Cardiac Output Responses in Rest and Work during Acute Exposure to Simulated Altitudes of 3,000, 4,500, and 6,000 m, and during Overnight Sleep at 4,500 m

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Abstract In order to assess the effects of hypobaric hypoxia on early cardiac responses, cardiac output during rest and work during acute and graded exposure to simulated altitudes of 3,000, 4,500, and 6,000 m, was estimated in 18 healthy male volunteers by impedance cardiography. The subjects were divided into two groups; 6 who had worked mainly at a desk without any accompanying sports activities (Group A) and 12 who had trained daily for their overseas high-altitude expeditions (Group B). The cardiac output (CO) at rest while sitting, at 3,000 m, showed a tendency toward a decrease for Group A, but not for Group B. At 4,500 m, the CO change was not significant in Group A, but showed an increase in Group B. At 6,000 m, the CO increase was about 30% in both groups. The consistent increase of heart rate (HR) with altitude was accompanied by a reduction of the stroke volume (SV), the remaining CO change being relatively small. The above discrepancy in the CO change at lower altitudes may represent a difference in sensitivity to hypoxia between the groups and may partly clarify the previous disagreement concerning the resting cardiac function at altitude.

A moderate workload at 0 m was still moderate at 3,000 m, where the moderate HR acceleration was well compensated for a reduction in SV leaving CO unchanged, but the exercise was almost at its maximum at 4,500 m, since HR approached a ceiling level (150–160 beats/min) which was attained at 6,000 m and CO increased remarkably.

Of 2 male volunteers (Group C) who slept overnight at 4,500 m, one showed a depression pattern in CO similar to 0-m sleep, while the other did not. In this CO reduction, the SV change was the determining factor as indicated previously for a 3,500-m sleep.

Key Words: hypobaric hypoxia, human, cardiac function, impedance cardiography.

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cardiac output, particularly in the early stage of exposure to acute hypoxia. Some authors have reported an increase, others a decrease, and still others no change in this parameter. Moreover, there are differences in the observations made on changes in stroke volume and heart rate (see Table 4). In these studies, the measurements were made at various altitudes, and also, the methods employed differed, as shown in the table.

Accordingly, the present study was undertaken to determine the effect of selected altitudes on cardiac function using a noninvasive, electrical impedance method. Furthermore, the subjects were divided into two groups wherein the daily physical activities were relatively low and high, respectively, because a group difference in cardiac responsiveness to hypoxia was expected in the form of a possible difference in oxygen intake capability. In addition, several subjects were obliged to take a moderate workload and overnight sleep at 4,500 m was conducted with other subjects in order to improve our understanding of the results obtained at rest.

Altitudes of 3,000, 4,500, and 6,000 m were chosen in the present study as representative of light, moderate and severe degrees of hypoxia. Acute exposure at 6,000 m is sometimes critical for those normally resident at sea-level for maintaining consciousness, but it was attempted in the present study in order to enhance the understanding of cardiac responsiveness to severe hypoxia. Each experiment was performed with the subjects' full agreement and understanding and with the special safety precautions described in METHODS.

METHODS

Subjects. All 21 subjects in this study were healthy male volunteers, whose normality had been demonstrated by a routine clinical examination which included a chest X-ray, electrocardiogram (ECG), and blood and urine analyses. In Group A, 4 of the 6 subjects were researchers (including the authors) and the other 2 were medical doctors working at universities. Since the group members worked mainly while sitting on chairs and had kept off sport for several years past, we classified the group as being of low physical activity. Most of the 12 subjects in Group B were clerks and foremen. They had plans for an overseas high-altitude expedition after the conclusion of the experiments. Most of them had exercised daily for 1–2 hr by running or swimming and the others with gymnasium equipment. We classified this group as being of high physical activity in the present study. The 3 subjects of Group C belonged to the latter group as regards their physical activities. All subjects were kept off mountain-climbing activities for at least 1 week before their individual experiments. When an experiment was repeated on the same subject, an interval of more than 1 week between the experiments was taken in order to avoid the effects of the preceding exposure. None of the subjects had had any overseas high-altitude experience during the
Table 1. Physical characteristics of and baseline data for the subjects.

