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Ventilatory responses to hypercapnia and hypoxia before and after high altitude mountaineering.

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The present study was designed to ascertain whether or not ventilatory response to hypercapnia at rest and to hypoxia during submaximal exercise at sea level increased after high altitude mountaineering. Two groups of subjects were studied: one (Andes) group consisted of 10 men and 4 women who had participated in the ascent of Mt. Huascaran (6,768 m) and the other (Himalaya) consisted of 10 men and 3 wemen who had participated in the ascent of Mt. Tent peak (5,760 m). Ventilatory response to CO_2 was determined by Read's rebreathing technique. In order to measure hypoxic ventilatory drive during exercise, the subject performed exercise on a bicycle ergometer for 8 min with a work load of 1.5 kp for males and 1.0 kp for females at a constant rate of 60 rpm. Minute ventilation breathing of room air ($\dot{V}_{E(nor)}$) and low (about 10%) oxygen ($\dot{V}_{E(hypo)}$) was measured: in this experiment, the ratio of $\dot{V}_{E(hypo)}$ to $\dot{V}_{E(nor)}$($\dot{V}_{E(hypo)}/\dot{V}_{E(nor)}$) was used as an index of hypoxic ventilatory response during submaximal exercise.

It was found in this study that average $\dot{V}_{E(nor)}$, $\dot{V}_{E(hypo)}$ and $\dot{V}_{E(hypo)}/\dot{V}_{E(nor)}$ values increased significantly ($p<0.05$-0.01) after mountaineering in both groups except $\dot{V}_{E(nor)}$ in the Andes group, while the slope of ventilatory respons to hypercapnia at rest was almost the same before and after high altitude mountaineering. These results suggest that elevated ventilatory response to hypoxia during submaximal exercise was still maintained for at least 1 or 2 weeks after returning to sea level, but not hypercapnia at rest.

Investigations of man at high altitudes have shown that high-altitude natives hypoventilatilate relative to sojourning lowlanders at rest, during exercise and in response to imposed hypoxic stimuli, while Hackett et al. (1980) found no difference in the hypoxic ventilatory reponse between Sherpas and Westerners. Previous studies also indicate that a lowlander sojourning at high-altitude becomes hypersenstive to hypercapnia (Rahn, 1953; Chiodi, 1957; Gray et al., 1971; Lefrancois et al., 1972) and to hypoxia (Lefrancois et al., 1968). In addition, it has been reported by Forster et al. (1971) that hypoxic response at rest increased 150% over prealtitude values and 20% over altitude values when a lowlander sojourned at 3,100 m for 45 days and returned to sea level. There is, however, no available data concerning the hypoxic ventilatory response during exercise at sea-level after high altitude mountaineering. The present experiments were designed to ascertain whether or not ventilatory response to hypoxia during exercise at sea-level increased sojourning at high altitude, and to compare hypercapnic ventilatory response at rest before and after mountaineering.

Methods

Two groups of subjects were studied : one group consisted of 10 men and four women aged 20-43 yr (herefter called Andes group) who had participated in the ascent of Mt. Huascaran (6,768 m) from June 29 to July 30, 1979. The other consisted of 10 men and three women aged 19-40 yr (hereafter called Himalaya group) who had participated in the ascent of Mt. Rosch (Tent) peak (5,760 m) from October 10 to November 2, 1980. All subjects had been born and lived in a city

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at sea level. With a few excepions, the subjects were not professional mountain climbers and at the time of the preliminary sea-level testing their general training conditions were relativly poor (Shimaoka et al., 1980). No general clinical examination was carried out, but all subjects were physically active and in good health. The subjects were briefly informed about the purpose of this study, but not about the detailed rsults of the experiment until the study had been completed.

