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Research Article

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HEMODYNAMIC RELATIONSHIPS OF ANAEROBIC METABOLISM AND PLASMA FREE FATTY ACIDS DURING PROLONGED, STRENUOUS EXERCISE IN TRAINED AND UNTRAINED SUBJECTS *

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Many of the physiological responses to exercise are known to be modified in physically trained subjects. Athletes, compared to untrained persons, are known to have a slower heart rate with increased work capacity per beat (1, 2), greater stroke volume (3), more efficient respiration with decreased minute ventilation (4), larger maximal oxygen intake (5), and less accumulation of lactic acid during exercise (6, 7). Red-cell and plasma volumes are probably larger in athletes than in untrained subjects (8). A measurable result of physical training is increased endurance for muscular exercise. The present investigation was designed to evaluate hemodynamic as well as certain carbohydrate and lipid responses that might help to explain the greater endurance in persons with increased capacity for strenuous exercise. A constant speed and grade of treadmill walking was chosen so that sedentary subjects would reach their limits of endurance within about 30 minutes. Since this same work load was only of moderate severity for physically trained persons, they were expected to continue exertion for a considerably longer time.

MATERIAL AND METHODS

Twenty-six studies were performed on 24 normal male volunteers, 19 to 44 years old (mean, 29 years). The subjects were recruited from the environs of the University of Washington and from a group of active mountain climbers. The sedentary group consisted of 6 university students, 3 physicians, and 5 white-collar workers. In the physically active group, there were 7 active mountain climbers, a varsity crewman, a semiprofessional bicyclist, and one university employee who walked several miles daily. The average age of the sedentary subjects was 31.2 years and that of the other group, 24.4 years. One subject in each group (no. 10 and 16) was studied twice; because of technical difficulties, the first study on Subject 16 was stopped after 30 minutes and repeated at a later date. The studies were performed in an air-conditioned laboratory during the morning when subjects were in the postabsorptive state. A Cournand needle was placed in the radial or brachial artery and either a polyethylene catheter was threaded into the axillary vein, or a cardiac catheter passed to the superior vena cava via an antecubital vein. Subjects were then allowed to rest in the supine position for approximately 45 minutes, when samples of arterial blood were taken and heart rate was recorded by an electrocardiograph.

Subjects then walked on a motor-driven treadmill at 3.0 miles per hour and an 18% grade to the point of severe fatigue, or for at least an hour. Severe fatigue and dyspnea forced the "sedentary" subjects to stop walking after 15 to 36 minutes, whereas the "physically active" men continued for at least an hour without evidence of significant fatigue or desire to rest.

Arterial blood samples for free fatty acids (FFA), lactate, pyruvate, and glucose were drawn at least once in the first 5 minutes of exercise and at 5- to 10-minute intervals throughout exercise. Samples were also taken during recovery (supine position) in most instances. The total amount of blood removed was 250 to 300 ml. Cardiac output, oxygen consumption, and pulmonary ventilation were usually measured 2 or 3 times during exercise. Heart rate was monitored frequently by the electrocardiograph.

Cardiac output was measured by the dye dilution technic with collection of multiple 1-second samples of arterial blood after injection of Evans' blue dye through the venous catheter (9). Ventilation was measured by collection of expired air through a low-resistance valve into a Douglas bag, and oxygen consumption was calculated from oxygen content of expired air as determined by the Scholander technic (10), or the Pauling paramagnetic oxygen analyzer. In six instances, ventilation and oxygen consumption during exercise were measured with a 13.5-L Collins respirometer before or after the prolonged exercise test.

Arterial concentrations of lactate were determined by the method of Barker and Summerson (11) with Huckabee's modification (12), pyruvate as described by Segal, Blair, and Wyngaarden (13), and FFA by Dole's

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TABLE I

Hemodynamic responses during exercise in sedentary normal men and in physically active men

