LACTIC ACID PRODUCTION DURING REST AND AFTER EXERCISE IN SUBJECTS WITH VARIOUS TYPES OF HEART DISEASE WITH SPECIAL REFERENCE TO CONGENITAL HEART DISEASE[1]

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The defects found in congenital heart disease are frequently of such character as to disturb the normal pathways of circulation through the heart. The common types of congenital lesions responsible for diverting the normal course of blood are interventricular septal defects with or without pulmonary stenosis, auricular septal defects, and patent ductus arteriosus. In these anomalies the hemodynamic relationship between the right and left side of the heart becomes so altered as to lead to a mechanical interference with the proper oxygenation of the blood. When this obtains, quantities of blood pass unaerated (venous-arterial shunt) from the right to the left side of the heart giving rise to varying degrees of oxygen unsaturation, cyanosis, and anoxemia. On the other hand, the course of the blood stream may be shunted from the left to the right side of the heart (arterial-venous shunt), thereby permitting oxygenated blood to pass back into the lesser circulation. Under the latter conditions there may be neither anoxemia nor cyanosis.

In this study we have sought to obtain data regarding the presence or absence of anoxemia and factors influencing its development. Information of this kind is of course important in congenital heart afflictions because prognoses, particularly of the potentially more serious defects, depend in general on the degree of anoxemia and the extent of the increase of the work of the heart. The degree of cyanosis is a valuable guide, but is not an accurate measure of anoxemia. If polycythemia is present, there may be a sufficient quantity of oxygen for the tissues and, in addition, enough reduced hemoglobin to cause cyanosis. Conversely, anoxemia may be present without visible cyanosis. We have attempted here to investigate this problem by studying the variations in blood lactic acid levels at rest and following slight exercise. The amount of lactic acid in the blood can be utilized as a measure of anoxemia since it is recognized that a reduction in the oxygen supply to the tissues can, by inhibiting the oxidative recovery process, prevent the combustion of lactic acid and its conversion to glucose, thus giving rise to the accumulation of this substance in the tissues and blood stream (1, 2).

[1] This study was carried out in the Medical Unit of Wilhelmina Hospital, University of Amsterdam, and the Cardiac Department of London Hospital, London.

METHOD

The investigation was carried out in the morning with the subjects in the fasting state. The patients rested at least thirty minutes before being placed in the chair-ergometer, and a sample of blood was drawn from the anterior cubital vein. With the exception of a few who were too ill, all subjects were subjected to a mild exercise test. The exercise on the chair-ergometer is simple and easily executed after the subject has been given a few simple instructions. Briefly, the apparatus consists of a comfortable chair projecting out from which is a double set of small tracks. The feet are fastened to two runners which in turn fit on the tracks. In the act of extension of the legs a set of weights, connected to the heels of the runners by a combination of bicycle chains, are raised a given distance. The work performed is calculated in terms of kilogrammeters. An average of about 1500 kgm. m. of work was done in ten minutes. We have considered this amount of physical work as equivalent to mild exercise. Several patients, however, were unable to carry out this amount of exercise because of fatigue and dyspnea. After exercise the subject remained sitting quietly in the chair. Seven minutes after the cessation of exercise a second sample of blood was removed from the anterior cubital vein. Lactic acid reaches a maximum concentration in the anterior cubital vein seven minutes after the termination of work on the chair-ergometer (3).

The samples of blood were then analyzed for lactic acid in duplicate or triplicate by the method of Freidemann, Cotonio, and Shaffer (4). The error involved in the method is no greater than 1 mgm. per cent.

MATERIAL

Thirty-nine persons were studied. In several instances the individual experiments were re-

peated. Of the total number tested eighteen were patients with congenital heart disease (Tables II and III) with clinical or radioscopic evidence of either intra or extra cardiac communications between the venous and arterial circulation. In this group eight were diagnosed as having interventricular septal defects; seven cases showed the classical findings of patent ductus arteriosus; two cases with permanent cyanosis were diagnosed as tetralogy of Fallot; and one case possessed either an interventricular septal defect or a patent auricular septal defect. The diagnosis in each of the eighteen cases of congenital heart disease was based on the auscultatory findings, radioscopic appearance of the heart, and electrocardiographic evidence. In two cases it was necessary to rely solely on the auscultatory findings because of the absence of enlargement of one or more chambers of the heart and the absence of enlargement of the pulmonary artery. In these two cases, however, the auscultatory findings were quite conclusive in respect to the location and character of the murmur and of the accompanying localized thrill.