The following measurents were made at sea-level on June 6-14 and August 7-18, 1979 for the Andes group, and on September 27-October 4 and November 8-15 for the Himalaya group, respectively. Experiments were usually conducted in the afternoon starting not less than 2 hours after a light meal. First, the ventilatory response to carbon dioxide at rest for each subject was determined in the sitting position by Read's rebreathing method (Read, 1967). The experimental set-up was similar to that described previously (Miyamura et al., 1976). A rubber bag with a capacity of about 10 liters was placed in an-airtight plastic box which was connected at one end to a respimeter (Benedict type, 13.5 liter) for recording ventilation. The bag was filled with 5-6 liters of a gas mixture about 7%CO_2 in O_2. Rebreathing started at the end of a maximal expiration and continued for 4 min. A continuous recored of alveolar P_{CO_2} (P_{ACO_2}) during rebreathing was obtained by drawing a sample of gas from the mouthpiece through an infrared CO_2 analyzer (Capnograph, Godart). After passing through the CO_2 analyzer, the sample gas was returned to the rebreathing bag to prevent changes in the bag volume. The CO_2 analyzer was calibrated by two gas mixtures of known CO_2 concentration that had been cheked by the Scholander micro-gas-analyzer. Minute ventilation ($\dot{V}_E$) was calculated for successive 30 sec intervals from spirographic recording, and the gas volume was corrected to BTPS conditions. From the P_{ACO_2} and $\dot{V}_E$ thus obtained, the slope of the ventilatory response line to hypercapnia was calculated by the least-square method : $\dot{V}_E = S(P_{ACO_2}-B)$, where S is the slope expressed as change in ventilation per unit change in P_{ACO_2} and B is the extrapolated intercept in the abscissa (P_{ACO_2} axis).

We chose to measure an index of hypoxic ventilatory drive during exercise at sea-level by comparing minute vention breathing of air ($\dot{V}_{E(nor)}$) with breathing of a hypoxic mixture ($\dot{V}_{E(hypo)}$) before and after the sojourn at high altitude. To measure the hypoxic ventilatory drive during submaximal exercise, subject performed execise on a bicycle ergomer for 8 min with work load of 1.5 kp for males and 1.0 kp for females, respectively. The subject inhaled air through a face-mask from the start of exercise to 5 min and low O_2 (about 10%) from 5 min 15 sec to 7 min. The pedaling rate was kept constant at 60 rpm and timed with a metronome. Expired gas during exercise was collected into the Douglas bag two times from 3-5 min and from 5.5-7 min, respectively. The collected gas volume was measured with a wet-gasometer, and mean minute ventilation of breathing air ($\dot{V}_{E(nor)}$) and a low oxygen ($\dot{V}_{E(hypo)}$) was estimated.

Results

Although all members of the Andes and Himalaya mountaineering group wanted to reach the top of Mt. Huascaran or Mt. Tent peak, several climbers in each group could not reach the top of mountain.

Table 1 and 2 show individiual data of ventilatory reponse to hypercapnia at rest and hypoxia during submaximal before and after high altitude moutaineering. Mean values and standard deviations for the slope (S) of the ventilatory

Table 1. Individual changes in ventilatory response to hypercapnia at rest and hypoxia during submaximal exercise in the Andes group before and after Mt. Huascaran (6,768m) mountaineering.

