The following is the abstract of the article discussed in the subsequent letter:

Wagner, Peter D., Mauricio Araoz, Robert Boushel, José A. L. Calbet, Birgitte Jessen, Göran Rådegran, Hilde Spievogel, Hans Sondegaard, Harrieth Wagner, and Bengt Saltin. Pulmonary gas exchange and acid-base state were compared in nine Danish lowlanders (L) acclimatized to 5,260 m for 9 wk and seven native Bolivian residents (N) of La Paz (altitude 3,600–4,100 m) brought acutely to this altitude. We evaluated normalcy of arterial pH and assessed pulmonary gas exchange and acid-base balance at rest and during peak exercise when breathing room air and 55% O₂. Despite 9 wk at 5,260 m and considerable renal bicarbonate excretion (arterial plasma HCO₃⁻ concentration = 15.1 meq/l), resting arterial pH in L was 7.48 ± 0.007 (significantly greater than 7.40). On the other hand, arterial pH in N was only 7.43 ± 0.004 (despite arterial O₂ saturation of 77%) after ascent from 3,600–4,100 to 5,260 m in 2 h. Maximal power output was similar in the two groups breathing air, whereas on 55% O₂ only L showed a significant increase. During exercise in air, arterial P CO₂ was 8 Torr lower in L than in N (P < 0.001), yet P O₂ was the same such that, at maximal O₂ uptake, alveolar-arterial PO₂ difference was lower in N (5.3 ± 1.3 Torr) than in L (10.5 ± 0.8 Torr), P = 0.004. Calculated O₂ diffusing capacity was 40% higher in N than in L, and, if referenced to maximal hyperoxic work, capacity was 73% greater in N. Buffering of lactic acid was greater in N, with 20% less increase in base deficit per millimole per liter rise in lactate. These data show in L, allowing maintenance of arterial PO₂ despite lower ventilation; and 4) better buffering of lactic acid. These results support and extend similar observations concerning adaptation in lung function in these and other high-altitude native groups previously performed at much lower altitudes.

Improved blood buffering in high-altitude natives?

To the Editor: Wagner et al. (8) have recently suggested that natives from La Paz (3,600–4,100 m above sea level) possess a better buffer capacity in blood than lowlanders acclimatized during 9 wk at 5,260 m of altitude. They conclude this from a reduced slope of the regression line for base excess (BE) on lactate concentration ([Lac]) in plasma during exercise in the latter group.

Buffer capacity (β) is defined as

$$\beta = \Delta [\text{base}] \times \Delta \text{pH}^{-1} = -\Delta [\text{acid}] \times \Delta \text{pH}^{-1}$$

where Δ means change. I wonder why the authors did not use this more direct approach.

If BE is determined experimentally, whole blood is titrated to pH 7.4 in plasma with fixed acid or base under standardized conditions (PCO₂ of 40 Torr, 37°C, constant oxygen saturation). The added amount yields exactly the excess or deficit of base per liter of blood without any influence of the buffer capacity (6); only the pH difference between start and end of titration depends on the latter.

Deviations from a 1:1 relationship between changes in BE and in [Lac] (as found in the natives) can result, however, from a variety of causes. These are detailed below.

First, plasma [Lac] is higher than blood [Lac] because BE is defined for whole blood or the red blood cells plus the extracellular fluid (see below).

Second, lactic acid is practically completely dissociated into Lac⁻ and H⁺ because of its low pK (3.9). However, the amount of Lac⁻ in plasma is not necessarily equal to the added amount of acid, if Lac⁻ and H⁺ transgress the cell membranes not in equimolar number. It is suggested that Lac⁻-H⁺ cotransporters in the muscles account for only 50–90% of lactic acid extrusion (4). The amount of these proteins might be influenced by hypoxia and training (e.g., Ref. 5).

Third, for routine use, BE is not experimentally determined in blood-gas analyzers, but it is calculated from actual pH, PCO₂, oxygen saturation, and hemoglobin concentration (equations can be found in the manuals or in Ref. 7). The latter is used as an estimate of blood buffer capacity, which is necessary for the computation; however, changes in the buffering properties of hemoglobin or in the properties of other buffers like phosphates and plasma proteins are not considered in the algorithms.

Fourth, in vivo, bicarbonate emigrates from blood to interstitial fluid during acidosis of either respiratory or nonrespiratory origin (1), thus reducing the BE of blood. A fixed blood-to-interstitial volume ratio is used in the calculation of the standard base excess to account for this effect (7). However, altitude and exercise may change this ratio.

Fifth, the actual base excess (defined for whole blood) accounts for variations in oxygen saturation because a decrease in oxygen saturation (occurring during exercise to a greater extent in the natives) increases BE. Wagner et al. (8) give no statement as to which BE they have used.

The buffer capacity only has some secondary influence for the calculated and not really for the experimentally determined BE. However, some of the abovementioned mechanisms influence the buffer capacity as well. Thus, despite my criticism, I feel that Wagner et al. (8) have observed an interesting phenomenon.