Subject	Age	BSA	Duration of exercise	Cardiac index				Heart rate				Stroke index				$\dot{V}O_2$
				4–6 min	10–14 min	18–27 min	>40 min	4–6 min	10–14 min	18–27 min	>40 min	4–6 min	10–14 min	18–27 min	>40 min	
no.	*years*	*m²*	*min*	*L/min/m²*				*beats/min*				*ml/beat/m²*				*L/min/m²*
A. Sedentary normal men																
01	33	1.95	20		9.35			149	178	177			51.7			1,141
02	32	1.95	22					161	182	192						
03	23	1.93	29	9.55	9.53	11.34		159	183	190		60.0	52.1	59.7		1,192
04	35	1.97	15	8.66	12.96			180	194			48.1	66.8			1,193
05	26	2.00	20	11.96	13.88			156	180	180		76.2	75.8			1,269
06	37	1.80	36	10.22	10.87	9.48		141	160	168		72.0	67.9	57.8		807
07	32	2.02	24		9.10	9.34		154	166	190			55.2	49.1		1,119
08	37	1.96	23		6.23			161	175	184			35.6			1,198
09	34	2.01	34					144	162	172						
10*	25	2.01	20	12.82	10.21	10.36		160	174	182		80.1	58.7	56.9		945
11*	25	2.01	36	11.05		9.03		159	178	190		69.5		48.3		1,228
12	30	1.87	19	9.31	12.01			160	175	183		58.2	68.6			1,010
13	44	1.98	23	8.62	11.25	8.36		169	174	185		51.0	64.6	45.2		915
14	25	2.19	21	11.69	11.32	13.00		175	180	191		67.6	62.9	68.1		1,180
15	30	2.12	14	6.77	9.70			167	175			40.5	55.4			1,410
Average	31	1.98	24	10.07	10.53	10.13		160	176	183		62.3	59.6	55.0		1,119
B. Physically active men																
16†	25	1.90	30‡	9.34	9.43	8.83		136	144	158		68.6	65.5	55.9		1,110
17†	25	1.90	66	8.67	9.27	9.42	9.60	141	155	165	179	61.6	60.0	57.1	53.7	1,145
18	20	1.82	76	7.69		7.02	8.97	138	140	153	172	55.7		45.9	52.1	1,143
19	29	2.15	60	9.96	11.00	11.44	11.97	159	167	178	189	62.6	65.9	64.3	63.3	1,307
20	19	1.83	66	10.29	12.32			138	159	160	164	74.6	77.5			1,107
21	22	2.08	82		7.13	8.27	5.84	116	123	132	141		54.5	62.7	41.4	633
22	27	2.00	60	11.41	10.56	13.40		130	136	144	162	87.7		76.0		1,267
23	33	2.03	61	12.52		13.11	10.20	128	132	128	136	97.8		100.1	75.0	1,124
24	23	2.19	66	11.60		9.35	10.23	120	120	121	146	96.6		77.3	70.1	1,093
25	21	1.91	60	10.26		8.18	9.24	125	136	148	160	75.5		56.0	57.8	907
26	24	1.75	60	6.79		7.86	7.73	129	133	135	150	53.9		55.0	52.2	893
Average	24	1.96	66	9.85	9.95	9.69	9.22	133	141	148	160	73.5	64.7	65.0	58.2	1.066

* Same subject, studied twice.
† Same subject, studied twice.
‡ Testing stopped because of technical difficulties after 30 minutes.

method (14) as modified by Trout, Estes, and Friedberg (15) to avoid interference by lactic acid. Glucose was determined by a modified glucose oxidase method (16). The blood samples for lactate and pyruvate were immediately denatured with ice-cold trichloroacetic acid. Excess lactate (XL) was calculated according to Huckabee's description (17), where $XL = (L_n - L_o) - (L_o/P_o)(P_n - P_o)$; L_n and P_n represent the molar concentrations of arterial blood lactate and pyruvate at time n, and L_o and P_o are the molar concentrations at rest.

The data were analyzed according to periods of exercise 4 to 6, 10 to 14, 18 to 27, and in the physically active group, beyond 40 minutes. Statistical computations were processed by an IBM 709 computer. Probability was estimated by t test.

RESULTS

Hemodynamic responses. The two groups demonstrated several noteworthy differences as well as similarities in the cardiac responses to exercise (Table I). Stroke index was greater in the physically active group during all comparable periods of exercise (Figure 1). The average stroke index in the first 40 minutes of exercise was 59.4 ml per beat per m² in the sedentary group and 68.3 ml per m² (15% greater) in the physically active group ($p < .02$). Heart rate, as might be expected, was greater during each period of exercise in the sedentary group, where all subjects developed marked fatigue and dyspnea and stopped walking after 15 to 36 minutes (average, 23.7 minutes). The average minute heart rates in the sedentary group were greater by 27, 35, and 36 beats during minutes 4 to 6, 10 to 14, and 18 to 27, respectively. Heart rate rose progressively and significantly during exercise in all subjects (Figure 1). In both groups, the increase in heart rate was accompanied by a significant reduction in stroke index. Compared to the stroke index during minutes 4 to 6, there was an average fall of 16% during minutes 18 to 27 of exercise in the sedentary group ($p = .03$) and 11% in the physically active group ($p = .03$). The final stroke index (40 to 60 minutes) in the physically active group was 14% less than the first determination during minutes 4 to 6 of exercise ($p < .001$).

The average oxygen consumption was 1,119 ml per m² in the sedentary group and was not significantly different from the mean of 1,066 ml per m² in the physically active group. Average total pulmonary ventilation was 60.7 L per minute in the sedentary subjects and 46.0 L per minute in the physically active group during the first 30 minutes of exercise. The average oxygen pulse in the sedentary group was 6.4 ml per beat per m² and was significantly less than the average of 7.5 ml per beat per m² in the other group ($p < .001$).

