PM R 8 (2016) S8-S15

www.pmrjournal.org

Advanced Sports Medicine Concepts and Controversies

Lactate: Friend or Foe

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Abstract

Lactic acid has played an important role in the traditional theory of muscle fatigue and limitation of endurance exercise performance. It has been called a waste product of anaerobic metabolism and has been believed to be responsible for the uncomfortable "burn" of intense exercise and directly responsible for the metabolic acidosis of exercise, leading to decreased muscle contractility and ultimately cessation of exercise. Although this premise has been commonly taught, it is not supported by the scientific literature and has led to a great deal of confusion among the sports medicine and exercise science communities. This review will provide the sports medicine clinician with an understanding of contemporary lactate theories, including lactate's role in energy production, its contributions to metabolic acidosis, and its function as an energy substrate for a variety of tissues. Lactate threshold concepts will also be discussed, including a practical approach to understanding prediction of performance and monitoring of training progress based on these parameters.

Introduction

Lactic acid has played an important role in the traditional theory of muscle fatigue and limitation of endurance exercise performance. It was thought that once exercise intensity exceeds the rate of maximal oxygen consumption ($V_{O_2}max$), then an "oxygen debt" occurs and metabolism switches from aerobic to anaerobic. This switch to anaerobic metabolism was thought to lead to an abrupt increase in blood lactate levels, resulting in metabolic acidosis. This lactic acidosis was believed to impair muscle contractility and, ultimately, to lead to fatigue, exhaustion, and cessation of exercise. The uncomfortable feelings within muscles working at these near-maximal efforts were believed to be directly associated with this lactic acidosis, as was the soreness that developed during subsequent days (now commonly referred to as delayed-onset muscle soreness). Thus lactic acid was believed to be little more than a metabolic waste product, the result of pushing our systems beyond our capacity to deliver an adequate oxygen supply to our working muscles. This line of thought led to the establishment of training programs that sought to increase maximal oxygen capacity through high-volume, lower intensity exercise and led many persons to be wary of exposing the body too frequently to bouts of lactic acid—producing intensity.

Scientific thought has evolved during the past 30 years, and new understandings of the role of lactate in energy metabolism have altered these traditional teachings. Unfortunately, many misconceptions continue to permeate the sports medicine and exercise science communities. It is not uncommon to hear phrases such as "lactic acid burn" and "flushing out lactic acid" even among well-respected coaches in the endurance community. Although the exact mechanisms by which lactate metabolism affects endurance performances continue to be defined in the literature, several key concepts are important for all sports medicine clinicians to understand. It is also important to understand basic concepts of how lactate measurements are used in predicting performance and designing training programs and the inherent limitations of individual lactate measurement.

Energy Production and Lactate Kinetics

Lactic Acid Versus Lactate: An Important Differentiation

Despite the ubiquitous use of the term "lactic acid" in both scientific and lay fitness and sports medicine

1934-1482/$ - see front matter
http://dx.doi.org/10.1016/j.pmrj.2015.10.018

communities, the actual presence of meaningful quantities of lactic acid in the human body has been called into question. It is true that the glycolytic production of lactate is associated with hydrogen ion (H^+) production, as represented in the following summary equations [1]:

$$\text{Glucose} \rightarrow 2 \text{ lactate} + 2\ H^+$$

$$\text{Glycogen} \rightarrow 2 \text{ lactate} + 1\ H^+$$

However, as detailed in the 2004 review of the biochemistry of exercise-induced metabolic acidosis by Robergs, Ghiasvand, and Parker, these summary equations do not imply that lactate is the source of H^+, but rather that the proton release of glycolysis is likely associated with the non-mitochondrial hydrolysis of adenosine triphosphate (ATP) [1]. Although other explanations for H^+ formation have been proposed, most investigators now agree that lactic acid is not produced in muscle [2]. Although the construct of "lactic acidosis" appears intuitive and continues to be propagated in physiology texts and medical education, no convincing evidence exists in support of this theory. Regardless of whether this stance represents an "entrenched sloppy nomenclature" as suggested by Lindinger et al [2] or a true inherent misunderstanding of lactate's production, it undoubtedly leads to confusion among many sports medicine clinicians. For this reason, we will only use the term *lactate*.

