 1000 l./min. The highest of three attempts was recorded.

Maximum Voluntry Ventilation

Maximum voluntry ventilation was measured using the 15 second sprint method. The measurement was made with the child seated on the bicycle ergometer. The volumes were read off the gasmeter trace and corrected to B.T.P.S.

Body Surface Area

Body surface area was calculated from the equation of Du Bois and Du Bois (1916) as given in Documenta Geigy Scientific Tables (1965).

Blood Samples

Ear lobe blood samples were taken as described by Godfrey et al (1971a). The samples were taken from an ear lobe in which vasodilation had been induced by applying a nicotine cream for five minutes. The ear lobe was then transected with a narrow pointed scalpel blade and the blood collected as a bubble-free sample in short section of small bore manometer tubing. The sample was

TABLE II - 1

SHOWING PO_2, PCO_2, AND pH VALUES FROM SIMULTANEOUS EAR BLOOD AND ARTERIAL BLOOD SAMPLES

	Source	PO_2	PCO_2	pH	
Rest	Ear	76.0	34.9	7.401	Subject 1
	Artery	77.0	35.9	7.383	
Exercise 25 watts	Ear	63.1	32.1	7.398	
	Artery	63.8	29.4	7.377	
After exercise	Ear	83.8	31.9	7.409	
	Artery	91.2	33.1	7.387	
	Ear	83.2	35.9	7.426	
	Artery	85.8	30.2	7.394	
	Ear	77.2	33.1	7.431	
	Artery	83.0	32.3	7.390	
Rest	Ear	87.0	37.0	7.47	Subject 2
	Artery	85.0	37.0	7.43	
40 watts exercise	Ear	93.5	30.0	7.53	
	Artery	101.0	28.5	7.53	
80 watts	Ear	101.0	25.8	-	
	Artery	103.5	25.8	7.510	
After exercise	Ear	108.0	20	7.525	
	Artery	110.0	18.2	7.590	
	Ear	102	18.0	7.67	
	Artery	112	17.5	7.63	
	Ear	98.5	20	7.587	
	Artery	101.0	21.5	7.587	
Arterial-ear value (Mean)		+3.6	-0.9	-0.015	
SD of difference		3.6	2.1	0.032	

analysed immediately for pH, PCO_2 and PO_2. A separate sample was taken for haemoglobin estimation. Godfrey et al (1971a) gave the following results for arterial minus ear blood differences in a comparison which they carried out:-

		PO_2	PCO_2	pH
Rest	Mean	+2.09	+0.65	-0.016
	SD	2.48	1.20	0.014
Exercise	Mean	+0.91	2.22	-0.024
	SD	3.10	1.27	0.020

A further comparison was carried out to check that the results were similar in the hands of the author (Table II - 1). These comparisons were made in adult patients in whom arterial catheters had been inserted for clinical investigation. Because of the small number of observations the results were not divided into 'rest' and 'exercise' groups. It can be seen from the table that there was reasonable agreement with the results obtained by Godfrey et al (1971a). A paired 't' test was used to assess the significance of the differences between the arterial and ear blood samples. There was no significant difference for the pH and PCO_2 values. The difference between the PO_2 values was significant at the 1% level. The present sample was small and the differences were close to those found by Godfrey et al (1971a) on a much larger sample. The correction factors from the larger

samples were used to adjust the ear sample results to arterial values, with the exception of the pH value for which a further correction was necessary because of an instrumental zero error (see below).

Correction factors added to ear blood values:-

PCO_2	Rest	+0.5 mm.Hg.
	Exercise	+2.0 mm.Hg.
PO_2	Rest	Nil
	Exercise	
pH	Rest	+0.08
	Exercise	

Blood Gas Electrodes

Eschweiler micro electrodes were used to measure the pH, PO_2 and PCO_2 of blood samples. The PO_2 electrode was calibrated using blood which had been tenometered with a CO_2, O_2 and N_2 gas mixture of known composition. It was also calibrated directly with the gas mixture and a correction factor set in to adjust for the blood-gas difference. The CO_2 electrode was calibrated using similar gas mixtures. Tenometered blood was used at intervals to check the accuracy of the equipment. Gas mixtures were used to calibrate the equipment during studies and the calibration was checked between blood samples. The calibrating gases were analysed by the Scholander technique (Scholander 1947).

TABLE II - 2

SHOWING COMPARATIVE VALUES OF pH USING THE INSTRUMENTATION LABORATORIES' (I.L.) AND ESCHWEILER pH ELECTRODES

	I.L.	Eschweiler
	7.323	7.303
	7.335	7.309
	7.322	7.325
	7.333	7.320
	7.308	7.312
	7.336	7.355
	7.335	7.311
	7.339	7.311
	7.339	7.320
	7.343	7.301
	7.336	7.305
	7.339	7.310
	7.343	7.301
	7.340	7.312
	7.340	7.300
	7.341	7.312
	7.333	7.312
	7.342	7.300
	7.325	7.315
	7.341	7.298
Mean	7.336	7.312
SD	0.0063	0.0127

Paired 't' test

Mean difference	0.0427
n	20
t	14.2531
p	***

pH Electrode

The pH electrode was standardised using buffers made for this purpose by Radiometer Limited. The manufacturer's tolerance of these buffers was ±0.005 pH units. It was found, however, that this pH measuring system gave consistently low pH readings. A comparison was therefore made with an Instrumentation Laboratories pH electrode.

Blood was taken into a sealed heparinised syringe. The two pH meters were placed in the same laboratory and pairs of samples were taken and analysed on each machine in turn. Both machines were standardised using ampoules of buffer from the same batch. It can be seen from the results of this comparison that the Eschweiler equipment gave a consistently lower result than the Instrumentation Laboratories' machine (Table II - 2).

The explanations of this difference probably lies in the flushing solutions used for the two electrodes.

Physiological saline was used as a flushing solution for the Instrumentation Laboratories' electrode while distilled water was used for the Eschweiler electrode. Kelman et al (1966) have shown that using water instead of saline results in low pH readings. They found that the mean reduction in pH brought about by using distilled water was 0.015 of a pH unit but that the difference could be as much as 0.05 of a pH unit.

This difference was therefore taken into account in the calculation of the arterial to ear sample' correction factors, so that a correction was made both for the arterial/ear blood difference and for the flushing solution difference.

Tissot Spirometer

The Tissot spirometer had a capacity of 100 litres. A line was fitted in parallel with the counter-weight line and drove a potentiometer which was linked to the Minograph recorder. The output of this system was checked by water displacement. Each sweep of the potentiometer was equivalent to 4.787 litres of gas. The figure obtained for this measurement by Godfrey (1971) was 4.785 litres per sweep.

The Gasmeter

A dry gasmeter (Parkinson Cowan CD4) was used to measure the volume of inspired air. It had a 10 litre sweep and its spindle was fitted to a rotary potentiometer linked to the Minograph recorder.

Once the calibration of the Tissot spirometer had been checked it was used to calibrate the gasmeter. The gasmeter read 0.55% high.

Tap, Valve Box and Rebreathing Circuit

The valve box was a simple flap valve type. The dead space was 53 ml. as measured by water displacement.

A sliding 'camera turret' type tap was used to switch the patient from the normal breathing circuit to a 2 litre rebreathing bag which was connected to a series of cylinders containing different concentrations of CO_2 in O_2. A suction pump was also connected to the rebreathing bag allowing the bag to be emptied rapidly.

Breathing Circuit Resistances

All of the tubing and taps in the breathing circuit, with the exception of the mouthpiece had an internal bore of 1½ inches (3.8 cm.). The resistances of the inspiratory and expiratory circuits were measured using a calibrated rotameter, an electric blower, and water manometers. The resistances are given below:-

	Flow (l./min.)	Resistance ($cm.H_2O/l./sec.$)
Inspiration	200	0.83
	400	1.55
Expiration	200	0.98
	400	1.80

Oxygen and Carbon Dioxide Meters

Oxygen concentrations were analysed using a paramagnetic oxygen analyser (Servomex O.A.150) the output of the analyser was displayed on the recorder with zero supression so that the range 14 - 20% was recorded. This oxygen analyser has a response time of 15 seconds to 95% of full deflection. Adequate time

was always given to allow the record to become stable when an analysis was being made.

Carbon dioxide concentrations were measured using an infra-red CO_2 analyser (URAS-4) the output of which was fed into two channels of the recorder to give adequate gain as each channel is only about 6 cm. wide. One channel recorded values of 0 - 6% and the other 6 - 14%. The response time of this meter is 0.5 sec. to 95% full deflection at a flow rate of 40 l./hour.

The analysers were calibrated simultaneously using four gas mixtures of varying proportions of carbon dioxide and oxygen in nitrogen. The composition of these mixtures was analysed using the Scholander (1947) technique. Scholander analyses were repeated until consecutive estimations agreed to within 0.05%. Calibration was performed after every study, or after every second study when several studies were done in rapid succession.

Mixed Venous CO_2

The estimation of mixed venous PCO_2 ($P\bar{v}CO_2$) relies on equilibration or near equilibration of PCO_2 between the mixed venous blood and the alveolar air. This must be complete before recirculation of arterial blood with a high PCO_2 causes a rise in the mixed venous PCO_2 (Jones et al 1967). Large intracardiac left to right shunts will rapidly recirculate blood with a high PCO_2 to the pulmonary artery and consequently disrupt

the normal rebreathing pattern. As the rebreathing method can be used to measure $P\bar{v}CO_2$ in normal subjects it appears that small left to right shunts as formed by the coronary circulation do not introduce a serious error. The degree of left to right shunting which causes an inacceptable inaccuracy of the rebreathing $P\bar{v}CO_2$ is not known. In the case of children with Fallot's tetralogy it had to be assumed that any left to right shunt was small and would not disturb the rebreathing pattern.

Collision Broadening

The oxygen concentration in the calibrating gases was in the physiological range and so the collision broadening effect was similar for both standardising and the unknown gases. However the oxygen concentration in the rebreathing bag was greather than physiological values being about 40% to 50% at the end of a rebreathing $P\bar{v}CO_2$ measurement. The exact concentration will vary depending on the composition of the initial gas mixture used, the amount of the gas mixture, the duration of rebreathing and the $P\bar{v}CO_2$. The collision broading effect was checked by analysing gas mixtures of CO_2 in O_2 by the Scholander (1947) technique and then by the infra-red carbon dioxide analyser. It was found that each 10% increase in oxygen concentration produced a 0.06% fall in the carbon dioxide reading. This would amount to an error of approximately 1.5 mm. in the estimation of $P\bar{v}CO_2$ at high work levels in large children.

Because this error is small was ignored in the study of normal children by Godfrey et al (1971) and as the values obtained in that study have been used for comparison with the present study the collision broading effect has again been ignored.

Recorder

All data from the exercise test were recorded on a Mingograf 81 recorder. This is an ink jet, 8 channel recorder with a channel width of approximately 6 cm. The frequency response is linear up to 500 Hertz. The amplitude linearity is better than 2.5%.

The Bicycle Ergometer

The bicycle ergometer (Lode) used in these studies used an electric 'eddy - current' breaking system. This system is designed so that over a wide range of pedalling speeds (40 to 80 revolutions for minute) the external work done in turning the pedals remains constant. The work rate setting of the bicycle can be adjusted continuously over the range 0 to 400 watts. Few physiology laboratories have the facilities to calibrate bicycle ergometers but as most exercise measurements are related to oxygen consumption and not to external work calibration of the bicycle ergometer is not a problem. Calibration of the bicycle is important when measurements related to external work are being considered, as in the progressive exercise test when oxygen consumption is not measured. Cumming and Alexander (1968) have shown that an electrically braked bicycle ergometer

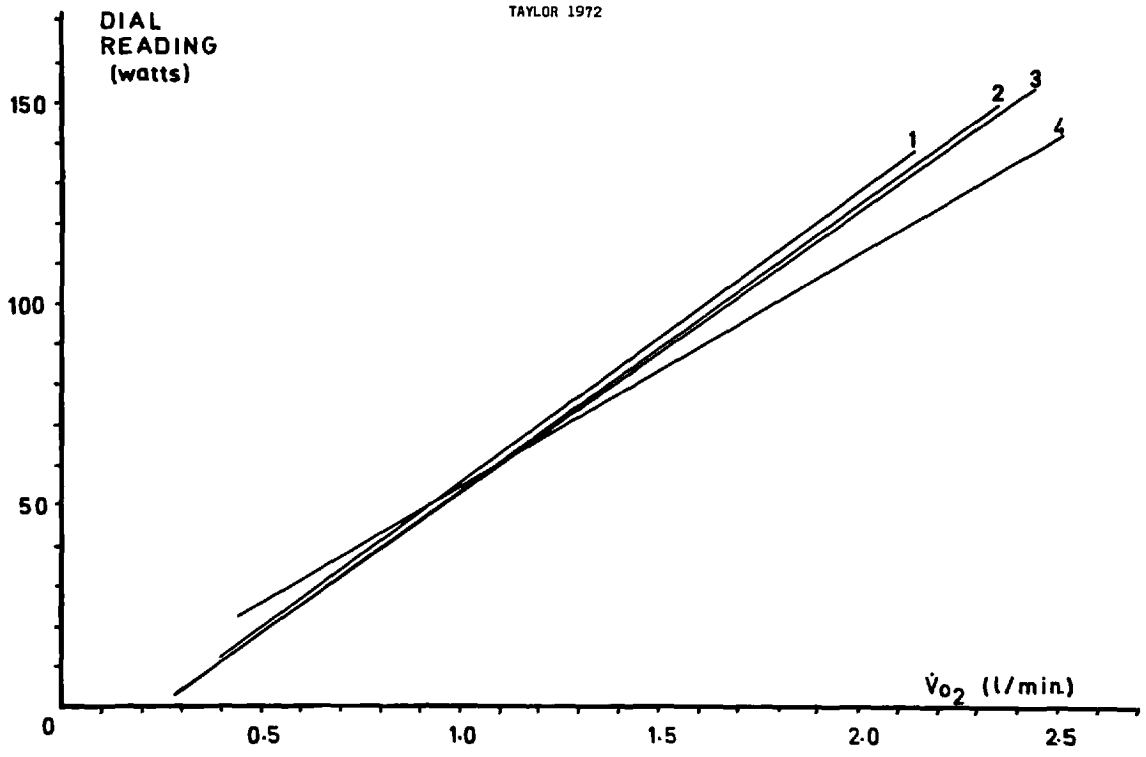
may differ as much as 20% from the factory calibration, though they found no significant variation in calibration over a period of 4 months. They found a variation of 10% from the rated work with variation in cycling speeds. In order to keep this to a minimum the cycling speed in the present study was kept as close as possible to 60 revolutions per minute.

Recently Clarke and Greenleaf (1971) have shown that running this type of bicycle ergometer at high work loads for several hours causes heating of the braking system and this can induce a large error in the work settings. The error increases as the temperature of the braking system rises. In short runs at low work loads the error was only +4% of the set work load.

The results presented in this thesis and the normal values with which they are compared were obtained using the same bicycle ergometer over a period of two and a half years. In order to obtain normal values for venous admixture in children and also as a check on the previous results ~~28~~ 27 of the 116 children first studied by Godfrey et al (1971) in 1969 were re-studied two years later. It was found that their maximum working capacity was lower than predicted and their oxygen consumption was higher than predicted from the 1969 values. The exercise tests performed in the past two years were then reviewed and the results grouped in six monthly periods. A regression line was calculated for the results from each six month period:-

FIGURE II - 2

Graph showing oxygen consumption and the work indicated by the bicycle ergometer dial. For explanation of regression lines see text.


TAYLOR 1972
DIAL
READING
(watts)
150
100
50
0
0·5
1·0
1·5
2·0
2·5
$\dot{V}_{O_2}$ (l/min.)
1
2
3
4

REGRESSION LINE NO.			
2	1969 Normals	work = 0.0707 VO_2 - 16.17	200=n
2	Feb. - July 1970	work = 0.0692 VO_2 - 14.25	48=n
2	Aug.1970 - Jan.1971	work = 0.0710 VO_2 - 17.27	94=n
3	Feb. - June 1971	work = 0.0701 VO_2 - 17.00	102=n
4	1971 Normals	work = 0.0576 VO_2 - 3.00	54=n
1	Post re-calibration	work = 0.0752 VO_2 - 20.95	29=n

These regression lines are shown in Figure II - 2 accompanied by the results from the studies of normal children. It can be seen that the regression lines for the sick children lie about that for the 1969 study of normal children. The difference in the oxygen consumption work relationship between the 1969 and 1971 study of normal children was appropriate to the difference between the observed and predicted mean maximum work load:-

Mean maximum work load 1971	114 watts
Predicted maximum work load from 1969 values	126 watts
Calculated oxygen consumption for 114 watts using 1971 regression line	1856 ml./min.
126 Calculated oxygen consumption for ~~1256~~ watts using 1969 regression line	1822 ml./min.

The bicycle ergometer was returned to the manufacturer's agents for recalibration. It was found that between 0 and 100 watts the bicycle was reading 12% low and between 100 and 200 watts it was reading 14% low. This was due to failure of a resistor in the braking circuit. The resistor was replaced and the bicycle reclaibrated. The regression line for the work:oxygen

consumption relationship of sick children studied after recalibration of the bicycle is shown in Figure II - 4. It can be seen that the lines lies close to that previously obtained for sick children.

In studies performed during the months encompassing the 1971 study of normal children the readings of watts have been corrected by the factors of 12% in the 0 to 100 watt range and 14% in the 100 to 200 watt range.

Electrocardiograph

The electrocardiograph was recorded using a bipolar lead system with the electrodes placed one in the fifth left intercostal space in the mid clavicular line and one in second right interspace in the mid clavicular line. A third electrode, the neutral electrode, was placed on the back over the trapezius above the spine of the right scapula. This configuration of electrodes was found to give an interference-free electrocardiograph during exercise. It is approximately equivalent to standard lead two. In most cases the elctrocardiograph was displayed on an osilloscope throughout the study so that alterations in the pattern could be seen immediately.

Cardiac Catheterisation

In the majority of cases cardiac catheterisation was carried out in the routine cardiac catheterisation laboratory at the Brompton or Guy's Hospitals. These investigations were carried out by the cardiological or

paediatric staff at these hospitals.

In a few children with pulmonary stenosis and one with Fallot's tetralogy the pulmonary outflow gradient was measured by the author using a float catheter (Bradley 1964). These investigations were carried out in the Paediatric Pulmonary Physiology Laboratory at the Institute of Diseases of the Chest.

The catheter used was of nylon with an external diameter of 0.63 mm. and a bore of 0.5 mm. A polythene canula was inserted into a cubital vein by percutaneous puncture under local anaesthetic. Aseptic technique was used throughout the procedure. The float catheter was inserted through the canula and advanced until the right ventricle was reached, as evidenced by the pressure trace. The catheter was then advanced centimetre by centimetre until the pulmonary artery was entered as shown by the pressure trace. Pressures were measured the same reference point (mid chest, patient supine) as in the cardiac catheterisation laboratory. No arrythmias other than ectopic beats were encountered. There were no complications. The full hospital cardiac arrest procedure was available at all times and resusitation equipment was ready to hand in the laboratory. In all cases in which float catheterisation was performed the investigation had been requested by the physician in charge of the child. The float catheter was connected to a Devices pressure transducer. Only a flushing system was interposed between the float catheter and the transducer as manometer tubing causes damping of the frequency

response. The output of the transducer was fed into an Exal patient monitor where it was displayed on an ossiloscope above the elctrocardiograph trace. It was also fed from the patient monitor to the Mingograf recorder to give a permanent record. The frequency response of the entire system (catheter to Mingograf trace) was 38 Hertz as measured by the square wave technique. This level of frequency response gives a 'shattered' trace which is difficult to interpret. An electronic filter was therefore placed in the system to reduce the response to 15 Hertz. The Devices transducer is moderately light sensitive. The illumination in the laboratory was maintained at a constant level and the equipment calibrated immediately after each pressure measurement to reduce any error due to light.

Gradients in all cases are given as systolic peak pressure differences in milimetres of mercury as measured with the patient at rest in the supine position.

SECTION III

NORMAL VALUES

TABLE III - 1

SHOWING THE AGE, SEX, WEIGHT AND HEIGHT
OF THE NORMAL CHILDREN IN 1969 AND 1971

1971					1969		
No.	Age	Sex	Wt.	Ht.	Age	Wt.	Ht.
2	14.1	M	74.5	167	11.8	59.5	157
5	14.7	M	52.7	165	12.5	36.6	147
6	15.8	M	56.0	171	13.6	39.8	156
8	14.4	M	61.1	172	12.6	47.6	152
37	11.5	M	30.5	147	9.4	26.1	137
38	11.4	M	33.0	147	9.3	27.5	137
46	11.1	M	35	141	8.9	28.1	132
57	9.9	M	36.5	144	7.8	29.2	133
58	9.3	M	30.0	131	7.3	27.6	120
59	9.4	M	28.0	131	7.4	22.2	121
71	9.8	M	32.0	141	7.8	26.5	131
72	9.4	M	27.5	133	7.4	23.4	124
92	15.2	M	72.2	179	13.3	55.5	171
99	16.9	M	82.0	187	14.9	76.5	185
111	8.2	M	29.5	129	6.2	22.3	117
112	8.8	M	25.0	126	6.8	19.0	115
10	14.0	F	47.5	151	11.8	43.6	147
35	11.4	F	54.1	152	9.4	42.9	139
45	11.8	F	47.0	147	9.8	31.5	131
68	9.3	F	34.0	131	7.4	23.9	120
75	16.8	F	40.0	153	14.8	43.5	153
84	9.2	F	27.0	128	7.2	21.0	117
86	9.2	F	38.0	140	7.2	28.1	127
97	16.8	F	64.7	161	14.8	52.3	160
109	17.8	F	57.5	164	15.8	62.6	164
113	8.8	F	23.5	127	6.8	19.9	119
117	8.3	F	24.5	129	6.3	19.8	119

INTRODUCTION

Normal children were studied in order:-

1. to check that in the hands of the author and his co-workers the results were comparable with those of Godfrey et al (1971),

2. to obtain estimates of parameters, such as venous admixture, for which normal values were not available, and

3. to discover whether a child's response to exercise remained consistent over a period of years and if so to within what limits; for example would a child with a cardiac output in the lower normal range in 1969 still have a low cardiac output in 1971?

MATERIALS AND METHODS

Twenty seven of the one hundred and seventeen children studied by Godfrey et al (1971) in 1969 were re-studied. Consent was obtained from both the children and their parents. One of these children (number 2) suffered from mild attacks of asthma. His spirometry results have been omitted from the statistical analysis. The details of the children are given in Table III - 1. The number used to designate each child is the same as that used in the original study. The individual results for each child obtained in 1969 are deposited

with the Librarian of the Royal Society of Medicine, London as Clinical Science Tables 40/2 and 40/3. The age distribution of the children as compared with those studied by Godfrey et al (1971) is given below:-

Age	No. of Boys		No. of Girls	
	Godfrey et al	Present study	Godfrey et al	Present Study
6.0-6.9	5		5	
7.0-7.9	6		6	
8.0-8.9	6	2	6	
9.0-9.9	5	5	6	3
10.0-10.9	7		8	2
11.0-11.9	5	3	6	2
12.0-12.9	7		6	
13.0-13.9	6		6	
14.0-14.9	5	3	6	1
15.0-15.9	5	2	5	
16.0-16.9		1		3

It can be seen that the present study was weighted towards older children as the children were now two years older and no 'new' young children were studied.

Statistical Analysis of the Steady State Results

The results obtained from the children in 1969 and 1971 were compared in two ways. Firstly a multiple linear regression computer programme (International Business machines Scientific Statistical Package) was used to

TABLE III - 3

SHOWING THE RESULTS OF PAIRED 't' TESTS ON THE OBSERVED AND EXPECTED VALUES FOR FEV_1, FVC, PEFR, & MAXIMUM WORK LOAD, ~~HEART RATE, MINUTE VENTILATION, AND CARDIAC OUTPUT BASED ON ASSUMED NORMAL DEAD SPACE.~~

'MEAN OF DIFFERENCES' IS THE MEAN OF THE OBSERVED-EXPECTED VALUES

Parameter	Mean of Differences	n	t	P
FEV_1 boys	-0.143	15	1.9301	NS
FVC boys	-0.131	15	1.3808	NS
PEFR boys	-1.2	15	0.0657	NS
FEV_1 girls	-0.0985	11	1.8067	NS
FVC girls	+0.1348	11	1.5675	NS
PEFR girls	+18	11	1.1264	NS
Maximum work load	+3	27	0.9110	NS

analyse the entire pooled data from 1969 and 1971. A weighting was given to the 1971 data which was then designated an an independent variable and the contribution of the 1971 data to the regression sum of squares was assessed using Snedecor's F test.

Secondly, for the twenty seven children restudied in 1971 the position of each child's result for 1969 and 1971 were recorded and the estimate given by the appropriate regression equation of Godfrey et al (1971) was subtracted from the observed value. A paired 't' test was then used to see whether the 'observed value - regression estimate' for each child for 1969 and for 1971 were significantly different. This is referred to in the text as the comparison of the individual results.

RESULTS

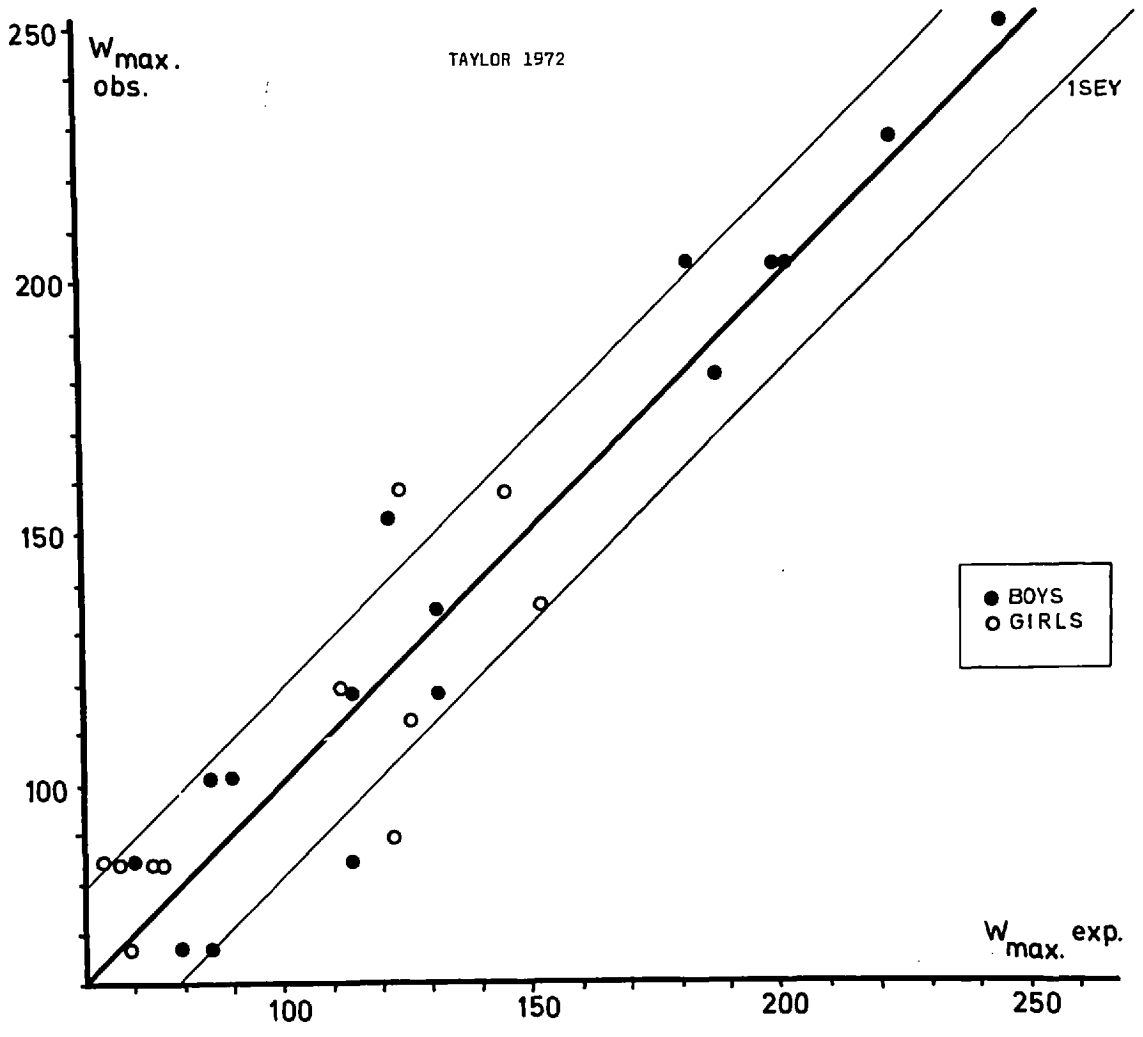
Lung Function

The FEV_1, FVC and PEFR of all the subjects, except subject number 2, were within the normal range (Table III - 2A). The mean values for each test did not differ significantly from the mean of the expected values (Table III - 3).

The maximum voluntry ventilation (Table III - 2A) was found to be significantly related to the FEV_1 ($r = 0.864$) and to height ($r = 0.798$)(Table III - 4A). This agrees well with the findings of Weng and Levison (1969)(Table III - 4A).

FIGURE III - 1

Showing a concordance plot for the observed and expected maximum work load of normal children. The girls are represented by open circles and the boys by filled circles. The lines are the line of identity and one standard error of the estimate.


250
200
150
100
$W_{max.}$ obs.
TAYLOR 1972
1SEY
BOYS
GIRLS
$W_{max.}$ exp.
100
150
200
250

Maximum work load completed

There was no significant difference between the mean values for the observed and expected maximum work loads (Tables III 2A and 3). This is shown graphically in Figure III - 1.

Dyspnoeic index

The dyspnoeic index, that is, the maximum ventilation reached in the progressive exercise test divided by the maximum voluntry ventilation and expressed as a percentage, was calculated for each child. The scatter of results was wide (Table III - 2A). The mean for boys was 77.2% with a standard deviation of 24.7%, and for girls 60.0% with a standard deviation of 10.5%. This wide scatter of results in normal children affords little prospect of the dyspnoea index being useful in distinquishing abnormal from normal children.

Steady State Results

Individual results for the steady state tests are given in Table III - 5A. Regression equations of normal values are given in Table III - 4A, which includes equations from other workers, from the present study, and where appropriate from pooled data. Blood gas, pH base excess and end tidal PCO_2 values for each child are given in Table III - 8A.

Heart Rate

The heart rates of boys and girls an exercise differed significantly, the girls having a higher heart rate than the boys for a given oxygen consumption. This is in keeping with the findings of Godfrey et al (1971). The results for boys and girls were therefore treated separately (Table III - 4A). Heart rate was significantly related tc height, weight and body surface area but the regression was significantly improved by the addition of the logarithm of the oxygen consumption to one of these three factors as independent variables.

The heart rates on exercise for both boys and girls did not differ significantly from the 1969 values when growth was allowed for. This indicates that the allowance for a fall in heart rate with increasing height which is given by the equation of Godfrey et al (1971) gave an adequate allowance for the changes in heart rate which accompanied the growth of the children over a period of two years. The equations for 1969 and 1971 are given below:-

Boys

1969 $HR = 159.1 \log 10 \dot{V}O_2 - 1.204 Ht - 143$

1971 $HR = 141.7 \log 10 \dot{V}O_2 - 1.185 Ht - 97$

Girls

1969 $HR = 173.0 \log 10 \dot{V}O_2 - 1.395 Ht - 140$

1971 $HR = 183.9 \log 10 \dot{V}O_2 - 1.249 Ht - 190$

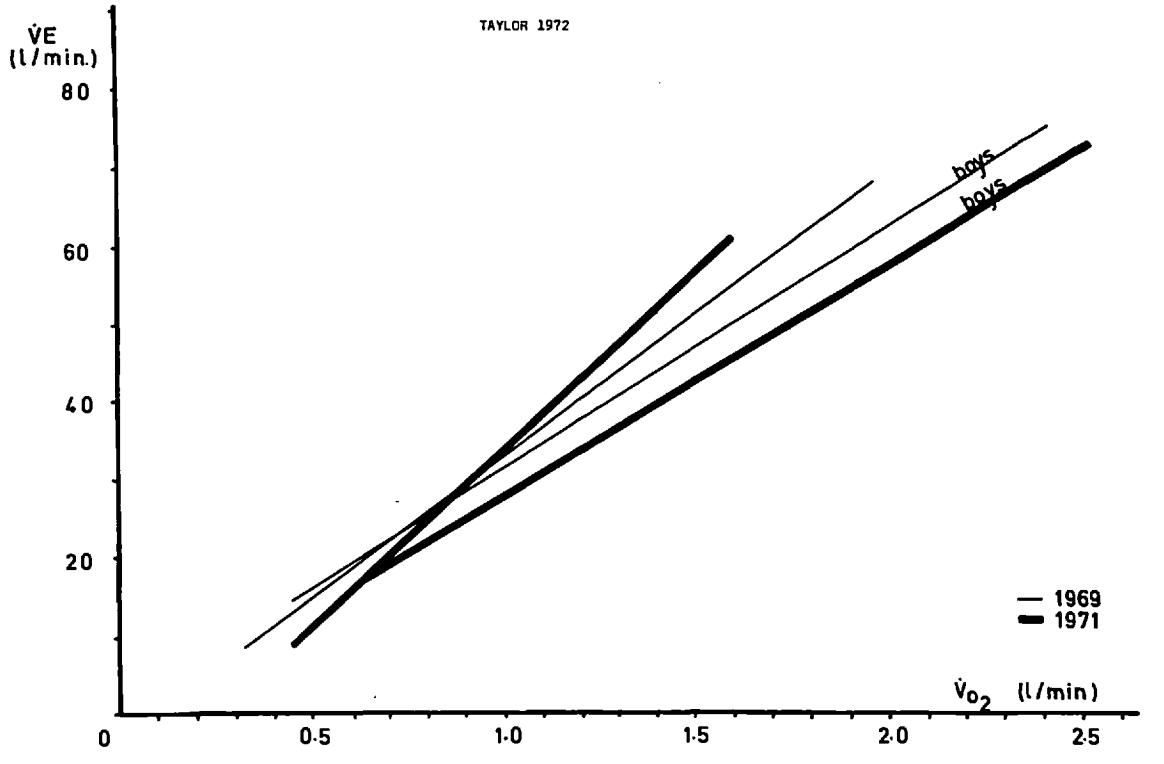
TABLE III - 7

Analysis of the results of the children who were studied both in 1969 and 1971. The table shows the results of comparing observed minus expected values for 1969 with observed minus expected values for 1971 using a paired 't' test. The expected values were calculated from the regression equations and data of Godfrey et al (1971) S.D. is the standard deviation of the differences of the values for (observed minus expected values 1971) minus (observed minus expected values 1969).

Parameter	Mean change	S.D. of difference	t	p
H.R. (boys)	-3.9	16.4	1.3330	N.S.
H.R. (girls)	-6.2	12.7	2.2995	*
$\dot{V}E$ (boys)	-1.3	5.9	1.2243	N.S.
$\dot{V}E$ (girls)	+3.2	5.0	2.9871	*
$\dot{Q}VD$ (boys + girls)	0.17	1.08	1.1815	N.S.
SV_{VD} (boys)	1.5	13.2	0.6473	N.S.
SV_{VD} (girls)	0.5	7.3	0.3133	N.S.

FIGURE III - 2

The relationship between oxygen consumption ($\dot{V}O_2$) and minute ventilation ($\dot{V}E$) for boys and girlst. The thick lines represent the values for 1971 and the thin ones those for 1969. All of the lines are calculated for a child of 150 cm.


TAYLOR 1972
V̇E
(l/min.)
80
60
40
20
0
0·5
1·0
1·5
2·0
2·5
boys
boys
— 1969
▬ 1971
V̇O2 (l/min)

When the individual results were compared it was found that the boys results had not changed significantly (Table III - 7). The mean change, in relation to the regression line, was a fall of 3.9 beats per minute. The girls however showed a mean fall of 6.2 beats per minute in relation to the regression line, which was significant at the 5% level. The standard deviations of the differences were similar for both groups being 16.5 for the boys and 12.7 for the girls.

Minute Ventilation

The minute ventilation of girls and boys differed significantly the girls having a higher minute ventilation than the boys (Figure III - 2). This is in keeping with the findings of Godfrey et al (1971). The results from the boys and girls were analysed separately. The boys minute ventilation in relation to oxygen consumption and height did not differ significantly from the 1969 results (Figure III - 2):-

1969 $\dot{V}E = 0.0305\ \dot{V}O_2 - 0.117\ Ht + 17$

1971 $\dot{V}E = 0.0306\ \dot{V}O_2 - 0.261\ Ht + 38$

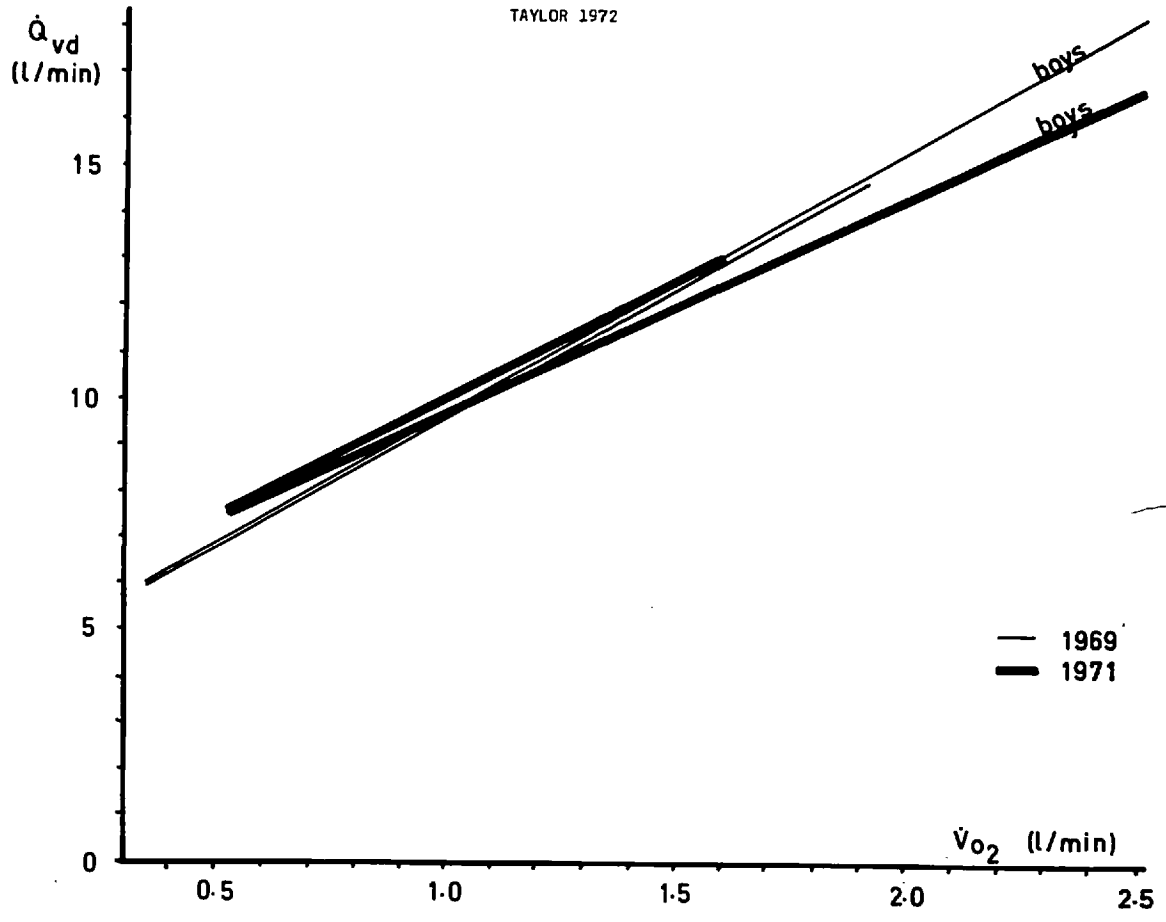
The girls however had a higher minute ventilation in relation to oxygen consumption and height than in 1969 (Figure III - 2):-

1969 $\dot{V}E = 0.0370\ \dot{V}O_2 - 0.211\ Ht + 25.7$

1971 $\dot{V}E = 0.0457\ \dot{V}O_2 - 0.364\ Ht + 42.4$

FIGURE III - 3

Cardiac output based on $PaCO_2$ (Calculated from an assumed normal dead space - $\frac{V_D}{V_T}$) plotted against oxygen consumption ($\dot{V}O_2$) for boys and girls. The thick lines represent the 1971 regression lines and the thin ones the 1969 regression lines. The lines are calculated for a boy of 150 cm. and a girl of 144 cm.


