Nagoya J. med. Sci. 29: 85-91, 1966

BREATH HOLDING DURING THE THREE WEEKS OF SOJOURN AT HIGH ALTITUDE

TETSUO NAGASAKA, SHIGERU ANDO[1], AND KENTARO TAKAGI[2]

Department of Physiology, Nagoya University School of Medicine, Nagoya and the 1965-1966, Nagoya University Scientific and Mountaineering Expedition to the Andes (Director: Prof. Kentaro Takagi)

ABSTRACT

This study is a part of the work which has been done in purpose of investigating the effects of a long term exposure to a lowered barometric pressure in the 1965-1966 Nagoya university scientific and mountaineering expedition to the Andes. Changes in breath holding time, P_{O_2} and P_{CO_2} of the expired air at the breaking point and alveolar P_{O_2} and P_{CO_2}, pulmonary ventilation and respiratory frequency were measured in the 14 male subjects during the 22 days of sojourn at an altitude of 4200 m. Breath holding time and P_{CO_2} of the expired air at the breaking point and alveolar P_{CO_2} became increasingly lower during the two weeks of sojourn. After the 2nd week the breath holding time, P_{CO_2} level at the breaking point reached the minimum while the alveolar P_{CO_2} continued to fall. Pulmonary ventilation and respiratory frequency as well as the alveolar P_{O_2} increased and reached a ceiling during the third week of sojourn. Those rather quick changes during the first two weeks would indicate an increased sensitivity of the respiratory center to CO_2 stimulus, but the discrepancy between the change in breathh olding time and that in alveolar P_{CO_2} after the third week of sojourn was difficult to be interpreted in this paper.

An augumented ventilatory response to CO_2 in the inspired air is one of the characteristics of acclimatization to high altitude[1,2], but the mechanism for this augumentation in the subjects acclimatized to high altitude is not yet fully understood. The hypotheses which have been advanced are in referring to 1) the importance of the lowered blood buffer capacity[3], 2) an accentuation of the centrogenic drive[4] and 3) the presence of an increased sensitivity of the respiratory center to the chemical stimulus of CO_2[1,5,6]. In the 1965-1966 Nagoya university scientific and mountaineering expedition to the Andes, the authors had an opportunity to measure the response of the respiratory system

---

永坂鉄夫，安藤　滋，高木健太郎

Received for publication, April 22, 1966.

1) Faculty member of Research Institute for Environmental Medicine, Nagoya University.

2) The leader of the 1965-1966, Nagoya University Scientific and Mountaineering Expedition to the Andes.

in the subjects at an altitude of 4200 m. With rather simple techniques of measuring breath holding time and alveolar gas tension, the authors have been provided to have a conclusion in verifying validity of the hypothesis that the increased sensitivity of the center to CO_2 would be an important factor in increasing ventilation in the subjects at high altitude. The results of the experiment and the outline of the expedition will be described in this paper.

METHODS

Fourteen male subjects aged 22–55 years were studied at the base camp (4200 m above sea level) of Mt. Aconcagua, Argentina. All subjects were Japanese, members of the Nagoya university scientific and mountaineering expedition to the Andes. The expedition traveled by ship from Japan to Valparaiso, Chile and then from Chile to Puente del Inca (2730 m above sea level) of Argentina by train in one day. The starting point of the expedition was actually Puente del Inca, where the members stayed for from 5 to 14 days for preparation and then moved to the base camp by mules in one day. Collection of the data was started immediately after the arrival of the subjects to the base camp.

In the first day at the base camp after the quick transition from Puente del Inca, no one complained any symptom of mountain sickness, but all subjects experienced rather severe headache, nausea and weakness after the third or fourth day of sojourn. Some had very unpleasant Cheyne Stokes type breathing. This type of respiration was marked at night, and the symptoms of mountain sickness were most noticeable in the morning. Since the physiological functions as well as the mental activity fluctuated very much in a day, the time of experiment was fairly strictly controlled to be at the same time of the day. Some members climbed to further higher altitude, and stayed there for 1 to several days (at altitudes of 4500 to 7000 m), but any measurement was carried out at the base camp.

Breath was started to hold at the end of normal expiration and breath holding time was measured by checking the point of breaking of the voluntary apnea. When the subjects reached the point not to be able to hold the breath any more, the air was expired and was collected into a 1 liter rubber bag and P_{O_2} and P_{CO_2} of the expired air at the breaking point were measured by Riken interferometers with an accuracy of $\pm 0.5\%$. Normal alveolar air was collected to the bag by expiring rapidly the air at the end of a normal expiration, and alverlar P_{O_2} and P_{CO_2} were checked by the interferometers. Normally expired gas was collected into a Douglas bag and pulmonary ventilation, respiratory frequency, P_{O_2} and P_{CO_2} of the collected expired air were measured. All those parameters were measured in the subjects sitting quietly in a tent.

