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THE EFFECTS OF MUSCULAR LEG EXERCISE ON
NEUROENDOCRINE BLOOD LEVELS

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INTRODUCTION

The combat soldier often depends upon his ability to perform sustained and sometimes severe levels of muscular exertion. For this reason an assessment of his capacity to work and a basic understanding of physical exhaustion is of great practical importance to the Army.

Man's capacity to work has been quantitated by exercise physiologists utilizing the measurement of maximal oxygen uptake and the determination of submaximal exercise endurance time. The measurement of maximal oxygen uptake requires specially trained personnel and is not suitable for assessment of work capacity outside of the laboratory. Endurance testing requires a considerable period of time and trained personnel, and the results from such testing are highly dependent upon the motivation of the subject.

A neuroendocrine profile consisting of growth hormone, nor-epinephrine, cortisol and epinephrine were measured during sub-maximal work loads of mild, moderate, and severe intensities. A comparison of the profile was made during exhaustive exercise at two different work loads (moderate and severe).

SUBJECTS

Two groups of eight volunteer subjects were studied in the Physiology Laboratory, U. S. Army Research Institute of Environmental Medicine. Group I was used in experiment No. 1, and Group II in experiments 2 and 3. All subjects were enlisted men assigned to the test subject platoon U. S. Army Natick Laboratories, Natick, Massachusetts (NLABS). Group I subjects were on 60 days temporary duty assignment to NLABS, had completed basic and advanced infantry training, and were to be assigned to combat units after their tour of duty at NLABS. Group II subjects were permanent members of the test subject platoon. Anthropometric data for the two groups are shown on Table 1.

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TABLE 1. Anthropometric Data

		Group 1	Group 2
Age (years)	\underline{n}	8	8
	\bar{X}	20.5	20.8
	Range	19-22	20-24
Height (inches)	\underline{n}	8	8
	\bar{X}	68	69
	Range	65-72	67-71
Weight (pounds)	\underline{n}	8	8
	\bar{X}	162	153
	Range	130-174	140-165
*Max $\dot{V}O_2$ (L/min)	\underline{n}	8	8
	\bar{X}	3.02	2.86
	Range	2.42-3.35	2.54-3.25
Participated in Experiment No.		1	2, 3

*Max $\dot{V}O_2$ = Maximal oxygen uptake. n = number of studies.
 \bar{X} = mean.

The mean maximal oxygen uptake for the two groups when expressed on the basis of body weight (Group I - 41.1 ml O₂/kg/min: Group II - 41.3 ml O₂/kg/min) are quite similar and both had aerobic capacities in the non-athlete or sedentary range (1).

METHODS AND PROCEDURES

All exercise tests were performed on an electrically braked bicycle ergometer in the upright position. Oxygen uptake was obtained by collecting expired gas through a low resistance respiratory valve into a Douglas bag and measuring the volume on a balanced Tissot spirometer. Gas samples were analyzed for O₂ and CO₂ fractions by the Scholander method. Arterial blood pressure was measured by the indirect (arm cuff) method. Hematocrit and hemoglobin were determined by routine methods, and blood lactate was measured by enzymatic assay.

Preliminary testing was performed to acquaint the subjects with the procedure and to establish their maximal oxygen uptakes. No exposure to strenuous exercise or undue stress of other types had occurred in the 24 hours preceding the morning of the study. On the day of the study the subjects had a light breakfast and at 0800 hours, were placed in bed and an indwelling polyethylene catheter was introduced into the antecubital vein by the Seldinger technique (2). The order of mean intensities of workloads, rest periods, and sampling times of all three experiments are shown in Figure I.

