THE RELATIONSHIP BETWEEN RESPIRATORY RESPONSE TO CONTROLLED HYPERCAPNIA AT REST AND THE ABILITY TO MAXIMIZE VENOUS SERUM LACTATE DURING EXERCISE

BY

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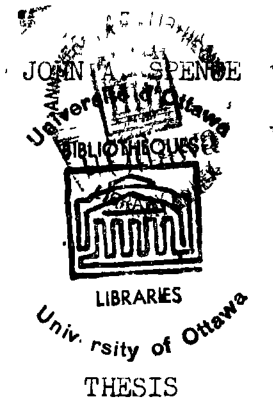

THESIS

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CHAPTER I

THE PROBLEM

Introduction

In the enduring effort to describe the athlete's enhanced capacity and tolerability in the performance of heavy work, virtually every organic system involved in the energy provision and utilization process has been examined. These investigations have established that systematic and progressive training has a positive effect on most of the energy producing and supporting processes (Ekbolm 1969, Faülkner 1968, Karlsson 1970, Gollnick et al. 1973a, Rowell 1974). This accounts for part of the athlete's superiority in the performance of work. However variations in work capacities are still observed among athletes who train equally hard (Banister 1969, Keul 1973). Therefore, it appears that the champion athlete may possess some special endowments which place his maximum work potential beyond the attainment of others. Although this speculation has led to the extensive use of oxygen uptake measurements as a classical index of athletic performance, Banister (1969) points out that this index alone cannot adequately identify superior athletic potential. Thus more sophisticated indices of exercise tolerance have been sought in order to enhance the ability to identify high caliber athletes. It is the suggested use of hypercapnic sensitivity as an index of anaerobic work potential for this purpose which has prompted the following investigation.

Statement of the Problem

The purpose of this investigation was to examine the relationship between the ability to maximize levels of lactate in venous blood during exhaustive exercise and the ventilatory response to controlled hypercapnia at rest.

More specifically, the experiment was designed to (1) measure post exercise levels of serum lactate in brachial venous blood following the exhausting performance of a work load chosen in relation to maximum voluntary work capacity measurements, (2) measure the sensitivity of breathing control mechanisms (expressed as respiration volume turnover per unit of excess CO_2 added to normoxic gas) in terms of the peak gas volume ventilated per mm Hg of alveolar PCO_2 (Peak $\dot{V}_E$ BTPS/$PaCO_2$ mm Hg), (3) quantitate the relationship between serum lactate levels and respiratory sensitivity to CO_2.

Subproblems

1. To establish if a significant difference exists between the athlete and the sedentary subject in their capacity to contract elevated levels of venous lactate during maximum exercise.

2. To establish if the athlete's ventilatory response to hypercapnia is significantly lower than the non-athlete.

3. To develop predictive indices of lactate potential from hypercapnic sensitivity response.

Definition and Abbreviation of Terminology

Acidemia

Any state of systemic arterial plasma in which the pH

is significantly less than normal value, 7.41 ± 0.02 in adult man at rest (Bartels et al. 1973).

Acidosis

The result of any process which by itself adds excess CO_2 (respiratory acidosis) or nonvolatile acids (metabolic acidosis) to arterial blood. Acidemia does not necessarily result since compensating mechanisms (increase in HCO_3^- in respiratory acidosis, increase of ventilation and consequently decrease of arterial CO_2 in metabolic acidosis) may intervene to restore plasma pH to normal (Bartels et al. 1973).

Alkalosis

The result of any process which, by itself, diminishes acids (respiratory alkalosis) or increases bases (metabolic alkalosis) in arterial blood (Bartels et al. 1973).

Hypercapnia

Any state in which the systemic arterial carbon dioxide pressure is significantly above 40 torr. It may occur when alveolar ventilation is inadequate for a given metabolic rate (hypoventilation) or during CO_2 inhalation (Bartels et al. 1973).

Hyperventilation

An alveolar ventilation which is excessive relative to the simultaneous metabolic rate. As a result the alveolar PCO_2 is significantly reduced below a normal of 40 torr.

Blood Lactate

Lactic acid or lactate ion is produced mainly via glycolytic metabolism and is measured in the blood in milligrams per 100

millilitres (mg%) (Astrand 1970). Lactacidosis is defined as a metabolic form of acidosis resulting from a higher than normal level (10 - 20 mg %) of lactic acid in the blood (Karlsson 1971b).

Ventilatory CO_2 Sensitivity

The ratio of variation of ventilation to variation in $PaCO_2$, ($\dot{V}E$ BTPS/$PaCO_2$ mm Hg), (Dejours 1966).

BTPS

Body temperature, barometric pressure and saturated with water vapor. These are the conditions existing in the gas phase of the lung. For man, the normal temperature is taken as 37° C., the pressure as barometric pressure, and partial pressure of water vapor, 47 torr (Bartels et al. 1973).

STPD

Standard temperature and pressure, dry. These are the conditions of a volume of gas at 0° C. at 760 torr, without water vapor. An STPD volume of a given gas contains a known number of moles of that gas (Bartels et al. 1973).

pH

The negative logarithm of hydrogen ion concentration in a solution (Davenport 1965).

Rationale for the Study

When CO_2 is inhaled, blood $[H^+]$ increases and ventilation increases (Balke et al. 1958, Leusen 1972, Sorensen 1970, Watkins et al. 1973). It has been demonstrated that at least part of this ventilation response results from a decrease in pH (Lambertsen 1961, Mitchell 1963).

It has been demonstrated that athletes have reduced ventilatory response to hypercapnia (Byrne-Quinn et al. 1971, Goff et al. 1957). Some evidence exists that under normal conditions hypercapnic drive is not subject to change (Schaefer 1958) while certain studies point out that it is modified under certain conditions of disease (Alexander et al. 1955, Cherniack 1965), obesity (Dempsey et al. 1966) and continued exposure to altitude (Forster et al. 1968, Byrne-Quinn et al. 1972). Whether or not it is changeable is not relevant to a simple demonstration of a relationship between athletic success and sensitivity levels.

Other investigations have indicated that for a given work load, the athlete exhibits lower serum lactate levels (Astrand 1970, Keul et al. 1972, Eriksson et al. 1973) but attains significantly higher peak blood lactates at his relative maximum work load (Karlsson 1971b, Cunningham and Faulkner 1969).

When the intensity of muscle metabolism is such that the oxidative resynthesis of ATP does not keep step with the consumption or there is an imbalance between the glycolysis and oxidative capacity of the muscle, lactate becomes greatly elevated in conjunction with the exercise (Keul et al. 1972, Jorfeldt 1971). The elevation of lactate titrates the blood in the direction of a low pH (Osnes and Hermansen 1972) which adds to the neurogenic activation of the respiratory centers (Asmussen 1950, Comroe 1964, Dejours 1966).

Since an increase of arterial CO_2 or lactate induces a decrease in pH and a resultant increase in ventilation, hypercapnic response can conceivably be qualitatively compared with lactate level accumulation during maximum exercise.

It was therefore hypothesized that a relationship may exist between maximum exercise levels of serum lactate and ventilatory response to inspired CO_2.

Limitations of the Study

1. The experimental group was comprised of ten fully conditioned male athletes who were selected from varsity football and regional track and paddling clubs. Five sedentary non-obese and non-smoking male subjects served as control. All subjects were between the ages of 17 and 27, and residents of the Ottawa area. The subjects were obtained through a selection rather than a randomization process in order to assure presence of successful athletes and sedentary young men in the study group. The results are thus limited to the study group.

2. Motivation was not controlled in this investigation except through a standard protocol of verbal persuasion.

3. Barometric pressure, relative humidity, temperature, and extraneous interference in the laboratory was not controlled in this experiment. However, all gas volumes were corrected for standard temperature and pressure.

4. It was not possible to control a fixed time of day for testing due to laboratory time tables. Each subject was tested at approximately the same time of day so that circadian rhythms were constant within individuals.

CHAPTER II

REVIEW OF THE LITERATURE

Introduction

The purpose of this chapter is to present the literature which is related directly and indirectly to the production and accumulation of lactate in exercise and the response of respiration to hypercapnia at rest. The material is presented under the following headings: Production, Role and Fate of Lactate in Exercise; Factors Regulating Lactate Production; Compensatory Mechanisms of Lactate Acidemia; Control of Respiration During Exercise; Respiratory Response to Hypercapnia; and Variations in Response to Hypercapnia.

Production, Role and Fate of Lactate in Exercise

In the performance of dynamic physical work, chemically bound energy is converted into mechanical work by muscular tissue (Karlsson 1971b). The immediate energy source for muscular contraction is adenosine triphosphate, ATP (Cain and Davis 1962). Since ATP stored in the muscle is limited, a continuous resynthesis of ATP must take place (Jorfeldt 1970). In the normal condition of steady-state homeostasis this resynthesis of ATP occurs mostly intramitochondrially through oxidative phosphorylation. Through this process NADH, NADPH, and FADH formed in the breakdown of fat and carbohydrate are oxidized with O_2 as the final electron acceptor (Jorfeldt 1971).

If the work rate is increased, an augmented ATP resynthesis is essential to sustain the work load. Under normal aerobic conditions the

cellular demands are not extensive and this increased rate of mitochondrial ATP resynthesis will be easily met by an increased O_2 supply by the respiratory and circulating convective systems. However if during intense muscular contraction adequate oxygen cannot be provided or utilized to meet metabolic needs the oxidative reduction systems must shift to a more reduced state of energy yield, anaerobic glycolysis (McGilvery 1970).

Through anaerobic glycolysis, ATP can nevertheless be sustained, since pyruvate under formation of lactate functions as an election acceptor for NADH. Pyruvate is reduced to lactic acid, while NADH is oxidized to NAD^+ (Pyruvate + NADH + $H^+ \rightleftharpoons$ Lactate + NAD^+) (Hirche et al. 1973b).

The energy yield of anaerobic glycolysis is significant. Karlsson (1971b) estimates that the breakdown of ATP and CP on one hand, and anaerobic glycolysis on the other, provide amounts of energy equivalent to one liter and 3 to 5 liters of O_2 respectively. He further states that anaerobic energy yielding processes can supply fifty percent of the total energy yield at high work loads resulting in exhaustion within two to three minutes.

Lactate, the end product of anaerobic glycolysis in the skeletal muscle is therefore produced by the reduction of pyruvate, when pyruvate cannot be oxidized and channeled into the citrate cycle (Keul et al. 1972) and by the necessity to reoxidize extra mitochondrially formed NADH in order to avoid complete arrest of glycolysis (Karlsson 1971b). Along with alactic energy stores CP and ATP, anaerobic glycolysis provides an important energy yield in short exhaustive work.

Maximal exercise of short duration has been shown to raise blood lactate concentrations up to values as high as 290 mg/100 ml (Hermansen 1971). More commonly, values of 140 to 200 mg/100 ml have been reported after vigorous exercise (Astrand et al. 1963, Haralambie and Frieburg 1973). These high levels of non-volatile lactate give rise to severe metabolic acidosis in the blood and the rest of the body. pH values of 6.8 to 7.1 have been reported (Osnes and Hermansen 1972, Laugh 1934).

Small deviations in pH have been shown to modify key enzyme activities thereby changing the rates of chemical reactions in the cells. Some reactions are accelerated while others are depressed (Hermansen and Osnes 1972). Low pH values negatively affect the "activation" and substrate binding capacity of the key enzyme of glycolysis, phosphofructokinase (Hofer and Pette 1968, for ref. see Haralambie and Frieburg 1973). Renal glutaminase is also less active at pH values less than 7.1 (Sayre and Robert 1966).

Elevated lactate levels with the concommittent depression of pH have also been shown to affect both skeletal and cardiac muscle contraction. Del Castillo et al. (1962) report that pH values below 7.1 in circulating blood may alter the neuromuscular function and the reactivity of skeletal muscle to acetylcholine. Pannier et al. (1970), demonstrated that isometric twitch and tetanic tension for a given stimulus is affected by a decrease in pH, particularly for tonic muscle fibers. An increase in tension is evident in solutions containing high lactate and low bicarbonate levels. In cardiac muscle, Katz (1970) points out that both hypercapnia and metabolic acidosis have long been known to depress myocardial contractility. He suggests that some of the defects in cardiac contractility seen in

metabolic acidosis may arise from the increased intracellular hydrogen ion concentration affecting the Ca^{++} troponin interaction. In support of Katz's suggestion, Fuch et al. (1970) provide evidence that decreased intracellular pH reduces the binding capacity for Ca^{++} through an inactivation of fibrillar protein, troponin.

Accretion of lactate might function as a physiological inhibitor of FFA mobilization in severe exercise (Issekutz and Miller 1962). Fredholm (1970) furnishes corroboration that FFA mobilization, induced by increased sympathetic nerve activity found in exercise, can be counteracted by lactate in concentrations that are achieved in exercise. They suggest that increased re-esterification is the major mechanism of action although some inhibition of lipolysis might also be present. It has however been demonstrated that when lactate concentration is sufficiently high to inhibit FFA mobilization and oxidation, its participation in the metabolic rate may compensate to a great extent for the lowering of energy derived from lipids (Freminet et al. 1974).

Freminet et al. (1974) further point out that when the lactate pool is augmented oxidation is limited and a greater flow of lactate is deviated to other metabolic pathways. They suggest that an increase in gluconeogenesis is possible since acetyl-CoA concentrations in the mitochondria will rise thus increasing the ratio of acetyl-CaA to CoA. It has been shown in vitro that pyruvate dehydrogenase is inhibited in such conditions while pyruvate carboxylase and PEP carboxykinase is elevated resulting in more use of pyruvate in gluconeogenesis (Gardland and Randle 1964). A study by Issekutz et al. (1972) suggests that this may be the case in vivo. They observed the participation of lactate in glucose

formation with increased lactate or with the rate of lactate turnover.

The role of lactate appears, therefore, important for the regulation of metabolic parthways, for the production of glucose, and as a prime source of energy for many tissues (Freminet et al. 1974).

Factors Regulating Lactate Production

The breakdown of carbohydrate to lactate is a chain of enzymatic processes whose rate and magnitude of production is subject to many influences. The following factors have been discussed in the literature as modifiers of lactate production:

Hypoxic Conditions

Hypoxia has been associated with lactate production since Von Liebig's hypothesis in 1847, that lactate accumulates in blood when O_2 supply is restricted (Keul et al. 1972). That production of lactate is caused by a lack of oxygen is suggested by the appearance of elevated lactate in clinical conditions with impairment of arterial inflow to exercising muscles (Pernow et al. 1973, Carlson and Pernow 1959), during heavy exercise, (Christensen 1960, Margaria 1970, Fagraesus 1974) and during exercise at altitude (Hermansen and Saltin 1966).

It has also been proposed that lactate production might also indicate an insufficient metabolic capacity to utilize oxygen. Carlson and Pernow (1961) and Keul et al. (1967) demonstrated that lactate is produced regardless of a high oxygen content and oxygen pressure in venous blood draining the exercising muscle. Keul et al. (1967) in explanation of this observation suggests an imbalance between glycolysis and oxidative

capacity of the cell. However, it has been pointed out that only a certain proportion of the total number of muscle fibers are activated even during maximal exercise (Hermansen et al. 1971), and that high glycolytic fast twitch or phasic fibers are recruited only when exercise exceeds seventy-five percent maximum oxygen consumption (Hermansen and Saltin 1966). Venous blood from an exercising muscle therefore consists of blood from activated and non-activated motor units within the same muscle group. Consequently, Hermansen (1971) suggests care when making inferences concerning intracellular processes from mixed blood samples.

Under hyperbaric conditions Kaijser (1973a) found elevated lactate despite a venous oxygen pressure of 65 mm Hg. These results imply aerobic glycolysis. Further observations by Kaijser that maximal heart rate was reduced and that there was no significant increase in work performance or O_2 extraction from femoral venous blood despite a large increase in O_2 content suggests insufficient metabolic capacity to extract or utilize oxygen. In answer to Kaijser's observations, Rowell (1974) points out that at 2-3 atm pulmonary ventilation is depressed by increased gas density and effects of hyperoxia. The result is that CO_2 elimination is impeded. When PCO_2 increases, blood and tissues become more acid (Banister et al. 1970), and $\dot{V}o_2$ peak is reduced (Luft et al. 1971 for ref. see Rowell 1974). Furthermore, in his review article on the deleterious effects of hyperoxia, Hauggaard (1968) with reference to the work of Horn et al. (for ref. see Hauggaard 1968) states that oxygen, at pressures above 1 atm, inhibits glyceraldehyde phosphate dehydrogenase and consequently causes marked changes in concentrations of glycolytic lactate

and ATP. It follows that care should be taken when making assumptions of normal O_2 extraction and utilization under hyperbaric conditions.

It is well established, therefore, that hypoxic conditions stimulate lactate production. However whether lactate occurs due to an insufficient supply or a rate limiting ability to utilize oxygen is unclear.

Alactic Stores (CP and ATP)

Karlsson (1971b) states that an increase in lactate concentration occurs only after an initial decrease in phosphogen stores. This occurence has been demonstrated in man, (Saltin and Karlsson 1971, Knuttgen and Saltin 1972) adolescent boys (Erikson et al. 1973), and in frogs (Danforth 1965). Karlsson (1971b) observed a marked depletion of CP stores even with submaximal loads but observed ATP depletion only at maximal or near maximal load.

Margaria et al. (1970) suggest that lactate is not produced in muscle during submaximal exercise nor until ATP and CP stores are spent. However Knuttgen and Saltin (1972) observed that at upper levels of exercise, high lactate levels were noted at the same time that muscle ATP and CP concentrations were reduced by 67%.

Whether there is a causal relationship between an initial decrease in phosphogen stores and the commencement of anaerobic glycolysis remains questionable (Karlsson 1971b).

Izosyme LDH and Muscle Fiber Type

The isozyme lactate dehygrogenase is present in mammalian tissue in five forms with different affinities for pyruvate and lactate

respectively. The M form favours lactate formation whereas the H form favours the formation of pyruvate from lactate (Karlsson 1971b, Keul et al. 1972, Mole et al. 1973). Mammalian muscle tissue is composed of different fiber types that have predominantly M or H type LDH (Keul et al. 1972). Kugelburg and Edström (1968, for ref. see Jorfeldt 1970) have shown that motor units consist of only one type of fiber, either phasic or tonic.

