

Respiratory Response and Muscle Function During Isometric Handgrip Exercise at High Altitude

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The purpose of this investigation was to determine if the hyperventilatory response to fatiguing isometric exercise at sea level could predict resting ventilation and acute mountain sickness (AMS) at 4300 m altitude. Exercise consisted of four successive endurance handgrips held to complete fatigue at 40% of maximum isometric handgrip strength (MHS). There was no relationship between the magnitude or pattern of exercise-induced hyperventilation at sea level and the severity of AMS later at altitude. Sea level hyperventilatory response was not predictive of resting ventilation at altitude. Altitude exposure progressively increased both the incidence and magnitude of the hyperventilatory response to exercise and prolonged it for 60-90 s into the recovery period, providing support for the "central command" theory of ventilatory control during isometric exercise. MHS was significantly increased at altitude—by 11% on day 2 and 16% on day 6. Endurance times to fatigue were reduced, but not always significantly so. A follow-up study involving more practice at sea level demonstrated MHS to be significantly increased throughout an entire 18-d stay at 4300 m and for 3, but not 5, days after descent. Significant changes in endurance could not be demonstrated. Neither AMS nor changes in body weight or circulating norepinephrine levels can account for the temporal pattern of increased grip strength, but the respiratory alkalosis occurring at altitude appears to be a likely mechanism.

A SCENT TO HIGH ALTITUDE results in an immediate and sustained increase in pulmonary ventilation. It is an adaptive response which increases alveolar O₂ concentration, thereby enhancing the gradient for O₂ diffusion into the blood and partially compensating for the decreased O₂ tension of inspired

air. The increase is a true hyperventilation, in view of the resultant decrease in plasma CO₂ tension (6). Those individuals showing the greatest hyperventilatory response at altitude have been reported to suffer less severe symptoms of acute mountain sickness (AMS) than those showing the least hyperventilation (12). Unfortunately, there is no way to identify such "hyperventilatory responders" prior to their initial ascent without exposing them to an hypoxic stimulus. Isometric endurance exercise (handgrip and leg extension), when performed to complete fatigue under normoxic conditions, has been reported to induce a hyperventilatory response in some individuals as they approach their endurance limit (22). It was not known whether such "exercise hyperventilators" possessed increased sensitivity to ventilatory stimuli in general and, thereby, might also exhibit the greatest hyperventilatory response to altitude exposure. If so, it could provide the basis for an easily administered test of AMS susceptibility or resistance. Therefore, in Study 1, ventilation was measured throughout fatiguing isometric handgrip exercise at sea level to determine whether ventilatory patterns during exercise would predict susceptibility to AMS during a subsequent week-long exposure to high altitude. During the course of this study, handgrip strength was found to be significantly increased at altitude, while handgrip endurance was consistently, but not always significantly, reduced. A follow-up study (Study 2) was undertaken to confirm the initial exercise results, extend them over a longer period of altitude exposure, and determine their fate upon return to sea level.

METHODS

Subjects: Subjects were relatively fit, 19-24-year-old male soldiers who volunteered to participate after

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receiving detailed explanations of the procedures and risks involved. In Study 1, 12 subjects completed the sea level baseline portion of the test and the initial remeasurement on the second day of a 7-d altitude exposure. The subject sickest with AMS voluntarily withdrew on the third day at altitude, which left 11 subjects for remeasurement on altitude day 6. In Study 2, eight subjects completed the sea level, altitude, and return-to-sea level phases.

Procedures: In Study 1, subjects performed the handgrip strength and endurance tasks, described below, three times per week (M,W,F) for three weeks at sea-level; control values were determined by averaging the results of the last 2 d at sea level. Subjects were then transported to Pikes Peak, CO (4300 m altitude) where they were retested on days 2 and 6 of a 7-d altitude residence. Ventilation was measured during the endurance tasks on the last day at sea level and on both measurement days at altitude. Subjects were engaged in concomitant studies, both at sea level and altitude, which required them to perform other exercise tasks. So as not to interfere, these other tests were scheduled on days when isometric handgrip testing was not performed, or (occasionally) after handgrip testing had been completed for that day.

In Study 2, subjects also performed the gripping tasks at sea level three times per week (M,W,F) for just over 5 weeks (16 trials). This was done to minimize the possibility that inadequate endurance practice had confounded the results of Study 1. Subjects then spent an 18-d period on Pikes Peak. They were retested every other day at altitude (except for day 10) and also on days 3 and 5 after return to sea level. Again, other exercise testing was performed, but only on days when handgrip testing was not scheduled. After ANOVA showed them not to differ, the results from the last 3 d at sea level were averaged to give a single control value for each parameter.

In both studies, subjects reported for testing at the same time each day, at least 90 min after eating and 60 min after smoking. Maximum handgrip strength (MHS) of the preferred hand was first determined with an isometric strain-gauge dynamometer (18) and then was used as the basis for setting the tension of the subsequent fatiguing endurance grips, which were performed at 40% of that day's MHS. MHS was determined as the peak force observed in a series of at least three maximum effort squeezes, separated by 1-min recovery periods. If the last squeeze exceeded the other two, the series was continued until a squeeze failed to exceed the previous one, with the highest value taken as MHS for that day. Spacing between the handles of the dynamometer was not set to be the optimal for each subject, but was fixed in each study at a spacing comfortable for the subject with the smallest hand. This has been shown previously to have no effect on endurance at a given percent of MHS (20).

Following the determination of MHS, the dynamometer indicator needle was set below its midpoint by 40% of MHS so that the midpoint reference mark could serve as a target for the endurance grips. Each subject then performed a series of four endurance grips to

utter fatigue of the gripping muscles. A recovery period of 11 min was allowed between grips. The series of four grips permitted each subject to reach the relatively consistent endurance times previously reported for the fourth and successive grips in a series using that length recovery period (5). Subjects were persistently exhorted to maintain the indicator needle right on the target until they could no longer do so, no matter how hard they squeezed. In Study 1, ventilation rate (\dot{V}_E) and respiratory exchange ratio (R) were measured for 3-min before, during, and for 2-min after each endurance grip.

