The Anaerobic Threshold Measurement to Evaluate Exercise Performance[1,2]

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SUMMARY During exercise, the oxygen consumption above which aerobic energy production is supplemented by anaerobic mechanisms, and which results in a significant increase in lactate, is termed the anaerobic threshold (AT). This power output has important functional implications because it is a demarcation of the work rate above which metabolic acidosis accelerates the stimulation to breathing, and exercise endurance becomes reduced. The justification for relating lactate increase to tissue anaerobiosis during exercise is presented, and the gas exchange methods for measuring the AT are described. The form of work affects the AT, treadmill being about 10% greater than cycling in sedentary subjects. It is useful for predicting the ability of the subject to sustain a given work rate for a prolonged period and for determining the $\dot{V}O_2$ above which there is cardiovascular insufficiency in meeting tissue O_2 requirements.

The primary and the most immediate function of the cardiovascular system is to supply oxygen in adequate quantity to the tissues. To perform exercise, the active muscles have a manifold increase in O_2 requirement as compared to rest. For example, to walk at a moderate pace, the metabolically active muscles increase their O_2 consumption approximately 20 times. Thus, meeting the increase in oxygen requirement to do physical work requires remarkable cardiovascular and respiratory adjustments to maintain $Paco_2$ and pH.

Anaerobic Threshold Hypothesis

The anaerobic threshold is defined as the level of exercise $\dot{V}o_2$ above which aerobic energy production is supplemented by anaerobic mechanisms. The hypothesis (1) states that (*a*) the O_2 required by the metabolically active muscles can exceed the O_2 supply to the mitochondria when the work rate is sufficiently high; (*b*) the imbalance between the O_2 supply and O_2 requirement (i.e., O_2 requirement greater than supply) brings about a net increase in anaerobic oxidation in the cytosol of the cell with pyruvate conversion to lactate (figure 1); (*c*) lactate is buffered in the cell primarily by HCO_3^- (figure 2); (*d*) the CO_2 generated from buffering increases CO_2 output while HCO_3^- exchanges for lactate across the muscle cell membrane according to the new electrochemical gradients; and (*e*) the buffering and acid-base disturbances produce predictable changes in gas exchange.

Lactic acid production increases during exercise when the glycolytic component of energy production proceeds at a rate such that reduced cytosol nicotinic adenine dinucleotide (NAD) cannot be reoxidized rapidly enough by the mitochondrial membrane H^+ (proton) shuttle (figure 1) for ultimate combination of cytosol H^+ with mitochondrial O_2. Consequently, pyruvate becomes the H^+ receptor and is converted to lactate while simultaneously reoxidizing the reduced cytosol NAD, allowing glycolysis to proceed. The production of lactate from pyruvate has been recognized since Pasteur's first description of this reaction as an oxygen-conserving mechanism that allows oxidation to continue even in a relative oxygen-deficient environment.

Information from Anaerobic Threshold Measurements

The information that is learned by measuring the anaerobic threshold (*AT*) includes:

1. *Sustainable work capacity.* In a study in which 10 young (22 to 31 yr of age) motivated male subjects were asked to exercise for 50 min at 3 different levels on different days on a cycle ergometer, the target work times could be achieved only for those work rates in which the arterial lactate increased less than 1.0 mM/L (figure 3). No subject with an increase in lactate above 2.5 mM/L could sustain pedaling for 50 min. The greater the increase in arterial lactate, the less the endurance.

2. *$\dot{V}O_2$ above which metabolic acidosis occurs.* Studies have been done that document the close reciprocal changes in lactate and bicarbonate during the performance of work above the *AT* (1–3) (figure 4). Work performed at levels above the *AT*, i.e., with a sustained elevation in lactate, has been

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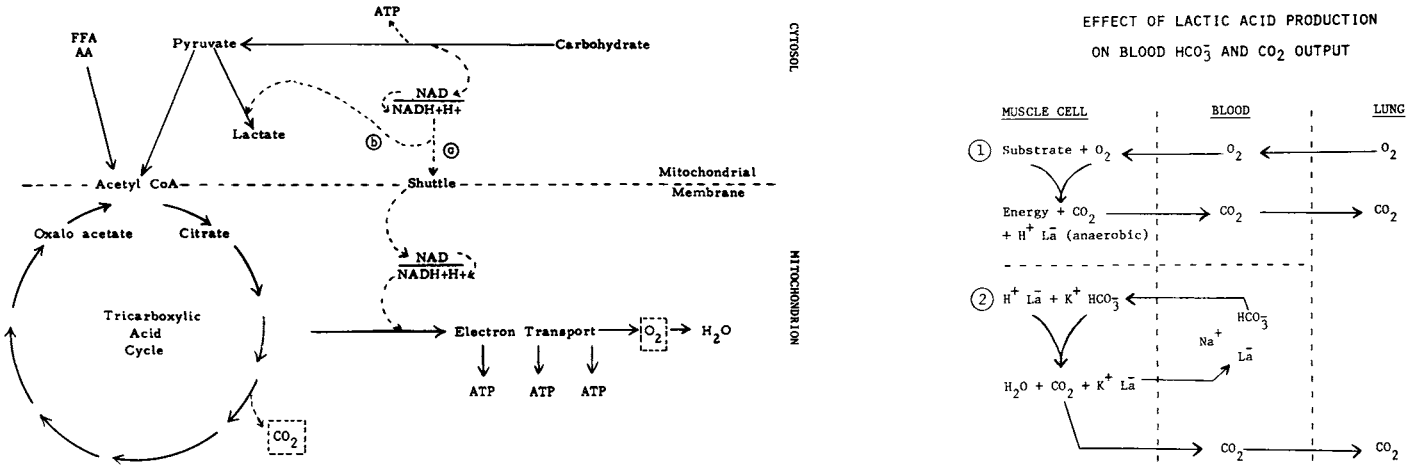

Fig. 1 (*left*). Schematic of metabolic pathways leading to production of adenosine triphosphate. Increased cellular lactate production depends on mechanism for reoxidation of cytoplasmic NADH. Pathway "a" is used for low to moderate intensity work rates. Pathway "b" supplements pathway "a" at heavy and very heavy work intensities. (See text for discussion of controlling mechanisms.) Fig. 2 (*right*). Cell buffering of the increase in lactic acid production when pathway "b", described in figure 1, contributes to the reoxidation of cytosol NADH. Immediate byproduct of buffering of the acid is CO_2. The increase in cell lactate and decrease in HCO_3 stimulates an anion exchange between cell and extracellular water causing blood lactate to increase and HCO_3 to decrease. (Reproduced from reference 41.)

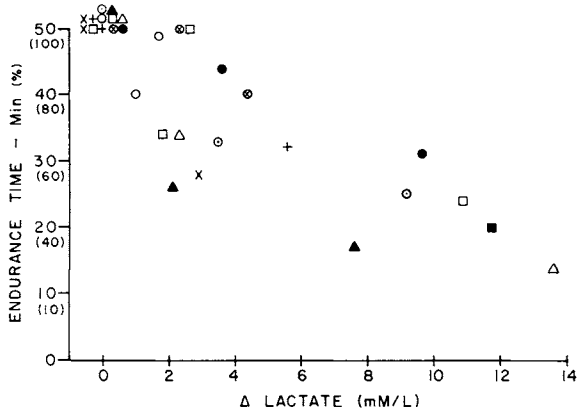

Fig. 3. The endurance time as related to the increase in lactate above control at the end of cycle ergometer exercise. Data are from 30 experiments on 10 male subjects studied at 3 work rates on 3 different days for a target time of 50 min. Endurance is curtailed when lactate is increased.

shown to be associated with an increased O_2 deficit and debt (2).

3. *$\dot{V}O_2$ above which there is a delay in steady-state.* The *AT* demarcates the work rate above which $\dot{V}O_2$ kinetics are slowed causing achievement of the steady-state to be delayed beyond 3 min (3). Thus, the increase in $\dot{V}O_2$ between the 3rd and 6th min of loaded cycling correlates with the lactate increase (figure 5). If the 6th minute $\dot{V}O_2$ is no greater than the 3rd min, then the 6th min lactate concentration is the same as control or minimally increased. The rise in $\dot{V}O_2$ beyond 3 min (observed for work rates above the anaerobic threshold) is probably caused by at least 2 mechanisms: (*a*) progressive vasodilatation to the muscle units by metabolic vasodilatators, such as [H^+], in response to relative O_2 lack, thereby increasing O_2 flow; and (*b*) the O_2 cost of conversion of lactate to glycogen in tissue taking up lactate as the concentration rises.

4. *$\dot{V}O_2$ above which the cardiovascular system limits endurance work.* The anaerobic threshold also describes the $\dot{V}O_2$ above which the cardiovascular system cannot provide the metabolically active tissues with sufficient O_2 to keep the cell redox state normal. The lactate/pyruvate ratio increases at work rates above the anaerobic threshold (figure 5). The mechanism of this increase must be a shift in the cytosol redox potential to a more reduced state. This depends on the rate of cytosol NADH reoxidation by the mitochondrial membrane proton shuttle (figure 1) (4, 5).

5. *$\dot{V}O_2$ above which $\dot{V}E$ increases with time.* Because of the acid-base disturbance associated with the increased blood level of lactate and reciprocal decrease in bicarbonate (figure 4B), ventilatory drive must be stimulated if respiratory chemoreceptors are intact. Thus, $\dot{V}E$ increases out of proportion to $\dot{V}O_2$ as work rates above the *AT* are sustained. The increase in $\dot{V}E$ is usually effected by an increase in frequency without an increase in tidal volume (figure 6).

6. *Adequacy of work effort.* During exercise testing to determine work level limitation, the effort made by the patient can be objectively assessed from the *AT* measurement. If the patient does not have breathing or orthopedic limitation, he should be able to exercise to a level above his *AT* (normally approximately 2 X). If the *AT* is not reached or is only slightly exceeded during an incremental exercise test in which the patient's $\dot{V}O_2$ max is significantly less than his predicted, the examiner should suspect that the patient's effort was poor.

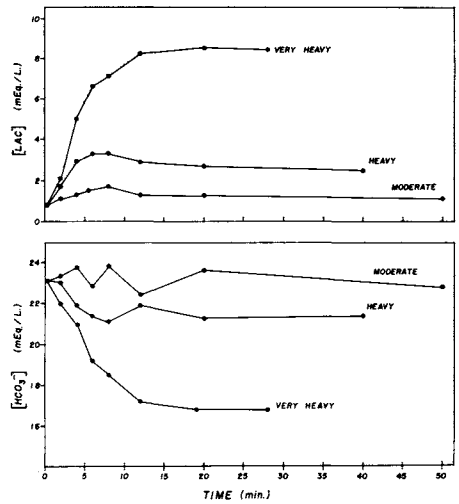

Fig. 4A. Lactate and bicarbonate change during exercise for moderate, heavy, and very heavy intensity cycle ergometer exercise. Each curve is the average of the same 10 normal subjects reported for figure 3. (From reference 2.)

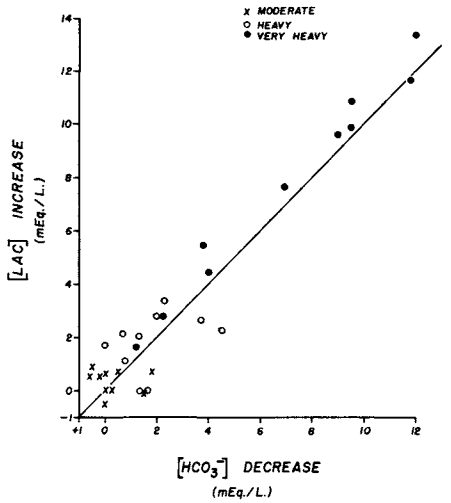

Fig. 4B. Simultaneous lactate and bicarbonate change at the end of exercise for the 30 studies shown in figure 3. Diagonal is the line of identity. (From reference 2.)

Justification of Term Anaerobic Threshold

Many experimental studies demonstrate that altering the balance between the exercise O_2 requirement and supply influences the lactate increase (table 1). Thus, when O_2 flow to the mitochondria is unable to meet all of the oxidative requirement for energy formation, anaerobic oxidation in the cytosol supplements mitochondrial oxidation, thereby conserving the O_2 that is ordinarily used in the mitochondria to reoxidize the mitochondrial membrane shuttle system (4, 5). This sparing of mitochondrial oxygen by the reoxidation of cytosol NADH by pyruvate (rather than by the mitochondrial membrane shuttle) allows maximal use of mitochondrial oxygen for ATP generation within the mitochondria. Functional adaptations to this low redox state are: (*a*) the increased acidity and related humoral factors that act to vasodilate the local vascular bed, thereby increasing blood (O_2) flow; and (*b*) the more acid pH shifting the oxyhemoglobin dissociation curve to the right, thereby raising capillary P_{O_2} in the ischemic bed and allowing O_2 to unload more readily from hemoglobin. Both mechanisms act to correct partially or completely the low redox state.

In studies in which muscle lactate has been studied during exercise, it is evident that muscle lactate does not significantly increase until a work level between 50 and 60% of the subject's Vo_2 max is reached (6–8). Blood lactate concentrations increase virtually simultaneously with the muscle increase (6, 8). Lactate/pyruvate ratios in the muscle also correlate with lactate/pyruvate ratios in the blood (9).

Some of the evidence supporting the concept that lactate increase during exercise is dependent on the balance between muscle O_2 requirement and O_2 availability are listed in table 1. When inspired oxygen tension is increased, whether by increasing the F_{IO_2} of the inspired air or increasing barometric pressure, blood lactate concentration during exercise decreases (10–16). In contrast, decreasing P_{IO_2} causes lactate to increase in the blood (10, 14, 16).

In states of isovolemic anemia, lactate is caused to increase in the blood during exercise above that of the nonanemic state (17–19). In studies on man, tying up 15 to 20% of the oxygen-binding sites of hemoglobin with carbon monoxide also causes lactate concentration to increase more during exercise than in the control state (20, 21). Moreover, reducing circulating blood volume in normal people has been demonstrated to result in an increase in exercise lactate concen-

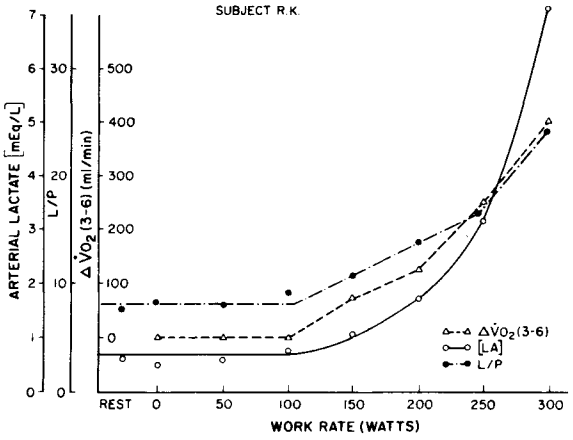

Fig. 5. Relation between lactate/pyruvate ratio, lactate and $\Delta\dot{V}O_2$ (6-3) for increasing work rate. (From reference 3.)

TABLE 1

EVIDENCE SUPPORTING THE CONCEPT THAT THE ANAEROBIC (LACTATE) THRESHOLD DURING EXERCISE DEPENDS ON ADEQUACY OF O_2 DELIVERY

1. Increasing P_{IO_2} decreases lactate (10-16).
2. Decreasing P_{IO_2} increases lactate (10, 14, 16).
3. Isovolemic anemia increases lactate and shifts threshold (17-19).
4. CO-Hb increases lactate and shifts threshold (20, 21).
5. Low cardiac output states increase lactate (25, 26, 33).
6. Reduced exercise $\dot{Q}$ with propranolol increases lactate in normal subjects (24).
7. Lactate increase correlates with size of O_2 deficit and debt (2, 8, 12).
8. Lactate increase correlates with V_{O_2} kinetics above *AT* (3).
9. Cardiac inotropic drugs decrease lactate (25).
10. Reduced circulating blood volume increases lactate (22, 23).
11. Lactate level in blood (7, 9, 15) and muscle (7, 9) is influenced by exercising muscle P_{O_2}.
12. Lactate increase in arterial blood occurs concurrently with a reduction in cell redox state (lactate/pyruvate ratio) in man (9).

tration presumably because of the accompanying vasoconstriction (22, 23).

By blocking the beta-adrenergic system with propranolol, Twentymen and associates (24) demonstrated blood lactate to increase in normal subjects during exercise without the RQ being affected. The authors conclude that the increase in lactate was brought about by the impaired cardiovascular response to exercise resulting from the beta-adrenergic blockade, thereby causing metabolically active muscle to become relatively anaerobic. Consistent with this, patients with heart diseases that cause the cardiac output response to exercise to be relatively low are known to have increased blood lactate levels (25, 26). Finally, in studies on cardiac patients with low exercise tolerance, Siskind and colleagues (27) were able to demonstrate that the lactate increase during exercise was reduced following the administration of the inotropic drug, amrinone.

The size of the oxygen deficit and debt had been shown to be increased at work rates that are accompanied by a lactic acidosis, and the increases in the debt and deficit are correlated with the increases in blood lactate (2, 8, 12). The lactate increase during exercise has also been correlated with the V_{O_2} kinetics above the anaerobic threshold. Thus, the rate of rise in $\dot{V}O_2$ after 3 min (3 min is when $\dot{V}O_2$ is in a steady-state below the anaerobic threshold) is correlated with the increase in lactate and lactate/pyruvate ratio (3).

Welch and coworkers (15) demonstrated, in man, that breathing O_2 increases the venous (capillary P_{O_2}) and decreases lactate in the effluent blood from the exercising muscle. Similarly, Jorfeldt and associates (7) and Bylund-Fellenius and colleagues (9) have demonstrated, in man, that lactate increase in the exercising muscle occurs only when the tissue or muscle venous P_{O_2} reaches critically low values. Finally, Bylund-Fellenius and colleagues (9) demonstrated that lactate increase in the arterial blood occurs concurrently with the reduction in muscle cell redox state as evidenced by an increase in lactate/pyruvate ratio in the muscle.

Despite the substantial evidence that links the lactate increase during exercise to the O_2 requirement-availability balance, a number of investigators believe that there is always adequate O_2 in the muscle mitochondria during exercise and that the increase in lactate is independent of oxygen availability. The study by Jobsis and Stainsby (28) is cited as evidence for this concept because these investigators, using fluorometry to detect change, could not find the mitochondrial NADH/NAD ratio in the isolated gastrocnemius muscle of dogs to change during exercise. However, in this study neither the blood nor muscle lactate was measured. In addition, according to their report, the method was not sensitive enough to detect cytoplasmic NADH/NAD ratio. Because lactate/pyruvate (L/P) ratio increases when *cytoplasmic*, not mitochondrial, NADH/NAD ratio increases, the findings in that report do not directly contradict the concept that lactate and L/P ratio increase at work rates during exercise in the presence of relative O_2 lack. However, the conclusions generally drawn from the latter studies do conflict with the more recent nuclear magnetic resonance studies done on the exercised gastrocnemius muscle of the rat (29). The latter studies demonstrate that the metabolic response of the muscle during exercise and recovery is controlled by the oxygen delivery to the muscle.

A second argument against the oxygen availability concept is proposed by Holloszy (30). Because $\dot{V}O_2$ during exercise is the same for the trained and untrained individual, he believes that O_2 lack could not account for the lactate increase in the untrained. This kind of reasoning fails to recognize two points in the anaerobic threshold-lactate increase concept: (*a*) lactate contributes toward the oxidative mechanisms only during the period of rising concentration; and (*b*) once a steady-state has been reached, all of the oxygen requirements of the muscle are met by oxygen transported through the mechanisms of external respiration regardless of fitness ($\dot{V}O_2$ would be the same in the unfit and fit for the same work rate). However, during the period when lactate is increasing, $\dot{V}O_2$ is below its steady-state response (2) and the unfit compared to the fit have slower O_2 uptake kinetics for the same work rate (3). It should also be noted that the anaerobic contribution to oxidation is very small compared to the aerobic and, therefore, to measure a difference in $\dot{V}O_2$ to evaluate the anaerobic contribution, measurements must be made at the right time (prior to lactate steady-state) and very accurately.

A nonanaerobic explanation for the in-

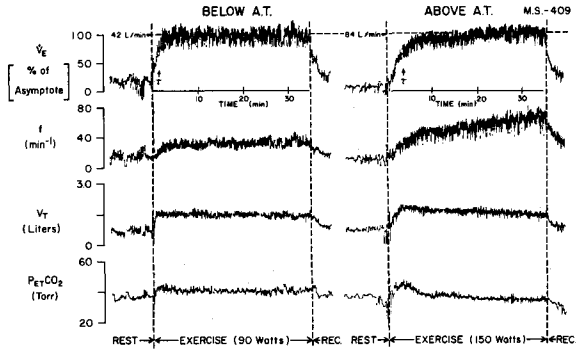

Fig. 6. Effect of prolonged exercise below and above the anaerobic threshold (AT) on $\dot{V}E$, VT, f and $P_{ET}CO_2$. The pattern of breathing remains unaltered during prolonged exercise below AT. In contrast, for work above the AT, $\dot{V}E$ and f increase with time and $P_{ET}CO_2$ decreases, presumably in response to the accompanying metabolic acidosis. (From reference 42.)

crease in lactate concentration in the blood during exercise has been proposed based on studies on muscle fiber type (31). Two predominant fiber types are present in human muscle: fast-twitch (type II) fibers poor in mitochondria and rich in glycolytic-pathway enzymes and slow-twitch (type I) fibers rich in mitochondria relative to glycolytic-pathway enzymes. Presumably, the fast-twitch fibers are important for short-burst, high-intensity work, while the slow-twitch, mitochondrial-rich fibers are important for endurance work.

To explain the pattern of increase in blood lactate as related to work rate by fiber type theory, the slow-twitch fibers must contract at low and moderate work rates, while the fast-twitch fibers must contract during heavy work. But there is as yet no data to support this type of sequential activation of muscle fibers during incremental exercise. Also, the changes that occur with deconditioning (32) and diseases associated with impaired O_2 transport (33), or acute changes in P_{IO_2} (10–16), hemoglobin content (17–19), and blood volume (22, 23) in normal subjects, do not make the fiber type sequential activation an attractive hypothesis to explain the lactate changes seen during exercise. Finally, it cannot readily explain the increase in lactate/pyruvate ratio that occurs simultaneously with the increase in lactate during exercise.

Another nonanaerobic explanation for the increase in lactate during exercise is based on the mitochondrial enzyme availability concept. Because training is associated with an increase in mitochondrial and Krebs cycle enzymes (34–36) as well as an increase in the work level at which lactate increases, it had been suggested that lactate might increase because of the limitation of the mitochondria to handle the products of glycolysis. Although it is easy to envisage that a shortage of these enzymes might prevent adequate utilization of pyruvate and thereby cause lactate to increase, there is no direct evidence for this unless the mitochondria are poisoned (37) or in the presence of severe iron deficiency (38). Furthermore, it cannot explain the observation that the lactate increase during exercise is affected by acute changes in hemoglobin concentration, inspired O_2 concentration, and blood volume (table 1). On the other hand, the stimulus for increase in mitochondrial enzymes might be secondary to inadequate O_2 availability because chronic muscle ischemia itself increases muscle mitochondrial enzymes (9).

Noninvasive Measurement of the Anaerobic Threshold

Lactic acid is the predominant fixed acid produced during exercise. It has a pK of approximately 3.8 and, therefore, is essentially totally dissociated at the cell pH (approximately 7.0). The HCO_3^- buffer system restricts the pH change that would otherwise come about from the formation of this relatively strong acid because the reaction $HCO_3^- \rightleftharpoons H_2CO_3 \rightleftharpoons CO_2$ continues to the right to form CO_2 gas. Because the resulting CO_2 is kept from accumulating by the respiratory control mechanisms that regulate P_{aCO_2} at its set-point or less (respiratory compensation for the metabolic acidosis), the pH change is small. Associated with the formation of H_2CO_3 during buffering, HCO_3^- concentration decreases in the blood almost mEq for mEq with the increase in lactate concentration (figures 4A and 4B). Because the buffering of the H^+ associated with lactate production must take place immediately within the cell, CO_2 production by the cell must increase (figure 2). The increase in cell lactate and decrease in cell HCO_3^- will be quickly balanced by transmembrane exchange of these ions. Consequently, the rapid efflux of additional CO_2 generated in the cell by buffering must be seen quickly in the lung gas exchange.

A relatively short progressive work rate test in which gas exchange is measured, breath-by-breath, can rapidly determine the $\dot{V}O_2$ at the anaerobic threshold because it allows measurement of the characteristic gas exchange phenomena associated with developing metabolic acidosis. A flow diagram describing the sequence of gas exchange and ventilation changes for a 1-min incremental exercise test is illustrated in figure 7 and the records of actual studies are shown in figures 8 and 9. As work rate is incremented, $\dot{V}O_2$, $\dot{V}CO_2$ and $\dot{V}E$ increase linearly. Above the anaerobic threshold, lactic acid production causes an increase in cell CO_2 production and the venous CO_2 load. This results in an acceleration of the increase in $\dot{V}CO_2$, which is usually accompanied by a parallel increase in $\dot{V}E$, thereby keeping P_{aCO_2} constant. Because the rate of rise of $\dot{V}O_2$ remains linear while $\dot{V}E$ accelerates, P_{ETO_2} increases at the anaerobic threshold while P_{ETCO_2} does not reciprocally decrease. As a corollary, ventilatory equivalent for O_2 ($\dot{V}E/\dot{V}O_2$) increases without an increase in the ventilatory equivalent for CO_2 ($\dot{V}E/\dot{V}CO_2$). The close parallel increase in $\dot{V}E$ and $\dot{V}CO_2$, seen initially above the *AT*, reflects a short period (2 min) of isocapnic buffering, i.e., $\dot{V}E/\dot{V}CO_2$ and P_{ETCO_2} do not change while $\dot{V}E/\dot{V}O_2$ and P_{ETO_2} increase. This is a sensitive gas exchange demonstration that the anaerobic threshold has been surpassed. As the work rate is increased, the pH falls further and the carotid bodies respond by causing ventilation to increase faster than CO_2 production. This causes P_{aCO_2} to decline and the pH decrease to be constrained. This respiratory compensation for the nonrespiratory lactic acidosis is reflected by an increase in $\dot{V}E/\dot{V}CO_2$ as well as by a further increase in $\dot{V}E/\dot{V}O_2$.

When the anaerobic threshold is measured as a metabolic stress, i.e., in units of O_2 consumption, it is unaffected by the type of exercise protocol employed for a given form of work. Moreover, the $\dot{V}O_2$ at the anaerobic threshold will not be affected by the duration of each work rate increment (39).

The reason for keeping the work rate intervals relatively short during testing is to take advantage of the fact that the increase in CO_2 is observed only during the buffering process and not after the lactate had been buffered, i.e., during the period of decreasing bicarbonate and increasing lactate.

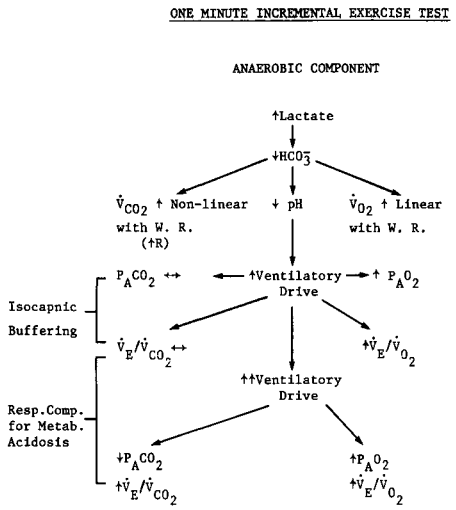

Fig. 7. Sequence of changes in gas exchange that accompanies anaerobic metabolism during a rapidly incrementing (1 min) exercise test. (From reference 43.)

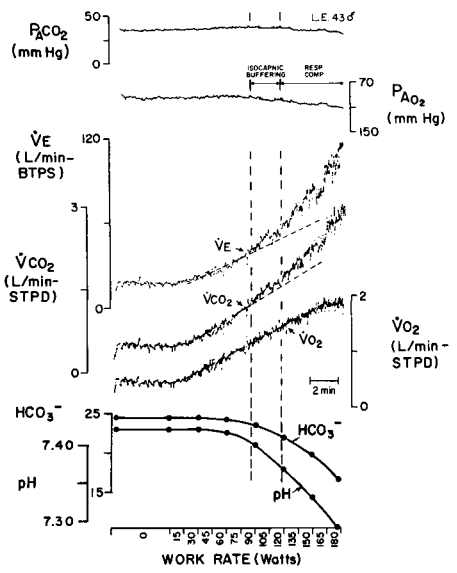

Fig. 8. Breath-by-breath measurements of alveolar (end-tidal) CO_2 and O_2 tension (P_{ACO_2} and P_{AO_2}) minute ventilation ($\dot{V}E$), CO_2 output ($\dot{V}CO_2$), O_2 uptake ($\dot{V}O_2$), arterial bicarbonate (HCO_3^-), and pH for a 1-min incremental work test on a cycle ergometer. The changes in gas exchange at the left vertical dashed line denote the AT. "Isocapnic buffering" refers to the period when $\dot{V}E$ and $\dot{V}CO_2$ increase, curvilinearly, at the same rate, thus retaining a constant P_{ACO_2}. This must be because of a developing metabolic acidosis. After the period of isocapnic buffering, P_{ACO_2} decreases, reflecting respiratory compensation for the metabolic acidosis of exercise. (From reference 43.)

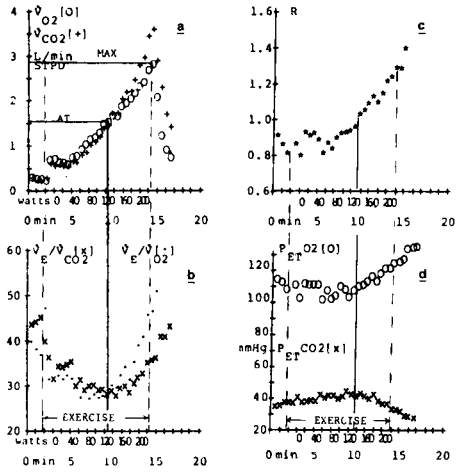

Fig. 9. Measurement of $\dot{V}O_2$ and $\dot{V}CO_2$ (*a*), $\dot{V}E/\dot{V}O_2$ and $\dot{V}E/\dot{V}CO_2$ (*b*), $P_{ET}O_2$ and $P_{ET}CO_2$ (*c*), and R (*d*) during a 1-min incremental exercise test. Points are at 30-s intervals with each point being the average of the closest number of whole breaths between the 15th and 20th s of the period.

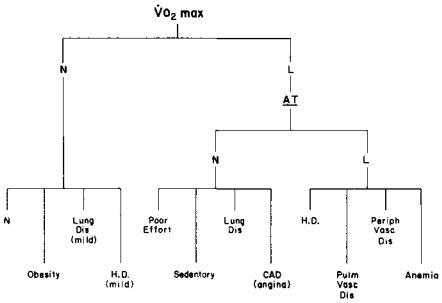

Fig. 10. Use of the anaerobic threshold (AT) for decision making in the differential diagnosis of exertional dyspnea. The disorders in which the AT is expected to be reduced are heart diseases, pulmonary vascular disease, peripheral vascular disease, and anemia. Reduced exercise performance in which the AT might be expected to be normal are poor effort by patients, lung disease without significant pulmonary vascular disease, and coronary artery disease in which cardiac output is not significantly impaired at moderate work rates.

Also, the ventilatory compensation for the buffered metabolic acidosis is delayed by approximately 2 min. Thus, for approximately 2 min, $\dot{V}E$ increases parallel to the rate of increase in $\dot{V}CO_2$, and the lack of decrease in $P_{ET}CO_2$ could be used to distinguish increased $\dot{V}E$ caused by metabolic acidosis from other mechanisms such as hypoxemia, pain, or psychogenic factors.

It should be noted that the anaerobic threshold, like the $\dot{V}O_2$ max, will differ depending on the muscle mass involved in the exercise. We find that the anaerobic threshold and $\dot{V}O_2$ max during cycle ergometer, incremental exercise testing is about 10% less than that for treadmill exercise in sedentary people.

Application of the Anaerobic Threshold Measurement

In testing patients with the complaint of exercise intolerance, we use the anaerobic threshold to complement our $\dot{V}O_2$ max measurement (figure 10). If the $\dot{V}O_2$ max is normal, then we conclude that the patient is normal, limited by obesity (a common condition that reduces exercise tolerance because of the high metabolic cost, but without cardiovascular or respiratory dysfunction), or we look for evidence of mild coronary artery disease or lung disease.

If the $\dot{V}O_2$ max is low, it is valuable to know if the *AT* is normal or low. Our lower limit for normal for *AT* is 40% of the *predicted* $\dot{V}O_2$ max with a mean of 56% for middle age to elderly men (40). We use the same method for predicting the *AT* for females.

The *AT* is reduced when O_2 flow to the metabolically active muscles is inadequate. Therefore, conditions that limit cardiac output during exercise, such as primary heart disease, pulmonary vascular occlusive disease, peripheral vascular disease, and anemia will cause *AT* to be reduced because of their effect on O_2 flow (figure 1).

If the *AT* is normal but the $\dot{V}O_2$ max is low (or the patient stops the exercise before reaching it), then the cardiovascular system is probably not limiting. The combination of reduced $\dot{V}O_2$ max and normal *AT* generally signifies either that the patient is limited by lung disease or is not willing to put forth the effort needed to achieve a normal $\dot{V}O_2$ max (figure 10).

Thus, the *AT* is an aid in the differential diagnosis of disorders of cardiorespiratory coupling to cellular respiration. Combined with other measurements, the pathophysiology of exercise limitation can be further subclassified. The *AT* can also be used for evaluating therapy because it is sensitively affected by changes in O_2 flow to the tissues. It is relatively independent of effort, in contrast to $\dot{V}O_2$ max.

Any increase in lactic acid production will cause an approximately equal decrease in bicarbonate. If normal chemoreceptors are present, ventilation should respond to the increased CO_2 released from the buffering reaction and decrease in pH. As described above, not all increases in ventilation are caused by an acidosis. In order to be sure that the increased rate of rise in ventilation reflects metabolic acidosis (work above the AT), it is important for it to be accompanied by the characteristic changes in gas exchange that reflect acid buffering.

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