Subjects	Sex	Age (yr)	S (1/min/mmHg)		B (mmHg)		$\dot{V}_E$ (nor) (1/min)		$\dot{V}_E$ (hypo) (1/min)		$\dot{V}_{E(hypo)}/\dot{V}_{E(nor)}$	
			B	A	B	A	B	A	B	A	B	A
A 1	M	26	2.36	2.45	37.2	37.2	31.8	31.1	46.7	62.1	1.47	2.00
A 2	M	22	1.90	1.26	43.8	37.3	32.4	34.2	47.3	64.0	1.46	1.87
A 3	M	31	1.28	1.14	41.6	33.2	32.1	33.9	57.9	65.7	1.80	1.94
A 4	M	28	1.31	1.44	34.4	30.1	35.6	26.6	53.1	54.8	1.49	2.06
A 5	M	43	1.23	1.74	43.8	39.1	27.0	28.0	63.9	54.1	2.36	1.93
A 6	M	20	0.91	1.60	34.2	38.5	38.4	36.9	56.1	65.6	1.46	1.78
A 7	M	32	2.50	3.02	45.5	40.9	33.5	–	48.1	–	1.43	–
A 8	M	22	1.62	1.57	37.3	40.7	31.2	42.3	50.2	73.8	1.61	1.74
A 9	M	35	0.81	0.72	24.8	24.7	31.2	31.0	41.4	51.1	1.34	1.65
A 10	M	36	1.78	1.24	41.0	38.9	30.9	34.9	50.9	53.2	1.65	1.52
A 11	F	27	1.28	0.89	36.1	35.9	29.0	27.0	36.8	43.0	1.27	1.59
A 12	F	38	0.32	0.19	0.8	0.8	28.3	26.0	40.5	51.7	1.43	1.98
A 13	F	29	1.21	0.93	39.9	41.3	30.3	29.2	38.4	39.6	1.27	1.36
A 14	F	29	0.87	1.35	25.8	40.4	30.4	26.5	43.4	44.7	1.63	1.69

M; Male, F; Female, B; Before mountaineering, A; After mountaineering

response to carbon dioxde at rest before and after mountaineering were 1.38±0.57 and 1.39±0.67 1/min/mmHg for the Andes group and 1.48±0.98 and 1.50±0±0.71 1/min/mmHg for the Himalaya group, respectively. There were no significant differences in the S before and after montaineering as shown in Fig. 1. It was also found that average values for the B before and after a sojourn at high altiude were 34.7± 11.1 and 34.2 ±10.3 mmHg for the Andes group and 40.0±5.4 and 40.7±5.3 mmHg for the Himalaya group, and the differences in the B values were again not significant.

Table 3 summarizes average values and standard deviation for minute ventilation breathing of room air ($\dot{V}_{E(nor)}$), minute ventilation breathing of low oxygen ($\dot{V}_{E(hypo)}$) and ratio of $\dot{V}_{E(hypo)}$ to $\dot{V}_{E(nor)}$ pre-and postaltitude in both groups. The average $\dot{V}_{E(nor)}$, $\dot{V}_{E(hypo)}$ and $\dot{V}_{E(hypo)}/\dot{V}_{E(nor)}$ values increased significantly ($p<0.05$-0.01) after mountaineering in both gorups except $\dot{V}_{E(nor)}$ in the Andes group. In these experiments, particular, the ratio of $\dot{V}_{E(hypo)}$ to $\dot{V}_{E(nor)}$($\dot{V}_{E(hypo)}/\dot{V}_{E(nor)}$) was used as an index of hypoxic Ventilatory response during submaximal exercise and it was increased in 11 out of 13

Table 2. Individual chnges in ventilatory response to hypercapnia at rest and hypoxia during submaximal exercise in the Himalaya group before and after Mt. Tent Peak (5,760m) mountaineering.

Subjects	Sex	Age (yr)	S (l/min/mmHg)		B (mmHg)		$\dot{V}_E$ (nor) (l/min)		$\dot{V}_E$ (hypo) (l/min)		$\dot{V}_{E(hypo)}/\dot{V}_{E(nor)}$	
			B	A	B	A	B	A	B	A	B	A
H 1	M	20	4.28	3.25	46.0	46.9	38.8	40.3	59.7	66.8	1.54	1.66
H 2	M	35	0.92	0.84	40.8	39.5	32.7	34.0	45.3	49.8	1.38	1.46
H 3	M	27	1.50	1.82	43.5	44.5	38.9	41.0	54.6	60.0	1.40	1.46
H 4	M	25	0.88	1.26	42.7	43.1	38.5	41.6	52.8	62.7	1.36	1.51
H 5	M	37	1.30	1.75	43.4	45.3	40.9	38.0	56.4	56.8	1.37	1.49
H 6	M	40	0.45	0.79	27.1	38.3	30.4	38.5	47.7	62.7	1.56	1.63
H 7	M	33	2.51	1.98	41.4	39.8	39.5	41.0	48.2	60.6	1.22	1.48
H 8	M	19	1.79	1.09	42.5	38.0	44.1	44.9	58.9	65.3	1.33	1.45
H 9	M	39	1.68	0.91	35.9	25.6	43.2	43.3	82.6	79.3	1.91	1.82
H 10	M	28	0.52	0.93	29.8	37.3	27.6	39.3	32.4	48.1	1.17	1.22
H 11	F	24	0.93	0.89	40.3	42.3	29.7	31.4	45.8	50.9	1.54	1.61
H 12	F	25	0.71	2.50	43.8	44.1	36.3	39.5	53.0	54.6	1.46	1.38
H 13	F	24	1.78	1.53	43.6	45.6	35.0	33.9	42.9	51.1	1.22	1.50

