letters to the editor

Exercise hyperventilation in patients with McArdle’s disease

To the Editor: I feel compelled to comment on a curious omission in the recent study by Hagberg et al. (3) regarding ventilatory control and acid-base regulation during exercise in patients with McArdle’s syndrome. Nowhere in this paper do the authors mention the cardinal symptomatic feature of high-intensity exercise in these patients: that of pain. In fact, this is pathognomonic for McArdle’s syndrome; if this did not occur then the categorization would be suspect. The literature on this point is consistent and is well summarized by Swash and Schwartz (8) who cite the main clinical features of this disease to be cramps and muscular stiffness on exertion (p. 208-209) and that management includes recommending avoidance of strenuous exercise and cessation of exercise when pain or cramps develop (p. 210). Hence, an acute respiratory alkalosis at the highest work rates in these patients, whether from pain itself or the apprehension of its impending induction, is by no means surprising, and is in fact to be predicted.

However, it is with the interpretation of the results of this study that I take exception. Hagberg et al. (3) cite these findings as evidence that the dominant component of the nonlinear increase in ventilation, which is out of proportion to the VO₂ at work rates which engender a metabolic (lactic) acidosis, is not mediated by the acidosis: the argument being that if subjects with McArdle’s syndrome hyperventilate without developing a metabolic acidosis, then metabolic acidosis is not normally the cause of hyperventilation during exercise.

Furthermore, on physiological grounds, the notion that an acute metabolic acidosis does not induce a respiratory compensation through alveolar hyperventilation must be challenged. In fact, if the increased ventilatory response and the lactic acidosis is only coincidence, then Hagberg et al. (3) might explain why subjects who do not have carotid bodies—the mediators of the dominant component of the acute ventilatory responses to a metabolic acidosis—do not hyperventilate at high work rates (10, 14), or why at such high work rates a ventilatory decrement is clearly induced in normal subjects by suppressing carotid body responsiveness with abrupt O₂ administration, a response which begins precisely with the transit delay to the carotid bodies (2, 7, 9, 13). It appears, therefore, that the weight of evidence strongly supports the carotid bodies as dominant mediators of this response. However, as argued elsewhere (11, 12), it is unlikely that all the hyperventilation at high-intensity exercise is mediated by the [H⁺]ₙ itself; other factors such as body temperature, catecholamines, osmolarity, hypovolemia in some subjects, and, of course, pain or “discomfort” can superimpose on the underlying acid-base regulatory mechanisms (which operate in diabetes, renal failure, and dietary, as well as exercise-induced, metabolic acidosis).

Further crucial information was omitted. For example, the actual ventilatory responses to the exercise were not presented. The authors should not have presented only percentages of the maximum ventilation without reporting the actual maximal values. The authors state that “the absolute increase in ventilation beyond the point of the abrupt increase was virtually identical in the two groups” (3) (p. 993). This must mean that the ventilation at low work rates in the subjects with McArdle’s syndrome (i.e., from Fig. 3 in Ref. 3) must have been inordinately high. Such a finding would be suggestive of pulmonary vascular impairment or possibly of unusually high breathing frequencies if the blood gases are normal. Presentation of the actual data would have either exposed this fact or obviated any such concern.

In conclusion, therefore, I agree with Hagberg et al. (3) that “further research is necessary to determine which signal or signals result in the altered cardiovascular, respiratory, and metabolic responses occurring at or very near the point where ventilation increases abruptly.” However, attempting to dispense with [H⁺], as a potent hyperventilatory stimulus on the grounds that some patients can hyperventilate without metabolic acidosis is unconvincing both on logical and physiological grounds.


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REPLY

To the Editor: Dr. Whipp has raised a number of questions regarding the results and interpretation of our study concerning exercise hyperventilation in patients with McArdle’s disease (5) which he has been thinking about for the past 17 months. These relate to the patients’ diagnosis and the possibility that pain mediated the hyperventilation.

The diagnosis of McArdle’s disease was made by two of the authors whose entire clinical practice is devoted to neuromuscular diseases. Muscle biopsy samples in all patients were found to lack phosphorylase activity determined histochemically and/or biochemically as stated in the original manuscript. Pain during dynamic exercise is not pathognomonic of McArdle’s disease for three rather obvious reasons: 1) its presence is highly variable among such patients with some having none whatsoever (3), 2) it can be highly variable within an individual patient, and 3) over 90% of patients with muscle pain do not have McArdle’s disease.

To invoke muscle cramps and pain, or the apprehension of their onset, as the mechanism initiating the patients’ hyperventilation seems strange. Two of the patients did develop mild muscle pain during exercise, but it occurred well after hyperventilation had begun. We are experienced in obtaining information regarding muscle symptoms from patients (cf. Ref. 1, 2, 4); if they had developed pain before or at the time of hyperventilation we would have elicited this information. In addition, because these patients had nothing to gain by taking part in the study, it is doubtful they would have volunteered if they had substantial apprehension about exercise-induced muscle cramps or pain.

Contrary to Dr. Whipp’s belief that our patients must have had “inordinately high” ventilations at low work rates, they actually had lower ventilatory volumes than the healthy subjects at the same relative work rates. However, this was a result of their lower V\textsubscript{E}/V\textsubscript{O\textsubscript{2}} max values, because their V\textsubscript{E}/V\textsubscript{CO\textsubscript{2}} ratios were identical to those of the healthy subjects at low work rates.

Various authors have been able to dissociate the ventilatory and blood lactate breakpoints (6, 7), however the absolute magnitude of the shifts have not been great. No evidence exists to show that patients with McArdle’s disease have abnormal ventilatory control and because their ventilatory breakpoint occurs at approximately the same relative exercise intensity as in healthy persons, we believe this demonstration of a complete dissociation of the ventilatory and blood lactate breakpoints to be a logical extension of previous work.

We hope we have cleared up Dr. Whipp’s questions concerning this study.


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