TAYLOR 1972
$\dot{Q}_{vd}$ (l/min)
15
10
5
0
boys
boys
1969
1971
$\dot{V}_{O_2}$ (l/min)
0·5
1·0
1·5
2·0
2·5

When the individual results were compared (Table III - 7) it was found that the boys minute ventilation had not altered significantly (mean change -1.3 l./min. SD 5.9) but the girls minute ventilation had increased by a mean of 3.2 litres per minute (SD 5.0) which was significant at the 1% level. It is difficult to see why this should have occurred other than as a result of the small sample (eleven girls) that was studied. As the boys mean minute ventilation fell in relation to the regression line it is most unlikely that any technical error was responsible for the change. The original study records were checked to make sure that the readings were correct but no error was found. The height range of the girls in the 1971 study falls within that of the 1969 study so that the two groups are comparable. The mean increase of 3.2 l./min. is not however very large in comparison with the mean minute ventilation on exercise of 29.8 l./min. It is not surprising to find that even at the age of 9 to 17 years females are inconsistent.

Cardiac Output Based on an Assumed Normal Dead Space

Cardiac output based on $PaCO_2$ calculated from an assumed normal dead space was found to be related to oxygen consumption. The regression line was not significantly affected by sex, height, weight or body surface area. The regression equations obtained by Godfrey et al (1971) and those of the present study are shown in Figure III - 3 and Table III - 4A. Godfrey et al (1971) found no significant difference between

the cardiac output of boys and girls, but gave separate equations for each. They did however find that height was a significant factor in determining cardiac output and this has been taken into account in comparing the two sets of data. The boys and girls results for 1969 and 1971 were pooled as there was no sex difference. There was no significant difference between the two sets of results:-

1969 $\dot{Q}VD = 0.0056\ VO_2 + 0.022\ Ht + 0.85$

1971 $\dot{Q}VD = 0.0044\ VO_2 + 0.025\ Ht + 1.60$

In the comparison of individual results the boys and girls results were again pooled and related to a regression equation for boys and girls calculated from the 1969 data (Table III - 4A). The cardiac output values had not changed significantly in relation to the regression line which took into acccunt height and oxygen consumption. The mean change was an increase of 0.17 l./min. with a standard deviation of 1.09.

The equation for cardiac output based on a $PaCO_2$ value calculated from the equation of Godfrey et al (1971) for normal dead space ($\dot{Q}VD$) was:-

$$\dot{Q}VD = 0.005\ \dot{V}O_2 + 4.7$$

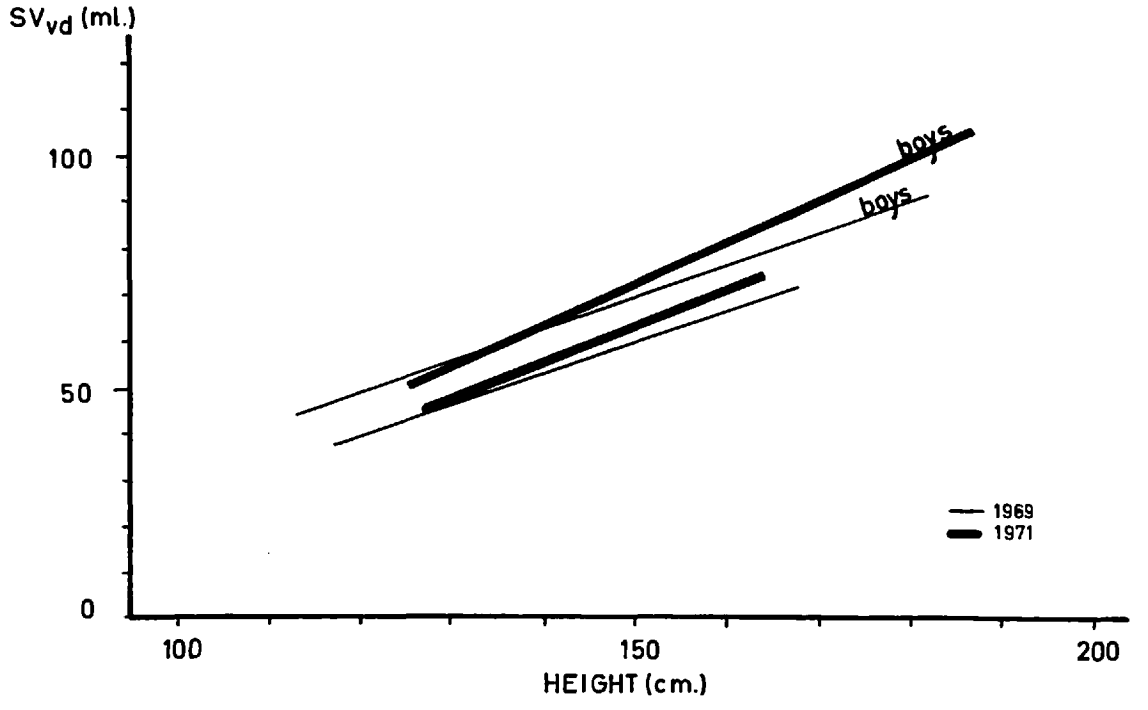
($r = 0.762$ $n = 79$ SEY 2.4)

This give lower results for cardiac output than do the pooled oxygen Fick results for adults calculated by Denison et al (1971):-

FIGURE III - 4

Showing the stroke voluem (SV_{VD}) (calculated from cardiac output based on an assumed normal dead space) plotted against height for boys and girls. The thick lines represent the 1971 values and the thin ones 1969 values. The stroke volume regression line for boys for 1969 was calculated for the boys' mean oxygen consumption on exercise in 1971.

TAYLOR 1972



$$\dot{Q} = 0.006\ \dot{V}O_2 + 6.0$$

(n = 228 SEY = 1.1)

They found good agreement between oxygen Fick values and indirect (CO_2) Fick estimates of cardiac output. They used corrected end tidal values for $PaCO_2$ and a rebreathing estimate of $P\bar{v}CO_2$.

Height did not make a significant contribution to the regression for the 1971 data though it did for the 1969 data. This is probably due to the smaller range of height of the children studied in 1971 compared with those studied in 1969. The increment for height is small being only 1.1 l./min. for every 50 cm. This is equivalent to approximately seven years growth in the 9 to 16 year age group - an increment of 0.17 litres/minute/year for a given oxygen consumption.

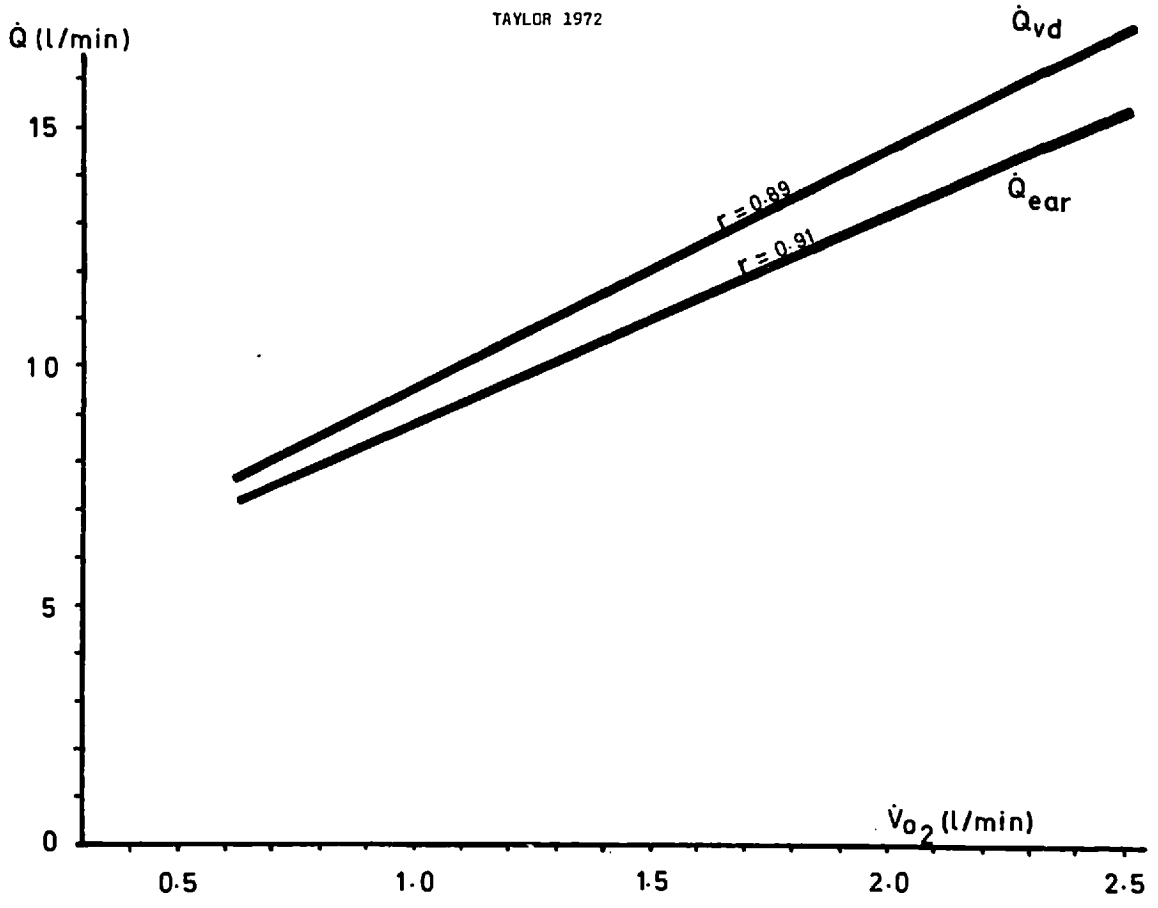
Stroke Volume Based on Assumed Dead Space

Stroke volume was significantly higher in boys than in girls (Table III - 4A and Figure III - 4). It was significantly related to height, weight and body surface area but when these parameters were known oxygen consumption did not have a significant effect. Godfrey et al (1971) found that oxygen consumption made a significant contribution in boys but not in girls.

No significant difference was found between the results for 1969 and 1971, nor was there any significant change in the individual results for boys (mean change + 1.5 ml. SD 13.2 ml.) or girls (mean change + 0.5 ml. SD 7.3).

FIGURE III - 5

Showing the relationship of cardiac output to oxygen consumption for (a) cardiac output based on a PCO_2 value calculated from an assumed normal dead space (QVD) and (b) cardiac output based on a PCO_2 value obtained from arterialised ear blood samples (QEAR). The line for QEAR is calculated for a child of 150 cm.


TAYLOR 1972
Q̇ (l/min)
15
10
5
0
0·5
1·0
1·5
2·0
2·5
V̇O2 (l/min)
Q̇vd
Q̇ear
r = 0·89
r = 0·91

The lack of change is not surprising in view of the agreement between the 1969 and 1971 values for heart rate and cardiac output.

Cardiac Output based on ear blood samples

The values obtained for cardiac output on exercise using ear blood samples were lower than those obtained by using an assumed normal dead space (Table III - 4A, Figure III - 5). A paired 't' test give the following results:-

Mean difference	n	t	P
-1.01	49	6.4663	***

Height, wieght and body surface area all had a significant effect on cardiac output but there was no significant variation with sex. These results are approximately one litre/minute lower than the results obtained by Godfrey and Davies (1970). The regression equation from the present study was used to provide the normal value when ear blood samples were used in the estimation of cardiac output. The 1971 regression coefficients of cardiac output based on ear blood estimates of PCO_2 ($\dot{Q}_{EAR}$) and on PCO_2 estimated from assumed normal dead space ($\dot{Q}VD$) in relation to oxygen consumption and height were similar as were the standard errors of the estimate:-

$\dot{Q}VD = 0.0044\ \dot{V}O_2 + 0.25\ Ht. + 1.6$

$(r = 0.899 \quad SEY = 1.2 \quad n = 54)$

$\dot{Q}_{EAR} = 0.0041\ \dot{V}O_2 + 0.78\ Ht. - 3.07$

$(r = 0.909 \quad SEY = 1.30 \quad n = 49$

These regression lines are shown in Figure III - 5.

Stroke volume based on ear blood samples

Stroke volume based on ear blood samples was significantly higher in boys than in girls (Table II - 4A). In both boys and girls stroke volume was significantly related to height, weight and body surface area and increased as these parameters increased. The relationship to oxygen consumption was not significant for either boys or girls when height, weight or body surface area were known.

Cardiac Output at Rest

Cardiac output at rest was calculated using values for $PaCO_2$ obtained from three sources, end tidal PCO_2, ear blood PCO_2, and $PaCO_2$ predicted from an assumed normal dead space (Table III - 5A). The mean values were as follows:-

PCO_2 Source	Mean $\dot{Q}$ (l./min.)	S.D.	n
Ear blood	4.0	2.3	24
Assumed dead space	6.3	3.6	24
End tidal	4.0	1.6	26

The standard deviation of the values obtained using the end tidal PCO_2 value was smaller than for either of the other values. The end tidal PCO_2 value also provided an estimate of cardiac output which, unlike the other two estimates, was significantly related to the resting oxygen consumption:-

PCO_2 Source	r	n	p
Ear blood	0.2361	24	N.S.
Assumed dead space	0.1695	24	N.S.
End tidal	0.6222	26	***

The equation for the cardiac output/oxygen consumption relationship at rest, based on end tidal PCO_2 is given in Table III - 4A.

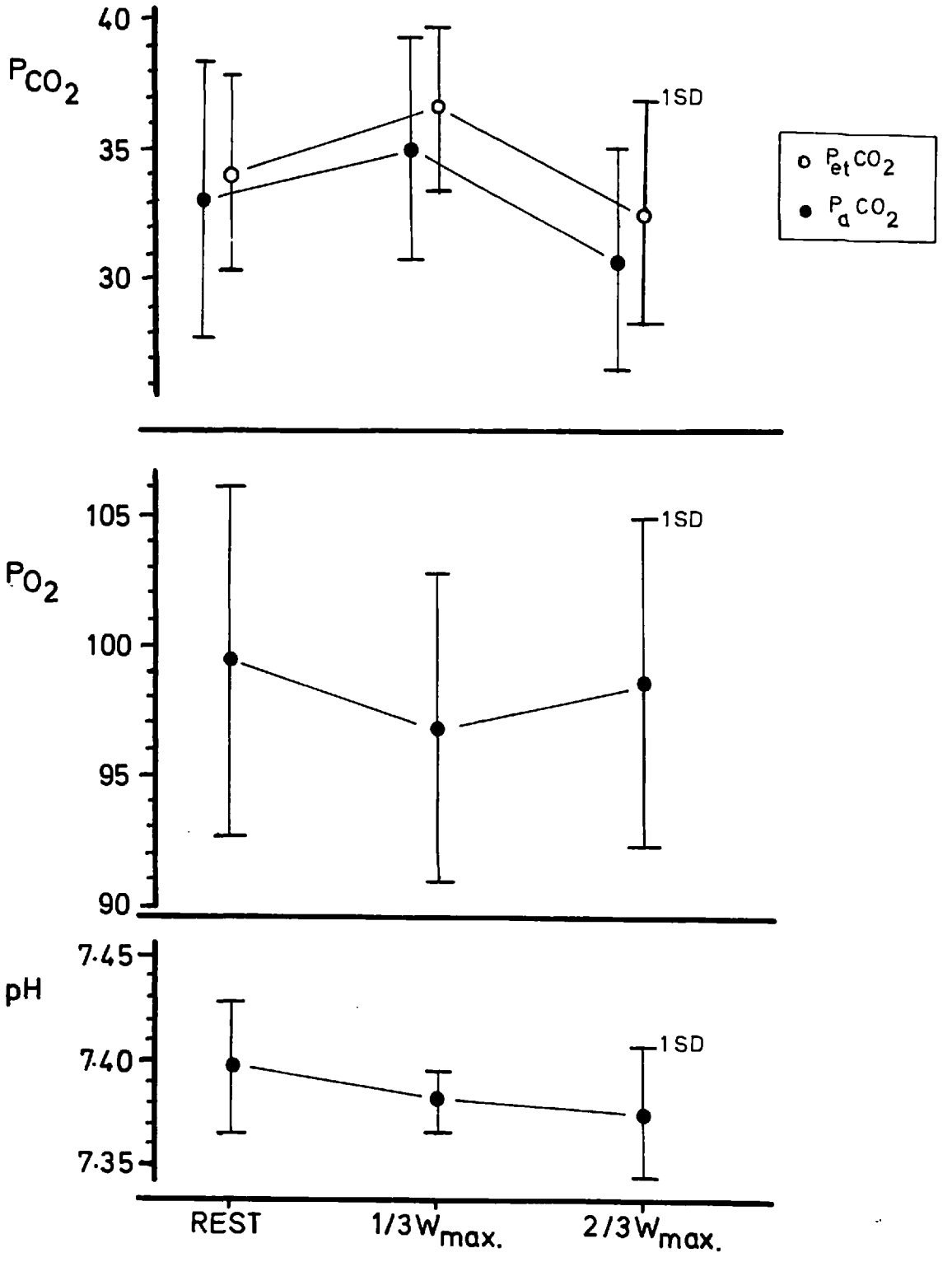
Venous Admixture

Venous admixture, that is the amount of venous blood not being oxygenated in the lungs, was expressed as a percentage of the systemic cardiac output (Table III - 5A). The values for venous admixture for each work load were as follows:-

	Mean	S.D.	n
Rest	3.0%	1.2	23
⅓ max.	1.9%	1.0	25
⅔ max.	1.9%	0.7	24

FIGURE III - 6

Showing the resting and steady state exercise values for CO_2 tension derived from end tidal air, and from arterialised blood, O_2 tension and pH derived from arterialised ear blood in normal children. The symbols represent the mean values and the range lines one standard deviation.


40
35
30
P_{CO_2}
1SD
$P_{et}CO_2$
P_aCO_2
105
100
95
90
P_{O_2}
1SD
7·45
7·40
7·35
pH
1SD
REST
1/3W max.
2/3W max.

TAYLOR 1972

These values are lower than those found by Jones et al (1966) in normal adults. They gave a mean resting value of 5.9% (S.D. 2.1) and on exercise 3.3% (S.D. 1.3). The lower values in children may be due to their smaller chest height reducing the ventilation/perfusion inequalities in the lung.

Blood gas, pH and oxygen saturation

Arterial blood gas values, pH and arterial oxygen saturation values (Table III - 8A) were derived from capillary ear blood samples. The means and standard deviations were as follows (the standard deviations are given in brackets):-

	Rest	⅓ Max.	⅔ max.
$PETCO_2$	34.0(3.7)	36.5(3.1)	32.4(4.1)
$PaCO_2$	33.0(5.3)	34.9(4.3)	30.6(4.1)
PaO_2	99.3(6.7)	96.7(5.9)	98.5(6.3)
SaO_2	97.4(0.4)	97.2(0.4)	97.3(0.4)
pH	7.398(0.033)	7.379(0.014)	7.374(0.032)

These results are expressed graphically in Figure III - 6.

It can be seen from this table that the pH fell as exercise increased and the arterial oxygen saturation scarcely altered at all. The end tidal and arterial PCO_2 followed each other closely with the mean end tidal value higher than the arterial but with the difference increasing slightly as exercise increased. This widening

of the end tidal arterial difference is to be expected with increasing work (Jones 1966).

Godfrey et al (1971) obtained the following values for PCO_2 in their study (standard deviations are given in brackets):-

	Rest	½ W max.	⅔ W max.
$PETCO_2$	32.8(3.9)	34.4(4.1)	32.0(4.0)
$PaCO_2$	35.5(3.3)	35.1(3.2)	34.0(2.9)

The fact that in these figures the $PaCO_2$ is higher than the $PETCO_2$ while in the present study the opposite was found, accounts for the difference in the estimates of dead space between the two studies. It also accounts for part of the difference between the values for cardiac output based on an assumed normal dead space calculated from the equation of Godfrey et al (1971) ($\dot{Q}VD$) and for cardiac output calculated using ear blood PCO_2 values ($\dot{Q}_{EAR}$).

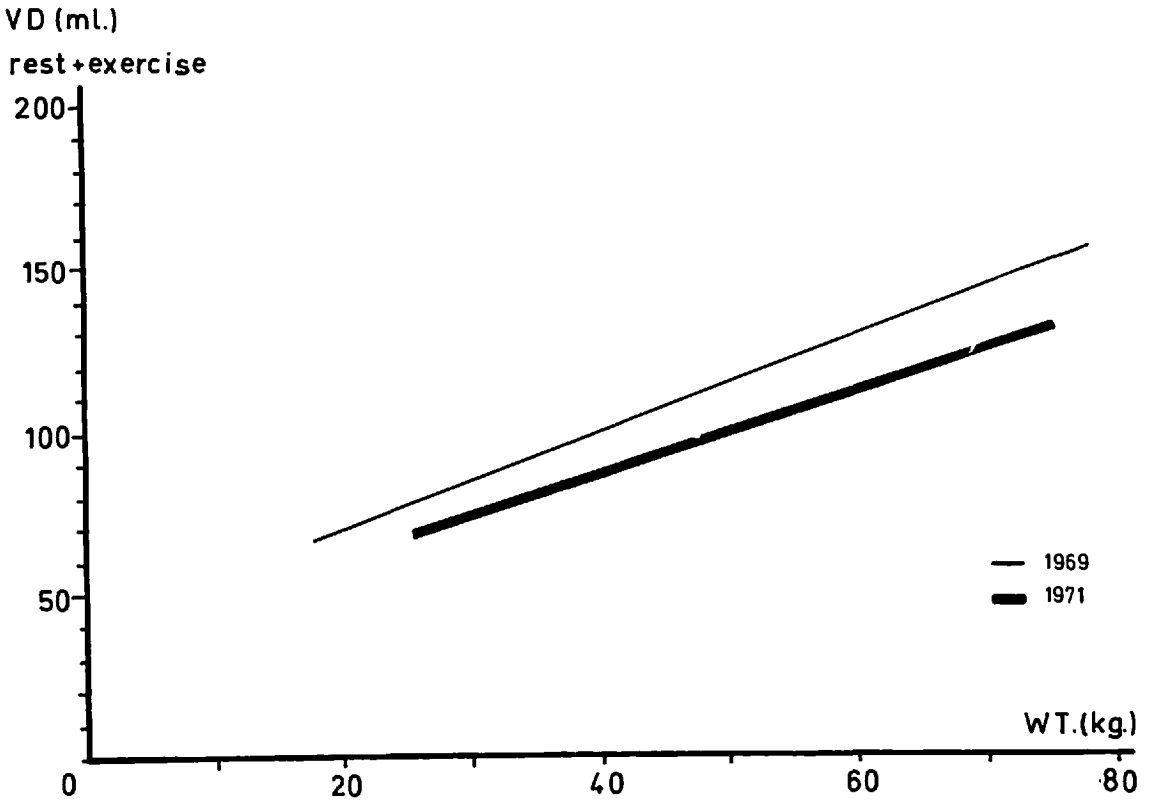
Dead Space

The value for dead space used by Godfrey (1971) was obtained from fourty pairs of results in which the end tidal and ear blood values for PCO_2 at rest and on exercise agreed to within 10%. The mean of each pair of results was used. Each mean value would therefore be close to the end tidal value. The equation obtained by Godfrey for the dead space/weight/tidal volume relationship was -

FIGURE III - 7

Showing the relationship of physiological dead space (VD) at rest and exercise to weight (wt.). The lines are calculated for a tidal volume of 850 ml. The thick line represents the values for 1971 dervied from end tidal PCO_2 and the thin line represents the equation of Godfrey et al (1971) based on the mean of the end tidal and ear blood PCO_2 values in selected cases (see text).

TAYLOR 1972



$$VD = 1.54 \times wt. + 0.049\ Vt + 2$$

(r = 0.78 SEY = 22 n = 40)

All of the end tidal values in the present study were used to calculate dead space irrespective of whether they agree closely with the ear blood values or not. The following equation was obtained (Figure III - 7):-

$$VD = 1.24\ wt. + 0.069\ Vt - 8.9$$

(r = 0.903 SEY = 22 n = 79)

The results obtained for dead space using corrected ear blood values for PCO_2 were lower and more scattered.

$$VD = 2.18\ wt - 37.5$$

(r = 0.541 SEY = 58.7 n = 72)

The effect of tidal volume on the regression was not significant. The values for PCO_2 given by corrected ear blood samples was lower than the end tidal values and the scatter was greater (Figure III - 6). This resulted in some very low and some negative values for dead space. All of the values, negative as well as positive were included in the regression analysis. The dead space was calculated from the adaption of the Bohr equation -

$$\frac{VD}{VT} = \frac{PaCO_2 - PECO_2}{PaCO_2}$$

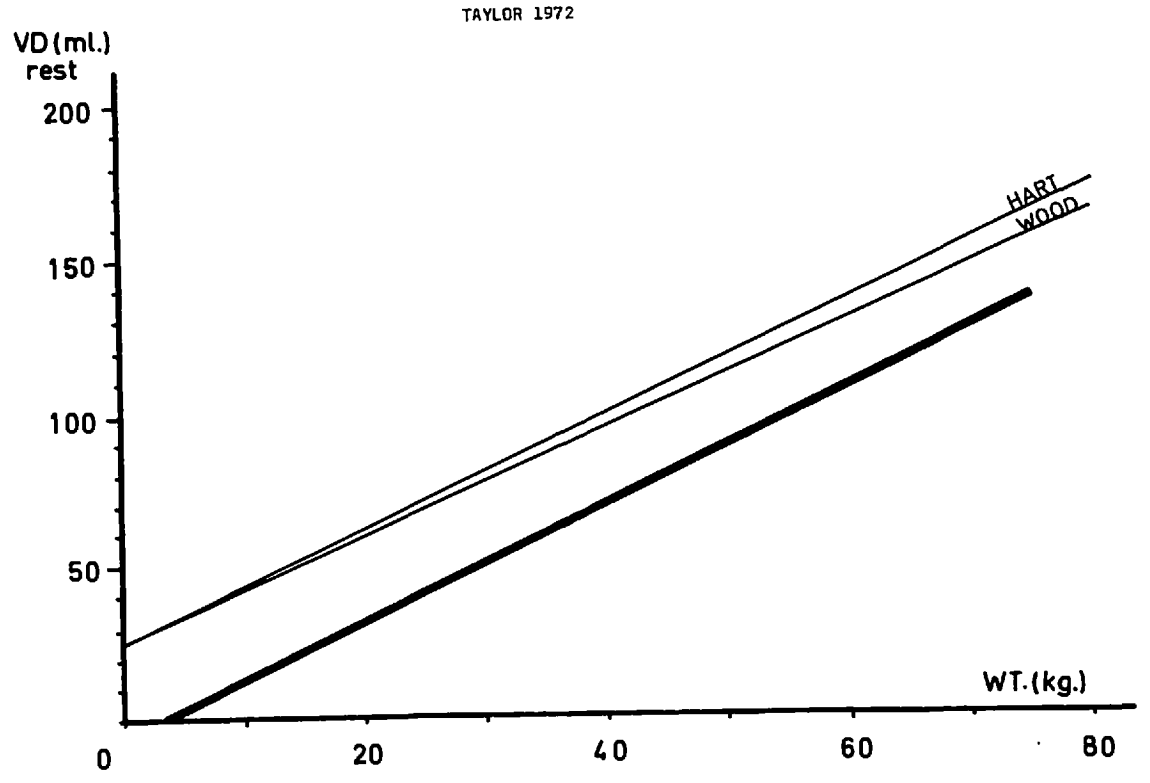
so that a change in the $PaCO_2$ value of one or two milimetres will produce a large change in the dead space value.

The equation given by Godfrey et al (1971) appears to be the only published assessment of physiological dead space in children (as opposed to infants). This equation is based on measurements made both at rest and on exercise. Hart et al (1963) and Wood et al (1971) measured anatomical dead space by a single or triple breath analysis after inhalation of 100% oxygen. Their measurements were made at rest and both series contained a large proportion of adults. They found significant relationships between anatomical dead space, and height, weight and body surface area. They found that the highest correlation was given by a curvilinear regression. Hart et al (1963) found that tidal volume made no significant contribution to the regression. Wood et al (1971) did not comment on the possibility of tidal volume being important. The increment for tidal volume found by Jones et al (1966) was 7.7 ml. per 100 ml., Assmussen and Neilsen (1956) obtained a value of 7 ml. per 100 ml., Godfrey et al (1971) one of 4.9 ml. and in the present study the increment was 6.9 ml./100 ml.

The correlation coefficients obtained in the present study using a multiple linear regression analysis with weight (or height) and tidal volume as independent variables were close to those obtained by Wood et al (1971) and Hart et al (1963) using a curvilinear regression:-

FIGURE III - 8

Showing dead space ($\dot{V}D$) at rest plotted against weight (wt.). The regression line for 1971 (heavy line) represents physiological dead space and is based on end tidal PCO_2. It is calculated for a tidal volume of 400 ml. The lines of Wood and Hart represent anatomical dead space.


TAYLOR 1972
VD (ml.)
rest
200
150
100
50
0
20
40
60
80
WT. (kg.)
HART
WOOD

Hart et al	$VD = 7.585 \times 10^{-4} \times Ht.^{2.363}$	$r = 0.91$
Wood et al	$VD = 4.5 \times 10^{-5} \times Ht.^{2.93}$	$r = 0.89$
Present study		
Rest only	$VD_{ET} = 1.46\ Ht. + 0.11\ VT - 180$	$r = 0.86$
Rest + exercise	$VD_{ET} = 0.82\ Ht. + 0.85\ VT - 146$	$r = 0.912$

No variation in dead space with sex has been found in the present study or in the studies of Godfrey et al (1971), Wood et al (1971) or Hart et al (1963).

The values obtained by Wood et al (1971) and Hart et al (1963) were in close agreement. The linear regression equations obtained by these workers give higher values than the values obtained at rest in the present study (Table III - 4A and Figure III - 8). In the present study it was found that both at rest and on exercise tidal volume made a significant contribution to the regression and as both the other studies contained a large proportion of adults with, presumably, large tidal volumes this may explain the discrepancy between the results. If the regression lines are extrapolated to 3 kg. the estimates of Hart et al (1963) and Wood et al (1971) are rather high for a baby while those of the present study are rather low.

CYANOTIC CONGENITAL HEART DISEASE

THE VENTILATORY RESPONSE TO EXERCISE DURING HYPOXIA

INTRODUCTION

Normal adults and children hyperventilate in response to hypoxia (Asmussen 1967 and Byrne-Quinn et al 1972) but Sorensen and Severinghaus (1968) and Edelman et al (1970) have shown a diminution in the ventilatory response to hypoxia, at rest, in cyanotic congenital heart disease.

However during the present study hyperventilation was noted during exercise in children with cyanotic congenital heart disease. Hyperventilation was most marked in those children who became deeply cyanosed.

MATERIALS AND METHODS

The results from seventeen patients (Table IV - 1) were analysed in this study. In a few children who had severe exercise intolerance a single steady state work load was used instead of the usual two work loads of one-third and two thirds of the maximum load completed in the progressive test.

A ventilatory index was used to relate the children's results to normal values. This was calculated as follows:-

$$\text{Ventilatory index} = \frac{\text{observed minute ventilation}}{\text{expected minute ventilation}} \times 100$$

The expected minute ventilation was calculated from the child's oxygen consumption, height and sex using the data from normal children reported by Godfrey et al (1971).

TABLE IV - 1

Showing the age, time of onset of cyanosis, sex, height, and diagnosis for each child. (V.S.D. = ventricular septal defect. T.C.F. = 'Totally corrected' Fallot's tetralogy).

Patient	Age (yrs.)	Age of onset of cyanosis	Sex	Height (cm.)	Diagnosis & Operations
1	7	Acyanotic	M	122	
2	6	1½ years	M	109	
3	6½	8 months	F	112	
4	6	Acyanotic	M	115	Fallot's tetralogy
5	8	Acyanotic	F	120	
6	7½	Acyanotic	F	120	
7	10½	3½ years	M	136	Fallot's tetralogy Blalock Shunt aged 4 years
8	13½	At birth	F	124	Fallot's tetralogy Pulmonary infundibular resection, aged 4 yrs.
9	8½	Acyanotic	M	133	Fallot's tetralogy
10	8½	2 years	M	127	Eisenmenger V.S.D.
11	14½	11 years	F	154	Eisenmenger V.S.D.
12	7½	5 days	F	120	T.C.F. aged 4 years
13a	10	At birth	M	135	T.C.F. aged 8 months
13b	11	At birth	M	140	T.C.F. aged 8 months
14	12	One week	M	145	T.C.F. aged 9 years
15	9½	One week	F	131	T.C.F. aged 8 years
16	9	5 years	F	130	T.C.F. aged 6 years
17	8½	10 months	M	125	T.C.F. aged 2½ years

FIGURE IV - 1

The relationship between ventilatory index and the change in arterial oxygen saturation from the resting value. ($y = 4.081 x + 96.96$ Patients 2, 3 and 7 omitted.) 95% confidence limits are given either side of the regression line. Asmussen's adult data is indicated:- Δ

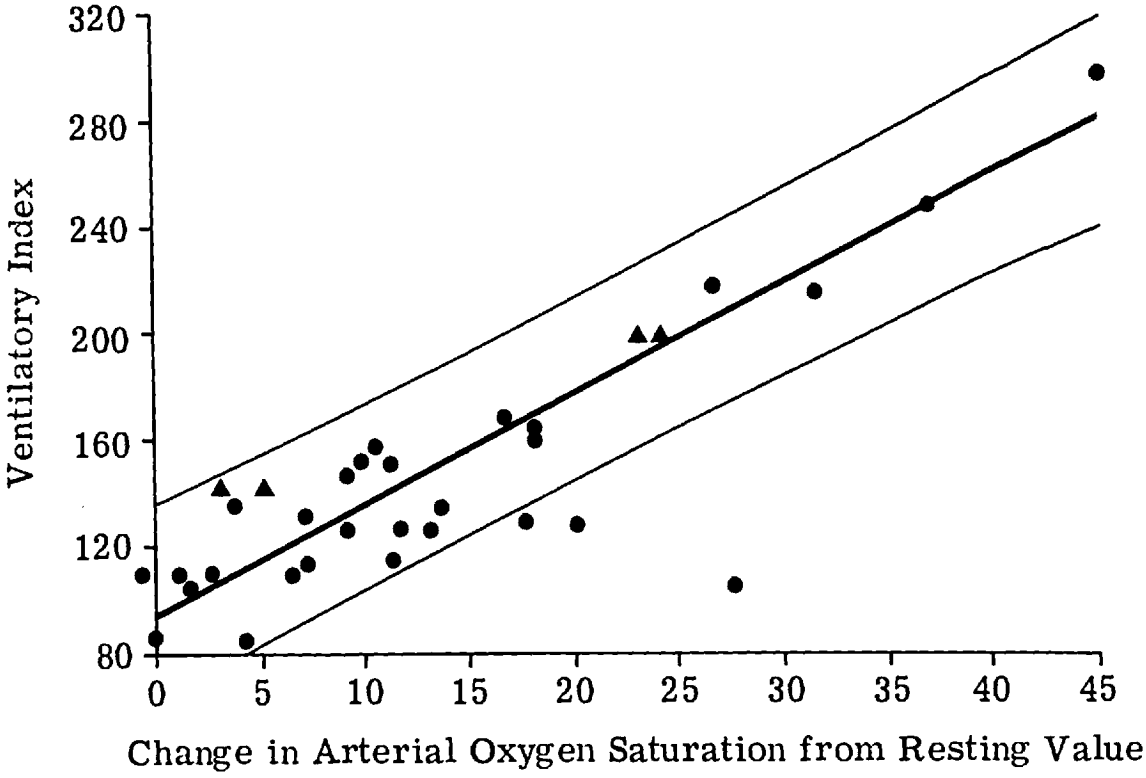
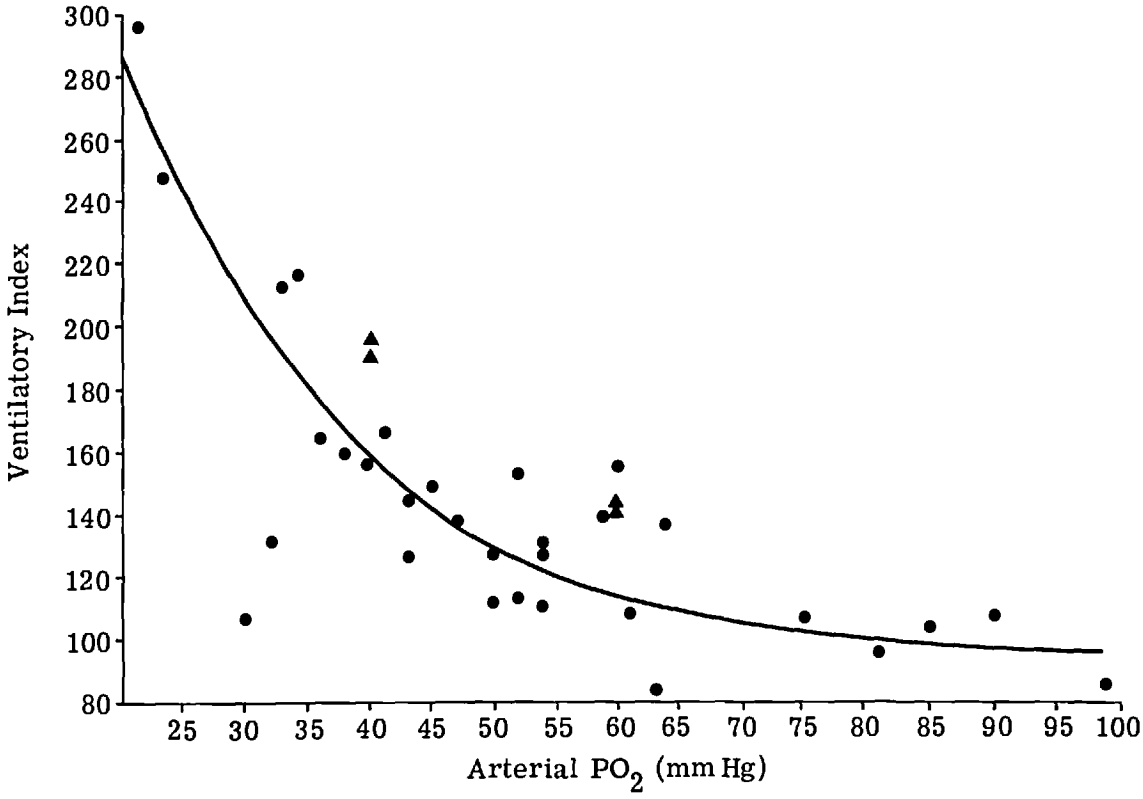

320
280
240
200
160
120
80
Ventilatory Index
0
5
10
15
20
25
30
35
40
45
Change in Arterial Oxygen Saturation from Resting Value

FIGURE IV - 2

The relationship between ventilatory index and arterial PO_2. The trend line was drawn by eye. Asmussen's adult data is marked:- Δ


Ventilatory Index
300
280
260
240
220
200
180
160
140
120
100
80
25 30 35 40 45 50 55 60 65 70 75 80 85 90 95 100
Arterial PO_2 (mm Hg)

RESULTS

At rest there was no significant difference between the mean minute ventilation of these children (mean 8.2 l./min. standard error 1.0) and that of normal children (mean 7.8 l./min. standard error 0.69).