Ten of the subjects studied had normal cardiovascular systems and their ages ranged from ten to fifty-nine years. There were six cases of acquired valvular defects, two of which were associated with auricular fibrillation. Of the remaining five cases there were two of coronary thrombosis, two of hypertension associated with coronary disease, and one of ventricular tachycardia.

RESULTS

The concentration of lactic acid in venous blood of the normal human at rest with the Freidemann, Cotonio, and Shaffer method (4) varies from 10 to 20 mgm. per 100 cc. of blood (5). Table I shows the lactic acid values obtained from ten normal subjects at rest and after the above described mild exercise. After these same individuals were submitted to our exercise test the concentration of venous blood lactate never exceeded 21 mgm. per 100 cc. The average concentration of lactic acid at the resting level was 13.8 mgm. per 100 cc. while after mild exercise it was 16.3 mgm., an average increase of slightly more than 2 mgm. per 100 cc. No patient showed nor complained of fatigue or dyspnea after the exercise and all stated they could carry on without any difficulty.

TABLE I

Lactic acid content of venous blood during rest and after exercise in normal subjects

Case	Age	Sex	Amount of work performed	Lactic acid	
				Before	After
	years		*kgm. m.*	*mgm. per 100 cc.*	*mgm. per 100 cc.*
1	22	F	1,260	12.8	15.0
2	23	M	1,440	10.3	12.9
3	11	F	1,050	13.6	16.6
4	19	F	1,287	11.4	13.7
5	13	M	1,350	15.0	17.0
6	24	M	1,920	15.8	16.4
7	13	F	1,092	12.6	16.8
8	59	M	2,000	15.3	20.5
9	10	F	350	12.0	17.2
10	24	M	1,700	15.4	15.8
11	35	M	1,500	17.7	17.8
			Average	13.8	16.3

The resting lactic acid levels and those following mild exercise for the cases with venous arterial shunts are tabulated in Table II. These patients are classified under the cyanotic group because of permanent cyanosis or its development after exercise (transient type). The changes in the concentration of the lactic acid following exercise are obviously marked, with the exception of Case 16. In every other instance there is more than a 65 per cent increase. Two separate experiments were carried out on Case 16 and the results were substantially in agreement, showing a 9 per cent increase from the resting value after the exercise test.

A fairly definite relationship exists between the lactic acid concentration and dyspnea, the patients with the highest lactic acid levels showed the greatest amount of dyspnea after exercise. (See Table II.)

Twelve cases comprise the acyanotic group (Table III). None showed visible cyanosis before or after mild exercise. The highest lactic acid concentration after exercise was found in Case 21. In this group the height of concentration of lactic acid after exercise was again related to the degree of dyspnea. In those cases in which the lactic acid response was within the normal range, dyspnea was neither observed nor noted by the patient. This table further indicates that the blood lactic acid values may rise well above the

TABLE II

Cyanotic group. Lactic acid levels of venous blood before and after standard exercise in those cases of congenital heart disease associated with venous-arterial shunts

Case	Age	Sex	Diagnosis	Work performed	Lactic acid		Hemoglobin*	Red blood cells	Remarks
					Before	After			
	years			*kgm. m.*	*mgm. per cent*	*mgm. per cent*	*per cent*	*millions*	
11	63	M	Interventricular septal defect	1200	18.44	43.25	121	7.5	Cyanotic; became dyspneic after this exercise and cyanosis more intense
12	19	M	Tetralogy of Fallot	540	17.98	40.94	106	11.0	Continuous cyanosis since birth; became extremely dyspneic and blue after this amount of exercise
13	17	F	Tetralogy of Fallot	1350	16.03	28.44	132	7.5	Cyanotic all her life. Cyanosis increased after work. Developed slight dyspnea after exercise
14	23	F	Patent ductus	875	13.20	28.68	90	5.0	Slight degree of cyanosis. Cyanosis did not increase after work. Slightly dyspneic and fatigued after exercise
14	23	F	Patent ductus	984	13.30	27.54			As above
15	21	F	Interventricular septal defect associated with patent ductus arteriosus	1720	20.88	47.10	82	5.0	No cyanosis but became cyanotic after exercise. Complained of fatigue. Moderate degree of dyspnea
15	21	F	Interventricular septal defect associated with patent ductus arteriosus	1475	18.48	29.56			As above
16	25	M	Interventricular septal defect with patent ductus	1512	20.78	22.01	130	7.0	Slight to moderate cyanosis. Not fatigued nor dyspneic after exercise. Cyanosis more marked after exercise
16	25	M	Interventricular septal defect with patent ductus	1800	18.85	22.57			As above
				Average	17.58	32.00			

