The following letters are in response to the Point:Counterpoint series “Lactic acid accumulation is an advantage/disadvantage during muscle activity” that appeared in the April issue (J Appl Physiol 100: 1410–1414, 2006; http://jap.physiology.org/content/vol100/issue4/2006).

To the Editor: Lamb and Stephenson (3) argue, based on reductionist approaches in isolated and skinned muscle fibers at rest, that lactate and proton accumulation during periods of contraction may augment force production by relieving inhibition of excitation-contraction coupling processes at the sarcolemma, SR and contractile apparatus. The reductionist approaches give insight to mechanisms that may be involved in the regulation of cellular processes, but the results are initially valid only for the experimental conditions used. Even with consideration of temperature effects (1), there are in vivo and in situ metabolic, biochemical and molecular evidence that lactate and proton accumulation within contracting muscle, directly and indirectly, contribute to fatigue and that this is effected by a number of factors including downregulation of pH-sensitive enzyme systems (2, 5). Although there may be simultaneous beneficial effects of increased lactate or protons on some E-C coupling processes at the sarcolemma, these are over-ridden by other, simultaneous, inhibitory effects on the contractile machinery (1) and energy production (5) that occur as a result of lactate and proton accumulation. The suggestion that fast glycolytic fibers benefit from lactate accumulation on the basis of the high $K_m$ for MCT4 (3) is illogical. Fast glycolytic fibers, during high intensity exercise, are tolerant of large excursions of metabolite and electrolyte concentrations, some of which are relatively slowly restored (4). However, retention of produced lactate by fast glycolytic fibers provides a preferred energy source for resynthesizing glycogen after cessation of contraction. Why get rid of a most important, readily usable postcontraction energy source?

REFERENCES

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To the Editor: We ask and answer a slightly different question: is lactate accumulation an advantage or a disadvantage during exercise in humans? It depends. During exercise intensities up to maximal lactate steady state, the modest concentration of lactate ($\sim4$ mM in whole blood) is likely an advantage in the context of distributing substrate and coordinating intermediary metabolism in different tissues, i.e., the cell-to-cell lactate shuttle (1, 2). However, it is incautious to infer that lactate is a performance-enhancing drug, as we are unaware of any studies...
demonstrating that ingestion or infusion of lactate improves performance.

During intense exercise, whole blood lactate levels may be ~20 mM and plasma pH <7.0, with even more extreme muscle values. At a minimum, it is likely under these conditions that a low tissue pH will cause pain and the blood acidosis will encourage arterial hemoglobin desaturation that diminishes aerobic performance (4). Furthermore, in isolated non-ischemic rat hearts, we observed a depression in contractility in response to low pH, high [lactate], and the combination of the two (5).

Specifically regarding skeletal muscle activity, Lamb and Stephenson (3) summarize intriguing studies suggesting that lactate accumulation and the resulting low pH via a decrease in the strong ion difference, may actually alleviate fatigue. However, studies of isolated, skinned muscle fibers at temperatures of 28–30°C and externally elevated [lactate] may not extrapolate accurately to contracting whole muscle groups in exercising humans where the muscle temperature may be as high as 42°C. Regardless of the final mechanism of action, it is premature to eliminate lactate accumulation as a potential cause of fatigue under at least some circumstances.

REFERENCES

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To the Editor: The long-held view that lactate accumulation has a detrimental effect on exercise performance is challenged by newer findings, indicating that lactate is more likely a surrogate marker for muscle fatigue, not the direct cause of it. Lactate is an important fuel for contracting skeletal muscle and not, as previously believed, merely a metabolic byproduct destined for the Cori’s cycle. Inborn errors of metabolism resulting in blocked [McArdle’s disease (MD)] or exaggerated [mitochondrial myopathy (MM)] production of lactate during exercise may hint at the role of lactate in muscle fatigue.

Premature muscle fatigue in MD, however, has little to do with the lack of muscle acidification, as argued by Lamb and Stephenson (1). In this setting, no muscle acidification and low Na+–K+ pump number, as mentioned by Bangsbo and Juel (1), are probably epiphenomena, which are outmatched by the patients’ inability to breakdown muscle glycogen, a fuel that is crucial for muscle energy balance during early and high-intensity exercise. It has also been argued that muscle acidification is a prerequisite for sympathoactivation and thus avoidance of fatigue during exercise (2). However, abolished or exaggerated muscle acidification in patients with MD and MM do not alter sympathetic responses to exercise (3, 4). Maximal levels of plasma lactate during low-intensity exercise in patients with MM were believed to impair exercise performance, but lowering of lactate to normal by treatment with DCA had no effect on fatigue or maximal exercise performance in the patients (5). Thus experimental models of nature suggest that lactate is a marker, but not the cause, of fatigue.

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To the Editor: All too often in physiology our discussions about muscle fatigue are based on a model of isometric contractions. In this context, Lamb and Stephenson (2) argue that lactic acid does not cause fatigue but actually helps delay the onset of fatigue in two ways: 1) by offsetting the negative effects of raised extracellular [K+] on membrane excitability and 2) by inhibiting the SR Ca2+ pump that would help increase cytoplasmic [Ca2+] and consequent force. On the basis of strong evidence cited by Lamb and Stephenson, I would agree that lactic acid accumulation appears to be an advantage during isometric contractile activity; however, it should be pointed out that reduced Ca2+ uptake would increase basal intracellular Ca2+, which is thought to be important in causing low-frequency fatigue (4).

Acidosis-induced slowing of Ca2+ removal by the SR would reduce muscle relaxation rate, which may be appropriate for isometric conditions, but sluggish muscle relaxation would not be optimal for muscle performance when viewed from a kinesiology perspective (3). From a kinesiology perspective,
muscle activity is viewed in the context of locomotion (i.e., running) that requires precise temporal recruitment between groups of agonist and antagonist muscles to coordinate rapidly alternating movements. In this context, slowed relaxation rate means that locomotion must also slow down to maintain coordinated alternating movements (i.e., fatigue).

Therefore, although lactic acid enhances the excitability of working muscle, I would agree with Bangsbo and Juel (2), that describing lactic acid as “the latest performance-enhancing drug” (1) is going a bit too far.

REFERENCES

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