Figure IV - 1 shows the relationship between the ventilatory index and the change in arterial oxygen saturation from the resting value. Figure IV - 2 shows the relationship between the ventilatory index and the arterial PO_2. There are no values available for the ventilatory response of normal children to hypoxia during exercise, with which to compare this data. However, the results calculated from the normal adult data of Asmussen (1967) (assuming normal resting arterial oxygen saturation and 3% venous admixture on exercise) agree with the present results (Figures IV - 1 and IV - 2).

Three children (patients 2, 3 and 7) had a lower ventilatory response than the others. Their results fall outside the 95% confidence limits estimated from the results of the other children. Direct measurement of ventilatory capacity in these children showed that they were all capable of a ventilation rate which would have brought their results within the 95% confidence limits. The arterial PCO_2 of these three children was not lower than that of the other children (Table IV - 2).

The ventilatory index was significantly related to the arterial pH, but statistical assessment of the multiple regression analysis of ventilatory index, change in arterial oxygen saturation, and pH showed that the contribution made by pH was not significant when the other two indices were known.

TABLE IV - 2

Showing the results for each patient. The abbreviations are explained in Section II.

Patient	Work (Watts)	Hb	$\dot{V}O_2$	Ventilatory Index	$PaCO_2$	PaO_2	SaO_2	pH
1	0	14.2			25	98	97.6	7.43
	10		427	139	30	59	91.0	7.41
	20		571	128	26	54	88.4	7.41
2	0	16.9			29	52	88.4	7.43
	10		366	106	27	30	60.7	7.43
3	0	19.7			27	42	79.0	7.41
	10		342	130	30	32	61.3	7.38
4	0	10.4			29	73	94.8	7.39
	15		445	137	30	47	81.3	7.37
5	0	14.2			27	64	93.8	7.46
	7		213	126	24	43	81.0	7.43
	14		445	166	23	41	72.2	7.39
6	0	14.4			27	46	85.2	7.47
	10		416	157	31	40	75.2	7.41
	20		489	164	29	37	67.4	7.38
7	0	17.5			32	43	80.3	7.43
	7		350	129	32	30	60.5	7.43
8	0	15.2			24	69	95.1	7.46
	10		359	151	29	52	85.5	7.37
9	0	14.9			32	78	96.2	7.45
	15		488	136	33	63	92.8	7.44
	30		650	155	27	60	91.0	7.40
10	0	15.6			31	40	77.0	7.42
	11		386	247	33	23	40.0	7.38
	22		373	298	31	21	32.0	7.34
11	0	18			29	56	88.6	7.37
	20		554	218	36	34	62.0	7.34
	40		680	215	42	33	57.0	7.39
12	0	12.5			30	84	96.5	7.41
	10		356	109	28	61	94.0	7.46
	20		490	129	33	54	89.5	7.45
13a	0	15.8			29	61	93.0	7.46
	20		640	112	34	50	86.0	7.40
	40		841	150	32	45	82.0	7.40
13b	0	15.0			32	70	94.1	7.40
	20		628	109	34	54	87.8	7.38
	40		923	127	31	50	82.7	7.32

Continued/.....

TABLE IV - 2 (CONTINUED)

Showing the results for each patient. The abbreviations are explained in Section II.

Patient	Work (Watts)	Hb	$\dot{V}O_2$	Ventilatory Index	$PaCO_2$	PaO_2	SaO_2	pH
14	0	12.5			33	85	96.7	7.38
	35		776	84	32	63	92.0	7.40
	75		1226	113	31	52	85.6	7.35
15	0	11.3			24	103	97.9	7.42
	35		553	109	33	90	96.8	7.38
	70		658	104	33	85	96.3	7.37
16	0	15.3			30	53	87.3	7.39
	15		412	145	27	43	78.5	7.37
	30		643	159	23	38	69.5	7.35
17	0	13.1			31	99	97.5	7.40
	10		545	86	34	99	97.4	7.38
	20		765	109	35	108	97.9	7.41

TABLE IV - 3

Dependant Variable (y)	Independent Variable (x)	Correlation Coefficient	P value	
Ventilatory Index	$PaCO_2$	0.08084	N.S.	Patients 2, 3 & 7 omitted
Ventilatory Index	PaO_2	-0.72440	***	
Ventilatory Index	SaO_2	-0.93810	***	
Ventilatory Index	ΔSaO_2	0.93865	***	
Ventilatory Index	CaO_2	-0.69961	*	
Ventilatory Index	pH	-0.43022	***	
Ventilatory Index	SaO_2	-0.80750	***	All patients included
Ventilatory Index	ΔSaO_2	0.83299	***	
Ventilatory Index	CaO_2	-0.66848	***	

As all the children with a poor response to hypoxia had high haemoglobin values it was possible that their arterial oxygen content might be normal despite low oxygen saturation, and the ventilatory response of all the children might be more closely related to oxygen content than saturation. However, statistical analysis showed that the ventilatory response was more closely related to both oxygen saturation and to change in oxygen saturation than to oxygen content (Table IV - 3).

An increase in $PaCO_2$ and fall in pH stimulate respiration (Leusen 1956) and could have been responsible for the raised ventilatory index on exercise. However, the highest $PaCO_2$ during exercise was 35 mm. Hg. and the $PaCO_2$ on exercise was not significantly related to the ventilatory index (Table IV - 3). Therefore the increase in minute ventilation was not due to an increase in $PaCO_2$. The ventilatory index was significantly related to the pH (Table IV - 3), but this was not significant when the arterial oxygen saturation was known.

DISCUSSION

The three patients (2, 3 and 7) who had a poor ventilatory response to hypoxia all had haemoglobin concentrations above 16 gm. per 100 ml., arterial oxygen saturations (Sa^0_2) of less than 88% at rest in air, and a history of cyanosis of at least 4½ years duration starting at or before 3½ years of age. Of the children who hyperventilated on exercise, four patients (7, 8 and 10) had a similar history of cyanosis and a low oxygen saturation at rest, but a haemoglobin concentration below 16 gm. per 100 ml. and one

(patient 11) had a low oxygen saturation at rest and a haemoglobin concentration of 18 gm. per 100 ml. but a late onset of cyanosis. It would appear that a raised haemoglobin concentration, arterial desaturation in air at rest and long-standing cyanosis starting early in life, were associated with relative insensitivity to hypoxia though it is not possible to say which is cause and which is effect from the data available at present.

Sorensen and Severinghaus (1968) using a steady state technique have shown blunting of the ventilatory response to hypoxia at rest, in 16 to 32 year old patients with surgically corrected Fallot's tetralogy. Edelman et al (1970) using transient hypoxia showed a diminished response in 8 to 37 year old patients with cyanotic congenital heart disease but a normal or nearly normal response after total surgical correction. This apparent disagreement may be due to the different techniques used or to the fact that the three post-operative patients studied by Edelman et al (1970) had normal arterial oxygen saturations and haemoglobin concentrations, while four of the five patients studied by Sorensen and Severinghaus (1968) were still hypoxic and had high haematocrits after total surgical correction. None of the 'poor responders' in the present study were among the six children with corrected Fallot's tetralogy although two of the six had low oxygen saturations at rest (Table IV - 2).

Weil et al (1970) have shown that a resting lowland native can acquire a progressive decrease in hypoxic ventilatory drive when exposed to the hypoxia

of altitude in adult life. They found that the decrease in ventilatory drive was dependent on time, being partial after 10 years' exposure to hypoxia and almost complete after twenty years. In a further study (Byrne-Quinn et al 1972) the ventilatory response to hypoxia of two groups of 9 to 10 year old children was compared. One group had been born and reared at 3,100 metres and the other at 1,600 metres. There was no significant difference between the response to hypoxia of the two groups. They concluded that the loss of hypoxic ventilatory drive in chronically hypoxia man does not occur in the neonatal period but is acquired over many years.

It must be emphasised that all of these studies were made at rest while the observations in the present study were made during exercise.

In the present study although the lowest PaO_2 at rest was 40 mm.Hg. the lowest arterial saturation was 77% thus providing relatively little stimulus to the respiratory centre. It is therefore not surprising that the mean ventilation rate at rest was not significantly different to that of normal children.

The duration of cyanosis in the 'poor responders' on exercise was considerably less than the 10 years at high altitude recorded by Weil et al (1970) for attenuation of hypoxic respiratory drive.

From the present study it appears that except in patients with the triad of long standing cyanosis from early life, a raised haemoglobin concentration and a low arterial oxygen saturation at rest, in air, exercise

releases the ventilatory response to hypoxia which is suppressed at rest. In cyanotic patients without this triad, it appears that the mechanism serving the acute hypoxic drive is merely blocked at rest and not damaged as has been suggested (Leader 1970).

SUMMARY

In contrast to the diminished ventilatory response to hypoxia which has been found at rest in cyanotic congenital heart disease, hyperventilation was noted on exercise in children who were cyanosed. Sixteen children had low arterial oxygen saturations on exercise and thirteen of these hyperventilated by an amount similar to that reported in normal adults breathing hypoxic gas mixtures. The three children who had little ventilatory response to hypoxia all had a triad of long standing cyanosis starting early in life, high haemoglobin concentrations and low arterial oxygen saturation at rest in air. It is concluded that except in children with this triad, exercise releases the ventilatory response to hypoxaemia which is absent or diminished at rest in cyanotic congenital heart disease.

OXYGEN CONSUMPTION DURING HYPOXIC EXERCISE

TABLE IV - 4

Showing the sex, age, height, haemoglobin concentration, diagnosis and operations of the children studied.

(VSD = ventricular septal defect)

TABLE IV - 4

Patient No.	Sex	Age (yrs.)	Height (cm.)	Hb (gm./100 ml.)	Diagnosis and Operations
1	M	7	122	14.2	
2	M	6	109	16.9	
3	F	6½	112	19.7	
4	M	6	115	10.4	Fallot's Tetralogy
5	F	8	120	14.2	
6	F	7½	120	14.4	
7	M	10½	136	17.5	Fallot's Tetralogy Blalock shunt aged 4 years
8	F	13½	124	15.2	Fallot's Tetralogy. Pulmonary infundibular resection aged 4 yrs.
9	M	8½	127	14.9	Fallot's Tetralogy
10	M	7	116	16.9	
11	M	8½	127	15.6	Eisenmenger V.S.D.
12	F	14½	154	18.0	

INTRODUCTION

It is generally accepted that for all subjects irrespective of health of disease, the increase in oxygen consumption for a given increase in external work remains constant provided the form of work remains the same (McIlroy 1963). However, Cassells and Morse (1958) reported that patients with cyanotic heart disease had a lower than normal oxygen consumption when running on a treadmill, but commented that as these children had severe limitation of exercise they frequently held onto the bars of the treadmill and so might have reduced the amount of work they were doing at a given treadmill setting. Kennaird (1971) found a lower oxygen consumption in cyanosed babies when active than when lying still, and further noticed that an oxygen debt was not built up during the period of activity.

During the present study it was noted that, for the same amount of external work the oxygen consumption of cyanosed children was lower than that of normal children.

MATERIALS AND METHODS

Details of the children whose results were analysed in this study are given in Table IV - 4. None of the children were receiving drug therapy at the time of the study. In all the children simple spirometry and peak expiratory flow rates were normal. In a few children with severe exercise intolerance only one steady state measurement

TABLE IV - 6a

Showing the results of paired 't' tests used to compare the observed and expected oxygen consumption levels during exercise in cyanosed children and in those with a variety of different acyanotic heart lesions. (ASD = atrial septal defect. V.S.D = ventricular septal defect)

TABLE IV - 6b

Showing the results of a paired 't' test comparing the observed and expected carbon dioxide production during exercise in cyanosed children.

TABLE IV - 6a

Group	No. of Patients	No. of Observations	Mean Difference (ml.)	Standard error	p
Cyanosed Patients	12	18	-64	16.8	**
Corrected Fallot's Tetralogy	10	22	+16	17.1	N.S.
Aortic Stenosis	8	18	+40	19.0	N.S.
Pulmonary Stenosis	11	23	+9	11.6	N.S.
Surgically Closed A.S.D. and V.S.D.	7	16	+49	24.9	N.S.

TABLE IV - 6b

Cyanosed Patients	12	18	-22	19.97	N.S.

FIGURE IV - 3

Showing the relationship of the oxygen consumption index and the arterial oxygen saturation. The equation for the regression line is $y = 0.41 x + 59.6$. The limit lines represent one standard error of the estimate.

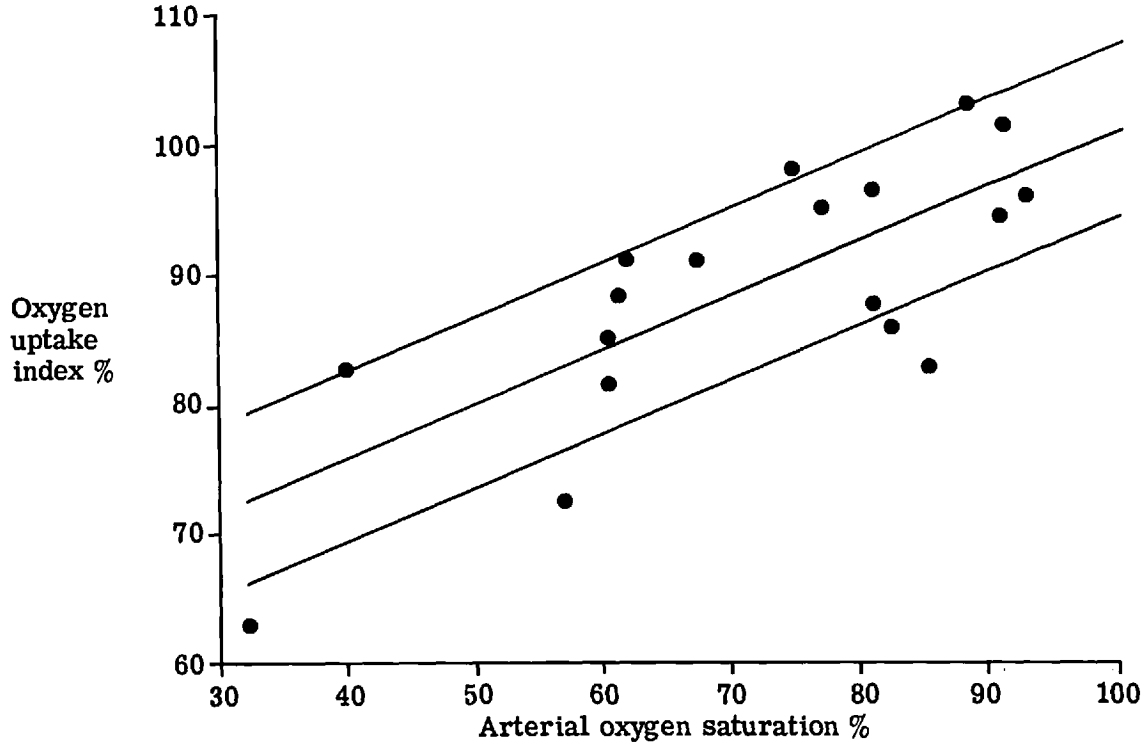

Oxygen uptake index %
110
100
90
80
70
60
30
40
50
60
70
80
90
100
Arterial oxygen saturation %

FIGURE IV - 4

Showing the relationship between the oxygen consumption index and the change in arterial oxygen saturation from rest to exercise (Δ $Sa0_2$). The equation for the regression line is -

$$y = -0.616\ x + 99.98$$

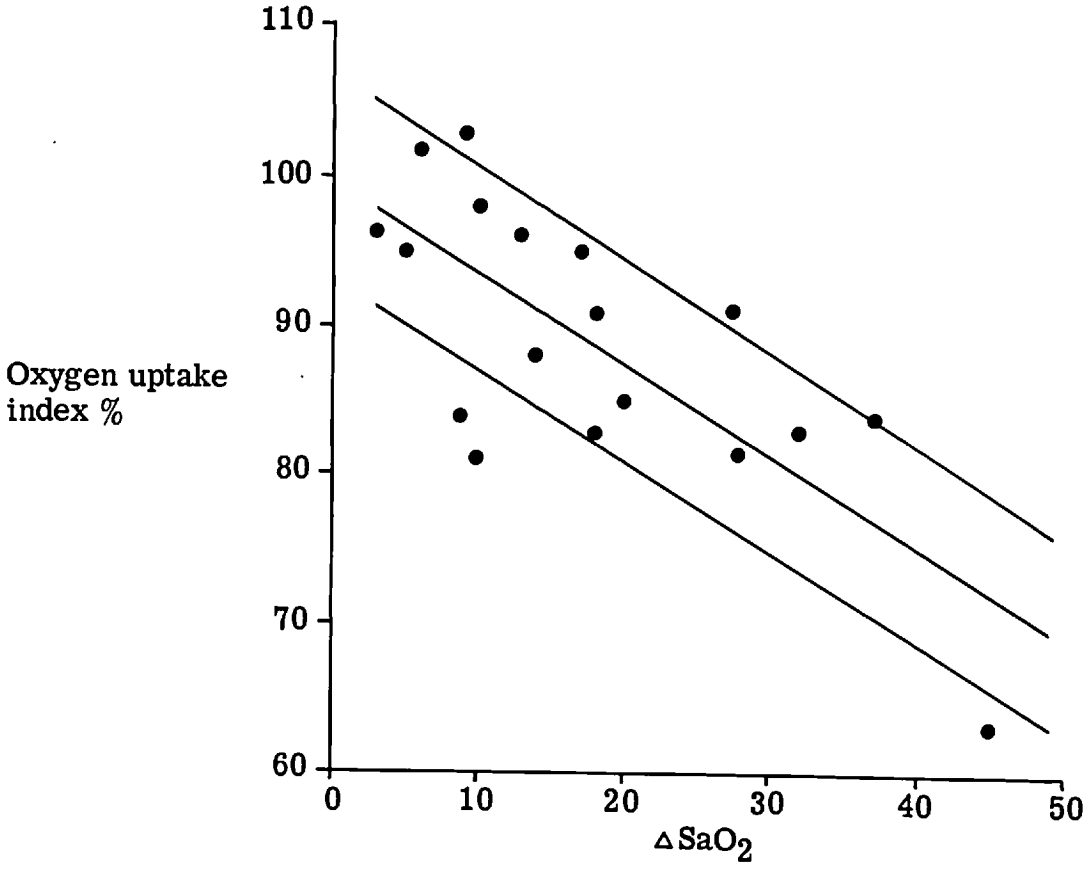

Oxygen uptake index %
110
100
90
80
70
60
0
10
20
30
40
50
ΔSaO2

TABLE IV - 7

Showing the results of a linear regression analysis of the relationship of the oxygen consumption index to arterial oxygen saturation, change in arterial oxygen saturation (ΔSaO_2), arterial oxygen tension, arterial pH, and arterial carbon dioxide tension.

TABLE IV - 7

Dependent Variable	Independent Variable (y)	Correlation coefficient	p
Oxygen consumption index	SaO_2	0.7585	***
Oxygen consumption index	ΔSaO_2	-0.7477	***
Oxygen consumption index	PaO_2	0.6843	**
Oxygen consumption index	pH	0.4285	N.S.
Oxygen consumption index	$PaCO_2$	-0.2783	N.S.

was made at either half or two-thirds of the maximum work load reached in the progressive exercise test.

In order to compare the results with normal values the oxygen consumption was expressed as a percentage of the normal value:-

$$\text{oxygen consumption index} = \frac{\text{observed oxygen consumption}}{\text{expected oxygen consumption}} \times 100$$

The expected oxygen consumption was calculated from the work performed using the data of Godfrey et al (1971) for normal children.

Both the normal values reported by Godfrey et al (1971) and the results reported here were obtained using the same equipment and techniques.

RESULTS

At rest the oxygen consumption of the cyanosed children was not significantly different from that of normal children. It was found that the oxygen consumption during exercise in the cyanosed children was significantly lower than that for normal children (Tables IV - 5A and IV - 6a). The reduction in oxygen consumption was related to the arterial oxygen saturation during exercise (Figure IV - 3) and to the fall in oxygen saturation from the resting value (Figure IV - 4). Both of these relationships were statistically highly significant (Table IV - 7).

The arterial pH and PCO_2 were not significantly related to the oxygen uptake index (Table IV - 7).

The carbon dioxide production of these children during exercise was not significantly different from that of the normal children studied by Godfrey et al (1971) (Table IV - 6b).

The oxygen consumption of children with aortic stenosis, pulmonary stenosis, surgically closed atrial and ventricular septal defects and totally corrected Fallot's tetralogy who have been studied in this laboratory did not differ significantly from normal values (Table IV - 6a).

DISCUSSION

It appears that a cyanosed child will perform a given work load for a lower oxygen consumption than a normal child. One might expect that a cyanosed child would produce less energy from aerobic metabolism and more energy from anaerobic metabolism than would a normal child. Anaerobic metabolism results in an increase in lactate production and consequently a rise in expired carbon dioxide. However, the carbon dioxide production of the cyanosed children was not significantly different from normal (Table IV - 6b) indicating that there was no compensating rise in anaerobic energy production. No direct measurement was made of the lactate levels in these children. The change in base excess has, however, been shown to be linearly related to the change in blood lactate (Anderson 1972). The mean change in base excess for these children between rest and the first work load was -0.7 (S.E. 1.1) and between

the first and second work loads -2.4 (S.E. 0.5). This is not significantly different from the values obtained in the normal children where the mean change from rest to the first work load was -0.1 (S.E. 0.6) and from the first to the second work load -2.6 (S.E. 0.6). Godfrey et al (1971) measured the lactate levels in ear blood samples and obtained the following results:-

Mean change in blood lactate m.mol./l.

	Boys	Girls
rest - $\frac{1}{3}$ max.	1.5	1.7
$\frac{1}{3}$ max. - $\frac{2}{3}$max.	2.2	2.6

Comparison of these values does not suggest an increase in anaerobic metabolism.

There are a number of possible explanations for the low levels of oxygen consumption; firstly faulty equipment and techniques, secondly production of energy by a pathway which does not require oxygen or produce carbon dioxide. Thirdly, reduction of oxygen consumption by tissues not directly concerned with external work and fourthly, increased efficiency of the normal energy producing pathways resulting in higher energy production for the same oxygen consumption.

Studies in patients one to six were made before the bicycle was re-calibrated. Studies in patients seven to twelve were made after the bicycle had been re-calibrated. The maximum correction which would have had to be applied to the first six studies was 2.4 watts. It is extremely difficult

to adjust the bicycle as accurately as this and so the correction was not applied in these studies. This small error would increase the oxygen consumption for the work load reading on the dial and would therefore tend to move the results towards normality not away from normality. The results of the cyanotic children stuied after the bicycle had been re-calibrated showed the same deviation from the norm as did those studied before re-calibration, and the greatest reduction in oxygen consumption was found in a patient studied on the re-calibrated bicycle. If there had been a technical error resulting in an abnormal oxygen consumption:work ratio then this should have applied to the acyanotic children as well as to the cyanotic children but this was not so (Table IV - 6a). If the reduction in oxygen consumption had been due to an imcomplete expired air collection then the carbon dioxide production and minute ventilation results should have been low. The carbon dioxide production was normal (Table IV -6b) and the minute ventilation of these children was increased (see Ventilatory Response to Hypoxic Exercise in this Section). A technical error does not seem to have been responsible for the reduction in oxygen consumption.

It seems unlikely that there is a major energy source in man which does not require oxygen or produce carbon dioxide, and so an increased efficiency of the normal metabolic pathways or reduction of oxygen consumption by tissues not directly contributing to external work,

when operating under hypoxic conditions, remain as the most likely explanations for the reduced oxygen consumption. Reduction in oxygen consumption by tissues not directly concerned with the production of energy for external work could be produced by diminishing their blood supply as occurs in the diving seal (Scholander 1960). Cross et al (1959) have shown that the oxygen consumption of the newborn lamb falls as hypoxia increases but that this response is absent in adult sheep except in extreme degrees of hypoxia.

Kennaird (1971) found that the oxygen consumption of babies with cyanotic congenital heart disease was lower when they were active than when they were at rest and noted that an oxygen debt was not built up. The ability to respond to hypoxia by a reduction in oxygen consumption could be advantageous in the immediate prenatal period. It may be that children with cyanotic congenital heart disease retain or regain this ability which is lost in normal children.

There are now three studies suggesting that children with cyanotic congenital heart disease may have a reduced oxygen consumption during hypoxic exercise Cassels and Morse (1962), Kennaird (1971), and the present study. However, the mechanism of the phenomenon is still open to conjecture.

The mechanical efficiency of patient 10 at the second work load (assuming an energy production of 20.61

Joules per ml. of oxygen) is 34.6% compared with the value of 25.4% found by Godfrey (1971) in normal children. As children with right to left shunts who are not cyanosed at rest tend to have only a small fall in arterial oxygen saturation on exercise it is not possible to tell from the present study whether long continued hypoxia at rest is essential to induce a lowered oxygen consumption on exercise. If it were ethically justifiable to perform muscle biopsy during exercise, in cyanosed patients, an assay of enzyme activities might help to elucidate the changes in their metabolism which results in a diminished oxygen requirement for work.

Because of the variation in bicycle ergometer calibration oxygen consumption has been used as a reference measurement for many aspects of the physiological response to exercise. Changes in cardiac output, heart rate, stroke volume and ventilation are normally quoted in relation to changes in oxygen consumption. The reduction in oxygen consumption by up to 37% of normal in severely cyanosed subjects presents the problem of whether the observed or the expected oxygen consumption should be used as a reference in such cases. In patient 12 the difference between the predicted and observed oxygen consumption at the 40 watt work load would represent a change of 1.4/1 minute in cardiac output in a normal child (Godfrey et al 1971). In general however, such extremes as this will not be encountered frequently as few patients will continue to ride a bicycle when their PaO_2 has fallen to 30 mm.Hg.

SUMMARY

It is generally accepted that the increase in oxygen consumption brought about by a given increase in work remains constant irrespective of health or disease. However, during exercise studies in cyanosed children, it was noted that oxygen consumption was consistently lower than normal. The amount by which the oxygen consumption was reduced was found to be related to the fall in arterial oxygen saturation. The largest reduction in oxygen consumption was 37% of the expected value, corresponding to a fall in arterial oxygen saturation of 45%. The carbon dioxide production remained normal in all children indicating that there had been no increase in anaerobic metabolism. It is suggested that cyanosed children may have a reduced oxygen consumption by tissues not directly concerned with external work, or an increased efficiency of the normal energy producing pathways.

FALLOT'S TETRALOGY:

THE RESPONSE TO EXERCISE

BEFORE AND AFTER TOTAL SURGICAL CORRECTION

INTRODUCTION

Total surgical correction is established as a successful treatment of Fallot's tetralogy. Initially reports of operative results were largely concerned with the high mortality of the operation. Later reports showed a gratifying reduction in mortality (Kirklin et al 1965, Goldman et al 1968). Post-operative cardiac catheterisation has, however, demonstrated residual haemadynamic abnormalities (Burnell et al 1968, Lillehei et al 1964) but these have generally been regarded as acceptable and the results of operation have been viewed with satisfaction. Few attempts have been made to discover the functional effects of these haemodynamic changes or indeed to discover what changes occur on exercise in Fallot's tetralogy whether corrected or uncorrected (Goldberg et al 1969, Snijders 1970). A few detailed exercise studies have been made in children after total surgical correction. Gotsman (1966) studied six patients during supine bicycle exercise and compared them to four adult controls. In some patients the exercise was performed only with one leg. Bristow et al (1970) studied ten patients during supine bicycle exercise but took his normal values from adult studies including treadmill exercise. Haider et al (1972) did not give details of the form of exercise which they used. No study of cardiac output during exercise in Fallot's tetralogy before operation has been found in the literature.

TABLE IV - 8

Showing the height, weight, sex, haemoglobin, arterial oxygen saturation at rest, and time since operation for each child.

Patient No.	Age		Sex	Ht.	Wt.	Hb.	SaO_2 at Rest	Months since operation	Diagnosis
	yr.	mth.							
1	7	0	M	122	40.0	14.2	97		
2	7	1	F	123	20.9	15.5	86		
3	5	11	M	109	18.5	16.9	87		
4	6	6	F	112	16.8	19.7	76		
5	6	3	M	115	19.2	10.4	95		Fallot's
6*	14	5	F	124	18.3	15.2	95		Tetralogy
7	8	4	M	133	25.4	14.9	96		
8	8	1	F	120	18.4	14.2	93		
9	6	0	M	116	18.7	16.9	92		
10	7	6	F	120	21.9	14.4	84		
11	6	6	F	120	20.7	12.5	96	21	
12	10	9	M	140	36.6	15.0	94	126	
13	12	3	M	145	35.0	12.5	96	3	
14	9	9	F	131	24.9	11.3	98	20	
15	8	1	F	131	23.4	15.3	87	42	Totally
16	6	3	M	109	20.2	13.6	97	3	corrected
17	8	7	M	125	24.9	13.1	97	71	of Fallot's
18	8	6	F	133	27.5	13.0	96	5	Tetralogy
19	11	7	F	142	35.5	15.9	97	25	
20	13	6	M	134	27.8	13.1	97	21	
21/	10	7	M	138	30.5	13.1	98	4	

* Pulmonary infundibular resection 2 yr. and 5 mnth. prior to study,

/ Blalock shunt 6 yr. and 2 mnth. prior to total correction.

The present study included measurement of maximum working capacity, pulmonary and systemic blood flow, and right to left shunting in a group of children with Fallot's tetralogy and in a second group who had undergone total surgical correction.

MATERIALS AND METHODS

Ten children with Fallot's tetralogy and eleven children who had undergone total surgical correction of Fallot's tetralogy were studied (Table IV - 8). Only two children (Nos. 2 and 3) were studied both before and after operation. Patient number 2's post-operative number is 18 and patient number 3's post-operative number is 16. Only one patient in each group had had a previous cardiac operation (Table IV - 8). The mean age for the Fallot's tetralogy group was seven years and eight months and for the totally corrected group nine years and six months. The operations were performed by four surgeons from the Brompton and Guy's Hospitals.

A child who could take part in all the activities of his peers but who became tired more easily than they did or had to rest occasionally was graded as having mild exercise intolerance.

A child who did not fall into the severe group but was unable to take part in all the activities of his peers or could only manage token participation in games with pauses at frequent intervals was graded as having moderate exercise intolerance.

TABLE IV - 10

Comparison of the values for each group for forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), peak flow rate (PFR), and maximum voluntary ventilation (MVV) with normal values using the paired 't' test 'mean' is the mean difference between the observed and expected values. Negative values indicate that the mean observed value is lower than the expected.

		Fallot's Tetralogy	'Totally corrected' Fallot's teralogy
FEV_1	mean	0.198	-0.355
	p	N.S.	*
FVC	mean	0.197	-0.380
	p	N.S.	*
PFR	mean	5.1	-46.4
	p	N.S.	**
MVV	mean	2.0	7.4
	p	N.S.	N.S.

TABLE IV - 11

Showing the observed and expected maximum work load and the observed work load as a percentage of the expected value (% expected) for each child.

Patient	W max.	Expected	% expected
1	40	59	68
2	30	55	55
3	20	22	91
4	15	29	52
5	35	40	88
6	20	27	35
7	45	89	51
8	20	46	43
9	20	42	48
10	30	46	65
11	30	48	63
12	65	111	59
13	120	125	96
14	45	74	61
15	45	70	64
16	25	30	83
17	60	68	88
18	60	77	78
19	60	99	61
20	65	92	71
21	60	105	57

TABLE IV - 12

Showing the mean values for maximum work load in the progressive exercise test and mean steady state values for minute ventilation ($\dot{V}E$), heart rate (HR), systemic blood flow ($\dot{Q}s$) and pulmonary blood flow ($\dot{Q}p$) all expressed as a percentage of the expected value. Venous admixture (V.A.) is expressed as a percentage of the systemic cardiac output. The significance of the difference between the pre-operative and post-operative groups and also between each group and the normal value are given for each parameter.

	Mean Value		p		
	Fallot	T.C. Fallot	Between Fallot & T.C.Fallot	Between Fallot & Normal	Between T.C. Fallot & Normal
W max.% expected	57	68	N.S.	***	***
$\dot{V}E$ % expected	142	114	***	***	***
H.R.% expected	110	100	N.S.	*	N.S.
$\dot{Q}s$ % expected	131	97	N.S.	**	N.S.
$\dot{Q}p$ % expected	68	75	N.S.	**	**
V.A. rest	26	9	*	**	N.S.
V.A. $\frac{1}{3}$ W max.	31	11	**	*	*
V.A. $\frac{2}{3}$ W max.	44	12	**	**	*

A child who was unable to run up one flight of stairs was graded as having severe exercise intolerance.

RESULTS

Spirometry, Peak Expiratory Flow Rate and Maximum Voluntry Ventilation

The FEV_1, FVC and PFR of the pre-operative children all fell within the normal range (Godfrey et al 1970)(Table IV - 9A). In the post-operative group however four of the eleven children had values for FEV_1 which were lower than normal. One of the four had an FVC lower than normal and another had a low value for PEFR (Table IV - 9A).

The paired 't' test was used to compare the mean values for each group with normal values. The results for the pre-operative group did not differ significantly from normal, but in the post-operative group the mean values for FEV_1, FVC and PFR were significantly lower than predicted (Table IV - 10).

Progressive Exercise

Maximum Working Capacity

The mean maximum working capacity of the pre-operative group, expressed as a percentage of the expected value was 58% (S.E. 5.8) and for the post-operative group 71% (S.E. 4.0)(Table IV - 11 and IV - 12). The difference between these results was not statistically significant but the mean for both groups was significantly lower than normal ($P < 0.001$). No child from either group reached the expected normal value.

FIGURE IV - 5

Showing the maximum work load reached in the progressive test and the history of exercise tolerance for children with Fallot's tetralogy and 'totally corrected' Fallot's tetralogy.

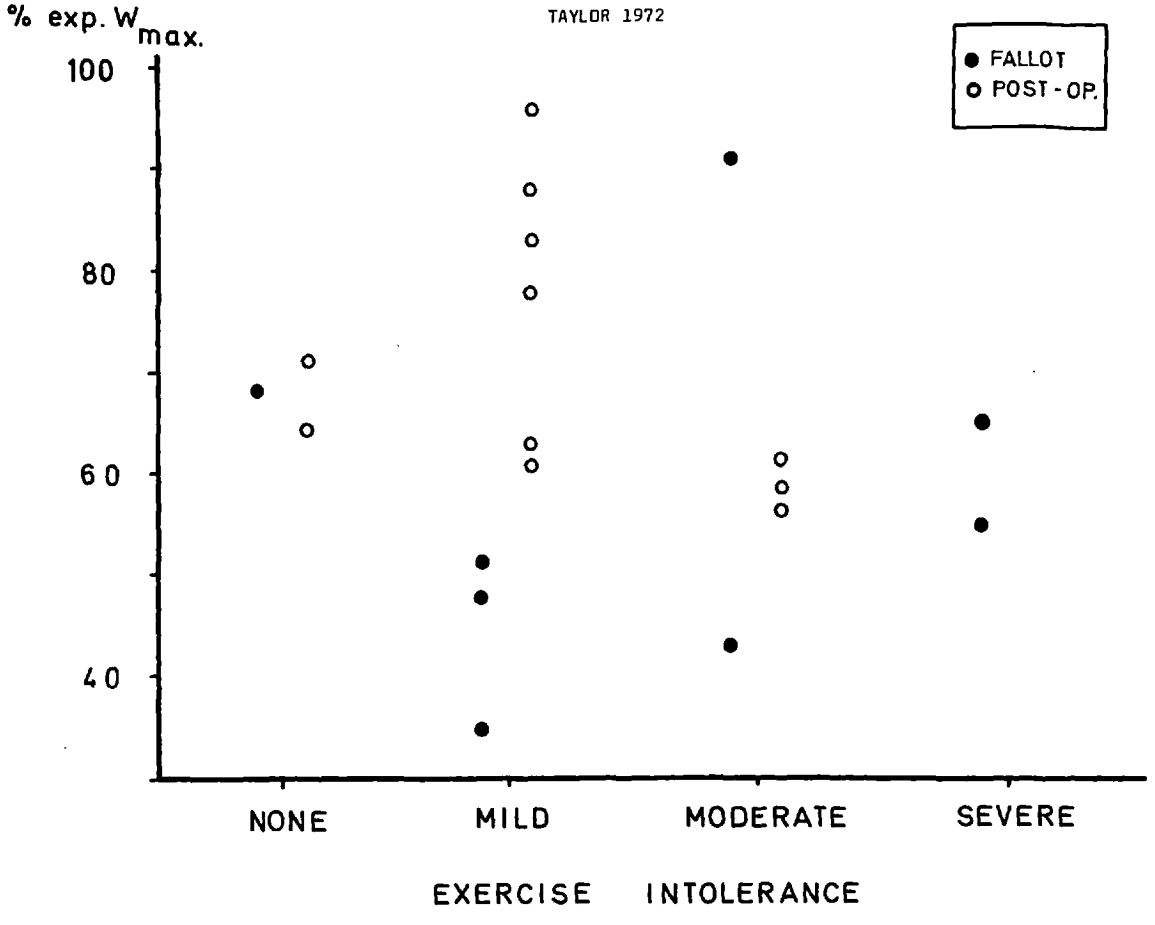

% exp. W max.
TAYLOR 1972
FALLOT
POST-OP.
100
80
60
40
NONE
MILD
MODERATE
SEVERE
EXERCISE INTOLERANCE

TABLE IV - 15

Showing the observed QRS duration at rest and the mean and upper limits for normal children.