* 17 grams of hemoglobin per 100 cc. of blood is equivalent to 100 per cent hemoglobin.

upper range of normal (Cases 17, 18, 21, 22, 23) without the development of cyanosis. Thus, the abnormal rise of lactic acid is not necessarily associated with cyanosis.

In Table IV are shown the lactic acid values in chronic valvular defects with and without auricular fibrillation. In the two cases of mitral stenosis associated with auricular fibrillation (Cases 31 and 32) there was a definitely abnormal rise in the lactic acid values following exercise. In Case 31 a slight amount of cyanosis developed but in Case 32 this phenomenon was absent, yet both developed dyspnea after the exercise test. In Case 29, likewise, an abnormal lactic acid rise was observed and even in the absence of auricular fibrillation, dyspnea developed after 1500 kgm. m. of work. In the remaining cases no abnormal response was obtained. In Case 35 a slightly elevated resting lactic acid value was obtained.

Several interesting findings are brought out in

TABLE III

Acyanotic group. Lactic acid levels of venous blood before and after standard exercise in those cases of congenital heart disease associated with arterial-venous shunt

Case	Age	Sex	Diagnosis	Work performed	Lactic acid		Remarks
					Before	After	
	years			*kgm. m.*	*mgm. per cent*	*mgm. per cent*	
17	32	M	Probably case of interventricular septal defect	1175	22.89	28.34	Some dyspnea after exercise
18	21	M	Patent ductus	2100	15.80	23.20	No dyspnea. No fatigue
19	31	F	Patent ductus	1275	19.65	21.73	Slight dyspnea after work. Short of breath on exertion all life
20	32	F	Patent ductus	750	13.34	15.19	Only complained of feeling tired. No dyspnea
21	28	F	Patent ductus	1250	15.44	37.87	Moderately dyspneic. Breathlessness since able to walk
22	22	M	Interventricular septal defect	1510	15.71	26.70	Slight dyspnea
23	47	M	Interventricular septal defect	2000	21.20	31.73	Slight dyspnea
24	12	F	Interventricular septal defect	1095	11.88	13.00	No dyspnea
25	5	F	Probably interventricular septal defect	120	13.54	14.36	No dyspnea
26	6	F	Probably interventricular septal defect	240	14.17	14.77	No dyspnea
27	10	M	Interventricular septal defect	1460	16.84	20.59	No dyspnea
				Average	16.40	24.31	
28	23	M	Interventricular septal defect	1000	28.64	53.90	Marked dyspnea (See Table V, Group VII)

Table V. Because of the poor condition of some of these patients it was impossible to submit them to the exercise. Cases 36 and 37 were elderly subjects with acute coronary closure but without apparent signs of congestive failure. Both showed moderately high lactic acid values at rest. It is very likely that the above cases would have developed dyspnea upon exertion. Case 38 had auricular fibrillation in addition to hypertension and coronary arteriosclerosis. His resting lactic acid level was at the upper limit of normal. Following exercise it rose to 30 mgm. and moderate dyspnea developed. Case 39 showed a high resting lactic acid value, 37 mgm. This was a case of congestive failure resulting from paroxysmal ventricular tachycardia of long duration. This patient was dyspneic and orthopneic.