M; Male, F; Female, B; Before mountaineering, A; After mountaineering

subjects of the Andes group and 11 out of 13 subjects of the Himalaya group, respectively.

Discussion

Concerning Ventilatory response to carbon dioxde, Forster et al. (1971) have reported that after 45 days of sojourn at 3,100 m altitude, 8 of the 10 individuals exhibited definite increase in ventilatory response to CO_2 over sea level values, and that the mean group index ($\Delta \dot{V}_E / \Delta P_{CO_2}$) of the lowlander in the postaltitude period was virtually the same as for under prealtitude conditions. It was found in this study that mean values for the slope of ventilatory response to hypercapnia at rest before and after mountaineering were 1.38 and 1.39 l/min/mmHg for the Andes group and 1.48 and 1.50 l/min/mmHg for the Himalaya group. There are no significant differences in the S before and after mouneering (Fig. 1). Our results basically agree with the data of Forster et al. who determined the ventilatory response to CO_2 at postaltitude 7 th day returning to sea-level. In our experiments, measurements of each subject were made on about one week before starting from Tokyo and were conducted after returning to Japan for 1 - 2 weeks for the Andes group and about 1 week for the Himalaya group. It was suggested, therefore, that elevated hypercapnic ventilatory drive at rest decreases suddenly within 1 or 2 weeks when the climber returns to sea level.

In this study average values for minute ventilation breathing of room air ($\dot{V}_{E(nor)}$), minute ventilation breathing a low oxygen ($\dot{V}_{E(hypo)}$), and ratio of $\dot{V}_{E(hypo)}$ to $\dot{V}_{E(nor)}$ during submaximal bicycle exercise increased significantly ($P<0.05$-0.01) after mountaineering in both groups except $\dot{V}_{E(nor)}$ in the Andes group. It is of interest that during submaximal exercise, $\dot{V}_{E(nor)}$ increased significantly in the Himalaya group after mountaineering, but not in the Andes group. The discrepancy of results in the Andes and Himalaya groups may be due to the difference in measurement time because postaltitude mesurements for each subject made for 1-2 weeks for the Andes and about 1 week for the Himalaya group after returning to Japan as described above.

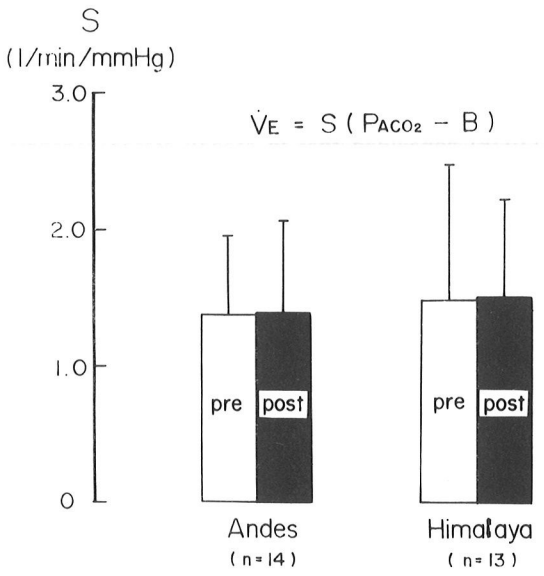

Fig. 1. Comparison of the slope of ventilatory response curve to CO_2 before and after mountaineering in the Andes and Himalaya groups.