Patient	QRS Duration sec.	Normal QRS Duration (sec.)	
		Upper Limit	Mean
1	0.06	0.08	0.07
2	0.08	0.08	0.07
3	0.06	0.08	0.07
4	0.06	0.08	0.07
5	0.07	0.08	0.07
6	0.09	0.10	0.07
7	0.09	0.09	0.07
8	0.08	0.09	0.07
9	0.06	0.08	0.07
10	0.08	0.08	0.07
11	0.12	0.08	0.07
12	0.06	0.08	0.07
13	0.12	0.10	0.07
14	0.11	0.09	0.07
15	0.13	0.09	0.07
16	0.12	0.08	0.07
17	0.09	0.09	0.07
18	0.08	0.09	0.07
19	0.11	0.10	0.07
20	0.14	0.10	0.07
21	0.12	0.09	0.07

The history of exercise intolerance as obtained from the mother was graded as 'none', 'mild', 'moderate' or 'severe' on an arbitrary scale as described above. The maximum work load achieved bore little relationship to the history of exercise intolerance (Figure IV - 5) and did not separate a child who could reach 35% of the expected value from one reaching 96%.

Steady State Exercise

Minute Ventilation

The mean minute ventilation for the pre-operative group was 142% of expected and for the post-operative group 114% of expected. The mean values for the two groups differed significantly both from each other and from the expected normal value (Tables IV - 12, IV - 13A, IV - 14A).

Heart Rate and Electrocardiograph

The mean heart rate of both groups was higher than normal during exercise. The mean for the post-operative group did not differ significantly from the expected value. The mean for the pre-operative group was significantly higher than normal (Table IV - 12).

The duration of the QRS complex on the resting electrocardiograph was much greater in the post-operative than in the pre-operative group. In the pre-operative group none were above the upper limit of normal

The duration of the QRs complex on the resting electrocardiograph was much greater in the post-operative than in the pre-operative group. In the pre-operative group none were above the upper limit of normal (Zeigler 1951) while in the post-operative group eight were above the upper limit of normal (Table IV - 15).

FIGURE IV - 6

Showing the pulmonary ($\dot{Q}_p$) and systemic ($\dot{Q}_s$) blood flows as a percentage of normal ($\dot{Q}exp$) in the pre-operative and post-operative children. The horizontal lines represent the mean values.

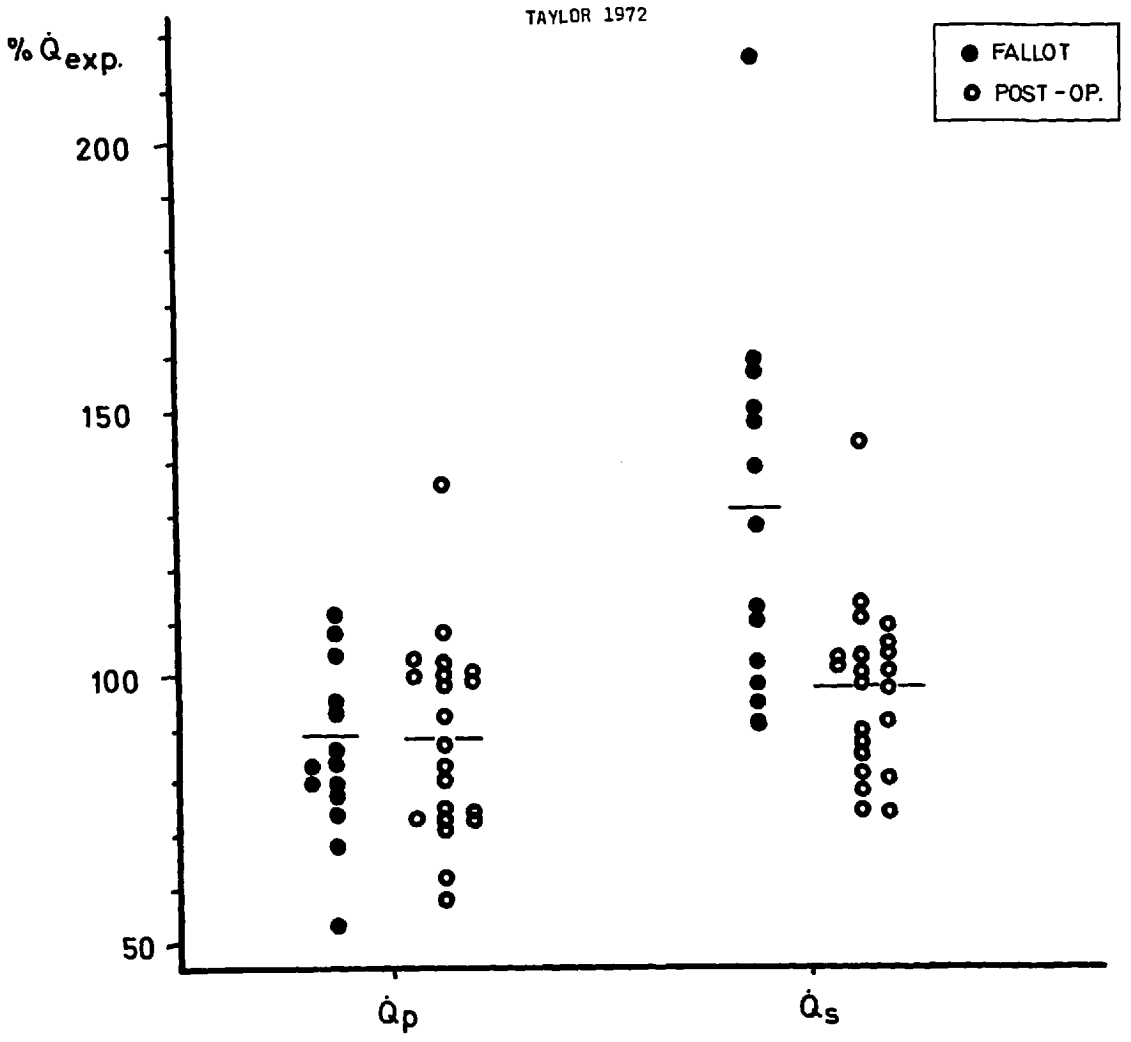

TAYLOR 1972
% $\dot{Q}_{exp.}$
200
150
100
50
FALLOT
POST-OP.
$\dot{Q}_p$
$\dot{Q}_s$

FIGURE IV - 7

Showing the mean and one standard error of the mean for venous admixture (L to R shunt %) at rest and on exercise for the pre-operative and post-operative children. The mean and two standard deviations are shown for normal children.

TAYLOR 1972

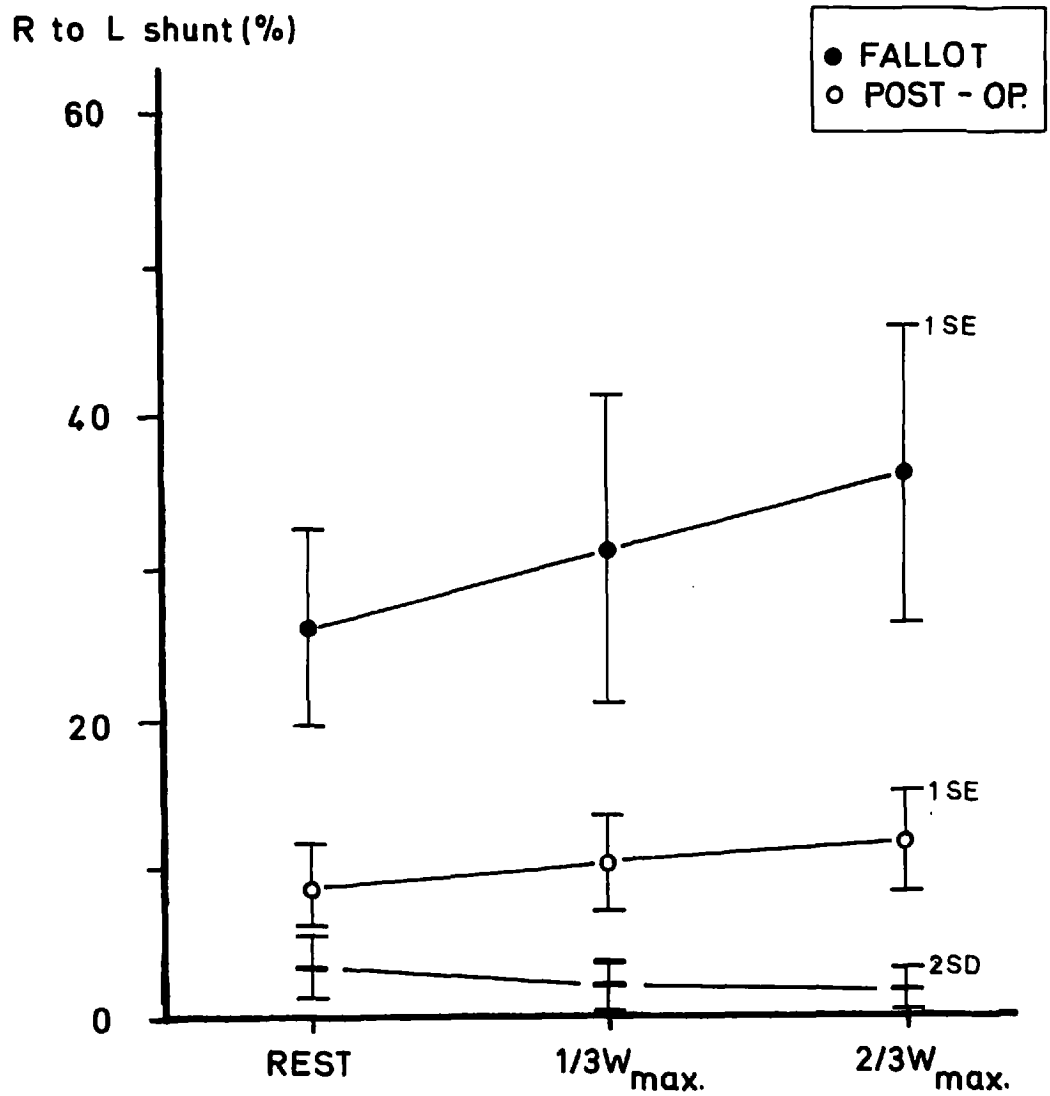
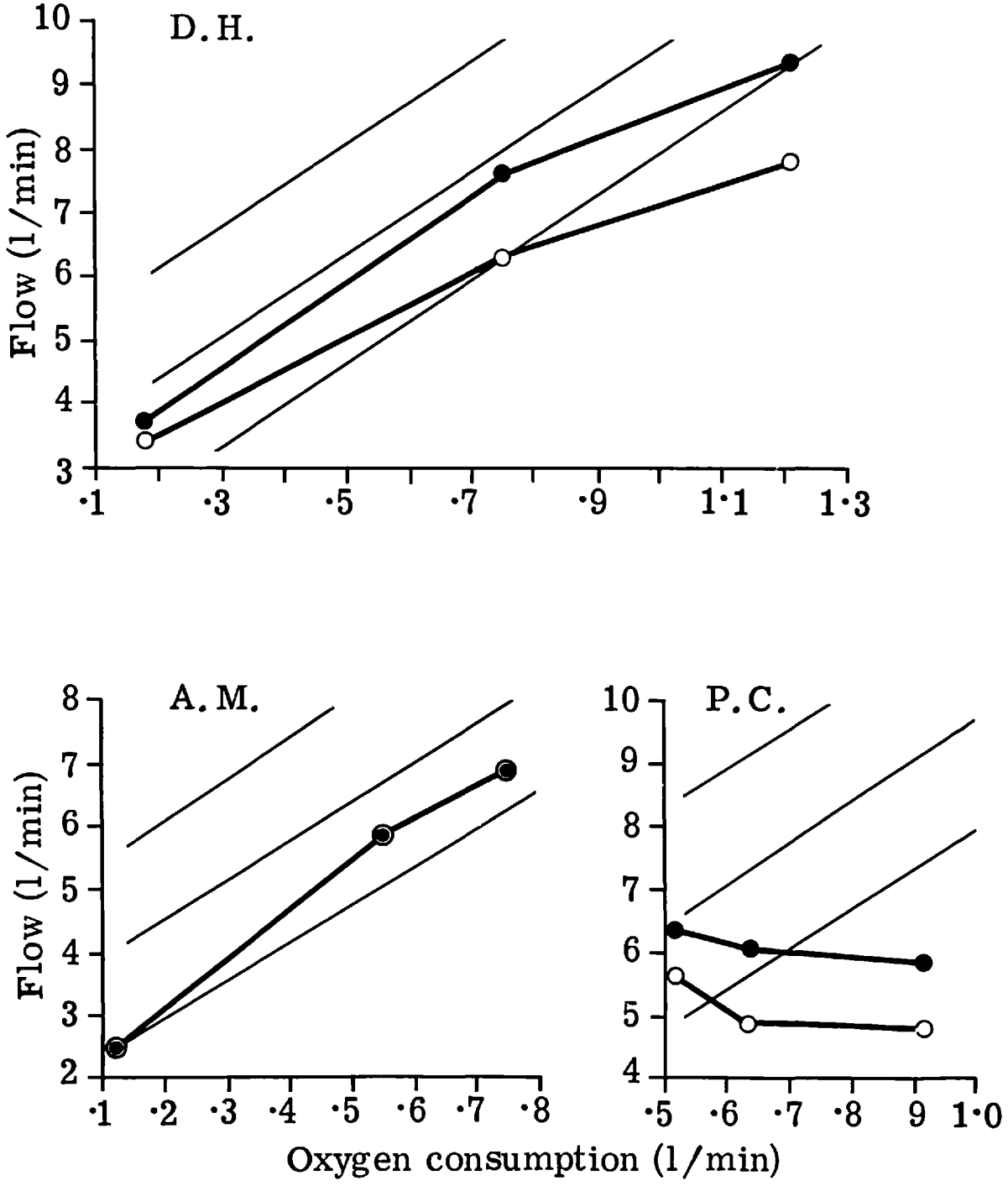

R to L shunt (%)
● FALLOT
○ POST - OP.
60
40
20
0
1 SE
1 SE
2SD
REST
1/3W max.
2/3W max.

FIGURE IV - 8

Changes in cardiac output on exercise in three patients with 'totally corrected' Fallot's tetralogy (see text). The regression line and two standard errors of the estimate for normal children are shown.

FALLOT'S TETRALOGY



Systemic and Pulmonary Blood Flow

In the pre-operative children the mean systemic blood flow was significantly greater than normal but the pulmonary blood flow was significantly lower than normal (Figure IV - 6). In the post-operative children the pulmonary blood flow was significantly lower than normal, but the systemic blood flow did not differ signficantly from normal. In both groups the mean pulmonary flow was lower than the systemic flow due to the right to left shunting. This shunting was much less in the post-operative than in the pre-operative children (Tables IV - 12, IV - 13A, IV - 14A and Figure IV - 6). In some post-operative children the right to left shunting was in the normal range (Table IV - 13A).

Right to Left Shunting

At rest eight out of nine of the pre-operative group had a right to left shunt outside the normal range, while in the post-operative group six out of eleven were in the normal range. On exercise the shunt became even greater in both groups (Figure IV - 7) and none of the pre-operative children fell in the normal range. In the post-operative group three of the eleven children were in the normal range at the first work load and only four were in the normal range at the second work load.

Individual Patterns of Response to Exercise

Some individual patterns of response to exercise in the post-operative patients are illustrated in Figure IV - 8.

Patient 17 (AM) had no significant right to left shunt, and a normal rise in cardiac output with increasing work, although the cardiac output was in the lower part of the normal range throughout the study. Patient 13 (DH) had a small right to left shunt at rest but on exercise the shunt increased greatly. His systemic blood flow remained within the normal range throughout the study although it was just at the lower limit of normal at the second work load. The pulmonary blood flow was normal at rest and at the first work load but was outside the normal range at the second work load.

In patient 12 (PC) the pulmonary and systemic blood flow both fell on exercise and the right to left shunt increased on exercise. The systolic pressure gradient between the right ventricle and the pulmonary artery was measured both at rest and on exercise using a flow catheter and rose from 27 mm. Hg. to 55 mm. Hg. even though there was no increase in pulmonary blood flow. This change in pressure gradient must have been due to pulmonary infundibular shut-down during exercise.

This child is the first recorded survivor of total surgical correction of Fallot's tetralogy carried out before the age of one year (Benson et al 1962). His operation included pulmonary infundibular resection, pulmonary valvotomy and insertion of a pericardial gusset into the right ventricular outflow tract.

Two patients were studied both before (Nos. 2 and 3) and after operation (Nos. 16 and 18). Their results expressed except in the case of venous admixture as a percentage of the expected value are given below:-

Study No.	Pre-Operation	Post-Operation	Pre-Operation	Post-Operation
	2	16	3	18
W max.	55	78	91	83
HR $\frac{1}{3}$ W max.	-	90	99	78
HR $\frac{1}{3}$ W max.	118	81	-	87
$\dot{V}E$ $\frac{1}{3}$ W max.	-	103	106	97
$\dot{V}E$ $\frac{2}{3}$ W max.	213	118	-	107
Q_P $\frac{1}{3}$ W max.	-	85	40	71
Q_S $\frac{1}{3}$ W max.	-	86	85	78
Q_P $\frac{2}{3}$ W max.	-	85		75
$\dot{Q}_S$ $\frac{2}{3}$ W max.	-	86		84
VA rest	52	2.8	31	5.7
VA $\frac{1}{3}$ W max.		1.7	53	5.7
VA $\frac{2}{3}$ W max.		1.0		5.7

Venous admixture is expressed as a percentage of the systemic blood flow. In study No.3 the exercise was performed at half the maximum work load but for convenience the results have been placed in the '$\frac{1}{3}$ W max.' now. In study 2 only one work study was performed. No pH value was obtained and so no cardiac output is given.

It can be seen that these two patients follow the overall trend in the changes brought about by operation. One patient has a rise in maximum working capacity while the other shows a small fall. In both cases the heart rates fall with operation. There is a large fall in minute ventilation between studies two and sixteen appropriate to the reduction of hypoxia but the second patient (study 3) was one of the 'poor responders' to hypoxia and there is little difference in his minute ventilation before and after operation. There is a marked change in venous admixture in both patients after operation although in the second child (study 18) the venous admixture is still outside the normal range both at rest and on exercise. The blood flows demonstrate low systemic flow after operation. In the second patient (studies 3 and 18) there was an increase in pulmonary blood flow after operation which was not seen in the group studies.

The most striking changes in these patients are the reduction in venous admixture, and, in the first patient, the reduction in minute ventilation.

DISCUSSION

The results from the pre-operative and post-operative children have been compared bearing in mind the differences between the two groups. Only in two cases were the same children studied before (Nos. 2 and 3) and after (Nos. 18 and 16) operation. The pre-operative group are selected in that they have all

(with the exception of patient 6) survived beyond the age of five years without surgical intervention. The post-operative group are selected in that they have all survived both the disease and the operation and have passed six years of age. All the children were selected in that they were co-operative enough to complete the exercise study.

Respiratory Function

Over all there was a small but significant reduction in respiratory function in the post-opperative group although only four children had spirometry or peak flow values outside the normal range (Table IV - 9A). Two of the four children with low FEV_1 values had MVV results close to the predicted value indicating that there was little disability from the point of view of function. It is possible that these children had some degree of airways obstruction which was reversed by the bronchudilator effect of exercise. This does not however explain the overall drop in three of the four measurements respiratory performance which are probably due to changes in chest wall and lungs following operation.

Maximum Working Capacity

The lack of correlation between the maximum working capacity and the history of exercise tolerance underlines the subjective nature of a history of exercise tolerance. A mother who knows that her child has congenital

heart disease cannot help but be emotionally biased when recounting his exercise performance; yet despite this the history of exercise tolerance is frequently taken into account when deciding the timing of cardiac surgery.

Snijders (1970) also noted this in his study of patients who had had total correction of Fallot's tetralogy - 'Although the majority of the patients or their parents reported unmistakable improvement in performance after the operation, the parent's concern and the patients willingness to exert themselves seemed to correlate more closely with the mere existence of a heart defect than with its severity'. He found that in eight 'well-corrected' cases of Fallot's tetralogy the mean maximum working capacity was 56% of normal. The figure for all the post-operative children in the present study was 68% (Table IV - 12).

Goldberg et al (1967) obtained similar results for the correlation of parental estimation of the child's exercise tolerance and maximum working capacity in a series of children after cardiac operation (none of the children had Fallot's tetralogy). However, they concluded that the parent's estimate correlated well with maximum working capacity! This underlines the subjective nature of the interpretation of scientific results.

No significant correlation was found between the maximum working capacity and the right to left shunt or pulmonary blood flow, but this is not surprising as despite the major changes in circulation brought about by

surgery there was little difference in the maximum working capacity between the two groups.

Minute Ventilation

As recorded earlier cyanotic children have a greater than normal minute ventilation during exercise and in general the increase in minute ventilation is proportional to the reduction in arterial oxygen saturation. All of the pre-operative group had an abnormal increase in minute ventilation on exercise as had some of the post-operative group. Two of the pre-operative group were 'poor responders' (3 and 4) having a lesser increase in minute ventilation than the other children. These two patients both had the triad of a long history of cyanosis starting early in life, a low resting arterial oxygen saturation and a haemoglobin concentration above 16 grams/100 ml.

The electrocardiograph

The finding of a prolongation of the QRS complex is in keeping with the finding of Landtman and Wolf (1965) who recorded a normal intraventricular conduction time in 109 out of 146 patients with Fallot's tetralogy but found that after total surgical correction only 8 out of 82 patients had a normal intraventricular conduction time. This last figure agrees closely with 1 out of 11 of the totally corrected group in the present study who had a normal conduction time.

Blood Flow

The main circulatory change brought about by the operation is attributable to closure of the ventricular septal defect. This produced a diminuation in the right to left shunting. The continued low pulmonary flow might be due to poor myocardial function (the electrocardiograph changes indicate some damage), a small outflow tract despite valvotomy with or without infundibular resection, raised pulmonary vascular resistance, or pulmonary incompetence following valvotomy. It is remarkable that despite such an extensive operation on the pulmonary outflow tract there is no significant difference in pulmonary blood flow between the pre- and post-operative groups. The systemic blood flow on exercise in the pre-operative group was significantly greater than normal (Table IV - 12)(mean increase 3.2 l./min.). In the post-operative group the systemic blood flow was slightly lower than normal though not significantly so (mean difference 0.2 l./min.).

Gotsman 1968 studied four patients aged 16 - 23 who had had a total correction of Fallot's tetralogy. The patients performed supine bicycle exercise and the results were compared with those of four adult normals. He concluded that the response of his patients to exercise was normal yet on exercise only one patient's systemic cardiac output was above the predicted value and two patients had systemic cardiac outputs outside the lower 95% confidence limits of normality.

Jonsson and Lee (1968) studied six adult patients before and after pulmonary valvatomy and found that the systemic cardiac output remained low despite relief of the obstruction. They suggested that the body's adjustment to a low systemic blood flow is an increased ability to extract oxygen from blood at low oxygen tensions (thus increasing the arterio-venous oxygen difference) and that this adaptation persists after operation. As the peripheral organs are able to extract their oxygen requirements from blood with a low oxygen tension there is then no need for the cardiac output to increase to normal values even though removal of the pulmonary stenosis has made this possible.

Right to Left Shunting

A reduction in right to left shunting was the second major difference between the pre- and post-operative groups. However, the finding of an abnormal degree of right to left shunting in five out of eleven of the post-operative group at rest and seven out of eleven on exercise is rather surprising. Lilihei et al (1964) reported that 20% of their patients had a residual shunt after total surgical correction. In contrast to these results Haider et al (1971) reported no significant abnormality of cardiac function at rest or on very mild exercise in twelve patients who had undergone total surgical correction. It is difficult to reconcile the results of Haider et al (1971) with those of the present study. Their limits

of normality appeared to be generous and included a pulmonary outflow trace gradient of 20 mm. As there are no published figures for venous admixture in normal children during exercise ~~in normal children during exercise~~ one wonders how these workers assessed the normality or otherwise of right to left shunting.

Most published reports of children after total correction refer to resting studies. When the right to left shunts of the post-operative children at rest are compared with those of the normal children there is no statistically significant difference between them, but exercise produces a significant difference (Table IV - 14A).

It is not possible to say at what level the shunt occurred in these patients. The two most likely sites for intracardiac shunting to occur are an incompletely closed ventricular septal defect or a patent foramen ovale. Many patients have pulmonary incompetence after total correction which in turn results in raised right ventricular end diastolic and right atrial systolic pressures (Gotsman 1968, Bristow et al 1970). This could lead to right and left shunting across a patent foramen ovale. In the majority of cases the operation notes did not contain any information about the state of the atrial septum and so the degree of right to left shunting could not be related to the condition of the foramen ovale.

CONCLUSION

This study shows that in the majority of cases the operation of 'total correction of Fallot's tetralogy' was far from total correction. The performance of both groups of children on exercise was below normal. The mean values for maximum working capacity and pulmonary blood flow did not differ significantly between the pre-operative and post-operative groups. Right to left shunting was less in the post-operative children but in the majority of them it was still greater than normal on exercise. The post-operative children exercised more comfortably as judged by their more normal minute ventilation and heart rate.

The history of exercise tolerance must be interpreted with caution. It is probably a better gauge of the optimism of the parents than of the ability of the child.

SUMMARY

Measurements of respiratory and cardiac function (including cardiac output) were made at rest and during exercise in ten patients with Fallot's tetralogy and in eleven patients who had undergone total surgical correction three months to 10½ years earlier. It was found that:-

1. FEV_1, FVC and PFR were significantly lower than normal in the post operative group.
2. The maximum working capacity ofthe two groups was not significantly different but in both it was significantly lower than normal.

3. The history of exercise tolerance gave little indication of a child's maximum working capacity.
4. The systemic blood flow was above normal in the pre-operative group but did not differ significantly from normal in the post-operative group.
5. There was no significantly difference in pulmonary blood flow between the two groups.
6. In the totally corrected group five of the eleven patients had an abnormal right to left shunt at rest but on exercise seven of the eleven had an abnormal right to left shunt.

These results are much less optimistic than those reported by other workers. It is suggested that this is in part due to the higher levels of work used in this study.

SECTION V

ACYANOTIC CONGENITAL HEART DISEASE

CONGENITAL HEART BLOCK

INTRODUCTION

Despite many studies of patients with congenital heart block (Holmgren et al 1959, Wright et al 1959, Paul et al 1958, Nakamura and Nadas 1964, Moss 1961, Wallgren and Winblad 1937, Cambell and Thorne 1956) there have been few reports of exercise tolerance, or of cardiac output measurements during exercise in patients with this condition who do not have artificial pacemakers (Ikkos and Hanson 1960, Holmgren et al 1959). Cardiac output at rest has been reported both as low (Wright et al 1959) and normal (Paul et al 1958, Moss 1961). On exercise too the reports have been conflicting.

Ikkos and Hansen (1960) studied two patients with complete heart block and found an increased cardiac output during exercise but no normal values were given and it is not clear whether the 'increased cardiac output' referred to an increase from that at rest or to an increase compared to that of normal subjects. Holmgren et al (1959) studied the cardiac output during exercise in two patients with congenital heart block. In one patient the cardiac output was normal on exercise and in the other the cardiac output was slightly low.

Ikkos and Hansen (1960) reported a normal maximum working capacity in their patients. Their normal values were predicted from atrial rates. Holmgren et al (1959) found a low maximum working capacity in three out of four patients when the expected value was calculated from the total body haemoglobin.

TABLE V - 1

Showing the age, sex, height, weight and associated cardiac abnormalities of the patients with heart block.

No.	Age	Sex	Height	Weight	Associated Cardiac Abnormalities
1.	23 years	F	160 cm.	51.3 Kg.	Nil
2.	21 years	M	172.5 cm.	73.4 Kg.	Dextrocardia and corrected transposition of the great vessels.
3.	15 years 9 months	M	169 cm.	58.0 Kg.	Nil
4.	9 years 3 months	M	124 cm.	25.5 Kg.	Dextrocardia

In order to investigate the response to exercise in congenital heart block, with particular reference to maximum working capacity and cardiac output, four patients were studied. None of them had an artificial pacemaker.

MATERIALS AND METHODS

The physical characteristics and diagnostic details of the patients are given in Table V - 1.

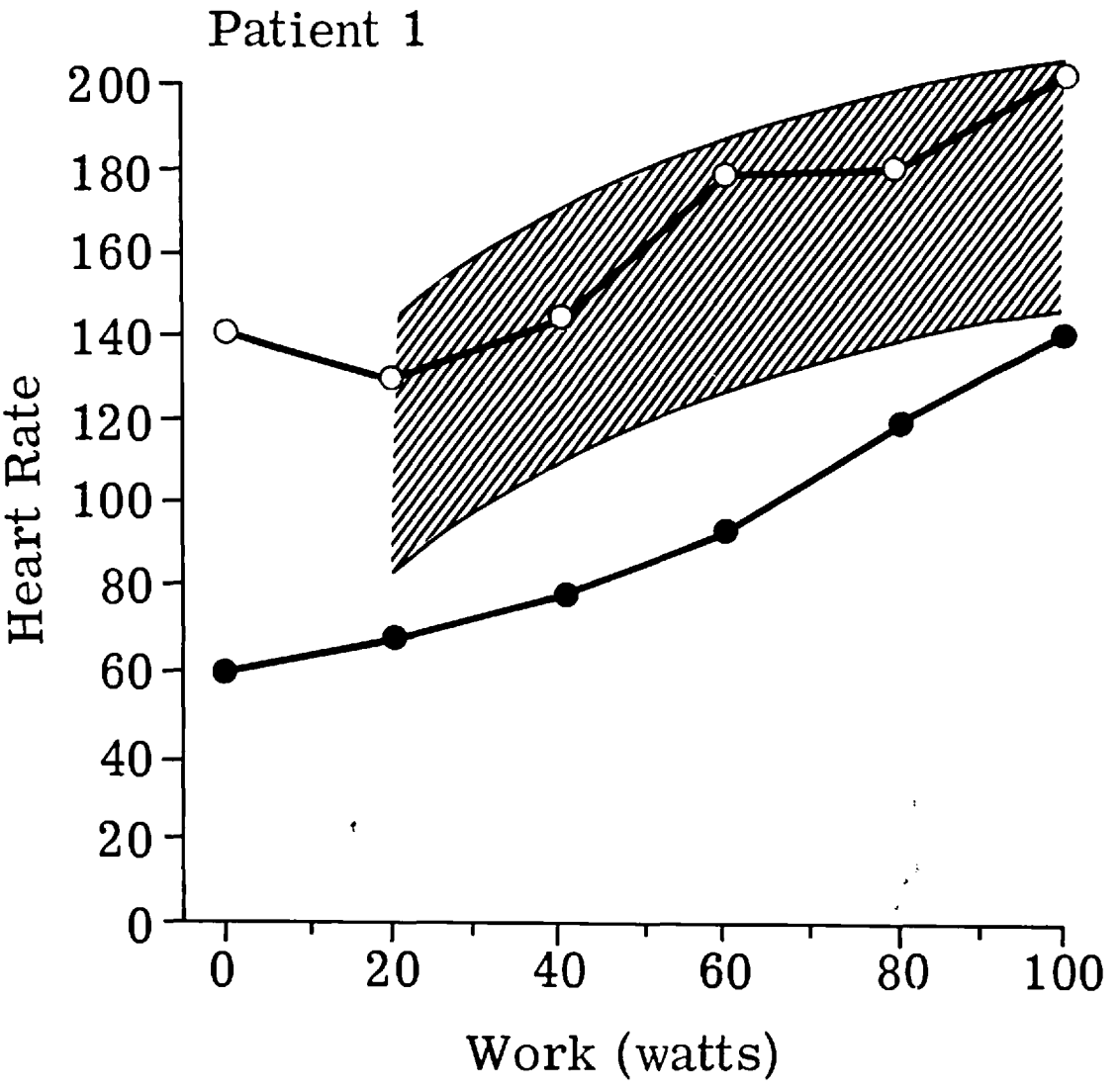
Congenital heart block was diagnosed in patient one at six year of age. She was instructed never to exert herself and so she never played games at school and has always led a sedentary life. Cardiac catheterisation revealed a normal cardiovascular system apart from the conduction defect.

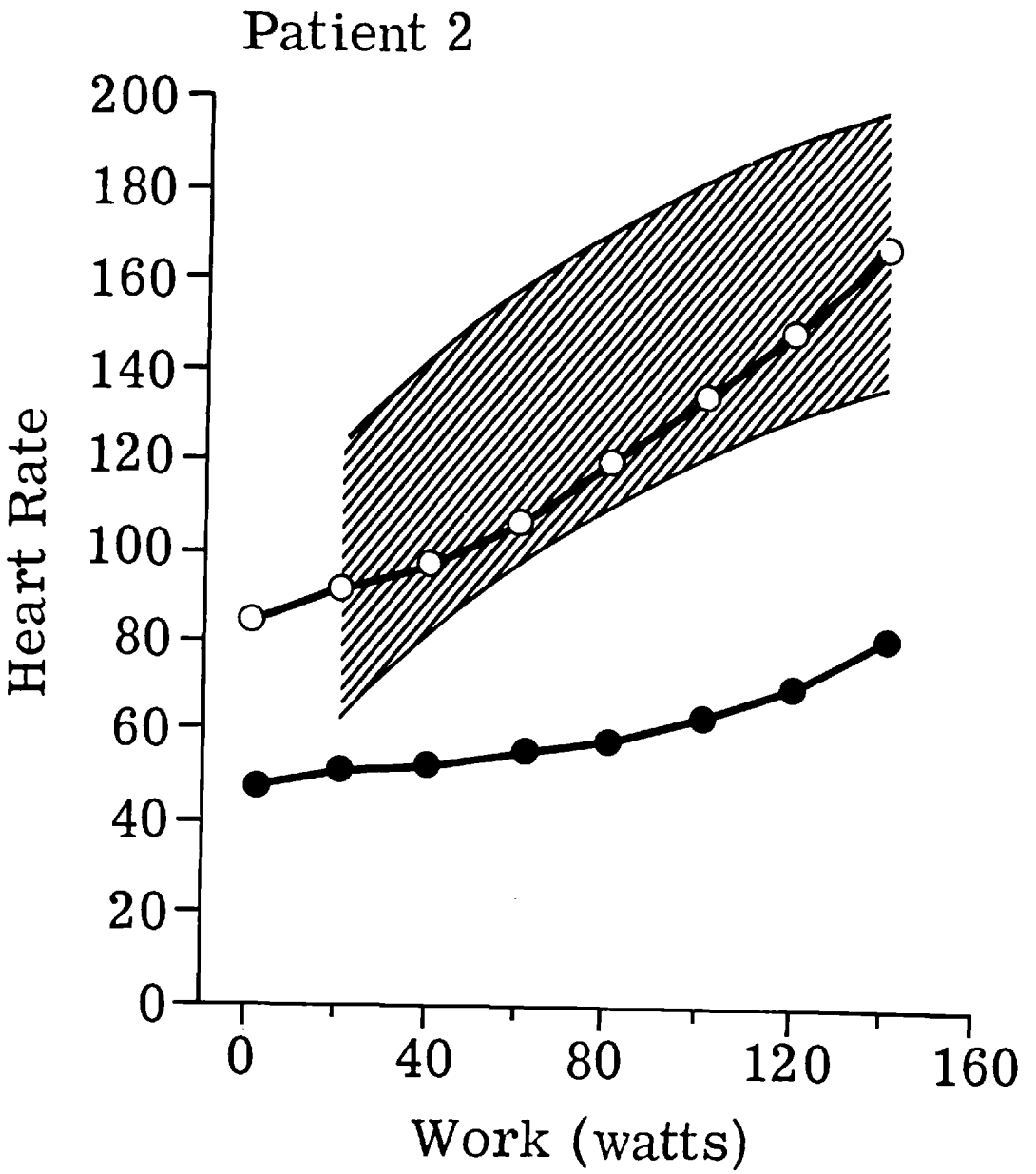
Congenital heart block was diagnosed at birth in patient two. He has had exercise intolerance from childhood. When playing football at school he had to stop about every ten minutes because of dyspnoea. He complains of being tired in his present work as a waiter. He suffers from mild bronchitis. Cardiac catheterisation revealed only minimally increased right ventricular and pulmonary artery pressures in addition to the anatomical lesions given in Table V - 1.