Measurement techniques: A semiautomated, open-circuit respiratory gas collection apparatus was used to determine \dot{V}_E and R. The subject breathed through a one-way, low-resistance Kögel valve into a calibrated turbine gasometer (Pneumoscan Model S-300, K&E Engineering), biased with a $1 \text{ L} \cdot \text{min}^{-1}$ flow. Expired O_2 and CO_2 concentrations were determined using Applied Electrochemistry model S3-A and Beckman model LB-2 analyzers, respectively.

Output signals from all sensors were digitized and collected on a Hewlett-Packard model 9815 printing calculator programmed to calculate $\dot{V}_E(\text{BTPS})$, $\dot{V}O_2(\text{STPD})$, $\dot{V}CO_2(\text{STPD})$ and R. Hyperventilation during the endurance grip was inferred from increases in \dot{V}_E sustained for at least 30 s, which were accompanied by values for $R > 1.05$ or increased 0.1 unit above pregrasp R. Fine distinctions on this point were not necessary; individuals either hyperventilated markedly ($\dot{V}_E > 20 \text{ L} \cdot \text{min}^{-1}$, $R > 1.10$) or not at all.

Several other variables were measured concomitantly in Study 1. Epinephrine and norepinephrine excretion rates were determined fluorometrically (1,9) from 24-h urine collections during three consecutive days at sea level and daily throughout the period of altitude exposure, because of the reported association between catecholamine excretion and AMS (15). The occurrence and severity of AMS symptoms were assessed each morning and evening by means of the Environmental Symptoms Questionnaire of Kobrick and Sampson (13). AMS was presumed if a subject vomited, reported a severity level of 4 (severe) for any single AMS-related symptom (headache, throbbing head, nausea, feel sick, upset stomach, dizziness, shortness of breath at rest, loss of appetite), or reported a severity level of 3 (moderate) for two or more symptoms. Again, fine distinctions were not necessary.

RESULTS

Study 1: Of the 12 subjects initially ascending to altitude, six definitely suffered from AMS during their initial 48 h, five suffered slight-to-moderate symptoms, and one was essentially symptom-free. These last six were considered to be "well." Both the number and degree of their symptoms were markedly different from their "sick" counterparts (Table I).

Peak \dot{V}_E observed during the endurance grips at sea level and on days 2 and 6 at altitude were averaged separately for the sick and well groups and are shown in Fig. 1. The data from altitude day 2 were collected during the period of pronounced AMS, while those from altitude day 6 were collected after the period of

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TABLE I. PEAK AMS SYMPTOM SCORES ON DAYS 1 AND 2 OF EXPOSURE TO 4300 M ALTITUDE BY CLASSIFICATION INTO SICK AND WELL GROUPS.

SYMPTOM	Subject-	SICK GROUP						WELL GROUP						
		Number	1	2	3	4	5	6	7	8	9	10	11	12
Headache		4	5	1	4	5	4		1	0	1	1	0	0
Head throbbing		4	5	0	4	5	4		2	0	1	0	0	0
Light-headed		3	3	2	3	5	2		2	1	1	0	0	0
Faint		1	3	2	2	1	2		2	0	0	0	0	0
Hard breathing		2	3	3	1	0	0		0	1	0	0	0	3
Nausea		2	3	5	1	5	1		0	0	1	0	0	0
Upset stomach		3	3	5	1	5	1		0	0	1	0	0	0
Vertigo		1	2	3	1	3	2		2	0	0	0	0	0
Insomnia		4	5	5	3	5	4		0	1	0	0	2	0

0 = none, 1 = slight, 2 = slight-to-moderate, 3 = moderate, 4 = severe, 5 = very severe

susceptibility had passed and the formerly sick subjects had recovered. At sea level, there were no significant differences in peak \dot{V}_E between the groups later to be sick and well at altitude. The altitude day 2 and 6 values also did not differ between groups. There were progressive increases ($p < 0.025$) in peak \dot{V}_E for both the sick and well groups at altitude, however. For both groups combined, the increases above sea level values averaged 18% on day 2 and 24% on day 6. For comparison, the resting \dot{V}_E was elevated 11% on day 2 and 32% on day 6.

The individual patterns of ventilation before, during, and after endurance grips 1 and 4 at sea level are shown in Fig. 2. Grips 2 and 3 were of similar pattern and are not shown. As anticipated, the exercise induced marked hyperventilation in some subjects, but not in others. There were no differences between members of the sick and well groups, however. Three of the subjects later to

be sick at altitude and three to be well hyperventilated markedly during the last half of each endurance grip or within 30 s thereafter ($\dot{V}_E > 30 \text{ L} \cdot \text{min}^{-1}$, $R > 1.05$). Neither the occurrence, timing, nor magnitude of the individual responses was characteristic of later illness or wellness at altitude. The hyperventilatory responses can be seen to occur in, or persist into, only the first minute of the recovery period, and usually only into the first 40 s.

Fig. 3 shows the ventilatory patterns during grips 1 and 4 on day 2 at altitude, when AMS symptomatology was maximal. \dot{V}_E at rest, during the handgrips, and after exercise were increased above those obtained at sea level, but there were no differences between those individuals either sick or well at the time. The hyperventilation during exercise was increased at altitude and was prolonged into the recovery period. Four of

