ANAEROBIC METABOLISM AND CARDIAC OUTPUT IN PATIENTS WITH SYMPTOMATIC HEART DISEASE[1]

by

Clarence Guenter[2]

1. From the Department of Medicine, University of Manitoba and the Cardio-pulmonary Division, Clinical Investigation Unit, Winnipeg General Hospital, Winnipeg, Manitoba.

2. Research Fellow of the Medical Research Council of Canada.

ANAEROBIC METABOLISM AND CARDIAC OUTPUT IN PATIENTS WITH SYMPTOMATIC HEART DISEASE

INTRODUCTION:

Since Hill in 1922 (1) introduced the concept of oxygen debt, and related this to lactic acid accumulation during exercise, these parameters have been considered indices of anaerobic metabolism. Numerous studies have been conducted measuring the oxygen debt (2-6) and blood lactate levels (6-16) in patients with heart disease. Several studies (4,7,8,9,) attempted to correlate cardiac output with oxygen debt or blood lactate levels. In general, although wide individual variability was present, the oxygen debt was somewhat higher and lactate levels increased more during exercise in patients with circulatory insufficiency than in normal subjects. The increased lactate accumulation and increased levels of oxygen debt were therefore thought to be due to an inadequate cardiac output, although none of the studies measured both parameters and correlated them with measured cardiac outputs.

This study was conducted to determine the oxygen debt, blood lactate and cardiac output response to exercise of sufficient severity to produce symptoms, in patients with heart disease. These changes were compared to those observed in normal subjects, in response to similar exercise.

METHODS AND MATERIALS:

Five female and five male patients were chosen from the wards and out-patient services of the Winnipeg General Hospital. The criteria for selection demanded that (1) they have a significant cardiac lesion; (2) they have symptoms attributable to this lesion, limiting their activity on mild to moderate exertion; and (3) they be fully ambulant at the time of the study. The physical characteristics and diagnosis of the patients are listed in Table I. Patients A-C had complete heart block, attributed to arteriosclerotic heart disease. Patients D-H had rheumatic valvular disease. Patient I had luetic aortic insufficiency and J had muscular subaortic stenosis. In patients D-H and J, the diagnosis was confirmed by cardiac catheterization. Only patient H had clinical evidence of congestive heart failure at the

time of the study. All patients suffered from dyspnea or excessive fatigueability on mild to moderate exertion and patients G and H had episodes of paroxysmal nocturnal dyspnea.

Four female and six male healthy active normal subjects, nine of whom were hospital personnel, were the control group for these studies. The physical characteristics of the subjects are listed in Table II. None of the subjects was familiar with the procedure from previous studies and none was considered physically trained. All the subjects had a normal chest x-ray within one year preceding the study, and the two who were more than 45 years old had normal electrocardiograms.

A preliminary run was carried out on the day prior to the test, to acquaint the subject or patient with the apparatus. On the day of the study, the subject came to the laboratory in the fasting state, and was allowed to rest comfortably in the supine position. A polyethylene catheter was introduced percutaneously into a median basilic or cephalic vein and advanced to the central venous system (generally mid subclavian vein). A teflon catheter was passed percutaneously into the brachial artery. Front-back E.K.G. electrodes were attached to monitor heart rate. The subject was then seated in a comfortable upholstered chair with a head rest, placed on the treadmill and again allowed to rest for 45 minutes. Immediately preceding the exercise, the subject was assisted from the sitting to the standing position, the chair was removed from the treadmill and the treadmill set in motion. When the treadmill was stopped at the end of the exercise period, the upholstered chair was immediately replaced onto the treadmill and the subject again comfortably seated. The oxygen consumption was determined for at least ten minutes while at rest before the exercise, throughout the exercise period and for thirty minutes after the cessation of exercise. Cardiac output determinations were made in duplicate at rest during the 15 minute period immediately preceding the onset of exercise, and at five minutes and nine minutes after the exercise was started. The latter two values did not differ significantly, suggesting that a

steady state had been achieved and they were considered as duplicate determinations. Arterial blood was sampled for the determination of pH, pCO_2, pO_2, lactate and pyruvate at rest, seven and nine minutes after the exercise started, and at two, five and forty five minutes after the exercise was stopped.

The treadmill was set at an incline of 4.4^{o} for all studies. In the patients, the treadmill rate was adjusted during the preliminary run, so that symptoms limited the duration of exercise to 10 minutes. The normal subjects were studied at approximately the same rate as the patients. The total exercise duration ranged from 10-12 minutes in all studies.

Repeat studies were carried out for all parameters in subjects 8 and 9 and for lactate, pyruvate and oxygen debt only in subjects 3 and 5. Studies were carried out at 2 treadmill rates in subjects 1 and 9. In patient D, a treadmill rate which did not produce symptoms was studied first, followed by a study in which the exercise was sufficient to produce symptoms. Only values for the second work load were used for comparison with the normal subjects. All studies in any given subject were carried out on the same day, with a one hour rest period between each exercise period.