DISCUSSION

Effect of cardiac shunts on blood lactic acid

If anoxemia can develop as a result of the shunting of venous blood from the right heart to the left through unaerated channels (veno-arterial) we should expect to find a corresponding increase in the blood lactic acid level following exercise. On the other hand, if the shunt is arterial-venous, then no rise of the blood lactic acid level would be expected. The findings in Table II showing the effect of exercise on the venous blood lactic acid level at rest and following exercise are striking in that they indicate that anoxic anoxemia (6) can occur without cardiac failure. The most obvious explanation of this situation is that adequate amounts of unaerated blood are shunted into the

TABLE IV

Lactic acid values of venous blood before and after standard exercise in cardiac disorders resulting from rheumatic valvular defects with and without auricular fibrillation

Case	Age	Sex	Diagnosis	Work performed	Lactic acid		Remarks
					Before	After	
	years			*kgm. m.*	*mgm. per cent*	*mgm. per cent*	
29	29	M	Mitral stenosis and aorta insufficiency	1500	19.22	28.22	Slight dyspnea after test
30	16	M	Mitral insufficiency with stenosis	1920	11.13	13.00	No dyspnea nor fatigue
31	45	M	Mitral stenosis with auricular fibrillation	718.5	21.63	23.93	Slight cyanosis, fatigue, and slight dyspnea after test
32	43	M	Mitral stenosis with auricular fibrillation	1575	16.01	25.17	Slightly fatigued and dyspneic after test
33	29	M	Aortic insufficiency	840	14.87	16.00	Severe headache. Refused to carry on with work
34	21	M	Aortic insufficiency	1900	13.61	15.88	No dyspnea nor fatigue
				Average	16.08	20.36	

TABLE V

Lactic acid values of venous blood before and after standard exercise in other cardiac conditions

Case	Age	Sex	Diagnosis	Work performed	Lactic acid		Remarks
					Before	After	
	years			*kgm. m.*	*mgm. per cent*	*mgm. per cent*	
CORONARY THROMBOSIS, GROUP V							
35	60	M	Coronary thrombosis with diabetes	No work	23.42		Occlusion six days old
36	59	M	Coronary thrombosis with hypertension	No work	19.83		No signs of congestive failure; angina pectoris for past seven years
				Average	21.67		
HYPERTENSION WITH CORONARY ARTERIOSCLEROSIS, GROUP VI							
37	50	M	Hypertension with coronary arteriosclerosis	No work	29.14		No signs of congestive failure
38	60	F	As above with auricular fibrillation	1.013	19.83	30.05	Dyspnea following exercise
				Average	24.40	30.05	
CONGESTIVE FAILURE, GROUP VII							
39	50	M	Ventricular paroxysmal tachycardia	No work	37.72		No cyanosis, pulse 170
28	23	M	Interventricular septal defect	1000	28.64	53.90	Marked dyspnea after exercise
				Average	33.18	53.90	

general circulation, thus creating an oxygen deficit (anoxemia). If, following the exercise test the recovery phase be prolonged because of this oxygen shortage, an excessive accumulation of lactic acid will be expected in the venous blood for some time after the termination of the exercise. The amount of unaerated blood shifted will depend on the size of the defect, and the height of blood pressure in the two circuits. As long as the pressure in the right heart or pulmonary artery is maintained higher than on the left side unaerated blood will pass through the defect.

In congenital heart disease, tissue anoxia is apparently not present during rest for the lactic acid values are essentially normal. While the circulation rate may be slowed somewhat if polycythemia is present, enough oxygen seems to be available to remove the lactic acid which is normally formed at rest.

When Table II (cyanotic group) is compared to Table III (acyanotic group) it will be noted that the lactic acid concentration, particularly after exercise, is with only a few exceptions consistently higher in the cyanotic group. The presence of cyanosis, though not directly responsible for higher blood lactic acid levels, indicates a potential state of oxygen deficiency which easily can be precipitated by mild physical exertion. It is a common clinical observation that in congenital heart defects with venous-arterial shunts, cyanosis becomes more intense upon such slight exertion as walking. This observation was made in the cyanotic cases following the exercise test. This is to be attributed to the fact, as pointed out by Haldane (7), that in morbus caeruleus after exercise, the blood returned from the musculature is extremely poor in oxygen. Furthermore, Lundsgaard and Van Slyke (8) point out that as much as one-third of the venous blood entering the right heart chamber must be shunted over directly into the systemic circulation before the cyanotic threshhold is exceeded. In extreme cases of cyanosis as much as two-thirds of the venous stream may be shunted, thus leading to a high degree of oxygen-unsaturation. It is reasonable to assume therefore that cyanosis in congenital heart disease indicates the presence and approximate extent of the shunt, though not in quantitative terms.

