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A COMPARISON OF THE TRANSITION FROM AEROBIC TO ANAEROBIC METABOLISM IN TRAINED AND UNTRAINED MEN.

by

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A thesis submitted to the School of Graduate Studies in partial fulfilment of the degree requirements of the Master of Science in Kinanthropology.

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ABSTRACT

The principle aim of this study was to define changes in blood parameters to describe the transition from aerobic to anaerobic metabolism during incremental work and to apply these criteria in the identification of the transition phase in endurance trained and untrained subjects. A secondary purpose was to investigate the relationship of changing blood responses through exercise transition with changes in respiratory gas response.

Nine endurance trained subjects were contrasted with nine untrained control subjects during an incremental work test to exhaustion on a cycle ergometer. During the test, each subject began pedaling at a pedalling frequency of 60 rpms. The workload was then gradually increased to a point that produced a steady state heart rate of 120 bpm. Subsequently the workload was increased 180 kpm/min every 2 minutes to exhaustion. Respiratory gas and venous blood samples were collected at rest, during the final 30 seconds of the warm-up period, and during the final 30 seconds of each subsequent workload.

From the respiratory gas samples, minute ventilation (VE), oxygen consumption (VO2), and carbon dioxide production (VCO2) were computed. Ventilatory equivalents for oxygen (VEO2) and carbon dioxide (VECO2) were then derived. Venous blood samples were analysed for blood lactate and pH.

The transition phase was initiated with the appearance of the first significant accumulation of lactate in the blood and concluded by the first significant drop in blood pH.

Blood lactate values rose significantly with increasing workloads in both trained and untrained subjects. Post-hoc analysis revealed that a significant accumulation of lactate was present when the blood concentration rose by 1.1 mM beyond the resting value in untrained subjects and by 0.9 mM beyond the resting value in trained subjects. This point identified the Lactate Threshold (LT) and delineated the initiation of the transition phase.

Blood pH values showed a significant decline across workloads in both subject groups. Post-hoc analysis indicated that a significantly lower pH coincided with a decline of pH of .08 units from rest in untrained subjects and a decline of .11 pH units in trained subjects. This point identified the Threshold of Decompensated Metabolic Acidosis (TDMA) and delineated the conclusion of the transition phase.

Neither the LT nor the TDMA was significantly related to a non-linear rise in VE or to the minimum value of the VECO2 in either of these groups.

The transition phase (as measured in terms of relative and absolute workloads) in trained subjects occurred at a greater proportion of the maximal oxidative capacity in comparison to untrained subjects. This shift was the result of a significantly elevated LT and a significantly higher TDMA. The total oxidative capacity located within the transition phase was independent of the training state.

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Chapter I
THE PROBLEM

1.1 INTRODUCTION

In the past, maximum oxygen consumption (VO2max) has been accepted as a useful measure of endurance capacity in events where oxidative energy use predominates. Athletes participating in these types of events, however, vary in the percentage of the VO2max which they are able to utilize effectively and consequently train to increase this ability.

More recently the concept of anaerobic threshold has been used as an index of endurance performance. During incremental work, when the workloads are gradually increased, there is a stage at which an activation of the anaerobic metabolism is followed by release of lactate from the skeletal muscle to blood. The onset of this process has been termed 'anaerobic threshold' (AT) (Wasserman et al, 1973) or the 'lactate threshold' (LT) (Ivy et al, 1980) and is believed to delineate the initiation of metabolic acidosis.

This intensity of exercise elicits an initial accumulation of lactate significantly different from resting levels. At this point mechanisms of respiratory compensation for the work induced lactic acidosis lead to a disproportional increase in ventilation with respect to oxygen uptake (Reinhard et al, 1979).

Nonetheless it has been noted that individuals may work above the anaerobic threshold as described for prolonged periods of time (Kindermann, et al., 1979). This indicates that even above the workload where the onset of anaerobiosis has occurred, lactate concentrations are not continuing to rise to work-limiting levels. The suggestion here is that

there are two separate thresholds; one that denotes the beginning of anaerobic metabolism and a second threshold that delineates a later workload which predisposes a lactate accumulation which becomes ever-increasing and work-limiting. Between these two points is a transition phase of aerobic/anaerobic metabolism within which plateauing of blood lactate values occurs (through an equilibration of its production and removal) and buffering of the exercise-induced acidosis is available through blood and respiratory mechanisms. As such, the upper limit of this phase denotes the workload up to which the exercise-induced acidosis is effectively compensated.

The second threshold has been described recently by several authors (Reinhard et al, 1979; Gutin and Young, 1980 ; Mader et al, 1976) and has been implicated as an important determinant of endurance performance (Kindermann et al, 1979).

Reinhard et al (1979) have called this point the 'threshold of decompensated metabolic acidosis' (TDMA) and for the purposes of this study their definition will stand. At this point the workload is such that the onset of an exponential increase in blood lactate concentration occurs. Because the buffering capacity of the blood is finite, and lactate metabolism cannot keep pace with lactate production and release from the muscle cells, blood pH drops significantly. Duration of work time at this intensity will be limited accordingly because of the inhibitory effect of acidosis on metabolism (Davenport, 1971).

Astrand and Rodahl (1977) have identified intensity and duration of exercise as important considerations in determining the effectiveness of endurance training.

The transition phase, (as delineated by the LT and the TDMA), defines that range of work intensities which allow

the highest possible stimulation of the oxidative energy supply mechanisms, while holding the anaerobic supplementation of energy to a degree that may be compensated physiologically. For this reason, exercise intensities in the transition are not unduly limited in duration and may be suitable for endurance training.

1.2 RATIONALE

Endurance athletes have the ability to utilize efficiently portions of their oxidative capacities above those normally recognized as their anaerobic threshold (Costill et al, 1970). Additionally, the AT has been demonstrated to be mutable with training (Davis et al, 1979). While the appearance of this point has been linked to performance (Costill et al, 1973; Weiser et al, 1978), it does not represent totally the major limiting factor of endurance performance. A more likely candidate is the aerobic-anaerobic transition phase, which may be delineated by the appearance of both the LT and the TDMA during incremental work.

This phase appears to be more representative of the body's ability to compensate physiologically for an exercise induced acidosis and it's ability to equilibrate lactate metabolism with it's production. If the location and duration of the aerobic/anaerobic transition phase could be established in subjects of variable oxidative capacities, more effective intensities for endurance training could be selected.

Previous authors have used empirical values of blood lactate to describe the transition phase (Mader et al, 1976; Kindermann et al, 1979), or have depended on changes in respiratory gas parameters (Reinhard et al, 1979; Gutin and Young, 1980). In the present study it was felt that these values may not be valid for a comparison of trained and untrained subjects because of a possible pH - dependent release of lactate from skeletal muscle (Mainwood and Worsely-

Brown, 1975), and differences in the responsiveness of the respiratory mechanisms (Stegeman et al, 1975). Instead the LT was defined by the workload just prior to the first statistically significant increase in blood lactate. Because lactate comprises the primary acid metabolite in the blood during exercise (Keul et al, 1973), blood pH should accurately reflect the compensatory capacity of the circulatory system for an acid load. Thus the TDMA was characterized by the workload just prior to the first significant drop in blood pH from resting values.

It should also be noted that, while the link between changes in blood lactate and respiratory gas parameters at AT have been well established (Wasserman et al, 1973; Davis et al, 1976), the degree to which respiratory parameters are tied to changes in blood lactate and pH throughout the whole range of transition is less understood.