In patients A-E cardiac output determinations were made on a bicycle ergometer rather than on the treadmill and consequently were not simultaneous with the oxygen debt determinations. The work load during the bicycle exercise was similar to the treadmill exercise, as demonstrated by the oxygen consumption. Cardiac output determinations were not carried out in patients G and I, because of severe regurgitant valvular lesions. In subject 4, the cardiac output was determined at rest only, since an urticarial rash appeared following the initial dye injection.

The oxygen consumption was determined by the open circuit technique. Expired gases were collected in a multiple bag system and analysed on a Beckman paramagnetic oxygen analyser and a Beckman infra red carbon dioxide analyser.

The total excess oxygen consumption due to exercise was calculated as the oxygen consumption throughout the exercise, and the recovery period following the exercise, minus the resting oxygen consumption for that period of time. (The resting oxygen consumption preceding the exercise was used in this calculation). The oxygen debt was calculated as defined by Hill (1); the resting oxygen consumption was subtracted from the oxygen consumption during the recovery period immediately following the exercise.

The Hamilton-Stewart indicator dilution technique was utilized in the determination of cardiac output. Five mgm. of indocyanine green were injected into the venous catheter from a calibrated syringe. The tubing was then rapidly flushed with five cc. of normal saline. Arterial blood was withdrawn at a constant rate of 23.1 cc/min. by a Harvard Apparatus Co. withdrawal pump, through the cuvette of a Gilford Densitometer. The dye curve was inscribed by a Honeywell recorder. At least five minutes transpired between injections at rest, and about four minutes between injections during exercise. Arterial blood was drawn for calibration about one hour after the exercise period; known quantities of the dye added to 10 cc. aliquots of the blood were then drawn through the cuvette of the densitometer in the same manner as during the determination of the cardiac output.

Arterial blood pH and pCO_2 were determined by the Astrup micro technique and pO_2 was determined on a Severinghaus electrode. Arterial blood lactate and pyruvate were measured by modifications of the enzymatic techniques previously described by Horn and Bruns (17) and Segal, Blair and Wyngaarden respectively (18).

RESULTS:

Cardiac Output, Heart Rate, Stroke Volume (Tables III & IV)

The mean cardiac output at rest was 3.32 l/min. for the patient group as compared with 4.85 l/min. in the normal subjects. This difference is highly significant ($p < .01$ t test analysis). As illustrated in Figure 1, there was little overlap in resting cardiac outputs between the two groups. The mean increase in cardiac output in response to exercise was .58 l./100 cc. increase in oxygen consumption in the normal subjects, and .52 l./100 cc. in the patients. The mean

cardiac output during exercise was 8.10 l./min. in the normal subjects and 6.10 l./min. in the patients. This difference is also highly significant ($p < .01$). Although patients A, D and J. demonstrated low cardiac outputs at rest, they were within the normal range during exercise as illustrated in Figure 1. All other patients in whom the cardiac output was measured showed a distinct difference from the normal subjects, both at rest and in response to exercise.

Patients A and B with heart block, increased their cardiac output during exercise, entirely by an increase in stroke volume. Patient C, who also had heart block, increased his rate by numerous extrasystoles, and elevated his cardiac output despite a small decrease in mean stroke volume. All the normal subjects and all the patients except A and B increased their cardiac output during exercise predominately by an increase in heart rate, with small changes in stroke volume. With the exception of the patients with heart block and patient D, the patients all had lower stroke volumes at rest and during exercise, than did the normal subjects.

An analysis of the heart rate response to exercise in the patients is obviously not valid since patients A-C had idioventricular rhythms, patients F-H had atrial fibrillation and several of the patients were fully digitalized.

Ventilation, Oxygen Consumption and Oxygen Debts.

As listed in Tables V and VI, the mean resting ventilation was 9.9 l./min. in the patients as compared to 8.9 l./min. in the normal subjects. During the exercise the ventilation increased similarly in the two groups, to a mean value of 24.5 l./min. in the patients and 22.9 l./min. in the normal subjects.

The mean resting oxygen consumption was similar in the two groups. During exercise the mean oxygen consumption was 695 cc./min. in the patients as compared with 810 cc./min. in the normal subjects. The mean total excess oxygen consumption due to exercise was 5449 in the patients and 6644 in the normal subjects. This difference probably reflects a difference in the external work done in the two groups, as can be seen in Figure 2.

The mean oxygen debt was 915 cc. in the patients and 855 cc. in the normal subjects. These values are not directly comparable, since the individual and group work loads were different. Therefore the oxygen debt was expressed as a proportion of the total excess oxygen consumption and this relationship is illustrated in Figure 3. In general, the patients had a higher oxygen debt for comparable levels of total excess oxygen consumption. This difference, however, is only significant statistically ($p < .01$) if patients A, D, and J, who had a normal cardiac output during exercise, are excluded from the group of patients.

Arterial Blood Gases, Lactate and Pyruvate (Tables VII & VIII)

Although several subjects and patients hyperventilated at rest, the mean arterial pH and pCO_2 were within normal range for both groups, and there was no significant difference between the groups. During exercise the pCO_2 showed no consistent change in either group. Patients D, F and I, were mildly hypoxic at rest.