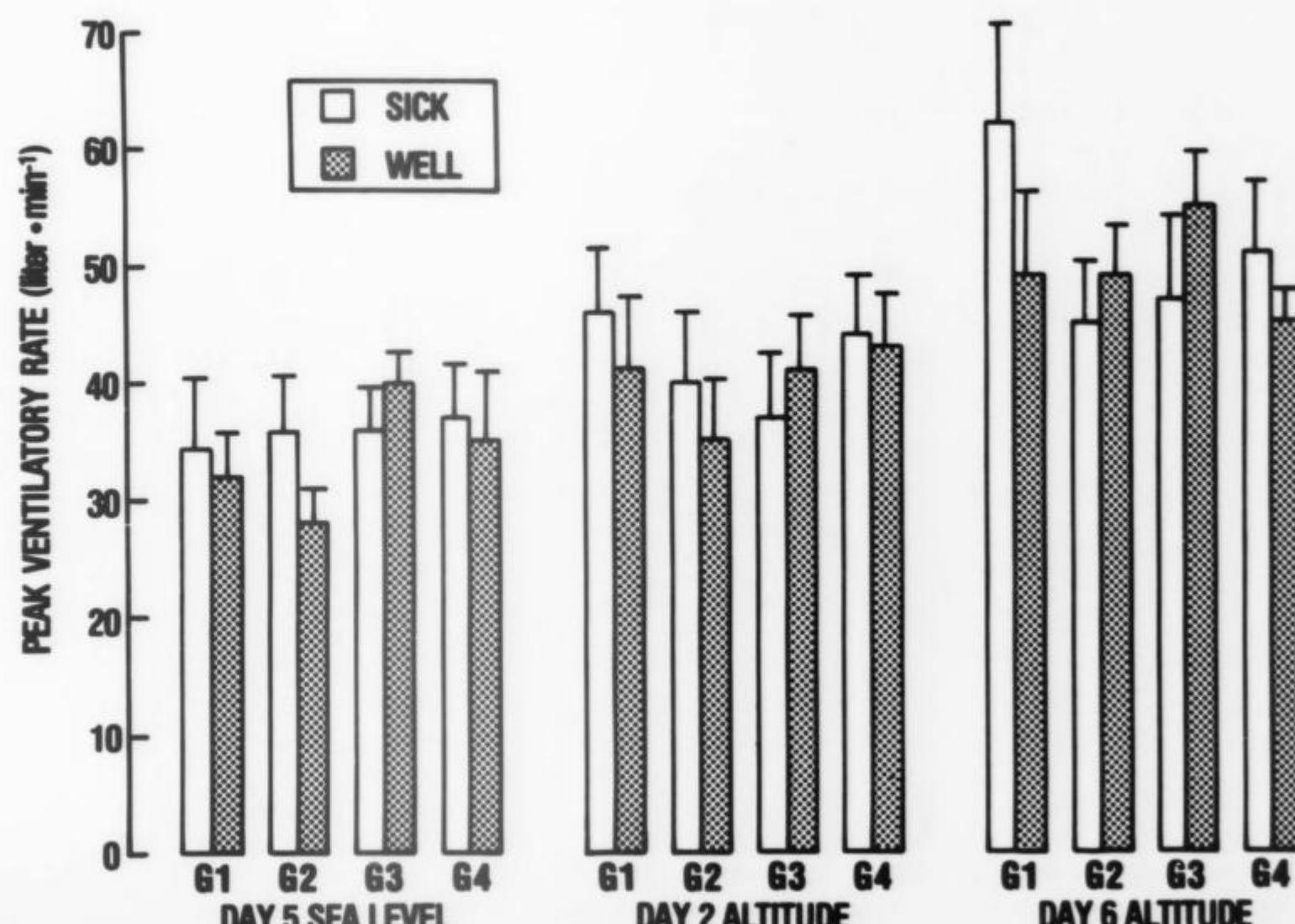


Fig. 1. Mean ventilatory rates (\pm S.E.) during isometric grips 1–4 (G1–G4) at sea level and after 2 and 6 d at 4300 m altitude; subjects separated into those SICK with AMS or WELL on day 2 at altitude.

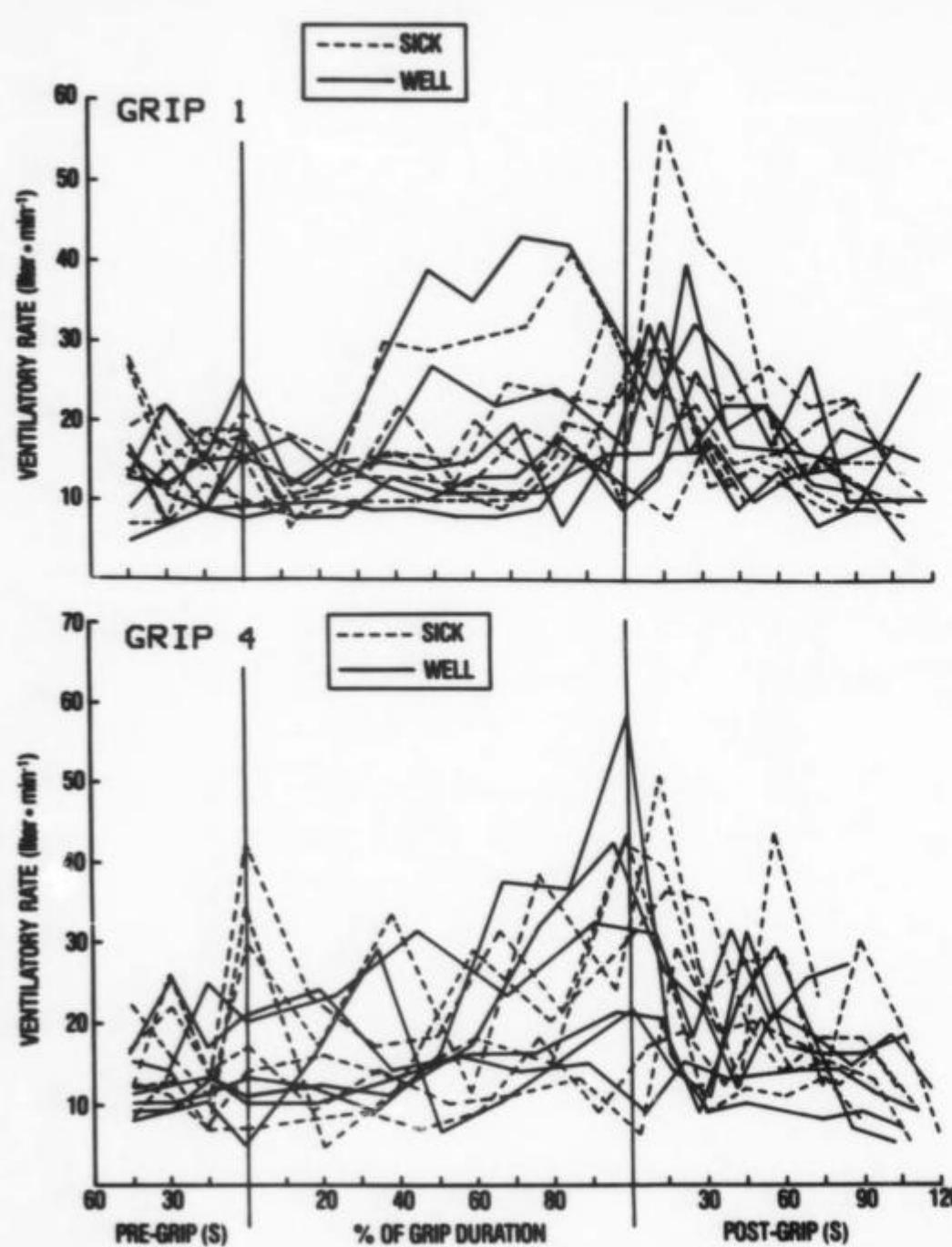


Fig. 2. Ventilatory rates (BTPS) at sea level for each subject before, during, and after the first and last of four isometric grips to complete fatigue. SICK and WELL same as Fig. 1.