Phasic fibers have a large content of glycogen and a high activity of glycolytic enzymes including M type LDH (Barnard et al. 1971, Baldwin et al. 1973a, b). These fibers are thus adapted for resynthesizing their ATP through glycolysis with consequent production of lactate (Jorfeldt 1970). It has been suggested that these fibers are recruited in the initial stages of exercise (Jorfeldt 1970) or when the exercise is chiefly anaerobic in nature (Hermansen and Saltin 1966). A recruitement of phasic, fast twitch motor units would therefore elevate lactate production.

Tonic fibers are adapted for a chiefly oxidative resynthesis of ATP. These fibers have abundant capillary networks, high myoglobin content, numerous mitochondria and high activities of the enzymes, including H type LDH, which are essential for complete oxidation of carbohydrates and free fatty acids (Baldwin et al. 1973 a, b, 1972a, Holloszy et al. 1971a). Their metabolism thus favours conversion of lactate to pyruvate (Jorfeldt 1971, Keul et al. 1972). These fibers appear to be recruited when the work load is not chiefly of an anaerobic nature. A recruitement of tonic fibers would consequently limit lactate production and enhance its catabolism.

The number and type of motor units recruited in the performance of muscular work will thus determine in part the rate of lactate production.

Lactate Levels

It is pointed out by Cerretelli and Ambrosoli (1973) that exhaustion occurs when the total lactic acid accumulation is much less than the body is capable of tolerating or the maximum amount that can be produced on the basis of glycogen stores of the body. Hultman and Bergström (1973) suggest that a critical lactate level may inhibit glycolytic activity or prevent the augmentation of lactate during the terminal part of exercise. It remains uncertain whether this possible self-regulating capacity of lactate is direct and/or indirect in nature.

As previously outlined, the augmentation of non-volatile lactate in the performance of heavy work is accompanied by a concomittant increase in acidity which may depress metabolic processes (MacDonald 1965, Pfhol 1965, Keul et al. 1966). In this connection it has been demonstrated that low pH values negatively affect the "activation" and substrate binding capacity of the rate limiting enzyme of glycolysis, phosphofructokinase (Hofer and Pette 1968, for ref. see Haralambie 1971). This observation lends support to a thesis of indirect inhibition by lactate.

Based on an in vitro study of human skeletal muscle, it has been hypothesized by Karlsson et al. (1974b) that elevated lactate may act directly as a product inhibition of LDH. He declares that it is conceivable that lactate or pyruvate, the products of LDH catylyzed reactions, could have a regulatory effect on both the anaerobic glycolysis and oxidation of lactate in the human skeletal muscle. Results of a

study by Fagraesus (1974) lends support to Karlsson's suggestion of lactate or pyruvate inducing an inhibition of LDH and thereby rate limiting lactate production. He found that peak blood lactate and muscle lactate at exhaustion remained unchanged whether exercise was performed in normoxia or hypercapnia. Since hypercapnia would induce a further reduction in pH this observation substantiates the hypothesis that lactate may act as a direct inhibitor with respect to its own production (Eldridge et al. 1974).

Availability of Carbohydrate

Astrand et al. (1963) discovered very low lactate values in contestants at the end of ski races lasting for one hour or more. In the same study these investigators observed that lower blood lactate concentrations were found in subjects given a standardized submaximal and maximal work loads after cross country skiing lasting 1-8 hours. They suggested a decreased glycogen store as one possible cause for the low lactate. Later studies by Karlsson (1971a) and Asmussen et al. (1974) confirmed the observations of Astrand et al.

Karlsson demonstrated (1971a) that maximal exhaustive exercise, preceeded by long-lasting exercise, resulted in a decrease in time to exhaustion, lower peak blood lactate concentrations, and a decrease in muscle lactate when the submaximal exercise had lasted 5 to 7 hours. Muscle glycogen was depleted to about 80% of normal values.

In a more recent, well controlled study, Asmussen et al. (1974) concluded that the ability to work anaerobically and to produce lactate decreased with decreasing amounts of available carbohydrate. They further advocate that this process is increasingly slowed down by lactic acid accumulation with decreasing substrate (glycogen) concentration.

It was also demonstrated in this study that glucose, which enters the glycogenolytic chain as glucose-6-phosphate, can partly restore the capability of lactate production.

The availability of the substrate glycogen, therefore may determine the amount of lactate production.

Intensity and Duration of the Work Load

Work intensity, duration, the type of work and amount of muscle mass involved play an important role for the amount of lactate that is produced per unit of time (Assmussen et al. 1948a, Hermansen 1971, Karlsson 1971b).

A release of lactate from the skeletal muscle takes place in man even in a basal state (Andres et al. 1956). The arterial and muscle concentration, production, and arterial-venous concentration difference of lactate all increase approximately exponentially with increasing intensity of work (Hermansen and Saltin 1966, Osnes and Hermansen 1972, Jorfeldt 1970, Keul and Doll 1973).

Through application of intermittent work load, Christensen et al. (1960), Margaria et al. (1969) and Wasserman et al. (1967) demonstrated that very heavy intermittent exercise can be maintained indefinitely and without marked elevation of blood lactate if the intensity of the exercise and its duration are such as not to deplete the alactic energy source and the recovery periods are sufficient (half reaction time being approximately 20 to 25 seconds) to allow repayment of the oxygen debt incurred.

Saltin and Essen (1971) showed that while blood lactate was only elevated above resting levels when work periods exceed 15 seconds in duration, muscle biopsies following very short supramaximal work loads

indicate a significant increase in lactate. Similar results were found by Osnes and Hermansen (1972). They state that if the work intensity is sufficiently high, large amounts of lactate are produced within ten seconds.

Knuttgen and Saltin (1972) revealed that lactate formation apparently has little or no involvement in exercises lower than 60% Max. $\dot{V}o_2$ but their results do not support the concept that lactate is not produced in the muscle during submaximal exercise. Bergström et al. (1967) observed that during continued exercise of long duration at a submaximal level the lactate level fell after an initial rise. Karlsson (1971b) further demonstrated that lactate concentrations at the end of work were found to be the same whether exhaustion was 2-3 minutes or about 7 minutes but were lower when exhaustion time amounted to 10-20 minutes.

Cortical Inhibition and Motivation

Since brain tissue pH is known to be strongly dependent on blood pH, Haralambie and Frieburg (1971) speculate that cortical inhibition as a consequence of the dramatic fall in pH is a defense mechanism against excessive changes induced by exercise. They further state that a marked fall in alkaline reserve is always accompanied by subjective sensations of fatigue.

Hermansen (1971) asserts that the motivation of the subject plays an important role in the establishment of peak blood lactate concentrations. He observed that all blood lactate values in the laboratory experiments were lower than those obtained after participation in important competitions. Keul (1973) contends that a direct relationship

was found between peak lactate, pH and the results in competition in rowers studied just after competition at the Olympic Games in Munich. The lower the athlete's lactate, the poorer they finished. He suggests that in this case the lactate level may be an expression of the intensity of exertion.

Endurance Training and Lactate Production

Trained competitors when compared with untrained individuals are characterized by the ability to maintain lower levels of blood lactate during moderate exercise (Eriksson et al. 1973, Karlsson 1971b, Astrand 1970). However, trained subjects attain significantly higher peak blood lactates following non-steady state maximum work loads (Karlsson 1971b, Cunningham and Faulkner 1969). The exact mechanism behind the athlete's enhanced capacity with respect to lactate production is yet to be fully understood.

Lactate Production in Submaximal Work

Training has been shown to decrease blood lactate for a given submaximal work load (Klausen et al. 1974, Hermansen 1971, Gollnick et al. 1973a). This is true even when performing exercise of the same relative intensity; when the rate of glycogenolysis in the working muscle are the same in the trained and untrained state (Saltin and Karlsson 1971).

The apparently low level of anaerobic metabolism at the same relative work load performed by trained subjects does not seem to be the result of enhanced muscle blood flow. Klausen et al. (1974) have

demonstrated muscle blood flow to be reduced at the same work load after training. An increase in capillarization is also an unlikely cause since Hermansen and Watchlova (1971) illustrated that the number of muscle capillaries per square millimeter did not differ in untrained and well trained subjects.

Several authors have shown that training induces structural and metabolic changes which may be related to higher oxidative phosphorylation capacity (Holloszy et al. 1971a, b, Mole et al. 1973, Staudte et al. 1973, Taylor et al. 1972, Bernard et al. 1970). Biochemical studies have provided evidence that endurance training increases the activity levels of enzymes, of fatty acid oxidation (Holloszy 1973, Mole et al. 1973), ketone oxidation (Winder et al. 1974), the citric acid cycle (Holloszy 1973) and the mitochondrial respiratory chain (Baldwin et al. 1972a, b, Gollnick et al. 1973a, Holloszy 1967). These changes can be partially explained by changes in enzyme activity rates and concentration levels as well as structural changes and increases in size and number of mitochondria (Holloszy 1973, Hoppeler et al. 1973). These changes in catabolic capacity are accompanied by increased volume density of intracellular lipids (triglyceride droplets) and muscle glycogen stores (Gollnick et al. 1973b) which would further support the functional capacity of the muscle for fatty acid oxidation and aerobic endoxidation of carbohydrate.

Moreover it is well documented that the oxidation of fatty acids inhibits the utilization of carbohydrate (Paul et al. 1966) and that trained individuals oxidize more fat and less carbohydrate than untrained when performing submaximal work at the same absolute intensity (Hermansen et al. 1967, Issekutz et al. 1966). Recently, it was

suggested that exercise induced increase in skeletal muscle mitochondria is responsible for the slower utilization of carbohydrate during submaximal exercise in trained as compared to the untrained state (Fitts et al. 1975).

Other authors have demonstrated that changes in the relative area of fiber types and LDH activity which may also explain a decreased lactate level at the same relative submaximal work load in the trained subject.

Gollnick et al. (1973a) have established that five months of endurance training increases the relative area of slow twitch fibers. Recently Karlsson et al. (1974b) found that LDH activity increased with an increase percentage of fast twitch fibers in humans. Along with the high LDH activity there was a decline in H type LDH contribution to the total LDH activity suggesting that the fast twitch fibers contained a greater concentration of M type LDH. In a later study, Karlsson et al. (1975) discovered that endurance athletes when compared to non-trained subjects had lower total LDH activity, a higher relative activity of the H specific isozymes and upon electrophoretic separation a complete absence of M isozymes in both arm and leg muscles. However, strength trained athletes when compared to untrained demonstrated a similar distribution of relative isozyme activities but tended to have a higher total LDH activity. In the leg muscles they also demonstrated a strong electrophoretic band corresponding to LDH 5, the most skeletal muscle specific isozyme.

With these changes in fiber type distribution and LDH activity the endurance trained athlete would tend to produce less lactate due to a decrease in M-type LDH activity and increase in H-type LDH

activity thus providing an enhanced ability to catabolize lactate.

Therefore possible reasons for decreased lactate levels during the performance of a submaximal work load of the same relative intensity include: 1. predominance of slow twitch fibers 2. enhanced mitochondrial structural and enzyme activity and 3. changes in substrate availability, mobilization and utilization.

Lactate Production in Maximal Work

It has been demonstrated that training will increase the maximal lactate concentration in muscle (Saltin and Karlsson 1971, Eriksson et al. 1973) and in blood (Hermansen 1969, Cunningham and Faulkner 1969).

Karlsson (1971b) found that blood lactate was higher ($P < 0.05$) in trained subjects compared with untrained subjects (14.6 mmoles x l^{-1} and 12.3 mmoles x l^{-1} respectively). He points out that the difference was less than might be expected from the muscle lactate concentration (22.7 and 16.9 mmoles x kg^{-1} wet muscle) in trained compared to untrained.

The enhanced ability to maximize serum lactate during exhaustive work despite the retarding effects of lactate uptake induced through endurance training is not clear.

It has been previously pointed out that the ability to work anaerobically and to produce lactate decreases with decreasing amounts of available carbohydrate (Asmussen et al. 1974). Gollnick et al. (1973b) estimated that muscle glycogen was 2.5 fold higher following training. Therefore an increase in available substrate may account for part of increased lactate levels in the trained subject.

In addition, training induces elevated activities of some glycolytic enzymes. Gollnick et al. (1973a) discovered an increase alpha-glycerophosphate activity in fast twitch fibers following strenuous endurance training. Furthermore an increase in phosphofructokinase (PFK) activity has been demonstrated following training (Eriksson et al. 1973, Gollnick et al. 1973a, Baldwin et al. 1972b). An increase in PFK activity would aid in the degradation of glycogen for muscular contraction by anaerobic pathways.

In conjunction with an increase in available substrate and glycolytic enzyme activity the trained subject may be able to compensate for or tolerate higher lactate levels before terminating the work load. Keul (1973) for example, suggests that differences in lactate levels among highly trained athletes may be an expression of the intensity of exertion.

Compensatory Mechanisms of Lactate Acidemia

Since inappropriate levels of acidity depress the metabolic processes of the organism (Haralambie and Frieburg 1971, Karlsson 1971b, Katz 1970), the degree of imbalance between lactate production and metabolic or buffer compensation of acidosis in severe exercise would define the duration of heavy work. Moreover the ability to offset or ignore acidemic stress would enhance one's anaerobic work potential.

Blood and Muscle Buffers

When non-volatile acids are added to the organism during exhaustive work, the buffer systems of the body take up excess hydrogen

ions and make the concentration lower than it would have if the buffers had not been present (Davenport 1958).

Blood proteins, particularly plasma proteins act as hydrogen acceptors since they ionize in blood to form negatively charged particles which then can accept the positively charged hydrogen ion. However the main buffer of blood is the protein hemoglobin. Its molecule contains a large number of acidic and basic groups (Astrand 1970). Reduction of oxyhemoglobin to reduced hemoglobin causes hemoglobin to become a weaker acid and remove hydrogen ions from solution, whereas the oxygenation of reduced hemoglobin causes the hemoglobin to become a stronger acid and give up H^+ to solution (Davenport 1958).

Osnes and Hermansen (1972) demonstrated that an increase of blood lactate up to 15 mmoles results in a nearly equivalent decrease in plasma bicarbonate. They state that if the increase in lactate concentration in plasma is the same for whole blood all lactate which enters the blood is buffered by the CO_2/HCO_3 system. However they further point out that when lactate levels increase to higher levels other buffer systems play an increasingly important role.

Bergström et al. (1971) have estimated that the concentration of lactic acid in intracellular water is about 3 times higher than the concentration of whole blood following exhaustive exercise. Thus the translocation process for lactate is not immediate between intracellular and extracellular space (Karlsson 1971b). Hirche et al. (1971) indicate that undissociated lactic acid is lipid insoluble and can permeate across a cell membrane only in an ionized form. This augmentation of acidity will be partially buffered by the splitting of phosphocreatine which takes place in the muscle (Hultman et al. 1967). The splitting of

phosphocreatine liberates base thus decreasing the acidity of the muscle cell (Lipman and Meyerhof 1964, for ref. see Bergström et al. 1971). However Rooth (1966) points out that the breakdown of phosphocreatine occuring during exercise would result in only a small pH change. In explanation he has postulated the elimination of hydrogen ions into the intracellular fluid via a cation pump.

Respiratory Compensation

The decreased pH produced by metabolic acidosis stimulates the respiratory centers (Dejours 1966) and thereby increases the ventilation of the alveolar and arterial PCO_2. The reduction of PCO_2 titrates the blood in the direction of a higher pH and lower bicarbonate concentration (Davenport 1958). Osnes and Hermansen (1972) found that the degree of respiratory compensation for metabolic acidosis during exhaustive work varies considerably from one subject to another and also for the same individual in the course of an experimental period.

Renal Compensation

The renal tubular secretion of acid increases during metabolic acidosis. The excretion of acid effectively increases blood alkalinity resulting in an increase in both plasma pH and bicarbonate (Davenport 1958).

However during exercise it is unlikely that the kidney offers compensation since its action is slow (Tenny and Lamb 1965) and in maximum exercise, renal blood flow diminishes to approximately 20% of its resting value (Kachadorian and Johnson 1970, Wexler and Kay 1970).

Lactate Uptake and Metabolism

During and following exercise, lactate is also taken up and oxidized in different tissues of the body. The liver, brain, kidney, heart, inactive muscles and fibers in the exercising muscles have been shown to extract and catabolize lactate (Eldridge et al. 1974).

Jorfeldt (1971) has demonstrated the existence of saturation kinetics with respect to lactate transport through the cell membrane. He observed a fractional uptake of 31% at an arterial concentration of 1.03 mmoles/l in human exercising forearm muscles. Jorfeldt further established that a better correlation existed between the rate of lactate and the product of arterial lactate concentration and muscle blood flow, than to the arterial concentration alone. He tentatively suggests, that perhaps a larger blood flow implies a larger open capillary surface area and therefore more favorable conditions for lactate uptake.

The fate of the majority of lactate produced during exercise appears to be a prompt conversion to CO_2 by the skeletal muscle (Brooks et al. 1973, Jorfeldt 1971) and the heart muscle (Keul et al. 1965, 1966, Reinhard et al. 1973). Brooks et al. (1973) by infusing 1-C^{14} labelled lactate into rats observed that 75% of the infused isotope was collected as CO_2. In an earlier study Depocas et al. (1969) demonstrated that 74% of the lactate formed during exercise is converted to CO_2, whereas approximately 10% is resynthesized into glucose and glycogen by the liver. However, a recent study by Freminet et al. (1974) illustrates that the percentage of lactate turnover which is oxidized decreases as the quantity of lactate goes up. They therefore concluded that when the

lactate pool is increased lactate oxidation is limited and an increased fraction of the lactate flow is deviated to other metabolic processes.

Through the oxidation of lactate by the heart and skeletal muscles the dramatic decrease in pH in muscle tissue, which may become a limiting factor for the optimal level of some enzymes can within limits be delayed or hindered (Keul 1973). It is also apparent that blood lactate concentration is a result of two opposing processes, production and removal (Eldridge et al. 1974).

Increase in Glutamate-Pyruvate Transaminase Activity

Felig and Wharen (1971) report that alanine production by muscle increases markedly during strenuous exercise. They estimate that conversion of pyruvate to alanine occurs at 35 to 60% of the rate at which lactate is formed. These findings in conjunction with the observation that endurance exercise induces an increase in glutamate-pyruvate-transaminase, (GPT), activity leads to the conclusion that GPT activity may have significance with lactate accumulation during exercise (Mole et al. 1973).

Mole and his co-workers (1973) hypothesize that by increasing the capacity of GPT to compete with LDH for pyruvate this adaptation could result in the conversion of a greater percentage of pyruvate formed in muscle during exercise to alanine and less to lactate. An increase in the rate of alanine production with a proportional decrease in lactate formation could, by resulting in less lactate and H^+ accumulation, possibly protect against or delay the onset of fatigue during very strenuous exercise in muscle that has adapted to exercise.