1.3 STATEMENT OF THE PROBLEM

The principal aim of this study was to define changes in blood parameters to describe the Lactate Threshold and the Threshold of Decompensated Metabolic Acidosis and to apply these criteria in the identification of the location of the aerobic to anaerobic transition of metabolism along a continuum of work intensities in endurance trained and untrained subjects. A secondary purpose was to investigate the relationship of changing blood responses through exercise transition with changes in respiratory gas response.

1.4 EXPERIMENTAL HYPOTHESIS

It was expected that the transitional phase from aerobic to anaerobic metabolism (as defined by the LT and the TDMA) would occur at a higher proportion of the maximal oxidative capacity in endurance trained athletes. Because of the role of the respiratory mechanisms in the compensation for acid/base disturbances, the relationship of changes in me-

tabolic characteristics to changes in respiratory parameters was expected to be high.

1.5 LIMITATIONS OF THE STUDY

The findings of this study were limited in their application to the general population for a number of reasons. Firstly, the cross-sectional design utilized to provide the comparison between trained and untrained groups, does not allow good control over genetic capacities which may affect the training state. Secondly, the narrow age range of the subjects and the homogeneity of their sex limited the implications to the specific groups stated. Thirdly, the use of venous, rather than arterial, blood must certainly be considered a limitation. Many of the physiolcgical adaptations to metabolic acidosis are initiated by changes in arterial blood. Sampling away from the active area may not be representative of changes occurring at the capillary level. Finally the selected dependent variables, while identified for their physiological importance, did not presume to cover all the changes in blood or respiratory gas parameters.

1.6 DEFINITIONS

ADP	adenosine diphosphate
AMP	adenosine monophosphate
AT	anaerobic threshold, the work rate or VO2 at which the onset of anaerobiosis occurs as measured by respiratory parameters
ATP	adenosine triphosphate
Buffer Base	total buffer available in the blood including both the bicarbonate and non-bicarbonate buffers.
VCO2	carbon dioxide production, the volume of carbon dioxide excreted by the body per unit time
FFA's	free fatty acids

FT fibers — fast twitch muscle fibers as classified by their myosin ATPase staining intensity

G-6-P — glucose-6-phosphate, an intermediate substrate of glycolysis

Hb — hemoglobin

HbO2 — oxyhemoglobin

LT — lactate threshold, the first significant elevation of blood lactate above resting values

VO2max — maximal oxygen consumption, the maximum volume of oxygen that may be consumed per unit time in the body; the product of the cardiac output and the arterio-venouus oxygen difference

NAD — nicatinamide adenine dinucleotide, a coenzyme of oxidation-reduction reactions containing the vitamin, nicatinamide, as its functional group. The oxidized form (NAD+) is reduced to form NADH by accepting two electrons as a hydride ion (H-)

VO2 — oxygen consumption, the volume of oxygen utilized in the body per unit time

PFK — phosphofructokinase, the enzyme catalysing the conversion of fructose-6-phosphate to fructose-1-6-diphosphate - the rate limiting reaction of glycolysis

pH — the hydrogen ion concentration

Pi — inorganic phosphate

ST fibers — slow twitch muscle fibers as characterized by their myosin ATPasa staining intensity

TDMA — threshold of decompensated metabolic acidosis, the work rate or VO2 at which compensatory mechanisms for the constraint of metabolic acidosis become saturated resulting in a precipitous drop in blood pH

Trained S — those subjects who have been involved in a systematic endurance training program for at least 6 months prior to the onset of experimentation

Untrained S — those subjects who have not been involved in a systematic endurance training program for at least 6 months prior to the onset of experimentation

$\dot{V}E/\dot{V}O_2$ — the ventilatory equivalent of oxygen, the ratio of ventilation to oxygen consumption

$\dot{V}E/\dot{V}CO_2$ — the ventilatory equivalent of carbon dioxide, the ratio of ventilation to carbon dioxide production

$\dot{V}E$ — ventilation, the volume of air expired by the body per unit time

Chapter II
REVIEW OF LITERATURE

2.1 INTRODUCTION

In order to evaluate the transitional phase of exercise, it is necessary to understand the factors that influence the relative contributions of the aerobic and anaerobic energy supply systems i.e. the metabolic response. Once established these factors will form the groundwork in the study of physiological adaptation to workloads of varying intensities and also in the comparison of the responses of trained and untrained individuals to incremental work.

To this end, the review of literature will be comprised of four sections:

1. Pathways of aerobic and anaerobic metabolism.
2. Factors affecting the metabolic response to exercise.
3. An overview of the metabolic response to submaximal work of varying intensities.
4. A comparison of the responses of trained and untrained individuals to incremental work.

2.2 PATHWAYS OF AEROBIC AND ANAEROBIC METABOLISM

The capacity to do work is controlled by the availability of energy. In this respect most of the physiological changes that occur during exercise are related to matching the energy supply to the muscles' utilization of energy to power their contractile processes. The method of supplying this energy, (in the form of ATP), varies with incremental work based on the intensity and duration of the exercise. Because the supply of ATP in the cell is limited, muscle cells must have a means of rapidly replacing ATP as it is

utilized during contraction. Muscle cells possess the enzymes necessary to resynthesize ATP from it's constituents, ADP and Pi.

The energy for this process may be provided by aerobic or anaerobic mechanisms, or through a combination of both. Thus the 'metabolic response' refers to the relative contribution of energy to the total energy pool by both the aerobic energy systems and the anaerobic energy systems. The basic pathways involved are illustrated in Figure 1.