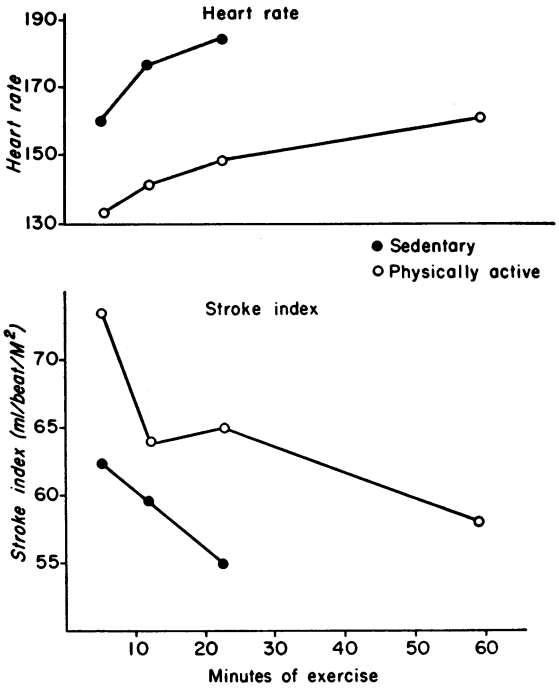

FIG. 1. AVERAGE HEART RATE AND STROKE INDEX DURING EXERCISE (walking at 3 mph, 18% grade).

In 12 subjects (4 sedentary and 8 physically active), measurements of oxygen consumption were repeated at intervals greater than 20 minutes. The variations in replicate oxygen consumption averaged 4.7% and ranged from + 16 to − 11%.

As mentioned above, heart rate in the sedentary group was considerably greater than in the physically active group. Stroke index in the former group averaged less, however, so that the cardiac index was virtually equal in the two groups (Figure 2). Cardiac index did not show any consistent change during the period of exercise, and the averages in the sedentary group were 10.1, 10.5, and 10.1 L per minute per m² during minutes 4 to 6, 10 to 14, and 18 to 27, respectively. In the physically active group, comparable values for average cardiac index were 9.9, 10.0, and 9.7 L per minute per m² (Figure 2). Although there was usually little variation of cardiac index in a given subject during the exercising period,

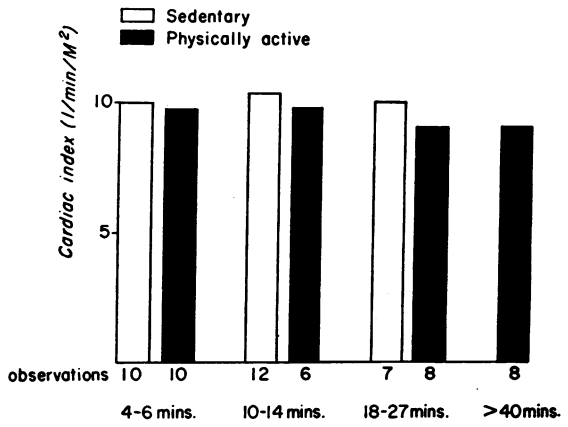

FIG. 2. AVERAGE CARDIAC INDEX DURING EXERCISE

the range of cardiac index in both groups was considerable, from 6.7 to 12.8 L per minute per m^2 in the first period of sampling. The calculated arteriovenous oxygen differences averaged 110.0 and 111.8 ml per L in the sedentary and physically active groups, respectively.

The arterial hematocrit did not change during the exercise (average change from the first to last determination was $-.001\%$), and the average hematocrit in both groups was 48%.

Anaerobic metabolism. Striking differences in arterial lactate and calculated excess lactate (XL) concentrations were observed (Figure 3). All subjects showed a prompt rise in XL in the first 5 minutes of exercise. The sedentary subjects continued to accumulate XL, and at the time of "maximal" endurance (24 minutes), the average XL was 5.28 mM. In contrast, XL was only 0.55 mM in the physically trained subjects after an average of 66 minutes of exertion ($p < .001$), and they noted little or no fatigue (Table II, Figure 3).

The rate of increase of XL was greatest in the first few minutes of exercise. The physically active group demonstrated an initial rise with a peak in minutes 2 to 5. This was usually followed by a decrease in XL and a subsequent plateau at a low level (Figure 3). Thus the average XL in this group was 0.84 mM in minutes 3 to 5 and fell to 0.45 mM in minutes 14 to 16, whereas average levels of XL in the sedentary group were 3.26 and 5.08 mM in the same periods ($p < .003$) (Table II). XL in the sedentary subjects tended to reach a plateau near the end of endurance, and in 3 instances it fell moderately in the final minutes (Figure 3). Nevertheless, XL continued to increase to a greater or lesser degree throughout exercise in the sedentary subjects. In contrast, the peak XL occurred at a much lower level within the first few minutes in the physically active sub-