Control of Respiration During Exercise

A great deal of investigation has been extended on the part of the respiratory physiologists to explain hyperpnia of exercise (Astrand 1970). However the degree and mechanisms through which the production, central integration and motor manifestations of ventilatory drives can be modified under varying environmental conditions and by varied physical activity is still unknown.

The primary function of the ventilation of the airways is the maintenance of adequate gas exchange during changing metabolic demands (Astrand 1970). The integration of the ventilatory process is carried out by respiratory centers located in the medulla (Leusen 1972). Functionally, the centers are divided into two parts. One part acts as the activity generator, producing a rising ramp of activity with each inspiration. The other, the timer, cuts off the inspiration at a given time (Von Euler 1970). The activity levels of these centers can be modified and regulated by fibers of central, cerebellar, or somatic origin. Besides the neurogenic input, the "centers" receive direct and indirect input from humoral agents of the blood which perfuse central and peripheral chemosensitive areas (Sorensen 1971, Dejours 1962, Comroe 1964).

The central chemoreceptors located in the brainstem are sensitive to pH changes in their environment (Leusen 1954, Mitchell et al. 1963 Pappenheimer et al. 1965). They respond slowly to metabolic acid-base changes in the blood, and therefore function mainly as PCO_2 sensors (Sorensen 1971). Control of respiration is therefore dependent upon both neurogenic and humoral input into the respiratory control centers.

There is little doubt that during exercise both neurogenic and humoral mechanisms can add to the hyperpnia of exercise (Dejours 1966). However, the relative contribution of the neurogenic and humoral component to the increase ventilation of exercise is still unclear.

It has been reported that unless the intensity of the work load is of a maximum nature, it is unlikely that humoral stimuli play an important part in control of ventilation during exercise (Dejours 1966, Flandrois et al. 1974). Cunningham et al. (1966) demonstrated that at the start of exercise, the rapid change in ventilation remains the same, regardless of the gaseous environment. This instantaneous response has therefore been attributed to result from stimulation of proprioceptors, ergoreceptors, or the muscle spindles in the exercising limbs and/or central nervous system (Comroe 1966, Campbell 1964, Eklund et al. 1964, Kao 1963).

It has also been established that during submaximal work comparatively small changes are observed in the PO_2, PCO_2, and H^+ concentration of arterial blood (Astrand 1970, Dejours 1968). The hyperpnia of mild exercise must therefore be attributed to a dominantly neurogenic component.

However Sipple and Gilbert (1966) could not show that the speed of limb motion affected ventilation using fixed work rate and varying the cycling frequencies. Wasserman et al. (1967) observed in graded exercise work tests in man, that steady state minute ventilation increased linearly with CO_2 production up to six times the resting metabolic rate and that the relationship intercepted at the origin. Thus a mechanism controlling ventilation which is independant of metabolism seems unlikely (Beaver and Wasserman 1970).

Respiratory Response to Hypercapnia

The physiological response of human organism to elevated arterial PCO_2 has been studied extensively. Observations of the ensuing biological responses following the administration of exogenous CO_2 has been instrumental in the description of the in-vivo mechanisms which compensate for endogenous humoral imbalance. The following is a summary of work which has been of primary importance in understanding these control mechanisms.

Kellog (1964) points out that as early as 1868, Pflüger demonstrated that both hypercapnia and hypoxia stimulate breathing. In 1905 Haldane and Priestly (1905) made observations of the sensitivity of breathing to slight deviations of carbon dioxide pressure. They found that a rise in 0.2% of an atmosphere in the alveolar CO_2 pressure was sufficient to double alveolar ventilation during rest. These early investigators pointed out that any cause that tends to increase or decrease the partial pressures of $PaCO_2$ and $PACO_2$ from this normal value initiates a ventilatory response which limits the deviations of gas tensions (Dejours 1966). Through the results of more recent studies Lambertsen et al. (1961) concluded that an increase in $PaCO_2$ of about 5 mm Hg was sufficient to double the average ventilation in steady state.

The ventilatory response to hypercapnia has been shown to increase during exercise (Craig et al. 1970, Byrne-Quinn et al. 1971, Dipps and Comroe 1947) and when hypoxia is induced through altitude exposure (Hansen et al. 1975, Forster et al. 1971) and experimentally at sea level (Lloyd et al. 1958, Naimark et al. 1965, Sorensen 1971). The response to elevated $PaCO_2$ is also augmented by increased levels of the thyroid and progesterone hormones.

When CO_2 is elevated in inspired air the alveolar gradient becomes such that a liter of alveolar ventilation is less effective in removing CO_2. This causes arterial and body stores of CO_2 to increase until mean pulmonary capillary PCO_2 and/or ventilation increases to restore equality between CO_2 production and CO_2 elimination (Menn et al. 1970). With the resultant increase of arterial carbon dioxide, the acid-base balance of the organism is disrupted. This effect is equivalent to the pathological condition of reduced ability to eliminate endogenous CO_2. The increase in arterial PCO_2 titrates the blood in the direction of a low pH (increased H^+) and bicarbonate levels rise (Davenport 1958).

CO_2 stimulates ventilation through its effects on both peripheral and central chemosensitive areas (Sorensen 1971). It has been well demonstrated that carbon dioxide tensions are fully sensed by the peripheral arterial chemoreceptors and are translated into a ventilatory response in less than two seconds (Gray 1968, Black et al. 1966, Dutton et al. 1967). In studies which involve inactivation or bypass of the arterial chemoreceptors, the ventilatory response to sudden alterations in arterial PCO_2 tensions, mediated by the central nervous system, lag behind changes in blood gas tensions for from 10 to 30 seconds (Cunningham et al. 1965, Fitzgerald et al. 1968). These findings suggest that ventilatory responses to rapidly changing transient stimuli will reflect the activity of peripheral chemoreceptors rather than that of the central receptors, while responses to steady-state stimuli will reflect the activity of both (Edelman et al. 1973).

The relative contribution of peripheral and central chemo-sensitive areas to total ventilatory response to CO_2 is difficult to

assess. In unanesthetized dogs the slope of the CO_2 response curve decreased 20 to 45% after denervation of the peripheral chemoreceptors (Mitchell 1965). Lahiri et al. (1975) and Von Euler (1970) found a decrease in response to CO_2 after vagotomy in cats. Lugliani et al. (1971) who studied CO_2 responses of asthmatic patients before and after denervation of the carotid bodies observed a 30% decrease in response following denervation. A similar conclusion was reported by Edelman et al. (1973). They report that in the intact unanesthetized man the peripheral chemoreceptors are responsible for approximately one third of the over all steady-state response.

It has been demonstrated that in absence of peripheral chemoreceptors hypercapnia stimulates breathing primarily through a tidal volume response (Von Euler et al. 1970, Lahiri et al. 1975). Rosentein et al. (1974) concluded that the influence on breathing of arterial chemoreceptors was exercised mainly if not completely through modulating action on the controls of tidal volume.

With respect to the separate quantitative role of H^+ and PCO_2 in CO_2 breathing, Lambertsen et al. (1961b) discovered that when H^+ was maintained stable in unanesthetized man, about two fifths of the ventilatory response to CO_2 breathing was removed. It has been further illustrated by Saito et al. (1960) and Lambertsen et al. (1961b) that if arterial CO_2 is maintained and arterial pH lowered, ventilation increases linearly with increases in H^+. When pH is maintained normal and arterial CO_2 is elevated, ventilation also increases in a linear fashion with CO_2. If H^+ and CO_2 are elevated together, the response tends to be additive.

Part of the CO_2 stimulus may be initiated by the cerebrospinal fluid (CSF) (Leusen 1972) bathing the proposed chemosensitive cells

localized in the floor of the fourth ventricle (Nicholson 1936). CO_2, unlike H^+, can diffuse from blood to CSF due to its high solubility coefficient (Mitchell et al. 1963). Leusen (1954) using a technique to perfuse the brain's ventricular system demonstrated that ventilation is stimulated when the H^+ of the perfusion fluid was raised by an increase in PCO_2. The response is characterized by a greater amplitude of respiratory movements (Leusen 1972). Mitchell et al. (1963) concluded that respiration was influenced by alterations of H^+ in the perfusion fluid induced either by modifying PCO_2 or HCO_3^- but that a more intense influence was noticed when the pH was changed by altering HCO_3^-. Pappenheimer et al. (1965) were able to produce a 2.5 fold increase in ventilation in unanesthetized goats when HCO_3^- of the perfusion fluid was lowered from its normal value of 22 mm to about 16 mm in a constant background of PCO_2. In addition they observed that for a given arterial PCO_2 increase the modification of respiratory response was much greater when HCO_3^- level in the ventricles was low. The pH of CSF was thus thought to have an important bearing on respiratory response.

The relationship of the acid-base composition of blood and CSF in acute and chronic states of alkalosis and acidosis has been studied extensively. It has been demonstrated that the effects of acute displacement of blood pH on CSF pH depends on whether the alteration of acid-base equilibrium is induced by a change in HCO_3^- or $PaCO_2$. Acute hypercapnia or hypocapnia causes respectively an increase in H^+ or a decrease in H^+ of the CSF (Manfredi 1962, Robin et al. 1958, Swanson and Rosingren 1962). However primary changes in blood pH produced by infusing bicarbonate or acids were found to cause little change in

CSF H^+ (Manfredi 1962, Robin et al. 1958, Bradley and Semple 1962). It has also been observed that infusion of bicarbonate into the blood causes a rise in CSF H^+ (Bradley and Semple 1962). Lactate formation by the brain tissue resulting in accelerating HCO_3^- breakdown in CSF during hypocapnia has been suggested as the compensatory mechanism for disturbances of acid-base equilibrium on the alkaline side of normal pH (Leusen 1972). Thus there appears to be a fundamental difference between the repercussions of acute respiratory and non-respiratory acid-base changes on CSF homeostasis. It has been suggested that this difference can be further explained by unequal diffusing characteristics of HCO_3^- and CO_2. CO_2 equilibriates rapidly between blood and CSF (Leusen 1972) while H^+ and HCO_3 apparently do not (Mitchell et al. 1963, Fencl et al. 1966, Sorensen 1970).

The isolation of CSF from acute metabolic or non-gaseous acidemia has been attributed to a blood-brain barrier (Leusen 1972, Mitchell 1965). The proposed barrier is hypothesized to hamper the passive exchange of $HCO_3^- + H^+$ between blood and CSF (Severinghaus et al. 1963, Mitchell 1965). Mitchell (1965) states that as long as plasma pH exceeds 7.3 there is an absolute barrier to the penetration of H^+ into CSF. Fencl et al. (1966) however suggest that this absolute barrier does not exist. They report the CSF changes continuously as a function of plasma HCO_3. Recent studies by Pavlin and Hornbein (1975 a, b) also provide evidence that the barrier is not so absolute and that passive diffusion of H^+ and HCO_3^- between CSF and blood may occur during metabolic and respiratory acidosis. Pierce et al. (1971) found that ventilatory response to acute uncomplicated base deficit correlated highly with arterial HCO_3^- ($r = 0.91$) or estimated (H^+) of cerebral interstitial fluid ($r = 0.93$) when the latter was assumed to

be determined by a HCO_3^- value intermediate between that of arterial blood and CSF. They suggest that HCO_3^- in blood and CSF each contribute to the control of ventilation.

At maximum work load, it appears that only arterial H^+ concentration increases whereas PO_2 remains relatively constant and PCO_2 following a slight increase of approximately 3 mm Hg (Bannister et al. 1954) may even decrease during the terminal part of maximum exercise (Wasserman et al. 1965, Bannister et al. 1954).

As previously mentioned, the rise in H^+ is the result of lactic production in the working muscles ($HLa + NaHCO_3 \rightleftharpoons Na\ La + H^+ + HCO_3^-$). Furthermore, to compensate for metabolic acidosis, respiratory alkalosis is imposed. This response is mediated through the peripheral chemoreceptors. Gray (1968) concluded that these receptors are capable of responding to even the most acute metabolic acid-base disturbances without significant delay. It appears that due to a blood brain barrier the central chemosensitive areas do not respond to acute metabolic acidosis (Leusen 1972). Lactate does not permeate readily from blood to CSF (Alexander et al. 1962) and is considered not to act as a direct stimulus to ventilation (Asmussen and Nielson 1946). Small elevations of lactate, however, have been found in CSF of dogs following twenty minutes of exercise (Van Vaerenbergh et al. 1965). The increase in ventilation due to metabolic agents stimulating the peripheral chemoreceptors will be partially offset by a decrease in central drive to ventilation due to hypercapnia (Robin et al. 1958, Sorensen 1971).

It appears therefore that the hyperpnia of mild exercise must be explained largely by factors other than chmeical agents. However in exercise of an anaerobic nature the resultant decrease in pH may add to the neurogenic input of the respiratory centers.

There appears to be little doubt that arterial PCO_2 exerts a direct influence on both central and peripheral chemoreceptors but non-gaseous influence of the central area is still to be determined. One apparent factor is that hypercapnia elevates H^+ content which has been demonstrated to be related to increased ventilation. The effects on respiration of changes in arterial PCO_2 and H^+ are not as yet readily distinguished from each other. In order to assess the extent to which hypercapnia affects the respiratory centers, measurements should be made on the number of efferent impulses going to the respiratory muscles in response to the change in respiratory center PCO_2. The proposed PCO_2 sensitive neurons at the level of the medulla are of course unobtainable in man (Dejours, 1966).

Variations in Response to Hypercapnia

It has been demonstrated that while the spontaneous ventilation is almost linearly related to alveolar carbon dioxide tension over a considerable range, there are marked differences in magnitude of response among individuals (Schaefer 1958, Cherniack 1965, Byrne-Quinn et al. 1971, Arkinstall et al. 1974). If ventilatory CO_2 sensitivity is defined as the ratio of variation of ventilation to variations in PaCO2 (Dejours 1966), a decreased response to inhaling a gas mixture with CO_2 may be interpreted as either a decrease of respiratory sensitivity in certain individuals or that certain individuals ignore the augmented CO_2 stimulus rather than increase their ventilation.

Cherniack (1965) observed that patients with emphysema demonstrate a decreased ventilatory response when a gas containing CO_2 is inhaled. These patients exhibit a diminished hypercapnic drive and a chronic CO_2 retention. The mechanism for such a response is unclear. However,

experimental and clinical data indicate that changes in CSF pH provoked by alterations of PCO_2 (respiratory acidosis) are progressively compensated by an adaptation of HCO_3^- concentration so that CSF returns towards normal pH values (Leusen 1972). It has been suggested that such an adaptation may reduce sensitivity to changes in carbon dioxide (Prime and Westlake 1954). Furthermore patients with chronic obstruction of airway passages or the addition of an obstruction in normal subjects causes a decreased response to hypercapnia (Brodovsky et al. 1960, Clark 1968, Flenley and Miller 1968, Tenny 1964).

The phenomenon of a diminished hypercapnic drive is not restricted to emphysema patients or by the addition of a mechanical obstruction to the airways. In a study with normal subjects Schaefer et al. (1958) found significant differences in ventilatory response when 5.4% and 7.5% CO_2 in a normoxic mixture was breathed at rest. They did not observe significant differences among subjects while breathing 1.5% and 3.3% CO_2 levels. The low ventilation group showed significantly lower respiratory rate, and larger tidal volume, inspiratory reserve capacity and vital capacity as well as higher alveolar CO_2 level (approximately 2 mm Hg) during normal breathing of air. Moreover subjects who exhibited a decreased hypercapnic drive approached a steady-state alveolar PCO_2 on exposure to hypercapnia faster than the high ventilatory group. When the study was repeated after an interval of five to six years it was found that in general the subjects' responses did not differ. In addition, Schaefer et al. (1958) demonstrated that subjects with a low ventilatory response to carbon dioxide also exhibited a low response to hypoxia. Shaeffer and his co-workers were unable to identify the cause

but suggested that differences in adrenal and sympathetic responses to hypercapnia might be responsible.

A number of studies have reported that specific groups are characterized by a decreased ventilatory response to hypercapnia. Song et al. (1963) found that the hae-nyo, the diving women of Korea, had lower ventilatory response to CO_2 than non-diving women but that their hypoxic response was not different.

Schaefer (1965) later pointed out that the characteristic of reduced CO_2 response and slow, deep breathing pattern in diving tank instructors diminished significantly after several months of non-diving and returned when they resumed diving. He also observed that active divers had a decreased response to hypoxia. Goff and Bartlett (1957) compared the response of trained and non-trained swimmers. The results of their study reveals that end-tidal CO_2 levels were elevated by 9 to 14 mm Hg in the trained experienced underwater swimmers. They suggested that the ability of trained swimmers to perform exercise efficiently under such hypercapnic conditions would indicate a reduced medullary CO_2 sensitivity or a conscious disregard of the stimulus or both. Their suggestion of a reduced medullary sensitivity to CO_2 is based on their observation that there was a significantly lower oxygen ventilation equivalent in the trained swimmer which would, especially in those swimmers without post-inspiratory pauses tend, to elevate the average alveolar and arterial CO_2 tension. In contrast Froeb (1960) compared 16 subjects having extensive scuba diving histories and found no difference between these groups in their response to exogenous CO_2 either at rest or during exercise.

In a recent study by Byrne-Quinn et al. (1971) resting hypoxic and hypercapnic drives together with ventilatory response to hypoxia during exercise in a group of 13 athletes were compared with a control of 10 non-athletes. They found that the ventilatory response to hypercapnia and hypoxia was significantly less ($P < 0.01$) in the athlete when compared to the control group. They suggest a diminished peripheral chemoreceptor function since they point out that it has been shown that high altitude natives with a decreased hypoxic drives also have a decreased ventilatory response to a single breath of carbon dioxide as well (Sorensen and Cruz 1969, Lefrançois et al. 1972). Byrne-Quinn and his fellow investigators also determined that both hypoxic and hypercapnic drives were inversely related with maximal oxygen uptake. At variance with this latter finding is the result of Hirshman et al. (1975). They found that both hypoxic and hypercapnic drive correlated poorly with maximal oxygen uptake in a group of non-athletes.