<table>
<thead>
<tr>
<th>Subj.</th>
<th>Age</th>
<th>Ht (cm)</th>
<th>Wt (kg)</th>
<th>HR (beats/min)</th>
<th>CO (liters/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. NNM</td>
<td>30</td>
<td>165</td>
<td>57</td>
<td>54</td>
<td>5.3</td>
</tr>
<tr>
<td>2. NNMM</td>
<td>30</td>
<td>165</td>
<td>57</td>
<td>61</td>
<td>4.1</td>
</tr>
<tr>
<td>3. MOR</td>
<td>38</td>
<td>171</td>
<td>72</td>
<td>88</td>
<td>4.9</td>
</tr>
<tr>
<td>4. MOR</td>
<td>38</td>
<td>171</td>
<td>72</td>
<td>90</td>
<td>4.4</td>
</tr>
<tr>
<td>5. SKK</td>
<td>29</td>
<td>170</td>
<td>62</td>
<td>65</td>
<td>4.9</td>
</tr>
<tr>
<td>6. SKK</td>
<td>29</td>
<td>170</td>
<td>62</td>
<td>58</td>
<td>6.7</td>
</tr>
<tr>
<td>7. HGS</td>
<td>32</td>
<td>170</td>
<td>65</td>
<td>64</td>
<td>4.4</td>
</tr>
<tr>
<td>8. HGS</td>
<td>32</td>
<td>170</td>
<td>65</td>
<td>64</td>
<td>4.3</td>
</tr>
<tr>
<td>9. SAT</td>
<td>30</td>
<td>163</td>
<td>53</td>
<td>78</td>
<td>2.8</td>
</tr>
<tr>
<td>10. TKB</td>
<td>32</td>
<td>169</td>
<td>55</td>
<td>70</td>
<td>5.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group B</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. KOT</td>
<td>33</td>
<td>177</td>
<td>70</td>
<td>52</td>
<td>6.7</td>
</tr>
<tr>
<td>2. KSH</td>
<td>28</td>
<td>168</td>
<td>60</td>
<td>69</td>
<td>7.2</td>
</tr>
<tr>
<td>3. SFU</td>
<td>31</td>
<td>170</td>
<td>80</td>
<td>50</td>
<td>7.3</td>
</tr>
<tr>
<td>4. SFU</td>
<td>31</td>
<td>170</td>
<td>80</td>
<td>54</td>
<td>5.7</td>
</tr>
<tr>
<td>5. MRM</td>
<td>30</td>
<td>168</td>
<td>66</td>
<td>87</td>
<td>5.2</td>
</tr>
</tbody>
</table>

Ht, height (cm); Wt, weight (kg). HR, heart rate (beats/min); CO, cardiac output (liters/min). * Exercise group. ** Arhythmia. † Experiment was discontinued or oxygen was administered at 6,000 m. Experiment was repeated on the subject whose name appears twice.

The physical characteristics of the subjects and some baseline data thereon are given in Table 1.

Experimental protocol. The studies were conducted in a decompression chamber (about 20 m²) with the temperature regulated at 20°C and a relative humidity of 60%. The experiment was usually started about 1 hr after lunch. After about 10 min rest in the chamber, the control measurements, from which the baseline values in Table 1 were obtained, were made; the subjects were then exposed stepwise to increasing altitudes of 3,000 (525 mmHg), 4,500 (432 mmHg), and 6,000 m (354 mmHg). Elevation was achieved at a speed of 100–150 m/min and the exposure time at each altitude was 30 min. No measurements were made during descent.

In the exercise group (see Table 1), moderate work intensities of 300 kpm for 3 min and 450 kpm for 3 min were provided via a bicycle ergometer (Monark, Sweden). Measurements were made with the subjects sitting on a couch for the resting data, and on bicycle ergometers for the exercise data which were taken immediately after the conclusion of exercise.