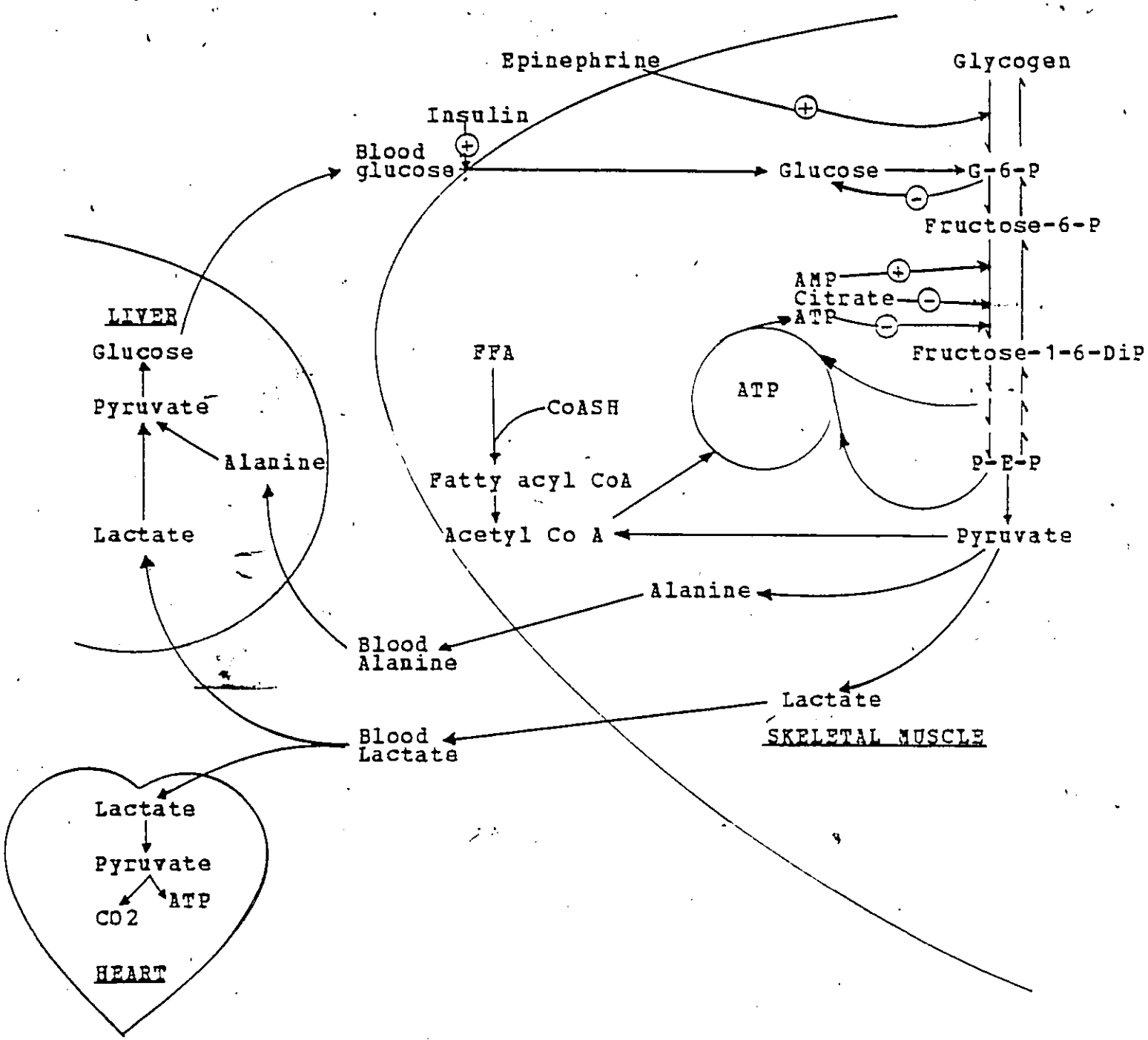
Aerobic metabolism refers to the production of energy in the presence of oxygen. In this type of metabolism , the phosphorylation of ADP to ATP takes place in the mitochondria. In skeletal muscle, the energy for this process is provided by the catabolism of fats and carbohydrates .

The final commomn pathways of carbohydrate and fat oxidation are the Kreb's cycle reactions and the oxido-reductions of the Electron Transport Chain (ETC).

Hydrogen pairs from the dehydrogenation reactions of substrate oxidations are bound and transported to the ETC by the reduced flavoproteins NAD and FAD.

In the ETC, a discrete series of oxido-reductions allow the transfer of each hydrogen pair from one molecule to the next with the sequential release of energy to be used in the phosphorylation of ADP to ATP. O2 acts as the ultimate electron accepter in this series of reactions, creating metabolic H20 in the process. For its continued functioning, the ETC has 3 major requirements (Armstrong,1979). These include: (1) an adequate supply of ADP and Pi, (2) oxygen, and (3) a continuing supply of hydrogen pairs.

Figure 1: Pathways of energy metabolism during muscular exercise. (from McMurray, 1977, p.152)



The most prolific supplier of hydrogen pairs in the muscle cell is the Kreb's cycle. In the Kreb's cycle the 2-C moiety of Acetyl Co A is transferred to a carrier molecule (oxalo acetic acid) that enters a series of reactions which convert the acetate (2C) to CO2 and H2. Eventually the original carrier molecule is regenerated. H2 is generated at four different dehydrogenase reactions in the Kreb's cycle. Three of these are NAD- linked and one is FAD-linked. These reducing equivalents are then passed to the ETC. One ATP is also produced during one of the metabolic steps in a process of substrate level phosphorylation (Lehninger. 1975). The CO2 produced diffuses down it's concentration gradient and into the blood forming the primary source of metabolic CO2 production in the cell (Clode and Campbell, 1969).

The free fatty acids (FFA's) are the major fat substrate utilized during exercise (McMurray, 1977). The catabolism of FFA's involves 3 different processes. The first of these is the activation of the fatty acid to a fatty acyl compound in an energy requiring reaction occurring in the cytoplasm of the cell. Since the rest of the reactions concerned with fat oxidation occur in the mitochondria, and the inner membrane is impermeable to all Co A derivatives, the muscle cell depends on carnitine mediated transport of the fatty acyl from the cytoplasm to the mitochondria. The second process is that of beta-oxidation. This involves the sequential removal of hydrogen pairs from the alkyl chain of the fatty acyl and the splitting off of 2-C units in the form of Acetyl-Co A molecules. The third process is the Kreb's cycle oxidation of the Acetyl Co A products yielding CO2 and hydrogen for oxidative phosphorylation and the subsequent oxidation of the hydrogen pairs in the ETC.

The other major substrate used for the production of reducing equivalents for oxidative phosphorylation is glucose. Generally as the intensity of exercise increases, the dependence on glucose as a substrate does likewise (Skinner and

Mc Lellan, 1980). This glucose may be derived either from the circulating blood or from intramuscular glycogen stores (Armstrong, 1979).

After entering the cell from the blood in a process of facilitated diffusion, glucose is phosphorylated to glucose-6-phosphate (G-6-P) effectively trapping the molecule within the cell. It then may be converted to glycogen or metabolized.

When glycogen is required for energy production it is reconverted to G-6-P and then catabolized in the process of glycolysis. Here G-6-P is phosphorylated again and split into 2 (3-C) phosphate molecules. Each of the triose phosphates is oxidized with the production of NADH. At 2 subsequent steps, substrate level phosphorylation of ADP occurs. The end product of glycolysis are 2 molecules of pyruvate. Pyruvate from this point may diffuse to the circulation (Keul et al, 1972) or be further metabolized in a number of pathways.

In the muscle, pyruvate may be oxidized to Acetyl Co A via the pyruvate dehydrogenase complex in the mitochondria. The Acetyl Co A may then be oxidized in the Kreb's cycle with the corresponding release of CO_2 and production of hydrogen pairs for the ETC. Thus the role of carbohydrate in oxidative phosphorylation.

Alternately, pyruvate may be converted to lactate in a reaction catalysed by lactate dehydrogenase (LDH) during anaerobic glycolysis- the second major energy supplier during prolonged activity. (Lactate and pyruvate are ionic forms of dissociated lactic and pyruvic acid, respectively. These acids dissociate in the following manner:

$$HA \text{ ----- } H^+ + A^-$$

Because of their high dissociation constants, lactic and pyruvic acids are normally found in the dissociated state under physiological conditions (Wasserman et al, 1973)).

Anaerobic glycolysis may produce energy at a much higher rate than may aerobic metabolism (Davis et al, 1979), and is thus most important when the rate of energy utilization is high. The maximum rate of energy utilization is ultimately dependent on the myosin ATPase activity of the contracting fiber.

The viability of this method of energy production is dependent on the relative LDH activity of the muscle fiber (Sjodin, 1976) and the cytosolic redox state (Edington, 1970). During lactate production, pyruvate may accept the hydrogen pair from NADH generated at previous glycolytic dehydrogenations, thus preventing the accumulation of NADH and regenerating NAD at the same time.

Hultman (1967) found that a significant proportion of muscle glycogen utilization during exercise could not be accounted for by lactate formation or CO_2 production. A third possibility for the removal of pyruvate may be its transamination to alanine via the reaction catalysed by alanine aminotransferase (Felig et al, 1970). Alanine may then diffuse out of the cell and become a key precursor for hepatic glucose production.