When polycythemia is present in congenital heart disease it appears to be a compensatory process arising from the stimulation of erythropoietic bone marrow tissue by anoxia. As a consequence the red cell count increases and therefore the capacity of the blood to carry oxygen is increased. In spite of its apparent beneficial effects, its presence indicates, as our studies show, that the liability to tissue anoxia is great even following mild exertion (Table II).

The degree of cyanosis is not necessarily an index of the amount of oxygen lack that will develop following muscular work. Case 16 (Table II) illustrates this point. Two separate sets of determinations were carried out on this individual, the results being in very good agreement. The resting values on both occasions were slightly elevated as compared with the normal group. Following exercise the average rise of lactic acid was about 2 mgm. per 100 cc. of blood. This patient had continuous cyanosis and following the exercise the cyanosis deepened appreciably, yet the lactic acid rise was only slight. Marked secondary polycythemia was present in this subject, and there was moderate cardiac enlargement. We must conclude from this case that tissue anoxia, at least to any marked degree, may be absent even in the presence of cyanosis and polycythemia. This patient complained of no fatigue after exercise and dyspnea was not noted. He stated he could easily carry on the work and was the only patient in this group who did not show evidence of fatigue or dyspnea. Obviously there was enough reduced hemoglobin to produce cyanosis, yet there was a sufficient amount of oxygen to prevent a muscle oxygen debt.

Blood lactic acid in acquired heart disease

When the five uncomplicated cases of mitral stenosis and aortic insufficiency (Table IV) are considered, it will be noted that the lactic acid levels before and after exercise are within normal limits and that the exercise response is the same as in normal subjects. On the other hand, the two cases of mitral stenosis associated with auricular fibrillation showed a moderate rise above the normal lactic acid level. Also, slight to moderate dyspnea was noted after the exercise. It would appear that in cases of valvular defects associated with auricular fibrillation a mild state of anoxia develops following exercise. In this group can also be included Case 38 with hypertension, auricular fibrillation, and evidence of marked en-

largement of the left ventricle. Dyspnea followed the exercise test and, while the resting level of lactic acid was at the upper limits of normal, the concentration after exercise rose to 30.05 mgm. The lactic acid rise in this case was undoubtedly consequent to left ventricular failure.

Of the two cases of coronary thrombosis studied, Table V, Group V, neither had any signs of congestive failure, still the resting blood lactic acid levels were slightly elevated.

Two cases of congestive failure were studied, Table V, Group VII. Both showed high blood lactic acids levels at rest. Case 28 was given the standard exercise test and the blood lactic acid rose to 53 mgm. per 100 cc. of blood. This was the highest value recorded in the series, indicating the great tendency to tissue anoxia when the cardiac reserve is impaired.

That the concentration of lactic acid may reach abnormally high concentrations even at rest in cases of circulatory failure was demonstrated by Meakins and Long (9) and confirmed by Jervell (10). They pointed out, furthermore, that the accumulation of lactic acid in the blood was in proportion to the severity of the circulatory failure and was excessively great after exercise. The results in our two cases were in entire accord with the findings of the above investigators.

The increase in the concentration of lactic acid following even mild exercise in cardiac failure must be attributed to a deficient oxygen supply to the tissues. With mild physical exertion the oxygen supply cannot be increased in proportion to the increased oxygen requirement, and a greater accumulation of lactic acid in the blood is found.