In Group C, the control measurements of a 0-m overnight sleep were taken first in the decompression chamber, and the 4,500-m sleep data were collected the next night. Measurements were made at 1-hr intervals during sleep. The subjects slept on beds under a dim light, following their daily rhythm for sleep.

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Subject KRW was excluded from the 4,500-m sleep, having shown clouding of consciousness and stiffness in the extremities during a short stay at 6,000 m which was performed as a fitness-checking procedure for the sleep experiment. Hematocrit values were checked each morning; no actual change resulted. Electroencephalograms were not recorded in this study, but irregular body movements were detectable on the ECG and respiration recordings.

Safety monitors for decompression experiments. We took particularly stringent precautions in our experiments as subjects were exposed to altitudes of above 4,500 m and consequently might have suffered acute illness or rapid loss of consciousness due to hypoxia. It was not infrequent for subjects, particularly those having no experience of high altitudes, to refrain from complaining of their discomfort albeit aware of the early signs of hypoxic disturbances. Thus, the early prediction of such illness or unusual states was extremely important not only for the safety of the subjects, but also for the correct interpretation of the data obtained.

We made it a routine that an experienced researcher, wearing an oxygen mask at high altitude, remained inside the chamber with the subjects. Continuous ECG and respiration monitoring and direct observation of the subjects by a TV system were other routine procedures. Abrupt slowing of heart rate indicated that the subject felt sick, unusual ST-T change of ECG marked a limit of performance, and dullness in response, behavior and appearance indicated a clouding of consciousness. Oxygen was immediately administered whenever any of the above signs were noted.

For subjects MOR and KOT in the present experiment, hypoxic exposure was interrupted at 6,000 m because of a rapid slowing of their heart rates. Subject SFU suffered a clouding of consciousness at 6,000 m without a reduction of heart rate, and KRW showed unusual behavior due to stiffness in his extremities at 6,000 m. They recovered from these troubles immediately after oxygen administration. No subject claimed significant discomfort after descent, supporting our belief that safety monitoring so far employed was reasonable.

According to our past experience the rate of incidence of subjects showing the above signs, at rest and during 6,000-m exposure, is less than 20% (unpublished observation). Such subjects had a tendency to show similar signs again when the exposure was repeated, suggesting their lower resistance to hypoxia.

Impedance cardiography. Since KUBICEK's (1966) first application, many reports have accumulated on estimating stroke volume and cardiac output by electrical impedance plethysmography (see references quoted by KOBAYASHI et al., 1978; DOERR et al., 1981). The instrumentation is now commercially available. We used an impedance plethysmograph (Nihon-Kohden, AI-600G) paired with a differentiator (Nihon-Kohden, ED-600G). These plug-in type units were connected to a polygraph system (Nihon-Kohden, RM-6000) which was also used for ECG and respiration monitoring. Two sets of these instruments were provided for the present study.
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Fig. 1. Arrangement of tape electrodes for impedance cardiography and sample records demonstrating thoracic impedance ($\Delta Z$) change and the differential of the $\Delta Z$, $dZ$, divided by the time differential $dt$.

Tape electrodes paired at a distance of 5 cm were attached to the neck and the lower chest respectively as shown in Fig. 1. Applying a constant alternating current of 0.35 mA to the outer electrodes (1 and 4 in Fig. 1), the impedance change ($\Delta Z$) was picked up by the inner electrodes (2 and 3 in Fig. 1). The differential of $\Delta Z$, “$dZ$”, divided by the time differential $dt$ were recorded simultaneously on a pen-writing oscillograph. Stroke volume (SV) can be given by the formula

$$SV = q \times (L/Z_0)^2 \times (dZ/dt)_{\text{min}} \times T,$$

where $q$ is the resistivity of blood which was taken as a constant of 150 (~ohm ~cm), $L$ the distance between the inner electrodes (cm), $Z_0$ the mean thoracic impedance (ohm) displayed on the unit panel, $T$ the ventricular ejection time (sec), and $(dZ/dt)_{\text{min}}$ the minimum value of $dZ/dt$ (ohm/sec). The latter 2 parameters were determined from the curve drawn on the paper, as shown in Fig. 1. Five consecutive pulses were measured and averaged for the calculation. Cardiac output (liters/min) was calculated from the stroke volume (ml) and heart rate (beats/min) at the point where the measurement was made.