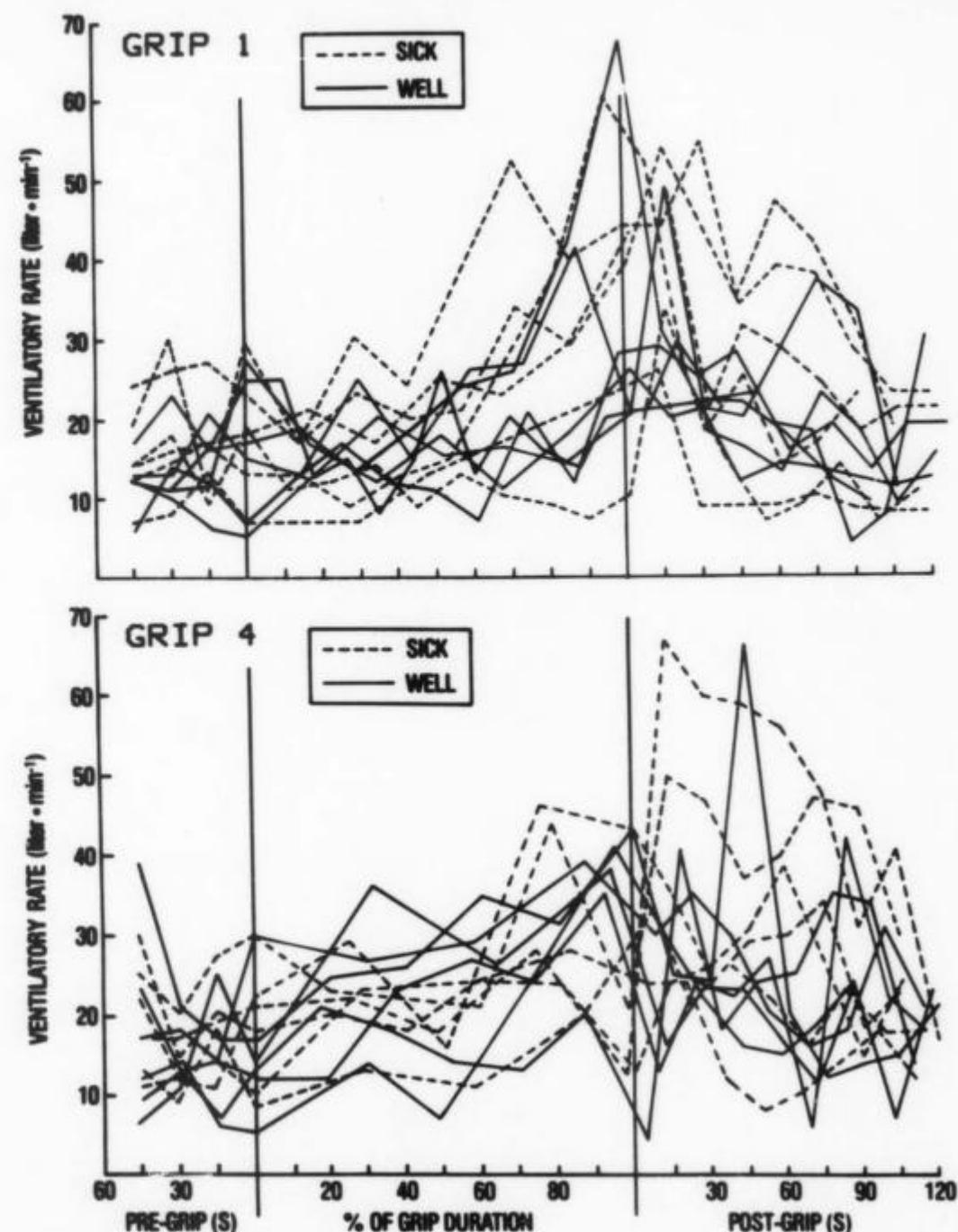


Fig. 3. Ventilatory rates (BTPS) on day 2 at altitude for each subject before, during, and after the first and last of four isometric grips to complete fatigue. SICK and WELL same as Fig. 1.

the sick subjects and five of the well hyperventilated markedly ($\dot{V}_E > 30 \text{ L} \cdot \text{min}^{-1}$, $R > 1.12$); nearly all sustained the hyperventilation for 90 s into the recovery period. The \dot{V}_E responses on day 6 at altitude, after symptoms had subsided, (not shown) were similarly patterned and of even greater magnitude, but, again, with no differences between groups. All five of the remaining formerly sick subjects and four of the well subjects had $\dot{V}_E > 30 \text{ L} \cdot \text{min}^{-1}$ during the exercise. Six of these nine individuals had the hyperventilation persist from 60–120 s into the recovery period.

Both handgrip strength and endurance time to fatigue were found to be significantly altered during the period of altitude residence (Fig. 4). MHS was increased by 11% over the sea level baseline value on day 2 at altitude ($p < 0.01$) and by 16% by day 6 ($p < 0.01$). Day 6 was not different from day 2 ($0.05 < p < 0.10$). The endurance times for all four grips on day 2 were less than the sea level baselines, but only grips 2 and 4 were significantly so (grip 2—17%, $p < 0.05$; grip 4—22%, $p < 0.01$). Endurance times on day 6, although still less than at sea level, had recovered to the extent that they were no longer significantly different.