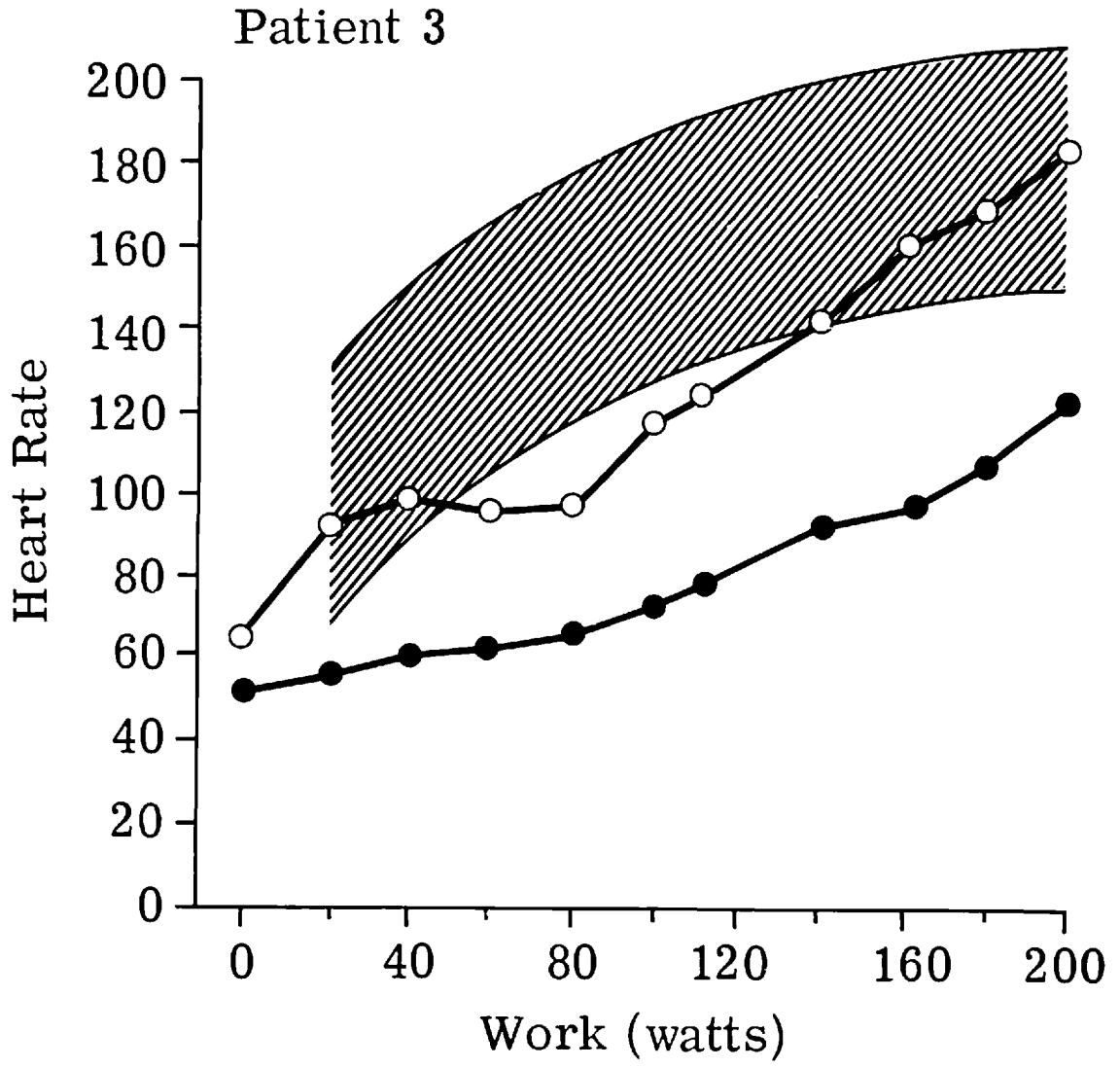
Congenital heart block was diagnosed in patient 3 at the age of 10 years when he attended hospital because of a chest infection. His heart block has never given rise to symptoms.

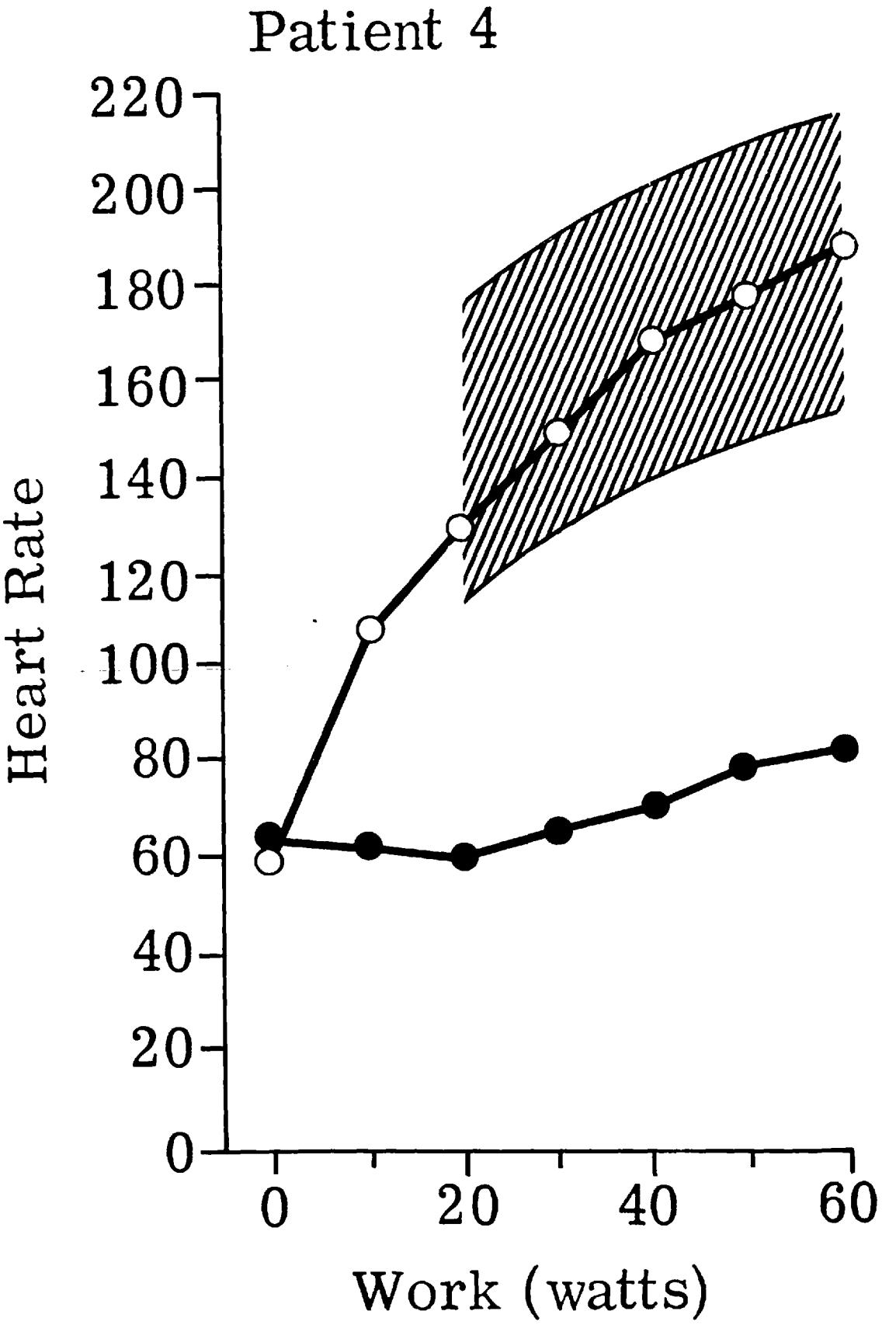
FIGURE V - 1

The atrial rate (O) and the ventricular rate (●) for each patient in the progressive exercise test plotted against the work load. The shaded area represents two standard errors either side of the regression line for normal subjects of the same height.


Patient 1
Heart Rate
200
180
160
140
120
100
80
60
40
20
0
0
20
40
60
80
100
Work (watts)


Patient 2
Heart Rate
200
180
160
140
120
100
80
60
40
20
0
0
40
80
120
160
Work (watts)


Patient 3
Heart Rate
200
180
160
140
120
100
80
60
40
20
0
0
40
80
120
160
200
Work (watts)


Patient 4
Heart Rate
220
200
180
160
140
120
100
80
60
40
20
0
0
20
40
60
Work (watts)

Patient 4 was delivered by caesarian section because of foetal bradycardia. The heart rate remained between 90 and 100 beats per minute after delivery and the diagnosis of congenital heart block was confirmed by electrocardiograph. Patients three and four both take part in athletics and football without any difficulty whatsoever.

It is not possible to be certain that the heart block in patients one and three was congenital but neither patient had a history of any illness which was likely to have produced heart block, this, and the fact that the diagnosis was made early in life made it very likely that the condition was congenital in origin.

None of the patients has ever suffered from Stokes Adams attacks, nor were any of them receiving any treatment at the time of the study. All of them had complete atrio-ventricular disocciation on their electrocardiographs.

RESULTS

The Progressive Exercise Test

On exercise all subjects showed an increase in both atrial and ventricular rates. On work the atrial rate rose faster than the ventricular rate (Figure V - 1). The rate of rise was greatest in the youngest subject. The atrial rate in all cases followed the same overall trend as in normal subjects and only in patient 3 did it fall outside the normal range at some work loads.

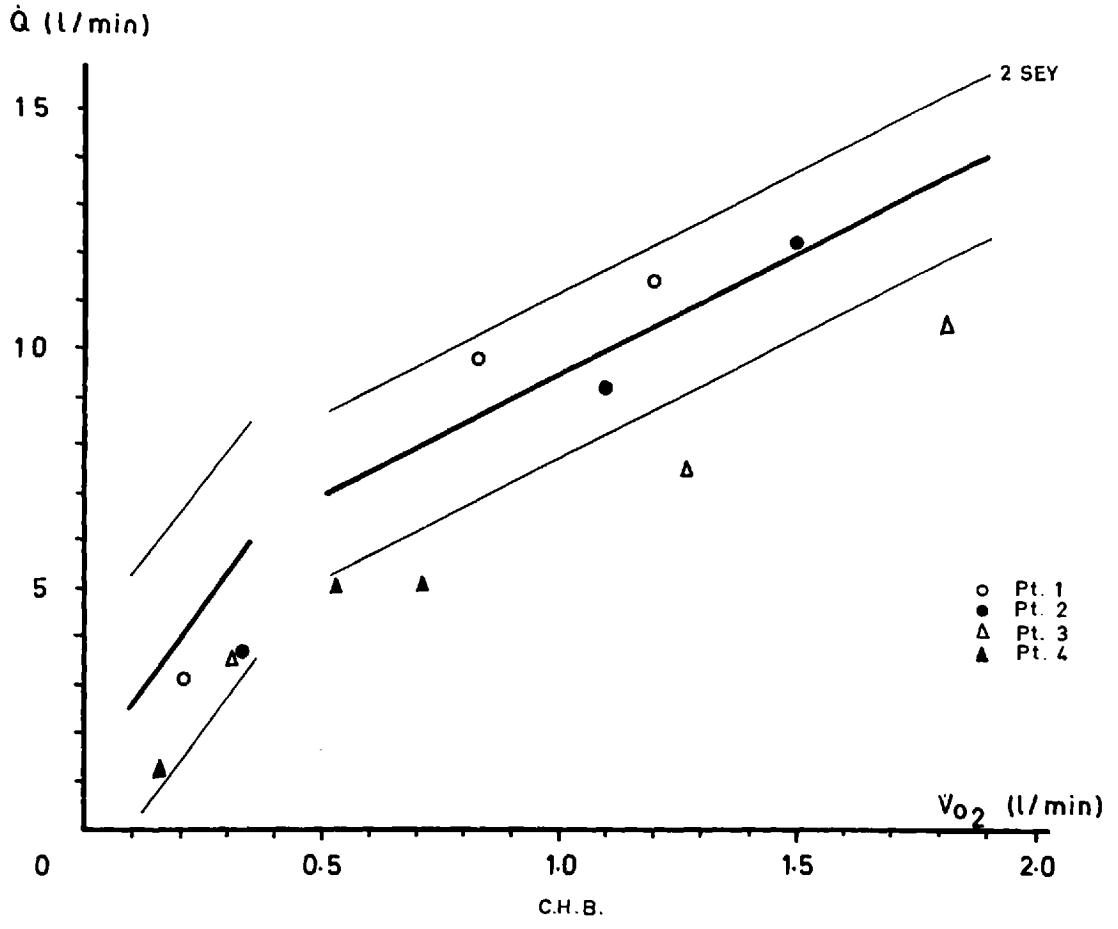
TABLE V - 2

Showing results for the steady state exercise test in the four patients. Expected values are given in brackets. The cardiac output at rest is based on end tidal PCO_2 values, on exercise it is based on an assumed normal dead space except in the case of Patient 2 (See Text).

Patient	Work (Watts)	Minute Ventilation (l/min BTPS)	Oxygen Consumption (l/min STPD)	Arterial PCO_2 mm.Hg.	Cardiac Output (l/min)	Ventricular Rate/min
1	0	10.8 (10)	214 (330)	21.5	3.1(4.2)	63
	33	32.9 (25)	827 (720)	31.2	9.8(8.5)	87 (143)
	66	52.0 (35)	1213 (1120)	28.2	11.4(11.0)	114 (190)
2	0	12 (10)	334 (320)	24.8	3.7(5.7)	52
	47	36.7 (32)	1105 (900)	34.2	8.7(10.2)	55 (134)
	95	56.8 (42)	1498 (1460)	33.9	12.2(12.8)	72 (155)
3	0	12.9 (10)	312 (320)	32.3	3.6(5.4)	56
	66	37.7 (36)	1268 (1120)	31.0	7.0(11.4)	63 (146)
	132	54.1 (50)	1810 (1880)	32.5	10.5(14.8)	87 (171)
4	0	5.3 (8)	158 (150)	33.8	1.2(3.4)	59
	20	18.9 (18)	528 (550)	33.0	5.0(6.5)	70 (139)
	40	26.0 (23)	712 (800)	30.3	5.1(7.8)	82 (160)

FIGURE V - 2

The cardiac output at rest and on exercise for each subject plotted against oxygen consumption (see text). The regression lines are those for normal subjects and the limit lines two standard errors of the estimate.


Q̇ (l/min)
15
10
5
0
0.5
1.0
1.5
2.0
2 SEY
Pt. 1
Pt. 2
Pt. 3
Pt. 4
V̇O2 (l/min)
C.H.B.

The increase in ventricular rate on work varied from subject to subject. From rest to maximum work patients 1 and 3 increased their ventricular rate by 60 beats per minute, patient 2 by 31 beats per minute and patient 4 by 20 beats per minute. The maximum work load that a patient was able to complete was not related to his rise in ventricular rate. Patient 4 who had the smallest rise in ventricular rate (20 beats/minute) reached a normal maximum work load for his size.

Most normal subject have a heart rate in the range 175 - 195 beats/minute at their maximum work load (Godfrey et al 1971). Three of the subjects in this study had atrial rates in excess of 180 beats per minute at their maximum work load. In general the atrial response to exercise was normal but the ventricular increase in rate was below normal.

Minute ventilation was normal throughout the progressive exercise test except in Patient 1 in whom it was increased during the last two work loads.

Steady State Tests

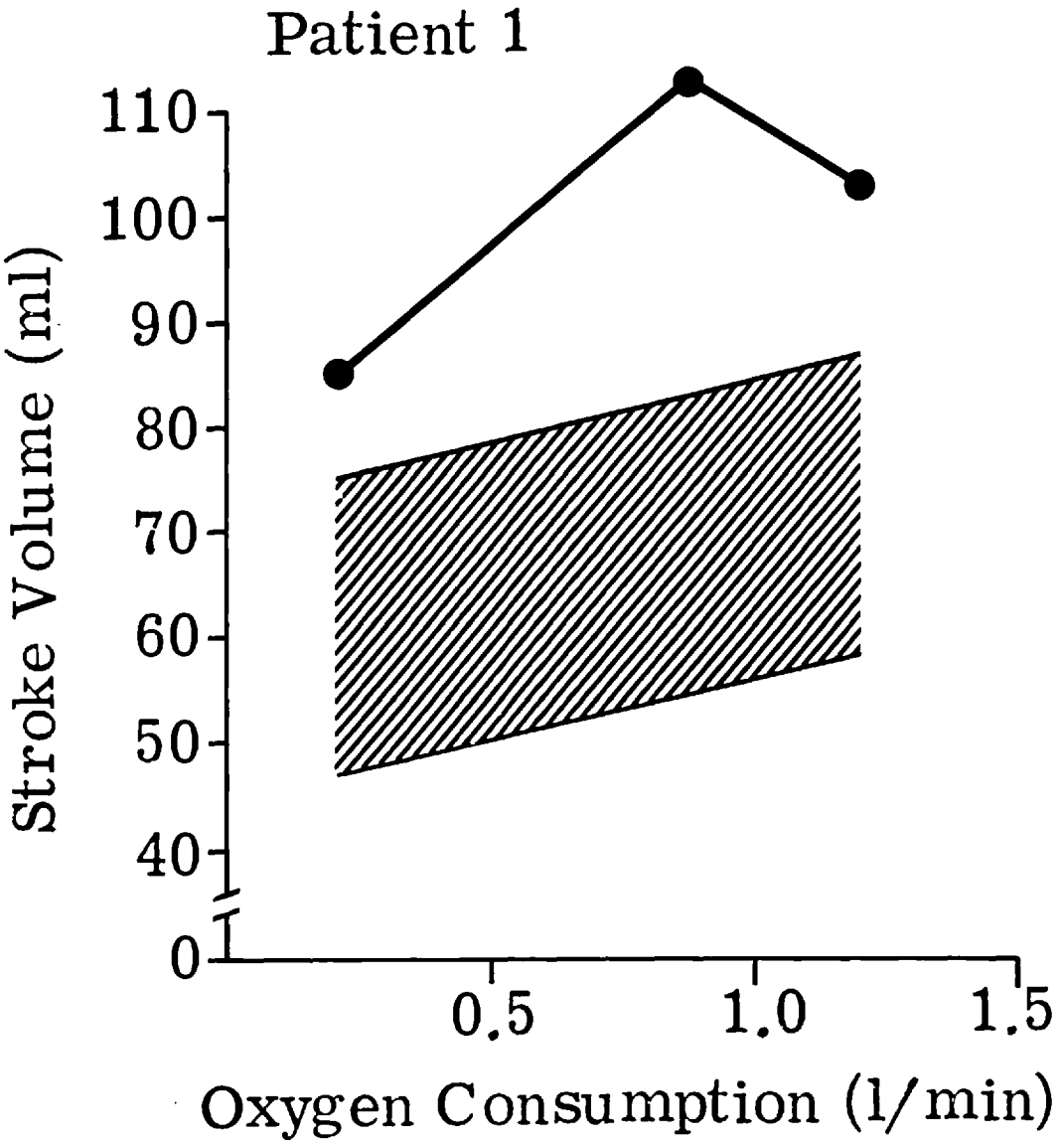
The results of the steady state tests are given in Table V - 2.

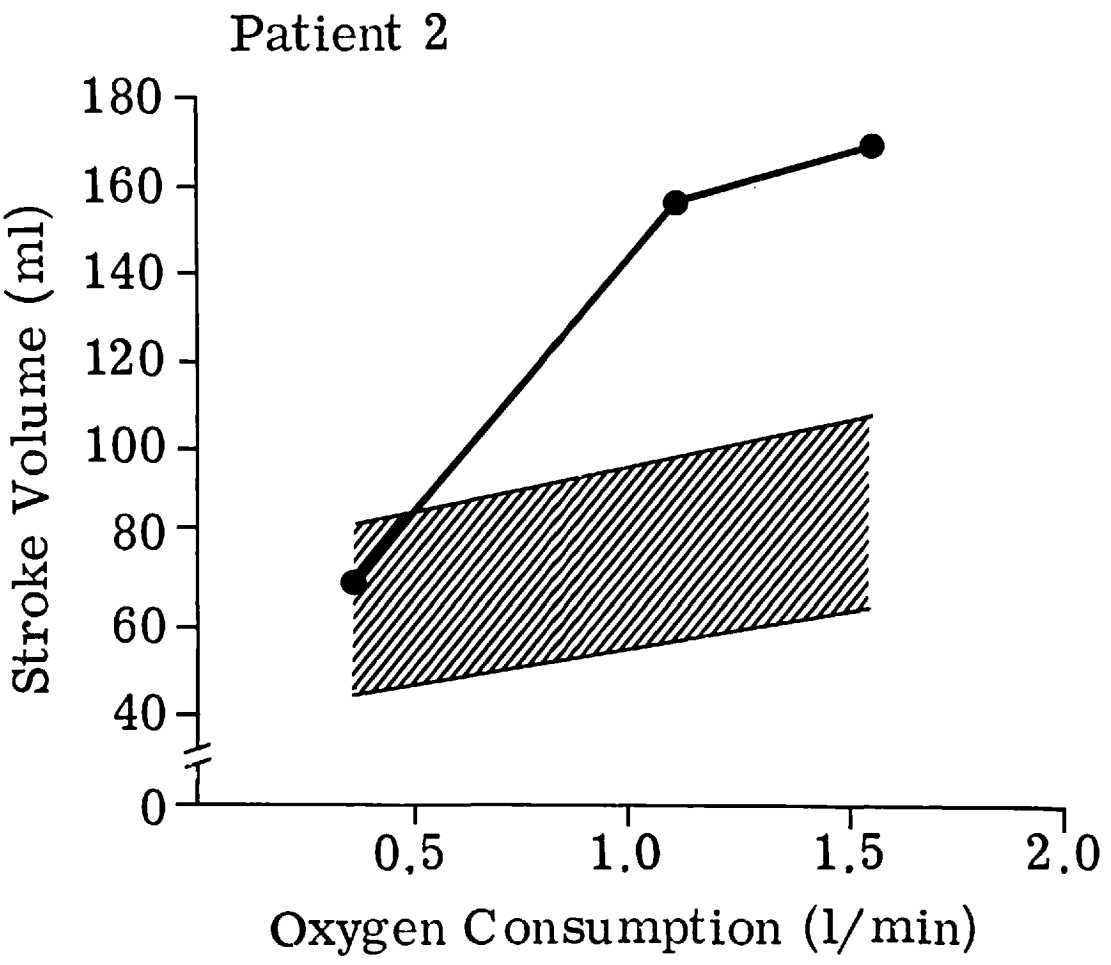
Cardiac Output

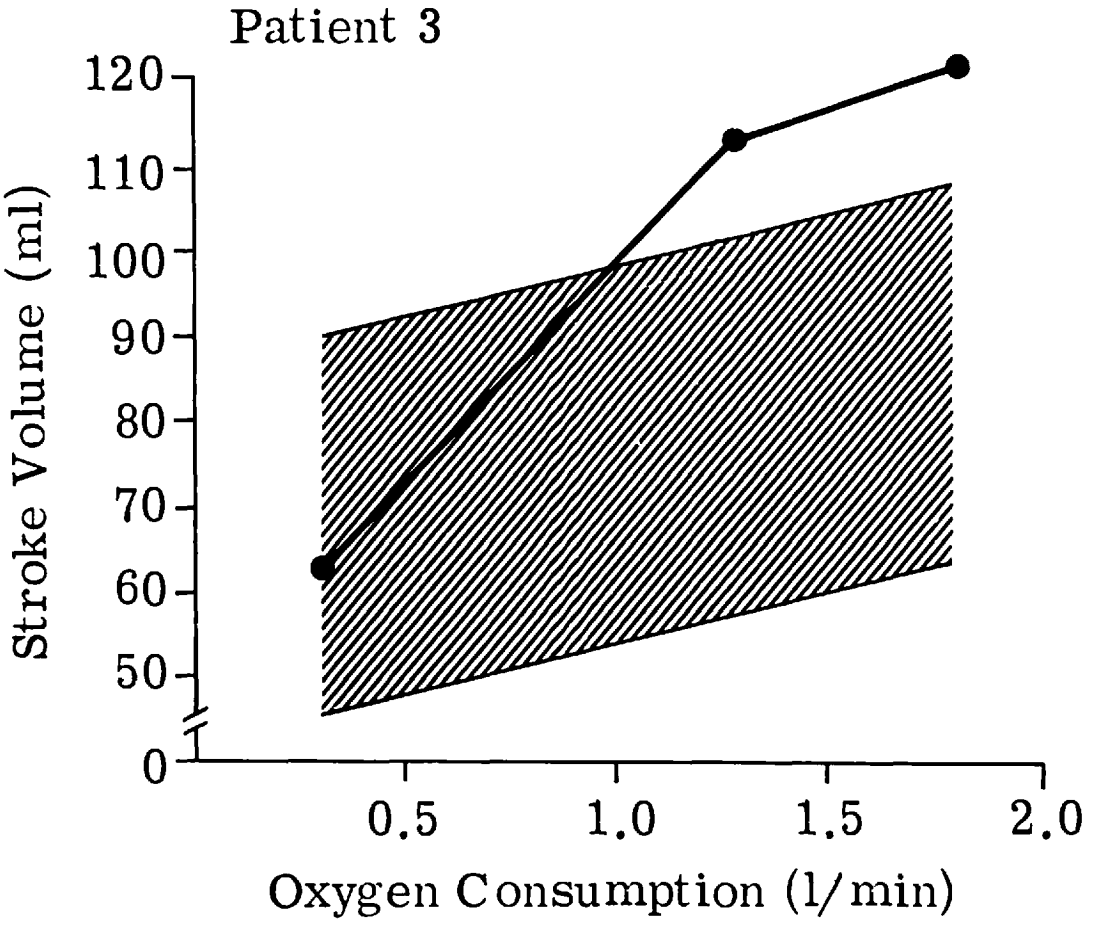
The results for cardiac output in relation to oxygen consumption are given in Figure V - 2. Cardiac output at rest was based on end tidal PCO_2 values. In

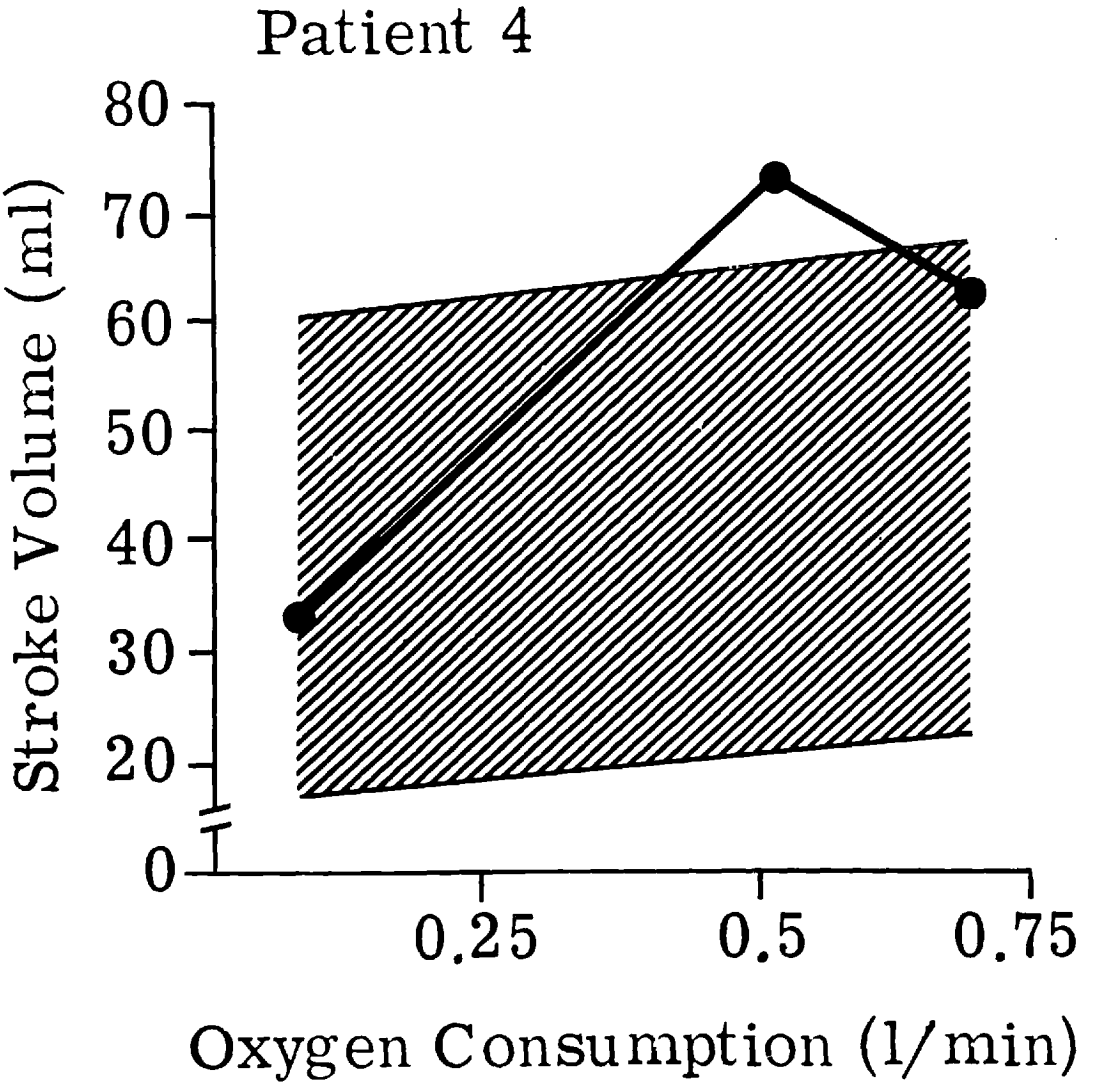
FIGURE V - 3

The stroke volume for each subject plotted against the oxygen consumption. The shaded area represents two standard errors either side of the regression line for normal subjects of the same height during exercise. (IN THIS INSTANCE ONLY REST VALUES ARE BASED ON AN ASSUMED NORMAL DEAD SPACE)


Patient 1
Stroke Volume (ml)
110
100
90
80
70
60
50
40
0
0.5
1.0
1.5
Oxygen Consumption (l/min)


Patient 2
Stroke Volume (ml)
180
160
140
120
100
80
60
40
0
0.5
1.0
1.5
2.0
Oxygen Consumption (l/min)


Patient 3
120
110
100
90
80
70
60
50
0
Stroke Volume (ml)
0.5
1.0
1.5
2.0
Oxygen Consumption (l/min)


Patient 4
Stroke Volume (ml)
80
70
60
50
40
30
20
0
0.25
0.5
0.75
Oxygen Consumption (l/min)

all cases the cardiac output was in the low normal range. On exercise cardiac output was based on PCO_2 derived from an assumed normal dead space except in patient 2. In patient 2 had a history of bronchitis which made it likely that he would have an abnormal dead space. His results have therefore been calculated from arterialised ear blood samples. On exercise cardiac output increased in all cases. The results for patients 1 and 2 were normal at both levels of exercise. Patient 4 had a cardiac output within normal limits at the first work load but a low cardiac output at the second work load. Patient 3 had a low cardiac output at both work loads.

Stroke Volume

In Figure V - 3 stroke volume for each subject is plotted against oxygen consumption and the normal ranges for exercise are given.

At rest the stroke volume calculated from the cardiac output based on end tidal PCO_2 was in the normal range:-

Patient	Observed Stroke Volume	Expected Stroke Volume	Expected value plus 2 standard errors of the estimate
1	50	42	66
2	71	56	80
3	64	54	78
4	20	35	59

All subjects had a large rise in stroke volume between rest and exercise with only a small further change between the first and second work loads. At work all subjects had a stroke volume greater than normal except patient 4 whose stroke volume was just within normal limits during the second work load.

Minute Ventilation

During the second steady state work load, patients 1 and 2 both had a raised minute ventilation. At rest and at the first work load they both had a normal minute ventilation. In patients 3 and 4 minute ventilation was normal.

DISCUSSION

Progressive Exercise Test

Maximum working capacity Ikkos and Hanson (1960) assessed the maximum working capacity of 10 patients with congenital heart block. They found that six of the patients had a normal working capacity and in four it was slightly reduced. Holmgren et al (1959) studied four patients with this condition and found that the maximum working capacity was low in three of them and normal in only one. Moss (1961) found a normal working capacity in all of the 4 children he studied with congenital heart block. In the present study two patients had a normal maximum working capacity as measured in the progressive test and in the other two it was low.

Heart Rate and Rhythm

Ikkos and Hanson (1960) using a two work load test noted that the rise in ventricular rate with work was not smooth. They found a large increase between rest and the first work load and a smaller increase between the first and second work loads. This occurred in the present study during the steady state test but in the progressive test, where small work increments were used, the ventricular rate rose smoothly as the work load increased (Figure V - 1).

Patient 1 was somewhat apprehensive at the start of her progressive test and had an atrial rate of 144 beats per minute and a ventricular rate of 59 beats per minute at rest. At rest, during the steady STATE study, when she was less apprehensive the figures were 119 beats per minute and 63 beats per minute respectively. It appears that emotion affects the atrial but not the ventricular rate.

Moss and Adams (1968) have stated that the ventricular and atrial rates generally parallel each other. it can be seen in figure 1 that this only occurred in one of the four patients in this study (patient 1). They also state that heart rate remains quite constant (40 - 80) from birth to the adult age group. Patient 4 had a ventricular rate of 90 - 100 beats/minute at birth and a rate of 80 - 90 beats/minute after 40 hours of age. His ventricular rate at rest is now 62 beats per minute.

Ikkos and Hanson (1960) noted ventricular extrasystoles on exercise in six of their eleven patients while Holmgren et al (1959) found them in two out of four patients and Moss and Adams (1968) in two out of ten patients during exercise. In the present study patient 2 had no extrasystoles. Patient 3 developed ventricular extrasystoles at the 100 watt load and they remained present at all higher work loads. The extrasystoles disappeared almost immediately he stopped work. Patient 1 followed the same pattern but the extrasystoles first appeared at the 80 watt load. Patient 4 had frequently ventricular extrasystoles both at rest and on exercise.

Steady State Test

The use of arterialised ear blood values for the estimation of cardiac output on exercise in patient 2 was necessary because a normal dead space could not be assumed in view of his history of bronchitis. The estimates of PCO_2 obtained from ear lobe blood agreed well with those obtained from end tidal PCO_2 corrected to arterial values using the method of Jones (1966):-

	PCO_2 corrected to arterial values	
	Ear Blood	End Tidal
$\frac{1}{3}$ W max.	34.2	32.9
$\frac{2}{3}$ W max.	33.9	33.1

TABLE V - 3

Showing calculated values for arterial oxygen content in ml. per 100 ml. blood (C_{aO_2}), mixed venous oxygen content in ml. per 100 ml. blood ($C\bar{v}_{O_2}$), mixed venous partial pressure of oxygen in mm.Hg. ($P\bar{v}_{O_2}$) and mixed venous oxygen saturation per cent. ($S\bar{v}_{O_2}$) at rest and on exercise in the four patients.

Patient	Work (Watts)	C_{aO_2}	$C\bar{v}_{O_2}$	$P\bar{v}_{O_2}$	$S\bar{v}_{O_2}$
1	0	21.5	14.6	41	71
	33	21.3	12.8	31	60
	66	21.1	10.8	33	50
2	0	20.9	11.6	33	53
	47	21.3	8.6	25	40
	95	21.1	8.8	26	41
3	0	20.5	11.9	26	57
	66	20.6	2.5	12	12
	133	20.6	3.4	13	16
4	0	17.9	4.4	20	22
	20	18.1	7.5	22	41
	40	18.1	4.1	15	22

These differences give rise to a difference in cardiac output of 0.3 l./min. at the first level of work and 0.2 l./min at the second level of work which make little difference to the results.

The two patients (3 and 4) who failed to reach a normal maximum work load in the progressive test had normal cardiac outputs in the steady state test. Both of the patients who reached a normal maximum work load in the progressive test had a low cardiac output at the higher work load in the steady state test. The increase in stroke volume which occurred on work, though greater than normal, was insufficient to compensate for the slow ventricular rate. In order to reach a normal maximum work load these patients had to tolerate a low cardiac output and, as a consequence an extremely low oxygen content of their venous blood (Table V - 3). The small changes in the calculated lactate rise suggest that anaerobic metabolism did not play a large part in energy production.

That the venous oxygen saturation may be a limiting factor for work in patients with heart block is suggested by the work of Edhag and Zetterquist (1968) in adults with artificial cardiac pacemakers. They found that the mean femoral venous oxygen saturation at which their patients stopped work was similar whether the ventricular rate was 47 or 72 beats per minute, although the duration and severity of work performed was higher at the higher ventricular rate. It may be that the ability to tolerate a low venous oxygen tension has to be acquired by training and this could explain

the differences in exercise tolerance in the present study. Both the subjects who had a normal exercise tolerance were very active and took part in field sports but this could be a reflection of their normal exercise tolerance rather than the cause of it.

The fact that two subjects were able to continue work with low cardiac outputs suggests that cardiac output alone is not a limiting factor for work in congenital heart block, and so heart rate and stroke volume will not be limiting factors either. In these four subjects the ability to reach a normal maximum work load was not related to the increase in ventricular rate, or in stroke volume on exercise.

Holmgren et al (1959) have reported one patient with congenital heart block who had a normal exercise tolerance and a normal cardiac output at work but this patient was able to increase his ventricular rate by 34 beats per minute between rest and exercise.

The two patients studied by Ikkos and Hanson (1960) both had low maximum working capacities and normal cardiac outputs (assuming a normal oxygen consumption) at low levels of work. Their findings agree with the findings in the two patients in this study who had normal cardiac outputs at work.

It appears that subjects with congenital heart block who can produce only a small increase in ventricular rate can only achieve a normal work output if they can tolerate a low cardiac output relative to the work done.

SUMMARY

Bicycle exercise studies were performed on four patients with congenital heart block. Two patients were found to have a normal capacity for work but they both had low cardiac outputs at high work loads. The two patients who were unable to perform a normal amount of work had normal cardiac outputs on exercise. The degree to which a patient increased his ventricular rate or stroke volume was not related to the maximum work which he could perform. It is suggested that in these patients with very slow heart rates at work normal amounts of work can only be done if the patient can tolerate a low cardiac output, a large arterio-venous oxygen difference and a low venous oxygen tension.

AORTIC STENOSIS

TABLE V - 4

Showing the age, sex, height, weight, left ventricular outflow gradient (outflow gradient), and site of obstruction for each child.

