Erythrocyte 2,3-diphosphoglycerate level and blood oxygen saturation at high altitude

MASATAKA YOSHINO¹⁾, RYOICHI HAYASHI²⁾, YOSHINAO KATSUMATA³⁾ and SHIGEO MORI⁴⁾

¹⁾Department of Biochemistry, Yokohama City University School of Medicine, Yokohama 232, ²⁾Institute of Equilibrium Research, Gifu University School of Medicine, Gifu 500, ³⁾Department of Legal Medicine, Nagoya University School of Medicine, Nagoya 466, and ⁴⁾Research Institute of Environmental Medicine, Nagoya University, Nagoya 464, Japan

ABSTRACT

The level of erythrocyte 2,3-diphosphoglycerate and arterial oxygen saturation were investigated as an adaptation to high altitude hypoxia. Exposure to simulated altitudes of 4,000, 5,000, and 6,000 m rapidly increased erythrocyte 2,3-diphosphoglycerate, which appears to reach a maximum value at an altitude of 5,000-6,000 m. The recovery of oxygen saturation in arterial blood was observed during a stay at high altitude for 5 hr, but the decreased oxygen saturation did not recover at altitudes above 6,000 m, which suggests that the mechanism of rapid adaptation to hypoxia for facilitating the supply of oxygen to tissues is not operative above this altitude.

KEY WORDS diphosphoglycerate / hypoxia / high altitude / adaptation

At high altitudes above 2,000 m the human organism leaves its accustomed environment and begins to feel stress because of an insufficiency of oxygen. Various adaptive mechanisms enable human organisms to overcome the hypoxic stress of high altitude and to attain physiological homeostasis under the conditions of high altitude hypoxia. The most important mechanisms triggered by exposure to high altitude hypoxia are directed toward increasing the availability of oxygen and increasing the pressure of oxygen at the tissue level (7). The increase in erythrocyte 2,3-diphosphoglycerate (2,3-DPG) during hypoxia can be considered as an aid to oxygen delivery to tissues (9), although the importance of the reduction in hemoglobin affinity has recently been questioned. Many studies on the adaptive mechanism to high altitude have been carried out concerning chron-

ic or prolonged exposure to hypoxia (3-5, 9), but little is known about the rapid adaptation to hypoxia. In this paper we report a correlation between the saturation of oxygen in arterial blood and the increase in erythrocyte 2,3-DPG during exposure to high altitude. The mechanism and the upper limit of acclimatization to acute high altitude hypoxia are discussed.

Five healthy untrained male students, aged 20-25 years, were subjected to simulated altitudes of 4,000, 5,000 and 6,000 m in an altitude chamber at the Research Institute of Environmental Medicine (Nagoya University). Oxygen saturation in arterial blood, which is correlated with the oxygenation at tissue level, rapidly decreased when the subjects were exposed to high altitude, and then gradually recovered in prolonged exposure to this altitude (Fig. 1). Although oxygen saturation can recover significantly during a stay at an altitude of 4,000 m for 5 hr, such recovery was not observed at an altitude of 6,000 m. We examined the relationship between the recovery of oxygen saturation and the increase in erythrocyte 2,3-DPG when the

Correspondence should be addressed to Masataka Yoshino, Department of Biochemistry, Yokohama City University School of Medicine, Urafune-cho 2-33, Minami-ku, Yokohama 232, Japan

Fig. 1 Oxygen saturation in arterial blood during exposure to simulated altitudes of 4,000 and 6,000 m. Five untrained healthy male students, aged 20–25 years, were subjected to simulated altitudes of 4,000, 5,000 and 6,000 m in an altitude chamber at the Research Institute of Environmental Medicine (Nagoya University). Blood oxygen saturation was determined non-invasively with an oximeter (OXIMET MODEL MET 1471, Mochida) at the indicated time.