Relation of blood lactate values to cardiac insufficiency

From the studies above it is apparent that the cause of hyperlacticacidemia in acquired heart disease is myocardial insufficiency. It is then necessary to inquire whether the high lactate values obtained in Table II (cyanotic type of congenital heart disease) and Table III (acyanotic type) can be accounted for on the basis of myocardial weakness. In order to obtain data in this direction we submitted the patients with congenital heart disease to radiocardiological and electrocardiographic examination of the heart, the purpose being not only to determine the type of enlargement for diagnostic purposes, but also to determine the degree of enlargement from a viewpoint of cardiac efficiency. The degree of enlargement is a fair index of the severity of the myocardial lesion and of the liability to failure (11, 12, 13). When Table VI is examined all the post-exercise values are abnormally high except in Case 16. Case 16 showed moderate enlargement of all chambers of the heart, yet the lactate concentration remains about stationary. Certainly from the point of view of enlargement the lactate values after exercise in this instance should be high if myocardial insufficiency were present. On the other hand Cases 11, 12, and 13 showed a very slight degree of enlargement with no evidence of myocardial disease by the electrocardiogram. Yet the lactate values doubled after exercise. From a consideration of these observations it would be inconsistent to attribute the high lactate values to myocardial insufficiency. In Cases 14 and 15 only are we justified in attributing the high lactate value to myocardial insufficiency. Yet in Case 14 gross failure was absent, for the venous pressure was 9 cm. H_2O.

When Table III (acyanotic group of congenital heart disease) is examined, abnormally high values are found in Cases 17, 18, 21, 22, and 23. Case 17 showed only slight enlargement. Case 18 showed no enlargement. Case 21 revealed a large pulmonary artery with very slight if any enlargement of the right ventricle. Case 22 showed no enlargement of the ventricles except slight enlargement in the region of the conus and Case 23 showed no enlargement. Of course, it is possible that temporary myocardial insufficiency could have manifested itself during exercise.

The above studies demonstrate that two factors may operate either singly or in combination to increase the lactic acid concentration of the blood in congenital heart disease. These are myocardial insufficiency and the presence of either intra or extra cardiac shunts. In the presence of cardiac enlargement, to at least a moderate degree, the cardiac reserve may be impaired and an increase in the blood lactate may be found after exercise. The co-existence of a veno-arterial shunt would heighten the blood lactate value. However, when cardiac enlargement is minimal or absent then the high lactate values may be preponderantly a direct result of the veno-arterial shunt. On the other hand, the elevation of the blood lactate in some cases of the acyanotic group (arteriovenous

TABLE VI

Significant cardiac findings in the congenital heart groups

Case	Diagnosis	Lactic acid		Radiocardiological findings	Electrocardiogram findings	Blood pressure	Auscultatory findings
		Before	After				
		mgm. per cent	*mgm. per cent*			*mm. Hg*	
				CYANOTIC GROUP			
11	Interventricular septal defect	18.44	43.25	Generalized enlargement slight. Rt. Vent.† Lt. Vent.† Pul. Art.†	Normal rhythm. Low voltage Lead I. P1 bifid. P2 P3 prominent. L.A.D.	135/80	Systolic murmur all areas. Loudest over pulmonic area
12	Tetralogy of Fallot	17.98	40.94	Rt. Vent.† Lt. Vent.† Pul. Art. normal. Conus †	Normal rhythm. T1 T2 prominent and upright. T3 inverted. P tendency to bifid all leads. R.A.D.	138/85	Rough, blowing systolic murmur over pulmonic area, but no thrill. 2d pulmonic absent
13	Tetralogy of Fallot	16.00	28.44	Dextrorotation of aorta. Pul. Art. not enlarged. Conus of Rt. Vent.† and slight generalized enlargement	Normal rhythm. R.A.D. P3 and T3 flat	135/82	Harsh, rough systolic murmur and systolic thrill over pulmonary area. 2d pulmonic sound absent
14	Patent ductus arteriosus	13.20	28.68	Pul. Art.†† Conus.†† Rt. Vent.† Lt. Vent.† Venous pressure 9 cm. H_2O	Normal rhythm. L.A.D. P.R. interval = 0.26 sec.	128/65	Machinery-like murmur heard maximum over pulmonic area. 2d pulmonic sound present
15	Interventricular septal defect associated with patent ductus arteriosus	20.88	47.10	Pul. Art.†† Rt. Vent.†† Conus.†† Lt. Vent.†	Notching of P waves in Leads I and II. Otherwise normal. Normal rhythm	125/85	Systolic murmur heard over 3d interspace just to left of sternum
16	Patent ductus arteriosus associated with interventricular septal defect	20.78	22.01	Pul. Art.†† Lt. Vent.† Conus.†† Rt. Vent.†† Venous pressure 13 cm. H_2O	R.A.D. High P2 T2. Increased amplitude of Q.R.S. complexes. Normal rhythm	130/82	2d pulmonic sound markedly accentuated. Systolic murmur heard best over 3d interspace to left of sternum preceded by snapping 1st sound and followed by snapping 2d sound followed by soft blowing diastolic murmur
				ACYANOTIC GROUP			
17	Probable case of interventricular septal defect	22.89	28.34	Pul. Art. sl. enlargement. Rt. Vent.† Conus †	Normal rhythm. T2 T3. Inverted. Rt. A.D.	100/60	Basal systolic thrill pulmonary region. Systolic murmur all areas, maximum over base
18	Patent ductus Botalli	15.00	23.00	No generalized enlargement. Pul. Art.†† and pulsating	Rt. A.D. Normal rhythm	145/95	Short blowing systolic murmur over apex. Systolic thrill over pulmonary area with systolic murmur. 2d pulmonic sound present

