Letter To The Editor: Comparison of Hypoxanthine and Lactate as Indicators of Hypoxia

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In a recent paper, "Comparison of Hypoxanthine, Lactate and ECG signs as Indicators of Hypoxia," Tuchschnid *et al.* (3) determined venous lactate and hypoxanthine levels in adults at an altitude of 6000 m. No alterations in hypoxanthine concentrations were found either during rest (27 min) or minimal exercise (4 min). During rest, the lactate levels were elevated, but did not exceed the normal range. During exercise, a small but significant increase in lactate levels was demonstrated. The authors concluded that "hypoxanthine in isolated, acute hypoxemic hypoxia in young adults is a less sensitive parameter than lactate" (3). Before such a conclusion can be drawn, however, it is important to be aware that hypoxanthine and lactate accumulation do not necessarily describe the same situation, but that different information may be given by these two measurements.

In addition to a series of conditions not associated with hypoxia, elevated lactate levels are found during hypoxia and reflect increased glycolysis to meet the increased energy demands of the hypoxic cell. Thus, even with high lactate level, the energy status of the cell is not necessarily altered. The elevation of hypoxanthine, on the other hand, probably reflects a deterioration of the energy charge. Therefore, there will be a dissociation between lactate and hypoxanthine patterns found, at least in mild hypoxia. An increased lactate level with normal hypoxanthine values thus can represent a compensated energetic stress situation. If the hypoxanthine level is elevated in addition to lactate, there is uncompensated energetic stress tending toward a hypoenergetic state.

In most of our experimental data, the hypoxia was too deep to discover such a dissociation between these two metabolites (1, 2), and there was an excellent correlation between lactate and hypoxanthine. The augmentation of hypoxanthine was so fast that there was no acidosis or cell destruction which could explain at

least the very early hypoxanthine elevation, as proposed by Tuchschnid *et al.* in their conclusion. Other authors have found elevated oxypurine levels at high altitude (4), although the duration was much longer than that reported by Tuchschnid *et al.* (3). There also was a close correlation between plasma oxypurine (hypoxanthine + xanthine) and oxygen saturation in arterial blood (4) in contrast to the finding of Tuchschnid *et al.* (3). The data presented by Tuchschnid *et al.* probably represent compensated energetic stress. This is not surprising if one looks at the very small lactate elevations these authors actually found. It is not surprising either that healthy adults have energy reserves which can compensate 4 min minimal work load, although performed at high altitude. We think care should be exercised in drawing firm conclusions from the data presented by Tuchschnid *et al.* Only four subjects were tested, and the lactate elevation was only from 1.08 ± 0.24 to 1.41 ± 0.42 mmol/liter after the working load was finished. It is obvious that factors other than hypoxia may be responsible for this modest lactate elevation. It has really not been ruled out, as discussed by the authors themselves, that, for instance, hyperventilation, which occurred in these subjects, can explain, at least partly, the moderate lactate elevations.

REFERENCES AND NOTES

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Letter to the Editor: Signs of Mild Hypoxia

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Neonatologists have been looking for a chemical indicator of mild and/or past hypoxia in newborns. Base-excess, standard-bicarbonate, and lactate were used. Concentration of hypoxanthine was recently found to be elevated in plasma of hypoxic newborns (1) and in animal-models of hypoxemic (3) and ischemic (4) hypoxia. Our investigation (6), published in the January issue of this journal, compared the sensitivity of this parameter with

lactate elevation and ECG-signs of myocardial-hypoxia as indicators of hypoxia. Altitude-induced hypoxemia associated with work in healthy adults was studied. The results show that lactate-elevation and ECG signs of hypoxia precede the elevation of hypoxanthine, which was augmented only in part of the cases where its *in vivo* breakdown was inhibited by allopurinol. We concluded that in mild hypoxia hypoxanthine is a less sensitive