RESULTS

A characteristic decrease in breath holding time with the lapse of sojourn was observed in all of the subjects in this expedition (Fig. 1). The mean breath holding time was 14.0±2.4 seconds at the first day of sojourn. It became increasingly lower in the first two weeks of sojourn. The value, however, reached the minimum at the beginning of the third week of sojourn and thereafter it was maintained at a constant level with 10.2±1.7 seconds. P_{CO_2} of the expired air at the breaking point (the end breath holding expiratory air) became also increasingly lower in all of the subjects during the three weeks of sojourn (Fig. 2). It was 27.0±1.7 mmHg at the first day of sojourn and 23.0±0.9 mmHg at the end of the three weeks of sojourn, but the rate of the decrement of the P_{CO_2} was much less in the third week than in the previous two weeks. P_{O_2} of the end breath holding expiratory air, on the contrary, increased with the lapse of sojourn. It was 32 5±0.6 mmHg at the first day of sojourn and 34.5±0.6 mmHg at the end of the three weeks of sojourn. Alveolar O_2 and CO_2 tension changed also characteristically (Fig. 3). Alveolar P_{O_2} increased linearly with the lapse of sojourn, and alveolar P_{OO_2} decreased inversely proportionally with the change of the alveolar P_{O_2}. Therefore the

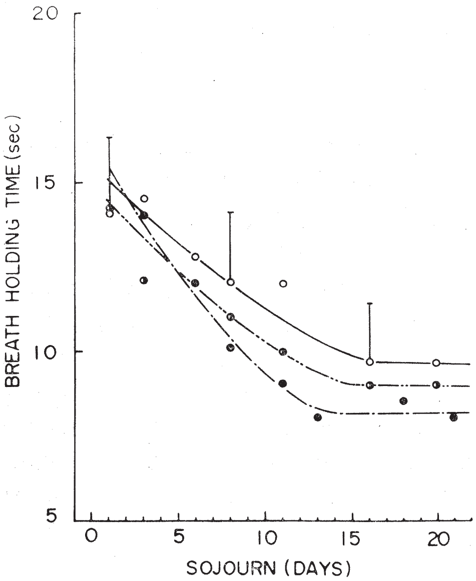

FIG. 1. Changes in breath holding time during the three weeks of sojourn at an altitude of 4200 m. -○- for the mean value, -●- and -◑- for the values obtained from two different individuals. Vertical lines indicate the standard deviations.

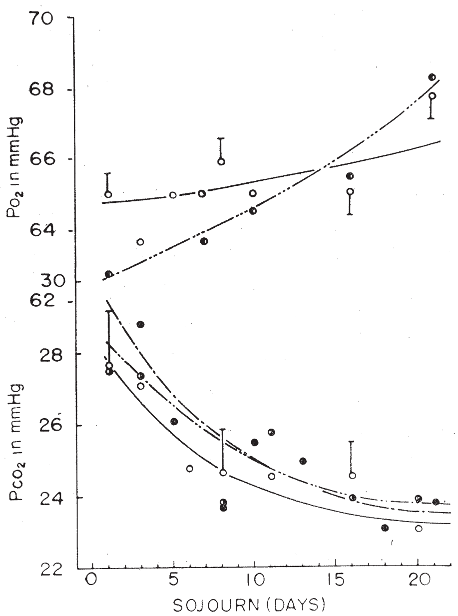

FIG. 2. Changes in alveolar P_{CO_2} and P_{O_2} at the breaking point during the three weeks of sojourn. -○- represents the mean values. -●-, -◑- and -◐- show the values obtained from three different subjects. Vertical lines represent the standard deviations.

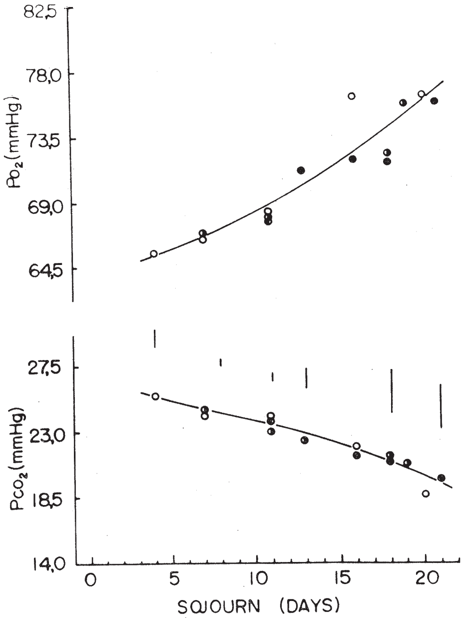

FIG. 3. Alveolar P_{CO_2} and P_{O_2} at the end of normal expiration. Vertical lines represent the difference between the alveolar P_{CO_2} at the breaking point and at the end of normal expiration.