TABLE VI—*Continued*

Case	Diagnosis	Lactic acid		Radiocardiological findings	Electrocardiogram findings	Blood pressure	Auscultatory findings
		Before	After				
		mgm. per cent	*mgm. per cent*			*mm. Hg*	
				ACYANOTIC GROUP (*Continued*)			
19	Patent ductus arteriosus	19.00	21.00	Pul. Art.†† with pulsation. R.V.†† Conus.†† Pul. branches †	R.A.D. Normal rhythm	120/90	Systolic thrill and murmur over 1st and 2d left interspaces
20	Patent ductus arteriosus	13.00	15.00	Pul. Art.†† Other changes slight	R.A.D. Normal rhythm	130/80	Machinery-like murmur heard over pulmonic area. 2d pulmonic sound heard
21	Patent ductus arteriosus	15.44	37.87	Pul. Art.†† with marked pulsation of pulmonary vessels. No aortic window. Conus.† Sl. enlargement of rt. vent. only	Bifid. P2 P3	110/65	Systolic and diastolic murmur over pulmonary artery and thrill
22	Interventricular septal defect	15.00	26.00	Slight enlargement in conus region	Normal	110/70	Loud rough systolic murmur heard maximum along sternal border with systolic thrill at level of 3d interspace
23	Interventricular septal defect	21.00	31.00	No definite enlargement	Normal	135/80	Loud rough systolic heard best over lower sternum with systolic thrill
24	Interventricular septal defect	11.00	13.00	No definite enlargement	Normal	110/60	Loud rough systolic murmur heard over entire sternum but heard maximum along left sternal louder at level of 4th interspace accompanied by systolic thrill
25	Probable case of interventricular septal defect	13.00	14.00	No enlargement	Normal	100/60	Loud rough systolic murmur heard maximum along left sternal border at level of 3d interspace accompanied by systolic thrill
26	Interventricular septal defect	14.00	14.77	Rt. Vent.†† Conus.†† Lt. Vent.†	R.A.D.	98/58	Thrill and loud systolic murmur elicited over level of 3d interspace just to left of sternum
27	Interventricular septal defect	16.00	20.00	Rt. Vent.† Conus.† Pul. Art. not enlarged	Normal	105/60	Systolic murmur loud rumbling, heard best over 3d interspace just to left of sternal borders. Level of 3d interspace
28	Interventricular septal defect. Congestive failure	28.64	53.90	Rt. Vent.††† Conus.†† Lt. Vent.† Pul. Art.† Lt. Aur. not enlarged	R.A.D.	130/78	Systolic murmur loud and harsh heard best along left sternal border at level of 2d interspace. Diastolic murmur questionable

†† = Moderate enlargement.
† = Slight enlargement.
L.A.D. = Left axis deviation.
Rt. Vent. = Right ventricle.
R.A.D. = Right axis deviation.
††† = Considerable enlargement.
Lt. Vent. = Left ventricle.
Pul. Art. = Pulmonary artery.

shunts) requires further explanation. The high values cannot be explained on the basis of myocardial insufficiency because it would be extremely difficult to comprehend how a heart normal in size and not showing any evidence of myocardial disease could become temporarily incompetent during mild exercise. It is our impression that the high lactate values obtained are probably due to the shunting of blood from the left to the right side of the heart through large defects and that therefore the output of blood through the aorta into the peripheral circulation does not increase in proportion to the oxygen demand of the muscles in exercise.