The relative contribution of either of these energy supply systems, i.e. either oxidative phosphorylation or anaerobic glycolysis, is dependent on the interplay of a number of factors which constitute 'determinants' of the metabolic response.

2.3 FACTORS AFFECTING THE METABOLIC RESPONSE TO EXERCISE

The major determinants of the metabolic response include:

a) Recruitment of muscle fibers

b) Substrate supply

c) Intracellular regulators

2.3.1 Recruitment

At least two separate fiber types can be discerned in human skeletal muscle based on their myosin ATPase activity at alkaline pH (Gollnick et al,1972). According to Barnard et al (1971), a high myosin ATPase activity under these assay conditions occurs in muscles with fast twitch characteristics and a low activity in muscle fibers with slow twitch characteristics. Thus the fibers may be designated as fast-twitch (FT) and slow-twitch (ST).

FT fibers always have a higher glycolytic capacity according to their alpha-glycerophosphate D-H and phosphofructokinase activities. ST fibers, on the other hand , are found to have a higher oxidative capacity based on their NADH diaphorase activity, although a wide continuum of staining intensities exists (Gollnick et al, 1972). ST fibers also have a high concentration of mitochondria and are accompanied by an enhanced capillary supply.

Isozymes of the enzyme lactate de-hydrogenase have been identified in both FT and ST fibers (Sjodin,1976; Thorstensson et al,1977). The LDH may be present as a heart specific (H-LDH) or as a muscle specific (M-LDH) isozyme. M-LDH facilitates the reduction of pyruvate to lactate while H-LDH catalyses the reverse reaction of lactate to pyruvate for utilization in the Kreb's cycle. ST fibers have been demonstrated to have a higher H-LDH activity (Sjodin,1976) whereas FT fibers have a greater M-LDH activity (Thorstensson et al,1977).

It appears that each of the two fiber types are specifically designed to preferentially sustain a particular type of metabolism; aerobic metabolism in the case of ST fibers or anaerobic metabolism in the case of FT fibers. This is not to say that either fiber type is incapable of supplying energy by any of the methods previously described. This implies simply that the aerobic or anaerobic capacity of the muscle cell is related to the fiber type (Ivy et al, 1980).

A summary of the metabolic potentials of FT and ST fibers is presented in Table 1. (as derived from Graham, 1978; Graham et al, 1976; Gollnick, 1972; Holloszy, 1976)

	FT fibers	ST fibers
Glycolysis	High	Low
Glycogenolysis	High	Low
CHO Oxidation	Low	Inter
Fat Oxidation	Low	High
Lactate Production	High	Low
Lactate Uptake	Low	High

Table 1: Summary of the metabolic potentials of FT and ST fibers.

(as derived from Graham, 1978; Graham et al, 1976; Gollnick, 1972; Holloszy, 1976)

Since muscle glycogen is stored intramuscularly in both muscle fiber types (Essen et al, 1975) and the utilization of this substrate varies with exercise characteristics (Essen, 1978), studies that monitor the depletion of glycogen with exercise may provide insight into the relationship between work characteristics and fiber recruitment. A summary of the depletion patterns in the fiber types as a function of exercise intensity, duration and mode is presented in Table 2.

AUTHORS	MODE OF EXERCISE	INTENSITY	DURATION	DEPLETION PATTERN
Gollnick et al, 1972	T-mill run	74% VO_2max.	30 min.	ST FT
Gollnick et al, 1973	cycle	150 "	6x1 min 10 min rest	FT fibers depleted first, some ST as continued in later intervals.
Gollnick et al, 1974	cycle	30 "	3 h.	Below VO_2max always ST depleted first then FT; Intensity increases the rate depletion. Above VO_2max FT fibers depleted before ST.
		65 "	2 h.	
		85 "	1 h.	
		120 "	exhaust.	
		150 "	"	
Gollnick et al, 1975	cycle	30 "		Initially ST fibers, some FT as continued
		60 "	2 - 3 h.	
		90 "		
		120 "	exhaust	Initially FT fibers, some ST as continued
		150 "	"	
	isometric	15% maximal	"	20% MVC = ST fibers
		40 voluntary contraction (MVC)	"	40% MVC = FT only.
Edgerton et al, 1973	cycle	120% VO_2max	4 - 6 min.	Greatest FT depletion
		120 "	10:10 sec. work:rest	Some FT depletion
		60 "	40 min.	Predominantly ST fibs
Costill et al, 1974	level and uphill running	75 "	2 h.	ST fibers depleted, some FT during uphill

AUTHORS	MODE OF EXERCISE	INTENSITY	DURATION	DEPLETION PATTERN
Essen, 1977	cycle	60% VO_2max	1 h.	ST fiber depletion greater than FT.
		100 "	15:15 sec. work:rest	FT fiber depletion greater than ST.
Essen, 1978	cycle	60 "	15:15 sec. work:rest	ST fiber depletion greater than FT.
		100 "	"	ST fiber depletion equivalent to FT.
		100 "	8 - 10 min.	FT depletion greater than ST.

Table 2: Selected studies of fiber depletion as a function of exercise mode, intensity and duration.

The fiber depletion studies support the existence of a relationship between fiber recruitment and the work intensity. At low work intensities preferential use of ST fibers, with their more highly developed oxidative systems occurs. Increasing work demands result in a quantitatively and qualitatively greater recruitment of FT fibers with their higher glycolytic capacities. In this way, fiber recruitment may influence the contribution of energy from aerobic and anaerobic mechanisms.

2.3.2 Substrate Supply

ATP for contraction can be regenerated from glycolytic and aerobic phosphorylations of ADP. The energy required for these processes is derived from the catabolism of fats and carbohydrates which may be obtained from both intracellular and extracellular sources.

The contribution of the extracellular substrates (i.e. glucose and FFA's) is dependent on their availability to the cell . This , in turn, depends on : (1) their mobilization from the extracellular storage areas (i.e.the liver and the adipose tissue), (2) the muscle blood flow to the working tissue , and (3) their uptake at the cell.

The mobilization of substrates is mediated primarily by neuro-endocrine mechanisms. The catecholamines, glucagon and insulin all show characteristic responses to exercise leading to an increased provision of fats from adipose tissue and regulation of blood glucose (Hartley et al,1972a,b; Galbo et al,1973;Galbo et al,1 978).

Fat mobilization is enhanced by the effects of epinephrine and glucagon on the balance between lipolysis and esterification cycling in adipose tissue. This effect is mediated through the activation of adenyl cyclase and lipase activity in the adipocyte (McMurray,1977). See Figure 2.