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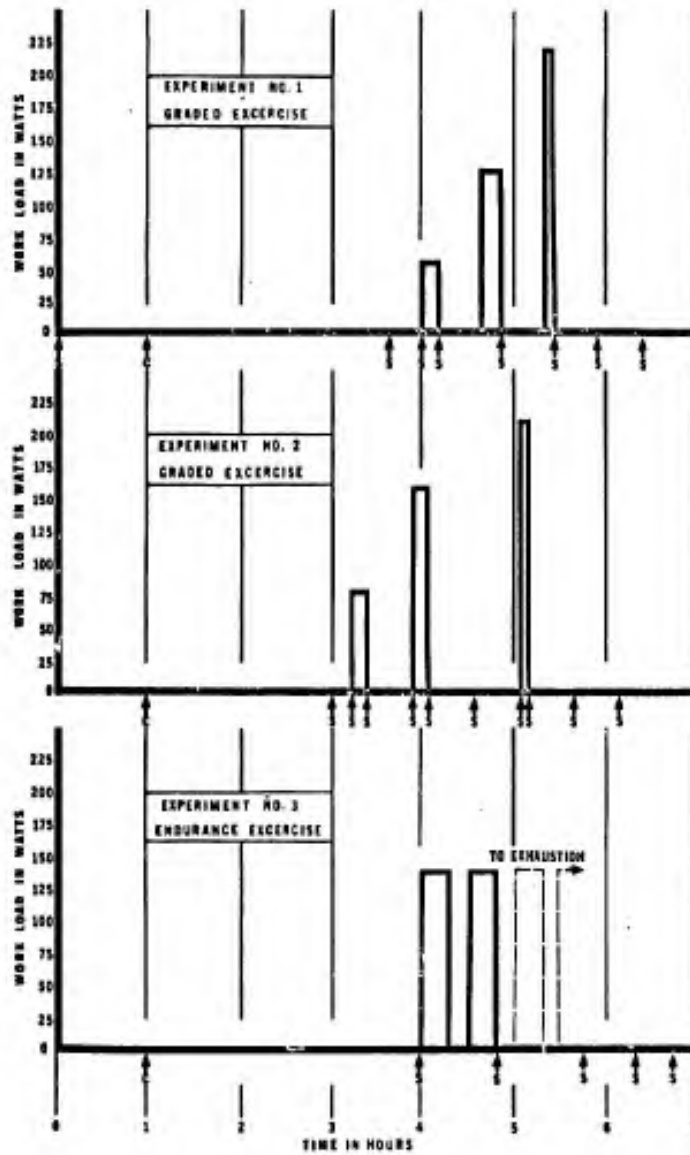


FIGURE 1. Schematic Representation of Experimental Procedures. C-indicates introduction of catheter. S-indicates blood sample taken. Heavily outlined bars indicate work periods. The ordinate is expressed as workload in WATTS and the abscissa is time in hours. In Experiment No. 3, work was continued in 20 minute increments until exhaustion occurred.

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Experiment No. 1. After three hours at bed rest three levels of steady state exercise were performed at work loads approximating 40, 70 and 100% of maximal oxygen uptake. Blood samples were taken at rest and during the last minute of submaximal and maximal exercise and 30 minutes and 60 minutes after the completion of work. Circulatory studies were obtained during the last two minutes of submaximal exercise and during the last three minutes of maximal exercise. Samples for blood lactates were taken during the last minute of submaximal work and five minutes after maximal work. In this experiment and Experiment No. 2 heart rate was obtained by electrocardiographic recording at rest, before each work load, and at one minute intervals throughout each exercise period. Blood pressure was measured at rest and during the last minute of each exercise period.

Experiment No. 2. Two hours of bed rest were allowed following introduction of the venous catheter. This was also a graded steady state exercise study at approximately 40, 70 and 100% of maximal oxygen uptake--but longer periods of recovery were allowed between workloads. Samples were obtained at rest and during the last minute of work. In addition, samples were taken following each of three workloads as indicated in Figure I.

Experiment No. 3. A period of three hours rest followed the introduction of the catheter. This was an endurance exercise test at approximately 70% of maximal oxygen uptake. Heart rate was obtained every five minutes, blood pressure every 15 minutes and circulatory studies every 30 minutes, and at exhaustion. Blood samples were taken before exercise began, at fifty minutes of exercise, and at exhaustion. In addition, recovery blood samples were obtained at 30 minutes and 60 minutes after exhaustion (See Figure I).

All blood samples were immediately centrifuged, the plasma decanted and frozen. The combined collections of several subjects were packed in dry ice in special shipping containers and air freighted to Walter Reed Army Institute of Research (WRAIR) in Washington, D. C., at least once per week. All biochemical determinations, with the exception of the blood lactic acids, were made in the laboratories of the Department of Neuroendocrinology, Division of Psychiatry, WRAIR, by methods previously described (3).

RESULTS

Maximal oxygen uptake is defined as a plateau of oxygen uptake with increasing workloads. This was determined in this study on each individual during the preliminary testing, by the method of Astrand (4).

Experiment No. 1 (Table 2).