Two recent reports suggest that the interindividual variability with respect to hypercapnic drive, may be due to genetic differences. In a comparative study between a population of Enga, New Guinea, natives and Caucasians, Beral and Read (1971) demonstrated a significantly lower ventilatory response to inhaled CO_2 in the New Guinea population. Rebuck and Read (1971) who studied highly trained athletes, reported a consistant difference between long distance runners who were low responders and sprinters who had a high response to CO_2. They observed a ten-fold difference in response between a marathon runner with a $\dot{V}_E / ET \ PCO_2$ of .57 l/min per mm Hg.and a sprinter with a corresponding value of 5.6. They point out that the observed difference appeared to be independant of the current intensity of training. In conclusion both pairs of

investigators stated the observed differences in ventilatory response to hypercapnia may reflect genetic differences.

In an attempt to gain insight into genetic differences with respect to hypercapnic drive at rest, Arkenstall et al. (1974) measured the ventilatory response to CO_2 in 17 sets of monozygous and 13 dizygous twins. The results of their study did not reveal a significant difference in the intrapair variance between the monozygous and the dizygous twins. They concluded that the variability in the ventilatory response to inhaled CO_2 can be attributed to environmental rather than genetic factors.

In contrast to Schaefer et al. (1958), Patrick and Howard (1972) state that the difference is apparently not related with total lung capacity or its subdivisions. They further found no relationship with age, body size, weight or smoking habits. They demonstrated a lower sensitivity in Caucasian women and that personality factors appear to influence the frequency of response.

There is evidence therefore that specific groups, which include experienced divers (Schaefer 1958, 1965), athletes (Byrne-Quinn et al. 1971), endurance swimmers and runners (Rebuck and Read, 1971), Highlanders (Forster et al. 1969), New Guineans (Bearl and Read 1971), and Caucasian women (Patrick and Howard 1972) have a decreased response to CO_2. There is also evidence to suggest that this decreased sensitivity occurs in the peripheral chemoreceptors (Byrne-Quinn et al. 1971, Edelman et al. 1973).

CHAPTER III

METHOD OF RESEARCH

The purpose of this investigation was to establish if a relationship exists between the ventilatory response to controlled hypercapnia at rest and the ability to maximize levels of lactate in blood during exhaustive exercise. In an attempt to resolve this problem subjects were screened into trained and untrained groups and their response to hypercapnia and ability to maximize blood lactate determined.

Subjects

All subjects were non-smokers between the ages of 17 and 27 without any history of cardiovascular or respiratory disease or obesity.

Ten fully conditioned male subjects were selected from varsity football or regional paddling and track clubs. No attempt was made to randomize selection but the trained subjects had to fulfill the following criteria for participation. They had to have achieved some measure of success in their particular sport and demonstrate a maximum oxygen consumption in excess of 55 ml kg^{-1} $min.^{-1}$.

In all twenty-six untrained subjects who did not participate in sports at the regional or university level were screened for participation. However only five subjects fulfilled the criteria for participation of a maximum oxygen consumption less than 47 ml kg^{-1} $min.^{-1}$. The untrained group was therefore limited to this number because of difficulty in finding young males with this low an oxygen consumption.

Testing Procedure and Methodology

Introduction to the Study

A full explanation of the proposed study and criteria for participation was given to all subjects and informed consent was obtained. Subjects were questioned with respect to past and present health status, athletic participation and achievement. Verbal and physical familiarization with the various apparatus to be utilized in the study was given. The subjects were then scheduled for two testing sessions to be carried out on non-consecutive days.

Session 1

The first session served to screen subjects based upon the aforementioned fitness criteria for participation. These included (1) pulmonary function tests and (2) maximum oxygen consumption (Max. $\dot{V}o_2$) tests. The Max. $\dot{V}o_2$ test also served to determine each subject's relative maximum work load (100% Max. $\dot{V}o_2$).

Resting Pulmonary Tests

Pulmonary function tests were administered to assure normal functional respiratory mechanics since either mechanical or pathological obstruction in the respiratory airways has been shown to reduce hypercapnic drive (Cherniack et al. 1956).

The following were determined from a standardized erect test position. The vital capacity and its subdivisions - Inspiratory Reserve Volume (IRV), Expiratory Reserve Volume (ERV), Tidal Volume (TV), along with dynamic measures of pulmonary function - Maximum Voluntary Ventilation (MVV) and Forced Vital Capacity (FVC) were recorded on a

Collins 13.5 liter Respirometer (model 2049). The manner of their determination is described elsewhere (Consolazio et al. 1963). Results were transformed to BTPS and STPD values.

Maximum $\dot{V}o_2$ Test

The Max. $\dot{V}o_2$ test served to assure that the athletic subjects satisfied original criteria for group separation (trained $<$ 55 ml kg^{-1} min.$^{-1}$; untrained $>$ 47 ml kg^{-1} min.$^{-1}$).

The incline of the treadmill was placed at 8.6% of its length. An initial speed of 6.5 mph and 5 mph was selected for trained and untrained subjects respectively. The subjects were required to run repeat exercise loads of five minutes duration. A rest period between each bout of exercise was permitted. Progressive increases in treadmill velocity were imposed with each successive load until the subject could not complete a 5 minute work bout.

The appropriate measurements were collected during the third and fifth minute of each exercise bout. To insure a final reading which may not have coincided with these collection intervals, the subjects were instructed to signal when they felt they were approximately 45 seconds from terminating the work load.

As shown in Figure 1 expired oxygen and carbon dioxide were analyzed by Rapox and Capnograph gas analyzers respectively. Gas analyzers were calibrated with gas from tanks calibrated by the Scholander micro technique. Minute ventilation was calculated from the collection of expired gas in a large and small Tissot Gasometer. Respiratory rate was measured by a potentiometer attached to the indicator mechanism of the Gasometer. The outputs for the four variables, $\dot{V}o_2$, $\dot{V}_E CO_2$, $\dot{V}_E$ and

KEY TO FIGURE 1 SCHEMATIC DIAGRAM OF EQUIPMENT

A.	Treadmill Control Amplifier Model No. 642	Quinton Ltd., Seattle, Wash.
B.	Programmed Exercise Control Amplifier Model No. 642	" "
C.	Exercise Cardiotachometer Model No. 609	" "
D.	ECG Isolation Amplifier Model No. 620	" "
E.	Treadmill	" "
F.	ECG Preamplifier Model No. 607	" "
G.	Triple J Valve	Warren E. Collins Inc.
H.	Triple J Valve	" "
I.	Mixing Box	" "
J.	Rampox O_2 Analyser	N.V. Godart Co., Holland
K.	Capnograph CO_2 Analyzer	Grass Inst. Co.
L.	Two 150 liter paritally filled Meterological Balloons	
LL.	Two Gas Tanks, 5% and 7% CO_2	
M.	Standard Hospital Bed	
N.	Larger Tissot Gasometer	Warren E. Collins Inc.
O.	Gas Collection Valve	" "
P.	Potentiometer	" "
Q.	Two way shut-off Valve	" "
R.	Small Tissot Gasometer	" "
S.	DC/AC Coupler Type 7170	Narco Bio Systems Inc., Houston, Texas
T.	DC/AC Coupler Type 7170	" "
U.	High Gain Coupler Type 7170	" "
V.	Servo Writer	" "
W.	Four B Polygraph	" "
X.	Event Marker	" "
Y.	Foot Switch for the Event Marker	" "
Z.	Switch for Solinoid Valve	" "

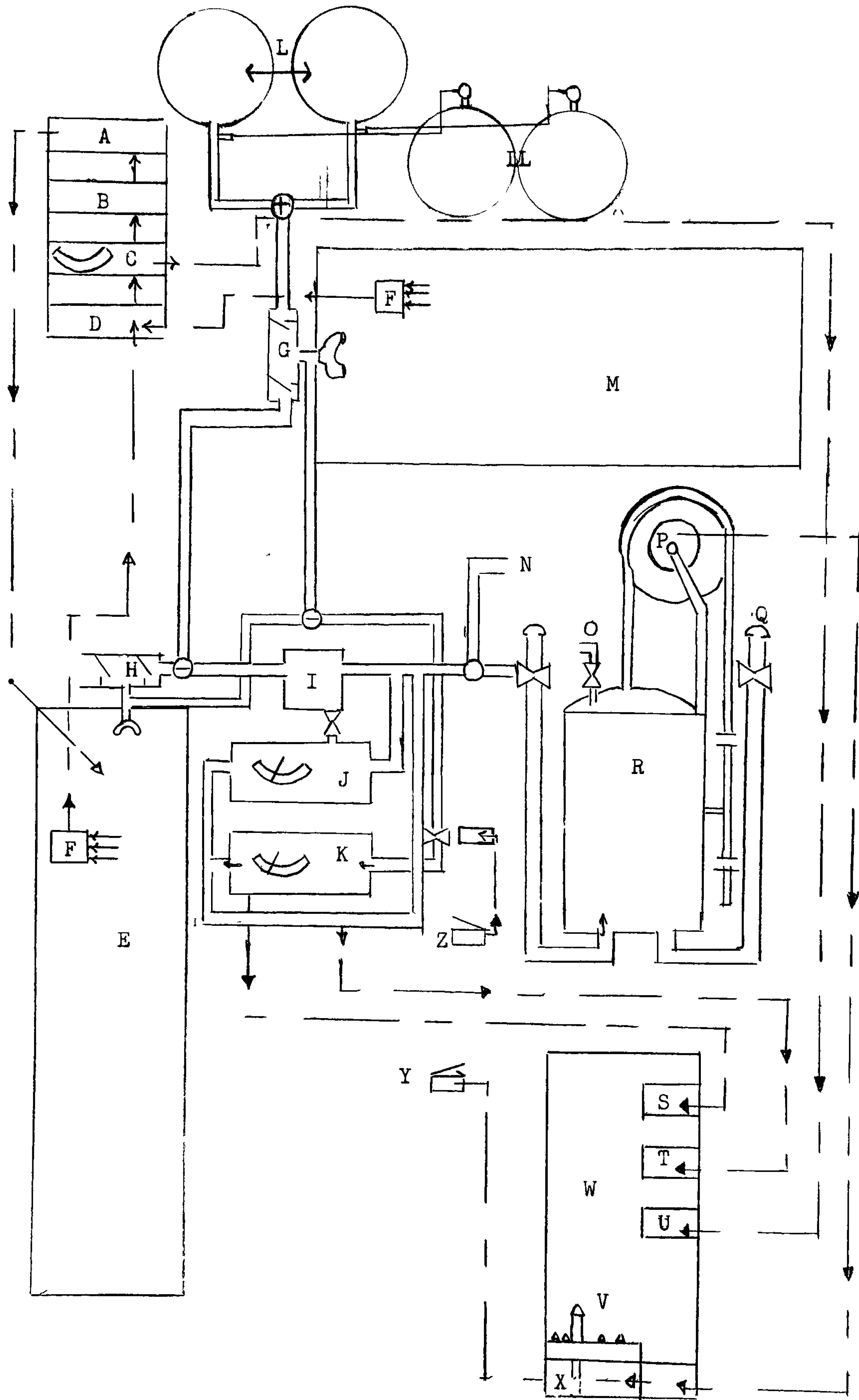


Figure 1 Schematic Diagram of Equipment

respiratory rate were monitored via separate channels of a Narco Bio systems Four B Polygraph which gave separate recordings for each variable.

Heart rate was recorded by a Quinton 609 Exercise Cardio Tachometer. A Quinton ECG Isolation Amplifier was also coupled to the Four B Polygraph to obtain continuous heart rate recordings.

Session 2

The purpose of this testing session was to attempt to determine each subject's ability to maximize levels of venous serum lactate following exhaustive exercise and his ventilatory response to controlled hypercapnia at rest.

Resting Oxygen Consumption and Blood Samples

The subjects were instructed to lie down and rest for a ten minute period. A five minute resting oxygen consumption was determined in the previously described manner (Appendix A).

Following this, ten cc of blood was drawn without stasis from the cubital vein into a vacutainer (Bechman-Sterile Disposal) with additive sodium heparin for lactate and pyruvate analysis. The venous blood samples were deproteinized immediately after collection according to the Biochemica Test Combination, Boehringer Mannheim GmbH, Mannheim Germany (see Appendix B). The deproteinized blood was then frozen for subsequent analysis. Ten cc were collected into a similar vacutainer but with additive EDTA N_2 for hemoglobin red and white cell count determination. A third vacutainer was taken for pH analysis. All samples were drawn by a qualified laboratory technician.

Hypercapnic Drive Determination

Upon completion of resting blood sampling, the subjects resumed their resting supine positions and breathed two mixtures of dry gas (approximately 5 and 7% in 20.93 O_2, balance N_2). To assure steady-state ventilation each gas mixture was breathed for a fifteen minute period (Saito et al. 1960). As shown in figure 1 the gases were breathed from 150 liter partially filled meteorological balloons. The two balloons were fed by tanks whose flow valves were adjusted to maintain the balloons in a constant partially filled position. The percentages of CO_2 and O_2 within the tanks were verified by the Scholander microtechnique. Continuous one minute readings were taken throughout the thirty minute periods with expired gas collected in a 350 and 150 liter Collins gasometer. One minute bell deflections and tissot temperatures were recorded to convert volumes to BTPS units. A continuous flow of expired gas was drawn from the dead space of the mouth piece and analyzed by the Godart Capnograph for end tidal (alveolar) carbon dioxide tensions and breathing frequency, and monitored via the physiograph. When the hypercapnic test was completed the subject breathed room air for a five minute period or until he felt fully recovered.

From the data collected peak ventilation per mm of alveolar PCO_2 was determined for comparison purposes.

Maximum Venous Lactate Determination

The subject was allowed the option of a brief warm-up before commencing his relative anaerobic work load (100% Max. $\dot{V}o_2$). The treadmill was then set at the standard 8.6% incline but at the speed which corresponded to the load at which each subject had attained his maximum

oxygen consumption. The subject ran at this load until exhaustion. Subjects were encouraged to put forth their maximum effort. Heart rate, breathing frequency mixed and end tidal O_2 and CO_2 were monitored and oxygen consumption determination carried out in a similar fashion as outlined previously for the Max. $\dot{V}o_2$ test. Upon voluntary termination of exercise the subject was placed in a lying position on a standard hospital bed. Five minutes after exercise similar blood samples were drawn and analyzed for post-exercise values.

Retesting Procedure

In order to obtain reliability coefficients the tests of the first session were repeated on half of the subjects and of session two, on all of the subjects. The order of gases in the hypercapnic tests was reversed in the retest of session 2 except in two trained and two untrained subjects to determine if the order of gases affected response levels.

Treatment of Data

Analysis of variance was used to compare trained and untrained subjects with respect to physical characteristic, maximum oxygen consumption, lung volumes and dynamics, post-exercise blood variables, RQ, and end tidal PCO_2 at the end of anaerobic work. A one-way analysis of variance, with repeated measures was run to determine differences between trained and untrained subjects ventilatory response to two levels of hypercapnia. Weighted t tests were run to see if significant differences existed between scores of repeated tests and correlation coefficients were obtained for major variables to obtain reliability of the test results. A correlation test was also run to determine the relationship between response to hypercapnia at rest and peak post-exercise venous serum lactate.

CHAPTER IV

RESULTS

Introduction

This section deals with the data which demonstrate the relationship between ventilatory response to controlled hypercapnia at rest and the ability to maximize levels of venous serum lactate during exhaustive exercise. The relationship and its related subproblems are summarized graphically and statistical comparisons are given in tabular form. A complete presentation of raw and calculated data is presented in Appendix D.

The material is presented in two sections. The first section contains the results of the screening session. In the second section, the results of the experimental sessions are presented.

Screening Session

A summary of one-way analysis of variance used to compare the physical characteristics of the athletes and controls is contained in Table 2. The non-significant F ratios ($P > 0.05$) indicate that the two groups did not differ in age, height, weight , or body surface area.

Maximum Oxygen Uptake (Max $\dot{V}o_2$)

Maximum oxygen uptake data for athletes and controls are listed in Table 3. The determination of Max. $\dot{V}o_2$ ml/kg was repeated for half the

TABLE 1

PHYSICAL DATA OF TRAINED AND UNTRAINED SUBJECTS

	AGE, YR	HT, IN"	WT, Kg	BSA, M^2
ATHLETES				
DS	24	71	81.36	2
RM	24	70.25	83.18	2.05
DM	24	71.5	77.88	1.99
JR	21	69.75	66.81	1.82
BS	21	71	76.36	1.96
PR	24	72.75	85.0	2.1
JE	18	71.75	61.82	1.81
RT	18	72	78.18	2.0
SF	18	71.75	61.82	1.81
BW	27	73.5	68.18	1.96
MEAN	21.9	71.5	76.5	1.95
SD	3.2	1.1	7.88	.10
CONTROLS				
DR	27	71	64.43	1.83
JC	18	71	66.59	1.85
BM	25	73.25	86.36	2.12
DM	24	70.5	77.73	1.98
RM	25	68.5	76.25	1.91
MEAN	23.8	70.85	74.27	1.94
SD	3.4	1.7	7.97	.12

TABLE 2

F TABLES OF ONE-WAY ANALYSIS OF VARIANCE OF TRAINED AND UNTRAINED SUBJECTS' PHYSICAL CHARACTERISTICS

CHARACTERISTICS	SOURCE	df	SS	MS	F
	B	1	12.03	12.03	1.13 (N.S.)
AGE	W	13	137.7	10.59	
	T	14	149.73		
	B	1	1.2	1.2	.69 (N.S.)
HT	W	13	22.675	1.74	
	T	14	23.875		
	B	1	16.74	16.74	.23 (N.S.)
WT	W	13	938.95	72.23	
	T	14	995.69		
	B	1	.0048	.0048	.48 (N.S.)
BSA, M^2	W	13	.136	.010	
	T	14	.1408		

TABLE 3

$\dot{V}o_2$ MAX. OF TRAINED AND UNTRAINED SUBJECTS

	$\dot{V}_E$ l/min. STPD	$\dot{V}o_2$ l/m	$\dot{V}o_2$ ml/kg
ATHLETES			
DS	147.44	5.07	62.31
RM	141.67	5.00	60.11
DM	127.85	4.58	58.81
JR	146.06	4.83	72.29
BS	155.93	5.59	73.2
PR	149.31	5.04	59.39
JE	162.19	5.05	60.62
RT	118.22	4.71	60.25
SF	130.26	4.68	75.83
BW	145.11	5.29	77.6
MEAN	142.41	4.98	66.04
SD	12.7	.29	7.27
CONTROLS			
DR	138.99	3.04	47.18
JC	103.45	2.67	40.16
BM	137.4	3.45	40.99
DM	104.42	3.27	42.07
RM	114.12	3.32	43.5
MEAN	120.28	3.15	42.78
SD	15.03	.27	2.47

TABLE 4

F TABLES OF ONE-WAY ANALYSIS OF VARIANCE OF $\dot{V}_E$ L/MIN. STPD, $\dot{V}o_2$ L/MIN., AND $\dot{V}o_2$ ML/KG FOR TRAINED AND UNTRAINED SUBJECTS

PARAMETER	SOURCE	df	SS	MS	F
	B	1	1803.58	1803.58	41.93***
$\dot{V}_E$ L/MIN. STPD	W	13	558.73	42.98	
	T	14	2362.31		
	B	1	11.21	11.21	120.83***
$\dot{V}o_2$ L/MIN.	W	13	1.206	.0927	
	T	14	12.418		
	B	1	1632.31	1632.31	7.738*
$\dot{V}o_2$ ML/KG	W	13	2742.32	210.95	
	T	14	4374.63		

* significant at the 0.05 level

*** significant at the 0.001 level

subjects to assure reliability. The resultant correlation of .944 and standard error of estimate of 4.04 ml kg^{-1}, for $\dot{V}o_2$ ml kg^{-1} $min.^{-1}$ is within the range of recently published values (Rowell 1974). One-way analysis of variance of Max. $\dot{V}o_2$ and its supporting variables for athletes and controls are summarized in Table 4. Significant differences were shown for the $\dot{V}_E$ l. $min.^{-1}$ STPD, $\dot{V}o_2$ l. $min.^{-1}$ and $\dot{V}o_2$ ml kg^{-1} measurements.