Glycolysis, Metabolic Acidosis, and Lactate Production: What is the Connection?

Detailed reviews of glycolysis, metabolic acidosis, and lactate kinetics are beyond the scope of this review [1-4]. However, it is important to discuss the key concepts so that the role of lactate in energy production and exercise performance can be better understood.

The energy molecule ATP is required for muscle contraction. With increasing exercise duration, phosphocreatine stores decline and muscle glycogen, or circulating blood glucose, is shuttled through the glycolytic pathway, forming ATP and pyruvate [5]. Both glycolysis and glycogenolysis produce the same number of pyruvate, but glycolysis is associated with the net release of 2 H^+, whereas glycogenolysis yields only 1 H^+, but also an additional ATP [1]. The pyruvate is then shuttled into the mitochondria, where it undergoes oxidative phosphorylation, which produces an abundance of ATP to allow for ongoing muscle contraction (Figure 1). As exercise intensity increases, the mitochondria are unable to oxidize all the available pyruvate. The increasing concentrations of pyruvate then trigger the conversion of pyruvate to lactate via the enzyme lactate dehydrogenase [3]. It has been argued that the lactate dehydrogenase reaction not only supports ongoing glycolysis via maintenance of cytosolic redox potential (oxidized nicotinamide adenine dinucleotide [NAD^+]/reduced NAD [NADH]) but that it also consumes a proton and effectively buffers against acidosis [1].

The origin of metabolic acidosis continues to be debated, but it seems clear that it is not directly related to lactic acid. Robergs et al [1] argue that non-mitochondrial ATP turnover is the source of H^+, as previously described. Lindinger et al [2] have proposed that, based on physiochemical principles, the strong acid anions (namely, $lactate^-$) that are produced with increasing glycolytic activity necessitate an increase in the net positive charge to maintain electroneutrality, and this positive charge is primarily provided by the dissociation of water.

More important than the exact mechanism of metabolic acidosis are the effects. Many of the misconceptions regarding lactate are directly related to the premise that acidosis is a primary cause of muscular fatigue and cessation of exercise. However, more recent studies have demonstrated limited effects on skeletal muscle contraction from induced acidosis, and in vitro studies have reported a protective effect of acidosis from hyperkalemic force depression in skeletal muscle [5]. Other beneficial effects of acidosis have been described, including greater release of oxygen from hemoglobin, ventilatory stimulation, enhanced muscular blood flow, and increased cardiovascular drive [5]. It is clear that the role of lactate in metabolic acidosis and fatigue must be reassessed.

Lactate Shuttles: What Happens to the Lactate Produced During Glycolysis?

Brooks [6] introduced the concept of cell to cell "lactate shuttles" more than 30 years ago. Ongoing research continues to expand and define the complex mechanisms at play both between cells and within cellular compartments. What has become clear is that lactate is not a waste product of anaerobic metabolism but rather an important fuel and potential signaling molecule that is continuously formed and utilized even under fully aerobic conditions [7].

The production of lactate, although likely oversimplified, was previously described. At this point, several pathways can be taken, all of which are facilitated by the monocarboxylate transport proteins (MCTs; Figure 2). Lactate can be transported into the mitochondria to be oxidized or transported into peroxisomes coupled with the reoxidation of NADH, which is required for function of β-oxidation [7].

Alternatively, lactate can be shuttled out of the cell via an MCT, possibly in conjunction with the extracellular transport of H^+ [1]. This blood lactate can then be taken up and used as fuel by adjacent skeletal muscle, as well as the heart, brain, liver, and kidneys [3,7]. During exercise, oxidation accounts for approximately