RESULTS

Heart rate (HR), stroke volume (SV), and cardiac output (CO) at rest

Since the resting HR peaked at the moment when each respective altitude was attained and then decreased to some extent during the following several minutes, measurements were taken 5 min after the attainment of each altitude. Percentage changes of resting HR, SV, and CO at altitude are shown in Fig. 2. HR increased in both groups with increasing altitude, but the increase tended to be greater in Group B (105, 116, 137% in Group A and 116, 142, 151% in Group B, at 3,000, 4,500, and 6,000 m respectively). Slopes of increases were close to each other when the same subject was exposed twice, suggesting that the HR response to altitude might be reproducible in nature. There was no relationship...
Fig. 2. Averaged per cent changes of resting heart rate (HR), stroke volume (SV), and cardiac output (CO) in Group A (○) and Group B (●). Changes in Group B are statistically significant against the reference at 0 m, while above 4,500 m for HR and only at 6,000 m for CO, they are significant in Group A (p<0.05, t-test). On a comparison between the two groups, significant differences are as indicated by asterisk (* p<0.05, ** p<0.01; t-test).

Table 2. Tendency of cardiac output change at altitude.

<table>
<thead>
<tr>
<th>Group</th>
<th>Altitude (m)</th>
<th>Decrease</th>
<th>Not significant*</th>
<th>Increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>3,000</td>
<td>5</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>4,500</td>
<td>2</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>6,000</td>
<td>0</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>B</td>
<td>3,000</td>
<td>1</td>
<td>11</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>4,500</td>
<td>1</td>
<td>5</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>6,000</td>
<td>1</td>
<td>2</td>
<td>14</td>
</tr>
</tbody>
</table>

* Within ±10% change.

between the baseline values of HR and the ratio of HR increase at altitude.

Contrary to the HR change, the resting SV tended to decrease at altitude. The rate of decrease was again greater in Group B (92, 96, 98% in Group A and 92, 83, 88% in Group B, for the respective altitudes of 3,000, 4,500 and 6,000 m), resulting in a smaller difference in CO between the groups (95, 106, 132% in Group A and 106, 118, 134% in Group B). Although CO changes at altitudes are statistically similar (p>0.05) between the two groups, we can see some different tendencies between them if attention is paid to changes in individual subjects.

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In Table 2, the individual CO change at each altitude is classified into "increase," "not significant," and "decrease" groups, where the reading error for SV calculation (see METHODS) is taken as only one factor to classify them; ±10% changes of CO at most were estimated for the error range. At 3,000 m, half of the trials undergone by Group A subjects belonged to the "decrease" group, while 11 of the 17 trials done by Group B subjects belonged to the "not significant" group. At 4,500 m, half of the Group A trials were in the "not significant" group, while 11 of 17 Group B trials were in the "increase" group. This observed tendency was considered sufficiently meaningful to merit later discussion.