Patient No.	Age (yr.)	Sex	Ht. (cm.)	Wt. (Kg.)	Outflow Gradient (mm.Hg.)	Site of obstruction
1	$9\frac{9}{12}$	M	136	33.6	75	Subaortic fibrous diaphram
2	$9\frac{11}{12}$	M	147	37.3	40	Valve
3	9	M	133	26.2	80	Valve
4	$13\frac{1}{2}$	M	143.5	35.2	72	Valve
5	$11\frac{2}{12}$	F	146	43.0	50	Valve
6	$7\frac{10}{12}$	M	127.5	24.0	20	Valve
7	$6\frac{7}{12}$	M	114.5	20.7	52	Valve
8	$6\frac{1}{2}$	M	115	19.3	60	Valve
9	13	M	153	39.1	77	Valve

INTRODUCTION

Limitation of exercise, in particular exclusion from competitive sports, is often advised for children with aortic stenosis yet few studies have been published of the working capacity or cardio-pulmonary response to exercise of these children (Duffie and Adams 1963, Goldberg et al 1958). The danger of sudden death is usually given as the reason for limiting exercise. Yet sudden death occurs infrequently in these children (Glew et al 1969) and is not usually related to strenous exertion (Reynolds et al 1960). The state of knowledge of the functional effects of aortic stenosis is such that there is doubt as to whether the cardiac output is raised (Brunwald 1963, Hancock and Fleming 1960) or lowered (Goldberg et al 1958, Lee 1970) in this condition. Lee (1970) studied thirty four patients with a mean age of 34 years both at rest and on exercise, and found a lowered cardiac output on exercise in patients with severe stenosis. In the present study the cardio-pulmonary and electrocardiographic changes produced in response to exercise by nine children with aortic stenosis was recorded in an attempt to identify the functional effects of this condition

MATERIALS AND METHODS

In all of the patients aortic stenosis had been shown by cardiac catheterisation. The details of these patients are given in Table V - 4. All had normal values for simple spirometry and peak expiratory flow rate (Table V - 5A),

TABLE V - 6

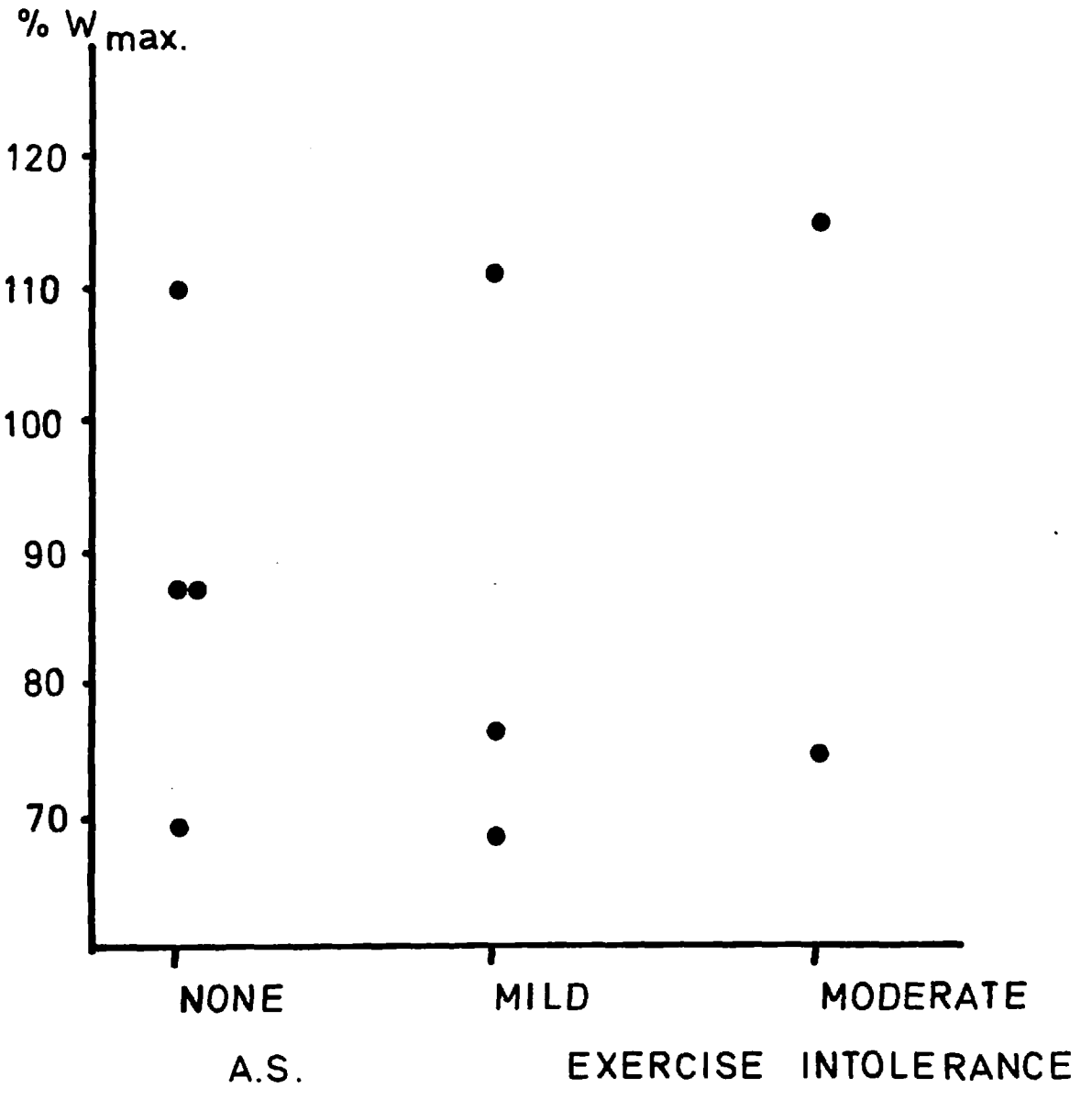
Showing for each child the maximum work load completed in the progressive test (W max.), the expected maximum work load, and the maximum work load expressed as a percentage of the expected value % W max.

Patient No.	W max.	Expected W max.	% W.max.
1	75	99	76
2	90	131	69
3	90	104	87
4	90	121	74
5	120	109	110
6	65	75	87
7	40	36	111
8	45	39	115
9	100	148	68

FIGURE V - 4

Showing the maximum work load completed in the progressive test as a percentage of the expected value (% W max.) plotted against the history of exercise intolerance.

TAYLOR 1972


% W max.
120
110
100
90
80
70
NONE
A.S.
MILD
EXERCISE
MODERATE
INTOLERANCE

although the mean FEV_1 was significantly lower than predicted. Patient 5 had a 10 mm. pulmonary valve gradient in addition to her 50 mm. aortic gradient. Estimates of cardiac output on exercise are based an assumed normal dead space. Estimates at rest are based on end tidal PCO_2. Exercise intolerance was graded on an arbitrary scale (as for Fallot's tetralogy) as none, mild, moderate or severe, from the parental observations. The criteria of Du Shane and Weidman (1965) were used to evaluate left ventricular hypertrophy on the electrocardiograph.

RESULTS

Progressive Exercise

Maximum Work Load

Three patients exceeded their expected maximum work load (Table V - 6). All of these patients had aortic gradients of 50 mm. or more. Of the remaining children (Nos. 1, 2, 4 and 9) had maximum work loads more than one standard error below the estimate for normal children. A paired 't' test was used to compare the observed ~~the~~ AND expected maximum work loads. The observed mean maximum work load was found to be significantly lower than normal ($P < 0.05$). The maximum work load reached was not significantly related to the outflow gradient ($r = 0.2813$ $P < 0.2$) nor was it related to the history of exercise tolerance (Figure V - 4).

TABLE V - 7

Showing electrocardiographic data for each child
(cw = clockwise, ccw = counter clockwise)
1 mV = 10 mm.

Patient No.	QRS Axis	R wave in aVF in mm.	$RV_6 + SV_1$ in mm.	QRS - T angle	Left ventrioular hypertrophy present	Horizontal QRS loop
1	+100°	22	28	140°	Yes	cw
2	+80°	10	30	70°	No	ccw
3	+60°	17	48	45°	Yes	ccw
4	+80°	30	48	75°	Yes	cw
5	+45°	9	48	30°	Yes	ccw
6	+75°	22	28	30°	No	ccw
7	+90°	9	30	80°	No.	ccw
9	+80°	25	57	75°	Yes	ccw

TABLE V - 8

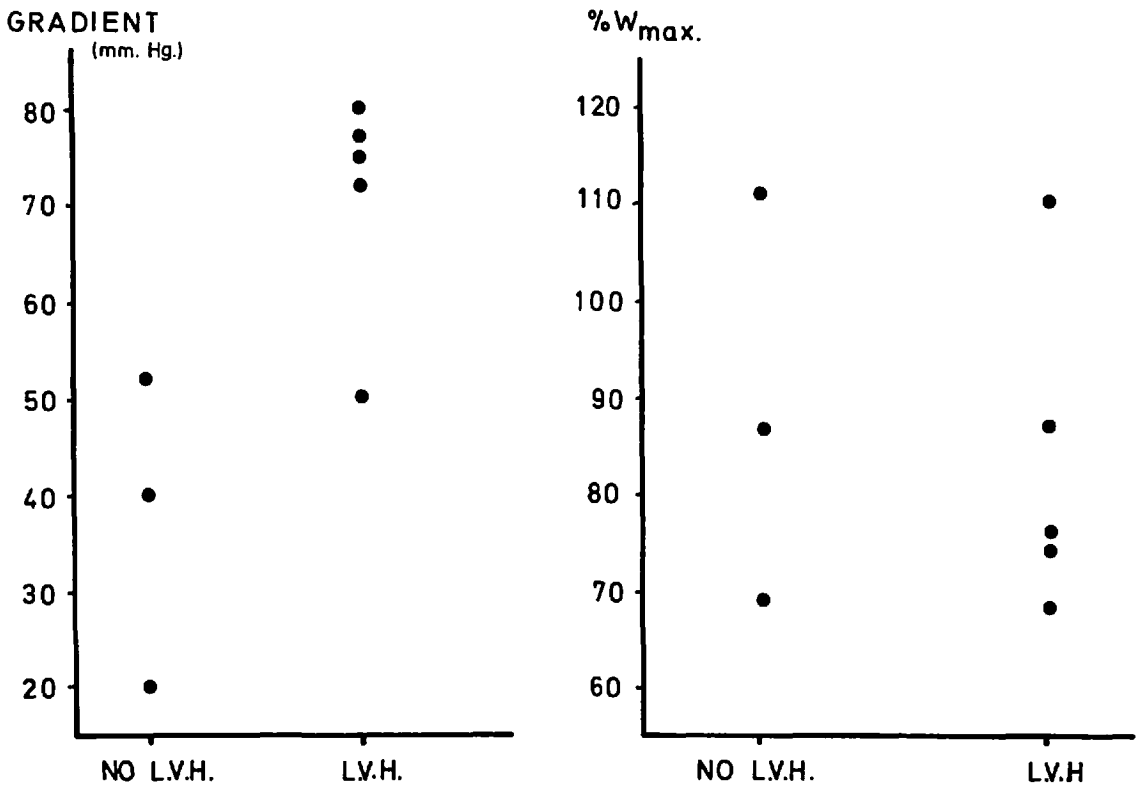
Showing the relationship between electrocardiograph indices of left ventricular hypertrophy and the left ventricular outflow gradient and the maximum work load as a percentage of the expected level.

Independent Variable	Dependent Variable	r	p
% expected maximum work load	QRS vector (horizontal axis)	0.409	N.S.
	'R' wave in AVF	0.073	N.S.
	R V_6 + SV_1	0.125	N.S.
	QRS-T angle	0.384	N.S.
Left ventricular outflow gradient	QRS vector (horizontal axis)	0.124	N.S.
	'R' wave in AVF	0.387	N.S.
	R V_6 + SV_1	0.591	N.S.
	QRS-T angle	0.487	N.S.

FIGURE V - 5

Showing the relationship of left ventricular outflow tract gradient (graddient) and the maximum work load as a percentage of the expected value (% W max.) to the presence or absence of left ventricular hypertrophy.

TAYLOR 1972



A.S.

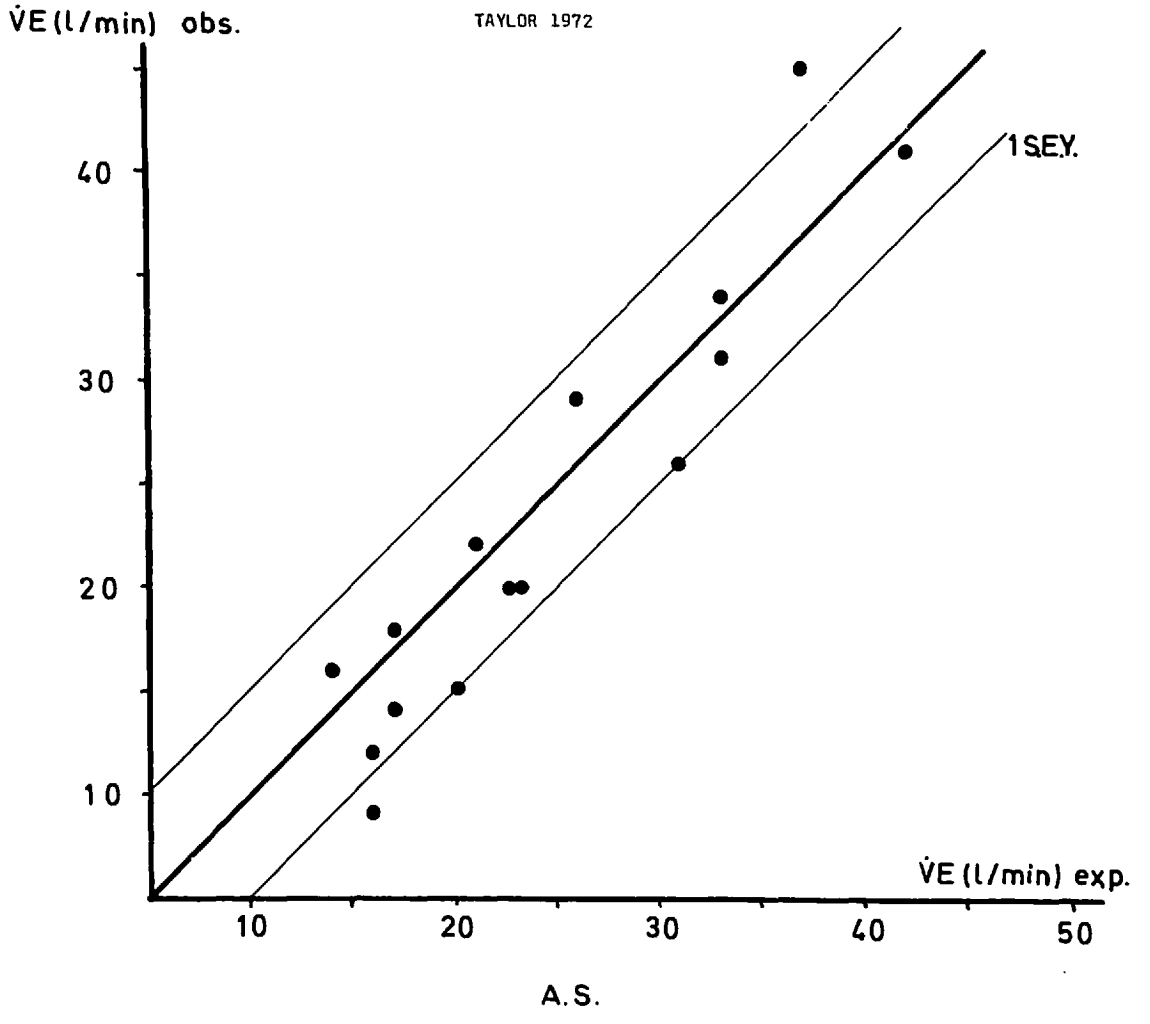
TABLE V - 10

The results of paired 't' tests comparing the observed and expected values for minute ventilation, heart rate, stroke volume and cardiac output in children with aortic stenosis. Negative values indicate results below the expected level.

Measurement	Work Load	Mean Difference	n	p
Minute Ventilation (l./min.)	1/3 W max.	+2.0	9	N.S.
	2/3 W max.	+0.1	9	N.S.
	1/3 + 2/3 W max.	+1.0	18	N.S.
Heart rate (beats/min.)	1/3 W max.	-1.6	9	N.S.
	2/3 W max.	+9.9	9	*
	1/3 + 2/3 W max.	+4.2	18	N.S.
Stroke volume (ml.)	1/3 W max.	-4.2	9	*
	2/3 W max.	-9.6	9	***
	1/3 + 2/3 W max.	-6.3	18	***
Cardiac Output (l./min.)	1/3 W max.	-0.9	9	***
	2/3 W max.	-1.3	9	***
	1/3 + 2/3 W max.	-1.1	18	***

FIGURE V - 6

Showing the relationship of the observed ($\dot{V}E$ obs.) to the expected ($\dot{V}E$ exp.) minute ventilation in aortic stenosis. The line of identity is shown. The limit lines represent one standard error of the estimate of the expected value.


V̇E (l/min) obs.
TAYLOR 1972
1 S.E.Y.
40
30
20
10
V̇E (l/min) exp.
10
20
30
40
50
A.S.

Electrocardiograph on Exercise

In none of the patients did the 'T' waves became inverted during exercise. At the maximum work load three patients had no ST depression (Patients 1, 2 and 6) two had a one milimetre depression (Patients 7 and 8). One had a 2 milimetre depression (Patient 5) and one a 10 milimetre depression (Patient 9). In two patients the tracing was not standardised.

The standard ECG for eight of the nine patients was assessed (Table V - 7) and various parameters compared with the maximum work load achieved. The direction of the QRS loop in the horizontal plane, the size of the 'R' wave in lead aVF, the sum of the height of the 'R' wave in V_6 and the 'S' wave in V_1 and the angle between the QRS and the T wave vectors in the horizontal plane were not related to the maximum work load (as a percentage of the expected value) or to the outflow gradient (Table V - 8). Children with left ventricular hypertrophy had a higher outflow gradient than those without it, but the presence or absence of left ventricular hypertrophy was not related to the maximum work load achieved (Figure V - 5).

Steady State

Minute Ventilation

At both levels of work the minute ventilation did not differ significantly from the expected value (Tables V - 9A and V - 10, Figure V - 6).

FIGURE V - 7

Showing the relationship of cardiac output to oxygen consumption in aortic stenosis. The regression lines for normal children are shown. The limit lines represent two standard errors of the estimate. The regression line on exercise is drawn for the mean height of the aortic stenosis group. Cardiac output on exercise is based on an assumed normal dead space. Cardiac output at rest is based on end tidal PCO_2.

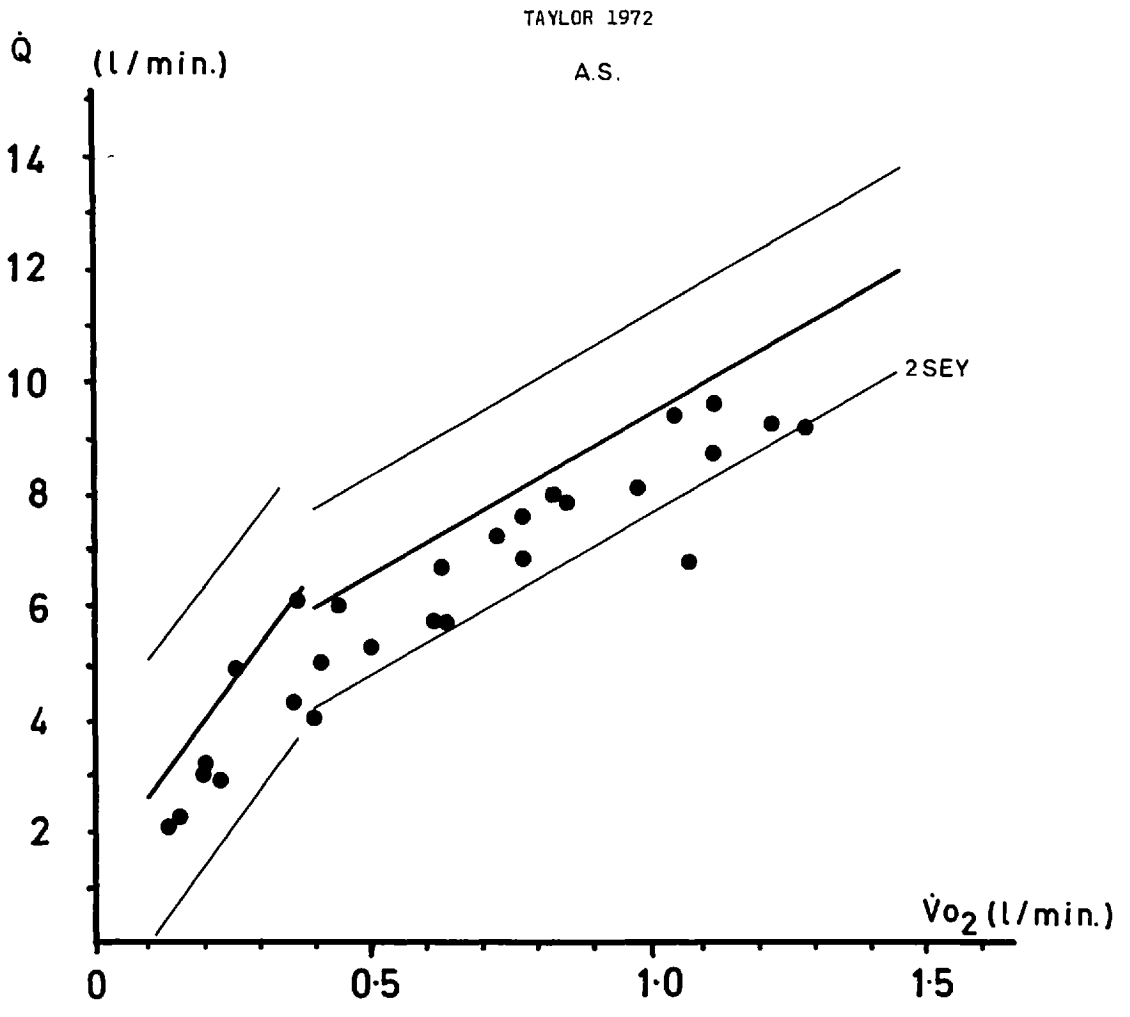

TAYLOR 1972
A.S.
Q̇ (l/min.)
14
12
10
8
6
4
2
2SEY
V̇o2 (l/min.)
0
0·5
1·0
1·5

TABLE V - 11

Showing for children with aortic stenosis -

1. the relationship between the left ventricular outflow gradient and the change in cardiac output minus the expected change between the $\frac{1}{3}$ W max. and $\frac{2}{3}$ W max. work loads and

2. the relationship between left ventricular outflow gradient and the change in stroke volume minus the expected change.

Independent Variable	Dependent Variable	r	p
Left Ventricular Outflow Gradient	Change in cardiac output between work loads minus expected change	0.878	***
	Change in stroke volume between work loads minus expected change	0.873	***

FIGURE V - 8

Showing the relationship of the observed minus the expected change in cardiac output between the $\frac{1}{3}$ W max. and $\frac{2}{3}$ W max. work loads ($\Delta \dot{Q}$ obs. - $\Delta \dot{Q}$ exp.) and the left ventricular outflow gradient. The equation for the regression line is,

$$y = -0.0332\,x + 1.67$$

($r = 0.878$ $n = 9$ SEY $= 0.44$)

TAYLOR 1972

A.S.

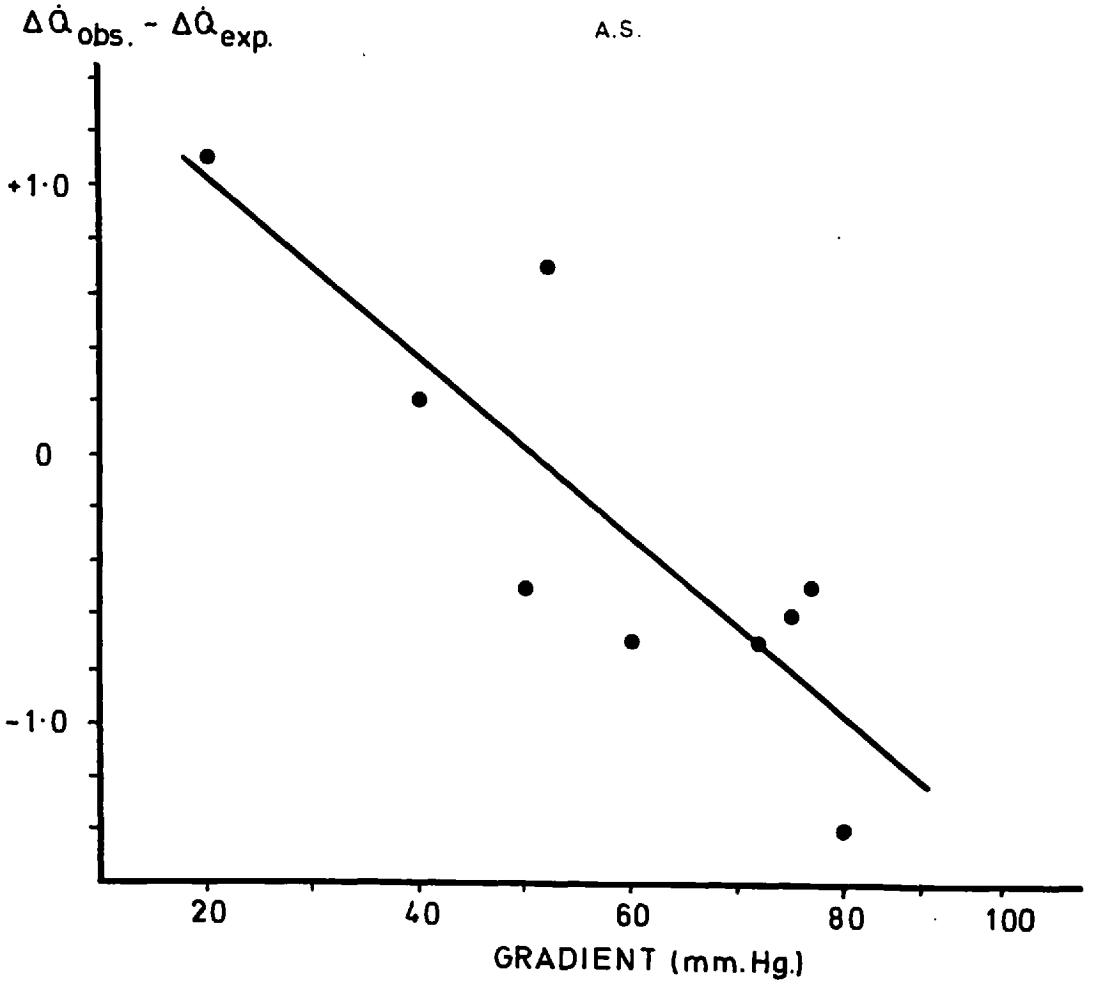
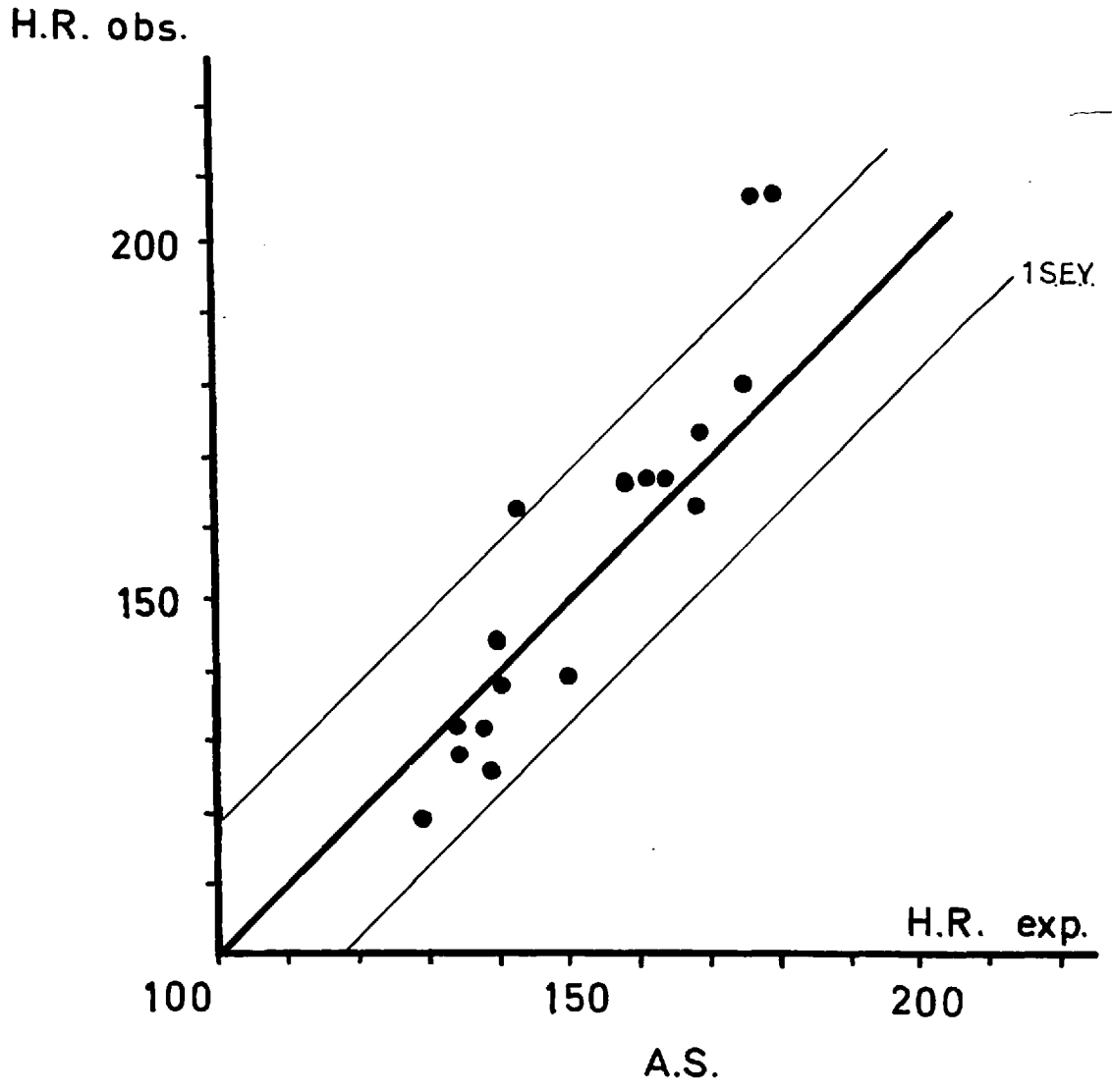


FIGURE V - 9

Showing the observed (H.R. obs.) and expected (H.R. exp.) heart rate in aortic stenosis. The line of identity is shown. The limit lines represent one standard error of the estimate of the expected value.

TAYLOR 1972



Cardiac Output

At rest the cardiac output was significantly lower than that of normal children (Tables V - 9A and V - 10 and Figure V - 7). On exercise too the cardiac output was lower than the expected value. The difference between the observed and expected change in cardiac output between the two work loads was found to be significantly related to the left ventricular outflow gradient (Table V - 11 and Figure V - 8).

Heart Rate

At the first work load the heart rate did not differ significantly from the expected value (Tables V - 9A and V - 10, Figure V - 9). At the second work load, however, the heart rate was significantly higher than normal with a mean increase in rate of 9.9 beats per minute.

Stroke Volume

The mean value for stroke volume was significantly lower than expected at both levels of work (Table V - 10). In two children the stroke volume increased from work load one to two; in one boy it remained the same; in all the other children it decreased.

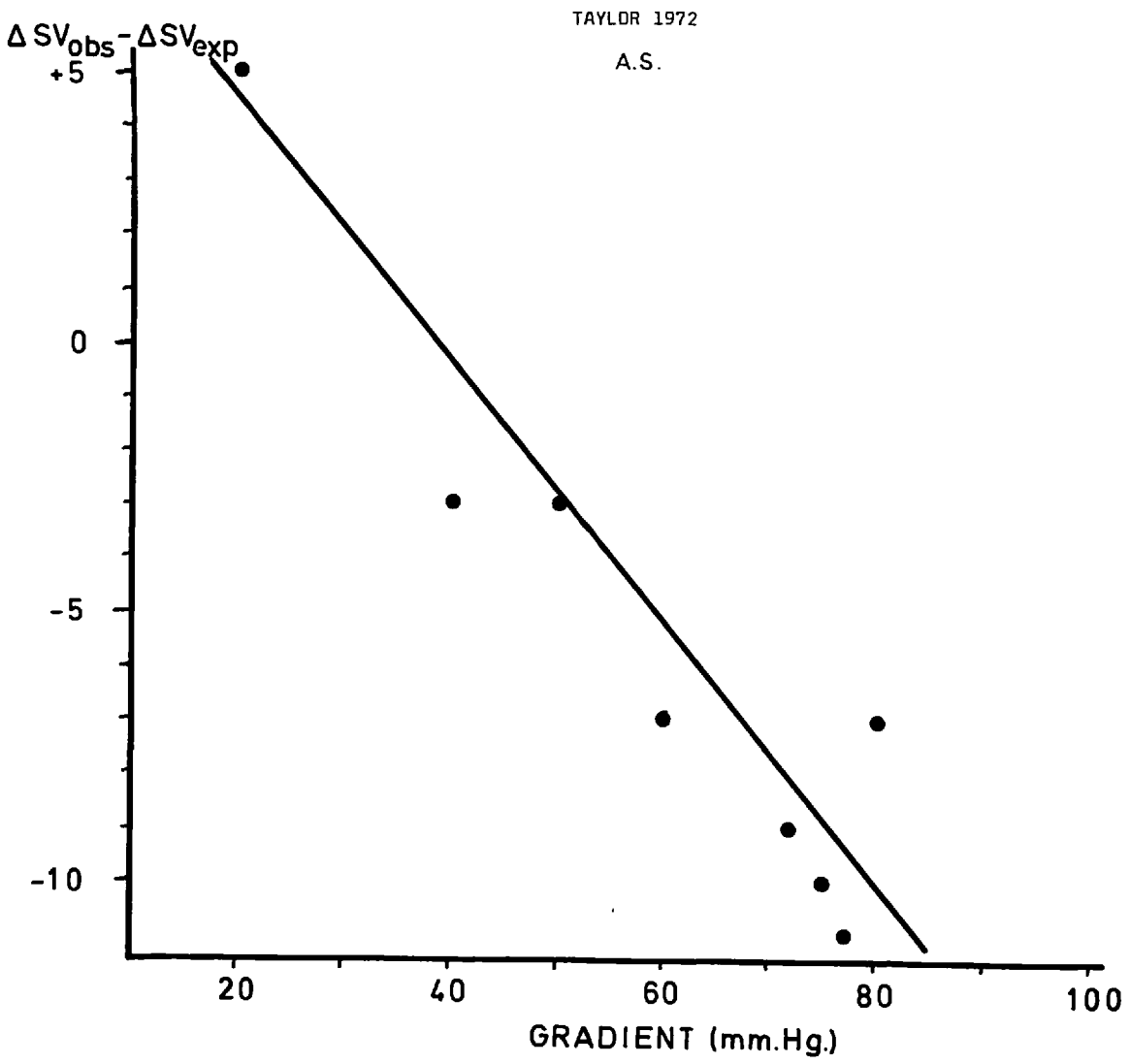
Stroke volume was higher than expected in only two patients (Table V - 9A). In only one patient was it higher than expected at the second work load and then only by 1 ml.

FIGURE V - 10

Showing the observed minus the expected change in stroke volume between the $\frac{1}{3}$ W max. and $\frac{2}{3}$ W max. work loads (Δ SV obs. - Δ SV exp.) plotted against the left ventricular outflow gradient (gradient). The equation for the regression line is,

$$y = -0.191\ x + 6.96$$

($r = 0.873$ $n = 9$ SEY = 2.28)


TAYLOR 1972
A.S.
ΔSVobs - ΔSVexp
+5
0
-5
-10
20
40
60
80
100
GRADIENT (mm.Hg.)

The difference between the observed and expected change in stroke volume between the two work loads was significantly related to the left ventricular outflow gradient (Table V - 11, Figure V - 10).

DISCUSSION

Respiratory Function

The forced expiratory volume in one second (FEV_1), the forced vital capacity (FVC), and peak expiratory flow rate (PEFR) fell within the normal range for all the children but the mean FEV_1 of these children was significantly lower than normal as assessed by a paired 't' test ($P < 0.05$). This might be due to bronchial changes as a result of raised left atrial pressure. The mean values for FVC and PEFR did not differ significantly from normal.

Progressive exercise

In this study it was found that some children with aortic stenosis could reach a normal maximum work load. This is in agreement with the findings of Duffie and Adams (1963) in children but in contrast with that of Lee et al (1970) who found that the exercise tolerance of adults was closely related to the severity of their aortic stenosis. Lee et al (1970) found that exercise tolerance was severely reduced, because of anginal pain and dyspnoea, or fatigue, in their patients with severe stenosis. These symptoms made the patients stop exercising when the heart rate was only 126 beats per minute. None of the children in

the present study had anginal symptoms or dyspnaea on exercise and their heart rates were between 184 and 218 beats per minute at the maximum work load completed. The main difference between children and adults with aortic stenosis is probably one of myocardial blood supply.

The fact that there was no relationship between the maximum work load completed (as a percentage of expected) and the outflow gradient suggests that other factors, such as myocardial compensation and the ability of the body to continue external work despite a sub-optimal cardiac output may be more important than the outflow gradient in determining the maximum working capacity.

Friedman et al (1971) reported a poor correlation between symptoms, the electrocardiograph, and the outflow gradient. In the present study too, electrocardiographic parameters were not related to the maximum working capacity or the outflow gradient, with the exception of left ventricular hypertrophy (Figure V - 5 and Table V - 8).

Halloran (1971) reported that in 14 out of 15 children with aortic gradients of 50 mm. or more there was depression of the ST segment of 2 mm. or more at the end of two minutes exercise at a maximum work load. In the present study in which the maximum work load was only continued for one minute three patients with gradients of above 50 mm. had ST depression of less than 2 mm.

Steady State

Minute Ventilation

Dyspnoea on exertion is not regarded as unusual in patients with heart disease. The finding of a normal minute ventilation in children with aortic stenosis emphasises the differences between the inappropriate effort required for breathing, which is dyspnoea (Campbell 1966) and the flow of air for a certain oxygen consumption which constitutes a normal minute ventilation. This normal minute ventilation on exercise contrasts with the increased minute ventilation found in children with cyanotic congenital heart disease in whom the ventilatory drive of exercise is supplemented by the drive due to increasing hypoxia (see section on ventilation during hypoxic exercise).

Cardiac Output at Rest

In the present study the cardiac output at rest was found to be significantly lower than normal. This is in keeping with the findings of Goldberg et al (1958), Goldberg et al (1954) and Lee et al (1970) but in contrast to the findings of Dexter et al (1956), Hancock and Fleming (1960) and Brunwald et al (1963). It does however seem reasonable to expect a lower than normal flow through a partially obstructed pipe.

~~Cardiac output, Heart Rate and Stroke Volume~~

~~The finding of a low cardiac output and stroke volume during exercise is in keeping with the observations~~

Cardiac Output, Heart Rate, and Stroke Volume

The findings of a low cardiac output and stroke volume during exercise is in keeping with the observations of Lee & al (1970) in adults with severe aortic stenosis. He did not however make any comment on heart rate during exercise. Cardiac output in aortic stenosis has been reported both as increased (Dexter et al 1956, Hancock and Fleming 1960, Brunwald et al 1963) and decreased (Goldberg et al 1954, Lee et al 1970) but in none of the studies in which an increased cardiac output was found were measurements made during exercise. Only the study of Goldberg et al (1958) included measurements of cardiac output during exercise in children with aortic stenosis. The measurements in their study were made at very low levels of work with a maximum oxygen consumption of 500 ml. per minute.