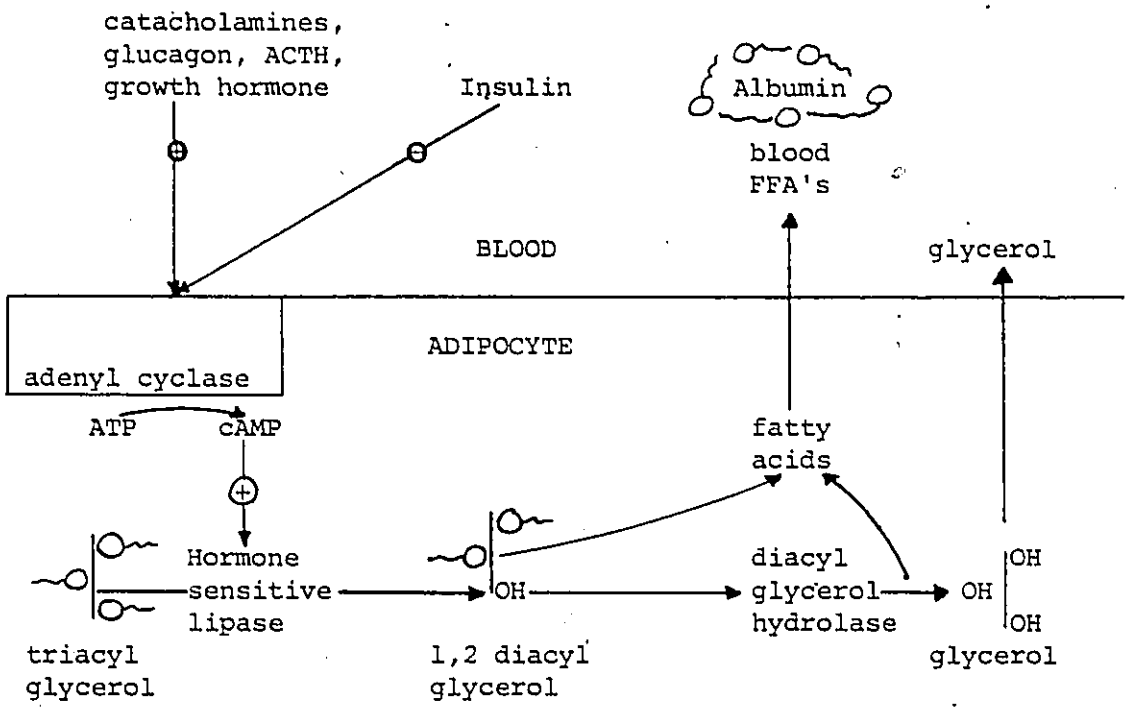


Figure 2; Intracellular lipolysis in adipose tissue and it's control by hormones (from Mc Murray, 1977,p. 197).

The release of the catecholamines, epinephrine and nor-epinephrine occurs during exercise with the stimulation of the sympathetic nervous system. The greater the activation, the greater the increase in blood levels. While nor-epinephrine is primarily a neurotransmitter, it does become blood borne and is able to influence other tissues (Terjung,1979). Epinephrine, on the other hand, is released directly into the blood.

Exercise brings about an increase in both epinephrine and nor-epinephrine levels in the blood. Several studies have shown that the degree of this response is dependent on the intensity of the exercise (Gray et al,1957; Haggendahl et al,1970; Hartley et al,1972a). The nor-epinephrine levels rise gradually as the work intensity increases and become disproportionately elevated at heavy workloads (>80% VO2max). Epinephrine response is somewhat slower with little increase at low and moderate intensities but increases markedly at high work intensities.

Control of blood glucose concentration is the role of insulin and glucagon.

Glucagon stimulates glycogenolysis in the liver through modulation of glycogen phosphorylase activity in response to declining blood glucose levels. It also stimulates gluconeogenesis with lactate, pyruvate, glycerol and amino acids being utilized as precursors of glucose production (Hultman,1978). During exercise, glucagon concentrations increase with the onset of activity and increase in a linear fashion with work intensity (Hartley et al,1972a).

The catecholamines can also rapidly increase glucose provision from the liver during times of stress. In addition they may stimulate the release of glucagon (Terjung,1979). It appears that the catacholamines aid in the initial increase in blood glucose, while glucagon provides the long term stimulus that includes gluconeogenesis.

Insulin acts on all tissues to increase the use of glucose and thereby decrease the blood levels. It specifically acts in the promotion of glucose transport into cells, enhancing glycogenesis and encouraging fat deposition (Terjung,1979). However during exercise insulin levels are known to drop (Galbo et al, 1976), preventing a serious decline in blood glucose levels.

Other hormones act synergistically in the provision of extracellular fat and glucose during exercise (Galbo et al,1978), including growth hormone, thyroid stimulating hormone, the corticosteroids and ACTH. However the time course of their release is more protracted than those mentioned above (Hartley et al,1972b).

Muscle blood flow is the product of the cardiac output and the distribution of that ouput to the active musculature. As such it comprises an integral component in the supply of extra-cellular substrates. Several studies have demonstrated a large increase in the blood flow to working muscle during heavy exercise in man (Pernow and Saltin,1971;Saltin et al,1976). The increased blood flow may be attributed to both an increase in the cardiac output during exercise (Rowell,1974) and the vasoactive effects of hypoxia, blood levels of K^+ and CO_2, acidity and the concentration of histamine and various metabolites (Skinner and Powell,1967; Clausen,1977;Keul et al,1972) and to variations in sympathetic nerve activity (Dehn and Mitchell,1979).

There is generally agreement that blood glucose plays a relatively minor role in the metabolism of the exercising cell (Reichard et al,1961;Saltin et al ,1976;Karlsson et al,1972) with estimations that it provides approximately 10% of the total carbohydrate oxidized (Gollnick,1978). This allows 'glucose sparing' for oxidation in nervous tissue. The mechanism of glucose sparing lies in the regulation of blood glucose uptake at the cell. Normally, glucose uptake

is a carrier mediated process under the influence of extracellular hormones such as insulin and the catachclamines and their effects on hexokinase activity, and intracellular substances such as ATP, citrate and FFA levels which may affect PFK activity and thereby the glycolytic flux. This control is mediated mostly through G-6-P and substrate inhibition (Gollnick, 1978).

The entry of circulating fatty acids into the cytoplasm of the cell is dependent on the concentration gradient (Newsholme, 1977). As a result the rate of entry of this substrate may be increased by (1) increasing the fatty acid concentration of the blood, or (2) increasing their rate of oxidation in the cell (Armstrong, 1979).

There is some dispute as to the role of intramuscular triglyceride in the provision of oxidizable fatty acids during activity. Originally it was thought that skeletal muscle lipids were of little importance in this capacity (Masaro et al, 1966; Froberg, 1971; Gollnick et al, 1969; Keul et al, 1972, p.151). Other authors, however , have demonstrated a significant utilization of intramuscular triglyceride during exercise (Paul, 1975; Carlson et al, 1971). Carlson et al (1971) demonstrated that during activity requiring 70% of the VO2max, 75% of the energy supplied by fatty acid oxidation came from intramuscular triglyceride and only 25% from fatty acids in the blood. Likewise, Paul (1975) calculated an intramuscular fat contribution of 48% of the total caloric cost during the initial 30 minutes of a long lasting activity in dogs. He concluded that plasma FFA's participated more when the activity was continued for longer periods of time.

Triglycerides are stored differentially in skeletal muscle as a function of the fiber type (Howald et al, 1978). Schmalbruch (1970) found that ST fibers contained propor-

tionately more intracellular triglyceride than did FT fibers. Their importance as a fuel source would appear to be more in line with the capacities of the ST fibers.

Intramuscular glycogen provides the most rapidly utilizable source of energy within the muscle after initial depletion of the high energy phosphagens (McMurray,1977) and is a substrate to some degree in exercise of virtually any intensity. The rate at which glycogen is utilized, however, is a function of the exercise demands.

At submaximal intensities of exercise demanding between 60 and 90% of an individuals maximal oxygen consumption the glycogen content of the working muscle declines linearly with the duration of the activity (Hultman and Bergstrom,1973). In this case intramuscular glycogen depletion is probably the limiting factor for muscular work (Hermansen et al,1967).