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The exercise workloads during the actual experiment were of mild, moderate and maximal intensity (36, 63, and 98% of maximal oxygen uptake respectively). Heart rate increased in linear fashion. Blood pressure increased from rest to maximal work by a mean of 40 mm Hg systolic and 12 mm Hg diastolic. Lactic acid levels increased in non-linear fashion with the greatest rise occurring from the moderate to the maximal work levels. The magnitude of the values of blood lactic acid during the last workload is compatible with maximal exercise (5).

The greatest levels of cortisol occurred at 30 minutes of recovery after the maximal exercise, but there was a significant rise in cortisol levels in the samples taken during the maximal workload. The lowest work load appeared not to have affected the blood levels of cortisol. Growth hormone was slightly elevated following insertion of the catheter but returned to control levels prior to the first workload. The levels of growth hormone rose with mild work and increased further to their greatest values at the moderate workload. The levels then declined during maximal work and returned to resting levels by the end of one hour of recovery. This pattern of declining levels of growth hormone from moderate to maximal exercise was seen in 5 of the 8 subjects in Experiment No. 1.

Experiment No. 2 (Table 3).

The three work levels used in this experiment were slightly higher during the submaximal exercise (44%, 74% and 100% of maximal oxygen uptake--mild, moderate, and maximal, respectively). Blood pressure showed less rise (mean systolic rise 23 mm Hg and diastolic rise 8 mm Hg) from rest to maximal work than was seen in Experiment No. 1. Heart rate showed a similar response as in Experiment No. 1. Lactic acid levels were taken five minutes after the maximal workload and were in the range considered compatible with maximal work. Cortisol levels measured both during and at 30 minutes after work did not change during light and moderate exercise. A mean rise of 4 uG/L occurred in response to the maximal exercise and it subsided by one hour of recovery. Growth hormone levels which were elevated following insertion of the catheter had not returned to control values prior to the onset of exercise, hence, declined from control samples to the least workload. It then rose to its peak level at the moderate workload and decreased during maximal exercise to the same level which was observed during mild exercise. This pattern of lower growth hormone levels during maximal than with moderate exercise was seen in five of the eight subjects studied. Norepinephrine levels show a pattern of increasing values with increasing workloads, with the greatest rise occurring during maximal work. By one hour the levels had returned to control values. Epinephrine shows a tendency to increase with greater workloads but the quantity of this change is small.

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TABLE 2. Experiment No. 1; Graded Exercise

	Control		Exercise			Recovery	Recovery
	1	2	1	2	3	30 min	60 min
Work Load (Watts)	0	0	4.57	7.38	8.39		
*VO ₂ (L/min)	0.26	0.26	1.11	1.89	3.02		
SE	0.004		0.056	0.121	0.102		
VO ₂ (% Max)	8	8	36	63	98		
SE	0		-	-	-		
Heart Rate (Beats/Min)	8	74	8	8	8		
SE	3		3.9	3.0	1.7		
B.P. (mm Hg)	8	122/73	8	8	8		
SE		1.8/3.2	0.9/4.1	5.0/4.4	5.1/4.7		
#Hla (mM/L)	8	1.20	8	7	8		
SE		0.055	0.094	0.394	0.508		
Cortisol (ug/L)	8	8	8	8	8	7	7
SE		1.2	0.8	1.0	1.1	1.5	1.8
Growth Hormone (ug/L)	8	8	8	8	8	7	7
SE		3.2	1.3	8.1	3.7	2.4	0.9

*VO₂ - oxygen uptake. #Hla - blood lactic acid. n - number of studies. X̄ - mean. SE - standard error of mean.