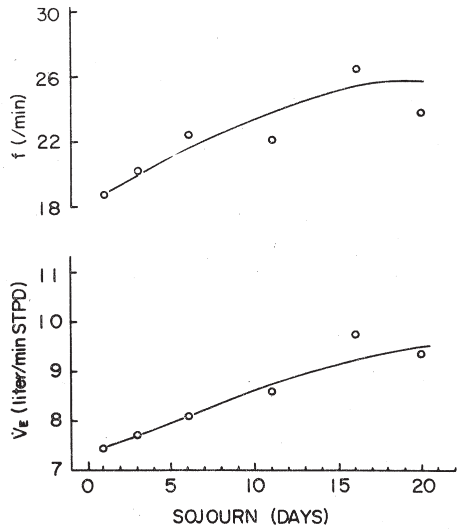

FIG. 4. Changes of mean pulmonary ventilation ($\dot{V}_E$) and respiratory frequency during the sojourn.

difference between the alveolar P_{CO_2} and P_{CO_2} of the end breath holding expiratory air was increasingly reduced in the first two weeks of sojourn and then it increased slightly during the following one week (Fig. 3).

Respiratory minute volume increased also linearly with the increased sojourn and this increased minute volume seemed to be caused by an increased respiratory frequency (Fig. 4). At the first day of sojourn $\dot{V}_E$ was 7.5 l/min STPD and frequency was 18.8/min. Both of those parameters increased to 9.4 l/min STPD and 23.7 l/min respectively after the three weeks of sojourn. They seemed to reach the maximum point at 14–16th day of sojourn. Analysis of the gas expired normally agreed with the data obtained by an analysis of the alveolar air and the end breath holding expiratory air. P_{CO_2} of the air decreased with an increased lapse of sojourn.

DISCUSSION

The definite and obvious results in this experiment were shortening of breath holding time, decreased P_{CO_2} of the end breath holding expiratory air and of the alveolar air, increased respiratory minute volume and frequency in the course of high altitude acclimatization. Those evidences are well known and the mechanism of the shortening of breath holding time and the increased minute volume during the course of high altitude acclimatization can be preferably attributed to the reduced response threshold of the respiratory center to CO_2 stimulus[7] or the increased sensitivity to CO_2 of the center[6][8][9]. Milledge[7] has suggested that there are two adaptive mechanisms to high altitude in increasing vetilation. One is a rather rapid mechanism, taking 5-7 days in completing itself, and the other is a slower one, taking 3-5 weeks in completing. He claimed that the rapid mechanism is a reduction in response threshold to CO_2 and the slower mechanism is due to an increase in CO_2 sensitivity. Most of the subjects in this experiment did not experienced respiratory discomfort in the first or second day of sojourn, but they complained very unpleasant discomfort after 3 5 days' staying at high altitude. Respiratory readjustment judged with the breath holding time and pulmonary ventilation seemed to be accomplished within the 2 weeks of sojourn and the respiratory discomfort was much improved by the time. The decrease of P_{CO_2} of the end breath holding expiratory air was only remarkable in the first two weeks. On the contrary alveolar P_{CO_2} in normal respiration continued to fall towards the end of the third week of sojourn. During the course of the two weeks of high altitude acclimatization, the difference between the alveolar P_{CO_2} and P_{CO_2} of the end breath holding expiratory air became increasingly lower (Fig. 3). This suggests that sensitivity of the respiratory center to CO_2 stimulus was increasingly elevated during this period. According to Takagi *et al.*[13], normal alveolar CO_2 level and the basic tolerable CO_2 level must be theoretically the same. The decreased rate of falling P_{CO_2} of the end breath holding expiratory air with the continued fall of alveolar P_{CO_2} after the third week may be explained by the other unknown mechanisms. It is, however, difficult in this paper to go further in discussing the mechanism through which ventilation can be augumented at high altitude, mainly because of a lack of further necessary parameters. Roles of the CSF Ph as well as the peripheral chemoreceptors responding to hypoxia on the augumented ventilation were discussed by many investigators[10][11][12], but it is not the purpose of this paper to discuss them in conjunction with the data obtained in this experiment.