In this experiment, the ratio of $\dot{V}_{E(hypo)}$ to $\dot{V}_{E(nor)}$($\dot{V}_{E(hypo)}/\dot{V}_{E(nor)}$) was used as an index of hypoxic ventilatory response during submaximal exercise, and it was increased in 11 out of the 13 subjects of the Andes group and 11 out of the 13 subjects of the Himalaya group, respectively. Forster et al. (1971) have reported that ventilatory response to hypoxia at rest increased in the lowlanders during their sojourn at 3,100 m altitude and that none of the individuals had returned completely to their pre-altitude on 45 days after return to sea level. These results suggest that in

Table 3. Average values and standard deviation for minute ventilation breathing of air ($\dot{V}_{E(nor)}$), minute ventilation breathing of a low oxygen ($\dot{V}_{E(hypo)}$) and ratio of $\dot{V}_{E(hypo)}$ to $\dot{V}_{E(nor)}$) before and after high altitude mountaineering in both Andes and Himalaya groups.

Group	Mountaineering	$\dot{V}_E$ (nor) (l/min)	$\dot{V}_E$ (hypo) (l/min)	$\dot{V}_E$ (hypo)/$\dot{V}_E$ (nor)
Andes	Pre	31.4 ± 2.9	48 2 ± 8.2	1.55 ± 0.27
(n = 13)	Post	31.4 ± 4.9	55.7 ± 10.1	1.77 ± 0.20
		n.s.	$p < 0.01$	$p < 0.01$
Himalaya	Pre	36.6 ± 4.9	52.3 ± 11.2	1.42 ± 0.20
(n = 13)	Post	38.9 ± 3.7	59.1 ± 8.3	1.51 ± 0.13
		$p < 0.05$	$p < 0.01$	$p < 0.01$

n.s.; not significant

the postaltitude, the lowlanders generally were hyperresponsive to hypoxia not only at rest, but also during submaximal exercise at sea level.

No conclusion can be reached from the results of this study regarding the site of hypersensitization to hypoxia or the mechanism reponsible for the hypersensitization. Few observations, however, are related to this question. First, Anderton et al. (1964) examined the ventilatory response to CO_2 without hypoxia, to hypoxia at constant P_{ACO_2} and combined with hypoxia in duplicate with an interval of 20 min between the two sets of measurement at sea level. They found that CO_2 sensitivity during hypoxia was significantly greater during the second set of measurements. Honda and Miyamura (1972) also observed progressive increase in ventilatory response evaluated by breath-by-breath recording after a simple large breath of hypercapnic and/or hypoxic test gases in consecutive daily trials for one week. Second, Gray et al. (1971) have reported that after exposure to an altitude of 5,400 m, the slope of CO_2 response curves incresed in most subjects who acclimatized well, but one subject with severe acute mountain sickness became flatter. These results were confirmed by Mathew et al. (1983) who found lower sensitivity to both hypoxia and CO_2 in maladapted subjects. Third, athletes have been shown to have diminished hypoxic and hypercapnic ventilatory responses (Byrne-Quinn et al., 1971; Miyamura et al., 1976). This may be beneficial at sea levl by reducing the work of breathing. But it has recently been reported by Schoene (1982) that a group of climbers who have successfully climbed to at least 7,800 m, had A values of hypoxic response parameter significantly higher than the group of outstanding long distance runners in that a blunted hypoxic response at altitude would be deterimental; the limiting factor is O_2 transnsport to brain and working muscle. A brisk ventilatory response to hypoxia may require insuring adequate alveolar O_2 and performing well at extreme high altitude as described by Schoene.