None of these workers reported a correlation between cardiac output and aortic gradient. In the present study the cardiac output on exercise was generally low and the change in cardiac output between the two work loads, minus the expected change ($\Delta \dot{Q} - \Delta \dot{Q}$ exp.), was closely related to the aortic valve gradient ($r = 0.848$) (Table V - 11 and Figure V - 8). The heart rate also rose above the predicted value on exercise (Table V - 10) and therefore the stroke volume would be expected to fall. This was found to be the case and the relationship between the observed minus the expected change in stroke volume on

exercise was significantly related to the aortic valve gradient ($r = 0.885$) (Table V - 11 and Figure V - 10).

Lee et al (1970) found a correlation between stroke volume as a proportion of heart volume and aortic valve area divided by body surface area ($r = 0.7$) in thirty four patients with aortic stenosis.

Congenital aortic stenosis in children has been shown to increase in severity with increasing age (Cohen et al 1968 and Friedman et al 1971). Friedman et al (1971) stated with regard to congenital aortic stenosis:

> "Of particular concern is the absence of a highly reliable indirect method for determination of a change in the severity of stenosis."

The good correlation between stroke volume changes on exercise and the left ventricular outflow gradient might well make serial exercise studies a suitable means of assessing the changes in the severity of aortic stenosis. This could, of course only, apply in a child in whom catheter studies had excluded any other lesion. Ziedifard et al (1972) have shown that stroke volume measurements during exercise are highly reproducible using the method employed in this study. It is important that increasing stenosis should be detected because children with severe stenosis are the most susceptable to sudden death (Glew et al 1969).

SUMMARY

The cardiopulmonary response to exercise of nine children with aortic stenosis was studied. Simple lung function tests were normal in all the children although the mean FEV_1 for the group was lower than predicted. The maximum working capacity of this group of children was signficantly lower than normal but three children with severe stenosis exceeded the expected maximum working capacity. The maximum working capacity was not related to the electrocardiographic pattern, the left ventricular outflow gradient or the history of exercise tolerance.

Cardiac output was significantly lower than expected both at rest and on exercise. Heart rate was significantly higher than expected and stroke volume was lower than expected, and fell as exercise increased. The change in heart rate and stroke volume on exercise were both significantly correlated with the left ventricular outflow gradient. It is suggested that serial exercise tests might provide a method for assessing changes in the severity of aortic stenosis provided that other forms of heart disease had been excluded.

PULMONARY STENOSIS

TABLE V - 12

Showing the age, sex, height (Ht.), weight (Wt.), and pulmonary valve gradient (Gradient) of each child. Patient 1 had a ventricular septal defect closed nine years previously.

Patient No.	Age (yrs.)	Sex	Ht. (cm.)	Wt. (Kg.)	Gradient (mm.Hg.)
1	13.1	M	145.5	39.2	13
2	8.6	F	117	21.9	11
3	13.8	F	161.5	51.9	12
4	7.8	F	120.5	21.0	32
5	9.2	F	145	32.0	30
6	11.3	M	148	39.2	9
7	11.7	M	152	38.5	9
8	8.2	M	130	29.1	65
9	10.3	M	131.5	31.2	115
10	12.4	F	159	38.4	10
11	9.5	M	115.5	20.5	48

INTRODUCTION

The response to exercise of 27 adult patients with pulmonary stenosis has been studied by Gazetopolous et al (1966). They found a diminution in cardiac output and an increase in minute ventilation in their patients. No similar study has been reported in children.

Duffie and Adams (1963) have reported a study of the maximum working capacity in 23 children with pulmonary stenosis but made no measurement of cardiac output. They found that the maximum working capacity of the children with pulmonary stenosis was lower than normal but was not related to the degree of stenosis.

The present study reports the maximum working capacity, cardiac output, minute ventilation and other cardiac-pulmonary data from eleven patients with pulmonary valve gradients from 9 to 115 mm. Hg.

MATERIALS AND METHODS

Eleven patients were studied with pulmonary valve graidents varying from 9 to 115 mm. Hg. (Table V - 12). These gradients were measured by cardiac catheterisation at rest. In three patients (11, 3 and 1) steady state studies were made only at half the maximum work load completed in the progressive test.

RESULTS

Respiratory Function

Respiratory function tests were performed on 10 of the 11 patients. Two patients (1 and 5) had

TABLE V - 14

The results of paired 't' tests on observed and expected values

Parameters	Mean Difference	n	t	p
FEV_1	-0.44	10	4.9394	***
FVC	0.2403	10	2.2010	N.S.
PEFR	8.7	10	0.5993	N.S.
MVV	9.1	10	1.1880	N.S.
W max.	14.6	11	1.6966	N.S.
$\dot{V}E$				
All work loads	-0.1	19	0.0769	N.S.
1/3 max.	1.5	8	1.8739	N.S.
2/3 max.	-0.9	8	0.7840	N.S.
$\dot{Q}$				
Rest	-0.1	9	0.2598	N.S.
All work loads	-1.3	19	7.0145	***
1/3 max.	-1.1	8	3.5590	**
2/3 max.	-1.6	8	7.0752	***
HR				
All work loads	-8.2	19	3.0458	**
1/3 max.	-13.1	8	2.8064	*
2/3 max.	-2.8	8	0.8255	N.S.
SV				
All work loads	-6.9	19	3.452	**
1/3 max.	-4.8	8	1.2153	N.S.
2/3 max.	-10.3	8	4.2385	***

TABLE V - 15

Showing the maximum work load completed by each child in the progressive test (W max.), the expected normal value (exp.) and the observed value expressed as a percentage of the expected value (% exp.).

Patient	W max.	Exp.	% exp.
1	165	127	130
2	50	40	125
3	100	146	68
4	44	49	90
5	84	107	79
6	84	134	63
7	135	145	93
8	50	82	61
9	84	86	98
10	89	140	64
11	50	40	125

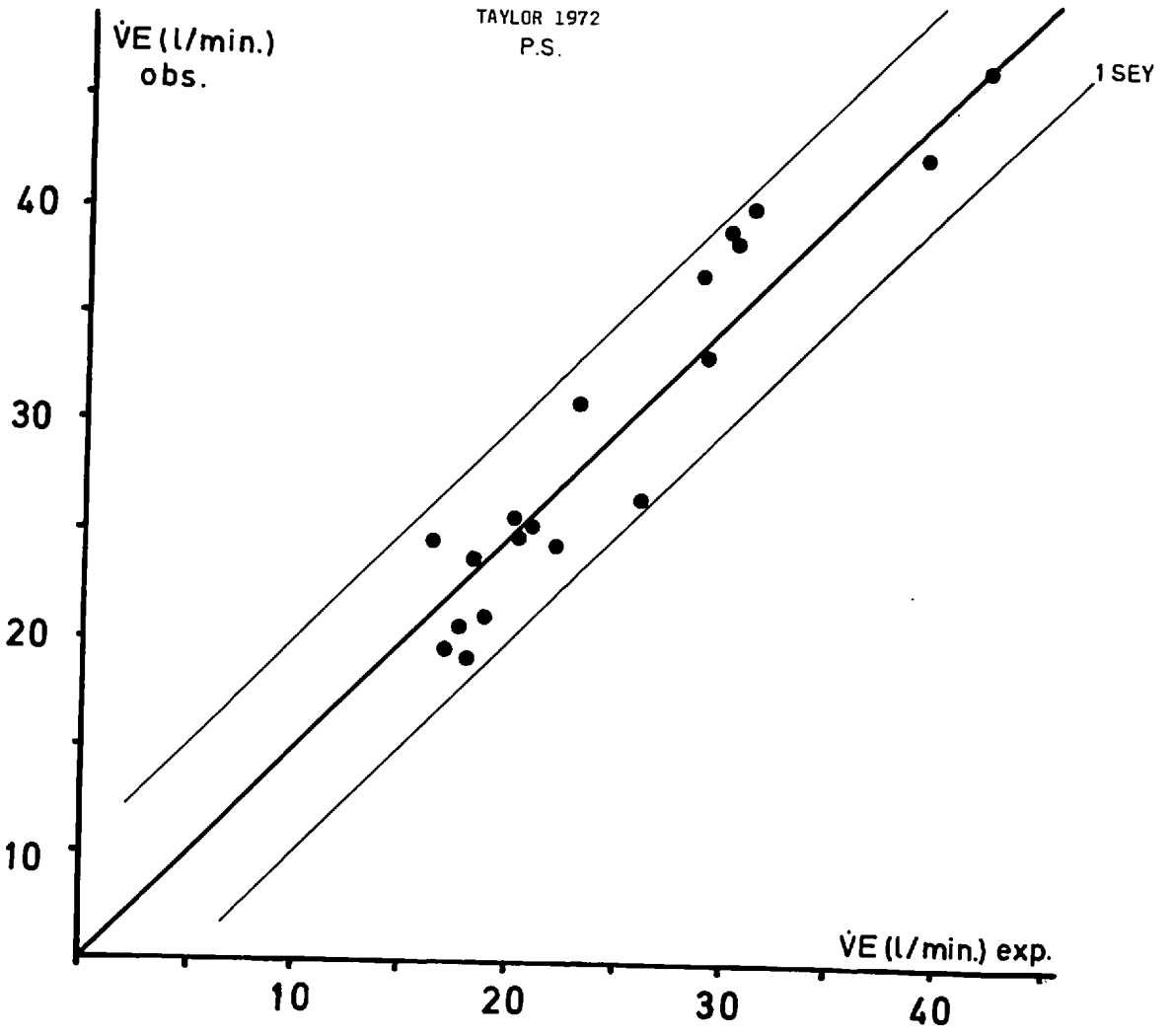
TABLE V - 16

Shows the correlation coefficients, 't' values and significance relationships between maximum work load as a percentage of the expected value (% W max.), the pulmonary valve gradient (valve gradient), the difference between the expected and observed cardiac output at the 2/3 W max. work load ($\dot{Q}$ exp. - $\dot{Q}$ at 2/3 W max.), the difference between the observed and expected stroke volume at the 2/3 W max. work load (SV - SV exp.) $\triangle$the change in cardiac output minus the expected change between the 1/3 and 2/3 W max. work loads ($\dot{Q}$ - $\dot{Q}$ exp.) and the change in stroke volume minus the expected change between the 1/3 W max and 2/3 W max. work loads ($\triangle$SV - $\triangle$SV exp.).

Dependent Variable	Independent Variable	r	t	p
% W max.	Valve gradient	0.0408	0.1225	N.S.
% W max.	SV - SV exp.	0.5029	1.7457	N.S.
$\dot{Q}$ exp. - $\dot{Q}$ at 2/3 W max.	Valve gradient	0.0507	0.1524	N.S.
$\dot{Q}$ - $\dot{Q}$ exp.	Valve gradient	0.1087	0.2679	N.S.
SV - SV exp.	Valve gradient	0.0915	0.2250	N.S.

FIGURE V - 11

Showing the observed and expected minute ventilation on steady state exercise in pulmonary stenosis. The line of identity is shown. The limit lines represent one standard error of the estimate of the expected value.


TAYLOR 1972
P.S.
V̇E (l/min.)
obs.
1 SEY
40
30
20
10
V̇E (l/min.) exp.
10
20
30
40

abnormal respiratory function tests. Patients 1 and 5 had FEV_1 values below the normal range but their values for FVC and PEFR were normal (Table V - 13A).

However, when the observed values for the respiratory function tests were compared with predicted values using a paired 't' test it was found that the FEV_1 values were significantly lower than normal (Table V - 14). The values for FVC, PEFR and MVV did not differ significantly from that of normal children (Table V - 14).

Maximum working capacity

Three patients (1, 2 and 11) exceeded their predicted maximum work load (Table V - 15) but the mean maximum working capacity of all the patients did not differ significantly from that of normal children (Table V - 14). The maximum working capacity expressed as a percentage of the expected value was not related to the pulmonary valve gradient (Table V - 16).

STEADY STATE RESULTS

Minute Ventilation

On exercise the minute ventilation in relation to oxygen consumption did not differ significantly from that of normal children (Table V - 14 and V - 17A, Figure V - 11).

Heart Rate

The heart rate of these children was significantly lower than normal on exercise. The reduction in heart rate

FIGURE V - 12

Showing the observed and expected heart rates on steady state exercise in children with pulmonary stenosis the line of identity is shown. The limit lines represent one standard error of the estimate of the expected value.

TAYLOR 1972
P.S.

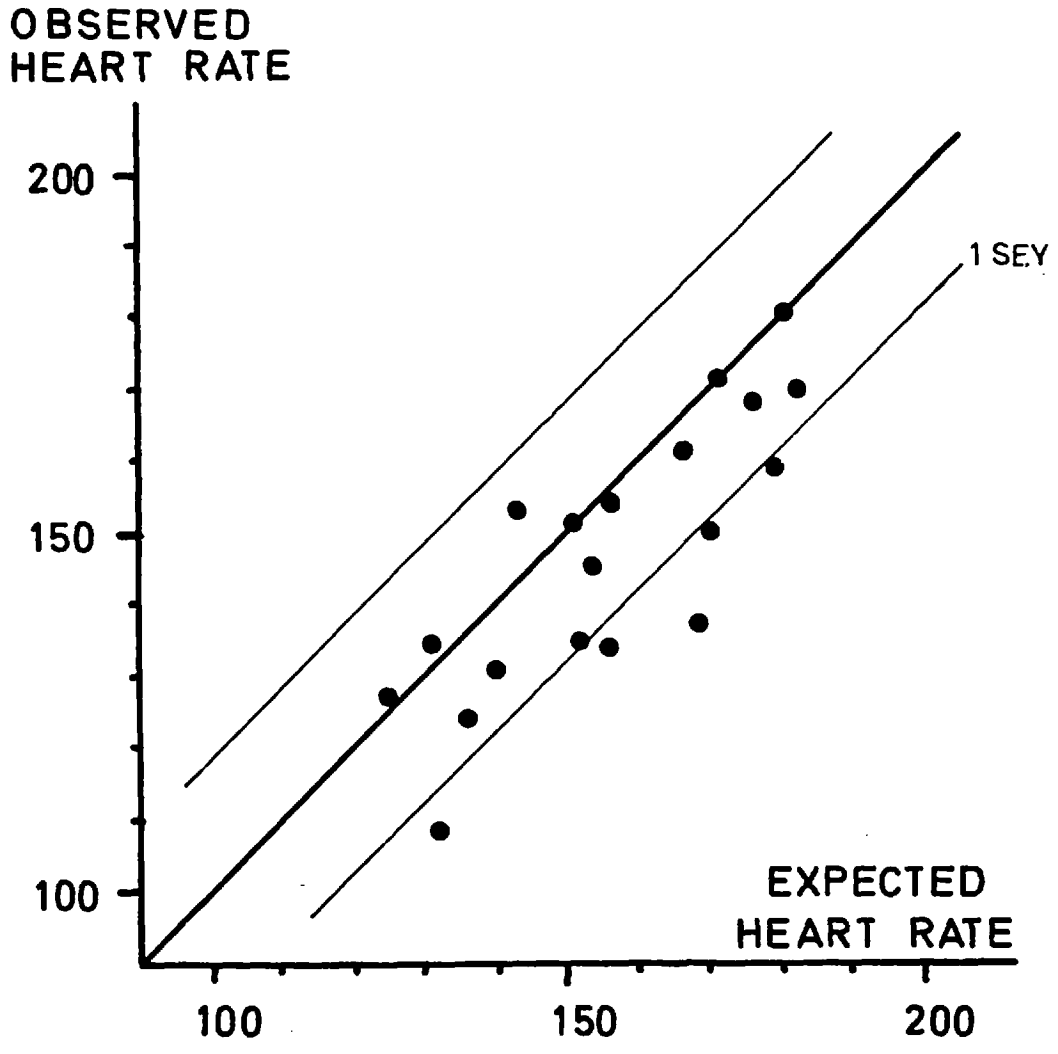
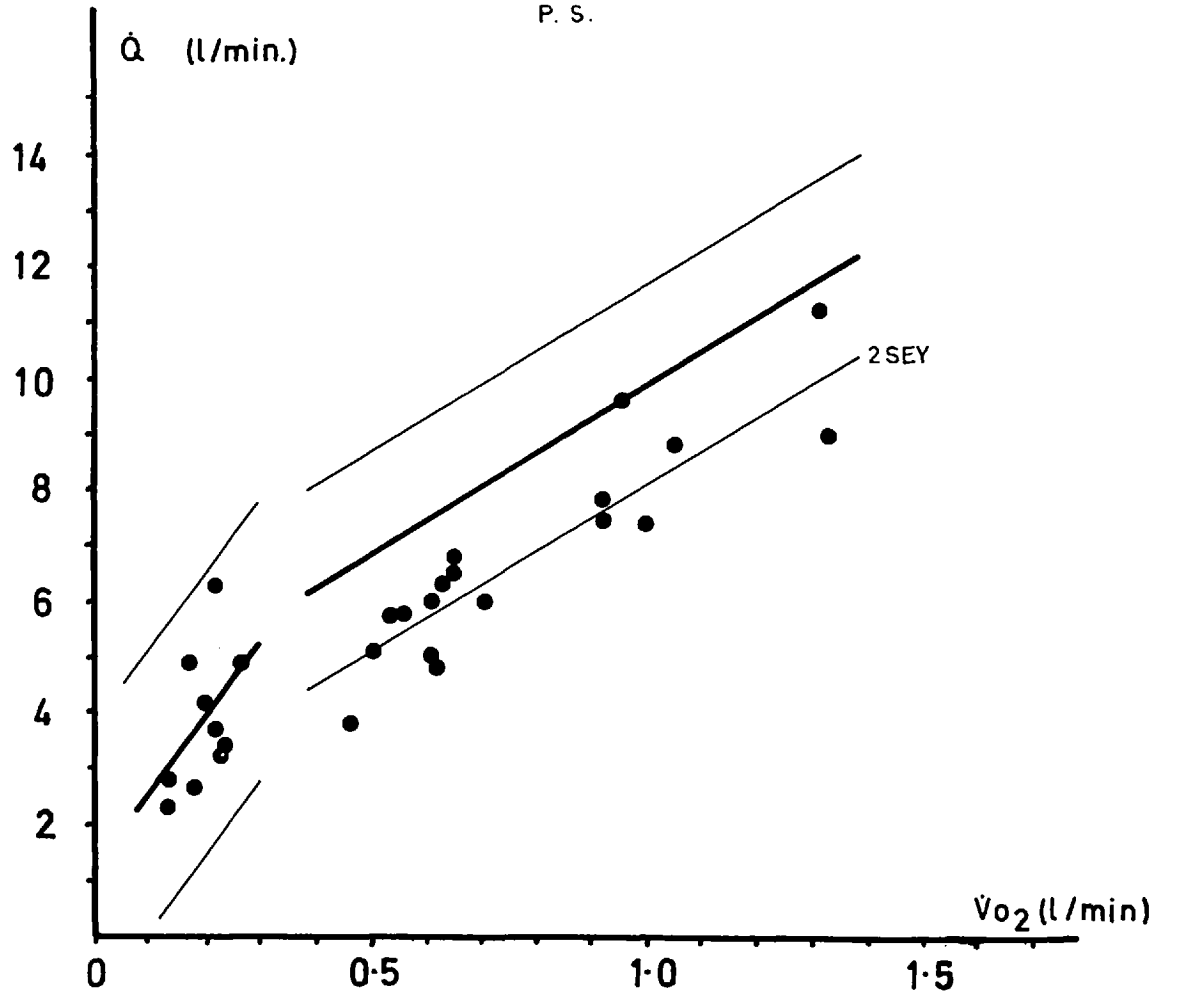


FIGURE V - 13

Showing the relationship between cardiac output ($\dot{Q}$) and oxygen consumption in pulmonary stenosis at rest and on exercise. The resting values for cardiac output are based on end tidal estimates of PCO_2, the exercise values are based on an assumed normal dead space. The regression line on exercise represents the value for normal children with a height equal to the mean of the children with pulmonary stenosis. The limit lines represent two standard errors of the estimate of cardiac output for normal children.

TAYLOR 1972

P. S.



was more marked at the first level of exercise than at the second level when it was not statistically significant (Table V - 14 and V - 17A, Figure V - 12).

Cardiac Output

The cardiac output at rest did not differ significantly from the normal values. On exercise however the cardiac output was significantly lower than normal at both levels of work (Table V-14). The reduction in cardiac output was greater at the higher level of work (Tables V - 14 and V - 17A, Figure V- 13).

Stroke Volume

Stroke volume on exercise was significantly lower than normal (Table V-14). As might be expected from the heart rate and cardiac output values the stroke volume was significantly lower than normal at the second level of exercise but not at the first (Table V - 14 and V - 17A).

DISCUSSION

Maximum working capacity

Three children exceeded the expected maximum working capacity. The mean maximum working capacity of all the children did not differ significantly from that of normal children (Table V - 14).

Duffie and Adams (1963), using a somewhat different method of measuring maximum working capacity, found that some children with pulmonary stenosis exceeded their expected maximum working capacity.

They too found that the maximum working capacity was not related to the pulmonary valve gradient. It appears that the measurement of maximum working capacity is of little value in determining the severity of the pulmonary gradient (Table V - 16) and that a child with a gradient of 115 mm. Hg. may achieve 98% of the expected value.

STEADY STATE

Minute Ventilation

Minute ventilation on exercise was normal (Table V - 14). This contrasts with the findings of Gazetapolous et al (1966). They studied 27 adults with pulmonary stenosis during mild supine exercise. They found that 7 of their patients hyperventilated during exercise but were unable to find any cause for the increased ventilation. They noted however that the increase in ventilation was related to the elevation of mean right atrial pressure. It may be that an elevation of right atrial pressure is only produced by long standing pulmonary stenosis and that this elevation in pressure and hyperventilation on exercise are only acquired in adult life.

Cardiac Output

The finding of a low cardiac output on exercise in pulmonary stenosis is in keeping with the findings of Howitt (1966), Gazetopolous et al (1966) and Ikkos et al (1966) in adults. Unlike Ikkos (1966) however no

relationship was found between the reduction in cardiac output and the pulmonary valve gradient (Table V - 16). The relationship between valve gradient and the change in cardiac output at work, minus the expected change, which had been found in aortic stenosis was not found in pulmonary stenosis; nor was the relationship between valve gradient and change in stroke volume found in pulmonary stenosis (Table V - 16).

Heart Rate

The heart rate at the first work load was significantly lower than normal (Table 3, Figure V - 12). A diminution in heart rate during exercise in pulmonary stenosis does not appear to have been reported previously. This relative bradycardia might be explained as a reflex response to distension of the right atium due to the pulmonary stenosis. If this were so one would expect the diminution in heart rate to be more pronounced at the higher than at the lower work loads but this is not so.

Stroke Volume

Stroke volume was lower than normal on exercise but not significantly so at the first level of work (Table V - 14). At the second level of work however the mean difference between the expected and observed stroke volume was 10.3 ml. Only in two patients (7 and 11) was the stroke volume higher than predicted (Table V - 17A).

Ikkos et al (1966) reported a lower than normal stroke volume: in relation to heart volume both at rest and on exercise in adult patients with severe pulmonary stenosis, but the mean heart volume of these patients was increased which could account for the reduction in the stroke volume: heart volume ratio.

SUMMARY

The response to exercise of eleven children with pulmonary stenosis with gradients ranging from 9 to 115 mm. Hg. was studied.

It was found that -

1. The maximum working capacity of the group did not differ significantly from normal.
2. The maximum working capacity was not related to the severity of pulmonary stenosis.
3. Minute ventilation on steady state exercise was normal.
4. Heart rate was lower than expected at low work loads.
5. Cardiac output was normal at rest but low on exercise, and
6. Stroke volume was low on exercise.

SECTION VI

APPENDIX

TABLE III - 2A

SHOWING THE VALUES FOR FEV_1, FVC, AND PEFR, MVV AND W MAX., FOR EACH CHILD. EACH OBSERVED VALUE, WITH THE EXCEPTION OF MVV IS FOLLOWED BY THE EXPECTED VALUE. FOR BOYS THE STANDARD DEVIATIONS OF THE EXPECTED VALUES ARE FEV_1 0.366 FVC 0.379 PEFR 49.9 AND FOR GIRLS FEV_1 0.355 FVC 0.365 PEFR 40.6

No.	FEV_1	exp.	FVC	exp.	PEFR	exp.	MVV	W max.	exp.	Dyspnoee Index
2	2.42	3.74	3.91	4.31	355	460	91	181	188	81.3
5	3.63	3.64	3.96	4.91	588	450	149	203	182	62.2
6	3.36	3.95	4.13	4.55	435	481	110	203	200	66.4
8	3.80	4.00	4.57	4.61	570	487	155	203	202	53.3
37	2.42	2.72	2.53	3.11	350	355	77	118	131	59.2
38	2.37	2.73	2.70	3.11	278	355	63	135	131	93.3
46	2.26	2.42	2.48	2.75	239	323	77	118	114	65.2
57	2.23	2.57	2.62	2.93	340	339	89	153	122	78.7
58	2.04	1.91	2.45	2.15	205	270	50	67	85	51.6
59	1.76	1.91	1.93	2.15	245	270	71	101	85	70.6
71	2.13	2.42	2.38	2.75	278	323	34	84	114	126.5
72	2.04	2.01	2.26	2.27	240	281	71	101	90	65.6
92	4.29	4.36	4.79	5.03	635	524	91	228	223	132.0
99	5.39	4.77	6.44	5.51	680	566	208	251	245	57.0
111	1.38	1.81	1.82	2.03	210	259	52	67	79	68.1
112	1.65	1.66	1.96	1.85	215	244	46	84	70	104.4
10	2.70	2.84	2.97	2.98	435	375	98	89	122	45.7
35	2.92	2.88	3.58	3.03	457	380	100	158	124	71.2
45	2.48	2.68	2.86	2.78	400	354	80	118	112	68.0
68	1.82	2.02	1.89	2.00	252	269	72	84	74	61.1
75	2.73	2.92	3.14	3.08	445	385	101	112	126	47.3
84	1.93	1.90	2.13	1.85	255	253	68	84	67	66.0
86	1.98	2.39	2.00	2.44	252	317	86	84	75	62.9
97	3.52	3.25	4.04	3.47	515	427	127	158	145	58.1
109	3.36	3.37	3.85	3.62	410	443	87	135	152	56.0
113	1.82	1.86	1.93	1.80	270	248	69	84	64	77.5
117	1.71	1.94	2.04	1.90	215	259	59	67	69	46.4

TABLE III - 4A

SHOWING THE REGRESSION EQUATIONS FOR THE NORMAL CHILDREN'S VALUES.
THE ABBREVIATIONS USED ARE EXPLAINED IN SECTION II

Source	Subjects	Equation	r	SEY	n
Weng and Levison 1969	Boys and girls	MVV = 1.50 Ht. - 134.6			139
Present study		MVV = 1.69 Ht - 161.3	0.798	22.8	27
		MVV = 34.5 FEV_1 - 1.52	0.864	19.1	27
Godfrey et al (1971)	Boys - exercise	HR = 159.1 log 10 $\dot{V}O_2$ - 1.204 Ht - 143	0.71	18	103
Present study		HR = 141.7 log 10 $\dot{V}O_2$ - 1.185 Ht - 97	0.722	18	32
		HR = 142.8 log 10 $\dot{V}O_2$ - 1.225 wt - - 225	0.719	18	32
		HR = 152.2 log 10 $\dot{V}O_2$ - 69.1 BSA - 214	0.749	18	32
Pooled 1969 + 1971 results		HR = 156.7 log 10 $\dot{V}O_2$ - 1.226 Ht - 134	0.718	18	141
		HR = 150.5 log 10 $\dot{V}O_2$ - 1.442 wt. -238	0.707	18	141

Continued/.....

TABLE III - 4A (CONTINUED)

Source	Subjects	Equation	r	SEY	n
Godfrey et al (1971)	Girls - exercise	$HR = 173.0 \log 10 \dot{V}O_2 - 1.395\ Ht - 140$	0.81	14	98
Present study		$HR = 183.9 \log 10 \dot{V}O_2 - 1.249\ Ht - 190$	0.752	19	22
		$HR = 187.9 \log 10 \dot{V}O_2 - 1.238\ wt - 330$	0.745	19	22
		$HR = 191.4 \log 10 \dot{V}O_2 - 70.4\ BSA - 301$	0.758	19	22
Pooled 1969 + 1971 results		$HR = 170.3 \log 10 \dot{V}O_2 - 1.34\ Ht - 140$	0.781	16	123
		$HR = 162.4 \log 10 \dot{V}O_2 - 1.407\ wt - 254$	0.777	16	123
Godfrey et al (1971)	Boys - exercise	$\dot{V}E = 0.0305\ \dot{V}O_2 - 0.117\ Ht + 17.0$	0.93	5.0	103
Present study		$\dot{V}E = 0.0292\ \dot{V}O_2 - 0.236\ Ht + 34.5$	0.913	6.1	32
		$\dot{V}E = 0.0296\ \dot{V}O_2 - 0.251\ wt. + 9.6$	0.912	6.2	32
		$\dot{V}E = 0.030\ \dot{V}O_2 - 13.6\ BSA + 16.6$	0.915	6.1	32
Pooled 1969 + 1971 results		$\dot{V}E = 0.0299\ \dot{V}O_2 - 0.145\ Ht + 21.4$	0.918	5.3	141

Continued/.....

TABLE III - 4A (CONTINUED)

Source	Subjects	Equation	r	SEY	n
Godfrey et al (1971	Girls - exercise	$\dot{V}E = 0.037\ \dot{V}O_2 - 0.211\ Ht + 25.7$	0.92	4.5	96
Present study		$\dot{V}E = \cancel{0.457}\ 0.0457\ \dot{V}O_2 - 0.363\ Ht + 42.4$	0.909	5.5	22
		$\dot{V}E = \cancel{0.468}\ 0.0468\ \dot{V}O_2 - 0.368\ wt + 4.7$	0.908	5.5	22
		$\dot{V}E = \cancel{0.463}\ 0.0463\ \dot{V}O_2 - 19.3\ BSA + 14.7$	0.905	5.6	22
Godfrey et al (1971)	Boys - exercise	$\dot{Q}VD = 0.0057\ \dot{V}O_2 + 0.022\ Ht + 0.71$	0.95	0.92	87
Present study		$\dot{Q}VD = 0.0045\ \dot{V}O_2 + 0.016\ Ht + 2.57$	0.907	1.32	32
		$\dot{Q}VD = 0.0049\ \dot{V}O_2 + 4.55$	0.904	1.32	32
Godfrey et al (1971)	Girls - exercise	$\dot{Q}VD = 0.0056\ \dot{V}O_2 + 0.021\ Ht + 1.02$	0.94	0.74	74
Present Study		$\dot{Q}VD = 0.0055\ \dot{V}O_2 + 0.039\ Ht - 1.18$	0.901	1.03	22
		$\dot{Q}VD = 0.0066\ \dot{V}O_2 + 3.51$	0.883	1.08	22

Continued/.....

TABLE III - 4A (CONTINUED)

Source	Subjects	Equation	r	SEY	n
Calculated from Data of Godfrey et al (1971)	Boys and girls exercise	$\dot{Q}VD = 0.0064\ \dot{V}O_2 + 3.23$	0.940	0.88	170
		$\dot{Q}VD = 0.0056\ \dot{V}O_2 + 0.022\ Ht + 0.85$	0.946	0.84	170
		$\dot{Q}VD = 0.0056\ \dot{V}O_2 + 0.031\ wt + 2.92$	0.947	0.82	170
Pooled 1969 + 1971 results		$\dot{Q}VD = 0.0059\ \dot{V}O_2 + 3.77$	0.923	1.01	224
		$\dot{Q}VD = 0.0051\ \dot{V}O_2 + 0.025\ Ht + 0.90$	0.929	0.97	224
		$\dot{Q}VD = 0.0050\ \dot{V}O_2 + 0.035\ wt + 3.29$	0.932	0.95	224
Godfrey et al (1971)	Boys - exercise	$SV_{VD} = 0.0114\ \dot{V}O_2 + 0.636\ Ht - 41$	0.85	10	87
Present study		$SV_{VD} = 0.007\ \dot{V}O_2 + 0.645\ Ht - 38.1$	0.781	13.2	32
		$SV_{VD} = 0.805\ Ht - 53.5$	0.769	13.3	32
		$SV_{VD} = 0.877\ wt + 29.2$	0.814	12.0	32
		$SV_{VD} = 45.93\ BSA + 5.70$	0.820	11.9	32
Pooled 1969 + 1971 data		$SV_{VD} = 0.0106\ \dot{V}O_2 + 0.724\ Ht - 51.2$	0.758	15.5	125
		$SV_{VD} = 0.0113\ \dot{V}O_2 + 0.826\ wt + 21.4$	0.738	16.0	125

Continued/.....

TABLE III - 4A (CONTINUED)

Source	Subjects	Equation	r	SEY	n
Godfrey et al (1971)	Girls - exercise	SV_{VD} = 0.645 Ht - 37	0.81	7	75
Present study		SV_{VD} = 0.724 Ht - 47.8	0.766	8.3	22
		SV_{VD} = 0.751 wt + 25.1	0.808	7.6	22
		SV_{VD} = 41.4 BSA + 3.0	0.818	7.4	22
Pooled 1969 + 1971 data		SV_{VD} = 0.669 Ht - 40.6	0.807	7.3	101
		SV_{VD} = 0.743 wt + 26.2	0.826	6.9	101
Present study	Boys and girls exercise	$\dot{Q}_{EAR}$ = 0.0054 $\dot{V}O_2$ + 3.15	0.887	1.43	49
		$\dot{Q}_{EAR}$ = 0.0041 $\dot{V}O_2$ + 0.051 Ht - 3.07	0.909	1.30	49
		$\dot{Q}_{EAR}$ = 0.0043 $\dot{V}O_2$ + 0.047 wt + 2.30	0.905	1.33	49
		$\dot{Q}_{EAR}$ = 0.0041 $\dot{V}O_2$ + 2.759 BSA + 0.80	0.909	1.31	49
Present study	Boys - exercise	SV_{EAR} = 0.928 Ht - 79.0	0.815	13.1	28
		SV_{EAR} = 0.926 wt + 20.6	0.808	13.3	28
		SV_{EAR} = 50.02 BSA - 6.6	0.830	12.6	28

Continued/.....

TABLE III - 4A (CONTINUED)

Source	Subjects	Equation	r	SEY	n
Present study	Girls - exercise	SV_{EAR} = 0.694 Ht - 51.8	0.813	6.5	21
		SV_{EAR} = 0.620 wt + 22.1	0.757	7.3	21
		SV_{EAR} = 35.9 BSA + 1.7	0.796	6.8	21
Denison et al (1971)	Adults Fick O_2 rest + exercise	$\dot{Q} = 0.006\ \dot{V}O_2 + 6$			
Present study	Boys and Girls Rest + exercise	$\dot{Q}VD = 0.0049\ \dot{V}O_2 + 4.7$	0.763	2.4	78
		$\dot{Q}_{EAR} = 0.0056\ \dot{V}O_2 + 2.8$	0.890	1.7	72
		$\dot{Q}_{EAR} = 0.0052\ \dot{V}O_2 + 0.027$ Ht - 0.97	0.898	1.6	72
		$\dot{Q}_{EAR} = 0.0052\ \dot{V}O_2 + 0.026$ wt + 1.94	0.897	1.6	72
		$\dot{Q}_{EAR} = 0.0052\ \dot{V}O_2 + 1.474$ BSA + 1.14	0.898	1.6	72
Godfrey et al (1971) calculated from data	Boys and girls rest	$\dot{V}E = 0.036\ \dot{V}O_2 + 0.276$	0.772	1.79	88
Present study		$\dot{V}E = 0.035\ \dot{V}O_2 + 0.359$	0.8095	1.97	26

TABLE III - 5A

Showing the steady state results for normal subjects. VD is the dead space value calculated from the equation of Godfrey et al, 1971. This value was used in the calculation of $\dot{V}O$.

No.	Work	$\dot{V}O_2$	$\dot{V}E$	HR	$\dot{Q}$(VD)	$\dot{Q}$EAR	$\dot{Q}$ET	SV(VD)	VD	VA
2	0	271	9.3	94	4.1	4.0	3.4	44	157	2.2
	59	1227	30.2	135	10.6	9.0		79	183	1.0
	119	2409	55.0	173	13.8	13.2		80	199	0.4
5	0	424	21.0	128	11.4	5.6	8.8	89	134	1.0
	67	1253	29.4	162	11.5	11.2		71	133	1.5
	135	1986	54.2	200	14.5	14.8		73	156	1.6
6	0	208	10.3	98	4.1	5.3	2.7	42	104	3.9
	67	968	25.4	119	7.2	6.5		61	130	1.6
	135	1651	44.5	158	10.6	10.8		67	148	1.6
8	0	403	9.3	83	7.0	4.1	5.6	84	126	3.0
	67	1685	28.6	116	12.1	12.3		106	157	0.8
	135	2149	53.3	166	15.7	13.1		95	178	1.6
37	0	163	6.1	96	3.0	4.2	3.2	31	63	2.9
	39	628	16.6	129	6.0	7.6		47	77	1.5
	78	1110	34.1	178	9.0	8.3		51	92	1.5
38	0	140	5.3	109	3.5	4.1	2.9	32	69	4.3
	44	675	19.5	149	7.3	8.6		49	86	5.4
	89	1151	40.0	187	9.7	8.3		52	98	3.8
46	0	187	5.5	88	18.0	3.0	5.0	205	70	3.9
	39	772	19.2	123	9.0	8.7		73	87	1.8
	78	1179	36.2	168	10.0	8.5		60	95	2.4
57	0	169	5.3	80	4.0	2.2	2.7	50	74	1.1
	50	837	20.8	123	8.6	5.6		70	92	0.8
	101	1359	44.4	171	11.1	8.5		65	99	1.6
58	0	189	6.9	105	10.6	-	4.9	101	61	5.3
	22	559	17.6	125	8.2	-		66	70	-
	44	819	30.8	173	10.2	-		59	72	-
59	0	135	6.0	94	6.8	2.4	2.6	72	55	2.8
	33	655	22.8	151	6.7	5.9		44	66	1.9
	67	1013	36.9	194	8.0	7.7		41	75	1.6
71	0	125	4.7	90	9.5	1.5	3.0	106	64	1.8
	27	555	15.4	119	6.9	5.8		58	77	0.5
	56	847	26.9	162	8.5	6.4		52	83	1.0
72	0	159	5.7	99	6.7	-	4.5	68	58	-
	33	622	18.1	130	8.2	-		53	73	3.3
	67	949	33.9	163	9.2	-		56	74	1.9
92	0	251	7.4	89	5.8	6.2	2.9	65	142	4.2
	74	1177	28.0	125	11.6	10.4		93	176	0.8
	149	2212	80.1	163	18.1	17.9		111	175	1.1

TABLE III - 5A (Cont'd)

Showing the steady state results for normal subjects. VD is the dead space value calculated from the equation of Godfrey et al 1971. This value was used in the calculation of $\dot{Q}VD$.