The mean arterial lactate at rest was .84 mM/l. of blood in the normal subjects and .96 mM/l. of blood in the patients, the pyruvates being .069 mM/l. and .065 mM/l. respectively. The maximum changes in lactate and pyruvate and in L/P ratio were seen by 7 minutes of exercise in almost all subjects. In general the 9 minute samples during exercise and the 2 minute and 5 minute recovery bloods demonstrated changes toward the initial resting level. For these reasons, the 7 minute exercise values only have been recorded here. During exercise the mean lactate increased to .92 mM/l. and the pyruvate was 0.67 mM/l. in the normal subjects, whereas in the patients the mean lactate increased to 1.51 mM/l. and the pyruvate to .70 mM/l. Statistical analysis failed to reveal a significant difference between the resting or the exercise values between the two groups, or the exercise as compared to the resting values within the groups. This of course is a result of the wide individual variability and the fact that one patient and four subjects demonstrated decreased levels of

lactate during exercise. The lactate levels during exercise are significantly higher ($p < .01$) in the patient group than in the normal subjects, only if patients A, D and J (whose cardiac outputs were normal during exercise) are excluded from the patient group. The pyruvate levels were similar in the two groups at rest and during exercise. The lactate:pyruvate ratios showed marked individual variability, predominantly due to low pyruvate levels in several individuals. Although the mean lactate:pyruvate ratio was higher in the patients than in the normal subjects, this difference was not statistically significant.

DISCUSSION:

The mean cardiac output at rest in the normal subjects was somewhat lower than the values of Astrand et al (19) who made their measurements sitting on a bicycle ergometer; however, their resting oxygen consumptions were also considerably higher than in our subjects. The cardiac outputs in our study compare well with the data of Reeves et al (20) who made their measurements standing on a treadmill. The increase in cardiac output in response to exercise in our normal subjects was also similar to previous studies (20,21).

Several aspects of this study have been investigated previously. Harris and Lipkin (4) measured cardiac output by the carbon dioxide method, and determined oxygen debt in a group of patients with clinical evidence of circulatory insufficiency, and in normal subjects. They found the oxygen consumption during exercise and the oxygen debt were considerably higher in the patients, than in the normal subjects. These did not correlate well with the cardiac output as they measured it. However the cardiac outputs in their patients were frequently as high or higher than their normal subjects. Harrison and Pilcher (6) found a lower oxygen consumption during exercise in their patients but most studies (2-5) have demonstrated a higher oxygen consumption during exercise and increased oxygen debt in patients with evidence of circulatory failure.

It is of interest that in our study, the oxygen consumption for a comparable work load was similar in the patients and in the normal subjects, but

the oxygen debt for comparable work loads was increased in the patients with low cardiac outputs. The discrepancies in these studies may be accounted for by differences in circulatory status of the patients, small numbers of patients in several investigations (3,5,6) and different methods of determination of cardiac output.

Blood lactate (5,8,10,12-16) and in some studies lactate and pyruvate (7,9,11) have been investigated in patients with heart disease and compared with normal subjects. Although a wide range of values for blood lactates were demonstrated in both normal subjects and in patients with heart disease, most studies demonstrated similar resting values in the two groups, with higher levels during exercise in patients with circulatory failure. Iseri, Evans and Evans (11) stated that there was no significant difference in blood lactates during exercise between their patients and normal subjects but they did not describe the circulatory status of their patients. Huckabee and Judson (7) were unable to demonstrate a significant difference in blood lactate levels in the patients with heart failure as compared to normal subjects. A difference between the two groups was only demonstrated when their lactates and pyruvates were converted to "Anaerobic Metabolic Rate". (The validity of the concept of "Excess Lactate" from which the "Anaerobic Metabolic Rate" is calculated, has been questioned by several authors (9,23)). Both Huckabee (24) and Harris, Bateman and Gloster (9) failed to demonstrate a correlation between cardiac output and blood lactate levels during exercise, however, Donald et al (8) found a good correlation of blood lactate levels with arterio-venous oxygen differences in patients and in normal subjects, thus perhaps relating the lactate levels to cardiac output. The high arterial lactate levels during mild exercise seen in their normal subjects (8) suggest that they were different from our normal subjects in some way. Further comparison of these reports is difficult because:-

1. Several studies (10,12) involved predominantly patients with cyanotic heart disease, and thus had arterial hypoxemia.

2. Venous, or ear lobe blood were used rather than arterial blood (5,13,15).

3. Stair climbing, treadmill walking, supine and sitting exercise on the

bicycle ergometer were employed in various studies, thus using different muscle groups.

4. The control subjects were from different populations, and as has been pointed out by Holmgren and Ström (16) considerable differences in blood lactate levels during exercise may be seen in different populations of normal subjects.