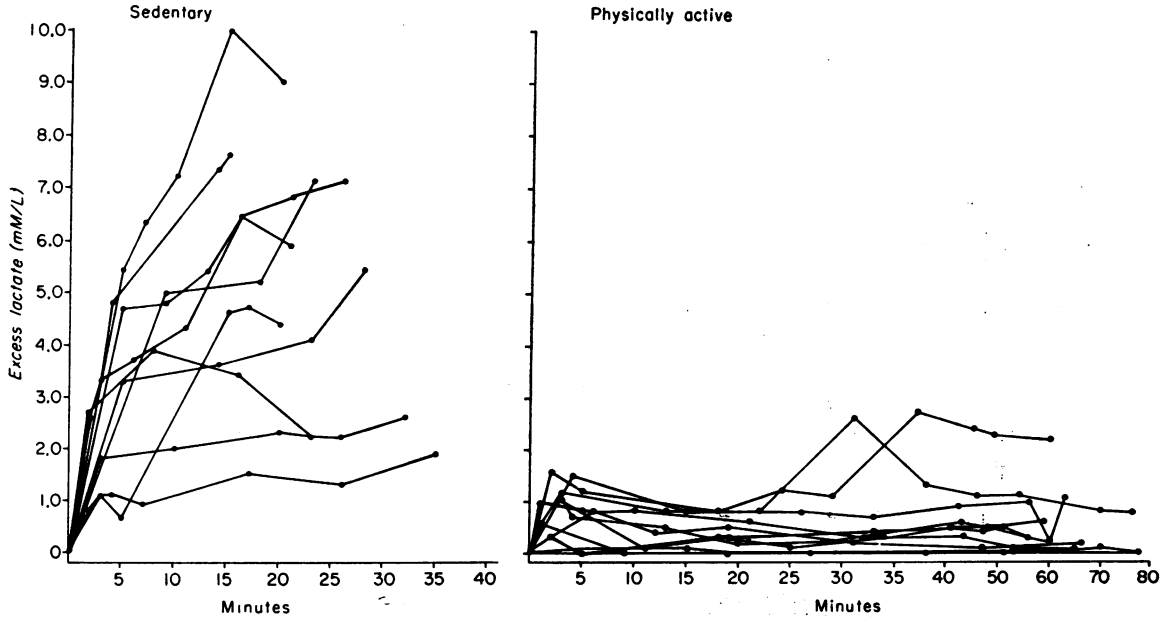

FIG. 3. ARTERIAL EXCESS LACTATE DURING EXERCISE.

TABLE II

Arterial lactate, pyruvate, excess lactate, and free fatty acids during exercise

Subject	Resting		3 to 5 min			14 to 16 min			Final				Free fatty acids			
	Lactate	Pyruvate	Lactate	Pyruvate	*XL*	Lactate	Pyruvate	*XL*	Lactate	Pyruvate	*XL*	Time	Control	Max.* fall	Final in exercise*	Max. in recovery*
no.	*mmoles/L*			*mmoles/L*			*mmoles/L*			*mmoles/L*		*min*			*μmoles/L*	
A. Sedentary men																
01	0.43	0.05	7.7	.26	5.4	12.5	.30	10.0	11.7	.31	9.0	20	710	− 91	− 61	
02	0.58	0.09	4.4	.18	3.3	8.3	.30	6.4	7.7	.29	5.9	21	573	−209	− 60	+ 328
03	0.66	0.09	4.5	.16	3.3	5.3	.25	3.6	7.2	.25	5.4	28	587	−313	−226	− 93
04	0.66	0.07	6.4	.17	4.8	10.1	.26	7.6	10.1	.26	7.6	15	620	−383	−213	+ 003
05	0.48	0.09	1.4	.14	0.7	5.6	.17	4.6	5.8	.26	4.4	20	473	−106	− 53	+ 295
06	0.77	0.11	2.9	.16	1.8	3.7	.20	2.2	4.1	.22	2.6	32	394	−142	− 50	+ 320
07	0.60	0.07	3.6	.12	2.6	4.8	.17	3.4	3.5	.17	2.1	23	398	−151	− 97	+ 631
08	0.81	0.12				6.7	.23	5.1	8.6	.22	7.1	23	865	−476	−476	+ 533
09	0.51	0.05	6.0	.12	4.7	7.8	.13	6.4	8.4	.13	7.1	26				
10	0.67		3.1			3.6			3.7			20				
11	0.40	0.07	1.8	.13	1.1	2.5	.20	1.4	3.2	.21	1.9	35	972	−315	−194	+1,102
12	0.86	0.06		.17		5.8	.24	2.6	5.8	.24	2.6	18				
13						6.6			7.0			22				
14	0.71		3.2			3.9			4.0			20				
15	0.62	0.09	6.1	.17	4.9	8.8	.18	7.6	8.8	.18	7.6	14				
Average	0.63	0.08	4.3	.16	3.3	6.4	.22	5.1	6.6	.23	5.3	23	621	−243	−159	+ 390
±SD	0.22	0.03	2.3	.06	2.0	3.2	.08	3.0	3.2	.09	3.0		297	160	150	403
B. Physically active men																
16	1.06		2.2			1.8			1.7			27				
17	0.72	0.10	2.7	.11	1.9	1.8	.14	0.8	2.0	.13	1.1	64	437	−220	+192	+ 571
18	0.60	0.09	2.2	.19	1.5	1.9	.15	0.8	1.9	.16	0.8	76	409	−140	+280	+1,542
19	0.58	0.06	2.1	.11	1.0	1.0	.08	0.2	1.1	.08	0.3	56	545	−248	−270	+ 881
20	0.60	0.08	1.7	.12	0.8	1.5	.11	0.7	0.6	.08	0.1	65	489	+012	+273	+ 886
21	0.84	0.11	1.1	.12	0.1	1.0	.12	0.1	0.6	.08	0.0	81	335	−133	+436	+ 843
22	0.67	0.10	2.5	.19	1.2	2.1	.17	0.9	3.4	.18	2.2	60	587	−257	+129	+1,150
23	0.31	0.05	0.7	.08	0.3	0.3	.07	0.0	0.3	.05	0.0	53	668	−114	+221	+1,141
24	0.20	0.05	1.3	.12	0.9	0.9	.11	0.4	0.6	.09	0.2	66	818	−195	+123	+ 807
25	0.61	0.11	0.9	.17	0.0	1.0	.13	0.2	1.4	.14	0.6	59	292	− 36	+313	+1,142
26	0.33	0.07	1.3	.12	0.7	1.0	.11	0.4	0.5	.07	0.2	60	826	−464	−267	+ 259
Average	0.59	0.08	1.7	.13	0.8	1.3	.12	0.5	1.3	.11	0.6	61	541	−180	+143	+ 922
±SD	0.31	0.04	0.9	.06	0.7	0.7	.05	0.4	1.0	.06	0.7		259	146	240	468
p†	>0.5	>0.5	<.003	<0.3	<.003	<.001	<.003	<.001	<.001	<.002	<.001		>0.5	>0.3	<.006	<.02