From the foregoing survey it is apparent that the hyperlacticacidemia which develops after exertion is constantly associated with the presence of dyspnea, regardless of the cause of anoxemia. When dyspnea is present one can predict the occurrence of abnormally increased amounts of lactic acid in the tissues and blood during exercise. Valentin (14) previously adduced evidence to show that blood lactic acid is high in all conditions involving dyspnea. The observations made in this study indicate that dyspnea invariably accompanies the anoxemic state.

CONCLUSIONS

1. An increased concentration of lactic acid in the venous blood is evidence of an inadequate supply of oxygen to the tissues.

2. There is only a slight increase of lactic acid in the blood following mild exercise in normal individuals, an average increase of about 2 mgm. per 100 cc. of blood above the resting value. The normal upper limit of concentration of venous blood lactic acid following our exercise test did not exceed 21 mgm. per 100 cc. of blood.

3. The blood lactic acid studies show that tissue anoxia is not present at rest in patients with congenital heart disease, either in the presence or absence of cyanosis.

4. Following mild exercise there is a definitely abnormal rise of blood lactic acid in the cyanotic group of congenital heart disease, indicating a greater liability to the development of tissue oxygen deficit after even slight physical exertion.

5. The presence of cyanosis and polycythemia in congenital heart disease does not necessarily indicate that oxygen deficit will develop following mild exertion for no significant rise of lactic acid level occurred in a case of morbus caeruleus.

6. Following mild exertion, a definitely abnormal rise may occur in some acyanotic cases of congenital heart disease, but the rise is not as great on the average as in the cyanotic group.

7. When dyspnea follows mild exercise the presence of tissue oxygen want may be assumed to be present regardless of what specific cardiac defect is ultimately responsible.

BIBLIOGRAPHY

1. (a) Hill, A. V., The mechanism of muscular contraction. Physiol. Rev., 1922, **2**, 310.
   (b) Hill, A. V., and Long, C. N. H., Muscular exercise, lactic acid and the supply and utilization of oxygen. Ergebn. d. Physiol., 1925, **24**, 43.
   (c) Hill, A. V., Long, C. N. H., and Lupton, H., Muscular exercise, lactic acid and the supply and utilization of oxygen. Part I. Introduction. Proc. Roy. Soc., s.B., 1924, **96**, 438.
2. Meyerhoff, O., Chemical Dynamics of Life Phenomena. Lippincott, Philadelphia and London, 1924.
3. Hallock, P., Blood lactic acid after exercise with particular reference to polycythemia rubra vera. Proc. Soc. Exper. Biol. and Med., 1938, **38**, 587.
4. Freidemann, T. E., Cotonio, M., and Shaffer, P. A., The determination of lactic acid. J. Biol. Chem., 1927, **73**, 335.
5. Peters, J. P., Van Slyke, D. D., Quantitative Clinical Chemistry. Vol. I. Interpretations. Chapter X. Williams and Wilkins Company, Baltimore, 1931.
6. Barcroft, J., Anoxemia. Lancet, 1920, **2**, 485.
7. Haldane, J. S., Respiration. Yale University Press, New Haven, 1922.
8. Lundsgaard, C. and Van Slyke, D. D., Cyanosis. Medicine Monographs. Williams and Wilkins Co., Baltimore, 1923.
9. Meakins, J., and Long, C. N. H., Oxygen consumption, oxygen debt and lactic acid in circulatory failure. J. Clin. Invest., 1927, **4**, 273.
10. Jervell, Otto, Investigations of the concentration of lactic acid in blood and urine. Acta med. Scandinav., 1928, Supp. 24, Chapter III, pp. 23 to 26.
11. Parkinson, J., Enlargement of the heart. Lumleian Lectures. Lancet, 1936, **1**, 1337 and 1391.
12. Grant, R. T., After histories for ten years of 1000 men suffering from heart failure. Heart, 1933, **16**, 275.
13. Hallock, P., Enlargement of the heart. Its recognition by the radiologic method. Minnesota Med., 1938, **21**, 303.
14. Valentin, F., Über den Milchsäuregehalt des Blutes. München. med. Wchnschr., 1925, **72**, 86.