In our study the patients as a group increased their arterial lactate levels during exercise more than the normal subjects, however, no correlation between cardiac output and lactate accumulation was demonstrable. Patient H, for example, had a very low cardiac output at rest and during exercise, but had a decrease in arterial lactate concentration (without a change in pyruvate concentration) during the exercise period. Similarly, although the oxygen debts were higher in the patients as a group, no correlation between the oxygen debt and the cardiac output was demonstrable. Perhaps the redistribution of blood flow seen in patients with impaired cardiac output (22) accounts at least in part for this poor correlation. If patients A, D and J who were found to have normal cardiac outputs during exercise are excluded from the patient group, a highly significant difference is found, between the patients and the normal subjects, with respect to cardiac output, oxygen debt and arterial lactate accumulation. The differences in oxygen debt and lactate accumulation, however, are not large.

Since patients A, D, and J had normal cardiac outputs during exercise, their symptoms can not be explained on the basis of a decreased cardiac output. It is also difficult to explain the symptoms of the patients on the basis of the oxygen debt and the lactate accumulation in their arterial blood, since several did not have increased oxygen debt or lactate accumulation. In addition, the highest values for oxygen debt and arterial blood lactate observed in these patients were considerably lower than those observed in exercise sufficient to produce symptoms in normal subjects. Nevertheless it is possible that oxygen debt, impaired cardiac output, or some combination of these parameters produces symptoms in patients with heart disease as a result of an altered sensitivity or threshold.

SUMMARY:

1. The cardiac output, oxygen debt and arterial blood lactate and pyruvate were measured at rest and during exercise in a group of patients with symptomatic heart disease and in normal subjects.

2. The mean cardiac output at rest and during exercise was lower in the patients than in the normal subjects; however, 3 of the patients had normal cardiac outputs during exercise.

3. No direct correlation was demonstrated between cardiac output and arterial blood lactate accumulation or oxygen debt, however, the mean oxygen debt and the mean increase in arterial lactate was greater in the group of patients who had abnormally low cardiac outputs than in the normal subjects.

4. If oxygen debt and lactate accumulation do indeed represent anaerobic metabolism, then the increases in anaerobic metabolism are small in patients with impaired cardiac output during mild exercise.

5. The symptoms of all the patients in this study are not readily explained by any one of the parameters investigated. The possibility of an altered sensitivity to lactate, oxygen debt, impaired cardiac output, or a combination of these factors is not excluded.

ACKNOWLEDGEMENT:

I wish to thank Dr. T. E. Cuddy for his constant interest and the many helpful suggestions offered throughout this study.

BIBLIOGRAPHY

1. Hill, A. V., Lupton, H.: Muscular Exercise, Lactic Acid and the Supply and Utilization of Oxygen. Quart. J. Med. 16:135, 1922-23.

2. Katz, L. N., Soskin, S., Schutz, W. J., Ackerman, W., Plaut, J. L.: A "Metabolic Exercise Tolerance Test" for Patients with Cardiac Disease. Arch. Int. Med. 53:710, 1934.

3. Campbell, J. M. H., Sale, F. J.: Effect of Exercise on Respiratory Exchange in Heart Disease II. Arch. Int. Med. 40:237, 1927.

4. Harris, I., Lipkin, I. J.: Cardiac Output and Oxygen Utilization in Some Types of Heart Disease. Edinburgh Med. J. 38:501, 1931.

5. Meakins, I., Long, C. N. H.: Oxygen Consumption, Oxygen Debt and Lactic Acid In Circulatory Failure. J. Clin. Invest. 4:273, 1927.

6. Harrison, R. T., Pilcher, C.: Studies In Congestive Heart Failure II. The Respiratory Exchange During and After Exercise. J. Clin. Invest. 8:291, 1930.

7. Huckabee, W. E., Judson, W. E.; The Role of Anaerobic Metabolism In The Performance of Mild Muscular Work. I. Relationship to Oxygen Consumption and Cardiac Output, and the Effect of Congestive Heart Failure. J. Clin. Invest. 37:1577, 1958.

8. Donald, K. W., Gloster, J., Harris, E. A., Reeves, J., Harris, P.: The Production of Lactic Acid During Exercise in Normal Subjects and in Patients With Rheumatic Heart Disease. Am. Heart J. 62:494, 1961.

9. Harris, P., Bateman, M., Gloster, J.: Relations Between The Cardio-Respiratory Effects of Exercise And The Arterial Concentration of Lactate and Pyruvate In Patients with Rheumatic Heart Disease. Clin. Sci. 23:531, 1962.

10. Hallock, P.: Lactic Acid Production During Rest and After Exercise In Subjects With Various Types of Heart Disease, With Special Reference To Congenital Heart Disease. J. Clin. Invest. 18:385, 1939.

11. Iseri, L. T., Evans, J. R., Evans, H.: Pathogenesis of Congestive Heart Failure. Correlation Between Anaerobic Metabolism and Plasma Volume Changes Following Exercise. Ann. Int. Med. 59:788, 1963.

12. Havel, R. J., Watkins, E.: The Metabolism of Lactate and Pyruvate in Children with Congenital Heart Disease. Circ. 2:536, 1950.

13. Cotes, J. E.: The Rate of Oxygen, Carbon Dioxide and Lactic Acid in the Ventilatory Response to Exercise in Patients with Mitral Stenosis. Clin. Sci. 14:317, 1955.