Pulmonary Function Tests

The results of the pulmonary function tests are listed in Table 5. The data is expressed in both BTPS and STPD units. One-way analysis of variance of the BTPS values obtained for vital capacity and its subdivisions: expiratory reserve volume, ERV, tidal volume, TV, inspiratory reserve volume, IRV, along with forced vital capacity, FVC, and maximum volume ventilation, MVV, are summarized in Table 6. No significant differences were shown for vital capacity and its subdivisions or for forced vital capacity. Athletes, however, demonstrated a significantly higher maximum volume ventilation capacity ($P < 0.05$).

Experimental Session

Maximum Serum Lactate (Subproblem 1)

Maximum work loads were repeated for all subjects on non-consecutive days. Oxygen consumption and its supporting variables were obtained for all subjects for both tests. However, due to technical difficulties, post-exercise lactate and pyruvate measurements were not obtained for two untrained subjects in one test. pH values were successfully determined for only three trained and two untrained subjects.

TABLE 5

PULMONARY FUNCTION DATA OF TRAINED AND UNTRAINED SUBJECTS

ATHLETES	VC		ERV		TV		IRV		FVC		MVV	
	BTPS	STPD	BTPS	STPD	BTPS	STPD	BTPS	STPD	BTPS	STPD	BTPS	STPD
DS	5654	4617	1746	1426	1474	1204	2324	1898	5676	4635	292.6	239.9
RM	5775	4715	1451	1185	1606	1311	2695	2200	5687	4642	257.4	210.2
DM	5847	4809	1758	1446	1758	1446	1594	1311	5935	4881	171.9	141.4
JR	5321	4303	2064	1669	742	585	1881	1521	5375	4346	250.5	202.6
BS	4971	4056	1320	1077	1562	1275	1826	1490	5169	4218	247.4	201.9
PR	6438	5246	2161	1761	1189	969	3134	2561	6915	5635	242.3	197.5
JR	7090	5912	2327	1940	1407	1173	2793	2329	7144	5957	270.6	225.6
RT	6201	5181	2002	1669	1689	1408	2468	2058	6494	5415	193.8	161.6
SF	4330	3611	1407	1173	1515	1263	1624	1354	4524	3773	236.5	191.2
BW	4885	4035	2008	1658	814	672	2443	2018	5026	4151	217.6	179.7
MEAN	5652		1824		1375.6		2278		5794.5		238.1	
± SD	772		326.7		333.8		499		798.9		33.8	
CONTROLS												
DR	5267	4316	2118	1735	782	614	2508	2052	5527	4529	194.4	159.3
JC	5292	4369	2095	1730	851	703	1964	1621	5183	4279	126.6	104.5
BM	6319	5085	2439	1963	2107	1696	2084	1677	6209	4996	187.4	150.8
DM	4814	3953	1313	1078	1149	944	1532	1258	4814	3953	197	161.8
RM	5661	4649	2068	1698	1524	1251	2123	1743	5878	4827	212.3	174.3
MEAN	5471		2006		1282.6		2042		5522		183.5	
± SD	502		372		488.4		313.5		492.9		29.6	

TABLE 6

F TABLES OF ONE-WAY ANALYSIS OF VARIANCE OF TRAINED AND UNTRAINED SUBJECTS' PULMONARY FUNCTION RECORD

CHARACTERISTIC	SOURCE	df	SS	MS	F
V.C.	B	1	110170.8	110170.8	.198 (NS)
	W	13	722332.6	555640.1	
	T	14	733492.4		
E.R.V.	B	1	110656	110656	.817 (NS)
	W	13	1759235	135325	
	T	14	1869891		
T.V.	B	1	28830	28830	.162 (NS)
	W	13	2306679	177436.8	
	T	14	2335509		
I.R.V.	B	1	185653.3	185653.3	.808 (NS)
	W	13	2986440	229726	
	T	14	3172093		
F.V.C.	B	1	247157.6	247157.6	.423 (NS)
	W	13	7598217	584478	
	T	14	7845374		
M.V.V.	B	1	9906.3	9906.3	8.14*
	W	13	15812.3	1216.3	
	T	14	25718.6		

TABLE 7

MEASUREMENTS OF MAX. $\dot{V}O_2$ AND ITS SUPPORTING VARIABLES DURING ANAEROBIC WORK FOR TRAINED AND UNTRAINED SUBJECTS

TRAINED	$\dot{V}_E$ STPD	$\dot{V}O_2$ L/MIN	$\dot{V}O_2$ ML/KG	R.Q.	END TIDAL PCO_2
DS	140.09	4.22	51.87	—	31.31
RM	137.99	4.48	53.89	1.11	26.65
DM	128.88	4.62	58.01	—	—
JR	143.06	4.37	65.35	1.16	31.07
BS	137.26	5.10	63.71	1.08	34.2
PR	148.08	4.22	49.88	1.23	31.18
JE	167.16	4.53	52.46	1.23	27.65
RT	143.48	4.37	55.92	1.05	26.53
SF	159.26	4.67	75.54	.97	21.96
BW	132.39	4.54	66.59	1.07	—
MEAN	143.77	4.51	59.36	1.11	28.82
SD	11.17	.24	7.75	8.44	3.61
CONTROLS					
DR	118.55	3.12	47.5	1.02	—
JC	103.31	3.07	46.0	1.18	—
BM	137.79	3.5	40.52	1.46	28.14
DM	110.94	3.61	46.44	1.14	30.45
RM	123.3	2.85	37.38	1.46	30.13
MEAN	118.78	3.23	43.57	1.25	29.57
SD	11.68	.28	3.92	.18	1.02

TABLE 8

F TABLES OF ONE-WAY ANALYSIS OF VARIANCE OF $\dot{V}_E$ L/MIN STPD, $\dot{V}o_2$ L/MIN, $\dot{V}o_2$ ML/KG, R.Q., AND END TIDAL PCO_2 FOR TRAINED AND UNTRAINED SUBJECTS DURING RELATIVE ANAEROBIC EXERCISE

PARAMETER	SOURCE	df	SS	MS	F
$\dot{V}_E$ L/MIN STPD	B	1	2081.33	2081.33	14.02**
	W	13	1929.48	148.42	
	T	14	4010.81		
$\dot{V}o_2$ L/MIN	B	1	5.478	5.478	71.59**
	W	13	.995	.0765	
	T	14	6.47		
$\dot{V}o_2$ ML/KG	B	1	831.50	831.50	15.94**
	W	13	677.87	52.14	
	T	14	1509.37		
R.Q.	B	1	.05987	.05987	3.06(N.S.)
	W	11	.215	.0195	
	T	12	.2749		
END TIDAL PCO_2	B	1	1.24	1.24	.104(N.S.)
	W	9	107.29	11.92	
	T	10	108.53		

** SIGNIFICANT AT THE 0.01 LEVEL

*** SIGNIFICANT AT THE 0.001 LEVEL

TABLE 9

MEASUREMENTS OF PRE-EXERCISE HEMOGLOBIN AND POST-EXERCISE BLOOD VARIABLES TAKEN 5 MINUTES AFTER COMPLETION OF A RELATIVE MAXIMUM WORK LOAD

ATHLETES	LACTATE	PYRUVATE	PH	Hb PRE-EX.
DS	87.3	2.14	—	15
RM	96.8	3.27	7.09	14.7
DM	129.2	4.11	—	15.4
JR	126.5	2.51	—	15.1
BS	86.4	2.41	—	15.1
PR	105.5	2.74	—	15
JE	144	1.13	7.027	16.2
RT	89	2.12	7.147	14
SF	116	1.33	7.075	15.7
BW	122.5	—	—	16.8
MEAN	110.32	2.42	7.085	15.3
SD	19.22	.86	.039	.744
CONTROLS				
DR	81.4	2.35	7.245	15
JC	69.1	1.86	7.201	15.7
BM	108.8	3.2	—	15.7
DM	81.6	2.13	—	—
RM	62.2	1.34	—	13.7
MEAN	80.62	2.18	7.225	15.02
SD	15.92	.61	.025	.82

The data of the two anaerobic tests were compared and showed the following reliability coefficients and standard error of estimates.

A correlation of .955 with a standard error of estimate of 3.31 ml kg^{-1} was found for the $\dot{V}o_2$ ml kg^{-1} measurement. Comparisons of post-exercise lactate and pyruvate values showed correlations of .78 and .80 with standard errors of estimates of 13.43 mg % and .42 mg % respectively. A correlation of .585 and standard error of estimate of .065 was calculated for post-exercise pH.

Since the intent of the study was to measure the ability to maximize blood lactate, the test results with the highest measured lactate were selected for further comparison. The values obtained are summarized in Tables 7 and 9.

One-way analysis of variance of the anaerobic test variables are summarized in Tables 8 and 10. Trained subjects were found to have significantly higher $\dot{V}o_2$ml kg^{-1} ($P < 0.01$), $\dot{V}o_2$ l. $min.^{-1}$, ($P < 0.01$) and $\dot{V}_E$ STPD ($P < 0.01$) than controls during the performance of their relative anaerobic work load. Trained subjects demonstrated significantly higher lactate ($P < 0.05$) and lower pH ($P < 0.05$) values than the untrained subjects. No significant differences were found in pre and post Hct, Hb, post-exercise venous serum pyruvate, RQ and end tidal PCO_2 measured during the last thirty seconds of the maximum workload.

Respiratory Response to Hypercapnia (Subproblem 2)

The determination of respiratory response to two levels of controlled hypercapnia at rest was repeated for all subjects. The order

TABLE 10

F TABLES OF ONE-WAY ANALYSIS OF VARIANCE OF PRE- AND POST-EXERCISE Hb AND Hct, AND POST-EXERCISE LACTATE, PYRUVATE AND pH DRAWN 5 MINUTES AFTER COMPLETION OF A RELATIVE MAXIMUM WORK LOAD FOR TRAINED AND UNTRAINED SUBJECTS

PARAMETER	SOURCE	df	SS	MS	F
LACTATE	B	1	2940.3	2940.3	7.7*
	W	13	4963.54	381.81	
	T	14	7903.84		
PYRUVATE	B	1	.1879	.1879	.26(N.S.)
	W	12	8.59	.7158	
	T	13	8.777		
pH	B	1	.0261	.0261	14.22*
	W	4	.007	.001	
	T	5	.0335		
PRE-EX. Hb	B	1	.21607	.21607	.32(N.S.)
	W	12	8.2075	.68395	
	T	13	8.42357		

TABLE 10(CON'T)

PARAMETER	SOURCE	df	SS	MS	F
POST-EX. Hb	B	1	.0472	.0472	.06
	W	11	8.929	.8117	
	T	12	8.976		
PRE-EX. Hct	B	1	.2440	.2440	.05
	W	12	56.79	4.733	
	T	13	57.03		
POST-EX. Hct	B	1	1.8349	1.835	.40
	W	12	55.02	4.5852	
	T	13	56.86		

* SIGNIFICANT AT THE 0.05 LEVEL

TABLE 11

DATA OF VENTILATORY RESPONSE TO 5% AND 7% CO_2

ATHLETES	5% CO_2			7% CO_2		
	P $\dot{V}_E$ BTPS	END TIDAL PCO_2 MM Hg ($PACO_2$)	$P\dot{V}_E/PaCO_2$	P $\dot{V}_E$ BTPS	END TIDAL PCO_2 MM Hg ($PACO_2$)	$P\dot{V}_E/PaCO_2$
DS	21.31	41.31	.516	58.4	54.9	1.064
RM	16.53	43.75	.378	31.29	55.39	.565
DM				50.41		
JR	25.4	40.99	.620	67.93	54.24	1.25
BS	22.04	40.64	.542	48.26	54.30	.889
PR	17.81	39.69	.449	58.8	53.32	.995
JE	25.4	48.02	.529	67.73	51.55	1.28
RT	37.39	44.30	.844	64.51	51.55	1.25
SF	26.27	47.19	.577	54.35	52.84	1.03
BW	28.98	42.72	.678	64.46	53.67	1.2
MEAN	24.57	43.18	.568	56.6	53.53	1.058
SD	6.3	2.9	.127	11.25	1.36	.216
CONTROLS						
DR	27.26	39.08	.698	78.08	50.77	1.54
JC	25.18	38.3	.657	77.31	50.02	1.55
BM	40.82	40.8	1.005	68.99	52.52	1.21
DM	25.8	44.07	.585	42.67	52.63	.811
RM	45.38	40.03	1.13	83.48	53.37	1.56
MEAN	32.88	40.5	.815	70.1	51.86	1.334
SD	9.5	2.2	.21	16.19	1.4	.293

of gases for test one was 5% CO_2, 21% O_2, balance N_2 followed by 7% CO_2 and was reversed for 11 subjects in test two. The average peak ventilatory response (P $\dot{V}_E$ l. min.$^{-1}$ BTPS) divided by end tidal PCO_2 or alveolar PCO_2 ($PACO_2$) of the 5% CO_2 treatment of test one and 7% CO_2 treatment of test two are listed in Table 11. Due to a calibration error, data for one of the reversed athletes had to be excluded. The P $\dot{V}_E$ l. min.$^{-1}$ BTPS/$PACO_2$ measurements of the two tests were analyzed for reliability coefficients. With the order of gases reversed (5-7, 7-5) a correlation of .36 with a standard error of estimate of .021 was shown for the 5% CO_2 treatments. The mean response of .671 $\pm$ .288 for test one and .803 $\pm$ .223 for test two suggested that the initial exposure to 7% CO_2 in test two may have inflated the 5% CO_2 response. A weighted t test however failed to reveal a significant difference between the mean ventilatory response of the two 5% CO_2 treatments. Comparison of the four subjects whose order of gases was not reversed revealed a correlation of .98 and a standard error of 0.023. Since the responses to 5% CO_2 of test one were void of any possible influence of 7% CO_2, they were selected for further comparisons.

The reliability coefficients of the 7% CO_2 treatments were .85 with a standard error of estimate of .17 when the gases were reversed and .84 and .08 respectively when the gases were not reversed. When the four P $\dot{V}_E$ l. min.$^{-1}$ BTPS/$PACO_2$ values for the three non-reversed subjects were added to those of the reversed subjects a correlation of .86 with a standard error of .17 was found. Comparison of the reversed and non-reserved mean values of 1.074 $\pm$ .265 and 1.45 $\pm$ .153 respectively did not demonstrate significant differences. Since the 7% CO_2 treatment

TABLE 12

GROUP MEAN, STANDARD DEVIATIONS AND t VALUES FOR 5% CO_2 AND 7% CO_2 TREATMENTS FOR TEST 1 AND TEST 2

VARIABLE	TEST 1	TEST 2	*t VALUE
5% CO_2	.65 $\pm$ .20	.77 $\pm$ .22	-2.0
7% CO_2	1.16 $\pm$ .29	1.196 $\pm$ .33	-.85

* The t values required for significance at the 0.05 and 0.01 levels, with 13 degrees of freedom, were 1.77 and 2.65 respectively.

TABLE 13

F TABLE OF ONE-WAY ANALYSIS OF VARIANCE WITH REPEATED MEASURES OF TRAINED SUBJECTS' VENTILATORY RESPONSE TO APPROXIMATELY 5%. AND 7% CO_2 NORMOXIC AIR (REMAINDER N_2) AT REST

SOURCE	df	SS	MS	F
BETWEEN SUBJECTS				
R	8	.458	5.73	
WITHIN SUBJECTS				
T	1	1.08	1.08	80.46***
TR	8	.107	.013	

*** SIGNIFICANT AT THE 0.001 LEVEL

TABLE 14

F TABLE OF ONE-WAY ANALYSIS OF VARIANCE WITH REPEATED MEASURE OF UNTRAINED SUBJECTS' VENTILATORY RESPONSE TO APPROXIMATELY 5% AND 7% CO_2 NORMOXIC AIR (REMAINDER N_2) AT REST

SOURCE	df	SS	MS	F
BETWEEN SUBJECTS				
R	4	.436	.109	
WITHIN SUBJECTS				
T	1	.726	.726	11.23*
TR	4	.258	.065	

* SIGNIFICANT AT THE .05 LEVEL

TABLE 15

F TABLE OF ONE-WAY ANALYSIS OF VARIANCE FOR TRAINED AND UNTRAINED SUBJECTS VENTILATORY RESPONSE TO APPROXIMATELY 5% CO_2 NORMOXIC AIR (REMAINDER N_2) AT REST

SOURCE	df	SS	MS	F
B	1	.1959	.1959	6.3*
W	12	.3731	.0310	
T	13	.5691		

* SIGNIFICANT AT THE 0.05 LEVEL

TABLE 16

F TABLE OF ONE-WAY ANALYSIS OF VARIANCE FOR TRAINED AND UNTRAINED SUBJECTS VENTILATORY RESPONSE TO APPROXIMATELY 7% CO_2 NORMOXIC AIR (REMAINDER N_2) AT REST

SOURCE	df	SS	MS	F
B	1	.2446	.2446	3.46(N.S.)
W	12	.8496	.0708	
T	13			

of test two was void of any possible influence of 5% CO_2, these response values were selected for further comparisons. The four non-reversed subjects were included in further comparisons since a weighted t test failed to reveal significance between the reversed and non-reversed 7% P $\dot{V}_E$ l. min.$^{-1}$ BTPS/$PACO_2$ mean values. A summary of group means, standard deviations and t values for 5% CO_2 and 7% CO_2 treatments for test one and two are summarized in Table 12.