Catecholamine excretion at sea level and altitude is shown in Fig. 5. The excretion of epinephrine was not altered at altitude while that of norepinephrine increased progressively, with the increase reaching significance ($p < 0.05$) on day 4 at altitude. It should be noted that the greater portion of the strength increase occurred on day 2, before the significant increase in norepinephrine.

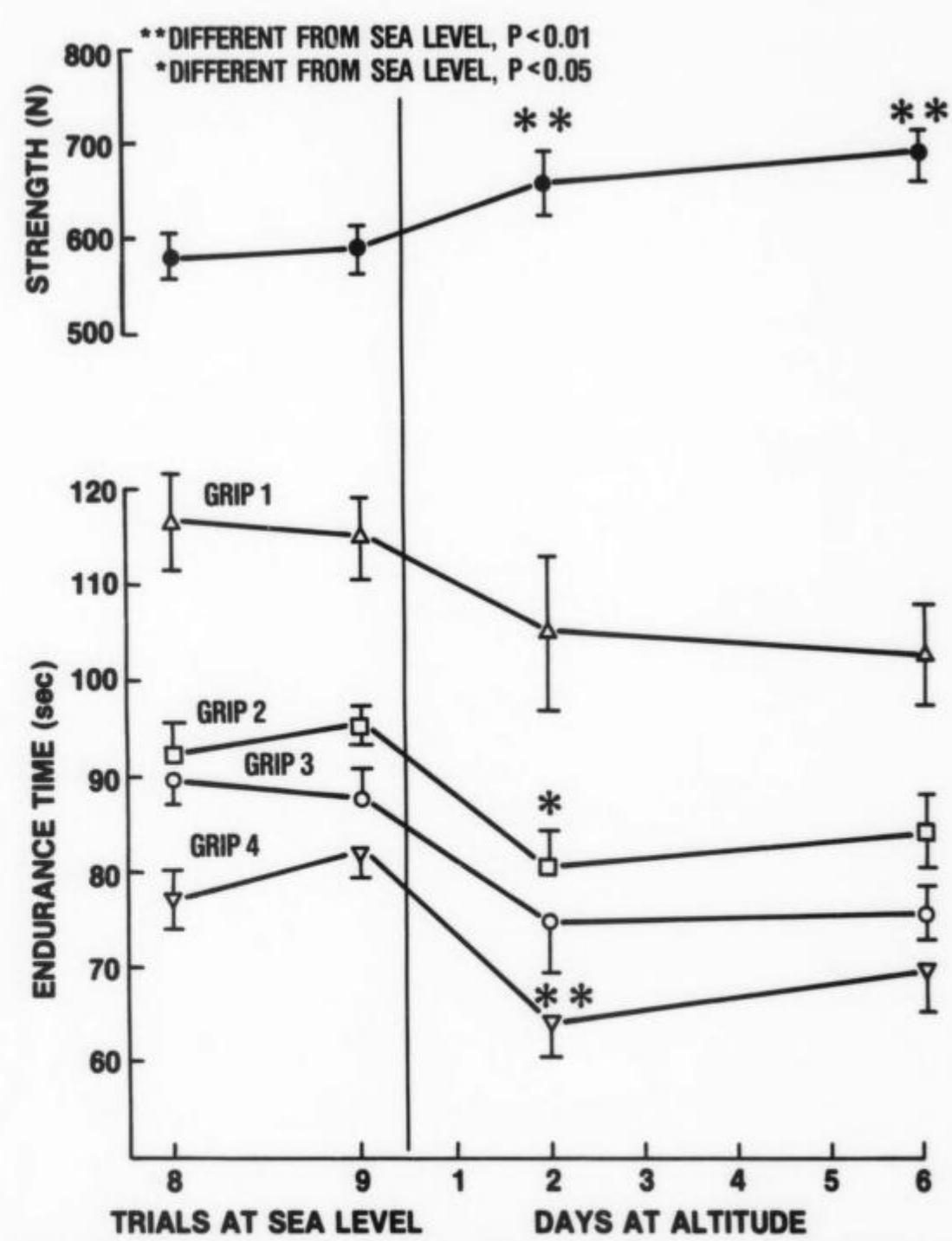


Fig. 4. Maximum isometric handgrip strength and endurance times of four handgrip contractions to complete fatigue: group averages ($\pm \text{S.E.}$) at sea level and at altitude.