Cardiac response with moderate workload

Work intensities of 300 kpm for 3 min and 450 kpm for 3 min seemed to be easily tolerable by the subjects at 0 and 3,000 m, since their CO did not increase at all with this workload as can be seen in Fig. 3; the decrease of SV fully compensated for the increase of HR. However, the same workload approached the maximum intensity for the subjects at 4,500 m, because HR in exercise had already reached a ceiling level of 150–160 beats/min which was the maximum level for 6,000 m. This ceiling level is about 20% lower than that at sea level. In addition, the marked elevation of CO was shared by the increase of SV. Of the 4 subjects to whom the workload was given, 3 showed a similar pattern. But subject SFU, to whom oxygen was administered at 6,000 m, showed a pattern different from the others; his CO had already increased with exercise at 0 and 3,000 m and was largely dependent on SV increase. As he was the heaviest in body weight among

![Fig. 3. Effects of constant exercise on cardiac output (CO), stroke volume (SV), and heart rate (HR) at various altitudes. Changes in the 1st (●, ○) and the 2nd experiments (▲, △) for the same subject ISY are shown together. Arrows connect changes occurring between the time when at rest (●, ▲) and after work (○, △), for each altitude. OU and OD indicate respective measurements at 0 m before and after exposure to altitude, and 30, 45, and 60 indicate the respective altitudes of 3,000, 4,500, and 6,000 m.](image-url)
the subjects, the work intensity applied should not have been too heavy. One point to be noticed in his characteristics was a low baseline value for HR (see Table 1).

**CO change during sleep at 4,500 m**

It is known that CO is attenuated during sleep, and is at its minimum in the early morning (Miller and Horvath, 1976, 1977; Miller and Helander, 1979). This was also demonstrated in the present experiment (Fig. 4). Such a reduction of CO was due to decreases in both HR and SV, but seemed to depend more on SV change, as found previously. The resting HR was high at 4,500 m and increased further during sleep in both subjects. On the other hand, the SV response between them was different. As can be seen in Fig. 4, in subject OGW, the reduction of SV was so marked that CO also dropped remarkably, and the pattern of CO decrease was similar to that of 0-m sleep. In subject IMA, on the other
hand, the reduction of CO was relatively small and the cardiac response not stable during sleep. Body movements, as shown in Fig. 4, demonstrate that the subject could not sleep well, particularly in the early morning.

The mean thoracic impedance \( Z_0 \) observed in both subjects changed irregularly, but within 1 ohm, during the total period of sleep. After descent from 4,500 m, the subjects complained of mild headache, but no other signs or symptoms of acute mountain sickness could be observed.

**Resting blood pressure at altitude**

In 4 subjects from Group A, 6 series of blood pressure measurements were made by use of the conventional method in the sitting position. The systolic pressure was stable at altitude, while the diastolic pressure decreased markedly at 6,000 m, as shown in Table 3, implying lowered peripheral vascular resistance associated with a CO increase at 6,000 m.

**DISCUSSION**

Although the validity of impedance cardiography is under debate, its great merits of convenience and non-invasion for CO measurement are attractive and promising, and many reports supporting its usefulness are being accumulated (see Impedance cardiography in METHODS). As can be seen in Table 1, we sometimes had difficulty in reproducing the absolute values when the same subject was checked on different days. Accordingly, the relative changes of each cardiac parameter were compared in the present study. Another difficulty we had was taking measurements during exercise, owing to the large fluctuation of recordings. We therefore chose a moment immediately after the conclusion of exercise, at the expense of some underestimation of the real exercise value.

Using this impedance method, Hoon et al. (1977) have measured the resting SV and CO for up to 10 days for sea-level dwellers airlifted to an altitude of 3,658 m. They found an immediate fall of SV and CO on arrival at this altitude, which reached a minimum on the 3rd day. Sime et al. (1974) showed a similar result at 2,364 m using a different method. On the other hand, in the report made by Klausen (1966), the resting CO and SV appeared to increase at 3,800 m. Vogel and Harris (1967) also reported an increase in CO and HR at a simulated altitude of 3,300 m and a further increase at 4,500 m. But in another report, Vogel et al. (1974) demonstrated a negligible change of CO at 4,350 m. All of

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**Table 3. Percentage change of blood pressure at altitude \( n = 6 \).**