A summary of one-way analysis of variance with repeated measures of the athletes and controls ventilatory response to two levels of hypercapnia is presented in Tables 13 and 14. The athletes' response was found to be significantly greater $P < 0.001$, for the 7% CO_2 treatment. A similar significant difference ($P < 0.05$) was shown for the controls. One-way analysis of variance comparison between the trained and untrained subjects' response to hypercapnia shows that trained subjects have a significantly decreased response to 5% CO_2 ($P < 0.05$). However, a significantly decreased response was not demonstrated for the 7% CO_2 treatment (Tables 15 and 16).

Relationship of Ventilatory Response to Hypercapnia and Elevation of Venous Serum Lactate During Exhaustive Work (Subproblem 3)

The relationship of ventilatory response to controlled hypercapnia at rest and elevated exercise lactate levels are summarized in figures 2 and 3. Initial graphical analysis suggested a possible relationship. However statistical analysis failed to support this

Figure 2 Relationship of Ventilatory Response to 7% CO_2 and Elevated Venous Serum Lactate Following Exhaustive Exercise

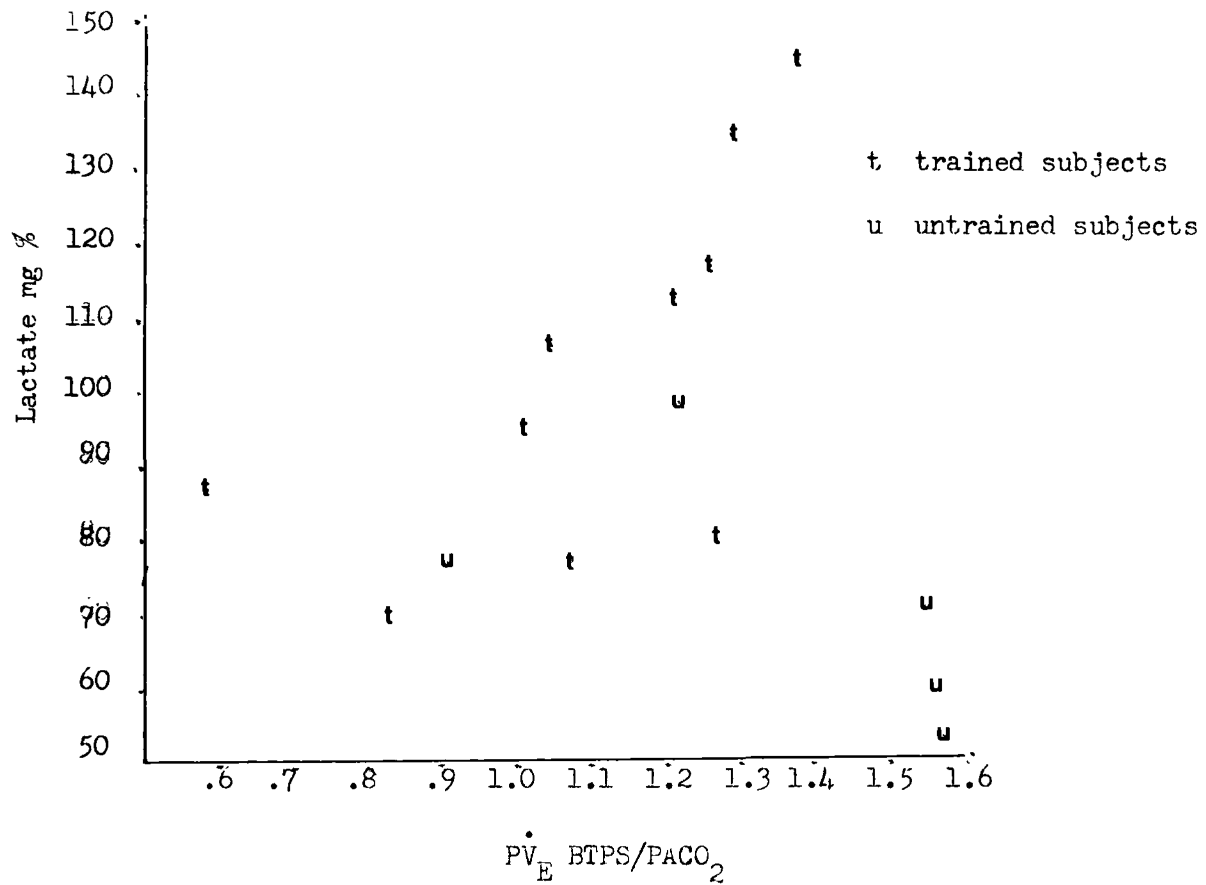
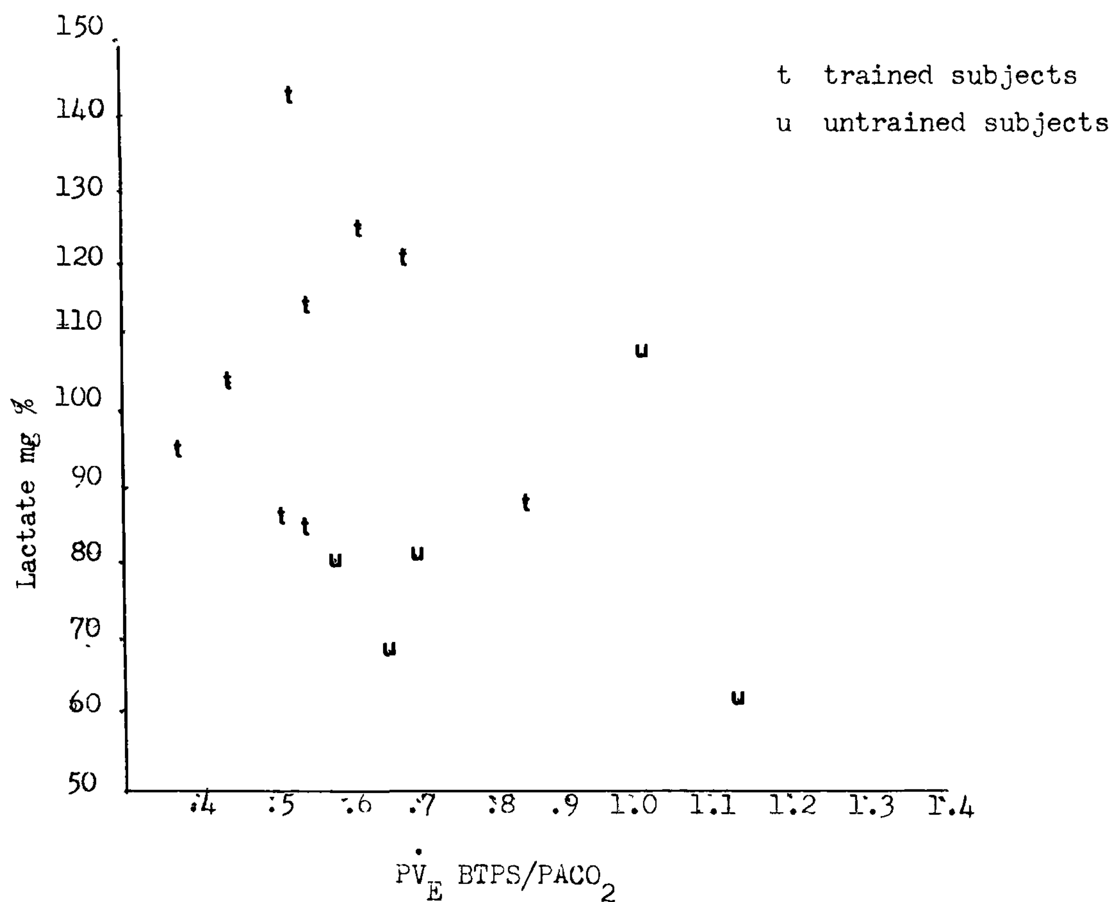


Figure 3 Relationship of Ventilatory Response to 5% CO_2 and Elevated Venous Serum Lactate following Exhaustive Exercise



observation. A correlation of -.18 with a standard error of estimate of 22.83 mg% and a correlation of -.33 with a standard error of estimate of 21.92 mg% was established for 7% and 5% response and peak lactate levels respectively.

CHAPTER V

DISCUSSION

Introduction

The discussion of results describing the relationship between ventilatory response to controlled hypercapnia at rest and the ability to maximize levels of venous serum lactate during exhaustive exercise is presented under the two major headings which were introduced in the previous chapter. The first section will discuss the results of the screening session. In the second section, a discussion of the data of the experimental session is presented.

Screening Session

Physical Characteristics

The trained and untrained groups were homogeneous with respect to their gross physical characteristics as shown by a lack of statistical significance (0.05) in age, height, weight or body surface area.

Maximum Oxygen Consumption

Mean values of 66.04 ml kg^{-1} and 42.8 ml kg^{-1} for the trained and untrained groups respectively adequately fulfilled the criteria for participation (trained $<$ 55 ml $kg^{-1} min.^{-1}$; untrained $>$ 47 ml kg^{-1} min^{-1}). Significant differences shown for $\dot{V}_E$ l. $min.^{-1}$, $\dot{V}o_2$ l. $min.^{-1}$ and $\dot{V}o_2$ ml kg^{-1} measurements was therefore to be expected between the two groups. The reliability of .94 for $\dot{V}o_2$ ml kg^{-1} is within the range reported by Rowell (1974).

Pulmonary Function

The results of the pulmonary function tests show that all subjects were within the normal range for vital capacity, expiratory reserve volume, tidal volume, inspiratory reserve volume, forced vital capacity and maximum voluntary ventilation (Baldwin et al. 1948, Needham et al. 1954). Therefore, these results together with the absence of a reported history of respiratory disease suggests that it is unlikely that the subjects suffered any physical obstruction of the airway passages which has been shown to decrease respiratory response to hypercapnia (Cherniack 1965, Clark 1968, Tenny 1964).

Analysis of variance shows that trained and untrained subjects did not vary significantly in vital capacity or its subdivisions even though mean values appeared slightly higher in the trained group in all but expiratory reserve volume. These differences may be expected since training, especially during adolescence, has been suggested to improve both vital capacity and total lung capacity because of its effects on the dynamics of pulmonary function (Sharkey 1975).

One-way analysis of variance demonstrates that the two groups differed significantly in maximal voluntary ventilatory capacity (MVV) ($P < 0.05$). The significantly enhanced ability of the breathing apparatus to pump air is probably due to trained respiratory musculature in the trained subject since all subjects of the study were of about the same age, non-smokers and free from disease (Sharkey 1975).

Experimental Session

Capacity to Maximize Serum Lactate (Subproblem 1)

The results of the study indicated that athletes possess

significantly higher peak serum venous lactate levels ($P < 0.05$) and lower pH levels ($P < 0.05$) than non-athletes following performance of a maximum work load (100% Max. $\dot{V}o_2$). This capacity was demonstrated despite the fact that athletes also displayed an enhanced aerobic capacity ($\dot{V}o_2$ ml kg^{-1}, ($P < 0.01$)) and no significant difference in Hct, in blood buffering as judged by total Hb ($P > 0.05$) or acidotically induced $PACO_2$ reduction as indicated by end tidal PCO_2 ($P > 0.05$).

These results are in accordance with observations of other investigators that training produces the potential for the development of higher maximum lactate levels (Saltin and Karlsson 1971, Cunningham and Faulkner 1969). Moreover it has also been reported that athletes demonstrate higher maximum lactate levels when compared to sedentary subjects (Karlsson 1971b, Astrand 1970). These observations seem true even though it has been demonstrated that endurance training induces metabolic changes which hinder or delay lactate production (Mole et al. 1973, Hoppeler et al. 1973, Fitts et al. 1975) and enhance lactate uptake (Gollnick et al. 1973a, Karlsson et al. 1975) during exercise. Consequently these groups seem to be demonstrating normal adaptational response to anaerobic exercise in accordance with their conditioning levels.

The mechanisms which enable the athlete to attain higher maximum lactate are not clear and are beyond the scope of this study. However, Karlsson et al. (1975) report that strength training increases M-type LDH activity which would enhance the velocity of lactate production (Jorfeldt 1970). It seems more than coincidental then, that all of the trained subjects in this study were currently engaged in strength training.

Lactate production is dependant upon the availability of glycogen and the activity level of glycolytic enzymes both of which have

been shown to increase with training (Assmussen et al. 1974, Eriksson et al. 1973, Baldwin et al. 1972). Therefore an increase in glycogen and glycolytic enzymes appear to be the major source of elevated peak lactates in the athletes.

In addition to possible increases of substrate and enzyme activity, the higher lactate levels in trained subjects ($P < 0.05$) may also be due to increased compensatory mechanisms or decreased sensitivity to acidemic stress.

The results of the study indicate that respiratory compensation as indicated by end tidal PCO_2 at the end of exercise was slightly greater in ahtletes but not significantly so ($P > 0.05$). The increased capacity to decrease end tidal PCO_2 (alveolar PCO_2) may be due in part to the higher level of MVV ($P < 0.05$). This would explain the insignificant trend by the trained subjects to employ respiratory compensation for their significantly higher metabolic acidosis.

Total hemoglobin, (Hb), the major blood buffer protein was not found to be significantly different between groups. This fact supports observations by Keul et al. (1972) who report that training apparently does not increase blood bicarbonate levels or blood buffering capacity. Furthermore, it is unlikely that the kidney has the time or blood volume to compensate for acidosis significantly during maximum work (Wexler and Kau 1970). Moreover, increased lactate uptake and alanine production (Mole et al. 1973) would only tend to lower lactate levels and make any differences seen here even smaller.

The lack of significant differences in compensatory mechanisms responding to acidemic stress in the face of significantly

higher lactate levels ($P < 0.05$) and lower pH ($P < 0.05$) in trained subjects provides an indication of a decreased sensitivity and/or enhanced tolerability to metabolic acidosis during exercise.

Respiratory Response to Hypercapnia (Subproblem 2)

A significantly greater respiratory response to a 7% CO_2 challenge than to a 5% CO_2 challenge occured in both trained ($P < 0.01$) and untrained subjects ($P < 0.05$). Trained subjects also demonstrated a significantly lower ventilatory response ($P < 0.05$) than controls for the 5% CO_2 concentration. This observation is corroborated by the results of Byrne-Quinn et al. (1971) who show that hypercapnic ventilatory drive as measured by the slope of the isoxic $\dot{V}_E$-$PACO_2$ lines was reduced in athletes to 47% of controls ($P < 0.01$). In light of this observation they suggested a decreased peripheral chemoreceptive hypercapnic drive in athletes. That the observed decrease in hypercapnic drive is of peripheral origin is further suggested by Sorensen and Cruz (1969) who showed evidence of a decreased response in high-altitude natives with a single breath of carbon dioxide.

Trained subjects demonstrated a lower but non-significant decreased response to hypercapnia at the 7% CO_2 concentration ($P > 0.05$). This observation appears to be in opposition to the results of Schaefer et al. (1958) who observed significant differences between low responders and higher responders at both 5.4% and 7.5% CO_2 concentrations. However the classification of the 65 normal subjects of their study was done arbitrarily. Subjects who responded with an increase in respiratory minute volume less than four times the resting volume while breathing 5.4% CO_2 and less than six times the basic volume on air for 7.5 were placed in the low responding group. Such exclusive criteria for low responders

may have potentiated statistically significant differences between their two groups for response to 7.5% CO_2.

The subjects of the present study were not classified on a criteria of response to various CO_2 concentrations but on athletic success and degree of fitness as indicated by $\dot{V}o_2$ ml kg^{-1}. Although such a classification generally resulted in the lowest responders being classified with the trained group and the highest responders being allocated to the untrained group, it was not universally the case. Subject RT of the trained group was a relatively high responder and DM of the untrained group was a relatively low responder. That this condition can exist has also been indicated by Rebuck and Read (1971). These authors report consistant differences between highly trained distance runners who were low responders and sprinters who had a high response to hypercapnia.

It is possible, therefore, that the different criteria used to establish participation in the experimental and control group by Shaeffer et al. may explain the variations of results at 7% CO_2 concentrations in the present study.

The different criteria of participation however does not explain the observation of athletes demonstrating a significantly decreased response for the 5% CO_2 but not for the 7% CO_2 gas mixture. It is also beyond the scope of the present study to establish the cause-effect relationship of this observation. But it is difficult not to hypothesize a tentative explanation through the following rationale.

The removal of the peripheral chemoreceptors in man has been shown to decrease approximately 30% of the overall response to hypercapnia (Lugliani 1971, Edelman et al. 1973). The contribution by

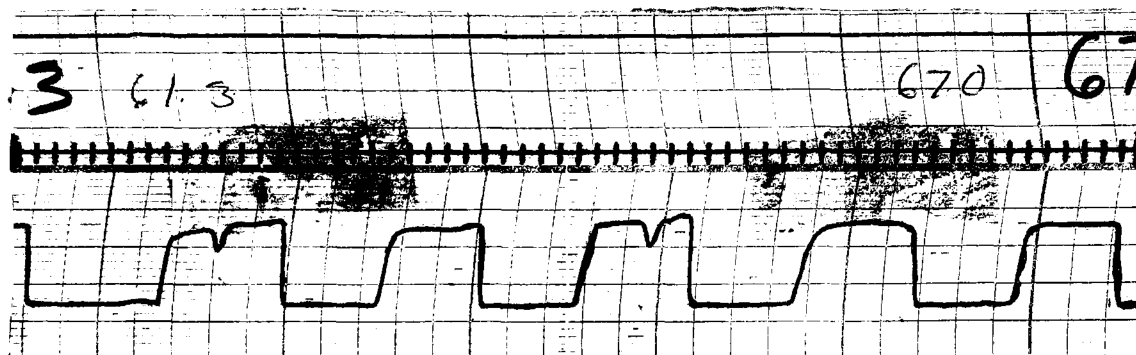
central chemoreceptors can therefore be estimated at approximately 70%. It has also been pointed out that in absence of peripheral chemoreceptors, the breathing pattern is characterized by a decrease of frequency and increase of amplitude under hypercapnic conditions (Von Euler et al. 1970, Lahiri et al. 1975). Rosentein et al. (1974) concluded that the influence of the arterial chemoreceptors was exercised predominantly if not totally through modulating the effects of CO_2 on the control of tidal volume. In addition Byrne-Quinn et al. (1971) suggest that the observed decrease in ventilatory response to hypercapnia in athletes is due to a decrease in peripheral chemosensitivity. This leads to the observation that the breathing pattern of a low responding athlete should be characterized by a decrease in frequency and increase in amplitude. Examination of the breathing pattern of an athlete and sedentary subject indicates that this is apparently the case (Figure #4).