* Change from control values.

† Probability of differences in means of the two groups due to chance.

jects and then fell without further significant change for the remainder of the exercise period.

There was no significant correlation between the final XL during exercise and either cardiac index ($r = -0.20$) or stroke index ($r = -0.35$). Similarly, the increment in heart rate was not correlated with XL at the end of exercise. The final level of XL, however, was correlated with the duration of exercise when all subjects were considered ($r = -0.81$).

Arterial pyruvate concentrations during exercise were also different in the two groups. The average resting values of 0.08 mM were identical; however, the pyruvate values during exercise

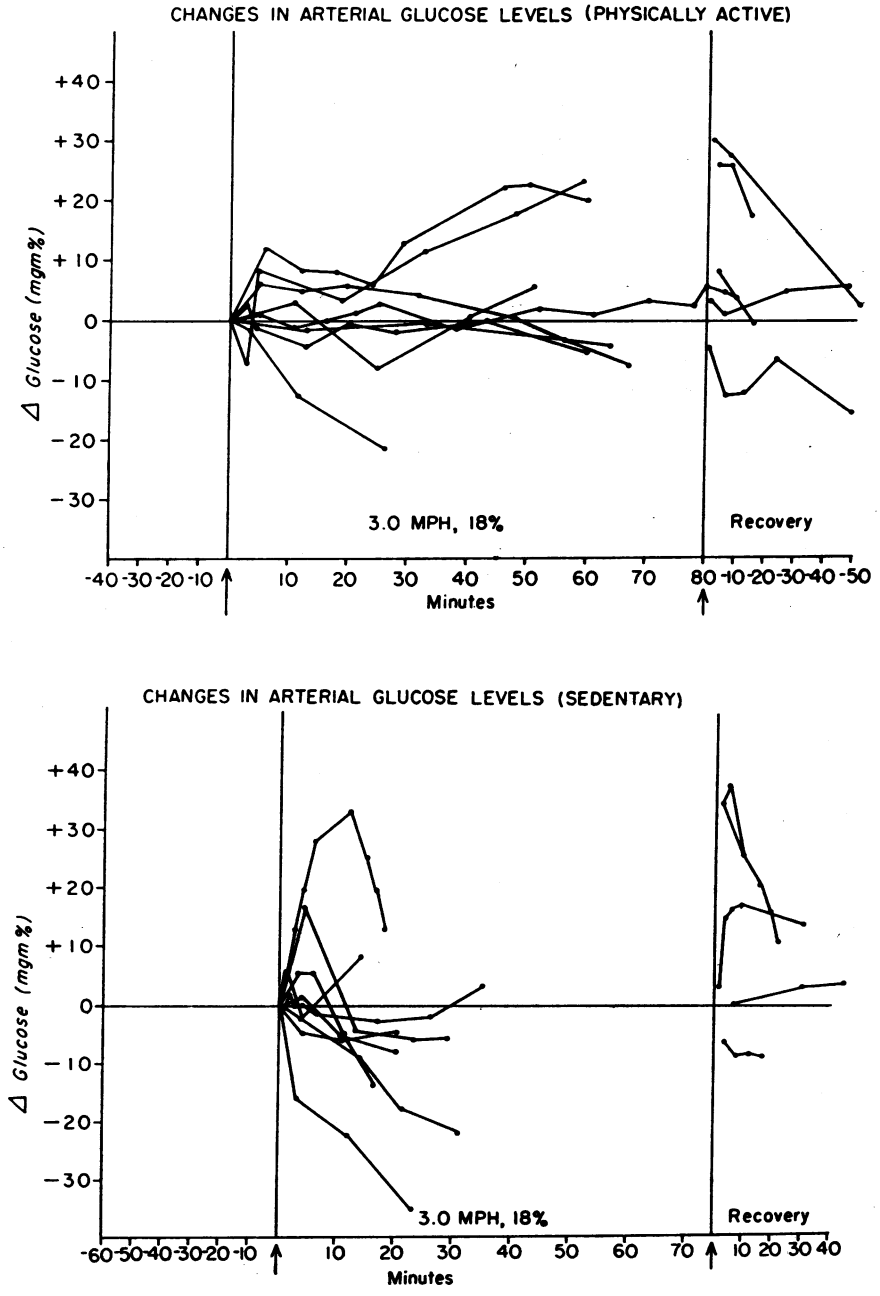

FIG. 4. CHANGES IN ARTERIAL GLUCOSE DURING EXERCISE.

were significantly higher in the sedentary group after the first few minutes of exercise (Table II). In minutes 14 to 16, the average concentration in the sedentary subjects was 0.22 mM, compared to 0.12 mM in the physically active group ($p < .003$). After an hour of walking, the pyruvate value in the latter group was essentially unchanged and significantly less than the final pyruvate in the sedentary subjects ($p < .002$).

Arterial concentrations of glucose in some subjects varied considerably in magnitude and direction during this exercise. By the end of exercise, the average change in glucose was -7.0 mg per 100 ml in nine sedentary subjects and $+0.5$ mg per 100 ml in eight of the physically active group so studied (Figure 4). The change in glucose was not correlated with cardiac index, change in heart rate, or stroke index. Final *XL* during exercise was poorly correlated with the change in glucose when both groups were examined ($r = 0.47$); however, in six sedentary individuals where correlation could be made, there was a relationship significant at the 5% level of confidence ($r = +0.83$).