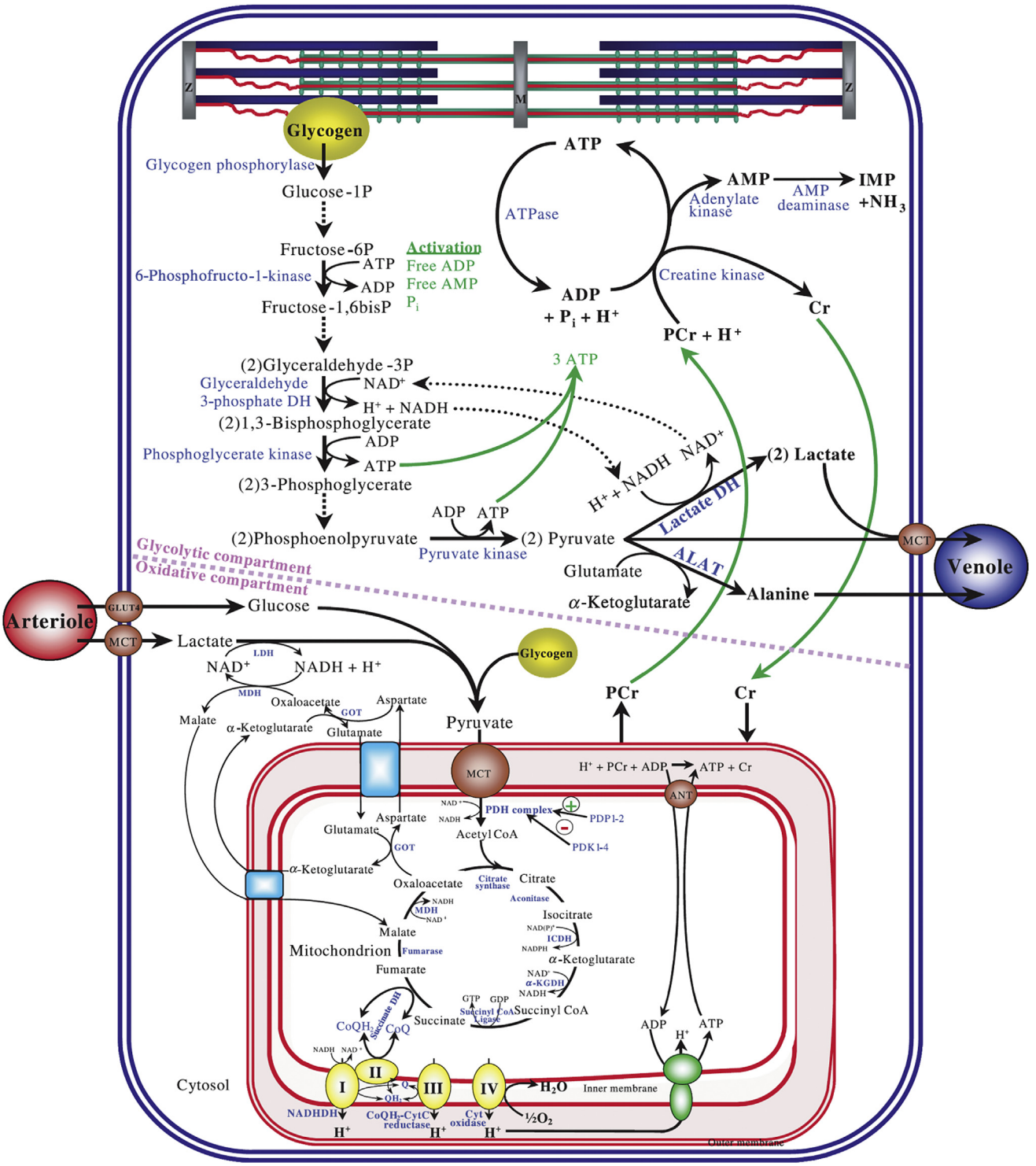

Figure 1. Skeletal muscle energy production. The process adjacent to the myofibril details the glycolytic (glycogenolysis/glycolysis) process of energy production. The oxidative component of energy production is detailed in the mitochondria (red rounded rectangle). Reproduced from Van Hall G. Lactate kinetics in human tissues at rest and during exercise. Acta Physiol (Oxf) 2010;199(4):499-508 [3], with permission. α = alpha; ADP = adenosine diphosphate; ALAT = alanine-aminotransferase; AMP = adenosine monophosphate; ANT = adenine nucleotide translocator; ATP = adenosine triphosphate; CoA = coenzyme A; CoQ = oxidized coenzyme Q; $CoQH_2$ = reduced coenzyme Q; Cr = creatine; Cyt = cytochrome; CytC = cytochrome C; DH = dehydrogenase; GDP = guanosine diphosphate; GOT = glutamate oxaloacetate transaminase; GTP = guanosine triphosphate; H^+ = hydrogen ion; H_2O = dihydrogen monoxide (water); ICDH = isocitrate dehydrogenase; IMP = inosine monophosphate; KGDH = ketoglutarate dehydrogenase; LDH = lactate dehydrogenase; MCT = monocarboxylate transport protein; MDH = malate dehydrogenase; $NAD(P)^+$ = oxidized nicotinamide adenine dinucleotide phosphate; NAD^+ = oxidized nicotinamide adenine dinucleotide; NADH = reduced nicotinamide adenine dinucleotide; NADHDH = nicotinamide adenine dinucleotide dehydrogenase; NADPH = reduced oxidized nicotinamide adenine dinucleotide phosphate; NH_3 = ammonia; O_2 = molecular oxygen; P = phosphate; PCr = phosphocreatine; PDH = pyruvate dehydrogenase; PDK = pyruvate dehydrogenase kinase; PDP = pyruvate dehydrogenase phosphatase; P_i = inorganic phosphate; Q = ubiquinone; QH_2 = ubiquinol.