A decrease in peripheral chemosensitivity resulting in a decrease of total ventilation would tend to increase the PCO_2 in the alveoli and arterial blood and consequently in the environment of the central chemoreceptors. The increase in $PaCO_2$ would therefore result in greater central chemoreceptor stimulation which would manifest itself by a greater amplitude in the breathing pattern. This process would tend to increase linearly with increasing PCO_2.

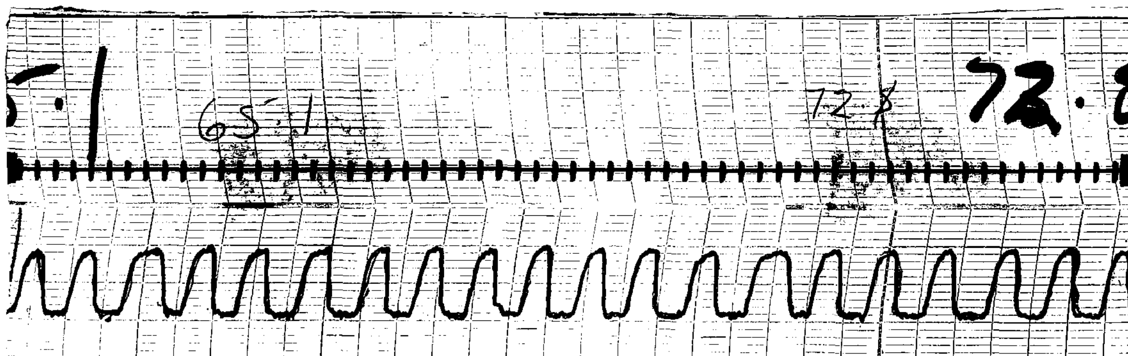
The peripheral chemoreceptors are not the only source of modulation affecting the control of tidal volume. Mechanoreceptors in the lungs also influence the time for inspiration (Dejours 1966).

Figure 4 Breathing Pattern of an Athlete or Low Responder and Sedentary or High Responder to the 5% CO_2 Treatment. The athlete, R.M., is characterized by an increase in amplitude and decrease in frequency as compared to the untrained subject, D.M.

Athlete, R.M.



Sedentary, D.M.



The larger the lung volume the greater the number of mechanoreceptors that are excited and the greater the frequency of afferent impulses (Dejours 1966). Therefore, the effect of increased lung volume, mediated through the mechanoreceptor afferrents might tend to stabilize amplitude through their inhibitory effect on inspiration and therefore generate higher frequency. If this were true, the effects of an increased peripheral mechanoreceptor input would result in an increase in overall ventilation.

Therefore it is tentatively suggested that the greater increase in CO_2 body stores while breathing 7% CO_2 would result in an even greater dominance of central drive in the athlete. The increased central drive would manifest itself by an increase in breathing amplitude or lung volume. The consequence of an increase in lung volume would be a proportionally greater discharge of mechanoreceptor afferent impulses which would tend to stabilize amplitude through an increase in frequency. The addition of a proportionately greater increase in central drive in the athlete, due to a decreased peripheral chemosensitivity, while breathing the 7% CO_2 concentration might therefore mask the significantly lower response to hypercapnia observed at the five percent concentration.

Relationship of Ventilatory Response to Hypercapnia and Elevation of Venous Serum Lactate During Exhaustive Work (Subproblem 3)

Statistical analysis failed to support the hypothesis of a relationship between respiratory response to controlled hypercapnia at rest and the capacity to maximize venous serum lactate during exhaustive work. The low correlations of -.18 with a standard error of estimate of 22.83 mg% and -.33 and 21.92 mg% respectively for 7% and 5% CO_2 treatments

with maximum exercise lactate levels did not provide for the development of predictive indices of glycolytic potential from hypercapnic sensitivity response.

Failure to demonstrate this relationship may be due to the fact that hypercapnia or respiratory acidosis is manifested mainly through a central chemoreceptor response (Sorensen 1970). The central chemoreceptor output is believed to be responsible for approximately 70% of the ventilatory response to hypercapnia in man (Edelman et al. 1973). On the other hand lactacidosis or the concomittant decrease in pH is believed to exert its influence mainly if not entirely on the peripheral chemoreceptors (Sorensen 1970, Leusen 1972).

Since any variation in chemosensitivity to hypercapnia is believed to be at the peripheral level (Byrne-Quinn et al. 1971) the inability to demonstrate a relationship between a decreased sensitivity to hypercapnia (respiratory acidosis) with a decreased sensitivity to lactacidosis (metabolic acidosis) may be due to the dominant central chemoreceptor participation in the ventilatory response to hypercapnia. In fact, this lack of relationship might be considered as partial documentation of the observations of Byrne-Quinn et al. (1971) at least to the extent that it does not antagonize their conclusions.

CHAPTER VI

SUMMARY, CONCLUSIONS AND RECOMMENDATIONS

Summary

This study was designed to examine the relationship between respiratory response to controlled hypercapnia at rest and the capacity to maximize venous serum lactate during exhaustive work. There were three subproblems in the study: 1. To establish if the athlete can contract significantly higher venous serum lactate during a relative maximum work load. 2. To establish if the athlete demonstrates a significant decrease in respiratory response to controlled hypercapnia at rest. 3. To develop predictive indices of lactate potential from hypercaphic sensitivity response.

It was assumed that since both an elevation of arterial CO_2 and lactate will induce a decrease in pH and a resultant increase in ventilation, hypercapnic response could be qualitatively compared with lactate accumulation during maximum exercise.

Fifteen subjects, ten of whom were trained athletes and five of whom were healthy untrained subjects as assessed by maximum oxygen consumption and athletic participation served respectively as members of trained and untrained groups. Each subject was exposed to two testing conditions. The first condition served to screen subjects on the basis of pulmonary function and maximum oxygen consumption in order to assure adequate categorization into trained and untrained groups. The Max. $\dot{V}o_2$ test also served to establish each subject's maximum voluntary work capacity (100% Max. $\dot{V}o_2$), for the purpose of establishing the load to be used in

the subsequent condition.

The second condition was designed to: 1. evaluate ventilatory response to hypercapnia and 2. determine each subject's ability to develop maximum levels of venous serum lactate through exhaustive exercise. Resting and hypercapnic response data were recorded for the following variables: HR, Bf, $\dot{V}_E$, TV, alveolar PCO_2 and Peak $\dot{V}_E$ $PACO_2$ mm hg. For the exhaustive work load, resting exercise and recovery data were measured for the following variables, $\dot{V}o_2$, $\dot{V}_E CO_2$, $\dot{V}_E$, HR, Bf and resting and recovery data for RQ, end tidal PCO_2, lactate pyruvate , pH, Hb, red and white blood cell count and Hct.

Group means and standard deviations were calculated for each variable. Analysis of variance was used to compare trained and untrained subjects with respect to maximum oxygen consumption static and dynamic lung volumes, post-exercise blood variables RQ and end tidal PCO_2 at the end of anaerobic work. One-way analysis of variance with repeated measures was used to determine group differences in ventilatory response to two levels of hypercapnia. Weighted t tests were used to determine if significant differences existed between scores of repeated tests and correlation coefficients were used to establish the degree of reliability in oxygen consumption and ventilatory test scores.

Athletes demonstrated significantly higher peak venous lactates ($P < 0.05$) and lower pH ($P < 0.05$) following performance of a relative maximum work load. The possibility of explaining these differences in lactate and pH values on the basis of an enhanced glycolytic capacity and/or tolerability for lactacidosis was discussed.

No significant differences were found in total Hb and end tidal

PCO_2 at the end of exercise. It was therefore suggested that the two groups did not differ in blood buffering capacity or respiratory compensation for incurred lactacidosis.

In the determination of hypercapnic sensitivity trained subjects had a significantly lower response when breathing 5% CO_2 in inspired air. The trained group mean response showed an insignificant trend to a lower hypercapnic drive under condition of 7% CO_2 in inspired air. It was suggested that a more dominant central drive at the 7% CO_2 concentration in the trained subject could result in an increase in mechanoreceptor afferent impulses which would tend to mask out the decreased peripheral chemosensitivity suggested to be the cause of the significant decreased ventilatory response at the 5% CO_2 exposure.

Graphic analysis pointed to a relationship between respiratory response to hypercapnia and peak lactate levels during exhaustive work. However, statistical analysis failed to support this relationship.

Conclusions

Within the scope and limitations of this study, the following may be concluded.

1. Trained subjects have an enhanced capacity to elevate venous serum lactate during maximum work (100% Max. $\dot{V}o_2$) and therefore possess either or both an enhanced glycolytic potential and higher tolerability for metabolic acidosis.

2. Trained subjects, within limits, demonstrate a significantly decreased sensitivity to respiratory acidosis as determined through test of hypercapnic drive.

3. Hypercapnic response fails to adequately predict glycolytic potential or tolerability for lactacidosis.

Recommendations

There is need for further investigation into the effects of training on respiratory response to hypercapnia. Although some evidence exists that a decreased response to hypercapnia is a characteristic of trained subjects, it has yet to be established if this characteristic is induced through training.

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APPENDIX A

RESPIRATORY CALCULATIONS

1A Respiratory Metabolism: Calculations
(Consolazio 1963)

Pulmonary Ventilation

Pulmonary or minute ventilation is expressed as liters of air expired per minute, the volume of gas being reduced to standard temperature and pressure $0^{o}C$ and 760 mm Hg, dry. The formula is

$$\frac{P_B - P_{H_2o}}{760\ (1 + 0.00367T)}$$

where P_B = ambient barometric pressure
P_{H_2o} = the vapor tension of water, mm Hg, at the temperature of the gasometer
T = the temperature of the gasometer ^{o}C

Oxygen Consumption and Carbon Dioxide Elimination

The volume of inspired air may be calculated from the expired air by the formula

(1) $\dot{V}$ inspired = V expired x $\frac{\%\ N_2 \text{ in expired air}}{79.04}$

The total volume of oxygen inspired (not all consumed) is then

(2) $\dot{V}o_2$ inspired = V air inspired $\frac{\%\ O_2 \text{ of inspired air}}{100}$

The percentage of oxygen in outdoor air is 20193; hence,

(3) $\dot{V}o_2$ inspired = $\dot{V}$ air inspired x $\frac{20.93}{100}$

The volume of oxygen expired (amount not consumed) is

(4) $\dot{V}o_2$ expired = $\frac{\%\ O_2 \text{ in expired air}}{100}$ x V air expired

The amount of oxygen consumed is

$$(5)\quad \dot{V}o_2 \text{ consumed} = \dot{V}o_2 \text{ inspired} - \dot{V}o_2 \text{ expired}$$

Substituting values from Eqs. (3) and (4),

$$\dot{V}o_2 \text{ consumed} = \dot{V} \text{ air inspired} \times \frac{20.93}{100} - V \text{ air expired} \times \frac{\%\ O_2 \text{ in expired air}}{100}$$

Substituting values from Eqs. (1),

$$\dot{V}o_2 \text{ consumed} = \dot{V} \text{ air expired} \times \frac{\%\ N_2 \text{ in expired air}}{79.04} \times \frac{20.93}{100}$$
$$- \dot{V} \text{ air expired} \times \frac{\%\ O_2 \text{ in inspired air}}{100}$$

Simplifying,

$$(6)\quad \dot{V}o_2 \text{ consumed} = \frac{\dot{V} \text{ air expired}}{100} \quad (N_2 \text{ in expired air} \times 0.265$$
$$- \%\ O_2 \text{ in expired air})$$

The factor ($\%\ N_2$ in expired air x 0.265 - $\%\ O_2$ in expired air) is the true oxygen, the number by which the volume of expired air (divided by 100) is multiplied to give the oxygen consumption. Using a formula similar to that for the derivation of oxygen consumption, the carbon dioxide expired becomes

$$Vco_2 \text{ expired} = \frac{\dot{V} \text{ air expired}}{100} \times (\ \%\ CO_2 \text{ in expired air}$$
$$- \frac{\%\ N_2 \text{ in expired air}}{79.04} \times \%\ CO_2 \text{ in inspired air})$$

When one uses outdoor air, this becomes

$$\dot{V}co_2 \text{ expired} = \frac{\dot{V} \text{ air expired}}{100} \quad (\%\ CO_2 \text{ in expired air} - 0.03)$$

The factor ($\%\ CO_2$ in expired air - 0.03) is the true carbon dioxide, the number by which the volume of expired air (divided by 100) is multiplied to give the carbon dioxide production.

Hence, the oxygen consumption in liters per minute is expressed as

$$\dot{V}o_2 \text{ (l./min.)} = \frac{\dot{V} \text{ gas (l./min.)}}{100} \times \text{ true } O_2$$

The carbon dioxide elimination in liters per minute is expressed as

$$\dot{V}_E Co_2 \text{ (l./min.)} = \frac{\dot{V} \text{ gas (l./min.)}}{100} \times \text{ true } Co_2$$

1B Hypercapnic Sensitivity: Calculations

Hypercapnic sensitivity is expressed as the ratio of variation of ventilation to variation in $PaCo_2$,

$$(\dot{V}_E \text{ BTPS}/PaCo_2 \text{ mm Hg})$$

$\dot{V}_E$ BTPS is calculated by selecting the highest repeatable $\dot{V}_E$ during each 15 minute hypercapnic test. This calculated volume is then corrected to BTPS

$PaCo_2$ mm Hg

The known Co_2 inspired air (tanks calibrated via Scholander Technique) = X cm deflection

$$\text{Therefore } Co_2 \text{ factors} = \frac{Co_2 \text{ inspired air}}{\text{X cm deflection}}$$

End tidal Co_2 = Y cm deflection

Therefore Co_2 factor x Y cm = End Tidal Co_2

End tidal PCo_2 = BP - 47 (water vapor) x end tidal Co_2

APPENDIX B

METHOD OF BLOOD ANALYSIS

Method of Lactate Analysis

Biochemica Test Combination
Cat. No.: 15972 TLAA

Preparation of solutions

1. Dilute solution in bottle 1 with redist. water and make up to 75 ml. Stable for one year at room temperature.

2. Dissolve contents of bottle 2 in 7 ml. redist. water. Stable for four weeks at approx. +4°C.

3. Use suspension in bottle 3 undiluted. Stable for one year at approx. +4°C.

In addition

Perchloric acid, approx. 0.6 N, Cat.-No.: 15902 TYAG or dilute 5.15ml. 70% (6.5 ml. 60%) perchloric acid with redist. water and make up to 100 ml.

Concentration of solutions:

1. 0.5 M glucine buffer, pH 9.0; 0.4 M hydrazine

2. 27 mM NAD

3. 2 mg. LDH/ml.

Deproteinisation

Pipette into 10 ml. centrifuge tube:

perchloric acid, ice-cold	1.0 ml.
blood (taken from the vein without stasis)	0.5 ml.

Mix well, centrifuge for 10 min. at approx. 3000 r.p.m.

Spectrophotometric measurements

Wavelength: 366, 340 or 334 nm
Glass cuvette: 1 cm. light path
Temperature: 25°C.

Measure agsinst air. One blank is sufficient for each series of determinations.

Pipette into test tubes:

	blank	sample
solution 1	2.00 ml.	2.00 ml.
supernatant fluid	--	0.20 ml.
perchloric acid	0.20 ml.	--
solution 2	0.20 ml.	0.20 ml.
suspension 3	0.02 ml.	0.02 ml.

Mix, incubate in water bath at 25°C for exactly 1 hour. Pour into cuvette, read optical densities of the sample (E_s) and the blank (E_b) against air.

$$E_s - E_b = \Delta E.$$

Please note

By using a quarter or half of the volumes given in the pipetting scheme, micro assays can be performed. The calculation factor remains the same.

In case the final volume used in the macro assay is not sufficient to fill the cuvette, take 3.0 ml. of solution1, 0.3 ml. of the supernatant fluid (or perchloric acid), 0.3 ml. of solution 2, and 0.03 ml. of suspension 3.

Controls can be prepared with 1 N l-lactate (Lactate calibration solution, Cat. No.: 15672 TYAK which is available together with instructions on request, free of charge). A 1:2000 dilution of this 1 N solution will give a solution of 9 ug. l-lactate/0.2 ml.

Method of Pyruvate Analysis

Biochemica Test Combination
Boehringer Mannheim

Solutions:

Perchloric acid 1.0 N (ice-cold)
Solution #1 0.7 M tripotassium phosphate
Solution #2 2.5 mM NADH
Solution #3 2 mg LDH/ml.

Deproteinisation:

Pipette 4.0 ml perchloric acid into test tube
Add 4.0 ml blood, cover and shake well
Centrifuge for 10 minutes
With Pasteur pipet aspirate supernatant fluid, transfer into clean test tube and centrifuge 5 minutes
Transfer clear supernatant into test tube (at this point supernatant can be frozen)

Analysis:

Pipette exactly 4.0 ml supernatant into test tube
Add 2.0 ml sol. #1
Mix, stand in ice bath for 10 min., filter. Allow filtrate to warm to approx. 25° C

Pipette into cuvette:

Filtrate	2.0 ml
Sol. #2	0.20 ml

Mix with plastic spatula, with spectro set at 366 nm, read transmittance t,
add sol. #3 0.02 ml
Mix and wait approx. 5 min., until reaction is completed,
Read transmittance t_2

Calculation:

Convert transmittance in optical density using chart
$O.D_1 - O.D_2 \times 8.21$ = mg pyruvate/ 100 ml blood
Normal values in venous fasting blood: 0.36 - 0.59 mg/100 ml

Determination of pH

Equipment: Corning pH Blood Gas Analyzer 165

Method:

1. Connect micro sampling adaptor to the sample chamber and insert catheter tubing.

2. Dip the tubing into the vacutainer tube of blood

3. Draw in sample by rotating the micro-sample wheel

4. Record reading when button light stops flashing

Sample size: Nominal 200 ul
Minimum 125 ul

Determination of Hemoglobin by Cyanmethemoglobin Method

Materials:

1. Hycel Cyanmethemoglobin Standard

2. Hycel Cyanmethemoglobin Reagent

3. Sahli pipettes of capacity 0.02 ml

4. Cuvettes

5. Spectrophotometer (set wavelength at 540 mu)

Method:

1. Preparation of Cyanmethemoglobin

2. Preparation of Standard curve
   Note: use dilutions for 5.0 ml; draw graph with optical density vs gm % of hemoglobin

Determination of Hemoglobin:

1. Into a blank test tube, pipet 5.0 ml of Reagent

2. Into the sample test tube, pipet 5.0 ml of Reagent

3. Using a 0.02 ml Sahli pipet, deliver 0.02 ml venous blood into the sample test tube

4. Rinse pipet several times with the diluted blood

5. Mix well and allow test tube to stand for 10 minutes
6. Set spectrophotometer at 540 mu
7. Transfer solutions from test tubes to cuvettes
8. Read %T against blank
9. Convert readings to optical density (O.D.)
10. Read the mg% of hemoglobin from standard curve

Principle:

Ferricyanide converts hemoglobin iron from ferrous to the ferric state to form methemoglobin in an alkaline solution. Methemoglobin then combines with potassium cyanide to produce the stable pigment, cyanmethemoglobin.