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	Experiment No. 1:		Experiment No. 2:		Graded Exercise		Recovery		Exercise		Recovery		Exercise		Recovery		Exercise		Recovery	
	Control	Control	Control	Control	Exercise	Recovery	Exercise	Recovery	Exercise	Recovery	Exercise	Recovery	Exercise	Recovery	Exercise	Recovery	Exercise	Recovery	Exercise	Recovery
Work Load (Watts)	8	8	8	8	79.4	2.20	142.5	4.53	212.5	6.20	8	8	8	8	8	8	8	8	8	8
VO ₂ (L/Min)	0.26	0.26	1.25	0.032	8	8	2.11	0.078	8	8	2.86	0.093	8	8	8	8	8	8	8	8
SE	0.00	0.00	0.032	0.00	0.032	0.00	0.078	0.00	0.078	0.00	0.093	0.00	0.00	0.093	0.00	0.00	0.093	0.00	0.00	0.113
VO ₂ (% Max)	8	8	44	8	8	8	74	8	8	8	100	8	8	8	8	8	8	8	8	8
SE	0	0	44	0	8	8	74	8	8	8	100	8	8	8	8	8	8	8	8	8
Heart Rate (Beats/Min)	8	8	114	8	114	8	161	3.0	189	2.4	8	8	8	8	8	8	8	8	8	8
SE	3	3	2.7	3	2.7	3	3.0	3.0	3.0	2.4	3	3	3	3	3	3	3	3	3	3
Blood Pressure (mm Hg)	114/77	114/77	121/78	1.0/0.8	132/80	2.0/0.9	137/85	1.4/0.5	137/85	1.4/0.5	137/85	1.4/0.5	137/85	1.4/0.5	137/85	1.4/0.5	137/85	1.4/0.5	137/85	1.4/0.5
SE	1.7/1.6	1.7/1.6	1.0/0.8	1.0/0.8	2.0/0.9	2.0/0.9	1.4/0.5	1.4/0.5	1.4/0.5	1.4/0.5	1.4/0.5	1.4/0.5	1.4/0.5	1.4/0.5	1.4/0.5	1.4/0.5	1.4/0.5	1.4/0.5	1.4/0.5	1.4/0.5
H1a (mM/L)	8	8	9.36	8	8	8	9.36	8	8	8	0.762	8	8	8	8	8	8	8	8	8
SE	0	0	9.36	0	8	8	9.36	8	8	8	0.762	8	8	8	8	8	8	8	8	8
Cortisol (ug/L)	4	4	7	4	7	4	7	4	7	4	7	4	7	4	7	4	7	4	7	4
SE	1.1	1.1	0.9	1.1	1.6	0.8	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2
Growth Hormone (ug/L)	8	8	6	8	6	8	11	5	4	8	4	8	4	8	4	8	4	8	4	8
SE	5.7	5.7	2.8	5.7	2.6	1.5	5.3	1.1	0.9	5.3	1.1	0.9	1.1	0.9	1.1	0.9	1.1	0.9	1.1	0.9
Nor-Epi nephrine (ug/L)	7	7	2.1	7	2.3	1.8	2.7	2.0	4.0	2.0	4.0	2.0	4.0	2.0	4.0	2.0	4.0	2.0	4.0	2.0
SE	1.7	1.7	2.1	1.7	2.3	1.8	2.7	2.0	4.0	2.0	4.0	2.0	4.0	2.0	4.0	2.0	4.0	2.0	4.0	2.0
Epi-nephrine (ug/L)	7	7	0.09	7	0.20	0.10	0.29	0.14	0.41	0.14	0.41	0.14	0.41	0.14	0.41	0.14	0.41	0.14	0.41	0.14
SE	0.055	0.055	0.046	0.055	0.110	0.057	0.132	0.087	0.149	0.087	0.149	0.087	0.149	0.087	0.149	0.087	0.149	0.087	0.149	0.087

(Symbols are the same as for Table 2)

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TABLE 4. Experiment No. 3; Endurance

		Control 1	Control 2	Exercise 1 Hour	Exercise Exhaustion	Recovery 1 Hour
Work Load (Watts)	<u>n</u>	8		8	8	
	<u>X</u>	0		138.1	138.1	
	SE	0		3.77	3.77	
$\dot{V}O_2$ (L/Min)	<u>n</u>	8		8	8	
	<u>X</u>	0.26		2.12	2.16	
	SE	0		0.064	0.051	
$\dot{V}O_2$ (% Max)	<u>n</u>	8		8	8	
	<u>X</u>	9		74	74	
	SE	0		-	-	
Heart Rate (Beats/Min)	<u>n</u>	8		8	8	
	<u>X</u>	75		176	176	
	SE	3.6		3.7	4.3	
Blood Pressure (mm Hg)	<u>n</u>	8		8	7	
	<u>X</u>	117/77		135/76	136/81	
	SE	1.1/0.7		3.5/4.3	1.6/0.9	
#H1a (mM/L)	<u>n</u>			7	8	
	<u>X</u>			4.72	4.02	
	SE			0.760	0.559	
Growth Hormone (uG/L)	<u>n</u>	8	8	7	8	8
	<u>X</u>	5	5	14	7	4
	SE	2.2	1.8	2.3	1.7	1.2
Nor- epinephrine (uG/L)	<u>n</u>	8	8	7	8	8
	<u>X</u>	2.0	2.6	4.3	4.2	2.5
	SE	0.19	0.29	0.41	0.45	0.26
Epineph- rine (uG/L)	<u>n</u>	8	8	7	8	8
	<u>X</u>	0.29	0.16	0.54	0.71	0.20
	SE	0.126	0.062	0.203	0.186	0.073