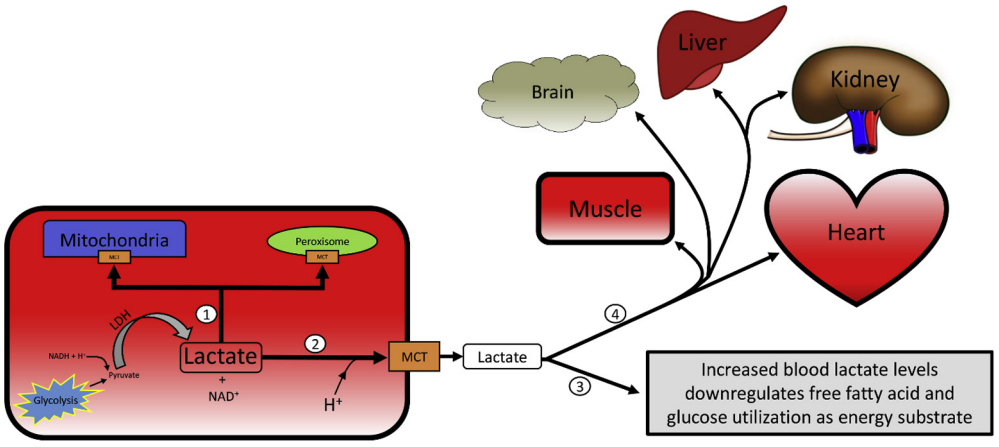

Figure 2. Intracellular and cell-cell lactate shuttle. 1 = Intracellular lactate shuttle, where lactate is transported via a monocarboxylate transport protein (MCT) into the mitochondria and oxidized or into peroxisomes for coupled reoxidation of reduced nicotinamide adenine dinucleotide (NADH). 2 = Extracellular transport of lactate and one hydrogen ion (H^+) via MCT. 3 = Signaling process by which cellular utilization of free fatty acids and glucose is downregulated. 4 = Utilization of lactate as an energy source (oxidation) by cells in the heart, brain, kidneys, liver, and other muscles. LDH = lactate dehydrogenase; NAD^+ = oxidized nicotinamide adenine dinucleotide.

75% of lactate removal, with the remainder being used for gluconeogenesis in the liver and kidney [7]. Elevated blood lactate levels have been shown to downregulate the use of glucose and free fatty acids as energy substrates [7]. In fact, in certain conditions, lactate may be a preferable energy source compared with glucose [3]. Lactate uptake is dependent on concentration gradients and is not limited in transport, as is insulin-dependent glucose. Also, because of a high capacity for lactate oxidation, the conversion of lactate to pyruvate does not appear limiting [3]. Thus lactate offers a fast and efficient fuel source.