Although the glycogen content of muscle is relatively evenly distributed between FT and ST fibers within the muscle (Essen,1977), the FT fibers have the potential to decrease their glycogen content more rapidly owing to their higher glycolytic and ATPase activity. Muscle glycogen utilization for ATP regeneration is approximately 18 to 19 times faster via anaerobic glycolysis as compared to oxidative phosphorylation (Davis et al,1979).

The control of glycogen degradation during exercise is through the unbalancing of the glycogenesis - glycogenolysis cycle in the muscle (McMurray,1977), and, more specifically, the activity of the enzymes involved - glycogen phosphorylase and synthetase.

Phosphorylase exists in 2 forms; an inactive 'b' form , which, following phosphorylation, becomes an activated 'a' form. Likewise, glycogen synthetase may be observed in an activated 'I'form or an inactive 'D' form. These conver-

sions are mediated by phosphorylase kinase and synthase kinase respectively within the muscle. The kinase activity is strongly activated by Ca2+ which is in low concentrations in the cell at rest but rises to high concentrations following its release from the sarcoplasmic reticulum during contraction. Ca2+ released during contraction therefore promotes the conversion of phosphorylase 'b' to 'a' and simultaneously, the conversion of synthetase from the 'I'to the 'D' form. In this way glycogenolysis is promoted (Gollnick,1978).

In addition to intracellular Ca2+ concentration, the glycogenesis- glycogenolysis cycle also responds to extracellular epinephrine via the adenylate cyclase system. Elevation of the intracellular concentrationn of cAMP promotes the conversion of phosphorylase 'b' to 'a' and ensures an enhanced substrate provision (G-6-P) to the glycolytic system.

Through these mechanisms the intracellular concentration of G-6-P is maintained even during heightened activity. This helps to moderate the activity of hexokinase and encourage blood glucose sparing (McMurray,1977).

2.3.3 Intracellular Regulators

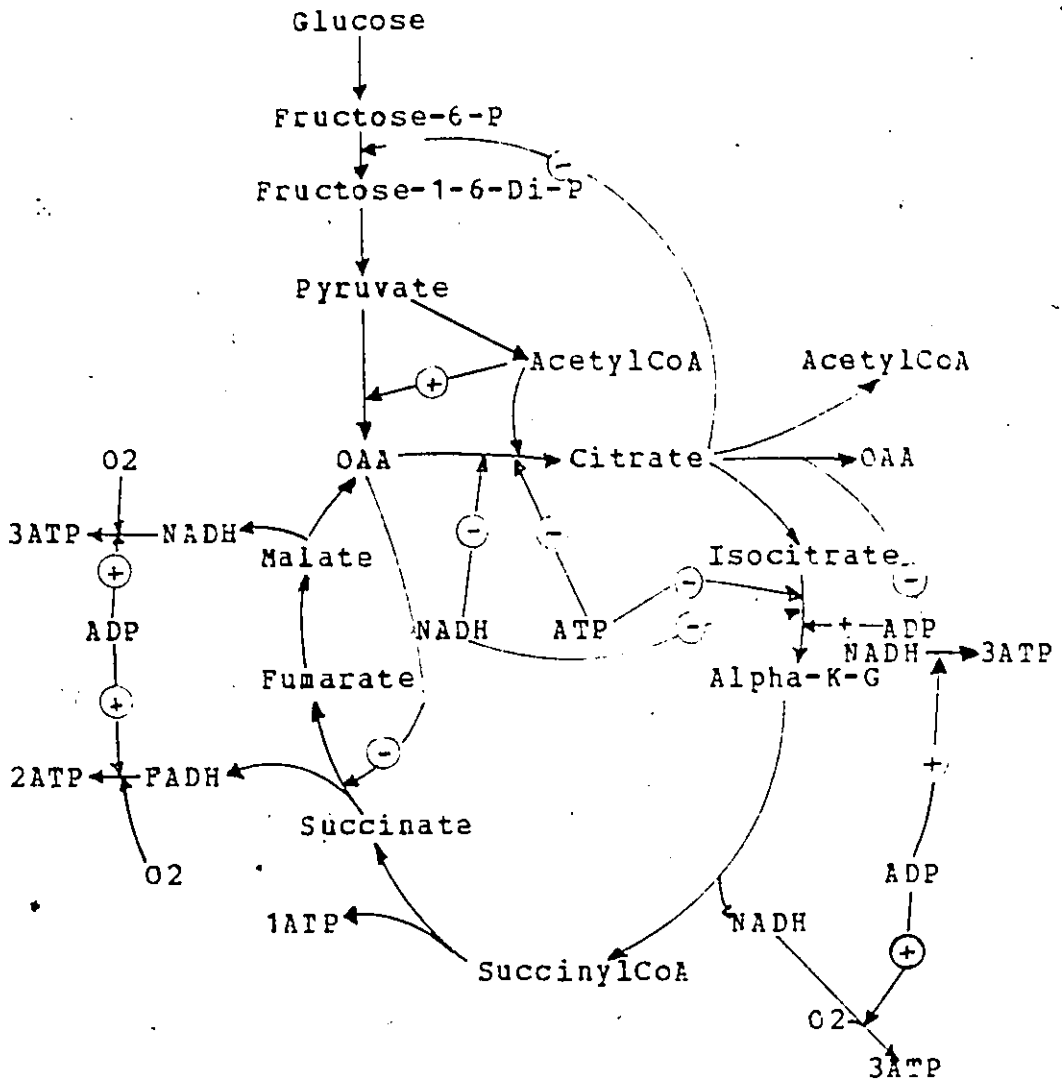
The rate at which metabolism takes place is dependent primarily on a number of intracellular regulators. Metabolic flux through aerobic and anaerobic mechanisms can dictate the contribution of each system within individual cells. Regulation may be in the form of inhibition and/or stimulation of certain regulatory enzymes but may also be related to the availability of reaction cofactors or intramuscular substrate provision (Newsholme and Start,1976). The regulation of oxidative phosphorylation is dependent primarily on the supply of oxygen, hydrogen pairs and ADP and Pi to the electron transport chain (Armstrong,1979).

In the ETC, ADP acts as the principle regulatory substance because of the obligatory coupling between electron flow and the phosphorylation of ADP in the respiratory chain (McGilvery,1975). ADP is made available to the mitochondria following the splitting of ATP during contraction and the exchange of ADP for ATP at the mitochondrial membrane (Newsholme,1978). Thus the energy transfer within the cell is related in the ATP/ADP couple (Newsholme and Start,1976). It is the ATP/ADP ratio, rather than simply the ADP concentration that is most significant in oxidative regulation (McGilvery,1975) possibly the result of competetive inhibitory effects between the 2 molecules (Newsholme,1978). High intramitochondrial ATP/ADP ratios retard oxidative phosphorylation, while low ATP/ADP ratios accelerate the ETC processes (McGilvery,1975).

The supply of reducing equivalents to the ETC is dependent on the Kreb's cycle flux as well as the delivery of hydrogen pairs from the cytoplasm via shuttle mechanisms (McMurray,1977).

Control of flux through the Kreb's cycle is provided by feedback mechanisms keyed to the concentrations of some of its carbon substrates and through the adenine nucleotides that serve as cofactors and end-products of the many reactions (McMurray,1977). These factors act as allosteric and substrate-level modulators of enzyme activity, particularly of citrate synthase and iso-citrate dehydrogenase - the flux generating steps in the Kreb's cycle (Newshlome and Start,1976). A summary of these regulatory mechanisms is presented in Figure 3.