No.	Work	$\dot{V}O_2$	$\dot{V}E$	HR	$\dot{Q}(VD)$	$\dot{Q}EAR$	Q_{ET}	SV(VD)	VD	VA
99	0	270	9.5	85	3.8	3.6	3.6	45	159	2.1
	81	1294	30.3	124	14.2	13.7		115	202	1.5
	165	2530	59.3	177	16.9	17.2		95	234	1.9
111	0	166	8.1	126	Neg.	3.8	5.4	-		4.9
	22	533	20.2	158	7.4	6.4		47	67	2.6
	44	830	30.6	189	8.2	5.8		43	74	2.2
112	0	172	5.9	96	3.6	2.6	3.4	38	56	2.8
	27	869	26.9	128	10.6	8.8		83	65	2.3
	56	914	33.2	160	9.1	8.1		57	68	2.1
10	0	162	6.5	75	5.5	5.4	4.1	73	87	4.5
	30	663	20.2	149	7.4	7.2		50	106	1.0
	60	951	39.0	188	11.5	11.3		61	117	1.9
35	0	174	6.0	95	5.1	3.5	2.8	54	116	4.2
	52	883	25.8	175	10.9	8.3		62	120	2.7
	105	1451	54.7	203	12.8	10.8		63	140	2.8
45	0	178	5.9	119	1.8	12.0	2.7	15	93	0
	39	714	21.0	159	9.2	9.7		58	112	2.8
	78	1109	34.7	190	10.9	9.3		57	122	1.5
68	0	-	-	-	-	-	-	-	-	-
	27	522	14.3	115	7.2	5.1		63	77	2.3
	56	877	29.4	172	8.3	6.5		48	82	2.9
75	0	241	9.4	104	8.0	Neg.	8.3	77	83	-
	36	705	16.0	154	7.4	8.1		48	108	1.4
	74	1166	34.0	193	9.8	10.3		51	116	1.6
84	0	165	5.3	96	5.3	2.1	4.0	55	60	3.4
	27	536	16.1	137	5.8	4.8		42	66	2.1
	56	865	35.2	185	7.4	6.0		40	75	2.1
86	0	128	4.4	106	10.5	2.0	2.6	99	75	2.1
	33	558	16.8	134	7.4	5.4		55	87	1.9
	67	919	33.7	187	8.2	7.4		44	98	1.6
97	0	258	7.0	123	7.7	3.9	4.0	63	123	2.4
	52	958	25.9	171	12.1	8.8		71	144	2.6
	105	1598	54.6	197	14.0	12.8		71	177	1.8
109	0	229	10.4	88	4.9	3.2	4.4	56	113	2.1
	44	840	26.7	113	9.1	7.7		81	134	2.2
	89	1254	44.1	145	11.7	-		81	149	-
113	0	162	7.5	104	4.0	2.3	4.1	38	51	1.5
	44	576	23.6	134	7.9	6.8		59	57	1.2
	89	803	50.3	188	9.6	7.5		51	74	1.4
117	0	147	5.8	108	2.7	1.8	2.8	25	55	3.3
	22	462	15.5	169	6.1	4.6		36	62	2.8
	49	651	24.7	194	7.8	6.7		40	67	2.8

TABLE III - 8A

Showing the results for pH, blood gas pressures and derived values in normal children. The pH and blood gas values were obtained from arterialised ear lobe blood and have been corrected to arterial values as described in Section II. The abbreviations are explained in Section II.

TABLE III - 8A

Rest						
No.	BE	$PETCO_2$	$PaCO_2$	PaO_2	SaO_2	pH
2	-2.2	31.0	33.1	101	97.7	7.420
5	-4.0	24.5	19.0	121	98.8	7.532
6	-4.1	27.8	35.0	100	97.4	7.377
8	-3.1	38.9	34.7	87	96.6	7.395
37	-2.2	36.2	38.8	97	97.2	7.378
38	-1.4	33.7	36.5	96	97.3	7.406
46	-5.1	36.9	32.5	93	97.0	7.382
57	-6.9	33.5	30.8	106	97.8	7.382
58	-	37.4	-	99	97.4	7.395
59	-1.4	36.7	35.8	101	97.6	7.411
71	-9.4	36.4	27.1	106	97.7	7.353
72	-	35.6	-	102	97.5	7.391
92	-1.8	32.4	36.5	94	97.1	7.399
99	-4.3	33.8	33.8	100	97.4	7.383
111	-6.8	30.2	27.5	100	97.6	7.395
112	-3.6	39.2	35.5	97	97.2	7.381
10	-2.3	31.0	32.7	100	97.6	7.422
35	-2.1	31.6	33.9	93	97.1	7.414
45	+0.7	36.2	43.8	99	97.2	7.383
68		F A I N T E D				
75	-2.0	30.2	36.5	95	97.1	7.388
84	-6.4	36.0	28.5	94	97.2	7.393
86	-6.5	37.4	33.8	103	97.5	7.358
97	-1.7	38.2	38.0	94	97.1	7.391
109	-7.4	30.0	25.9	105	97.9	7.398
113	-8.2	33.2	26.5	110	98.0	7.380
117	-2.5	35.6	29.6	94	97.5	7.445
mean	-3.95	33.9	32.7	99.3	97.4	7.398
S.D.	2.6	3.7	5.2	6.7	0.41	0.033
n	24	26	24	26	26	26

TABLE III - 8A (CONTINUED)

⅓ W max.						
No.	BE	$PETCO_2$	$PaCO_2$	PaO_2	SaO_2	pH
2	-4.9	36.0	33.2	102	97.5	7.378
5	-2.4	38.9	37.8	95	97.1	7.382
6	-5.1	36.0	34.2	95	97.1	7.368
8	-1.6	42.2	41.4	89	96.5	7.368
37	-0.4	39.0	41.9	93	96.9	7.381
38	-1.9	35.1	38.3	80	95.7	7.385
46	-2.0	37.6	37.7	94	97.1	7.389
57	-5.8	37.1	27.5	104	97.8	7.412
58	-	37.0	-	97	97.0	7.348
59	-4.2	36.4	33.4	98	97.4	7.388
71	-3.1	37.8	35.4	107	97.8	7.389
72	-	37.7	-	94	96.9	7.364
92	-6.6	30.8	35.0	104	97.4	7.338
99	-0.9	41.4	40.0	98	97.3	7.388
111	-4.5	33.1	32.3	98	97.4	7.393
112	-5.1	38.9	33.3	95	97.1	7.375
10	-5.3	35.0	33.3	107	97.7	7.372
35	-4.9	33.4	31.2	91	97.0	7.395
45	-2.6	38.3	38.1	94	97.0	7.377
68	-4.9	37.4	33.2	95	97.1	7.378
75	-2.4	40.0	40.2	96	97.0	7.366
84	-5.5	34.9	32.6	95	97.1	7.374
86	-4.5	37.8	32.9	99	97.4	7.388
97	-4.7	38.5	33.1	94	97.1	7.382
109	-5.3	32.5	30.3	95	97.3	7.395
113	-7.7	28.5	28.2	108	97.9	7.375
117	-5.8	35.3	30.3	95	97.2	7.388
mean	-3.95	36.5	34.9	96.7	97.18	7.379
S.D.	1.938	3.06	4.25	5.9	0.43	0.0141
n	26	27	26	27	27	27

TABLE III - 8A (CONTINUED)

⅔ W max.						
No.	BE	$PETCO_2$	$PaCO_2$	PaO_2	SaO_2	pH
2	-4.8	33.5	33.2	103	97.6	7.380
5	-4.0	37.1	36.8	96	97.1	7.366
6	-2.6	30.1	36.4	94	97.1	7.389
8	-5.3	38.2	31.7	96	97.3	7.383
37	-7.1	35.1	32.3	98	97.2	7.351
38	-6.1	34.1	29.4	81	96.0	7.390
46	-4.7	32.3	29.9	90	97.0	7.408
57	-6.8	31.0	25.5	103	97.8	7.414
58	-	30.6	-	98	97.1	7.326
59	-7.0	33.5	32.9	101	97.3	7.348
71	-5.9	34.9	28.2	107	97.9	7.404
72	-	30.9	-	100	97.4	7.375
92	-4.9	27.0	31.8	107	97.8	7.388
99	-4.1	40.0	37.0	96	97.0	7.363
111	-6.8	30.2	24.0	93	97.4	7.428
112	-5.6	32.4	31.5	97	97.3	7.382
10	-6.9	30.6	31.9	106	97.7	7.356
35	-8.7	28.4	26.8	90	96.8	7.368
45	-6.0	35.5	31.2	101	97.5	7.377
68	-13.0	33.1	28.0	94	96.5	7.276
75	-6.6	36.4	36.5	100	97.1	7.328
84	-9.5	29.2	25.2	97	97.3	7.368
86	-7.3	33.5	30.9	103	97.5	7.357
97	-5.9	32.8	31.1	101	97.5	7.378
109	-	-	-	-	-	-
113	-9.7	18.9	20.7	111	98.2	7.411
117	-4.9	33.1	30.2	96.5	97.4	7.403
mean	-6.38	32.4	30.6	98.46	97.3	7.3737
S.D.	2.15	4.09	4.08	6.28	0.44	0.0316
n	25	26	25	26	26	26

TABLE IV - 5A

Showing the results for each patient
at each level of work.

(Oxygen consumption during hypoxic exercise)

TABLE IV - 5A

Patient No.	Work (Watts)	$PaCO_2$	PaO_2	SaO_2	pH	$\dot{V}O_2$	$\dot{V}O_2$ expected
1	0	25	98	97.6	7.43		
	10	30	59	91.0	7.41	458	448
	20	26	54	88.4	7.41	586	567
2	0	29	52	88.4	7.43		
	10	27	30	60.7	7.43	366	448
3	0	27	42	79.0	7.41		
	10	30	32	61.3	7.38	343	412
4	0	29	73	94.8	7.39		
	15	30	47	81.3	7.37	445	507
5	0	27	64	93.8	7.46		
	7	24	43	81.0	7.43	376	391
	14	23	41	77.2	7.39	445	469
6	0	27	46	85.2	7.47		
	10	31	40	75.2	7.41	416	424
	20	29	37	67.4	7.38	489	536
7	0	32	43	80.3	7.43		
	7	32	30	60.5	7.43	350	412
8	0	24	69	95.1	7.46		
	10	29	52	85.5	7.37	359	432
9	0	32	78	96.2	7.45		
	15	33	63	92.8	7.44	488	507
	30	27	60	91.0	7.40	650	686
10	0	31	59	91.6	7.43		
	10	29	43	82.4	7.47	384	448
11	0	31	40	77.0	7.42		
	11	33	23	40.0	7.38	386	460
	22	31	21	32.0	7.34	373	591
12	0	29	56	88.6	7.37		
	20	36	34	62.0	7.34	544	594
	40	42	33	57.0	7.39	680	934

TABLE IV - 9a

Showing values of forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), the FEV_1/FVC ratio expressed as a percentage (FEV_1/FVC). Maximum voluntary ventilation (MVV) for all the children. Expected values (exp.) follow each observed value. The expected value for MVV is calculated from the expected FEV_1. The starred values are abnormal.

Patient		FEV_1	Exp.	%	FVC	Exp.	%	FEV_1/FVC	MVV	Exp.	PEFR	Exp.
1	Fallot's tetralogy	1.21	1.1	100	1.21	1.2	101	100	54	36.5	290	175
2		1.43	1.5	95	1.60	1.6	100	89	32.5	50.3	190	220
3		0.88	0.8	110	0.88	0.8	110	100	33.3	26.1	165	255
4		0.94	1.05	89	0.94	1.05	89	100	20.2	34.7	95	160
5		0.72	1.1	65	0.72	1.2	65	100	42.4	34.5	130	190
6		0.86	1.55	57	0.88	1.65	53	100	53.5	52.0	210	220
7		1.27	2.0	63	1.27	2.25	56	100	55.4	67.5	310	280
8		1.32	1.35	98	1.38	1.4	98	96	37.7	45.1	230	200
9		0.99	1.25	79	1.16	1.25	93	85	27.9	41.6	180	190
10		1.49	1.4	106	1.8	1.4	129	78	58.2	46.8	240	200
11	Totally corrected Fallot's tetralogy	1.29	1.4	92	1.37	1.45	95	94	46.8	46.8	145	205
12		2.04	2.35	87	2.04	2.7	76	100	50.0	79.6	320	320
13		1.54*	2.65	58	2.53	3.0	84	61	82.2	89.9	300	345
14		1.19*	1.85	64	1.30	2.0	65	92	40.6	62.3	180*	265
15		0.83*	1.8	46	1.54	1.95	79	54	53.6	60.6	190	260
16		0.99	0.9	110	1.16	1.0	116	85	28	29.6	140	170
17		1.7	1.6	106	2.09	1.8	116	81	56	53.7	200	240
18		1.65	1.9	87	1.98	2.05	97	83	74	64.5	300	270
19		1.76	2.25	78	2.09	2.45	85	84	75	76.1	280	325
20		1.50	1.4	107	1.61	2.25	71	93	48	46.8	210	285
21		1.27*	2.25	56	1.32*	2.55	52	96	50	76.1	220	310

TABLE IV - 13a

Showing the steady state exercise results for the children with Fallot's tetralogy.

Patient	Work (watts)	$\dot{V}O_2$	$\dot{V}_E$	$\dot{Q}_p$	$\dot{Q}_s$	$\dot{Q}$ exp.	V.A.	H.R.	H.R. exp.
1	0	128	6.5	2.1	2.2		3.9		
	10	458	22.0	4.7	5.6	6.9	16.3	158	130
	20	586	28.2	4.3	5.2	7.7	15.8	187	148
2	0	194	10.9	1.2	3.4		52.2		
	20	514	39.6	-	-	6.4	83.9	181	154
3	0	143	5.6	1.7	2.4		30.7		
	10	366	16.3	2.1	4.4	5.2	52.9	134	135
4	0	98	5.5	0.9	2.1		55.5		
	10	343	19.1	3.8	6.0	5.3	64.9	152	140
5	0	130	5.8	1.8	2.0		8.5		
	15	445	23.4	5.1	7.3	5.7	30.2	155	140
6	0	112	5.3	1.0	1.1		8.2		
	10	359	18.1	3.5	4.8	5.6	27.7	170	156
7	0	148	5.5	1.7	1.9		6.6		
	15	488	22.3	4.9	5.6	6.4	12.4	134	127
	30	650	33.3	5.1	5.8	7.3	12.5	150	146
8	0	110	5.2	1.7	2.1		17.4		
	7	376	18.2	5.0	9.9	5.6	48.8	150	-
	14	445	28.2	4.1	7.2	6.0	42.2	186	148
9	0	156	6.4	2.5	3.5		28.1		
	10	384	18.7	3.5	6.1	5.5	38.9	112	138
10	0	180	12.3	3.0	5.8				
	10	416	25.0	3.9	7.4	5.8	5.8	142	144
	20	489	30.4	3.4	6.4	6.3	6.3	170	156

TABLE IV - 14A

Steady-state exercise results for the children with 'totally corrected' Fallot's tetralogy

Patient	Work (watts)	$\dot{V}O_2$	$\dot{V}E$	$\dot{Q}_p$	$\dot{Q}_s$	$\dot{Q}$ exp.	V.A.	H.R.	H.R. exp.
11	0	108	5.5	1.2	1.3		5.1		
	13	457	14.8	3.5	3.8	6.1	8.6	138	130
	26	565	26.0	4.6	5.3	6.6	12.9	176	156
12	0	514	18.4	5.6	6.3		10.6		
	20	628	21.6	4.8	5.9	7.4	17.7	134	134
	40	923	36.6	4.8	5.8	9.1	17.3	167	160
13	0	178	5.1	3.4	3.6		6.8		
	35	766	20.0	5.5	6.0	8.3	8.4	137	141
	70	1226	42.4	7.7	9.1	10.9	15.3	185	174
14	0	226	9.0	4.0	4.1		2.5		
	20	533	16.9	7.9	8.3	6.8	4.4	155	146
	30	659	23.3	6.3	6.5	7.5	3.5	176	162
15	0	378	16.5	4.2	5.8		27.2		
	15	412	19.7	3.0	4.5	6.1	33.2	137	127
	30	643	35.2	4.5	5.4	7.3	35.1	169	162
16	0	127	5.2	2.3	2.4		5.7		
	8	342	13.9	3.6	3.8	5.1	5.7	107	137
	16	422	18.0	4.3	4.6	5.5	6.7	131	151
17	0	145	5.2	2.2	2.3		2.8		
	20	545	16.4	5.6	5.7	6.6	1.7	124	139
	40	759	28.0	6.6	6.7	7.8	1.0	172	162
18	0	164	6.6	2.5	2.6		4.7		
	20	605	20.6	4.5	4.6	7.2	2.1	141	156
	40	1172	48.2	8.4	8.5	10.4	1.3	167	206
19	0	173	7.1	3.0	3.3		8.4		
	20	584	18.9	5.8	7.1	7.3	17.2	135	139
	40	865	30.8	5.8	7.0	8.8	17.2	163	170
20	0	151	5.4	1.8	1.9		4.1		
	20	528	16.7	5.8	6.1	6.7	4.1	116	132
	40	830	32.7	7.7	8.0	8.4	3.8	155	162
21	0	127	4.1	2.6	2.6		0		
	20	514	15.6	4.9	4.9	6.7	1.0	150	122
	40	720	22.8	6.9	7.0	7.9	1.4	193	146

TABLE V - 5A

Showing the values for forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), peak expiratory flow rate (PEFR) and maximum voluntary ventilation ($M\dot{V}V$) in each child. Each observed value is followed by the expected value (exp.).

Patient No.	FEV_1	Exp.	FVC	Exp.	PEFR	Exp.	MVV	MVV Exp.
1	1.6	2.166	2.31	2.45	210	296	70.1	68.5
2	2.42	2.727	2.84	3.11	350	355	59.6	87.1
3	1.8	2.013	1.9	2.27	315	281	61.2	63.5
4	2.2	2.549	2.69	2.90	360	336	89.4	81.2
5	2.36	2.636	2.69	2.734	350	348	85.3	85.4
6	1.6	1.733	1.76	1.94	250	251	69.5	54.2
7	1.10	1.070	1.32	1.160	155	183	29.4	32.2
8	1.32	1.095	1.54	1.19	200	185	41.8	33.1
9	2.42	3.033	3.025	3.47	390	386	88	97.3

TABLE V - 9A

Steady state results for each child. The cardiac output and stroke volume values at rest are based on the end tidal PCO_2. On exercise these values are based on an assumed normal dead space.

Patient	$\dot{V}O_2$	$\dot{V}E$	Exp.	HR	Exp.	$\dot{Q}(VD)$	Exp.	$\dot{Q}ear$	SV(VD)	Exp.
1	-	5.7	-	-	-	-	-	-	-	-
	630	15.3	20.3	126	139	6.7	7.3	6.7	53	53
	981	25.8	31.0	173	169	8.1	9.3	8.1	47	57
2	258	20.5	-	-	-	6.5	4.9	4.7	-	-
	774	26.8	23.4	138	140	7.6	8.3	7.5	56	61
	1052	37.9	31.9	167	161	9.4	9.9	9.9	56	64
3	147	5.9	-	-	-	2.2	3.3	2.6	-	-
	634	21.6	20.8	163	143	5.7	7.2	6.1	35	51
	1069	33.4	34.0	207	179	6.8	9.7	8.2	33	56
4	357	10.5	-	-	-	4.3	6.0	6.1	76	-
	851	27.7	26.1	139	150	7.9	8.7	7.9	57	60
	1221	44.9	37.4	180	175	9.3	10.8	9.3	52	64
5	229	8.5	-	-	-	2.9	4.4	4.0	-	-
	769	19.9	23.3	144	140	6.9	8.4	7.8	48	53
	1279	40.5	42.2	207	176	9.2	11.2	9.1	45	53
6	119	6.9	-	-	-	3.2	4.0	3.0	-	-
	499	14.0	17.3	132	134	5.3	6.4	4.8	40	46
	827	25.7	27.3	165	168	8.0	8.2	7.2	49	50
7	125	3.3	-	-	-	2.1	3.0	-	-	-
	413	9.3	15.7	138	132	4.9	5.6	-	35	37
	622	17.8	16.9	167	164	6.0	6.8	-	35	39
8	371	10.8	-	-	-	6.1	6.2	4.9	-	-
	405	12.3	15.9	128	134	3.7	5.5	5.0	39	37
	622	19.6	22.5	171	163	5.4	6.9	5.7	34	39
9	204	7.0	-	-	-	3.1	4.0	3.2	-	-
	731	13.5	15.8	119	129	7.3	8.2	5.7	62	65
	1122	30.6	33.4	167	158	9.1	10.5	8.4	55	69

TABLE V - 13a

Showing the FEV_1, FVC, PEFR and MVV for each child. Each observed value is followed by the expected normal value.

	Ht. (cm)	FEV_1	Exp.	FVC	Exp.	PEFR	Exp.	MVV	Exp.
1	145.5	1.9	2.65	2.42	3.02	315	347	78	84.6
2	122.5	1.49	1.673	1.77	1.583	245	224	51.7	45.7
3	161.5	3.08	3.272	3.74	3.494	460	430	73	111.6
4	120.5	1.15	1.59	1.43	1.485	225	214	46.4	42.3
5	145	1.815	2.595	2.31	2.685	280	343	79.6	83.8
6	148	2.145	2.778	2.585	3.170	275	360	63.8	88.8
7	152	2.31	2.982	2.8	3.41	340	381	88.0	95.6
8	130	-	1.86	-	2.09	-	265	63.6	58.4
9	131.5	1.980	1.937	2.310	2.18	310	273	61.2	60.9
10	159	2.585	3.169	2.850	3.371	400	417	82.8	107.4
11	115.5	0.88	1.12	1.0	1.22	240	188	-	33.9

TABLE V - 17A

Showing the results of the steady state tests of children with pulmonary stenosis. Both the observed and expected values for cardiac output at rest are based on the end tidal PCO_2. Those on exercise are based on an assumed normal dead space.

Patient	$\dot{V}O_2$	$\dot{V}E$	Exp.	HR	Exp.	$\dot{Q}(VD)$	Exp.	$\dot{Q}ear$	SV(VD)	Exp.	VD pred.
1	240	11.7	-	81	-	3.4	4.5	4.0	-	-	-
	1332	41.5	40.6	159	179	9.1	11.5	9.0	57	66	80
2	133	5.9	-	91	-	2.8	3.1	3.0	-	-	-
	500	14.0	18.4	134	156	5.1	6.4	4.2	38	42	63
	705	21.5	25.9	170	182	6.0	7.5	5.4	35	42	69
3	265	10.1	-	116	-	4.9	4.8	5.2	-	-	-
	964	32.2	27.3	151	151	9.6	10.0	9.9	63	67	125
4	126	4.3	-	100	-	2.3	3.0	2.0	-	-	-
	455	14.6	17.1	135	152	3.7	6.1	3.3	28	41	51
	617	26.0	23.1	180	175	4.9	7.1	4.1	27	41	58
5	196	7.2	-	95	-	4.2	3.9	2.8	-	-	-
	612	15.6	17.7	131	140	6.0	7.5	4.2	46	57	78
	923	28.0	29.2	171	171	7.5	9.3	6.2	44	57	86
6	216	6.9	-	114	-	6.3	4.2	3.8	-	-	-
	647	18.7	19.4	134	126	6.5	7.7	4.8	48	61	89
	1004	33.6	30.3	154	156	7.4	9.7	6.3	48	65	94
7	170	5.0	-	73	-	5.9	3.6	4.8	-	-	-
	753	19.5	22.2	108	132	9.1	8.4	9.3	84	64	97
	1306	37.5	39.0	150	170	11.2	11.5	9.7	75	71	108
8	232	8.0	-	115	-	3.2	4.4	3.4	-	-	-
	550	16.0	18.6	124	136	5.8	6.7	4.9	47	48	69
	605	19.7	20.2	153	143	5.0	7.0	5.0	33	49	70
9	216	7.4	-	96	-	3.7	4.2	3.2	-	-	-
	631	20.2	20.9	137	168	6.3	7.2	6.3	46	50	85
	924	34.1	29.8	168	171	7.7	8.9	7.1	46	53	95
10	-	-	-	-	-	-	-	-	-	-	-
	650	19.6	16.2	127	125	6.8	8.0	7.7	54	66	93
	1047	35.1	30.9	161	161	8.7	10.3	7.1	54	66	109
11	-	-	-	-	-	-	-	-	-	-	-
	542	20.4	20.0	145	154	5.8	6.3	5.3	40	39	55

BIBLIOGRAPHY

Anderson, S.D., (1972) Physiological aspects of exercise induced asthma, Ph.D. Thesis, London University.

Astrand, P-O. (1952), Experimental Studies of Physical working capacity in relation to sex and age, E. Munksgaard, Copenhagen.

Asmussen, E. (1967) Exercise and the regulation of ventilation, Circulation Research Suppl. to Vols. 20 and 21, 132 - 145.

Benson, P.F., Joseph, M.C. and Ross, D.N. (1962), Total surgical correction of Fallot's tetralogy in the first year of life, Lancet, 2, 326 - 327.

Braunwald, E., Goldblatt, A., Aygaen, M.M., Rukoff, D. and Morrow, A.G. (1963), Congenital aortic stenosis I. Clincial and haemadynamic findings in 100 patients, Circulation, 27, 426 - 462.

Bristow, J.D., Kloster, F.E., Lees, M.H., Menashe, V.D., Griswood, H.E. and Starr, A., (1970), Serial cardiac catheterisations and exercise haemadynamics after correction of tetralogy of Fallot, Circulation, 41, 1057 - 1066.

Burnell, R.H., Woodson, R.D., Lees, M.H., Bristow, J.D., and Starr, A. (1969), Results of correction of Fallot's tetralogy in children under four years of age, Journal of Thoracic and Cardiovascular Surgery, 57, 153 - 159.

Byrne-Quinn, E., Sodal, I.E. and Weil, J.V., (1972), Hypoxic and hypercapnic ventilatory drives in children native to high altitude, Journal of Applied Physiology, 32, 44 - 46.

Campbell, E.J.M. (1966), The relationship of the sensation of breathlessness to the act of breathing, 'Breathlessness' Ed. Howell, J.B.L. and Campbell, E.J.M., Blackwell, Oxford, 55 - 63.

Campbell, M. and Thorne, M.G. (1956), Congenital Heart Block, British Heart Journal, 18, 90 - 102.

Cassells, D.E.and Morse, M. (1962), Cardiopulmonary data for children and young adults, Thomas, Springfield, Illinois.

Cayler, G.G., Rudolph, M. and Nadas, A.S. (1963), Systemic blood flow in infants and children with and without heart disease, Paediatrics, 32, 186 - 201.

Clark, J.H. and Greenleaf, J.E. (1971), Electronic bicycle ergometer: a simple calibration procedure, Journal of Applied Physiology, 30, 440 - 442.

Coates, J.E. (1968), Lung Function, Blackwell, London.

Cohen, L.S., Buanwald, E., Ross, J., and Morrow, A.G. (1968), The natural history of mild congenital aortic stenosis in patients studied by serial left heart catheterisation, Annals of Internal Medicine, 68, 1152 - 1153.

Cross, K.W., Dawes, G.S. and Mott, J.C. (1959), Anoxia, oxygen consumption and cardiac output in new born lambs and adult sheep, Journal of Physiology, 146, 316 - 343.

Cumming, G.R. and Alexander, W.D. (1968), The callibration of bicycle ergometers, Canadian Journal of Physiology and Pharmacology, 48, 917 - 919.

Denison, D., Edwards, R.H.T., Jones, G. and Pope, H. (1971), Estimates of the CO_2 pressures in systemic arterial blood during rebreathing on exercise, Respiration Physiology, 11, 186 - 196.

Dexeter, L., Harken, D.E., Cobb, L.A., Novack, P., Schlant, R.C., Phinney, A.O. and Hayes, F.W. (1958), Aortic stenosis, Archives of Internal Medicine, 101, 254 - 266.

Duffie, E.R. and Adams, F.H. (1963), The use of the working capacity test in the evaluation of children with congenital heart disease, Paediatrics, 32, 757 - 768.

Du Shane, J. and Weidman, W. (1965), Five congenital heart defects: A study of the profile and natural history, Circulation, 32 (Suppl. 3) III - 1 to III - 3.

Documenta Geigy Scientific Tables (1962), Geigy, Manchester.

Edelman, N.H., Lahiri, S., Braud, O., Cherniack, N.S., and Fishman, A.P. (1970), Blunted ventilatory response to hypoxia in congenital heart disease, New England Journal of Medicine, 282, 405 - 411.

Edhag, O., and Zetterquist, S. (1968), Peripheral circulatory adaptation to exercise in restricted cardiac output, Scandanavian Journal of Clinical and Laboratory Investigation, 21, 123 - 135.

Friedman, W.F., Modlinger, J., and Morgan, J.R., (1971) Serial haemodynamic observations in asymptomatic children with valvar aortic stenosis, Circulation, 43, 91 - 97.

Gadhoke, S. and Jones, N.L. (1969), The response to exercise of boys aged 9 to 15, Clinical Science, 37, 789 - 801.

Gazetopoulos, N., Davies, H., Oliver, C. and Deuchar, (1966), Ventilation and Haemodynamics in heart disease, British Heart Journal, 28, 1 - 15.

Glew, R.H., Varghese, P.J., Krovetz, L.J., Dorst, J.P. and Rowe, R.D. (1969), Sudden death in congenital aortic stenosis, American Heart Journal, 78, 615 - 625.

Godfrey, S., (1970), Manipulation of the indirect Fick Principle by a digital computer programme for the calculation of exercise physiology results, Respiration, 27, 513 - 532.

Godfrey, S., (1971), The study of physiological responses to exercise in children, M.D. Thesis, London University.

Godfrey, S. and Davies, C.T.M. (1970), Estimates of arterial PCO_2 and their effect on the calculated values of cardiac output and dead space on exercise, Clinical Science, 39, 529 - 537.

Godfrey, S., Davies, C.T.M., Wozniak, E. and Barnes, C.A. (1971), Cardio-respiratory response to exercise in normal children, Clinical Science, 40, 419 - 431.

Godfrey, S., Kamiburoff, P.L. and Nairn, J.R. (1970) Spirometry, lung volumes and airway resistance in normal children aged 5 to 18 years, British Journal of Diseases of the Chest, 64, 15 - 24.

Godfrey, S., Wozniak, E., Courtenay-Evans, R.J. and Samuels, C.S. (1971a), Ear lobe blood samples for blood gas analysis at rest and during exercise, British Journal of Diseases of the Chest, 65, 58,- 64.

Goldberg, S.J., Adams, F.H. and Hurwitz, R.A. (1967), Effect of cardiac surgery on exercise performance, Journal of Paediatrics, 71, 192 - 197.

Goldberg, H., Bakst, A.A. and Bailey, C.P. (1954), The dynamics of aortic valvular diseases, American Heart Journal, 47, 527 - 559.

Goldberg, H., Denton, C., Bender, S. and Uricchio, J. (1958), The haemodynamic and clinical characteristics of rheumatic aortic stenosis, Diseases of the Chest, 33, 201 - 213.

Goldberg, S.J., Mendes, F. and Hurwitz, R. (1969), Maximum exercise capability of children as a function of specific cardiac defects, American Journal of Cardiology, 23, 349 - 353.

Goldman, B.S., Mustard, W.T., and Trusler, G.S. (1968), Total correction of Fallot's tetralogy, British Heart Journal, 30, 563 - 568.

Gotsman, M.S. (1966), Haemodynamic and cine-angiocardiographic changes after one stage repair of Fallot's tetralogy, British Heart Journal, 28, 448 - 460.

Haider, R., Finnegan, P., Sanchos-Fornos, S., Abrams, L.P., Singh, S.P. and Parsons, C.G. (1971), Twelve year follow-up after surgical correction of Fallot's tetralogy, British Heart Journal, 34, 205 - 206.

Halloran, K.H., (1971), The tetemetered exercise electrocardiogram in congenital aortic stenosis, Paediatrics, 47, 31 - 39.

Hancock, E.W. and Fleming, D.R. (1960), Aortic Stenosis, Quarterly Journal of Medicine, 29, 209 - 234.

Hart, M.C., Orzalesi, M.M. and Cook, C.D. (1963), Relation between anatomic respiratory dead space and body size and lung volume, Journal of Applied Physiology, 18, 519 - 522.

Holmgren, A., Karlberg, P. and Pernow, B., (1959), Circulatory adaptation at rest and during muscular work in patients with complete heart block, Acta Medica Scandanavica, 164, 119 - 130.

Howitt, G (1966). Haemodynamic effects of exercise in pulmonary stenosis, British Heart Journal, 28, 152 - 160.

Ikkos, D. and Hanson, J.A. (1960), Response to exercise in complete atrio ventricular block, Circulation, 22, 583 - 590.

Ikkos, D., Jonsson, B. and Linderholm, H. (1966), The effect of exercise in pulmonary stenosis with intact ventricular septum, British Heart Journal, 28, 316 - 330.

International Business Machines (1954), Scientific Statistical Package based on Ostle. B., Statistics in Research, Iowa State College Press.

Jones, N.L., McHardy, G.J.R., Naimark, A. and Campbell, E.J.M. (1966), Physiological dead space and alveolar arterial gas pressure differences during exercise, Clinical Science, 31, 19 - 29.

Jones, N.L., Campbell, E.J.M., McHardy, G.J.R., Higgs, B.E. and Clode, M. (1967), The estimation of carbon dioxide pressure of mixed venous blood during exercise, Clinical Science, 32, 311 - 327.

Jonsson, B. and Lee, S.J.K. (1968), Haemodynamic effects of exercise in isolated pulmonary stenosis before and after surgery, British Heart Journal, 30, 60 - 66.

Kelman, G.R., Coleman, A.J. and Nunn, J.F. (1966), Evaluation of a microtenometer used with a capillary glass pH electrode, Journal of Applied Physiology, 21, 1103 - 1107.

Kennaird, D.L. (1971), Oxygen consumption and evaporative water loss in infants with congenital heart disease, Ph.D. Thesis, London University.

Kirklin, J.W., Wallace, R.B., McGoon, D.C. and Dushane, J.W. (1965), Early and late results after intracardiac repair of tetralogy of Fallot: 5 year review of 337 patients, Annals of Surgery, 162, 578 - 589.

Landtman, B. and Wolf, M.D. (1965), Total correction of Fallot's tetralogy II: changes in the electrocardiogram after surgery, Circulation, 31, 394 - 402.

Leader, (1970), Control of Breathing, British Medical Journal, 3, 720 - 721.

Leusen, I.R. (1956), Chemosensitivity of the Respiratory centre, American Journal of Physiology, 176, 45 - 51.

Lee, S.J.K., Jonsson, B., Bevegard, S., Karlöf, I. and Astrom, H. (1970), Haemodynamic changes at rest and during exercise in patients with aortic stenosis of varying severity, American Heart Journal, 79, 318 - 331.

Lillehei, C.W., Levy, M.J., Adams, P., Anderson,R.C. (1964), Corrective surgery for tetralogy of Fallot, Journal of Thoracic and Cardiovascular Surgery, 48, 556,-576.

McIlroy, M.B. (1963), The respiratory response to exercise, Paediatrics, 32, 680 - 682 (October supplement).

Moss, A.J. (1961), Congenital complete atrioventricular block. Clinical features, haemodynamic findings and physical working capacity, The Journal - Lancet, 81, 542

Moss, A.J. and Adams, F.H. (1968), Heart disease in infants, children and adolescents, Williams and Wilkins, Baltimore.

Nakamura, F.F. and Nadas, A.S. (1964), Congenital complete atrioventricular dissociation due to complete or advanced atrioventricular block., New England Journal of Medicine, 270, 1261 - 1268.

Paul, M.H., Rudolph, A.M. and Nadas, A.S. (1958), Congenital complete atrioventricular block: problems of clinical assessment, Circulation, 18, 183 - 190.

Reynolds, J., Nadas, A.S., Rudolph, A.M. and Gross, R.E. (1960), Critical congenital aortic stenosis with minimal electrocardiographic changes, New England Journal of Medicine, 262, 276 - 282.

Scholander, P.F. (1947), Analysis for accurate estimation of respiratory gases in one-half cubic centimeter samples, Journal of Biological Chemistry, 167, 235.

Scholander, P.F. (1960), Experimental studies in asphyxia in animals, In Walker, J. and Turnbull, A.C., Oxygen supply to the foetus, Blackwell Scientific Publications, Oxford,

Snijders, H. (1970), De Totale Correctie Van de Tetralogie van Fallot, Thesis, University of Leiden, Holland.

Sorensen, S.C. and Severinghaus, J.W. (1968), Respiratory Insensitivity to hypoxia persisting after correction of tetralogy of Fallot, Journal of Applied Physiology, 25, 221 - 223.

Tanner, J.M. (1958), Modern trends in paediatrics, Butterworths, London.

Wallgren, A. and Winblad, S. (1937), Congenital Heart Block, Acta Paediatrica, 20, 175.

Weil, J.V., Byrne-Quinn, E., Sodal, I.E., Friesen, W.O., Underhill, B.E., Filley, G.F. and Grover, R.F. (1970), Hypoxic ventilatory drive in normal man, Journal of Clinical Investigation, 49, 1061 - 1072.

Weng, T.R. and Levison, H., (1969), Standards of Pulmonary Function in children, American Review of Respiratory Diseases, 99, 879 - 894.

West, J.B., (1965), Ventilation/blood flow and gas exchange, Blackwell, Oxford, England.

Wright, F.S., Adams, P. and Anderson, S.C. (1959), Congenital atrio ventricular dissociation due to complete or advanced atrioventricular block, American Journal of Diseases of Children, 98, 72.

Wood, L.D.H., Prichard, S., Weng, T.R., Kruger, K., Bryan, A.C. and Levison, H. (1971), Relationship between anatomic dead space and body size in health, asthma and cystic fibrosis, American Review of Respiratory Disease, 104, 215 - 222.

Ziedfard, E. (1972), Personal communication.

Zeidfard, E., Silverman, M. and Godfrey, S. (1972), Reproducibility of the indirect (CO_2) Fick method for the calculation of cardiac output, Journal of Applied Physiology, 33, 141.

Zeigler, R.F. (1951), Electrocardiographic studies in normal infants and children, Thomas, Springfield, Illinois.