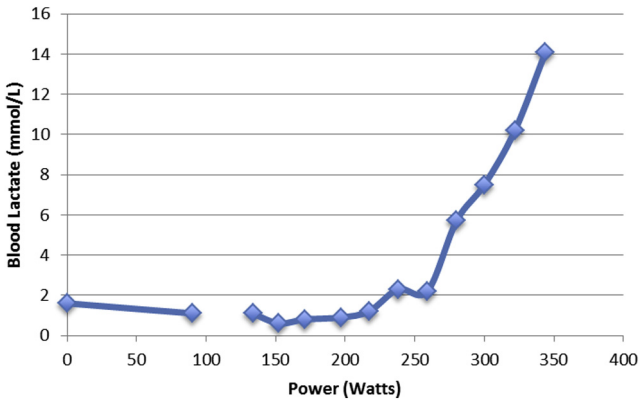

Figure 3. The blood lactate curve. Blood lactate concentrations are plotted against power during an incremental exercise challenge on a cycle ergometer. A brief warm-up period preceded the first recorded measurement, which resulted in increased blood lactate levels prior to cardiorespiratory responses to exercise. Blood lactate levels decline as increases in heart rate and muscular capillary dilatation deliver more oxygen to working muscles and likely transport blood lactate for utilization in other tissues. As exercise intensity increases, blood lactate levels will begin to rise above baseline, which is referred to as the onset of blood lactate accumulation. Exercise intensity will then be reached, above which a continuous increase in blood lactate is unavoidable; this state is referred to as the maximal lactate steady state.

The Blood Lactate Curve

A typical blood lactate curve from an incremental exercise challenge is presented in Figure 3. This curve is a useful illustration of how lactate production and consumption change with exercise. At the initiation of exercise, blood lactate levels will increase slightly. An increase in ATP demand by the working muscles triggers glycolysis, but there has not yet been an adequate increase in heart rate (HR) and capillary dilatation to deliver adequate oxygen to the working muscles. Pyruvate accumulation leads to lactate conversion and increased blood lactate levels. As the cardiovascular responses to exercise ensue (thus delivering more oxygen), the blood lactate levels decrease and stabilize. With increasing exercise intensity, pyruvate will once again begin to accumulate and be converted to lactate. Blood lactate levels will begin to rise when the rate of production exceeds the rate of uptake. Multiple factors may contribute to this increase in blood lactate, including oxygen delivery, mitochondrial capacity, and the ability to clear and utilize lactate by other cells throughout the body. Knowledge of these contributing factors is important because the opportunity exists to modify many of these variables via training. For example, increasing capillary density and mitochondrial numbers have been shown to occur with training, which increases the oxygen delivery capacity. Studies have also shown the ability to increase the density of MCTs, which would be expected to improve lactate uptake and utilization and be reflected as lower blood lactate levels [8].

Lactate Threshold Concepts: Utility in Training and Predicting Performance

What Is the Lactate Threshold?

The first difficulty in using the lactate threshold as a training aid or performance predictor is the confusion in terminology. The terms "lactate threshold," "anaerobic threshold," "aerobic threshold," "lactate turn point," "onset of blood lactate accumulation (OBLA)," and "maximal lactate steady state (MLSS)" are used somewhat interchangeably, although precise definitions may be quite different. However, these terms refer to two specific phenomena. First, during a graded exercise challenge, there is a point at which blood lactate begins to increase above resting values. This point was described as the "anaerobic threshold" by Wasserman et al [9] but as the "aerobic threshold" by Kindermann et al [10]. In most scientific literature this point is now called the "aerobic lactate threshold," but for the sake of clarity, we will call this point the "onset of blood lactate accumulation" (OBLA). Second, there exists a maximal exercise intensity above which a continuous increase in blood lactate is unavoidable. Kindermann et al [10,11] have called this point the "anaerobic threshold," and most scientific literature now refers to this point as the "anaerobic lactate threshold." However, for the sake of clarity, we will call this point the "maximal lactate steady state" (MLSS). In addition, some authors advocate for identifying the lactate threshold by visually inspecting a graph of work rate versus blood lactate accumulation (such as in Figure 3), whereas others advocate identifying the lactate threshold by taking the log of each measurement and intercepting the slope of the first few measurements and the slope of the last few measurements [12]. However, recent studies suggest that the method of visualizing the lactate curve to estimate the OBLA and MLSS is more reproducible [13]. Some investigators advocate using fixed blood lactate levels (for example, the workload that produces a blood lactate of 2 mmol/L might correlate with OBLA, and the workload that produces a blood lactate of 4 mmol/L might correlate with MLSS) to estimate OBLA and MLSS, but strong evidence shows that these methods are poor indicators of these physiologic phenomena [14]. Despite this evidence, these methods are commonly used in commercial endurance testing and coaching.