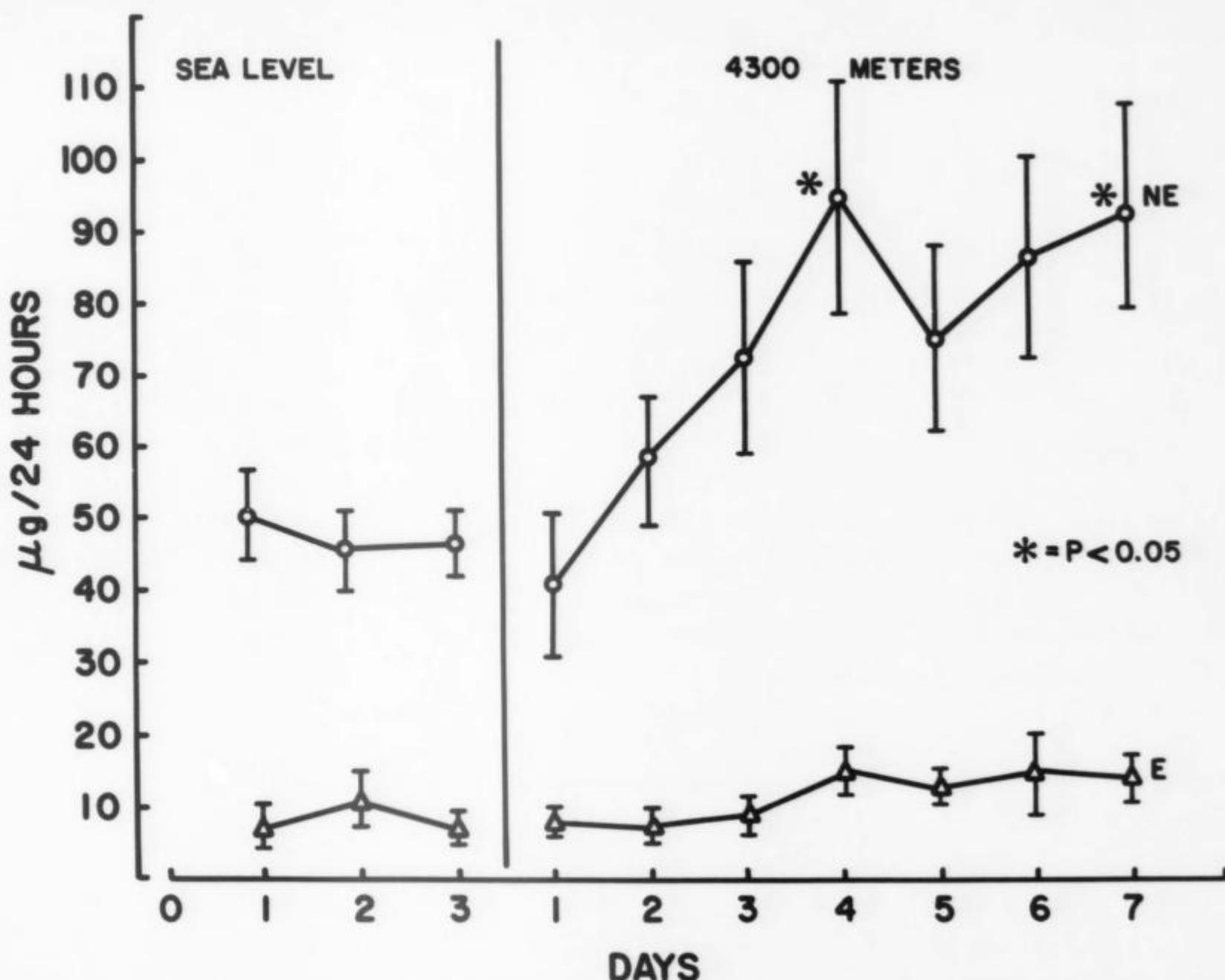


Fig. 5. Mean urinary norepinephrine (NE) and epinephrine (E) excretion at 50 m (sea level) and throughout 7 d at 4300 m altitude. Handgrip testing performed at sea-level and on days 2 and 6 at altitude.

The nonsignificant change in MHS from day 2 to day 6 occurred during the period of maximal norepinephrine excretion.

Study 2: The mean values for MHS and endurance time for grips 1–4 are shown in Table II. MHS throughout the period at altitude was significantly greater than at sea level ($p<0.05$) and remained so for 3, but not 5, days after return to sea level. Endurance times

did not change significantly upon ascent to altitude or descent to sea level. There were no significant changes in either strength or endurance throughout the 18-d period of acclimatization. On day 3 after return to sea level, MHS was identical to the last measurement at altitude; by day 5 after descent, MHS had reverted to within 1 N of the original sea level baseline. This abrupt and significant decrease in strength from the

TABLE II. MAXIMUM HANDGRIP STRENGTH (MHS) AND ENDURANCE TIME FOR FOUR CONSECUTIVE HANDGRIPS HELD TO FATIGUE AT SEA LEVEL, DURING AN 18-D EXPOSURE TO ALTITUDE AND AFTER RETURN TO SEA LEVEL. MEAN \pm S.E. N=8.

Condition	Day	MHS (N)	Endurance time (s)			
			Grip 1	Grip 2	Grip 3	Grip 4
sea level	14	701 \pm 34	80.2 \pm 7.8	70.0 \pm 6.5	67.2 \pm 5.2	65.9 \pm 6.8
	15	718 \pm 28	77.0 \pm 6.5	68.1 \pm 7.4	68.4 \pm 6.0	64.2 \pm 6.4
	16	707 \pm 30	85.8 \pm 11.3	71.1 \pm 10.3	74.1 \pm 1.9	70.0 \pm 9.3
	Mean	709 \pm 29	81.0 \pm 8.2	69.8 \pm 7.6	69.9 \pm 7.1	66.8 \pm 7.0
Altitude	2	772 \pm 29	74.4 \pm 7.3	64.4 \pm 6.2	55.2 \pm 4.2	56.1 \pm 2.5
	4	727 \pm 32	74.6 \pm 8.4	68.0 \pm 6.5	60.8 \pm 4.0	60.8 \pm 3.1
	6	733 \pm 38	91.6 \pm 11.1	67.5 \pm 4.7	64.0 \pm 5.1	61.5 \pm 4.4
	8	764 \pm 39	89.6 \pm 8.8	61.4 \pm 7.1	56.8 \pm 6.3	60.5 \pm 3.6
	12	765 \pm 49	97.0 \pm 10.3	71.6 \pm 3.7	68.2 \pm 6.9	65.8 \pm 4.6
	14	736 \pm 47	92.9 \pm 11.2	72.2 \pm 8.1	72.2 \pm 5.9	63.1 \pm 5.3
	16	736 \pm 43	89.5 \pm 10.9	73.4 \pm 7.4	63.0 \pm 7.2	64.0 \pm 6.8
	18	751 \pm 42	86.2 \pm 8.4	65.4 \pm 6.8	63.9 \pm 4.5	60.8 \pm 3.5
	Mean	748 \pm 37*	86.9 \pm 8.0	68.1 \pm 5.1	63.2 \pm 4.3	61.6 \pm 3.2
Return to sea-level	3	751 \pm 44*#	86.6 \pm 8.4	67.1 \pm 7.8	66.2 \pm 6.1	65.0 \pm 5.7
	5	710 \pm 38	92.2 \pm 8.6	79.4 \pm 9.0	72.4 \pm 9.8	72.8 \pm 9.0

*Significantly greater than sea level ($p<0.05$)

#Significantly greater than return to sea level ($p<0.05$)

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third to the fifth day after descent was accompanied by a uniform rise in all four endurance times, but these changes did not reach the level of significance.