At present, we can not explain based on physiological grounds why elevated hypoxic ventilatory response submaxmal exercise was still maintained for one or two weeks after returning to sea level. Since Crawford and Severinghaus (1978) concluded that in steady states cerebral spinal fluid (CSF) pH value reflects the strength of peripheral chemoreceptor and other ventilatory drives, and Fencl et al. (1979) suggest that the fluid surroundig the central chemoreptor may contribute to ventilatory acclimatization to high altitude, it will be neccessary to further investigate an increase of ventilatory response to hypoxia and/or submaximal exrcise after high altitude mountaineering with respect to CSF pH.

References

1) Anderton, J. L., E. A. Harris and K. B. Slawson. The repeatability of ventilatory responses to excess of carbon dioxide and lack of oxygen. Quart. J. Exp. Physiol. 49: 43−51, 1964.

2) Byrne-Quinn, E., J. V. Weil, I. E. Sodal, G. F. Filley and R. F. Grover. Ventilatory control in the athlete. J. Appl. Physiol. 30: 91−98, 1971.

3) Chiodi, H. Respiratory adaptations to chronic high altitude hypoxia. J. Appl. Physiol. 10: 81−87, 1957.

4) Crawford, R. D. and J. W. Severinghaus. CSF pH and ventilatory acclimatization to altitude. J. Appl. Physiol.: Respirat. Environ. Exercise Physiol. 45: 275−283, 1978.

5) Fencl, V., R. A. Gabel and D. Wolfe. Composition of cerebral fluids in goats adapted to high altitude. J. Appl. Physiol.: Respirat. Environ. Exercise Physiol. 47: 508−513, 1979.

6) Gray, G. W., D. Sinclair, A. C. Bryan and C. S. Houston. Carbon dioxide reponse curves at altiude. Aeropace Med. 42: 1069−1073, 1971.

7) Hackett, P. H., J. T. Reeves, C. D. Reeves, R. F. Grover and D. Rennie. Control of breathing in Sherpas at low and high altitude. J. Appl. Phy-

siol.: Respirat. Environ. Exercise Physiol. 49: 374−379, 1980.
8) Honda, Y. and M. Miyamura. Increased ventilatory respnse to CO_2 by rebreathing in consecutive daily trials. Jap. J. Physiol. 22: 13−23, 1972.
9) Lefrancois, R., H. Gautier and P. Pasquis. Ventilatory oxygen drive in acute and chronic hypoxia. Respir. Physiol. 4: 217−228, 1968.
10) Lefrancois, R., H. Gautier, P. Pasquis, A. M. Cevaer, M. F. Hellot and J. Leroy. Chemoreflex ventiatory response to CO_2 in man at low and high altitudes. Respir. Physiol. 14: 296−306, 1972.
11) Mathew, L., P. M. Gopinathan, S. S. Purkayastha, J. Sen Gupta and H. S. Nayar. Chemoreceptor sensitivity and maladapation to high altitude in man. Eur. J. Appl. Physiol. 51: 137−144, 1983.
12) Miyamura, M., T. Yamashina and Y. Honda. Ventilatory responses to CO_2 rebreathing at rest and during exercise untrained subjects and athletes. Jap. J. Physiol. 26: 245−254, 1976.
13) Rahn, H., R. C. Stroud, S. M. Tenney and J. C. Mithoefer. Adaptation to high altitude: Respirtory response to CO_2 and O_2. J. Appl. Physiol. 6: 158−162, 1953.
14) Read, D. J. C. A clinical method for assessing the ventilatory response to carbon dioxide. Aust. Ann. Med. 16: 20−32, 1967.
15) Schoene, R. B. Control of ventilation in climbers to extreme altitude. J. Appl. Physiol.: Respirat. Environ. Exercise Physiol. 53: 886−890, 1982.
16) Shimaoka, K., M. Hara, H. Takeya and H. Matsui. The relationship between maximum oxygen uptake per body weight and performance in the high altitude mountaineering (Japanese). Nagoya J. Hlth. Phys. Fit. 3: 41−46, 1980.

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