Reliability of Lactate Testing

The limiting factor in lactate threshold testing and training might be how accurately it can be measured. Van Schuylenbergh et al [15] investigated the validity of multiple different lactate and ventilatory threshold measurement methods and found very poor correlation between the methods and with MLSS power or MLSS HR. They concluded that it is not possible to precisely predict MLSS power or HR in individual elite cyclists without verification by a longer (30-minute) constant-load test. Grant et al [16] demonstrated that using a fixed blood lactate threshold was correlated with HR and rate of perceived exertion in a group of runners, but it had sufficiently high variance to limit its applicability in individual athletes [16]. It has been argued that the method of identifying the lactate inflection point for OBLA or MLSS is the source of the difficulty in reproducing lactate threshold test results. However, Zuniga et al [17] demonstrated that the methods of analyzing a blood lactate curve were unimportant but that differences in testing protocols had large effects on estimated OBLA and MLSS. Furthermore, glycogen status, which is related to nutritional factors or prior exhaustive exercise, may have effects on the blood lactate curve and must be considered when interpreting results [18-22]. Although lactate threshold may be a useful tool for evaluating a group of athletes (either for predicting performance or for monitoring improvement), the fidelity of traditional lactate threshold measuring techniques may limit its applicability for the individual athlete.

Predicting Performance

Predicting performance with MLSS can be confusing and is often misinterpreted. The absolute value of blood lactate at MLSS does not predict performance on endurance tasks. That is, if one subject has an MLSS with a blood lactate of 4 mmol/L, there is no reason to suspect that this subject will perform better on endurance tasks than a subject with a blood lactate of 2 mmol/L at MLSS. However, the workload at MLSS strongly predicts performance and is not correlated with the absolute blood levels of lactate at MLSS [23].

In recreational runners, V_{O_2}max is not a strong predictor of running performance, but V_{O_2} at MLSS and running velocity at MLSS are strong predictors of running performance [24]. However, among well-trained distance runners, V_{O_2}max and running velocity at V_{O_2}max explains differences in performance better than velocity at lactate threshold or percentage of V_{O_2}max at the lactate threshold [25]. Maximal 1 hour power, power at lactate threshold, and V_{O_2} at the lactate threshold are strong predictors of endurance cycling performance, but absolute V_{O_2}max is not a strong predictor of endurance cycling performance [26]. Lucia et al [27] compared professional with good amateur cyclists and demonstrated that V_{O_2}max is not sensitive enough to detect the differences in endurance capacity that exist between these very different athletes. Although V_{O_2}max was similar between the 2 groups, the professional racers were able to sustain much higher workloads at their MLSS. These investigators concluded that the main physiologic advantage of the professionals was their

ability to maintain very high workloads without intolerably high lactate concentrations in their blood. In reality, this likely represents superiority in both oxygen delivery and lactate utilization, as discussed previously, but this does not change the interpretation of their findings. Cycling performance can vary dramatically between cyclists of equal V_{O_2}max; however, lactate threshold is tightly correlated with cycling performance (although not as much as body weight and years of racing experience) [28].