DISCUSSION

Hyperventilation: The original hypothesis which prompted Study 1 was that hyperventilation during the course of fatiguing isometric exercise at sea level might serve to predict those individuals having greater ventilation during a subsequent exposure to high altitude and, therefore, less severe AMS. This hypothesis was clearly refuted by the results of the first study. There were no differences between those sick and well at altitude in the incidence, extent, or pattern of their hyperventilatory responses during handgrip exercise. This held true at sea level before the exposure, at altitude during the period of greatest AMS symptomatology, and at altitude after recovery had occurred. The exercise did induce a frank, pronounced hyperventilatory response in 6 of 12 subjects at sea level. The incidence and extent of this hyperventilation ($V_E > 20 \text{ L} \cdot \text{min}^{-1}$) was comparable to that observed earlier; Wiley and Lind (22) reported 4 of 7 subjects to have $V_E > 18 \text{ L} \cdot \text{min}^{-1}$ during fatiguing handgrips at 30% and 40% MHS. There are no similar studies of hyperventilation during isometric exercise at altitude for comparison. In Study 1, peak exercise V_E increased progressively at altitude, averaging 18% above sea level V_E on day 2 and 24% above on day 6. The incidence and extent of the hyperventilatory responses also increased at altitude, and the responses were prolonged for 60–90 s into the recovery period (Fig. 2 and 3). The progressive increases in the magnitude and duration of the hyperventilatory response to isometric exercise follow a time course similar to that of the resting ventilation. This suggests that there is a progressive increase in the general sensitivity of ventilatory control during the first 6 d at altitude.

Reduced incidence and severity of AMS symptoms have been reported for those individuals showing the greatest increase in resting ventilation at altitude (12). Presumably, those individuals with the greatest alveolar ventilation had the least arterial hypoxemia and, thereby, the best maintained supply of O_2 to the CNS. They were able to maintain their enhanced ventilation at altitude despite the increased arterial O_2 tension, which lessens the stimulus to the peripheral respiratory chemoreceptors (6). Therefore, they displayed a greater sensitivity in their ventilatory responses to hypoxia. There was no theoretical reason for supposing *a priori* that individuals with greater sensitivity to the hyperventilatory stimulus of isometric exercise might also be the same individuals with the greater ventilatory sensitivity to hypoxia; the results show clearly that they are not. The failure of the exercise stimulus at sea level to identify those individuals with the higher resting ventilation at altitude (Fig. 2) implies an additional difference in the control mechanisms for the ventilatory responses to hypoxia and to isometric exercise, despite their similar increases at altitude. Mechanisms mediating ventilatory response to hypoxia have been summarized extensively (6) and need no elaboration here. One

feature of the response pattern to isometric exercise warrants attention, however, because it contributes an additional clue to understanding ventilatory control during exercise.

Wiley and Lind have examined a number of possible mechanisms for hyperventilation during isometric exercise (22). They have provisionally eliminated muscle ischemia *per se*, the stimulation of either local or central chemoreceptors by muscle metabolites, and the stimulation of afferent pain fibers. They were not able to rule out two other possibilities, however—the afferent input from stretch receptors in muscle or tendon or the increased “central nervous drive” (16) accompanying motoneuron outflow.

Either of these possibilities is compatible with the greater incidence and magnitude of the hyperventilatory responses observed at altitude. The tension at which the 40% maximum endurance grips were performed had to be increased at altitude because the maximum grip strength was greater. Such increased tension stimulated greater central nervous drive in parallel with the enhanced motoneuron outflow recruiting additional motor units; it also increased the neural output from the muscle and tendon stretch receptors, which received a greater mechanical pull. However, only increased central nervous drive can account for the prolongation of the hyperventilatory response for 60–90 s into the recovery period. Stretch receptor activity, no matter how intense, would have ceased immediately upon muscle relaxation and all ventilatory effects would have ended shortly thereafter.

Handgrip strength and endurance: In Study 1, MHS was significantly elevated on days 2 and 6 at altitude. Endurance time to full fatigue was consistently reduced below sea level values on those days, but significantly so only for grips 2 and 4 on day 2. In Study 2, the fate of these alterations in muscular performance was determined over a longer period of altitude exposure and upon return to sea level. In order to reduce the variability in the endurance measures, more handgrip practice was provided before ascent. Study 2 showed that the significant increase in MHS at altitude was a reproducible phenomenon which persisted throughout at least 18 d of exposure and for at least 3, but not 5, days after descent. Despite the additional practice, grip endurance was not significantly altered, either upon ascent or throughout altitude exposure.

Studies of isometric muscle functions at altitude with which to compare these results are few. There is a single report of a 13% increase in isometric pull-down strength after 48 h at 4500 m (23), but there are no reports concerning strength after a week or more at altitude, or after descent. Endurance times at several percentages of MHS measured at sea level were reported not to change after 30 min at 3700 m (2), but MHS was measured only quasi-isometrically on a spring-loaded dynamometer, and only at sea level prior to the altitude exposure.

Examination of other variables measured concomitantly in Study 1 eliminated several potential mechanisms for the significant increase in MHS at altitude. AMS could have impaired motivation to

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TABLE III. AVERAGE CHANGES IN BODY WEIGHT, MAXIMUM ISOMETRIC HANDGRIP STRENGTH, AND ENDURANCE ON DAYS 2 AND 6 AT ALTITUDE FOR SICK AND WELL SUBJECT GROUPS IN STUDY 1.

PARAMETER	CHANGE (% OF SEA LEVEL VALUE)			
	SEA LEVEL TO DAY 2		DAY 2 TO DAY 6	
	SICK	WELL	SICK	WELL
Body Weight	-4	0	-1	-2
Strength	+15	+8	+5	+5
Grip 1 Endurance	-14	-5	+6	-8
Grip 2 Endurance	-19	-13	+1	+6
Grip 3 Endurance	-30	0	+8	-5
Grip 4 Endurance	-29	-16	+6	+6

perform the gripping tasks, thereby affecting both strength and endurance. The relationship between AMS and muscle function was assessed in Study 1 by examining changes in MHS and endurance in the sick and well groups separately (Table III). Comparisons were made both on day 2 and at altitude, when AMS symptoms were present in the sick group, and on day 6, after recovery had occurred.

On day 2, MHS was significantly increased by 15% in the sick group and 8% in the well group; these changes were significantly different between groups. Such a result is exactly the opposite of what would be expected if AMS or one of its symptoms was diminishing motivation to exert maximum force. Since both groups increased their MHS, neither AMS nor altitude exposure was deleterious to grip strength. The data from day 6, after symptoms had resolved, reinforce this conclusion. If AMS had been inhibiting potentially greater increases in MHS on day 2, the gain from day 2 to day 6 should have been greater in the sick group. It was not; both groups increased an additional 5%.