Figure 3: Regulation of metabolism via carbon substrates and adenine nucleotides (McMurray, 1977, p.104).



In order that the hydrogen pairs generated during glycolysis be fully oxidized it is necessary that the reducing equivalents be transferred from the cytoplasm to the mitochondria. This is the role of the shuttle mechanisms. At least 2 major shuttle mechanisms are thought to operate in skeletal muscle; the alpha-glycerophosphate shuttle and the malate-aspartate shuttle (Hochachka et al,1978). It appears that each shuttle mechanism is predominant only in one of the 2 major fiber types (Baldwin et al,1973). The capacity of the muscle to oxidize alpha-glycerophosphate is inversely related to its capacity for aerobic metabolism (Van Dam et al,1971).

If oxygen is not available at the inner membrane of the mitochondrion in sufficient quantities, the electron transport chain is unable to discharge its hydrogen pairs since O2 acts as the ultimate electron acceptor. This causes the chain to back up and effectively blocks ATP production by this process.

A reduction of the mitochondrial NAD/NADH ratio has been used as an index of such hypoxia (Jobsis and Stainsby,1968;Wendt and Chapman,1976). These studies demonstrated hypoxic changes during tetanic contractions, ischemia or anaerobiosis but not when the muscle was stimulated rhythmically. In fact, the muscle levels of NAD during steady state exercise are high enough to suggest sufficient mitochondrial O2, even when lactate is being produced (Jobsis and Stainsby,1968;Wahren,1977). Only at maximal exercise intensities has hypoxia been shown tc be present (Graham,1978).

Control over glycolytic energy production is exerted primarily through the modulation of phosphofructokinase (PFK) activity- the rate limiting enzyme of glycolysis (Danforth,1965) - by the adenine nucleotides and citrate and lactate.

The activity of PFK is inhibited by high levels of ATP as well as by the accumulation of citrate (Berger et al,1976;Newsholme and Start,1976;McGilvery,1975). Since both of these conditions are thought to exist during submaximal fatty acid oxidation, it appears that this is one way that the body is able to spare glucose. This inhibition is lifted by increased levels of AMP (via AMP amplification) and Pi (Newsholme and Start,1976). ADP is also a positive modulator since it is required for production of ATP in substrate level phosphorylation at the 3-P-glycero kinase and pyruvate kinase levels (McGilvery,1975).

The production of lactate, as the end-product of anaerobic glycolysis, is a primary cause of inhibition in the glycolytic system. In this way lactate production is self-limiting. Lactate accumulation causes the decline of intramuscular pH and retards the reaction velocity of PFK (Sahlin,1977) thereby limiting ATP formation in this process.

For anaerobic glycolysis to proceed from glycogen to lactate formation the hydrogen acceptor NAD+ is required in sufficient quantities (Edington,1970). The availability of this acceptor is reflected in the cytoplasmic NAD/NADH ratio. Because the production of lactate from pyruvate results in the formation of NAD from NADH in the lactate dehydrogenase reaction, the rate of lactate production will dictate the NAD/NADH relationship. The rate of lactate production, in turn, depends on the M-LDH activity of the fiber in question (Tesch,1978). FT fibers have been found to have a greater M-LDH activity than do ST fibers (Thorstenssen at al,1978). Thus the dominance of anaerobic glycolysis in the FT fibers .

Intramuscular glycogen depletion has also been suggested as a regulator of glycolytic flux (Wenger and Reed,1976). When glycogen reserves become low the rate of glycolysis is slowed due to substrate inhibition of PFK as G-6-P levels drop (Newsholme and Start,1976).

2.3.4 Summary

The metabolic response, i.e. the relative contribution of the aerobic and anaerobic energy supply systems, is the result of the interplay between the fiber type recruited, the substrates available and the balance of regulators within the cell. While authors disagree as to the absolute importance of each of these factors, each appears to have a role in the limitation of exercise. Recruitment of either FT or ST fibers is an important consideration in establishing the capacity of the cell for either aerobic or anaerobic metabolism, while the intracellular regulators govern the rate of energy production. Subsequently, the substrates available dictate the overall work output of the cell.

2.4 AN OVERVIEW OF THE METABOLIC RESPONSE TO SUBMAXIMAL WORK OF VARYING INTENSITIES

At low exercise intensities (below approximately 40% VO2max) the oxidative phosphoylation of free fatty acids provides the predominant energy supply mechanism (Armstrong,1979). Several factors assure the dominance of this system. Firstly, the recruited fibers at this intensity are predominantly ST (Gollnick et al,1975;Essen,1977) thereby establishing a good potential for oxidative metabolism. The neuro-endocrine mediated mobilization of FFA's combined with an increase in muscle blood flow allow an enhanced delivery of FFA's to the cell membrane and create an elevated concentration gradient for diffusion (Newsholme,1977). Because the energy requirements of this intensity of exercise are within the activities of the dehydrogenases and shuttle mechanisms of the Kreb's cycle, the NAD/NADH ratio in the mitochondria remains low ensuring a sufficient supply of reducing equivalents to the ETC (Wenger and Reed,1976). The accumulation of citrate and high concentrations of ATP in the cytoplasm inhibit PFK and as a result the glycolytic flux (Newsholme and Start,1976). Accumulation of G-6-P retards glycogenolysis and glucose entry into the cell via endproduct inhibition of hexokinase and glycogen phosphory-

lase (McMurray, 1977). Finally, the increased rate of fatty acid oxidation increases the ratio of acetyl Co A:coenzyme A causing inhibition of pyruvate oxidation (Newsholme and Start, 1976)

The increased metabolism of exercise causes the O2 extraction and consumption to rise in a linear fashion with the workload, and a similar increase in metabolic CO2 production. From the cell CO2 diffuses freely into the blood where it combines with H2O in the presence of carbonic anhydrase to form carbonic acid for transport on the erythrocyte to the lungs.

$$H2O + CO2 \text{ ----- } H2CO3$$

An accentuated flux of CO2 to the lungs is instituted in this way, with this stimulus providing the most likely source of ventilatory control information (Davis and Whipp, 1979). While the mechanism of ventilatory control is not clearly apparent, it is known that ventilation (VE) closely tracks the kinetics of CO2 flux through the lungs thereby maintaining the alveolar and arterial content of CO2 (Swanson, 1979). As a result ventilation rises in proportion to the VO2 and metabolic CO2 production.

As exercise intensity increases, a point is reached, between 40 and 70% VO2max, where aerobic mechanisms are unable to supply energy at a sufficient rate to meet energy demands (Skinner and McLellan, 1980). At this point supplementation from anaerobic energy producing mechanisms is necessary to sustain work intensities.

Centrally there is a recruitment of some FT fibers to accompany the already active ST fibers (Essen, 1977; Gollnick et al, 1975a) and an increase in the sympathetic nervous system response leading to enhanced catacholamine release (Hartley et al, 1972b).

The increased utilization of ATP through contraction leads to an increased concentration of ADP, Pi, AMP, and NH_4 intracellularly and the removal of some of the inhibititory effect of citrate on PFK (Newsholme,1977). In combination with the epinephrine activated increase in glycogenolysis, the increased glycolytic flux accentuates the importance of carbohydrate as a substrate. Pyruvate now appears as an important cross roads product.