<table>
<thead>
<tr>
<th></th>
<th>0 m</th>
<th>3,000 m</th>
<th>4,500 m</th>
<th>6,000 m</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic</td>
<td>100</td>
<td>99.6 (±2.97)</td>
<td>99.4 (±7.47)</td>
<td>98.0 (±5.48)</td>
</tr>
<tr>
<td>Diastolic</td>
<td>100</td>
<td>99.2 (±8.26)</td>
<td>94.2 (±8.38)</td>
<td>72.0 (±6.27)**</td>
</tr>
</tbody>
</table>

**Significant \( t \)-test, \( p < 0.01 \).**

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Table 4. Cardiac responses of a resting man at the early stage of altitude exposure.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Altitude and measurement time</th>
<th>Number of subjects</th>
<th>CO</th>
<th>SV</th>
<th>HR</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>KLAUSEN (1966)</td>
<td>3,800 m 1st day</td>
<td>3</td>
<td>↑</td>
<td>n.s.</td>
<td>↑</td>
<td>Fick's method</td>
</tr>
<tr>
<td>VOGEL and HARRIS (1967)</td>
<td>3,300 m* 10-40 hr</td>
<td>16</td>
<td>↑</td>
<td>(18%)</td>
<td>↑</td>
<td>Dye dilution</td>
</tr>
<tr>
<td>VOGEL et al. (1974)</td>
<td>4,350 m 2nd day</td>
<td>4</td>
<td>↓</td>
<td>n.s.</td>
<td>↑</td>
<td>Dye dilution</td>
</tr>
<tr>
<td>SME et al. (1974)</td>
<td>2,364 m 4-6 hr</td>
<td>8</td>
<td>↓</td>
<td>(10%)</td>
<td>↓</td>
<td>Fick's method</td>
</tr>
<tr>
<td>HOON et al. (1977)</td>
<td>3,658 m 0-4 hr</td>
<td>50</td>
<td>↓</td>
<td>(19.5%)</td>
<td>n.s.</td>
<td>Impedance method</td>
</tr>
</tbody>
</table>

* Decompression chamber.  n.s.: not significant.

these results are garnered up from the earliest measurements appearing in the respective reports and are summarized in Table 4.

In our data, cardiac responses were relatively small in both groups at 3,000 m, but the tendency in Group A was close to the results of HOON et al. (1977) and SME et al. (1974), while the tendency in Group B was similar to the results of VOGEL and HARRIS (1967). Also, at 4,500 m, our results correlate to some extent with those of VOGEL and HARRIS (1967) and VOGEL et al. (1974). This suggests that physical conditioning before exposure to altitude may be one of the factors which affect the cardiac output responses at altitude, though a direct comparison among the reports referred to is difficult to make because of the incomplete description of the physical condition of the subjects. The report quoted by MILLER (1974) which showed an extension of the “time of useful consciousness” at 24,000 ft from 2 min to 6 to 8 min, as a result of a physical conditioning program at sea level, seems to favor this idea. Moreover, a tendency at 3,000 and 4,500 m for a greater increase in the resting HR and CO of Group B than of Group A, as shown in Fig. 2, is also favorable to this idea, because it implies that Group B is more sensitive to hypoxia than Group A; it is reasonable that one can respond to increasing hypoxia as early as possible with an increase of the circulatory flow. Thus, it may well be promising for acceleration of adaptation to hypoxia to maintain high physical activity before exposure. However, why CO at 6,000 m did not reflect the difference in physical activity level between the two groups is a problem to be further explored.

It may be that, at 3,000 m, such an altitude effect does not decisively activate circulatory adjustments. The strong compensatory action of SV against the HR increase (see Figs. 2 and 3) supports this conjecture. Similarly, an altitude of 4,500 m would not be absolutely sufficient to activate the mechanism of circulatory adjustment, as seen from the inconsistent results of VOGEL and his group (1967, 1974), and also from the large range of deviation found in the present
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study (Fig. 2). In the 4,500-m sleep experiment, one of two subjects maintained a lowered CO level where the SV decrease overcompensated for the HR increase. This fact may also indicate that the hypoxic stimulus used is too weak to activate the mechanism.