Normal values:	Males	12-17 mg%
	Females	11-15 mg%

Determination of Hematocrit

Materials:

1. Plain capillary tubes (75 mm length)
2. Adams Autocrit Centrifuge
3. Tube sealer

Method:

1. Fill two capillary tubes with whole venous blood (up to $\frac{3}{4}$ of the length of the tube)
2. Seal one end of the tube with tube sealer
3. Place the tube in the centrifuge with sealed end facing outside
4. Balance the tube by placing the second tube in the opposite position
5. Centrifuge for 5 minutes
6. Read the % of hematocrit using the scale in the centrifuge

Normal values:	Males	40-54%
	Females	37-47%

APPENDIX C

STATISTICAL FORMULAE

F ratios, analysis of variance with repeated measures and t tests were computed with the use of an IBM, APL computer terminal.

F test

The observations for a given variable were arranged as follows:

Subject	Test I	Test II
1	X1I	X1II
2	X2I	X2II
3		
4		
5		
.		
.		X_{ij}
.		
Mean		

Where X_{ij} signifies a score in row i and column j.

F Test Analysis Table

Calculations were based on the following formulae:

Source	Sum of Squares (SS)	Degrees of freedom (df)	Mean Square	F Ratio
Treatments (between groups)	$\sum \frac{(\sum_i X_{ij})^2}{n_j} - \frac{(\sum_j \sum_i X_{ij})^2}{N}$	J-1	$\frac{SSbetween}{J-1}$	$\frac{MSbetween}{MSwithin}$
Error (within groups)	$\sum_j \sum_i X^2_{ij} - \sum \frac{(\sum_i X_{ij})^2}{n_j}$	N-J	$\frac{SS\ within}{N-J}$	
Totals	$\sum_j \sum_i X^2_{ij} - \frac{(\sum_j \sum_i X_{ij})^2}{N}$	N-1		

Analysis of Variance with Repeated Measures

Total variance is partitioned into "between persons" and "within persons" variance. If persons are represented by r the analysis of variance table is as follows:

Repeated Measures Analysis Table

	d.f.	SS	MS	F
Between persons	r - 1	$\frac{\sum^{r}\left[\sum^{d} X\right]^2}{d} - (1) = 287.33 - \frac{3136}{12} = 26$	8.67	
Within persons	r(d - 1)			
Treatment	d - 1	$\frac{\sum^{d}\left[\sum^{r} X\right]^2}{r} - \frac{\left[\sum^{dr}\sum X\right]^2}{dr} = 52.67$	26.33	79.8*
Error	(r - 1)(d - 1)	$\frac{\sum^{dr}\sum(X^2)}{1} - \frac{\sum^{d}\left[\sum^{r} X\right]^2}{r} - \frac{\sum^{r}\left[\sum^{d} X\right]^2}{d} + \frac{\left[\sum^{dr}\sum X\right]^2}{dr} = 2$	.33	
Total	rd - 1			

Example of a t Test for Correlated or Paired Groups

Scores:

Pretest	8	3	7	2	4	6	6	8	2	4
Posttest	10	6	11	4	5	4	6	12	6	6

$m_1 = 5 \quad m_2 = 7 \quad S_1 = 2.19 \quad S_2 = 2.76 \quad r = 0.75$

When group measurements are correlated the standard error is decreased. As a result,

$$S_{m_1 - m_2} = \sqrt{S_{m_1}^{2} + S_{m_2}^{2} - 2rS_{m_1}S_{m_2}}$$

The standard error of $m_1 - m_2$ must be calculated

$$S_{m_1} = \frac{2.19}{\sqrt{9}} = 7.3$$

$$S_{m_2} = \frac{2.76}{\sqrt{9}} = 0.92$$

Therefore,

$$S_{m_1 - m_2} = \sqrt{.5329 + .8464 - 2(.75)\ (.6716)}$$

$$= \sqrt{0.3719}$$

$$= 0.61$$

$$t = \frac{D}{S_D} = -\frac{2}{0.61} = -3.28$$

$$_{0.95}t_9 = t_{2.26}$$

Since $t = 3.28$ exceeds $_{0.95}t_9$, the $m_2 - m_1$ difference is significant. In other words, the null hypothesis that there is no difference between the means is rejected with 95% confidence.

APPENDIX D

INDIVIDUAL AND GROUP DATA FOR SCREENING AND EXPERIMENTAL TESTING SESSIONS

TABLE D1

MAX. $\dot{V}O_2$ TEST ONE RESULTS

SUBJECTS	$\dot{V}_E$ STPD	$\dot{V}O_2$ STPD	$\dot{V}O_2$ ML/Kg	HR	Bf
DS	152.9	4.97	61.09	198	54
RM	141.7	5.00	60.11	186	60
DM	127.9	4.58	58.81	200	60
JR	146.1	4.83	72.29	190	52
BS	155.93	5.59	73.2	200	55
PR	149.3	5.04	59.39	180	54
JE	154.75	5.05	60.62	174	57
RT	118.2	4.71	60.25	186	49
SF	130.26	4.68	75.83	183	48
BW	141.49	5.02	73.59	201	60
DR	138.99	3.04	47.18	---	47
JC	103.45	2.67	40.16	192	42
BM	137.4	3.45	40.99	180	45
DM	107.42	3.27	42.07	180	54
RM	114.12	3.32	43.50	---	52

TABLE D2

MAX. $\dot{V}O_2$ TEST TWO RESULTS*

SUBJECTS	$\dot{V}_E$ STPD	$\dot{V}O_2$ STPD	$\dot{V}O_2$ ML/Kg	HR	Bf
DS	147.44	5.07	62.31	194	54
RM	150.65	4.98	59.22	184	66
BS	144.56	5.25	65.2	190	60
JE	162.19	5.03	60.35	---	48
SF	141.16	4.40	71.22	194	60
BW	145.11	5.29	77.58	196	60
DR	142.22	3.07	46.74	---	42
JC	103.45	2.50	37.47	186	--

* Repeated for only half of the subjects to obtain reliability of measurement

TABLE D3

MAXIMUM WORK LOAD TEST ONE RESULTS

SUBJECTS	$\dot{V}_E$ STPD	$\dot{V}o_2$ STPD	$\dot{V}o_2$ ML/Kg	HR	Bf	RQ
DS	139.15	4.14	50.88	200	54	
RM	141.83	4.38	51.96	182	50	1.24
DM	128.88	4.62	58.01	200	60	-
JR	143.06	4.37	65.35	188	50	1.16
BS	137.26	5.10	63.71	190	48	1.08
PR	154.18	4.74	56.11	192	48	1.23
JE	129.30	3.97	46.18	172	48	1.23
RT	143.48	4.37	55.92	182	42	1.05
SF	147.61	4.61	74.57	196	62	1.02
BW	132.39	4.54	66.59	200	--	1.07
DR	125.94	3.04	46.29	---	52	1.04
JC	109.41	2.71	40.51	---	44	1.19
BM	131.42	3.42	39.60	180	48	1.38
DM	110.94	3.61	46.44	---	46	1.14
RM	123.3	2.85	37.38	180	48	1.46

TABLE D4

MAXIMUM WORK LOAD TEST TWO RESULTS

SUBJECTS	$\dot{V}_E$ STPD	$\dot{V}O_2$ STPD	$\dot{V}O_2$ ML/Kg	HR	Bf	RQ
DS	140.09	4.22	51.87	186	54	
RM	137.99	4.48	53.89	194	52	1.11
JR	134.15	4.53	67.85	180	48	1.09
BS	127.14	4.75	59.43	186	48	1.08
PR	148.09	4.22	49.88	180	48	1.30
JE	167.16	4.53	52.46	184	45	1.45
RT	124.69	4.23	54.18	174	42	1.18
SF	159.26	4.67	75.54	198	63	.97
BW	122.32	4.46	65.43	200	--	1.23
DR	118.55	3.12	47.50	180	44	1.02
JC	109.31	3.07	46.00	---	44	1.18
BM	137.79	3.50	40.52	192	42	1.46
DM	103.99	3.60	46.31	198	51	1.18
RM	123.16	2.66	34.88	180	58	--

TABLE D5

POST-EXERCISE TEST ONE BLOOD RESULTS

SUBJECTS	Hct	Hb	LACTATE	PYRUVATE	pH
DS	51.0	16.4	83.51	2.54	--
RM	46.5	--	82.90	2.72	--
DM	--	17.9	129.2	4.11	7.09
JR	46.5	16.4	126.5	2.51	--
BS	49.	--	86.40	2.41	--
PR	50	16.4	92.24	2.83	--
JE	49.5	17.8	145	.52	7.08
RT	45.5	16.1	89.0	2.19	7.15
SF	48	16.7	102	.62	7.15
BW	50.5	17.9	122.5	--	--
DR	47.5	16.7	67.7	3.21	7.17
JC	48	17.4	55.9	1.78	7.25
BM	51.0	17.3	99.4	2.75	--
DM	52.5	--	81.6	2.13	--
RM	47.0	15.5	62.2	1.34	--

TABLE D6

POST EXERCISE TEST TWO BLOOD RESULTS

SUBJECTS	Hct	Hb	LACTATE	PYRUVATE	pH
DS	51.0	16.4	87.3	2.14	--
RM	49.0	16.4	96.8	3.27	--
DM	--	16.9	98	2.79	7.13
JR	44	--	119.0	2.74	--
BS	51	--	76.4	2.09	--
PR	50.5	16	105.46	2.74	--
JE	46.5	16.6	144	1.13	7.03
RT	45.5	15.6	70	--	7.16
SF	49.	16.7	116	1.33	7.08
BW	49.5	18	104	--	--
DR	47	16.7	81.4	2.35	7.25
JC	50	18.1	69.1	1.86	7.20
BM	52	17.6	108.8	3.2	--

TABLE D7

HYPERCAPNIC DRIVE TEST ONE RESULTS (5% CO_2)

SUBJECTS	$P\dot{V}_E$	TIME	CO_{2_I}	CO_2F	ET mm	ET CO_2	BP-47	ET CO_2 mm Hg	$P\dot{V}_E/PACO_2$ mm Hg
DS	21.3	11	4.33	4.33/32	43	5.82	709.7	41.31	.516
RM	16.5	11	4.33	4.33/32	46	6.22	703.4	43.75	.378
JR	25.4	10	4.33	4.33/32	43	5.82	704.3	40.99	.62
BS	22.0	11	4.33	4.33/32	43	5.82	698.3	40.64	.542
PR	17.8	11	4.33	4.33/32	42	5.68	698.7	39.69	.449
JE	25.4	11	4.87	4.87/29	41	6.89	697	48.02	.529
RT	37.4	8	4.87	4.87/29	37	6.2	713.3	44.3	.844
SF	26.3	13	4.87	4.87/29	39.5	6.63	711.8	47.19	.557
BW	28.98	8	5.12	5.12/34	40	6.02	709.6	42.72	.678
DR	27.3	12	4.45	4.45/28.5	35.5	5.54	705.5	39.08	.698
JC	25.2	13	4.45	4.45/37	45	5.41	708	38.3	.657
BM	39.6	10	5.03	5.03/37	43.5	5.9	694.7	41.06	.965
DM	25.8	12	5.03	5.03/37	46	6.25	705	44.07	.585
RM	45.4	10	5.03	5.03/37	42.5	5.78	697.4	40.31	1.13

TABLE D8

HYPERCAPNIC DRIVE TEST TWO RESULTS (5% CO_2)

SUBJECTS	$P\dot{V}_E$	TIME	CO_{2_I}	CO_2F	ET mm	ET CO_2	BP-47	ET CO_2mm Hg	$P\dot{V}_E/PACO_2$ mm Hg
DS	26.9	11	4.33	4.33/32	41	5.55	704.8	39.12	.688
RM	21.6	10	5.03	5.03/37	49	6.66	703.8	46.87	.460
JR	37.9	8	5.03	5.03/37	44	5.98	710.0	42.46	.893
BS	28.8	10	5.03	5.03/37	46.5	6.32	698	44.11	.652
PR	20.2	10	4.33	4.33/32	44	5.95	698	48.3	.418
JE	32.4	10	4.87	4.87/30	38.5	6.25	697.5	43.59	.745
RT	40.71	10	4.87	4.87/30	36	5.84	720	42.05	.967
SF	53.6	11	4.87	4.87/30	39	6.33	720	45.58	1.18
BW	41.1	11	5.12	5.12/39	43	5.65	710.9	40.17	1.02
DR	30.4	7	4.45	4.45/37	46	5.53	712	39.37	.772
JC	31.6	12	4.45	4.45/37	47	5.65	714	40.34	.783
BM	40.8	11	5.03	5.03/36	42	5.87	695	40.8	1.0005
DM	22.8	11	5.03	5.03/34	43	6.36	708.4	45.05	.506
RM	31.1	10	5.03	5.03/36	42	5.87	705.9	41.44	.751

TABLE D9

HYPERCAPNIC DRIVE TEST ONE RESULTS (7% CO_2)

SUBJECTS	$P\dot{V}_E$	TIME	CO_{2I}	CO_2F	ET mm	ET CO_2	BP-47	ET CO_2mm Hg	$P\dot{V}_E/PACO_2$ mm Hg
DS	68.1	11	7.19	7.19/48	51.5	7.71	709.7	54.72	1.24
RM	31.4	10	7.19	7.19/47	52	7.96	703.4	55.99	.560
JR	87.8	7	7.19	7.19/48	50.5	7.56	704.3	53.25	1.65
BS	49.9	10	7.19	7.19/47	50.5	7.73	698.3	53.98	.925
PR	64.0	7	7.19	7.19/47	50	7.65	698.7	53.45	1.2
JE	67.5	10	6.77	6.77/41	46	7.60	697	52.97	1.27
RT	79.3	9	6.77	6.77/41	45	7.43	713.3	53	1.5
SF	41.5	12	6.77	6.77/41	47.5	7.84	711.8	55.81	.743
BW	58.3	10	6.81	6.81/46	50	7.40	709.6	52.51	1.11
DR	78.0	7	6.78	6.78/43	45	7.1	705.5	50.06	1.56
JC	69	12	6.78	6.78/60	61	6.89	708	48.78	1.41
BM	64	10	7.18	7.18/47	49.5	7.56	694.7	52.52	1.21
DM	42.9	12	7.19	7.19/50	53	7.62	705.1	53.73	.797
RM	80.5	6	7.19	7.19/49	51	7.48	697.4	52.17	1.54

TABLE D10

HYPERCAPNIC DRIVE TEST TWO RESULTS (7% CO_2)

SUBJECTS	$P\dot{V}_E$	TIME	CO_{2I}	CO_2F	ETmm	ET CO_2	BP-47	ET CO_2mm Hg	$P\dot{V}_E/PACO_2$ mm Hg
DS	58.4	10	7.19	7.19/48	52	7.79	704.8	54.9	1.064
RM	31.3	10	7.19	7.19/47.5	52	7.87	703.8	55.39	.565
JR	67.9	8	7.19	7.19/47.5	50.5	7.64	710	54.24	1.25
BS	48.3	9	7.19	7.19/47.5	51.5	7.78	798	54.3	.889
PR	58.8	10	7.19	7.19/47.5	50.5	7.64	698	53.32	1.10
JE	65.7	12	6.77	6.77/44	48	7.39	697.5	51.55	1.28
RT	64.5	12	6.77	6.77/51.5	54.5	7.16	720	51.55	1.25
SF	54.4	11	6.77	6.77/50	54.2	7.34	720	52.84	1.029
BW	64.5	11	6.81	6.81/55	61	7.55	710.9	53.67	1.2
DR	78.0	9	6.78	6.78/59.5	62.5	7.12	712	50.77	1.54
JC	77.3	12	6.78	6.78/60	62	7.01	714	50.02	1.55
BM	64.3	7	7.18	7.18/47.5	49.5	7.48	695	51.98	1.24
DM	42.7	11	7.18	7.18/56.5	58.5	7.43	708.4	52.63	.811
RM	83.5	8	7.18	7.18/47.5	49.5	7.56	705.9	53.37	1.56

ABSTRACT

This study investigated the relationship between respiratory response to controlled hypercapnia at rest and the ability to maximize venous serum lactate during exercise. Recent studies have demonstrated that athletes have a reduced ventilatory response to hypercapnia and also attain significantly higher peak lactates during a relative maximum work load. Since an increase in arterial CO_2 or lactate induces a decrease in pH and resultant increase in ventilation, it was hypothesized that hypercapnic response could conceivably be qualitatively compared with lactate level accumulation during maximum exercise.

Ten fully conditioned male subjects who achieved some measure of success in their particular sport and demonstrated a maximum oxygen comsumption in excess of 55 ml kg^{-1} $min.^{-1}$ and five untrained subjects who demonstrated a maximum oxygen consumption less than 47 ml kg^{-1} $min.^{-1}$ were selected for the study. All subjects were non-smokers between the ages of 17 and 27 without any history of cardiovascular or respiratory disease or obesity.

All subjects breathed two gas mixtures containing approximately 5% and 7% CO_2 in 20.93 O_2, balance N_2 and their respiratory response was recorded. Maximum peak blood lactates were measured following exhaustion induced through the performance of a relative maximum work load (100 Max. $\dot{V}o_2$).

Trained subjects demonstrated a significantly higher blood lactate level following maximum exercise. They further demonstrated a significantly decreased respiratory response to a gas mixture containing approximately 5%

CO_2, in inspired air and an insignificant trend to a lower hypercapnic drive under conditions of 7% CO_2 in inspired air. Graphic analysis pointed to a relationship between respiratory response to hypercapnia and peak lactate levels during exhaustive work. However, statistical analysis failed to support this relationship.