Plasma FFA. The concentration of arterial plasma FFA fell promptly after exercise was initiated, as shown by the mean curves for the two groups in Figure 5. The average nadir in these curves occurred at 10 and 9 minutes in the sedentary and physically active groups, respectively, and represented respective decreases of 39 and 33% (Table II). These values of FFA are not corrected for the reduction in plasma volume known to occur with exercise. If a correction were made, the exercise values would be approximately 15% lower and the changes somewhat greater (18).

After the initial fall, FFA slowly rose as exercise was continued. In the sedentary subjects, the average FFA was still 26% below the control level at the time of "maximal" endurance. A similar rise in FFA was seen in the other group (Figure 5), where capacity for exercise was markedly greater and the continued rise of FFA more apparent; just before exercise was stopped, after an average of 63 minutes, the mean FFA was 26% greater than the pre-exercise concentration.

After exercise, a rapid increase in FFA was seen in all subjects (Table II), usually reaching

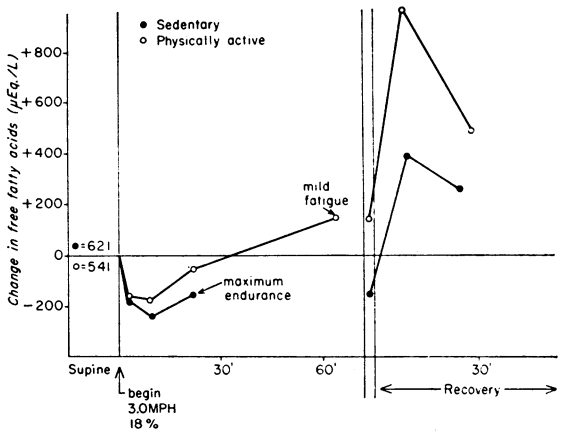

FIG. 5. AVERAGE CHANGES IN ARTERIAL FREE FATTY ACIDS DURING EXERCISE. The mean control values of 621 and 541 μM per L are indicated at the left.

a peak in the first 10 minutes of recovery. In the physically active group, the mean peak increase was 922 μmoles per L above the pre-exercise value, a significantly greater rebound than that of 390 μmoles per L observed in the sedentary subjects ($p < .02$). If, however, the recovery concentrations are compared to FFA in the last minute of exercise, the "rebound" of 779 μmoles per L in the physically active subjects is not significantly different from that of 561 μmoles per L observed in the sedentary group ($p > 0.2$).