It is difficult to consider the subjects of this experiment as a physiologically homogeneous group, because their age ranged from 22 to 55 years and activity of the subjects varied throughout the sojourn. Some of them stayed at the level of 4200-4400 meters altitude and some were at 7000 meters' summit of Mt. Aconcagua. Rather scattered mean value of P_{CO_2} and P_{O_2} of the end breath holding expiratory air and of the breath holding time may be interpreted by this difference of degree of high altitude acclimatization. It was expressed by many subjects that even after being accustomed to a certain hypoxic level they suffered from respiratory discomfort again when they climbed to further higher altitude and it may be quite natural to suppose that during their staying at the level their adaptive process is much accelerated in some form. Psychological tension and physical activity should also be the factors to disturb the results, but the adaptive changes above mentioned seem to be too definite for those unwellcomed factors to disturb the curves.

ACKNOWLEDGMENTS

The authors acknowledge the assistance received from many sources during the preparation, execution and analysis of the study. This investigation was conducted under the IBP subcommittee of JHA, of which chairman is Dr. H. Yoshimura, Professor of Kyoto Prefectural University of Medicine. The expedition was partially supported by the Ministry of Education and was given backing of the Ministry of Public Welfare and Nagoya University without financial support. The expedition was given great helps and advices from the Japanese Ambassies in Argentina, Chile and Peru.

The authors are particulary indebted to Captain O. G. Driollet and the officers and soldiers of the Compaña de Esquidors de Alta Montaña 8, Puente del Inca, Mendoza and the Army force of Argentina for their great help in accomplishing the expedition. The authors are also indebted to the staff of Research Institute for Environmental Medicine, Nagoya University for their assistance during preliminary experiments and to Dr. T. Satake for his interest and advice. The help of all members of the expedition is also greatly acknowledged.

REFERENCES

1. Hurtado, A. *Animals in high altitudes: Resident man.* In: Handbook of Physiology. Sect. 4, Adaptation to the environment. 1964. Amer. Physiol. Soc. Washington, D. C. pp. 843.
2. Chiodi, H. Respiratory adaptation to chronic high altitude hypoxia. *J. Appl. Physiol.* **10**: 81, 1959.
3. Rahn, H. and Otis, A. B. Man's respiratory response during and after acclimatization to high altitude. *Amer. J. Physiol.*, **157**: 445, 1949.
4. Bjurstedt, A. G. H. Interaction of centrogenic and chemoreflex control of breathing during oxygen defficiency at rest. *Acta Physiol. Scand.*, **12**: Suppl. **38**: 1, 1946.
5. Nielsen, M. and Smith, H. Studies on the regulation of respiration in acute hypoxia with an appendix on respiratory control during prolonged hypoxia. *Acta Physiol. Scand.*, **24**: 293, 1951.
6. Rahn, H., Bahnson, H. T., Muxworthy, J. F. and Hagen, J. M. Adaptation to high altitude: Changes in breath holding time. *J. Appl. Physiol.*, **6**: 154, 1953.
7. Milledge, J. S. *Repiratory regulation at* 19000 *ft.* (5900 m). In: The regulation of human respiration: Proceedings of the J. H. Haldane Centenary Symposium, 1961. Oxford; Blackwell, 1963. pp. 397.
8. Rahn, H., Stroud, R. C., Tenny, S. M. and Mithoefer, J. C. Adaptation to high altitude: Respiratory response to CO_2 and O_2. *J. Appl. Physiol.*, **6**: 158, 1953.
9. Kellogg, P. H. *The role of* CO_2 *in high altitude acclimatization.* In: The regulation of human respiration: Proceedings of the J. H. Haldane Centenary Symposium, 1961.

Oxford, Blackwell. 1963. pp. 379.
10. Severinghaus, J. W. and Mitchell, R. A. *The role of cerebrospinal fluid in the respiratory acclimatization to high altitude in man.* In: The physiological effects of high altitude. Oxford, Pergamon Press. 1964. pp. 273.
11. Dejours, P. *Regulation of breathing in exercise at high altitude.* In: The physiological effects of high altitude. Oxford, Pergamon Press. 1964. pp. 201.
12. Åstrand, P. O. The respiratory activity in man exposed to prolonged hypoxia. *Acta Physiol. Scand.*, **30**: 343, 1954.
13. Takagi, K. and Kobayashi, S. *Alveolar gas exchange during breath holding and consideration on the breaking point.* In: Physiology of breath-hold diving and the ama of Japan. National Academy of Science. Washington, D. C. 1965. pp. 147.