14. Weiss, S., Ellis, L. B.: Oxygen Utilization and Lactic Acid Production in the Extremities During Rest and Exercise. Arch. Int. Med. 55:665, 1935.

15. Jervell, O.: Investigation of the Concentration of Lactic Acid in Blood and Urine. Acta. Med. Scand. Supp. 24, 1928.

16. Holmgren, A., Ström, G.: Blood Lactate Concentration in Relation to Absolute and Relative Work Load in Normal Men and in Mitral Stenosis, Atrial Septal Defect and Vasoregulatory Asthenia. Acta. Med. Scand. 163:185, 1959.

17. Horn, H. D., Bruns, F. N.: Quantitative Bestimmung von L(+)- Milchsaure mit Milchsauredehydrogenase. Biochem. et Biophysica Acta. 21:378;1956.

18. Segal, S., Blair, A. E., Wyngaarden, J. B.: An Enzymatic Spectrophotometric Method for the Determination of Pyruvic Acid in the Blood. J. Lab. Clin. Med. 48:137;1956.

19. Astrand, P. O., Cuddy, T. E., Saltin, B., Stenberg, J: Cardiac Output During Submaximal and Maximal Work. J. Appl. Physiol. 19:268;1964.

20. Reeves, J. T., Grover, R. F., Blount, S. G. Jr., Filley, G. F.: Cardiac Output Response to Standing and Treadmill Walking. J. Appl. Physiol. 16:283;1961.

21. Donald, K. W., Bishop, J. M., Cumming, G., Wade, O. L.: The Effect of Exercise on the Cardiac Output and Circulatory Dynamics of Normal Subjects. Clin. Sci. 14:37;1955.

22. Donald, K. W.: Exercise and Heart Disease (A study in Regional Circulation). Brit. Med. J. 1:985;1959.

23. Olson, R. E.: "Excess Lactate" and Anaerobiosis. Ann. Int. Med. 59:960;1963.

24. Huckabee, W. E.: The Role of Anaerobic Metabolism in the Performance of Mild Muscular Work. II The Effect of Asymptomatic Heart Disease. J. Clin. Invest. 37:1593;1958.

TABLE I

PHYSICAL CHARACTERISTICS OF PATIENTS

PATIENT	AGE	SEX	HT.(cms.)	WT.(Kgm.)	B.S.A.(M^2)	DIAGNOSIS
A	59	M	176	92.7	2.07	Complete Heart Block
B	65	M	173	73.0	1.89	Complete Heart Block
C	70	M	180	71.2	1.90	Complete Heart Block
D	55	M	175	65.2	1.80	Aortic Stenosis
E	24	F	160	49.5	1.51	Mitral Stenosis
F	50	F	160	75.0	1.82	Mitral Stenosis
G	28	F	160	52.2	1.53	Mitral Stenosis and Insufficiency
H	48	F	163	73.5	1.79	Mitral Stenosis
I	77	M	161	50.4	1.52	Aortic Insufficiency
J	21	F	157	42.5	1.37	Subaortic Stenosis
MEAN	49.7		165	64.5	1.73	

TABLE II

PHYSICAL CHARACTERISTICS OF NORMAL SUBJECTS

SUBJECT	AGE	SEX	HT.(cms.)	WT.(Kgm.)	B.S.A.(M^2)
1.	32	M	178	72.9	1.90
2.	29	F	160	48.9	1.49
3.	67	M	167	79.0	1.88
4.	50	M	168	67.5	1.77
5.	45	M	170	69.3	1.80
6.	35	M	168	71.8	1.81
7.	20	F	181	81.9	2.06
8.	41	F	163	77.0	1.82
9.	27	M	163	60.0	1.64
10.	24	F	163	54.8	1.56
MEAN	37.0		167.9	68.3	1.77

TABLE III

HEMODYNAMIC DATA OF PATIENTS

PATIENT	C.O.		C.I.		H.R.		S.V.		$\dot{V}O_2$	
	R.	E.	R.	E.	R.	E.	R.	E.	R.	E.
A	4.1	9.6	2.0	4.7	48	48	86	200	274	1196*
B	2.5	4.5	1.3	2.4	27	27	91	167	222	801*
C	3.1	4.7	1.6	2.5	30	48	103	99	243	557*
D	4.2	7.2	2.3	4.0	65	96	64	75	261	803*
E	3.2	6.1	2.1	4.0	82	126	39	48	208	931*
F	3.6	5.6	2.1	3.2	64	92	56	61	209	615
G					68	156				
H	2.6	3.7	1.5	2.1	64	84	40	44	215	534
I					63	84				
J	3.4	7.5	2.5	5.5	66	156	52	48	201	746*
MEAN	3.32	6.10	1.93	3.55					229	773

C.O. = Cardiac Output in l./Min.
H.R. = Heart Rate per minute.
S.V. = Stroke Volume in ml.

C.I. = Cardiac Index in l./Min./M^2
$\dot{V}O_2$ = Oxygen Consumption in ml. per minute.
R = Rest
E = Exercise

*(This differs from treadmill exercise $\dot{V}O_2$ in those patients whose cardiac outputs were measured during bicycle exercise).