Lactate threshold testing has significant limitations for predicting performance. Strong evidence shows that MLSS is sport specific, with dramatically different values within the same subject between rowing, cycling, speed skating, and running tasks [29]. Evidence is conflicting about whether blood lactate levels are similar at different sites of measurement (fingertip, toe, and earlobe) [30,31]. Test-retest reliability of incremental treadmill test—based measurements of MLSS is remarkably poor [32]. Baron et al [33] demonstrated that exercise failure above MLSS intensity was not associated with evidence of failure in any physiologic system, making the true physiologic underpinnings of lactate threshold testing and training unclear. Interestingly, there seems to be little to no relationship between effort or performance on resistance exercise tasks and lactate threshold [34]. In addition, it has been recognized for at least 2 decades that although velocity at MLSS is a strong predictor of endurance running performance in a large group of runners, it also has a high risk of both over- and underestimating performance [35].

In summary, the adage that "performance predicts performance" seems to be most correct. In a study of elite endurance runners, maximal sustainable speed on a treadmill predicted 5000-m running performance better than V_{O_2}max, running economy, V_{O_2} at lactate threshold, OBLA, or MLSS [36].

Does the Lactate Threshold Improve With Training?

A common adage among endurance coaches is that V_{O_2}max is a measure of an athlete's maximal potential, whereas V_{O_2} at lactate threshold or pace/power at lactate threshold is a measurement of the athlete's current ability. This adage seems to be borne out by the available data. A meta-analysis of studies that measured training intensity and changes in lactate threshold (both OBLA and MLSS were included) demonstrated that any training stimulus, including very light exercise, increased the lactate threshold of sedentary subjects but that very intense exercise was necessary to increase the lactate threshold of well-conditioned athletes, whereas V_{O_2}max proved to be minimally trainable [37].

It is not uncommon for endurance training zones to be based on HR or percentage of laboratory-measured V_{O_2}max. Good evidence shows that if the goal is to place individuals into specific training zones to normalize exercise intensity, percentage of V_{O_2}max and percentage of maximal heart rate are ineffective methods. However, percentage of OBLA or MLSS are reliable for normalizing exercise intensity [38].

In elite runners, running velocity at MLSS and V_{O_2} at MLSS are very trainable and account for nearly all improvement in running performance. V_{O_2}max, however, demonstrates limited improvement in response to training and correlates poorly with improvements in athletic performance [39]. However, measuring lactate threshold is somewhat cumbersome and, in runners, evidence shows that using rate of perceived exertion is as effective as laboratory-measured blood lactate levels for determining training zones [40]. In addition, critical power and critical velocity have proven to be closely correlated with power and velocity at MLSS and OBLA [41]. For this reason, many cyclists and runners have transitioned away from lactate threshold—based training plans and toward training plans and zones based on critical pace (typically a 5- or 10-km running pace—that is, the maximal running pace that is sustainable for more than a few minutes) or functional threshold power (the maximal sustainable power output for a 1-hour maximal effort). Additionally, the term "critical pace" or "critical power" is used to describe the maximal workload over a given time or distance. For example, the "1K critical pace" is the maximal speed that a runner can maintain over a 1000-m effort, and the "20-minute critical power" is the maximal power output a cyclist can maintain for 20 minutes. These functional measures of performance are easier to measure, likely more repeatable (although the evidence for such a claim is lacking), and easier for most self-coached endurance athletes to understand.

Conclusions

Although the role of lactate in exercise physiology continues to be debated, it is clear that lactate is a vital energy substrate, provides key functions in energy metabolism, likely functions in cell signaling during exercise, and is not confined to anaerobic conditions. The concept of lactate thresholds is confusing in the literature, but when interpreted with contemporary understanding of lactate metabolism, it can provide useful information. Several limitations confound the utility of lactate threshold testing for the individual, and functional tests are likely more practical for most athletes.

Key Points

1. *Lactic acid* is an inappropriate term that contributes to ongoing confusion regarding energy metabolism

and models of muscular fatigue. The term *lactate* should be used in its place.
2. Lactate is not responsible for muscular fatigue but rather is an important energy substrate that is readily utilized by multiple tissues throughout the body and is not confined to anaerobic conditions.
3. Although the lactate threshold may be a useful tool for evaluating a group of athletes (either for predicting performance or for monitoring improvement), the fidelity of traditional lactate threshold measuring techniques may limit its applicability for the individual athlete.

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Disclosure

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Submitted for publication August 21, 2015; accepted October 4, 2015.