(Symbols are the same as for Table 2)

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Experiment No. 3 (Table 4)

This experiment consisted of repeated 20 minute exercise periods at a mean value of 74% of the individual's maximal oxygen uptake, interrupted by 10 minute rest periods, until he was exhausted. The total duration of this exercise time was a mean of 106 (range, 72 to 140) minutes. Oxygen uptake did not change during the exercise test, and although heart rate rose with the passage of time, its peak value at the end of one hour was not different than at exhaustion. Blood pressure showed little change during work. Lactic acid levels increased to a mean of 4.72 mM/L and decreased slightly at exhaustion to a mean of 4.02 mM/L. Growth hormone which was at control levels immediately preceding the beginning of exercise, then increased to a peak value at one hour and decreased, at exhaustion, to near control levels. This pattern of decrease at exhaustion was seen in six of seven subjects studied. Norepinephrine increased to levels similar to those seen at maximal exercise by the end of one hour and remained at essentially the same levels to exhaustion. Recovery was completed by one hour. Epinephrine, as with the graded exercise experiment, showed a rise during exercise, but the magnitude was small.

No more than 250 ml of whole blood was withdrawn during any one of the graded exercise experiments -- and less than 200 was withdrawn during the endurance study. Experiments 2 and 3 were done on all subjects in Group II and at least 4 days were allowed between studies. The effect on hemoglobin and hematocrit was minimal.

DISCUSSION

This study shows a clear relationship of a variety of parameters to the stress of the workload during graded steady state muscular exercise. Heart rate is directly related to the per cent of maximal oxygen uptake. This finding is in agreement with that of Astrand and Rhyning (6). Blood lactic acid is related in a non-linear way to the per cent of maximal oxygen uptake as described by others (7). The blood lactate samples during the severe work load were taken after exercise when lactate has been shown to peak (8) and were within the range of values compatible with maximal oxygen uptake. Norepinephrine levels were related to the per cent of maximal oxygen uptake in a non-linear fashion. This relationship extends even to workloads which were greater than 100% of maximal oxygen uptake, as shown by others (9). Epinephrine shows only a slight rise. With exercise, growth hormone reached its' highest levels at 70% of maximal oxygen uptake. Elevations of growth hormone during exercise have been reported (10) but the workload was not quantitated. Cortisol, because of its slower response to the stimulus of stress (3), is probably best reflected in blood samples taken at 30 minutes to one hour after the end of an exercise period. Cortisol rose only during maximal workloads. Other studies have reported both increases (11) and decreases (12) in cortisol levels, but the intensities of the workloads under which these changes occurred were not clearly defined. All hormones studied

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had returned to resting levels by one hour after maximal exercise. Growth hormone levels declined to control values in virtually every subject despite the fact that most subjects were sedentary. Thus, this study did not confirm an earlier report by Sutton et al (11) of prolonged growth hormone elevations during recovery from exhaustive exercise in untrained individuals. The pattern of response described related well to the workload when described as per cent of maximal oxygen uptake but not to the work load when expressed in Watts.

A different pattern of response was noted if the moderate (70% of maximum oxygen uptake) workload was continued to exhaustion. Heart rate gradually increased with the progress of time, reaching its highest levels by one hour of exercise and changing little to exhaustion. Blood lactic acid rose from resting to peak levels at the end of one hour and then declined, a pattern which has been previously described (13). Norepinephrine levels increased with time and were maximal at the end of one hour, remaining at this level to exhaustion. Epinephrine levels showed little change, as in the graded exercise studies. Growth hormone rose to peak levels at one hour then declined at exhaustion almost to control levels. The patterns of high levels of norepinephrine and low levels of growth hormone characterized exhaustion at both maximal and submaximal work intensities. These findings suggest that the approach of using a neuro-hormonal profile may be of value in determining not only metabolic factors leading to fatigue, but also may be a basis for developing an index of the appearance of fatigue.

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