TABLE IV

HEMODYNAMIC DATA OF NORMAL SUBJECTS

SUBJECT	C.O.		C.I.		H.R.		S.V.	
	R.	E.	R.	E.	R.	E.	R.	E.
1. (a)	4.5	7.0	2.4	3.7	60	90	75	78
(b)		9.2		4.8		114		81
2.	5.0	8.0	3.4	5.3	80	104	63	77
3.	4.7	7.9	2.5	4.2	60	80	79	98
4.	4.6		2.6		72	92	63	
5.	6.1	10.3	3.4	5.7	76	98	81	94
6.	5.0	8.1	2.8	4.5	78	112	64	72
7.	5.5	10.1	2.7	4.9	74	115	74	88
8. (a)	4.9	7.6	2.7	4.2	62	84	79	80
(b)	4.2	7.4	2.3	4.2	62	88	68	84
9. (a)	4.7	7.1	2.9	4.4	66	84	71	85
(b)	5.1	7.0	3.1	4.3	66	78	77	90
(c)	5.2	7.8	3.2	4.7	66	94	79	83
10.	3.5	6.9	2.3	4.5	54	92	65	75
*MEAN	4.85	8.11	2.77	4.60	68.2	95.1	71.4	83.0

The oxygen consumption at rest and during exercise for each cardiac output determination is listed in Table VI.

*Mean value includes only the first determination in each subject.

Abbreviations as listed in Table III.

TABLE V

VENTILATION, OXYGEN CONSUMPTION, OXYGEN DEBT AND TOTAL EXCESS OXYGEN CONSUMPTION OF PATIENTS

PATIENT	RATE	TIME	$\dot{V}_E$		$\dot{V}O_2$		O_2 DEBT	EXCESS VO_2
			R.	E.	R.	E.		
A	23.2	10.00	12.0	31.7	274	794	723	5657
B	26.0	10.00	9.6	26.9	222	786	1015	5876
C	18.0	10.67	11.5	23.2	243	623	1194	4853
D (1)	19.5	10.00	9.3	16.6	261	641	480	4326
(2)	47.6	10.00	9.6	24.9	262	994	838	8270
E	50.0	11.00	9.3	31.3	208	832	1560	7875
F	27.2	10.00	8.1	18.6	209	615	575	4375
G	38.1	10.00	9.8	29.7	203	643	1011	5044
H	16.1	10.50	7.9	14.1	215	534	1122	4924
I	15.0	10.00	11.4	25.7	261	588	784	3920
J	38.6	10.50	9.3	18.8	201	545	329	3698
*MEAN	30.0	10.28	9.9	24.5	230	695	915	5449

Rate = Treadmill rate in Meters/Min.
$\dot{V}_E$ = Minute Ventilation in l/Min. B.T.P.S.
O_2 Debt = Oxygen Debt in ml.

Time = Duration of Exercise in Minutes.
$\dot{V}O_2$ = Oxygen Consumption in ml./min.
Excess VO_2 = Total Excess Oxygen Consumption due to Exercise in ml.

*Mean includes only study (2) of patient D.

TABLE VI

VENTILATION, OXYGEN CONSUMPTION, OXYGEN DEBT AND TOTAL EXCESS OXYGEN CONSUMPTION OF NORMAL SUBJECTS

SUBJECT	RATE	TIME	$\dot{V}_E$		$\dot{V}O_2$		O_2 DEBT	EXCESS VO_2
			R.	E.	R.	E.		
1. (a)	26.6	10.00	9.1	20.3	227	665	840	5298
(b)	55.5	10.27	8.7	29.9	244	1009	853	9353
2.	29.4	12.00	8.2	18.0	203	543	626	5026
3.	27.2	10.00	10.7	29.0	270	796	1169	6030
4.	32.6	10.00	11.4	19.8	238	820	685	6570
5. (a)	32.6	10.15	7.7	22.2	220	894	1223	7131
(b)	32.6	11.33	9.2	21.8	248	691	510	5486
6.	35.4	10.55	9.1	23.2	306	991	564	7397
7.	38.1	10.52	8.2	33.6	262	1113	1045	9744
8. (a)	32.1	11.67	8.5	23.9	238	883	802	7923
(b)	32.1	11.67	9.1	23.7	229	852	1088	7898
9. (a)	27.7	11.00	8.9	18.8	239	695	580	5315
(b)	27.7	11.02	9.4	18.6	251	674	522	4880
(c)	55.5	10.04	9.8	25.9	249	964	893	7908
10.	27.2	10.47	7.3	20.0	175	700	1014	6002
*MEAN	30.9	10.64	8.9	22.9	238	810	855	6644

Abbreviations as listed in Table V.

*Mean includes first study only in each subject.