Buffers consist of bicarbonate and nonbicarbonate buffers. Because the preexercise bicarbonate concen-
tration in the natives was higher than that in the acclimatized lowlanders, the natives had indeed more bicarbonate buffers in blood and interstitial fluid. However, Wagner et al. (8) are probably speculating on nonbicarbonate buffers. Instead of using the relation between BE and [Lac], a more direct and quantitative approach to this question is to calculate the difference between $-\Delta [\text{Lac}] \times \Delta \mathrm{pH}^{-1}$ and $\Delta [\text{HCO}_3^-] \times \Delta \mathrm{pH}^{-1}$ in plasma during exercise, which yields an estimate of the nonbicarbonate buffer capacity in red blood cells and extracellular fluid.

Interestingly, my laboratory (2, 3) has found a marked increase of this difference after a high-altitude expedition and in moderate-altitude inhabitants by a marked increase of this difference after a high-altitude expedition. The unexpected acidosis and ventilation, as the likely primary differences that the experimental plan for this project focused on some cogent points. However, it must be remembered that the experimental plan for this project focused on some cogent points.

Our finding of a difference in the relationship between plasma lactate and calculated base deficit is indeed not the most direct way of examining acid-base activity. We had chosen that relationship because $\mathrm{H}^+$ concentration ($[\mathrm{H}^+]$) is obviously affected not only by lactate levels but also by $\mathrm{PCO}_2$, and we wished to separate these influences on pH. In response to Prof. Boning’s ideas, we have calculated the change in $[\mathrm{H}^+]$ from rest to peak exercise as well as the change in plasma lactate concentration from rest to exercise. Natives increased $[\mathrm{H}^+]$ by $10.4 \pm 0.9$ (SE) nmol/l, whereas lowlanders increased $[\mathrm{H}^+]$ by $10.3 \pm 1.4$ nmol/l, a nonsignificant difference. On the other hand, plasma lactate levels increased by $10.1 \pm 0.9$ nmol/l in natives, whereas those in lowlanders increased by only $6.7 \pm 0.6$ nmol/l ($P = 0.009$). This direct comparison does confirm greater ability to buffer lactate in the natives, noting that arterial $\mathrm{PCO}_2$ changed similarly in both groups from rest to exercise (as reported in Ref. 1).

As Prof. Boning points out, we indeed agree that we have observed an interesting phenomenon, but this is one that requires further study.

REFERENCES


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REPLY

To the Editor: The letter of Prof. Dieter Bönig concerning our recent paper in the Journal of Applied Physiology on pulmonary gas exchange at high altitude in natives and acclimatized lowlanders (1) contains some cogent points. However, it must be remembered that the experimental plan for this project focused on pulmonary gas exchange, especially diffusion limitation and ventilation, as the likely primary differences between natives and lowlanders. The unexpected acid-base differences we noticed came from post hoc examination of the data. Because we did not anticipate acid-base differences, there was never a conscious plan to measure acid-base behavior in the two groups, an obvious error of omission given the intriguing results.

Our finding of a difference in the relationship between plasma lactate and calculated base deficit is indeed not the most direct way of examining acid-base activity. We had chosen that relationship because $\mathrm{H}^+$ concentration ($[\mathrm{H}^+]$) is obviously affected not only by lactate levels but also by $\mathrm{PCO}_2$, and we wished to separate these influences on pH. In response to Prof. Bönig’s ideas, we have calculated the change in $[\mathrm{H}^+]$ from rest to peak exercise as well as the change in plasma lactate concentration from rest to exercise. Natives increased $[\mathrm{H}^+]$ by $10.4 \pm 0.9$ (SE) nmol/l, whereas lowlanders increased $[\mathrm{H}^+]$ by $10.3 \pm 1.4$ nmol/l, a nonsignificant difference. On the other hand, plasma lactate levels increased by $10.1 \pm 0.9$ nmol/l in natives, whereas those in lowlanders increased by only $6.7 \pm 0.6$ nmol/l ($P = 0.009$). This direct comparison does confirm greater ability to buffer lactate in the natives, noting that arterial $\mathrm{PCO}_2$ changed similarly in both groups from rest to exercise (as reported in Ref. 1).

We also have data on strong ion concentrations, and, in the natives, the strong ion difference did not change from rest to exercise (0.2 ± 3.6 meq/l), whereas in the lowlanders, this tended to fall, by $-2.8 \pm 2.5$ meq/l. This suggests that a part of the natives’ enhanced ability to buffer lactate is via movement of $\mathrm{Na}^+$ and $\mathrm{Cl}^-$ out of plasma such that no change in strong ion difference occurs despite the large increase in lactate. However, as we did not measure ammonia, albumin, or phosphate concentrations or hemoglobin buffer ability (note, however, that hemoglobin concentration was the same in the two groups, as reported in Ref. 1), we are not in a position to explain the entire nature of the complex differences in the acid-base behavior between the high-altitude natives and acclimatized lowlanders.

As Prof. Bönig points out, we indeed agree that we have observed an interesting phenomenon, but this is one that requires further study.

REFERENCES


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