At 6,000 m, several cases were observed in which the CO increase at rest was not significant: MOR's 1st and 2nd, SKK's 2nd, and SAT's experiments in Group A, and KOT's, KSH's, and IWM's experiments in Group B. MOR became sick in both trials. SAT had continuing sinus arrhythmia from 0 to 6,000 m. SKK had a complaint of strong drowsiness, and KOT became sick. KSH and IWM, however, had no complaints during the whole stay at 6,000 m and even appeared to have higher ability to resist hypoxia than the other members. Thus, there may be two types for such unchanged resting CO at 6,000 m; the 1st type due to failure of circulatory adjustments and the 2nd type resulting from full activation of another adaptive system such as respiratory compensation, which was not investigated in the present study.

The effects of workload on cardiac response were not intensively studied in the present experiments, but an apparent relationship of $HR \times SV = k$ (constant) below 3,000 m and $HR/SV = k'$ above 3,000 m for moderate exercise (see Fig. 3) must surely be an interesting aspect for future analysis. This relationship suggests the presence of a possible switching mechanism which detects the circulatory demand and changes the SV factor from subtractive to additive against the HR factor. Peripheral vascular resistance might be one of the main factors in the activation of the mechanism. It is suggested (Vogel and Harris, 1967) that peripheral vasodilatation may be a factor responsible for the CO increase under hypoxia. Supporting this, in the present study, the fall in total peripheral resistance appears to correspond well with the enhancement of CO (see Table 3).

A limit to the increase in HR could also be observed in the present experiments at high altitudes, as noted earlier (Åstrand and Åstrand, 1958; Pugh, 1964; Hartley et al., 1974). It is an additional finding, however, that such limitation of HR increase occurs immediately after high altitude exposure. Hartley et al. (1974) have proposed a hypothesis that parasympathetic nervous activity contributes to a reduction in the maximal HR occurring during work at altitude, since atropine improves the maximal HR at altitude while being ineffective at sea level.

Miller and Horvath (1976, 1977) have measured the change in CO occurring during sleep with impedance cardiography and compared it between sea level and a simulated height of 3,500 m. They found that the attenuation of CO was similar in both conditions. In the present study of 4,500 m sleep, subject OGW showed a similar result, while IMA did not. There was no change in the baseline thoracic impedance ($Z_0$), and symptoms of acute mountain sickness were very mild in both subjects when they awoke in the morning. Thus, such a discrepancy as observed between them may be attributable to a different level of sensitivity to hypoxia in
that part of the central nervous system which controls sleep. As indicated by MILLER and HORVATH (1977), HR was elevated during sleep at altitude and SV became the determining factor in the reduction of CO. This dominancy of SV change may be a characteristic feature during sleep, since it was present in the 0-m sleep. MILLER and HELANDER (1979) thought that such an SV-reducing process might be mediated by the sympathoinhibitory properties of the medullary raphe function, based on the report by CABOT et al. (1979).

In the present study, 4 subjects (MOR, KOT, SFU, and KRW) could not tolerate severe hypoxia at 6,000 m. It is interesting that the baseline HR was very low for 3 of them, suggesting high parasympathetic tone. In the other subject MOR, on the contrary, the baseline HR was very high, and he was extremely insensitive to hypoxia from the point of cardiac responsiveness. In a supplementary check at sea level, he could accelerate HR with exercise but the recovery was delayed, and furthermore he had a tendency of orthostatic disorder. It must be true that such imbalance in the autonomic nervous system is strongly related to low tolerance and low resistance to hypoxia, as already postulated by MCFARLAND (1937) and MALHOTRA and MURTHY (1977).

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REFERENCES


MCFARLAND, R. A. (1937) Psycho-physiological studies at high altitude in the Andes. IV. Sensory and circulatory responses of the Andean residents at 17,500 feet. Comp. Psychol.,

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