TABLE VII

ARTERIAL

PATIENT NO.	REST pH	REST pCO_2	REST pO_2	REST L	REST P	REST L/P	7 MIN. EXERCISE pH	7 MIN. EXERCISE pCO_2	7 MIN. EXERCISE pO_2	7 MIN. EXERCISE L	7 MIN. EXERCISE P	7 MIN. EXERCISE L/P
A	7.44	35	86	.30	.063	5.0				.79	.065	12.2
B	7.44	38	84	1.12	.041	27.3	+7.43	38		1.70	.039	43.6
C	7.44	43	89	.76	.072	10.6				1.55	.087	17.8
D (1)	7.42	42	74	1.04	.063	16.5				.88	.041	21.5
(2)				.85	.064	13.3				.90	.051	17.6
E	7.45	35	87	1.80	.064	28.1	+7.42	32	89	3.20	.086	37.2
F	7.44	38	73	1.11	.107	10.4	7.41	41	90	1.32	.103	12.8
G	7.47	40	96	1.22	.120	10.2	7.48	34	94	3.11	.160	19.4
H	7.43	38	97	1.06	.063	16.8	7.41	42	92	.95	.065	14.6
I	7.46	46	67	.99	.022	45.0				1.11	.029	38.3
J	7.42	34	96	.35	.030	11.7	7.41	34	95	.44	.023	19.1
*MEAN	7.44	38.9	84.9	.96	.065	14.7	7.43	36.8	92	1.51	.070	21.6

*Mean includes second run only of subject D.
+Blood samples drawn at 5 minutes rather than 7 minutes of Exercise.

L = Lactic acid in mM/L of blood.
P = Pyruvic acid in mM/L of blood.
L/P = Ratio of lactic to pyruvic acid.

TABLE VIII

ARTERIAL BLOOD GASES, LACTATE AND PYRUVATE IN NORMAL SUBJECTS

SUBJECT NO.	REST pH	REST pCO_2	REST pO_2	REST L	REST P	REST L/P	7 MIN. EXERCISE pH	7 MIN. EXERCISE pCO_2	7 MIN. EXERCISE pO_2	7 MIN. EXERCISE L	7 MIN. EXERCISE P	7 MIN. EXERCISE L/P
1. (a)				.60	.061	9.8				.63	.065	9.8
(b)				.78	.080	9.8				.95	.076	12.5
2.	7.41	33	93	.63	.064	9.8	7.40	34	93	1.07	.080	13.4
3. (a)	7.41	34	84	1.47	.117	12.6	++7.42	35	84	1.11	.068	16.3
(b)				1.33	.092	14.5				+ .63	.057	11.1
4.	7.53	23	94	.81	.071	11.4	7.37	46	75	1.41	.090	15.7
5. (a)	7.41	42	84	.62	.027	22.9	7.41	42	98	.98	.052	18.8
(b)	7.41	41	86	.61	.024	25.4	7.40	40	88	1.03	.038	27.1
6.	7.37	46	88	.91	.079	11.5	7.38	47	90	.68	.050	13.6
7.	7.41	41	94	.84	.064	13.1	7.42	43	90	.98	.078	12.6
8. (a)	7.40	33	88	.49	.022	22.3	7.42	33	95	.69	.049	14.1
(b)	7.42	33	94	.72	.038	18.9	7.43	36	92	.59	.045	13.1
9. (a)	7.41	43	97	.77	.070	11.0	7.39	42	97	.49	.041	11.9
(b)	7.41	42	101	.54	.063	8.6	7.39	43	93	.36	.042	8.6
(c)	7.39	41	96	.70	.047	14.9	7.38	46	88	.50	.041	12.2
10.	7.38	42	92	1.25	.110	11.4	7.39	41	90	1.13	.092	12.3
*MEAN	7.41	37.4	90.4	0.84	.069	12.2	7.40	40.3	90.2	.92	.067	13.7

Abbreviations as listed in Table VII.
*Mean of first run only each subject.

++Sample taken at 5' Exercise.
+ Sample taken at 10' Exercise.

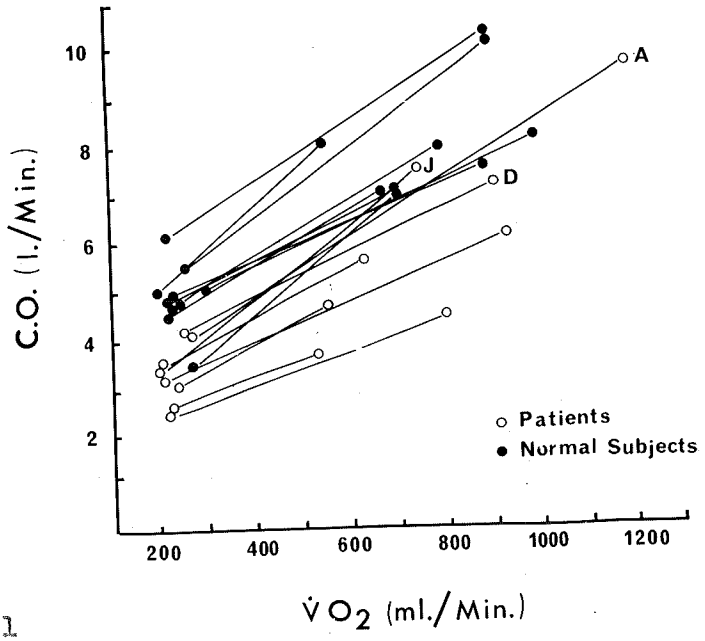
C.O. (l./Min.)
10
8
6
4
2
200
400
600
800
1000
1200
V̇O2 (ml./Min.)
A
J
D
Patients
Normal Subjects