AMS may have deteriorously affected endurance in Study 1, as the sick group showed the greater average loss in endurance on day 2 and the greater regain from then until day 6. In Study 2, endurance was not changed significantly at any time during the exposure, whether AMS symptoms were present or not. The lack of change in the second study cannot refute the possibility that AMS lowers isometric endurance in unpracticed individuals, however.

AMS might also have had an indirect effect on muscle function at altitude; sharply curtailed appetite is a principal symptom of AMS and can result in major losses in body weight. Weight loss has been reported to increase isometric endurance at sea level, without affecting MHS (19). The authors concluded that this occurred because heat dissipation during the exercise is enhanced by loss of body fat insulation over the gripping muscles, thereby maintaining muscle temperature at a more favorable point on the temperature-endurance curve. The relationship between isometric muscle function and weight loss at altitude is not known, however, and might

well be different. The weight changes for the sick and well groups were calculated, therefore, and are included in Table III.

Body weight losses by day 2 at altitude were greater in the sick group, as might be expected (Table III). That group lost an average of 3% in weight and 23% in endurance (all four grips combined, $p < 0.025$). The well group lost no weight and was down only 8% in endurance ($0.20 < p < 0.10$). This was the opposite of the reported relationship between weight loss and endurance at sea level. From day 2 to day 6, the sick group lost 2% more weight and regained 5% of its original endurance. The well group also lost 2% in weight but showed no further change in endurance. Weight changes played no part in the increase in MHS, as strength increased in both groups irrespective of weight loss. Taken together, these results indicate that weight loss did not contribute meaningfully to the changes in isometric function.

Urinary excretion of norepinephrine and epinephrine is a measure of sympatho-adrenal activity. Consistent with previous reports (8,15), epinephrine excretion did not change significantly during the altitude exposure, while norepinephrine excretion progressively increased. The norepinephrine increase reached significance on day 4. Because changes in excretion necessarily must lag changes in circulating concentration, the significant increases in grip strength seen on day 2 may have been due in part to increased circulating norepinephrine concentrations; catecholamines have long been known to affect muscular perfusion at sea level (3). This cannot be the sole mechanism responsible for the increased MHS, however, as a lesser and nonsignificant increase occurred from day 2 to day 6, which was the period of maximal norepinephrine excretion. It must also be recalled that, in Study 2, MHS remained significantly elevated for 3 d after descent. Elevated catecholamine excretion has been shown to decline precipitously during the first 24 h after descent (11); because of the time lag, the circulating concentration of norepinephrine must decline even more rapidly. This makes norepinephrine or increased sympathetic activity a most unlikely mechanism for the preservation of MHS at altitude levels for 3 d after descent.

The respiratory alkalosis which occurs in response to altitude exposure may have been at least partially responsible for the increased grip strength seen in the present studies. Alkalosis has been shown to enhance the contractility of canine heart muscle (7) and to increase the maximal twitch tension of canine skeletal muscle (14). Acidosis has the opposite effect, reducing contractility, twitch tension, and voluntary muscle strength in animals and humans (4,7,17,21).

The time course of the increased grip strength during and after the altitude exposure closely matches that of the respiratory alkalosis of high altitude. Upon ascent, the hypoxia stimulates an immediate increase in ventilation, which reduces plasma PCO_2 and raises pH. Partial renal compensation for the alkalosis occurs after 2–3 d, as bicarbonate is excreted. Ventilation and plasma pH are maintained above normal levels for 2–3 d after return to sea level, despite the increase in the O_2 content of inspired air, until plasma and CSF bicarbonate have

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been restored to their pre-ascent values.

The degree of respiratory alkalosis of the present subjects was not measured but should match that of six men of similar age and fitness levels measured at the same location (unpublished results). At sea-level, mean (\pm S.D.) PCO_2 was 33 ± 2 mm Hg and pH was 7.41 ± 0.02 . On the second day at altitude, the values were 25 ± 2 mm Hg and 7.47 ± 0.02 , respectively. Over the next 4 d, PCO_2 ranged from 24–26 mm Hg while pH stabilized at 7.47. These increases of 0.05–0.06 pH unit are encompassed by the changes of 0.03–0.16 pH unit which have been reported to significantly increase twitch tension of canine gastrocnemius-plantaris muscle electrically stimulated *in situ* (14). Direct evidence of the effect of alkalosis on human isometric strengths is lacking, unfortunately.

One sketchy report does exist of the deleterious effect of hypercapnic acidosis on human muscle strength, however. A pilot study (unpublished results cited in reference 10) in one man breathing 10% CO_2 in air (duration and endtidal PCO_2 unspecified), showed the contractile force of the *adductor pollicis longus* to be reduced by 10% during electrical stimulation of the ulnar nerve. Strength loss consequent to acidosis proves no point about alkalosis, but it does serve to indicate the sensitivity of human muscle strength to small departures from normocapnia.

SUMMARY

The present investigations have shown that maximum isometric handgrip strength increases upon ascent to high altitude; it remains elevated throughout the exposure and for at least 3 d after descent. Neither AMS nor changes in body weight or circulating norepinephrine levels appear to be the source of the increase, but the altitude-induced respiratory alkalosis is a likely candidate. Isometric grip endurance is changed but little at altitude. Hyperventilation during isometric endurance grips held to fatigue at sea level does not predict either resting ventilation or mountain sickness experience during subsequent altitude exposure. Hyperventilation during isometric endurance exercise shows a progressive increase in magnitude and duration over 6 d at altitude; this suggests a generalized increase at altitude in sensitivity to ventilatory stimuli. The prolongation of exercise hyperventilation for 60–90 s into the post-exercise recovery period lends additional support for the “central command” theory of ventilatory control during isometric exercise and diminishes the possible role of mechanoreceptors linked to working muscle.

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department of the Army position, policy, or decision, unless so designated by other official documentation.

Human subjects participated in these studies after giving their free and informed voluntary consent. Investigators adhered to AR 70-25 and USAMRDC Regulation 70-25 on Use of Volunteers in Research.

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