Fig. 2 2,3-Diphosphoglycerate levels (○) in human erythrocytes after 5 hr of exposure to different simulated altitudes, and the recovery of arterial oxygen saturation (△) during a stay at the altitude for 5 hr. Blood oxygen saturation was determined as indicated in Fig. 1. Blood samples were collected from the antecubital vein in heparinized syringes before and after the experiments. Erythrocytes were immediately separated by centrifugation of the heparinized blood. 2,3-DPG was determined according to the method of Keitt (8). Recovery of oxygen saturation was calculated as the ratio of the value determined immediately after the altitude to that after the stay at the altitude for 5 hr. Data are given as mean $\pm$ S.D. Standard statistical methods were employed.

subjects were exposed to altitudes of 4,000, 5,000 and 6,000 m. Blood samples were collected from the antecubital vein in heparinized syringes after the exposure to each altitude. Exposure to simulated altitude rapidly increased 2,3-DPG, which appears to reach a maximum value at an altitude of 5,000–6,000 m (Fig. 2). The recovery of oxygen saturation was observed during a stay at altitudes of 4,000 and 5,000 m for 5 hr; however, the decreased oxygen saturation in arterial blood did not recover at altitudes above 6,000 m (Fig. 2). A close correlation was observed between the increase in 2,3-DPG and the recovery of oxygen saturation in arterial blood during the stay at high altitude. These results suggest that the mechanism of rapid adaptation to hypoxia for promoting the supply of oxygen to tissues is not operative above this altitude.

Attention has been given to the rapid adaptation mechanism to high altitude hypoxia. Exposure to hypoxia initiates a series of physiological and biochemical changes that tend to maintain normal oxygen delivery and also induce a metabolic adaptation to lower oxygen availability (10). The supply of oxygen is set by its availability in the environment and by the efficiency with which it can be transported from the environment to the tissues. The most important adaptational mechanism at high altitude remains obscure: some infer that the increased ventilation is by far the most important mechanism (11, 12), while others attach importance to the factors favoring oxygen transport to tissues (3, 4, 6). The mechanism by which impaired oxygen supply can be effectively and rapidly corrected is improved delivery of oxygen from the lung to tissue capillaries. This improvement can occur in two ways: (a) improved oxygen transport and (b) alteration in the oxygen affinity of hemoglobin. The first mechanism, that is, an improvement in oxygen transport can be produced by an increase in the hemoglobin level which increases the oxygen capacity, and by an increase in the cardiac output. A change in hemoglobin level occurs slowly, while the advantage of compensation by increased cardiac output is that it can occur immediately. It has however the considerable disadvantage that it increases significantly the basal oxygen requirement; this offsets the advantage. Another mechanism available to the organism for promoting the supply of oxygen to the tissues is by decreasing the blood affinity for oxygen. This change, which results in a rightward displacement of the oxygen dissociation curve, improves oxygenation because more oxygen can

be delivered at the same or higher oxygen tension. Chanutin (2) and Benesch *et al.* (1) have convincingly shown *in vitro* that intraerythrocytic 2,3-DPG is a powerful modifier of the oxygen affinity of hemoglobin. The relationship between oxygen dissociation and 2,3-DPG in the red cells was studied in subjects moving from low to high altitude: a change in hemoglobin affinity for oxygen, and a parallel change in 2,3-DPG content of the red cells occurs (9). Thus, the increase in erythrocyte 2,3-DPG has been considered to be the most important factor favoring the increased availability of oxygen to tissues. Our results also support the central role of 2,3-DPG in regulating oxygen transport. A close correlation between the increase in erythrocyte 2,3-DPG and the recovery of oxygen saturation in arterial blood during the stay at high altitude suggest that this adaptive mechanism, whereby oxygen was more effectively transported to the tissues, does not occur above an altitude of 6,000 m. These results, concerning the improved transport mechanism demonstrated by some biochemical and physiological parameters, are consistent with the results concerning the upper limit of acclimatization toward acute high altitude hypoxia.

Received for publication 22 July 1980

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