DISCUSSION

The quantitative differences in the hemodynamic responses to exercise between the two groups are of interest. In one group, this level of exercise represented the subjects' maximal endurance after an average of 24 minutes. On the other hand, for the physically active group, largely represented by well-trained mountain climbers, this same level of exercise was submaximal even after an hour. This latter group exhibited a significantly lower heart rate and greater stroke index during exercise. Since the average cardiac index was nearly equal in the two groups (Figure 2), the greater endurance of the physically active group cannot be accounted for by enhanced cardiac output. It would appear more likely that under the specific conditions of these studies, the basis for the prolonged endurance and lack of fatigue was related to peripheral circulatory or metabolic adaptions, or both, associated with physical conditioning.

Freedman and colleagues (19) studied three members of a track team, two of them before and after 2 months of competitive running. These investigators, using cardiac catheterization technic and direct measurement of pulmonary arteriovenous differences, found no changes in cardiac outputs or arteriovenous differences after further physical conditioning. Their observations were made at moderate levels of exercise and for short periods of time. They did not study sedentary subjects or maximal responses to exercise; however, they speculated that local tissue factors might be more important than cardiorespiratory phenomena in accounting for the benefits of training.

A continuous increase in heart rate was observed in both the sedentary and physically active groups (Figure 1). Although heart rate during light exercise is known to be quite stable for long periods, heavier work is frequently accompanied by a secondary rise, and exhausting work by a continuous increase in heart rate (20, 21). The mechanisms responsible for the slowly increasing heart rate are not known; possibly this may be due to elevated body temperature. Since the physically active group accumulated almost no *XL* after the first few minutes, anaerobic metabolism and its consequences probably were not of significance in augmenting the heart rate of this group. The larger increment in heart rate observed in the sedentary subjects, however, may have been in part secondary to the metabolic changes of anaerobiosis. The reduction in stroke index observed during prolonged exercise is not readily explained. Although stroke index did not fall regularly in all subjects, the changes between the first and last observations during exercise appear to be significant, particularly in the physically active group. Whatever the mechanisms, a "steady state" of stroke volume and heart rate was not realized in either group under the conditions of this study. It is unlikely that the removal of approximately 250 ml of blood over this period would account for the reduction in stroke index. Previous studies (22) have shown that acute bleeding of 2 to 3 times the amount slowly removed in the present study produced a 12% reduction in resting stroke volume. Since the hemodynamic effects of acute bleeding are to some extent transient (23) and since the amount removed was relatively small, we believe that the observed reduction of stroke index was largely unrelated to loss of blood volume.

Accumulation of *XL* in the sedentary individuals clearly separated them from the physically active subjects (Figure 3). Since the accumulation of *XL* probably reflects intracellular oxidative potential and appears to be a good estimate of the degree of anaerobic glycolysis (17), we conclude that the sedentary group responded to this strenuous exercise with increased anaerobic muscle glycolysis. It has been known for some time that athletes, compared to untrained persons, have lower levels of blood lactic acid during exercise (6, 24, 25), and previous investigators have attempted to correlate venous lactic acidemia with oxygen debt (26, 27). Since blood lactic acid includes variable amounts of lactate unrelated to hypoxia, Huckabee's concept of *XL*, compared to the use of forearm venous lactic acid, affords considerable theoretical advantage for the recognition and quantitation of anaerobic metabolism (17).

Bang (24) as well as Tepperman and Tepperman (28) suggested that lactic acid accumulation during exercise was secondary to inadequate cardiorespiratory responses immediately after the onset of muscular exercise. The initial rapid increase in *XL* in our subjects tends to support this. The continued rise of *XL* in the sedentary subjects, the fall of *XL* in the physically active group, and the finding of nearly equal cardiac outputs in both groups suggest, moreover, that anaerobic metabolism, after the first few minutes, was probably a consequence of peripheral muscle factors rather than secondary to an "inadequate" cardiac output.

It seems probable that anaerobic pathways may be utilized as a result of several hemodynamic mechanisms, including reduction of cardiac output and oxygen transport capacity of blood, alterations in the distribution of blood flow, vascular obstruction, and arteriovenous shunting, all of which may produce relative inadequacy of oxygen diffusion in the capillaries. Two mechanisms that might facilitate muscle oxygen transport in physically trained persons come to mind. First, the capillary bed of hypertrophied muscles may be increased (29). If this is the case, a greater diffusing area per unit of muscle mass would tend to promote oxygen transport to the working muscles.

Secondly, vasomotor control of small vessels might function so as to reduce arteriovenous shunting or otherwise alter circulatory pathways, thereby increasing the perfusion of contracting muscles. In this regard, the responses to the hyperthermia of prolonged exercise might be of considerable importance. The possibility of pulsatile blood flow facilitating cellular metabolism is also an interesting one that would seem to merit further study (30). Also, adaptive metabolic mechanisms might be implicated in facilitating the utilization of more efficient aerobic pathways by athletes and "physically conditioned" persons. In this regard, Reynafarje (31) has reported higher concentrations of myoglobin and certain oxidative enzymes in muscles of persons adapted to high altitude. Studies of muscle biopsies in our subjects are currently in progress.

