Point:Counterpoint: The lactate paradox does/does not occur during exercise at high altitude

Point: The lactate paradox does occur during exercise at high altitude

First, a definition. The term lactate paradox is used here to refer to the unexpectedly (paradoxically) low blood lactate concentration during exercise at high altitude in acclimatized subjects compared with subjects exposed to acute hypoxia. Another definition refers to the reduction in blood lactate concentration during exercise when a newcomer acclimatizes to high altitude. But since the newcomer is essentially exposed to acute hypoxia, this amounts to the same thing.

The word “paradox” was first used in this context following the 1981 American Medical Research Expedition to Everest, when very low lactate concentrations were seen in the blood of well-acclimatized subjects pedaling a bicycle ergometer to exhaustion at an altitude of 6,300 m (25, 27). When combined with previous measurements mainly from Cerretelli et al. (4), extrapolation of the points relating maximal blood lactate to altitude predicted that above an altitude of 7,500 m there would be no increase in blood lactate concentration at all during maximum exercise. Since it is well known that severe exercise during acute hypoxia results in high levels of lactate concentration, presumably related in some way to tissue hypoxia, the low blood lactate concentrations high on Everest elicited the statement, “This is a paradox indeed, because such a climber is apparently more hypoxic during maximal exercise than in any other known situation” (25). Two years later, Hochachka (14) introduced the term “lactate paradox.”

However, the first clear demonstrations of the reduced lactate concentrations in the blood during high-altitude exercise following acclimatization were made some 50 years earlier by Edwards (10) following the 1935 International Expedition to Chile. Measurements on several well-acclimatized subjects at an altitude of 5,340 m showed that the venous blood lactate concentration rose as work rate increased but that the points fell along the same line relating lactate to work rate as that obtained during normoxic exercise at sea level. The only exceptions were in subjects who had spent only a short period at high altitude, which was insufficient for acclimatization. Since acute hypoxia was known to greatly elevate blood lactate levels during exercise, this observation implied that acclimatization had markedly reduced the lactate concentrations. In fact the initial (although brief) description of the lactate paradox was made on Edwards himself a few years earlier when he spent a summer at Leadville, Colorado, altitude 3,100 m. It was reported that his “lactate acid concentration for a given metabolic rate decreased uniformly throughout the summer” (8).

Over the last 70 years there have been repeated demonstrations of the lactate paradox during exercise at high altitude in both acclimatized lowlanders and high-altitude residents (1–3, 5–7, 9, 11–13, 15, 16, 18, 19, 20–23, 26, 28, 29). No claim is made that the lactate paradox occurs in everybody? Perhaps not. Is it possible that in some people the lactate concentration during exercise falls with acclimatization but then tends to recover if additional time is spent at high altitude? There is some evidence to support this (20, 24). Is the lactate paradox more pronounced at very high altitudes, for example, above 5,000 m? That may well be the case. But does it occur as in the title of this essay? Without question.

There are two striking features of the lactate paradox at very high altitudes. The first, as initially pointed out by Cerretelli et al. (4), is that maximal blood lactate concentrations, that is, those concentrations associated with the highest level of exercise, fall in a roughly linear fashion as altitude increases. The second striking feature, as already alluded to, is the extremely low maximum blood lactate concentrations during maximal exercise at extreme altitudes. These two features are illustrated in Fig. 1, which is redrawn from Cerretelli and Samaja (6). A straight line of best fit has been drawn through the points above an altitude of 1 km. Below this modest altitude there appears to be no fall in maximum blood lactate concentrations compared with sea level. In drawing this line, the data points from Operation Everest II shown by the four black triangles have been omitted because of this and other evidence that the subjects were not well acclimatized to extreme altitudes. This topic has been extensively discussed elsewhere (26) and the evidence for poor acclimatization includes lower alveolar PO2 values and higher alveolar PCO2 values than those found in field studies, the relatively high blood lactate concentrations during exercise, and the failure of maximal exercise ventilation to fall at extreme high altitude as has been observed in the field. Indeed, the inadequate acclimatization of the Everest II subjects was recognized by the leader of the study, C. S. Houston, when he wrote, “. . . they [the subjects] were not as well acclimatized as members of an expedition who have spent months on a big mountain . . . . Was ascent too fast, time at altitude too short? . . . we don’t know” (17). As pointed out

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Fig. 1. Maximal blood lactate concentration ([La]max) as a function of altitude in both acclimatized lowlanders and high-altitude residents. Most of the measurements were carried out a few minutes after maximal exercise to voluntary exhaustion. The line of best fit includes all the points above an altitude of 1 km, except the four from Operation Everest II shown by ●, r = 0.91. Redrawn from Cerretelli and Samaja (6).
earlier, Edwards (10) in his initial study showed that subjects who had not been at high altitude long enough for good acclimatization had higher maximum blood lactate levels than well-acclimatized subjects.

The data in Fig. 1 predict that there would be no rise in blood lactate concentration on maximal exercise above the resting level at altitudes above ~7,600 m and indeed the highest data point (6) seems to confirm this. It is very extraordinary that under these conditions of extreme tissue hypoxia, blood lactate levels are so different from those seen in acute hypoxic exposure. Irrespective of whether this strange state of affairs does not occur in everybody (although the data in Fig. 1 are from a large number of subjects including both acclimatized lowlanders and high-altitude residents), and there may be some recovery of blood lactate levels with increased time spent at high altitude, this extreme reduction in blood lactate is certainly intriguing.

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REFERENCES


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COUNTERPOINT: THE LACTATE PARADOX DOES NOT OCCUR DURING EXERCISE AT HIGH ALTITUDE

Some 75 years of research has been undertaken studying lactate metabolism at acute and chronic exposure to altitude. Despite these endeavors there are no data providing either an explanation or convincing evidence for a change in muscle lactate production and accumulation in the blood during exercise at chronic exposure to altitude. The simple reason is that the lactate paradox does not exist. Hochachka (11) tried to explain the phenomenon. He suggested a reduced glycolytic potential and tighter coupling between ATP production and lactate use, based on observation that Quechus (altitude natives in the Andes) accumulated less lactate in blood than lowlanders and that they had a lower muscle lactate dehydrogenase activity (12, 13). However, these observations have been questioned as the subjects were anemic and the metabolic adaptation observed was due to anemia rather than to genetic or developmental hypoxia-induced adaptations (7). Indeed, we did not find any differences in muscle lactate dehydrogenase activity or isoform or other proteins involved in acid/base balance or lactate transport in Aymaras compared to lowlanders (15). Moreover, maximal lactate levels were similar, pointing at a similar glycolytic potential in altitude natives. Since Aymaras