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

Maltais, François, Jean Jobin, Martin J. Sullivan, Sarah Bernard, François Whittom, Kieran J. Killian, Marc Desmeules, Marthe Bélanger, and Pierre LeBlanc. Metabolic and hemodynamic responses of lower limb during exercise in patients with COPD. J. Appl. Physiol. 84(5): 1573–1580, 1998.—Premature lactic acidosis during exercise in patients with chronic obstructive pulmonary disease (COPD) may play a role in exercise intolerance. In this study, we evaluated whether the early exercise-induced lactic acidosis in these individuals can be explained by changes in peripheral O2 delivery (DO2). Measurements of leg blood flow by thermodilution and of arterial and femoral venous blood gases, pH, and lactate were obtained during a standard incremental exercise test to capacity in eight patients with severe COPD and in eight age-matched controls. No significant difference was found between the two groups in leg blood flow at rest or during exercise at the same power outputs. Blood lactate concentrations and lactate release from the lower limb were greater in COPD patients at all submaximal exercise levels (all P < 0.05). Leg DO2 at a given power output was not significantly different between the two groups, and no significant correlation was found between this parameter and blood lactate concentrations. COPD patients had lower arterial and venous pH at submaximal exercise, and there was a significant positive correlation between venous pH at 40 W and the peak O2 uptake (r = 0.91, P < 0.0001). The correlation between venous pH and peak O2 uptake suggests that early muscle acidosis may be involved in early exercise termination in COPD patients. The early lactate release from the lower limb during exercise could not be accounted for by changes in peripheral DO2. The present results point to skeletal muscle dysfunction as being responsible for the early onset of lactic acidosis in COPD.

Skeletal Muscle Dysfunction vs. Muscle Disuse in Patients With COPD

To the Editor: From the outset of this communication it is important to acknowledge the different definitions of the terms “dysfunction” (abnormal or impaired function) and “disuse” (a lack of use) (9). The latter most certainly exists in patients with chronic obstructive pulmonary disease (COPD), as from the onset dyspnea limits their physical activity, whereas the former has recently been suggested to accompany the prominent lung pathology in the same population (5, 7, 8). Verifying the existence and then understanding the contribution of a skeletal muscle dysfunction in COPD is not only important because of its effect on the general function of patients both before and after lung transplant (3, 12) but also because such a myopathy may manifest itself in the respiratory muscles, thereby compounding respiratory problems (2). Thus it is clear that the recent paper by Maltais et al. (6) addresses an important and current issue. However, the authors concluded that skeletal muscle dysfunction (“an intrinsic muscle abnormality”) associated with COPD explains the elevated lactate release and a consequential reduction in venous pH at a similar O2 delivery at the same absolute submaximal work rates in the patients with COPD in comparison with the control subjects. The problem here is that a comparison of lactate efflux at absolute work rates between two groups with vastly different maximum work rates (almost three times greater in the controls) means that any submaximal effort will always be a far greater relative effort for the group with the lower maximum work rate. Recognized in the text, but dismissed as not measured, is the role of catecholamines in the stimulation of glycolysis (predominantly by epinephrine via cAMP) and the subsequent relation to lactate production. There is a strong positive correlation between epinephrine concentration (and blood lactate concentration) and exercise intensity (4, 10). At altitude, maximum work rate is diminished, leading to elevated epinephrine levels (and lactate concentrations) at any given submaximal absolute work rate (1). Is this considered to be evidence of skeletal muscle dysfunction or an intrinsic abnormality? Similarly, when subjects are studied and then confined to bed rest, the second series of exercise tests reveals a reduced maximum work rate and elevated epinephrine levels (and lactate concentrations) for a given submaxi-
mal absolute work rate (11). Again, is this considered to be evidence of skeletal muscle dysfunction or an intrinsic abnormality? It seems that the answer in all three cases (COPD, altitude, and bed rest) is no. What is being seen is an elevated relative intensity and (probably a catecholamine-mediated) increase in lactate concentration for any given submaximal work rate. In the case of the present COPD data (6), if we replot the lactate release data from Fig. 1D in Ref. 6 as a percentage of maximum work rate, we see no difference in the response between the patients and the controls (Fig. 1). In fact, we see a typical skeletal muscle lactate release in response to an increasing relative intensity of work. Since this analysis reveals no difference between the control subjects and the patients with COPD, these data appear to be suggestive of skeletal muscle disuse and not dysfunction. A positive indication of true skeletal muscle dysfunction would still be apparent when the data were analyzed in this fashion.

REFERENCES


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REPLY

To the Editor: In our study (3), the term "muscle dysfunction" was used to signify that the faster increase in blood lactate during exercise was indicative of a modified muscle metabolism. No assumptions were made regarding the underlying cause of this modification in muscle metabolism, whether it is entirely due to chronic inactivity and muscle deconditioning or whether there is a specific muscle disorder. This will have to be addressed in further investigations.

To speculate that the muscle metabolism was modified in our patients appears reasonable for several reasons. The rapid rise in blood lactate in our patients with COPD could not be explained by a low peripheral O2 transport. We agree that direct evidence of skeletal muscle dysfunction was not provided in this study. However, previous studies using skeletal muscle biopsy (2, 4), and 31P-magnetic resonance spectroscopy have convincingly shown that enzyme activities, fiber type proportion, and energy metabolism are modified in the peripheral muscles in patients with COPD. By further influencing muscle metabolism, an increased adrenergic drive may have contributed to the rapid rise in blood lactate during exercise in our patients.

We chose to report the response to incremental exercise using absolute work rate value; in real life situations, patients perform absolute and not relative work. Stair climbing or walking at a certain pace represents the same work whether they are done by a patient with a 50% reduction in his/her total work capacity or by a normal individual with a preserved exercise tolerance. The normalization of the lactate-work rate relationship when the work rate is expressed in relative units is not helpful in clarifying the origin of the rapid rise in blood lactate in patients with COPD and the nature of the underlying process in their skeletal muscles. For instance, the ventilation-work rate relationship in patients with COPD or the heart rate-work rate relationship during exercise in patients with chronic heart failure during cycling exercise shows the same (and even more pronounced) phenomenon when the work rate is expressed in relative units. Clearly, the pseudonormalization of these relationships should not be interpreted as indicating the absence of lung or heart disease in these patients.

Richardson’s comments are appreciated, and we hope that these clarifications will help in a better understanding of our paper (3).
REFERENCES


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