Fig. 1

Fig. 1:

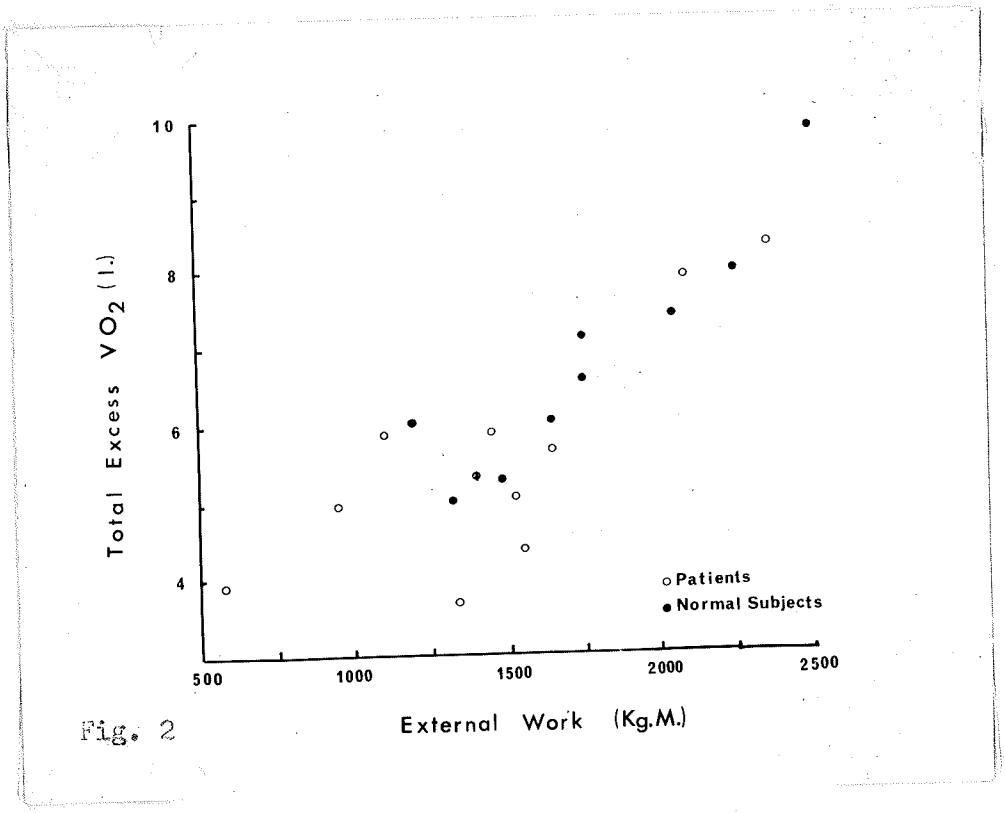

Fig. 2

Fig. 2: The work done in walking up the slope of the treadmill was calculated for each subject and patient. (The horizontal component was not included). As demonstrated in the graph, there was considerable overlap between the groups, but in general the patients did less work and had a proportionately lower total excess oxygen consumption than the normal subjects.

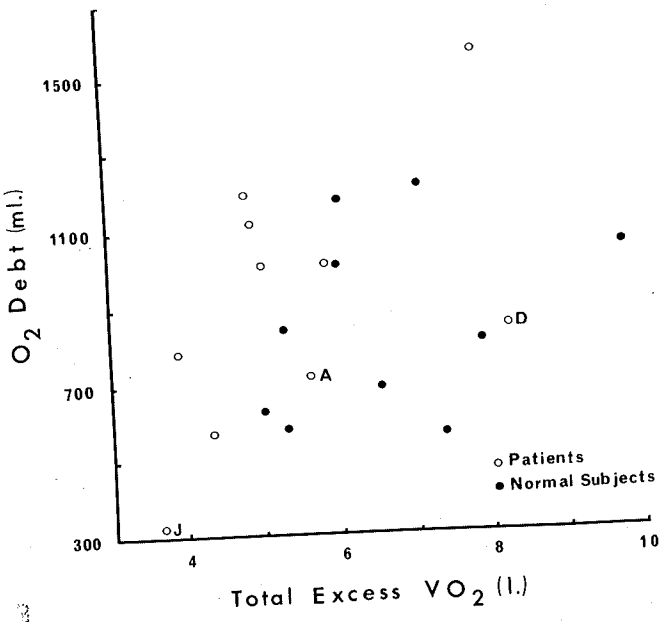
1500
1100
700
300
O_2 Debt (ml.)
4
6
8
10
Total Excess VO_2 (l.)
D
A
J
Patients
Normal Subjects

Fig. 3

Fig. 3: