KARST, GREGORY MARK

VENTILATORY AND LACTATE THRESHOLDS DURING SUPINE AND UPRIGHT CYCLING

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VENTILATORY AND LACTATE THRESHOLDS DURING SUPINE AND UPRIGHT CYCLING

by

Gregory Mark Karst

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This thesis has been approved on the date shown below:

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VICTOR A. CONVERTINO — Date

Assistant Professor of Physical Education

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ABSTRACT

Maximal, incremental exercise tests were performed using a cycle ergometer in both the supine and upright positions in order to examine ventilatory responses and changes in arterialized venous blood H^+ ion, lactate and HCO_3^- concentrations. Eight male subjects performed tests in both positions using a protocol of 8 minutes at 180 kpm/min followed by 180 kpm/min increases in work rate until exhaustion. Ventilatory threshold (T_{vent}) and lactate threshold (T_{lac}) were identified for each test.

Mean peak oxygen uptake (VO_2) values were 14.1% lower ($p<.01$) in the supine position and peak heart rates were 166 (±8.5) bpm (mean ± S.D.) supine compared with 181 (±8.0) bpm upright ($p<.01$). Comparison of the absolute VO_2 at which T_{vent} and T_{lac} occurred resulted in significant ($p<.05$) correlations of .756 for the supine tests and .765 for the upright tests. Comparison of concurrent changes in arterialized venous blood pH, lactate and bicarbonate concentrations during the 3 min prior to and the 4 min following the onset of T_{vent} indicated a strong correlation between the changes in those blood parameters ($p<.01$ for all comparisons in either position).

These results support the validity of using T_{vent} as a predictor of T_{lac} in supine as well as the upright position and are consistent with the concept that T_{vent} indicates respiratory compensation in response to increasing H^+ ion concentration during

incremental exercise. In addition, the strong correlation between changes in pH and lactate concentration suggests that any differences in rates of efflux of H^+ and $lactate^-$ from working muscle are not apparent when sampling arterialized venous blood from the upper extremity during cycling in either the supine or upright position.

CHAPTER 1

INTRODUCTION

The ability of the human body to effectively control pulmonary ventilation in order to match metabolic demands and maintain a homeostatic internal environment represents adaptation through physiologic regulation. The mechanisms by which the body compensates for disturbances such as muscular exercise or changing air pressure at altitude are complex, and as yet not completely understood. The study of the ventilatory response to exercise, during which many of the humoral and neural factors thought to influence ventilation undergo marked change, is one means of obtaining information regarding how and when these various stimuli interact in influencing external respiration.

During steady-state exercise of light to moderate intensity, minute ventilation (V_E) exhibits a linear relationship to metabolic demand as measured by O_2 uptake (VO_2) or CO_2 production (VCO_2). However, as the intensity of exercise becomes more severe, a point is reached at which V_E begins to increase in a curvilinear fashion with respect to O_2 uptake. This ventilatory threshold (T_{vent}) has been described as "hyperventilaton with respect to O_2" uptake (48). This deviation from the prior linear relationship between V_E and VO_2 suggests a change in the basic response pattern of the respiratory

centers. Consequently, much work has been done in an attempt to relate changes in known and proposed ventilatory stimuli to this observed change in ventilation.

In order to study the dynamics of various ventilatory stimuli in the appropriate range of O_2 uptake where $\dot{V}_E$ begins to increase nonlinearly, investigators have used incremental exercise tests during which various ventilatory and humoral factors can be serially measured and analyzed. Data derived from such tests on normal subjects and cardiac patients resulted in the formulation of a theory correlating the T_{vent} with the threshold of increased blood lactate levels (T_{lac}), and the term anaerobic threshold (AT) to describe this point. The AT has been defined as "the highest VO_2 beyond which lactate begins accumulating in the blood causing metabolic acidosis" (48). The T_{lac} in this case is attributed to anaerobic glycolysis resulting from local muscle hypoxia occurring when O_2 demand exceeds utilization in the active muscle groups during heavy exercise. The lactic acid dissociates to a large degree and is buffered by the bicarbonate system, resulting in the formation of non-metabolic CO_2 and H^+ion, which in turn stimulates the increased ventilatory response noted at the AT. This exercise-induced ventilatory response results in respiratory compensation for the metabolic acidosis by increasing the expired CO_2 with a subsequent hypocapnia.

Central to this theory is the observation that T_{vent} occurs at the same time as T_{lac} during incremental exercise. Thus, the use of ventilatory indices such as $\dot{V}_E$, ventilatory equivilent for oxygen uptake ($\dot{V}_E/VO_2$), ventilatory equivilent for carbon dioxide ($\dot{V}_E/VCO_2$),

and respiratory exchange ratio (R) have been advocated as a noninvasive method of delineating the T_{lac} and hence, the onset of anaerobic metabolism during exercise. This concept has been supported by numerous validation studies comparing the ventilatory indices with T_{lac} , but other recent studies have questioned the causal relationship of T_{lac} to T_{vent}based on both experimental and theoretical models.

The issue of the validity of T_{vent} as an indicator of T_{lac} is important both from a theoretical standpoint in regard to understanding the control mechanisms of ventilation during heavy exercise, and from a practical standpoint since the concept of AT has been widely used and accepted for the assessment of cardiac patients, exercise prescription, assessment of aerobic capacity and effects of training, and prediction of endurance performance.

The AT is known to vary widely among individuals, with values ranging from 50% to 80% of maximal oxygen uptake (VO_2 max) reported in the literature. Several factors have been reported which may account for the interindividual as well as intraindividual differences. Endurance training has been shown to increase the AT. An increase in local blood flow, oxidative capacity of muscle, or delayed recruitment of fast-twitch muscle fibers following endurance training have been suggested as possible mechanisms. Similarly, different modes of exercise (e.g., treadmill vs. cycling) and variance in the amount of active muscle mass (e.g., arm vs. leg work) have been shown to change the intraindividual AT.

However, several recent publications have reported an uncoupling of these two measures and have questioned the causal

relationship. Factors reported to uncouple T_{vent} from T_{lac} include changing muscle substrate utilization by using dietary manipulation plus repeated maximal exercise to induce muscle glycogen depletion, and also by inducing lactic acidosis via a prior bout of exercise. In addition, there is conflicting evidence regarding the effect of the test protocol on the determination of AT and evidence that the AT determined by a graded exercise test is not applicable to steady-state work. The relationship of increases in expired CO_2 to increased blood lactate has also been questioned on the basis of recent evidence regarding uptake and oxidation of blood lactate and the relative rate of efflux of lactate and H^+ ions from exerising muscle.

Further investigation is needed to resolve apparent conflicts in the literature and, more importantly, to clarify test conditions which may alter the relationship of the ventilatory indices to T_{lac}. Such clarification will serve not only to improve the accuracy and versatility of exercise testing involving the use of the AT concept, but may help to clarify the basic mechanisms of ventilatory control by illustrating the relative importance of various ventilatory stimuli which can be manipulated by carefully designed experiments.

As noted above, the uncoupling of T_{lac} and T_{vent} has been reported following manipulation of lactate levels via diet and prior exercise. The question arises whether factors affecting ventilation operate independently of T_{lac} during exercise in regard to the onset of hyperventilation during exercise. Varying posture from supine to upright during exercise appears to be an appropriate method of examining this question, since the supine posture has been shown to

result in a lower V_E at rest and during exercise at a given level of O_2 consumption when compared to the upright posture.

While considerable work has been done on circulatory adaptations to variations in posture during exercise, information regarding the relationship of V_E to blood parameters during supine and upright exercise is minimal and conflicting. Bevegard et al. (3) compared physiological responses to arm and leg exercise in both the supine and sitting position using two submaximal work rates. They reported that VO_2 was not significantly different between the two positions for leg work while pulmonary ventilation was greater in the upright position. However, the increase in V_E during exercise was proportional to the increase in VO_2 regardless of position. They also found no significant differences in arterial lactate concentration during submaximal cycling in the two positions. In contrast, Fukunaga et al. (17) reported higher lactate concentrations in the supine position for all work rates when comparing graded maximal exercise in both positions, while still finding lower V_E in the supine position. They also calculated T_{lac} (defined as 4mM/L blood lactate concentration) as occurring at 60% of VO_2 max independent of posture. No ventilatory indices of the AT were reported in either study.

The purpose of this study is to compare changes in arterialized venous blood lactate, pH and HCO_3^- concentrations during incremental cycle ergometer exercise in both supine and upright positions in order to clarify the relationship of those blood parameters to the changing ventilatory response occurring at the ventilatory threshold.

CHAPTER 2

LITERATURE REVIEW

During exercise of intensity below the AT, minute ventilation correlates highly with VO_2 and VCO_2 while arterial pH, PO_2, and PCO_2 remain essentially unchanged (45). Precise control of ventilation during exercise is necessary to maintain these blood parameters in the face of increased metabolic demand. Numerous neural and humoral mechanisms have been proposed for transmission of the "exercise stimulus" to the ventilatory control centers of the medulla. These mechanisms include peripheral mechanoreceptors, thermoreceptors and chemoreceptors acting via neural pathways as well as chemical changes in arterial or mixed venous blood or cerebrospinal fluid, blood temperature changes, pressure changes in the central circulation and rate of CO_2 flux to the lungs (31). Reviews by Wasserman (45) and Levine (31) present detailed analysis of evidence supporting and opposing the viability of these proposed mechanisms. Although the precise interaction of these mechanisms is not fully understood, some combination of these ventilatory stimuli appears to cause an increase in V_E in proportion to the metabolic rate until the exercise intenity reaches the ventilatory threshold (T_{vent}).

In order to explain this deviation from linearity in the relationship of V_E to VO_2 which occurs at T_{vent}, several additional

mechanisms have been proposed. These include metabolic acidosis (46), increased ventilatory response to hypoxia resulting from the multiplicative interaction of peripheral and central ventilatory drives (15), increased circulating catecholamines (31), and increased temperature (44).

The metabolic acidosis attributed to lactic acid production during severe exercise has been implicated as the cause of T_{vent}. Wasserman and associates (46,48) proposed the mechanism of local muscle hypoxia resulting in lactic acid production followed by buffering of the dissociated H^+ ions by the bicarbonate buffering system. The resultant shift of the equation $H^+ + HCO_3^- \rightleftharpoons H_2CO_3 \rightleftharpoons H_2O + CO_2$ to the right causes additional, non-metabolic CO_2 and H^+ production which serves as a stimulus for increased ventilation. As the HCO_3^- stores are diminished due to excess CO_2 exhalation, blood pH decreases, suggesting that H^+ sensitivity of the carotid bodies (30,49) or a combination of both central and carotid chemoreceptors (1,35) might mediate the hyperventilatory response. Supporting this theory are numerous studies showing that induced metabolic acidosis tends to increase the ventilatory response to exercise while induced metabolic alkalosis decreases minute ventilation (1,29,35). Linking the coincident onset of this increase in V_E with the onset of increased blood lactate levels resulted in the concept of AT and use of the gas exchange data as a non-invasive means of determining the onset of blood lactate accumulation during graded exercise.

Since the use of ventilatory indices of the AT was first advocated as a means of detecting the onset of blood lactate

accumulation (46) without the added complications of serial blood sampling, many uses of the AT have been proposed. These include use of the AT to evaluate physical fitness and detect circulatory insufficiency (48), measurement of training effects (11), use in formulating exercise prescription (14), and use as a predictor of endurance exercise performance (43) and muscle fiber oxidative capacity (27). Use of the gas exchange AT in testing and exercise prescription for patients is especially attractive in that it gives an estimate of exercise capacity without the risks of a maximal exercise test. Use of the AT in predicting endurance performance has been advocated on the basis that the AT is a major determinant of the ability to perform sustained, high intensity exercise.

Many different gas exchange indices have been used as indicators of the AT. Even before the term "AT" was coined, the respiratory exchange ratio (R) was seen as an indicator of the extent of anaerobic metabolism during exercise (25) and as a predictor of maximal aerobic capacity (24). Increases in R have since been used to delineate the AT on the grounds that a rapid increase in the VCO_2/VO_2 ratio is due to the non-metabolic CO_2 production during the buffering of lactic acid (7,12,34,46,48). Abrupt or nonlinear increases in V_E (12,22,27) or VCO_2 (12,48) have also been used to define the AT, as has a systematic increase in the ventilatory equivilent for oxygen (V_E/VO_2) without a concurrent increase in the ventilatory equivilent for carbon dioxide (V_E/VCO_2) (6,11,38). This dual criterion is intended to avoid complications caused by hyperventilation unrelated to a metabolic acidosis during the test.

Because of the variety of indices used to define AT, attempts have been made to compare the various indices and correlate them with the onset of blood lactate accumulation during a graded exercise test. Reinhard et al. (38) reported a strong correlation (r = .94) between the onset of increased capillary lactate and V_E/VO_2 increase. They also noted that the fraction of expired O_2 (FeO_2) is analagous to V_E/VO_2 and could be substituted as an index of AT. Caiozzo et al. (6) compared the onset of venous blood lactate accumulation with each of the indices mentioned above and found V_E/VO_2 to have the highest correlation with lactate (r = .93) followed by V_E and VCO_2 (r = .88 and r = .83, respectively) while R showed the poorest correlation with venous lactate (r = .39). Several other studies have lent support to the validity of gas exchange indices as predictors of the onset of blood lactate accumulation (12,27,55). However, some authors have reported mixed results in correlating gas exchange and blood lactate data. Recently, questions have been raised regarding the ability of independent observers to agree in either the lactate or ventilatory thresholds when evaluating the same data sets (54) and several studies have directly challenged the validity of the gas exchange indices as predictors of the blood lactate accumulation (22,37,39,54).

The disparity over the validity and reliability of T_{vent} as a predictor of T_{lac} may stem in part from methodological factors such as the criteria for defining the lactate and ventilatory thresholds, the exercise test protocol and the site of blood sampling for determination of T_{lac}. Yeh and associates (54) recently reported an average of 16% variability among four experienced exercise

physiologists in determining T_{vent} from gas exchange data despite the use of a standard definition of T_{vent}. However, other studies report good inter-reviewer agreement in detecting the T_{vent} (6,12) and in many cases, the question of test-retest reliability of a single reviewer may be the more important point. In an attempt to minimize the variation in picking inflection points off of data plots, Orr et al. (36) reported the use of a computerized multiple linear regression model to determine the T_{vent}. Although they found good correlation between computer derived results and those of several independent reviewers, they did not validate the method with simultaneous invasive determination of T_{lac}.

A second methodological concern is the site of blood sampling for the determination of T_{lac}. Arterial, venous and capillary blood has been used for such determinations. Since lactate uptake by resting and exercising muscle is known to occur (20,26,41) and could thus alter the ratio of lactate production/clearance which determines blood lactate levels, the validity of sampling venous blood from the arm during leg exercise has been questioned. Studies comparing simultaneous arterial and venous blood lactate levels taken from the resting arms during upright cycling have shown both lower venous lactate levels and a lag between the onset of arterial and venous blood lactate accumulation (54,56). This lag in venous lactate accumulation has been reported to introduce errors averaging 1.5 minutes in determining T_{lac} (54) and cause the T_{lac} expressed as $\%VO_2$ max to vary from from 37% to 55% based on arterial and venous samples, respectively (56). Some investigators have advocated the use of

"arterialized venous blood" obtained from a dorsal hand vein while the hand is heated to 41-43 degrees C by a heating pad, resulting in a-v shunting. Forster et al. (16) utilized this method in a variety of conditions including submaximal and maximal exercise and found good correlation when comparing pH (r=.98), PCO_2 (r=.95), and lactate concentration (r=.92) from simultaneously drawn arterial and arterialized venous blood samples. Mean differences between arterialized venous blood and arterial blood were 1mmHg for PCO_2 , .005 for pH, and 1 mg% for lactate, with the arterialized venous blood showing slightly higher PCO_2 and lactate values and slightly lower pH than arterial blood. PO_2 measurements obtained in this manner did not correlate well. Use of this technique was reported to be accurate for evaluation of lactate and acid-base changes in the blood without the risks associated with arterial punctures.

Another variable found in the literature concerning AT determination is the protocol of the exercise test. T_{vent} has been reported to vary in the same individual between arm and leg exercise tests (12). Some investigators have reported differences in treadmill vs. cycle ergometer tests for trained runners but not for trained cyclists (53), while others found no overall significant difference (12). Many different types of incremental and ramp work protocols have been used and there is some disagreement regarding the effect of the test protocol on AT determination. Increments in duration of 1 minute (6,11,47,48,54,55,56), 2 minutes (22,39) or a continuous ramp work protocol (23,52) appear most common, but some increments were as long as four minutes per work load (19,48). The rate of work increase

used in AT testing varied from 15 to 50 watts/minute, with most values around 25 watts/minute.

Comparison of AT values during 1 minute and 4 minute incremental tests by Wasserman et al. (48) showed no difference in VO_2 at the AT despite differences in the absolute values of V_E and blood lactate. However, Hughson and Green (23) reported differences in T_{vent} when comparing fast (49-65 watt/min.) vs. slow (6-8 watt/min.) ramp tests, while Whipp et al. (52) reported minimal differences in T_{vent} when comparing a 50 watt/min. ramp protocol with a 15 watt/min. incremental test.

Given a standard methodology for determining T_{vent} and T_{lac}, there is still disagreement regarding the validity of T_{vent} as a predictor of T_{lac}. While many studies have reported the coupling of these two events (6,12,27,48), several recent studies have reported uncoupling of T_{vent} and T_{lac} and concluded that the relationship is merely coincidental rather than causal.

Simon et al. found that during constant-load work at a rate just above the point of T_{vent}, the V_E/VO_2 peaked well before plasma lactate, suggesting that "exercise hyperventilation is not necessarily proportional to changes in plasma lactate" (39).

Hughes et al. (22) reported an uncoupling of T_{vent} from T_{lac} following muscle glycogen depletion, with T_{vent} occurring at a lower work rate and T_{lac} occurring at a significantly higher work rate and VO_2 following glycogen depletion. Other investigators have reported finding lower lactate concentrations and higher minute ventilation at any given work rate of an incremental test following glycogen

depletion (19). These data would seem to support the findings of Hughes et al., although threshold points were not identified.

Further evidence of the uncoupling of T_{vent} and T_{lac} is presented in studies in which metabolic acidosis is induced via prior bouts of exercise. H.A. Davis et al. (9) used two successive incremental tests on a cycle ergometer separated by a 5 minute rest period. They reported that T_{vent} occurred at a similar work rate during both tests although lactate concentration was actually decreasing at the time of T_{vent} during the second test. However, careful inspection of their lactate plot reveals that T_{vent} did coincide with the point where lactate changed slope in the second test. This suggests that the de nova lactate generated by the second exercise test occurred at the same work rate observed in the first test.

While the experimental findings suggesting uncoupling of T_{lac} from T_{vent} are not fully explained by the theory of exercise hyperventilation with respect to O_2 uptake proposed by Wasserman et al. (48), several additional theories have been proposed which might help explain the apparent dissociation of these two events. One reason for the possible discrepancy between the onset of T_{vent} and T_{lac} may lie in the relationship of the relative rates of efflux of hydrogen and lactate ions from exercising muscle into the blood. Jones (28) points out that the net production of H^+ ions during exercise is dependent on muscle pH and phosphocreatin concentration. He states that proton release via hydrolysis of ATP decreases as pH decreases, while absorption of protons via the phosphocreatin kinase

reaction (PCr_2^- + $ADP_3^- \rightleftharpoons Cr$ + ATP_4^-) increases with decreasing intracellular pH. In addition, the decreasing intracellular phosphocreatin concentration during exercise affects the impact of this latter reaction on the net production of H^+ ions. Because of this capacity for changing net H^+ production, the relationship between production of hydrogen and lactate ions may not be stoichiometric. Benade and Heisler (2) studied the relative rates of efflux of H^+ and lactate ions from isolated rat diaphram and frog sartorius muscles and found that hydrogen ion efflux exceeded lactate ion efflux by factors of 14 and 50 for the diaphram and sartorius muscles, respectively, leading to the conclusion that lactate content of a body compartment is not representative of the hydrogen ion load for that compartment, especially during the early stages of efflux. The rate of lactate efflux from exercising muscle has also been reported to be altered by changes in HCO_3 concentration (32), pH (18), and PCO_2 (21) of the perfusing fluid.

Another factor which may be relevant to the variability of the relationship of T_{vent} to T_{lac} is the alteration during exercise of the two factors ultimately responsible for blood lactate levels, the production and clearance rates of lactate. Jones et al. (29) measured blood lactate concentration during exercise after inducing changes in blood pH by oral administration of $NaHCO_3$ or NH_4Cl. They found that the ventilatory response was consistent with pH changes (V_E higher during acidosis than during alkalosis) while lactate concentration was lowest following acidosis and highest during exercise in the alkalotic condition. Suggested reasons for these results included the changes

in lactate efflux noted above as well as increases in lactate uptake by the liver and muscle tissue and decreased lactate production secondary to inhibition of lipolysis. The inhibitory effect of lactate and/or pyruvate on lipolysis has been supported by Boyd et al. (5) in a study of lactate infusion during exercise in man. Lactate uptake by both resting and exercising muscle has been reported by many investigators. Stainsby and Welch (41) used contracting dog skeletal muscle in situ and found that approximately 50% of the muscle preparations showed a net uptake of lactate after 10-60 minutes of electrically induced twitch contractions. Issekutz and associates (26) utilized isotopically labeled glucose and lactate to determine the rates of lactate disappearance, oxidation and conversion to glucose during rest and exercise in dogs. They found that exercising muscle produces and utilizes lactate at the same time, with oxidation of lactate accounting for a larger portion of lactate disappearance than liver gluconeogenesis. These results are supported by the results of Hermansen et al. (20) which indicate that "human skeletal muscle possesses a pronounced capacity to oxidize lactate" and show that lactate oxidation during exercise of up to 60-80% of VO_2 max is greater than lactate oxidation at rest. Hence, changes in the onset of blood lactate accumulation would appear to be influenced by factors other than the onset of anaerobic glycolyis due to local muscle hypoxia.

In light of the questions raised by the studies showing an uncoupling of T_{vent} and T_{lac} as well as the aforementioned theoretical considerations, further study in this area is indicated for the

following reasons: First, although the theoretical basis of the AT concept is currently being challenged, there is little doubt that the concept itself is useful in some contexts and will continue to be used in certain clinical and research applications. Thus, further study is needed to delineate the exact conditions in which T_{vent} is or is not a valid predictor of T_{lac}. Secondly, since the studies showing a dissociation of T_{vent} from T_{lac} have basically relied on models which manipulate blood lactate by diet or induced acidosis prior to exercise, other approaches, such as the supine vs. upright exercise model proposed here, seem warranted. Finally, the supine vs. upright model is especilly relevant in view of the widespread use of supine cycle ergometer testing in clinical settings. Results of this study will demonstrate the degree of validity associated with use of T_{vent} as a predictor of T_{lac} in the supine position and will also allow comparison of absolute and relative changes in T_{vent} and T_{lac} between the supine and upright postures.

The model of supine vs. upright exercise has previously been used to study circulatory adaptation to exercise. In one such study, McGregor et al. (33) noted lower ventilation volumes in the supine position both at rest and at comparable work loads despite no significant difference in VO_2 between the postures. Bevegard et al. (3) also reported lower V_E at equivalent VO_2 both at rest and during exercise in the supine position, but they also noted that V_E remained proportional to VO_2 regardless of posture. Other investigators have also reported lower minute ventilation at rest (3,4,40,51) and during exercise (17) in the supine position. Recently, the supine vs.

upright model has been used in studying ventilatory control at the initiation of exercise (50).

Review of the literature has revealed two prior studies which provide at least some data regarding ventilation and lactate accumulation during exercise in the supine and upright postures. Bevegard et al. (3), in a study primarily focused on circulation and stroke volume, reported that "body position did not cause any significant increase in lactate concentration during leg exercise or combined arm and leg exercise" at either of two steady-state work rates studied. These findings are not in agreement with those of Fukunaga et al. (17) who studied four male subjects performing incremental cycle ergometer tests in both supine and sitting positions. They reported higher lactic acid concentrations at a given work rate in the supine position while V_E, VO_2 and HR all remained lower while supine. Using a lactate concentration of 4 mM/L as an arbitrary designation of the T_{lac}, they found that the absolute VO_2 at T_{lac} was lower in the supine position than while upright (1.44L/min. and 1.98L/min., respectively) but the relative VO_2 (%VO_2 max) was equivilent to 60% VO_2 max independent of posture. No ventilatory thresholds were reported in either study. The purpose of this study was to clarify this apparent discrepancy regarding lactate accumulation in the two postures and at the same time answer the question of whether or not the relationship between T_{vent} and T_{lac} is altered by exercising in the supine position.

CHAPTER 3

METHODS

Eight healthy males ranging in age from 22 to 29 years volunteered to serve as subjects for the experiment. Each subject was familiarized with the testing procedures and signed a consent form approved by the Human Subjects Committee of the University of Arizona (see Appendix A). Physical activity levels of the subjects varied widely, ranging from competitive cycling and running to mostly sedentary, although all but one subject reported engaging in some form of regular aerobic activity. Subjects were asked to continue with their normal activities during the course of the experiment and to avoid any extreme changes in activity level.

All eight subjects performed two incremental exercise tests on a Monarch cycle ergometer, one in the supine position and one upright, during which serial blood sampling was carried out in addition to collection of heart rate and gas exchange data. In addition, six of the subjects performed a second test in each position during which only heart rate and gas exchange data were collected. Testing order was randomized. Supine testing was accomplished by mounting the Monarch ergometer on a padded table and stabilizing the subject by means of a padded waist belt which maintained the subject at the proper distance from the pedals. Toe clips were used in both the

supine and upright positions, and an additional strap was placed behind the heel during the supine tests to provide a necessary counterforce against the effect of gravity. During upright testing, the same cycle ergometer was used in a conventional manner, although the subjects were required to sit with the trunk in a vertical position rather than flexed forward over the handlebars, thus more closely approximating the biomechanics of the supine cycling position. Subjects stabilized the trunk by grasping a support with the right hand and leaning the left elbow and forearm on a horizontal support. This allowed for ease of blood sampling from the left hand and minimized the use of the hand and forearm musculature which might effect blood chemistry of the samples.

Protocol for all tests was the same, beginning with 8 minutes of cycling at 180 kpm/min followed by 180 kpm/min increases each minute to volitional fatigue, after which resistance was decreased back to 180 kpm/min for a 5 minute cool-down period. A metronome was used to maintain a pedaling frequency of 60 rpm and a frequency counter attached to the ergometer was monitored to assure that the frequency was maintained at 60 ± 2 rpm.

During all tests, the subject breathed through a Hans-Rudolph low resistance valve, with the inspiratory side connected to a Parkinson-Cowan CD-4 gas meter and the expiratory side to a 5-liter mixing chamber. Air from the mixing chamber was then drawn through a drying column and analyzed for fraction of expired CO_2 ($FeCO_2$) and fraction of expired O_2 (FeO_2) by Applied Electrochemistry CD-3A and S-3A analyzers, respectively. The analyzers were calibrated before

and after each test using reference gases analyzed by the Scholander technique (8). Inspiratory volume (V_I), FeO_2 and $FeCO_2$ data were fed on line to a microprocessor for calculation of gas exchange data using the Haldane transformation to calculate V_E from V_I. Those values were used to calculate and display 1 minute averages for VO_2 (in L/min and ml/kg), VCO_2 , R, V_E/VO_2, V_E/VCO_2, and VCO_2 each 15 seconds thoughout the test. Following post-calibration, any change in sensitivity of the gas analyzers was corrected for, (assuming a linear drift throughout the test), and corrected values were printed.

The highest 1 minute average VO_2 recorded during the test was considered to be the VO_2 max for that position. T_{vent} values for comparison with blood variables were identified by a single experienced reviewer who was not involved in the testing. Identification of the T_{vent} was accomplished by analysis of plots of V_E/VO_2 , V_E/VCO_2 and V_E plotted against VO_2 using the criteria of a systematic increase in V_E/VO_2 without a concomitant increase in V_E/VCO_2 , as described by Caiozzo et al. (6).

Heart rate data was collected via a modified V5 EKG configuration and recorded on a Gilson chart recorder at 5 mm/second for later analysis. One minute heart rate values were obtained by averaging the rate during the first and last 5 seconds of each minute of exercise. Palpation of the carotid pulse was used to determine heart rate in the event of problems with the EKG signal during a test.

Serial arterialized venous blood samples were obtained from each subject during one supine and one upright test. A 21 gauge over-the-needle teflon catheter (Quickath, Travenol) was inserted into

a branch of the dorsal venous network of the left hand 10 to 20 minutes prior to the exercise testing, and the hand was heated prior to and during the test, using an electric heating pad to maintain skin temperature at approximately 43 degrees C. This technique was reported by Forster et al. to allow close approximation of arterial values for blood pH, PCO_2 and lactate concentration without the possible risks associated with arterial sampling (16). The teflon catheter was connected by polyethylene tubing (capacity approxiately 1 ml) to a three-way stopcock. The tubing and catheter were flushed prior to starting the test and as needed to prevent clotting during the test with heparinized saline solution (100 units/ml; maximum 12 ml/test). Four samples were drawn during the 8 minute warm-up period (at 2, 4, 6, and 8 minutes) to establish baseline values and additional samples were then drawn at the end of each minute of incremental exercise. A final sample was taken at the end of the 5 minute cool-down period in an attempt to determine peak blood lactate levels. One ml of blood was drawn and discarded prior to each sample in order to clear the tubing and catheter, with an addiional 3 ml drawn for analysis of hematocrit, pH, PCO_2 and lactate concentration.

Samples to be analyzed for pH, and PCO_2 were collected in oiled, heparinized glass syringes and placed in an ice bath until analysis was completed, usually within 1 to 2 hours of sampling. A Radiometer BMS3 Mk2 blood gas analyzer was used for pH and PCO_2 measurement, with calibration procedures performed after every fourth sample to minimize drift. Each sample was tested in duplicate and a third analysis was performed if the initial two differed by more than

.01 for pH or 2 torr for PCO_2 . The Henderson-Hasselbalch equation was used to determine HCO_3^- concentration.

Lactate concentration was determined in duplicate for each sample using an enzymatic spectrophotometric technique (826-UV, Sigma Diagnostics, St. Louis, MO). Hematocrit readings were obtained in duplicate after centrifuging the heparinized microhematocrit tubes for 10 minutes at 11,500 rpm.

Lactate threshold points (T_{lac}) were determined from plots of lactate concentration versus time using the criterion of a systematic increase above baseline warm-up values, with VO_2 at T_{lac} then determined from individual regression equations of VO_2 on time (6).

Mean values for VO_2 at T_{vent} and T_{lac} in each position were compared by the use of paired t-tests and Pearson correlation coefficients, and least squares linear regression equations were calculated for VO_2 at T_{vent} versus VO_2 at T_{lac} in each position. Paired t-tests were used to compare mean VO_2 and heart rate values between the two positions during both the steady state and incremental portions of the test. Pearson correlation coefficients were used to compare changes in blood pH, lactate and HCO_3^- concentrations at the onset of the ventilatory threshold. The .05 level of significance was used in statistical analysis.

CHAPTER 4

RESULTS

Peak oxygen uptake values were significantly less during supine cycling as opposed to upright cycling (Table 1). Mean (±S.D.) peak VO_2 values were 3.18 ± .62 L/min supine and 3.71 ± .73 L/min upright, representing a mean difference of 14.1% ($p<.001$). Comparison of individual peak VO_2 values between the two positions revealed a correlation of .945. The maximum work rate in the supine position averaged 1822.5 ± 262 kpm/min as compared with 2070 ± 304 kpm/min in the upright position, and total work time was 1.5 ± .76 minutes longer for the upright tests. Mean VO_2 values (Figure 1) during the steady portion of the test (minutes 1 through 8) were .13 ± .06 L/min lower during the supine tests ($p<.05$). During the incremental portion of the test, min 9 through 14 (the last minute completed by all 8 subjects in both positions), the mean VO_2 was .08 ± .05 L/min lower in the supine as compared with the upright position (ns).

Maximal heart rate response during the supine tests was 166 ± 8.5 bpm compared with a maximum rate of 181 ± 8.0 bpm in the upright position ($p<.01$). Mean heart rate values (Figure 2) for minutes 1 through 8 were 4.1 ± 1.6 bpm lower in the supine position (ns) while means during the incremental portion of the tests (min 9-14) were 4.3± 1.8 bpm lower supine (ns). Due to technical problems with the heart rate data for one subject, n=7 for all heart rate data.

TABLE 1. Subject's weight and peak VO_2, supine and upright.

Peak VO_2 is expressed in absolute and relative terms for both positions. Final column expresses supine peak VO_2 as a percentage of upright peak VO_2.

	Weight	Peak VO_2 Upright		Peak VO_2 Supine		%VO_2 S/U
Subject	(KG)	(L/min)	(ml/Kg)	(L/min)	(ml/Kg)	
GD	77.0	5.26	68.3	4.34	56.4	82.5
CK	71.2	3.90	54.8	3.15	44.2	80.8
ML	74.8	3.67	49.1	3.29	44.0	89.6
GK	74.0	3.53	47.7	2.91	39.3	82.4
SK	73.4	3.56	48.5	3.13	42.6	87.9
PD	70.3	3.18	45.2	2.56	36.4	80.5
MB	81.6	2.75	33.7	2.39	29.3	86.9
KH	80.3	3.80	47.3	3.66	45.6	96.3
Mean	75.3	3.71	49.3	3.18	42.2	85.9
±S.D.	4.1	.73	9.7	.62	7.8	5.4

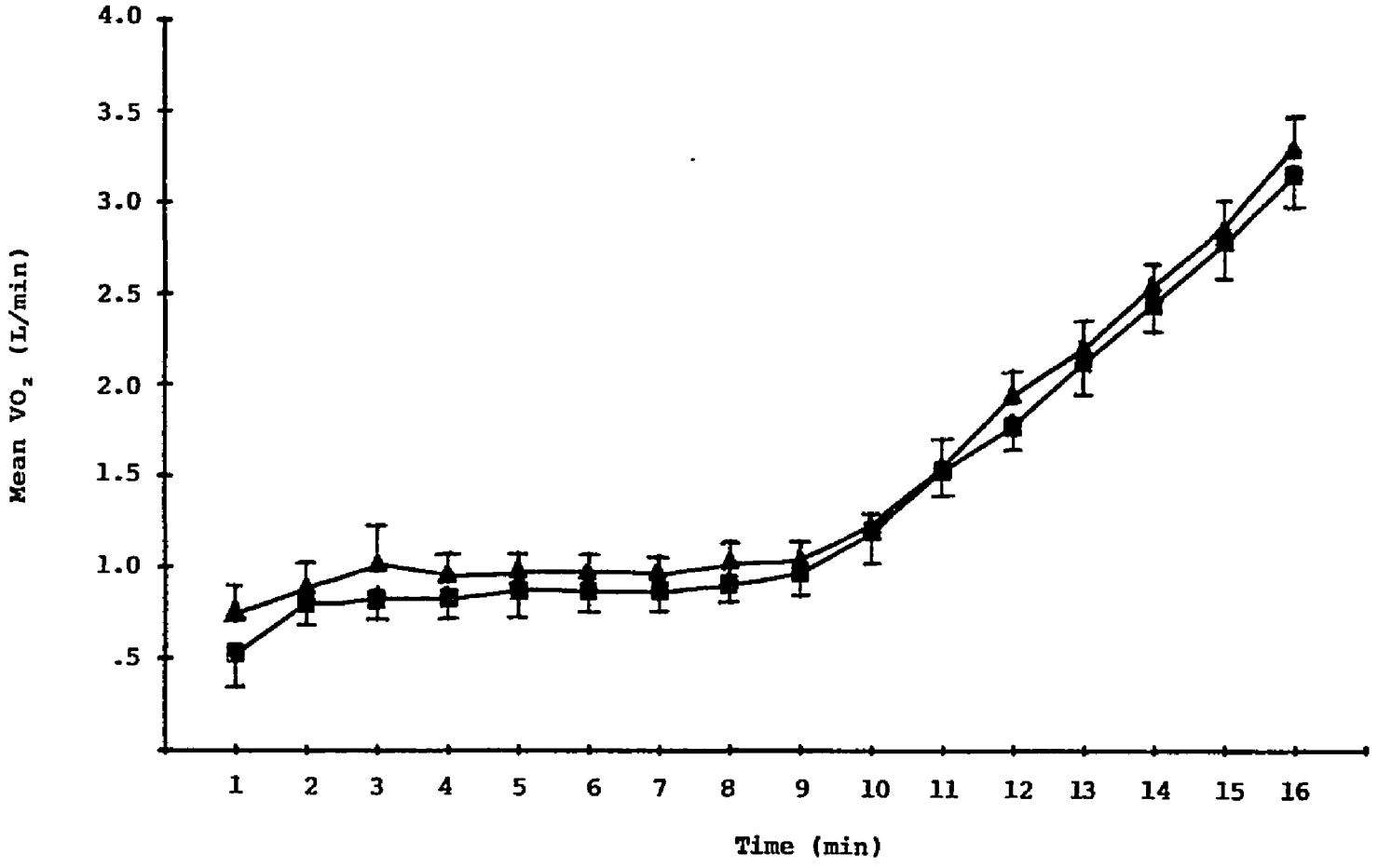

Figure 1. Mean oxygen uptake (L/min), supine and upright.

Values are means ±S.D. for the supine (■) and upright (▲) positions. N = 8 except for minute 15 (n=7) and minute 16 (n=6).

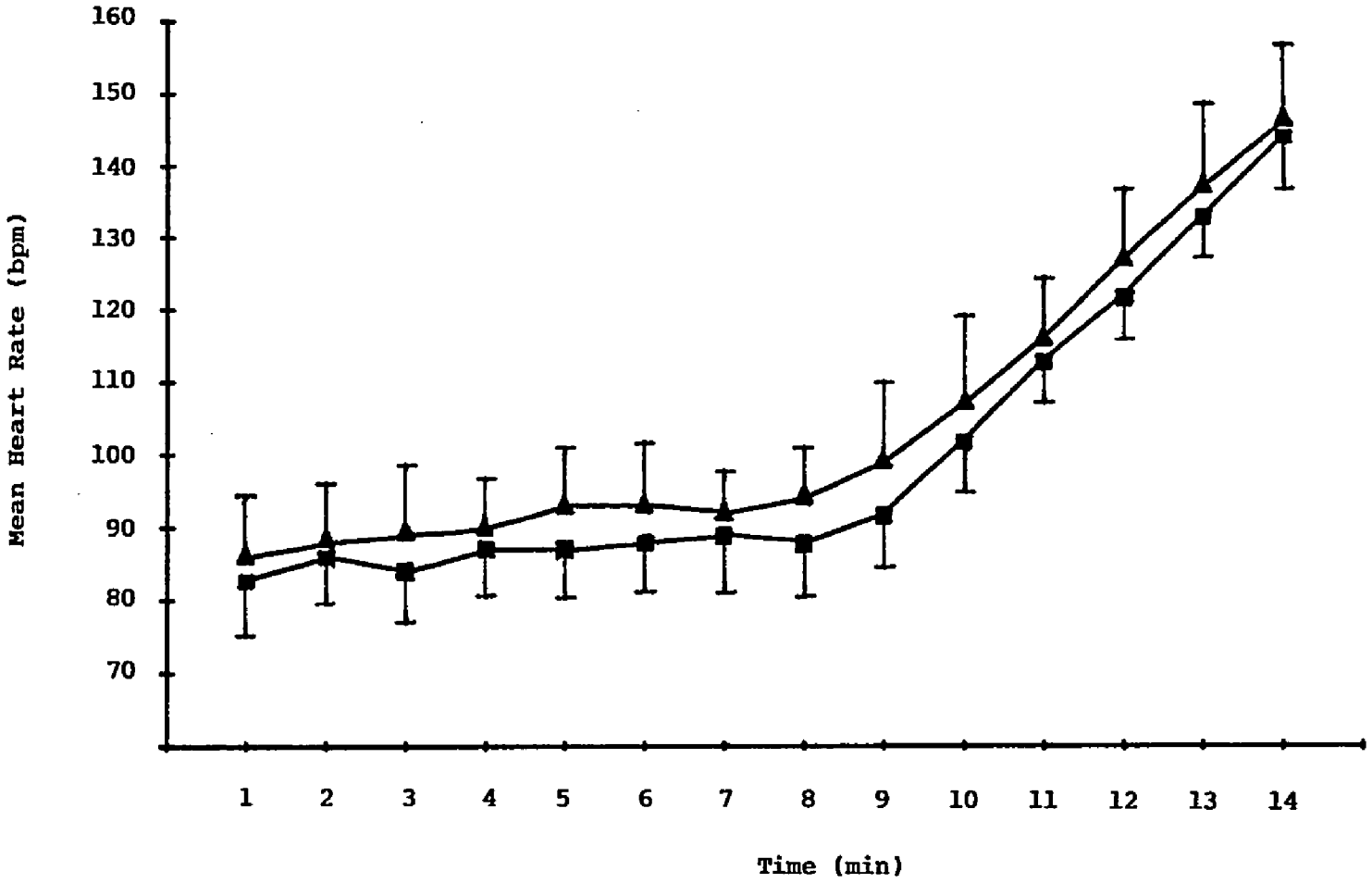

Figure 2. Mean heart rate (bpm), supine and upright.

Values are means ± S.D. for the supine (■) and upright (▲) positions. N = 7 for all minutes.

TABLE 2. Ventilatory and lactate thresholds (L/min), supine and upright.

	T_{vent} (L/min)		T_{lac} (L/min)	
Subject	Supine	Upright	Supine	Upright
GD	2.20	2.85	2.29	2.76
CK	1.47	1.83	1.54	1.25
ML	1.21	1.43	1.29	1.26
GK	1.57	1.35	1.71	1.84
SK	1.80	2.02	1.16	1.51
PD	1.25	1.61	0.87	1.22
MB	1.21	1.49	1.14	1.19
KH	1.50	1.57	1.66	1.69
Mean	1.53	1.77	1.46	1.59
±S.D.	.34	.49	.44	.53

TABLE 3. Ventilatory and lactate thresholds (% peak VO_2), supine and upright.

	T_{vent} (% Peak VO_2)		T_{lac} (% Peak VO_2)	
Subject	Supine	Upright	Supine	Upright
GD	50.7	54.2	52.8	52.5
CK	46.7	46.9	48.9	32.1
ML	36.8	39.0	39.2	34.3
GK	54.0	38.2	58.8	52.1
SK	57.5	56.7	37.1	42.4
PD	48.8	50.6	34.0	38.4
MB	50.6	54.2	47.7	43.3
KH	41.0	41.3	45.4	43.9
Mean	48.3	47.6	45.5	42.4
±S.D.	6.7	7.4	8.4	7.4

Individual values and group means for T_{vent} and T_{lac} in the two positions are expressed in terms of absolute VO_2 (L/min) in Table 2 and in terms of relative VO_2 (% peak VO_2 for that position) in Table 3. T_{vent} occurred at a higher absolute VO_2 in the upright position than in the supine position, with mean (±S.D.) values of 1.53 ± .34 L/min supine and 1.77 ±.49 L/min upright ($p<.05$). Corresponding mean T_{lac} values were 1.46 ± .44 L/min supine and 1.59 ± .53 L/min upright (ns). When expressed in terms of % peak VO_2, mean T_{vent} values were 48.3 ± 6.7% supine and 47.6 ± 7.4% upright (ns), and T_{lac} mean values were 45.5 ± 8.4% supine and 42.4 ± 7.4% upright (ns). Paired comparison of T_{vent} and T_{lac} values showed the differences to be nonsignificant in either position.

Correlation coefficients for T_{vent} versus T_{lac} were .756 supine and .765 upright ($p<.05$ for both positions). In addition, the slopes of the linear regression equations for T_{vent} on T_{lac} were not significantly different (Figures 3 and 4). When T_{vent} and T_{lac} were expressed in terms of peak VO_2 for each position, correlation coefficients were .211 supine and .096 upright (both ns).

VO_2 values at the points where blood lactate concentrations reached 2mM and 4mM were also calculated in order to compare the results of this study with previous work in which those criteria were used to define the lactate threshold. Mean (±S.D.) VO_2 at 2mM lactate levels was 2.30 ± .6 L/min supine and 2.39 ± .45 L/min upright, corresponding to 72.6 ± 13.6% and 65.1 ± 13.6% of peak VO_2 respectively. VO_2 at 4mM lactate was 2.90 ± .62 L/min supine and 3.05 ± .89 L/min upright, with corresponding relative VO_2 values of 88.3 ± 10.1% and

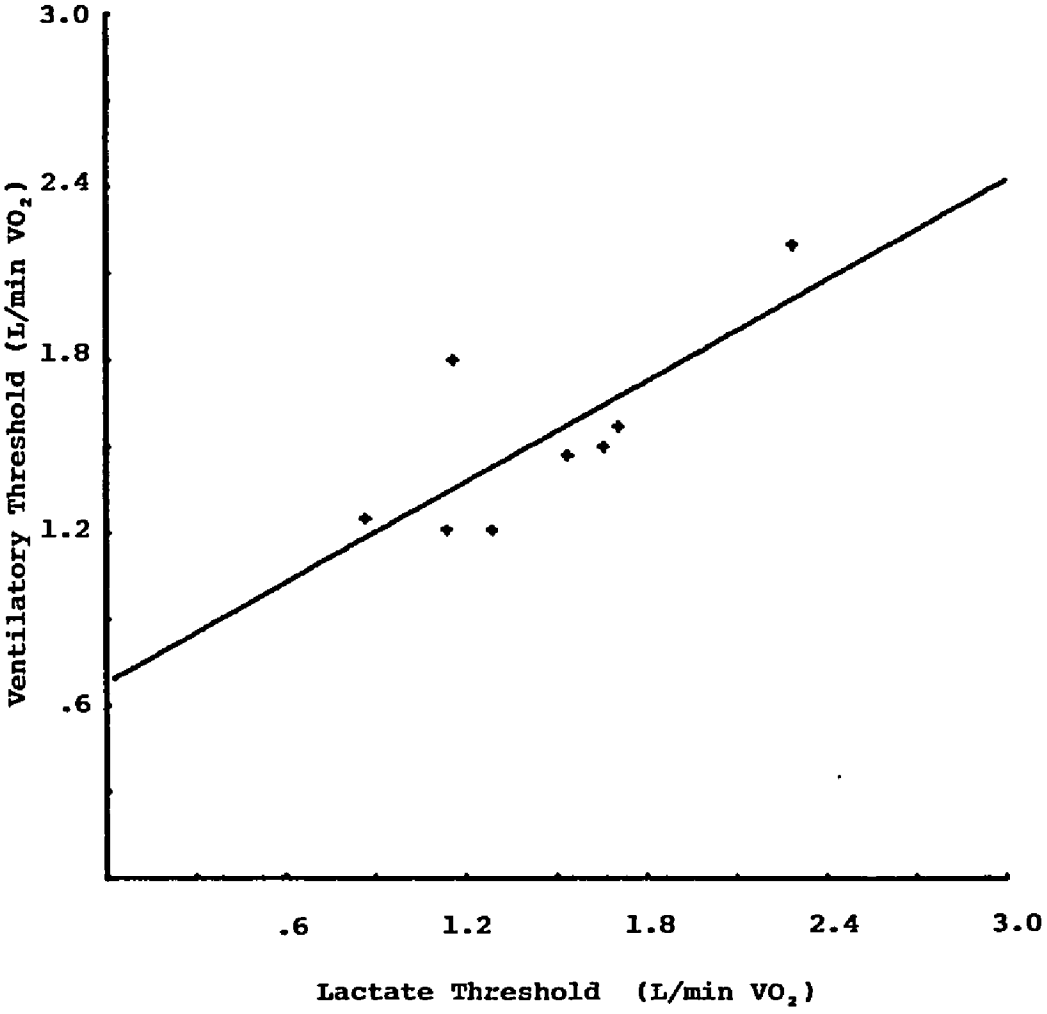

Figure 3. Least squares linear regression of T_{vent} on T_{lac}, supine.

Values are VO_2 (L/min) for T_{vent} (Y) on T_{lac} (X).
Y = .582(X) + .677; r = .756; SEE = .241.

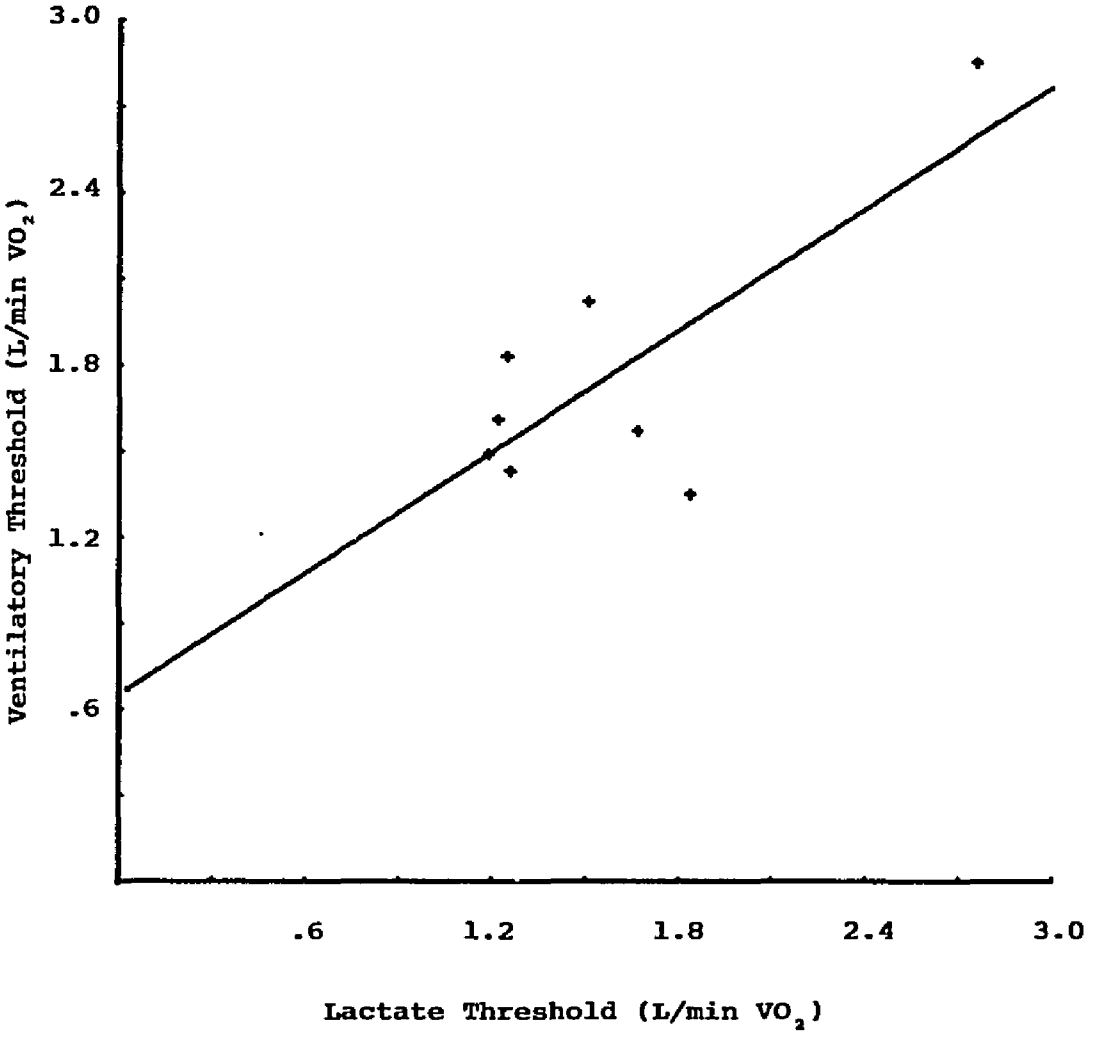

Figure 4. Least squares linear regression of T_{vent} on T_{lac}, upright.

Values are for VO_2 (L/min) for T_{vent} (Y) on T_{lac} (X). Y = .705(X) + .65; r = .765; SEE = .340.

81.7 ± 12.4% of peak VO_2. (Values for 2mM and 4mM blood lactate levels are both for n=7 due to one subject having >2mM baseline lactate levels during the upright test and a second subject failing to reach the 4mM level during the supine test.) VO_2 at both 2mM and 4mM lactate levels is significantly greater than VO_2 at T_{lac} as defined in this study, regardless of posture.

Test-retest comparisons of T_{vent} and peak VO_2 were made for the six subjects who completed a second test in each position. T_{vent} for these 12 additional tests was determined by a second reviewer using the same criteria as before. The test-retest correlation coefficient for the 12 pairs (6 supine and 6 upright) of T_{vent} values was .801 ($p<.01$). Peak VO_2 for the repeated tests also showed a strong .871 correlation ($p<.01$). Pooling the T_{vent} values from the two tests for those six subjects also resulted in a stronger correlation with T_{lac} than the single test T_{vent} values reported above. When comparing the mean T_{vent} for the two tests with the T_{lac}, $r=.868$ ($p<.05$; n=6) supine and $r=.912$ ($p<.01$; n=6) for the upright posture.

CHAPTER 5

DISCUSSION

Recent studies have suggested that the relationship between the onset of lactic acidosis and the ventilatory threshold might be altered by varying the test protocol (23) or by dietary manipulation prior to the exercise test (22,39). Other studies have demonstrated differences in the initial rate of ventilatory response to exercise performed in the supine and upright positions (50) as well as lower peak values for minute ventilation when exercise is performed supine as opposed to upright (17,33). The major purpose of this study was to examine the effect of posture on the lactate and ventilatory thresholds during graded exercise in an attempt to describe the ventilatory stimulus to exercise. Comparison of T_{lac} and T_{vent} in the two postures should help to clarify the conditions under which T_{vent} can be assumed to predict the onset of lactic acidosis during graded exercise. A second objective of this study was to compare changes in blood lactate concentration to changes in blood pH and HCO_3^- concentration during exercise in supine and upright body positions to determine if the appearance of $lactate^-$ ion in the blood corresponded temporarily with acid-base changes, since some research has shown changes in the relative rate of efflux of H^+ and $lactate^-$ ions from active muscle (2,18,31,32). Comparison of $lactate^-$ concentration and

acid-base changes in both positions was carried out to determine if any disassociation of these variables was noticeable when sampling arterialized venous blood during exercise, and if so, which variables were most closely associated with the onset of T_{vent} during the exercise.

The experiment was designed with the change in posture to be the only difference between the two test conditions. Ideally, this would result in equal oxygen uptake at any given time, thus simplifying the comparison of other physiological variables. Although mean values for oxygen uptake were generally higher at a given work rate when exercise was performed upright, the difference during the incremental portion of the test, including the region of the ventilatory and lactate thresholds, was not significantly different at the $p=.05$ level (Figure 1). Previous studies have shown no significant difference (3,32) or higher oxygen uptake during upright as opposed to supine exercise (17,42). Altered mechanical efficiency or decreased muscular activity for trunk stabilization in the supine position might account for the lower oxygen uptake in the supine position which has been reported by some investigators. In order to further minimize the statistically insignificant differences in VO_2 between positions, comparisons such as the onset of T_{lac} and T_{vent} were made in terms of VO_2 rather than work rate.

The 14.1% lower mean peak VO_2 values in the supine position were in close agreement with the findings of Stenberg et al. (42) and in general agreement with those of Fukunaga et al. (17), although the latter group reported a larger mean difference of 27% in peak VO_2

values between the two positions. The lower peak values are attributable to both the higher VO_2 at a given work rate and the 1.5 minute increase in mean work time in the upright position.

Consistent with the changes seen in oxygen uptake in the two positions, both mean and peak heart rate values were lower when exercising supine. The 4.2 ± 1.9% difference in mean heart rate found in this study is similar to the 6.7% difference reported by McGregor (33), and is in general agreement with the findings of Bevegard et al. (3), who reported no significant difference in mean heart rate between the two positions when performing leg or combined arm-leg exercise.

Analysis of the data gathered in this experiment in regard to the onset of lactic acidosis and changes in ventilatory response requires care in the definition of terminology used and the range of situations to which the results can be extrapolated. There is apparent controversy in the literature in regard to the use and meaning of such terms as "anaerobic threshold" and "lactate threshold". The lactate threshold (T_{lac}) values used in the present study were determined from individual plots of blood lactate concentration versus time using the criterion of a systematic increase above baseline warm-up levels, with VO_2 at T_{lac} then determined from individual regression equations of VO_2 on time. All T_{lac} determinations were made by a single experienced investigator who was naive as to the subject and test position corresponding to the plots. This definition of T_{lac} was chosen rather than the 2mM or 4mM criteria used by some investigators (17,43) on the basis of studies by J.A. Davis et al. (10) which demonstrated poor correlation of specified

blood lactate levels with ventilatory threshold values. The term "ventilatory threshold" (T_{vent}) was chosen to denote the point at which minute ventilation increased nonlinearly with respect to oxygen uptake during graded exercise. Although the term is defined in the same manner as the "anaerobic threshold" originally described by Wasserman and associates (46,48) and the criteria used for determination of the T_{vent} were chosen on the basis of work done by Caiozzo et al. (6), who also use the term "anaerobic threshold", T_{vent} was used to emphasize the descriptive nature of the term and to avoid any implication as to the cause of the ventilatory phenomenon it describes. The T_{vent} was determined as described by Caiozzo et al. (6) using plots of V_E/VO_2 and V_E/VCO_2 versus VO_2. The use of the "dual criteria" of a systematic increase in V_E/VO_2 without a concomitant increase in V_E/VCO_2 was reported to correlate most highly with T_{lac} when compared with other gas exchange indices. The use of this dual criteria is based on the concept of "isocapnic buffering" proposed by Wasserman (47) in reference to the period during an incremental exercise test during which V_E/VO_2 increases while V_E/VCO_2 remains stable. This represents "hyperventilation with respect to oxygen uptake" without any change in alveolar PCO_2 due to the increased CO_2 load resulting from early buffering of lactic acid and is said to distinguish the ventilatory response associated with exercise induced lactacidemia from hyperventilation due to pain, anxiety, etc., as the latter conditions would result in both V_E/VO_2 and V_E/VCO_2. These criteria for T_{lac} and T_{vent} were chosen because they have been shown to correlate well in most upright exercise

conditions, resulting in widespread use of T_{vent} as a predictor of T_{lac} in research and clinical situations.

Values for T_{vent} and T_{lac} (Table 3) were not significantly different from each other in either exercise position, although mean T_{vent} values were slightly higher than mean T_{lac} values in both exercise postures when expressed in absolute VO_2 (Table 2). Correlation coefficients between VO_2 at T_{vent} and T_{lac} in the two positions were similar ($r=.756$ supine; $r=.765$ upright; both $p<.05$) and statistical comparison of the slopes of the linear regression lines (Figures 3 and 4) demonstrates no significant difference between the two positions. When T_{vent} and T_{lac} were expressed in terms of relative VO_2 (% of peak VO_2 in that position) the mean values of T_{vent} and T_{lac} remained similar (2.8% difference supine and 5.2% difference upright) with mean T_{vent} higher in both cases (Table 3). However, the correlation coefficients between T_{vent} and T_{lac} were much lower when those threshold values were expressed in terms of relative VO_2 rather than absolute VO_2 values ($r=.211$ upright and $r=.096$ supine). The lower correlation between threshold values when expressed as % peak VO_2 may be due to the added variable of peak VO_2 compounding the inherent problem of outliers on correlations involving a relatively small sample size. The effect of outliers can be seen to a lesser degree in the correlation of the absolute T_{vent} and T_{lac}, where removal of a single outlying point strengthens the correlation coefficients from $r=.756$ to $r=.928$ for the supine case and from $r=.765$ to $r=.925$ for the upright case. Although the correlation is non-significant when expressing T_{vent} and T_{lac} in relative terms, i.e., % peak VO_2, there

was no indication that this represented any "uncoupling" of T_{vent} and T_{lac} due to the change in posture, since the correlation decreased significantly in both exercise postures.

Postural change did cause the T_{vent}, expressed as an absolute VO_2, to change, with a significant 13.6% decrease observed in the supine position as compared with upright exercise. Relative VO_2 values at T_{vent} or T_{lac} did not differ significantly between positions. These findings were both in agreement with those reported by Fukunaga et al. (17) who based their T_{lac} values on the 4mM lactate criterion. However, using the 4mM criterion on the present data resulted in a complete reversal of those relationships, with the relative VO_2 at T_{lac} being significantly different between positions (88.3% supine and 81.7% upright). The reason for this discrepancy was not clear, but the much larger value for the 4mM threshold compared with T_{vent} and T_{lac} as defined in this study was in agreement with J.A. Davis et al. (10) who also found that both the 2mM and 4mM thresholds occurred at a significantly higher VO_2 than either T_{vent} or T_{lac} as defined in this study. One other discrepancy between these results and those reported by Fukunaga et al. concerned lactate accumulation in the blood relative to position of exercise. While they reported significantly higher blood lactate concentrations at a given work rate while supine, the data presented here showed no significant change in lactate concentrations when comparing the two postures at a given work rate.

A final point of concern with regard to the T_{vent} and T_{lac} data is the reliability of determining the inflection points from the

aforementioned plots. Yeh and associates (54) recently reported poor agreement between experienced reviewers when determining ventilatory and lactate inflection points off of plots similar to those used in this study. To test the reliability of both the exercise test data and the reliability between two reviewers in the present study, six of the subjects underwent an additional pair of exercise tests identical to the first except that no blood sampling took place. The gas exchange data was then plotted as in the other tests and was then analyzed by a second reviewer under the same "blind" conditions. This simulated a "worst case" reliability test where both the reproducibility of the gas exchange data and the degree of intra-reviewer reliability were potentially confounding variables. The correlation coefficients were r=.801 for the T_{vent} determination and r=.871 (both $p<.01$), indicative of good reproducibility on both counts in the current study.

The second major objective of this experiment was to examine the blocd pH and HCO_3^- concentration data in order to determine whether those data corresponded temporarily with changes in lactate concentration values, and if so, which changes correlated most closely with the T_{vent} . Several investigators have reported differences in rates of efflux of H^+ and $lactate^-$ ions from isolated, perfused muscle preparations (2,18,21,32), with changes in pH, PCO_2 and HCO_3^- concentration all suggested as having possible interactions with the efflux of those ions from active muscle. Therefore, correlation coefficients were determined from changes in blood pH, HCO_3 and

lactate concentrations were analyzed in both the supine and upright tests.

In order to compare the changes in these three variables and their relation to the onset of the T_{vent} during the incremental exercise test, it was necessary to standardize the data in relation to the individually determined T_{vent} for each particular test. Thus, the values for the three blood variables being examined could be compared directly from T_{vent} minus 3 minutes to T_{vent} plus 4 minutes even though the point at which T_{vent} occurred varied from subject to subject and between positions for the same subject. This approach avoided the inherent errors resulting from the use of "pooled" data in comparing such threshold values, as recently pointed out by J.A. Davis et al. (10). Figure 5 shows the concurrent changes in blood pH, lactate and HCO_3^- concentrations relative to T_{vent} for both positions. Although there were slight differences in absolute values in the two positions, the pattern of change in relation to T_{vent} was similar, with pH, and HCO_3^- curves displaying the classical "mirror-image" of the lactate curves in both the supine and upright positions. This similarity is supported by the data presented in Table 4, demonstrating the zero-order correlation coefficients between the three variables. The strong correlations between all three variables when plotted in relation to T_{vent} supports the use of lactate$^-$ concentration as an indicator of acid-base changes in arterialized venous blood during incremental exercise tests in either position. These data do not address the possibility of differences in those variables at the level of the muscle cell and capillary which might

well be masked by the location and technique of sampling used in this study. Therefore, it would appear that in situations where arterialized venous sampling is being used to determine the onset of lactic acidosis during incremental cycling exercise, whether supine or upright, determination of lactate concentration alone should suffice, without the added complexity of pH and PCO_2 determination.

The data in Table 4 and Figure 5 demonstrate that each of the three blood parameters measured in this study reflected consistent changes in relation to the onset of the ventilatory threshold regardless of posture during the exercise test. The strong correlations between changes in pH, $lactate^-$ and HCO_3^- concentrations in relation to the ventilatory threshold support the concept that lactic acid produced during heavy exercise is largely buffered by the bicarbonate buffering system and that the eventual depletion of the bicarbonate stores corresponds with the fall in blood pH reflected in the data. Furthermore, the fact that these changes in blood pH and related variables remained closely associated to the ventilatory threshold even though the work rate and VO_2 at which the threshold was reached varied between the supine and upright postures supports the hypothesis that the change in ventilatory response observed at the ventilatory threshold is mediated largely by chemoreceptor response to changes in blood H^+ concentration.

TABLE 4. Zero order correlation coefficients for pH, lactate and HCO_3^- concentrations and ventilatory equivalent for oxygen uptake relative to the ventilatory threshold.

Coefficients of correlation are for mean values (n=8) taken from 3 min prior to T_{vent} through 4 min after T_{vent}.

ZERO ORDER CORRELATION COEFFICIENTS

IN SUPINE POSITION

	pH	HCO_3^-	Lactate
pH	---	.982	-.985
HCO_3^-	---	----	-.973
Lactate	---	----	-----

ZERO ORDER CORRELATION COEFFICIENTS

IN UPRIGHT POSITION

	pH	HCO_3^-	Lactate
pH	---	.953	-.970
HCO_3^-	---	----	-.995
Lactate	---	----	-----

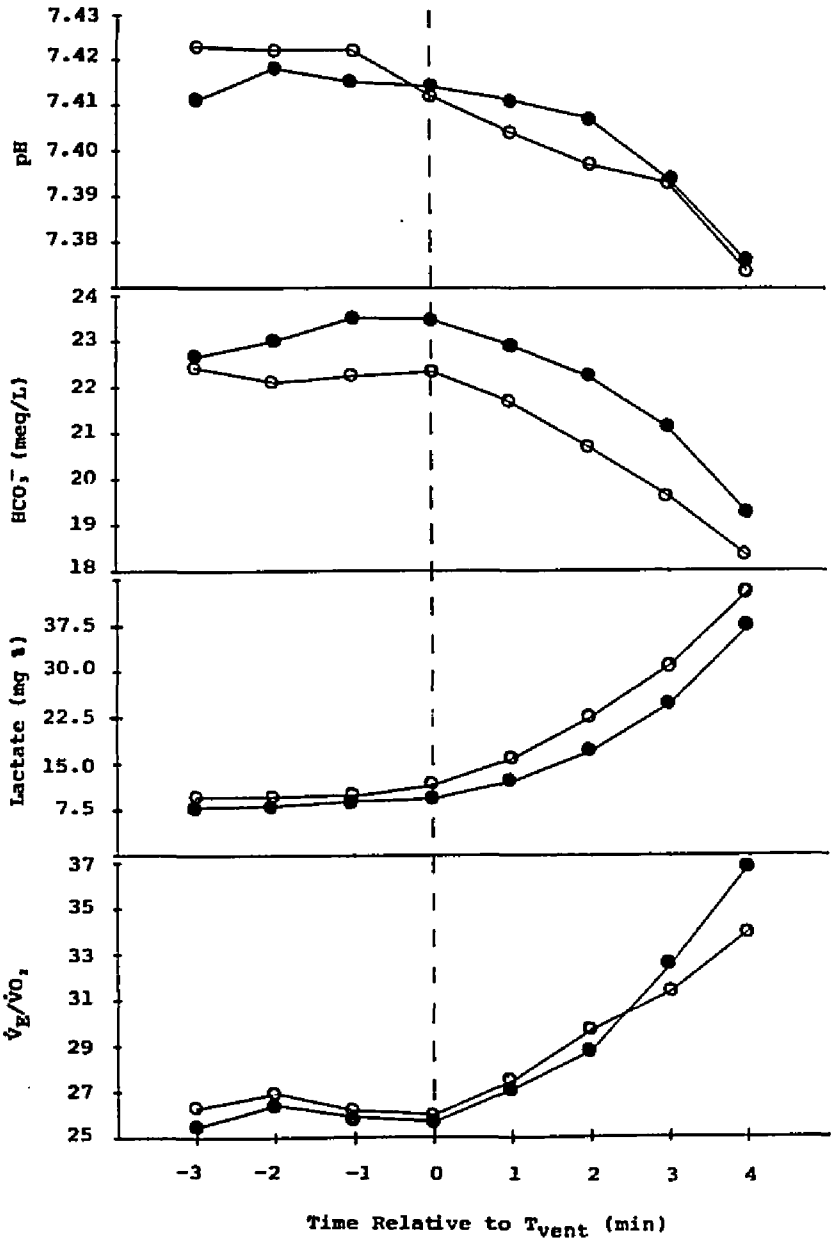

Figure 5. Arterialized venous blood pH, lactate and bicarbonate concentrations and ventilatory equivalent for oxygen uptake in relation to the ventilatory threshold, supine and upright.

Values are means for the supine (●) and upright (○) tests from T_{vent} minus 3 min to T_{vent} plus 4 min. Differences between postures are nonsignificant for all four parameters.

CHAPTER 6

SUMMARY

The concept of using the ventilatory threshold as a non-invasive indicator of the onset of lactic acidosis during an incremental exercise test has been widely accepted and is currently used in a variety of research and clinical applications, some of which involve the application of the concept during supine cycle ergometry. Recent findings questioning the validity of linking the ventilatory threshold to the lactate threshold under certain exercise conditions and in some metabolic conditions, such as following muscle glycogen depletion, coupled with evidence of possible changes in ventilatory response to exercise when comparing the supine and upright postures raises the possibility that posture may effect the relationship between the ventilatory and lactate thresholds during an incremental exercise test. This study attempted to address that question by comparing ventilatory and blood lactate thresholds during maximal, incremental cycling tests in both supine and upright positions.

A related issue addressed by this study concerned the possibility that the use of blood lactate measurements might not provide an accurate estimate of changes in blood acid-base balance, thus resulting in misconceptions regarding the factors involved in control of ventilation as the ventilatory threshold is reached in an

incremental exercise test. While there is evidence that the rate of efflux of H^+ ions and $lactate^-$ ions from active muscle is not necessarily proportional (2,18,21,32), it is not known whether these tissue-level factors change the relationship of H^+ and $lactate^-$ concentrations in remotely sampled peripheral blood in a manner which might alter the results of studies such as this one. In order to evaluate that possibility, blood pH and PCO_2 data were collected in addition to lactate concentration data in both the supine and upright positions in order to compare the changes in blood pH, $lactate^-$ and HCO_3^- concentrations relative to the ventilatory threshold.

As expected, peak values for oxygen uptake, minute ventilation, heart rate and lactate accumulation were all lower in the supine position. Oxygen uptake at a given work rate was slightly lower in the supine position, as were mean heart rate and lactate accumulation values. However, at a given oxygen uptake, differences in heart rate and lactate accumulation were not significant. Lactate accumulation at a given oxygen uptake was similar for the two positions. Test-retest correlations for peak VO_2 and ventilatory threshold values were found to be highly significant in either position.

Values for T_{vent} and T_{lac} were determined from individual plots and were found to correlate significantly and to a similar degree when expressed in terms of absolute oxygen uptake at the respective threshold points. Mean absolute values for T_{vent} were significantly higher upright than supine, and T_{lac} values exhibited a similar but nonsignificant trend. Expressing the threshold values in

terms of % peak oxygen uptake in each position resulted in nonsignificant correlation coefficients, but paired comparison of mean relative T_{vent} and T_{lac} values did not differ significantly in either position. Correlation coefficients were found to be very sensitive to outlying data points due to the small number of subjects and relative homogeneity of the data. Both T_{vent} and T_{lac} as defined in this study occurred at a significantly lower VO_2 than 2mM or 4mM blood lactate concentration.

Comparison of arterialized venous blood lactate accumulation with changes in pH and bicarbonate concentration was accomplished by standardizing the values in relation to the onset of T_{vent} during each individual test. Correlation of these three blood parameters from 3 minutes prior to T_{vent} until 4 minutes after T_{vent} resulted in r values of greater than .95 in all cases, indicating no apparent advantage in the use of pH or bicarbonate concentration over the technically easier lactate assay when using the type of blood sampling technique and testing protocols used in this study.

These findings suggest that although the absolute values at which T_{vent} and T_{lac} occur differ between supine and upright exercise, the use of T_{vent} (expressed in terms of absolute oxygen uptake) as an indicator of the onset of increasing lactate accumulation in arterialized venous blood does not appear to be affected by changing from upright to supine positioning during incremental cycling tests. In addition, the use of lactate concentration as an indicator of blood acid-base levels under the conditions of this study appears to be an equally valid assumption irrespective of posture. The fact that the

ventilatory threshold corresponded closely with changes in the H^+ ion concentration regardless of the posture during exercise supports the concept of chemoreceptor mediated sensitivity to blood H^+ concentration as a major factor of the control of ventilation during exercise above the ventilatory threshold.

APPENDIX A

HUMAN SUBJECTS COMMITTEE APPROVAL

THE UNIVERSITY OF ARIZONA
HEALTH SCIENCES CENTER
TUCSON, ARIZONA 85724

HUMAN SUBJECTS COMMITTEE
1609 N. WARREN (BUILDING 220), ROOM 112

TELEPHONE: (602) 626-6721 or 626-7575

15 November 1983

Mr. Gregory M. Karst
2307 North Forgeus
Tucson, AZ 85716

Dear Mr. Karst:

We are in receipt of your project, "Ventilatory and Lactate Thresholds During Supine and Upright Cycling", which was submitted to this Committee for review. The procedures to be followed in this study pose no more than minimal risk to the participating subjects. Regulations issued by the U.S. Department of Health and Human Services [45 CFR Part 46.110(b)] authorize approval of this type project through the expedited review procedures, with the condition that subjects' anonymity be maintained. Although full Committee review is not required, a brief summary of the project procedures is submitted to the Committee for their information and comment, if any, after administrative approval is granted. This project is approved effective 15 November 1983.

Approval is granted with the understanding that no changes will be made in either the procedures followed or in the consent form(s) to be used (copies of which we have on file) without the knowledge and approval of the Human Subjects Committee and the College or Departmental Review Committee. Any physical or psychological harm to any subject must also be reported to each committee.

A university policy requires that all signed subject consent forms be kept in a permanent file in an area designated for that purpose by the Department Head or comparable authority. This will assure their accessibility in the event that university officials require the information and the principal investigator is unavailable for some reason.

Sincerely yours,

Milan Novak

Milan Novak, M.D., Ph.D.
Chairman
Human Subjects Committee

MN/jm

cc: Patricia C. Fairchild, Ph.D.
Departmental Review Committee

THE UNIVERSITY OF ARIZONA
HEALTH SCIENCES CENTER
TUCSON, ARIZONA 85724

HUMAN SUBJECTS COMMITTEE
1609 N. WARREN (BUILDING 220), ROOM 112

TELEPHONE: (602) 626-6721 or 626-7575

27 February 1984

Mr. Gregory M. Karst
2307 North Forgeus
Tucson, Arizona 85716

Dear Mr. Karst:

We are in receipt of your 23 February 1984 letter and the accompanying revised consent form for your project, "Ventilatory and Lactate Thresholds During Supine and Upright Cycling". The changes reflected in this revision are minor and pose no further risk to the subjects involved. Therefore, approval for these changes is granted effective 27 February 1984.

The changes approved are:

1. Addition of a procedure to prevent clotting between blood collections through the use of sterile saline solution and/or heparin lock flush solution.

2. Expansion of subject population to include females.

Approval is granted with the understanding that no further changes or additions will be made either to the procedures followed or to the consent form used (copies of which we have on file) without the knowledge and approval of the Human Subjects Committee and your College or Departmental Review Committee. Any physical or psychological harm to any subject must also be reported to each committee.

A university policy requires that all signed subject consent forms be kept in a permanent file in an area designated for that purpose by the Department Head or comparable authority. This will assure their accessibility in the event that university officials require the information and the principal investigator is unavailable for some reason.

Sincerely yours,

Milan Novak

Milan Novak, M.D., Ph.D.
Chairman
Human Subjects Committee

MN/jm

cc: Patricia C. Fairchild, Ph.D.

Departmental Review Committee

APPENDIX B

SUBJECT CONSENT FORM

VENTILATORY AND LACTATE THRESHOLDS DURING SUPINE AND UPRIGHT CYCLING

Subject's Consent Form

I am being invited to participate in a research study entitled **"Ventilatory and lactate thresholds during supine and upright cycling."** I have received an oral explanation of the study and I understand the following:

Purpose: The study is designed to see how different postures (lying supine and sitting) affect breathing and the accumulation of lactic acid (a waster product formed in the muscles during severe exercise) in the blood during exercise on a stationary bicycle. This study will help to explain how the body is able to correctly control the rate of breathing during exercise.

Subjects: There will be approximately eight subjects involved in the study, all of whom will be volunteers. Subjects will be normal, healthy males between the ages 18 and 35. There will be no cost to the subjects, and they will receive no pay for participating. I understand that I may withdraw from the study at any time without any ill will.

Location: All testing will take place in the Exercise and Sport Sciences Laboratory in Room 228 of McKale Center on the University of Arizona campus.

Procedures:

The main part of the experiment will consist of performing four (4) exercise tests (2 while sitting and 2 while lying supine) in which I will pedal a stationary bicycle at a constant speed while the resistance is gradually increased until I am too exhausted to continue exercising. The test generally takes 10 to 15 minutes depending upon the fitness of the subject. During the test, my blood pressure will be taken periodically and my heart rate will be monitored by an electrocardiograph using three electrodes taped to the chest. Abnormal changes in those measurements (a very remote possibility) as well as symptoms of chest pain, shortness of breath, dizziness, or unusual fatigue would be reasons for stopping the test. During all four tests, I will wear a nose clip and a headgear/mouthpiece apparatus which will allow the air I expire to be measured for volume and amount of oxygen and carbon dioxide. In addition, during two of the tests, one sitting and one supine, blood samples will be taken as outlined below.

Blood Samples:

Venous blood samples will be drawn during one of the upright and one of the supine exercise tests. Prior to those tests, a needle will be inserted into a vein of the forearm and will remain in place throughout the exercise test. Approximately every minute, a small blood sample will be taken using a syringe attached to the needle by a short tube. Each sample will be no larger than 4 ml. (about ¼ tablespoon) and no more than 18 samples will be taken during each test. Thus the maximum amount of blood taken during each of these two tests will not exceed 72 ml (about 5 tablespoons).

On the two days when exercise tests are performed without blood samples during the test, a blood test will be performed before the exercise test in order to determine the amount of plasma (blood water) in the body. This test consists of taking 6 ml of blood from a forearm vein both before and after injection of the Evans Blue dye (see #3 below) for a total of 12 ml (less than 1 tablespoon) for each test. The total maximum amount of blood drawn during the entire study is outlined below:

Maximum blood drawn during exercise tests = 72 ml x 2 tests = 144 ml
Maximum blood drawn for plasma volume tests = 12 ml x 2 tests = 24 ml
Maximum total blood drawn during study = 168 ml (approximately 1/3 pint)

This 168 ml is less than 1/3 of the amount normally given in a single blood-bank donation.

Injections:

1. Each of the two tests which will measure plasma volume requires the injection of about 5 ml (less than ½ tablespoon) of Evans Blue dye solution. Evans Blue dye is a non-toxic, greenish-blue powder which is mixed with water and injected into a forearm vein. Although the dye is harmless, if some of it should leak out of the vein during the injection, it might cause a slight burning sensation lasting several minutes and a bluish discoloration of the skin lasting several days. As described in #2 above, a 6 ml blood sample will be taken both before and after the injection. No exercise is performed during this test.

2. Body composition will be determined by comparing dry weight with underwater weight. Underwater weighing will require keeping my head underwater for several seconds, but swimming ability is not required as the tank is only 3½ feet deep.

3. Lung function measurements involving forcefully expiring through a mouthpiece after taking a deep breath will be performed once during the study.

Miscellaneous:

1. I understand that participation in this study is voluntary and that I may quit the study at any time and for any reason without incurring any ill will.

2. I realize that I should not participate if I have a history of heart disease or any current medical problem which might be aggravated by exercising on a bicycle.

3. I understand that I will be required for testing at McKale Center on as many as six separate days with each test lasting up to two hours.

4. I will be asked to abstain from caffeine, alcohol, and other prescription or non-prescription drugs for 12 hours prior to the exercise-testing sessions.

5. I will be required to provide my own clothing and shoes suitable for exercising on a stationary bicycle.

6. I understand that the investigators will answer any questions regarding the testing procedures and will discuss with me the results of my tests. I will remain anonymous in all publications of the results of this study.

Risks:

I understand that although the risks of this study are considered minimal, the following could conceivably occur:

1. Inconvenience and discomfort due to the headgear/mouthpiece apparatus worn during the exercise tests.

2. Muscle soreness in the legs from cycling.

3. Minor discomfort during the venipunctures used to draw blood samples with a possibility of slight swelling or discoloration in the area for a few days.

4. Possible burning and discoloration if the Evans Blue dye is not kept entirely in the vein when it is injected.

Benefits:

I will be given a detailed explanation of my test results by the investigators, including an assessment of my aerobic fitness and body composition. In addition, I will have the opportunity to gain understanding of scientific methods as applied to Exercise Physiology research.

Compensation for injuries:

I understand that in the event of physical injury resulting from the research procedures, financial compensation for wages or time lost is not available, and the costs of medical care and hospitalization are not available and must be borne by the subject. I understand that Gregory M. Karst (326-0182) and/or Victor A. Convertino (621-2712) will provide more information on my request.

I have read the above subject's consent. The nature, demands, risks, and benefits of the study have been explained to me. I understand that I may ask questions and that I am free to withdraw from the study at any time without incurring ill will. I also understand that this consent form will be filed in an area designated by the Human Subjects Committee and that my data will be kept in strict confidence with access restricted to the principal investigators or authorized representatives of the particular department.

_____ _____

Subject's Signature Date

_____ _____

Witness' Signature Date

I have carefully explained to the subject the nature of the above study. I hereby certify that, to the best of my knowledge, the subject signing this consent form understands clearly the nature, demands, benefits, and risks involved in participating in this study. A medical problem or language or educational barrier has not precluded a clear understanding of his involvement in this study.

_____ _____

Investigator's Signature Date

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