The two groups could also be separated by the average levels of arterial pyruvate during the later periods of exercise, when pyruvate was significantly less in the physically active subjects. A decreasing pyruvate level during exercise in athletic young men has been reported previously (32, 33). The mechanisms responsible for this phenomenon are not known.

The early fall in FFA with exercise confirms previous reports (34–36). Studies designed to demonstrate the contributions of mobilization and utilization of FFA during short periods of exercise have led to somewhat different conclusions. Friedberg, Harlan, Trout, and Estes (35) concluded that the early effect of exercise was to lower plasma FFA by accelerating its removal from blood. They also estimated a significant increase in FFA flux (the amount of FFA entering and leaving the vascular compartment per minute) during strenuous exercise. Carlson and Pernow (18) infused albumin-bound C^{14}-labeled palmitic acid in a subject, and measured the specific activity of the FFA fraction during and after exercise. In spite of a considerable fall in arterial FFA in exercise and a rebound in recovery, they found no appreciable change in specific activity. They concluded that plasma outflow of FFA regulated FFA concentration in the first minutes of exercise and that the rate of addition to plasma of FFA probably remained rather constant. Our data showing a progressive rise in FFA with prolonged exercise and very high rebounds in recovery are certainly consistent with increased mobilization, as well as utilization, of FFA. The difference in recovery FFA between our two groups is more likely to be related to the longer duration of exercise in the physically active group rather than to fundamental differences in lipid metabolism between the two groups.

It has been suggested that the early fall in FFA with exercise is consequent to the increased blood flow in exercising muscles (37). Supporting evidence for this was the correlation between the augmentation of heart rate and the change in FFA reported by Carlson and Pernow (18) and confirmed to some extent in this study ($r = -0.49$,

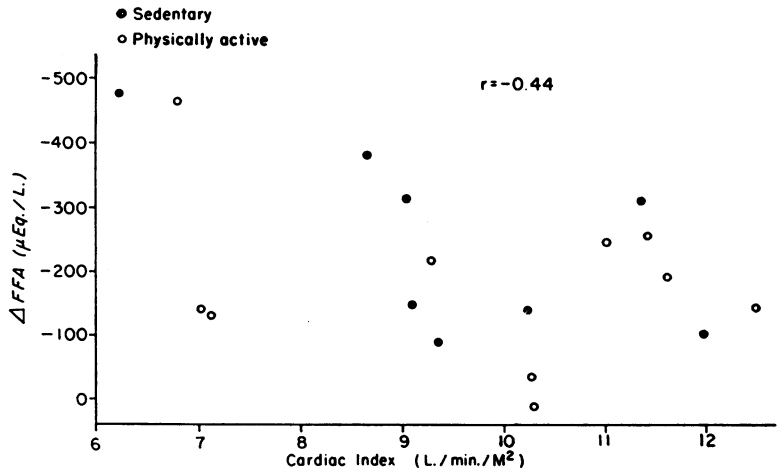

FIG. 6. RELATIONSHIP BETWEEN THE EARLY CHANGE IN FREE FATTY ACID CONCENTRATION AND CARDIAC INDEX.

$p < .05$). The interpretation that this was related to blood flow, however, was not documented (Figure 6); in fact, there was a tendency for those with the largest outputs to show the least change in FFA ($r = 0.44$). It would appear that the reduction in FFA and the increased heart rate of exercise are associated phenomena, their correlation being independent of cardiac output per se. It is possible, however, that direct measurements of muscle blood flow might correlate with FFA reduction.

There was a correlation between early FFA change and simultaneous XL ($r = -0.48$, $p = 0.02$), indicating a tendency for the sedentary persons with more rapid heart rates and greater anaerobiosis to show a somewhat larger fall in FFA in the first minutes of exercise.

SUMMARY

Responses to prolonged strenuous exercise were compared in a group of sedentary subjects and in a group of well-conditioned, physically active men. An identical speed and grade of treadmill walking was used for all studies. Anaerobic metabolic pathways were utilized to a much greater degree in the sedentary subjects, who became exhausted after an average of 24 minutes. In the physically active group, excess lactate initially rose slightly and subsequently fell to a low plateau for an hour. Although stroke volume was greater and heart rate less in the physically active group, cardiac output was virtually the same in both groups. Thus, the anaerobiosis and poor endurance in the sedentary group could not be explained on the basis of inadequate cardiac output.

These data suggest that increased endurance for exercise in trained persons is, at least in part, a circulatory phenomenon related to distribution of muscle blood flow, or an undefined metabolic adaptation associated with skeletal muscle hypertrophy.

Plasma free fatty acids fell initially and slowly rose above the resting value during prolonged exercise. Further rebound of free fatty acids in recovery was consistent with increased mobilization persisting after exercise. Free fatty acid changes were similar in both groups.

Arterial hematocrits during exercise were equal in both groups and did not change during the exercise period.

Heart rate rose progressively during the constant work load in all subjects, and the average stroke index fell significantly by an average of 11 to 16%, indicating that the so-called "steady state" of exercise does not apply to these measurements under the conditions of prolonged, strenuous, upright exercise.

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