Part of the pyruvate produced is transaminated resulting in the production of Kreb's cycle intermediates and alanine (Felig et al,1970).

Lactate may act as the electron acceptor from pyruvate during anaerobic glycolysis. Because the FT fibers have a greater relative M-LDH activity (Sjodin,1976), favoring the conversion of pyruvate to lactate, some lactate will be produced in the contracting muscle. Since lactate production is attributable to the LDH isozyme pattern of the muscle (Jorfeldt,1970), the rate of lactate production is mostly the result of the qualitative and quantitative recruitment of FT fibers, which in turn is dependent on the metabolic demand. As a result, the first significant accumulation of lactate should occur at this point.

Lactate and pyruvate are non-volatile acid metabolites which will alter the cellular acidity if left to accumulate in the cell (Sahlin,1977). Of the two, lactate is the most significant during exercise since its concentration is many times higher (Keul et al,1972). Because changes in the cellular acidity may affect enzyme reactivity, the cell depends on buffering and removal of the acid metabolites for its continued functioning.

The intracellular buffering capacity has been divided into: (1) physico-chemical buffering - dependent on the amount of weak acids and bases and their dissociation con-

stants, and (2) transmembrane fluxes of H+ and HCO3- (Heisler and Piiper, 1972).

Because lactate is also removed into the blood, some authors have used blood lactates as indicative of cellular anaerobiosis (Davies et al, 1970; Wasserman et al, 1967; Davis et al, 1976).

When using blood lactate to indicate the quantity of anaerobic work, it is important to establish the relationship of muscle to blood lactate. Mader et al (1976) described blood lactate as the result of lactate production release, distribution and metabolism.

A number of studies have demonstrated that lactate is not freely diffusable from the muscle cell to the blood (Karlsson, 1971; Jorfeldt, 1978; Mainwood and Worsley-Brown, 1973) and demonstrates saturation kinetics (Jorfeldt, 1978). A translocation mechanism with a finite capacity is suggested. Hence, during exercise, muscle to blood lactate gradients are established (Graham et al, 1976). The steepness of this gradient is different between fiber types - FT fibers having gradients 3 times as high as ST fibers (Graham et al, 1976). This is thought to be the result of a higher rate of production or a slower rate of release from FT fibers. It was also suggested that perfusion by means of surface area and diffusion distance was regulating release (Graham, 1978).

The existence of concentration gradients dictates that muscle to blood lactate equilibration is not instantaneous. Mader et al (1976) have identified a time constant of approximately 2 minutes from intracellular lactate production till its arrival in the extracellular space. Other authors (Karlsson, 1971; Jorfeldt et al, 1978) suggest longer times (up to 5 minutes) based on higher intracellular concentrations, more likely to cause saturation of the translocation mechanism.

The metabolism of lactate during exercise has been shown to be significant (Jorfeldt,1970; Hubbard,1973;Essen et al,1975;Jorfeldt et al,1978).

Hubbard (1973) injected a bolus of sodium L-lactate which was radioactively labelled into normal individuals during heavy exercise. The intensity of the exercise was such that lactate levels and oxygen consumption were held constant for the duration of the activity. Lactate removal and metabolism from blood was found to be greater during exercise than at rest as most of the labelled lactate was recovered as labelled CO2 and little took part in gluconeogenesis.

The uptake of lactate occurs largely in muscles that are still operating aerobically during exercise including both skeletal (Essen et al,1975) and cardiac muscle (Keul et al,1966). Here the lactate is converted back to pyruvate and then oxidized in the Kreb's cycle.

Jorfeldt (1970) suggested that, within the muscle, the FT fibers produce the lactate. Simultaneously, ST fibers are continually taking up lactate, both from the blood and from the FT fibers directly. Lactate released into the blood is therefore the net effect of its production and simultaneous oxidation.

In the blood, lactate is considered to be the most significant acid metabolite during exercise (Keul et al,1972). If left unchecked, the efflux of muscle lactate to the blood would lead to an increase in the H+ concentration of the blood and a decline in blood pH - a situation of metabolic acidosis.

In deference to a declining pH the blocd provides a buffer system consisting of a relatively unimportant HPO4/H2PO4 component, numerous protein buffers (most notably hemoglobin) and the HCO3-/CO2 portion (Comroe,1968).

During exercise, the buffering of the base bound as bicarbonate is considered to be the most important in dealing with exercise-induced metabolic acidosis (Bouhuys and Pool,1966). This stems from this systems end product removal (CO2) during respiration and regeneration of the original bicarbonate molecule (Sutton and Jones,1979). Bicarbonate buffering of lactate is illustrated in the following reaction:

$$H^+ + La + NaHCO_3^- \longrightarrow NaLa + H_2CO_3$$

$$H_2CO_3 \longrightarrow H_2O + CO_2$$

In this way the buffering of H+ becomes an additional source of CO2, over and above the metabolic CO2 production of aerobic metabolism (Clode and Campbell,1969).

The bicarbonate system does not, however, reflect the total buffer capacity of the blood. Hemoglobin and other protein buffers are also important in the maintenance of acid/base status (Davenport, 1971; Siggaard-Anderson, 1974). Buffer base is the term which is utilized to describe the total buffer capacity of the blood. This includes both bicarbonate and non-bicarbonate (HPO_4, Pr, Hb, HbO_2) sources.

Of the non-bicarbonate buffers, hemoglobin (Hb) and its oxidized form oxyhemoglobin (HbO_2) play the most important role in the buffering of exercise-induced acidosis (Comroe, 1967). A protein such as hemoglobin is a buffer because it's molecule contains a large number of acidic and basic groups. Much of the buffering by hemoglobin in the physiological range is done by the imadazole groups of histidine. The buffering power of Hb varies depending on whether O_2 is being carried by the molecule. When oxygen is removed from HbO_2, the remaining molecule becomes less strongly acidic thereby taking up hydrogen ions from solution (the Haldane effect). Hb, therefore, is a better buffer than HbO_2. An increase in blood acidity facilitates the dissociation of O_2 from HbO_2 (the Bohr effect) thereby enhancing the buffering power of the blood.

Increases of total Hb have been found in dogs and humans as the result of training (Davis and Brewer, 1935; Kjellberg et al, 1949; Brotherhood et al, 1975). These increases seem to parallel increases in blood volume such that no increase in Hb concentration (Hb per unit blood volume) occurs. Indeed, Dill and associates (1974) found Hb concentration to be 4% lower in highly trained runners than in controls. They concluded that endurance athletes have thin blood, but increases in blood volume coincident with training allow their total Hb to exceed that of non-athletes.

Since VCO2 flux is tied to ventilation and VO2 is linear with workload (Astrand and Rodahl,1977), exercise intensities above the appearance of lactate (i.e. the LT, Ivy et al,1980), lead to a disproportional increase in the VE with respect to VO2. This corresponds to the 'anaerobic threshold' described by Wasserman et al (1973).

Ventilation at this point is still tied to CO2 production so the arterial content of CO2 remains unchanged (isocapnic hyperpnea) but the fraction of O2 in the expired ventilation increases (Hollmann and Kastner,1968). The end result is respiratory compensation for the lactacidosis and a stable pH in the blood.

Further increments of exercise intensity (between 65 and 90% VO2max) are accompanied by the recruitment of qualitatively and quantitatively more FT fibers (Essen,1977;Gollnick et al,1975) and a relatively greater sympathetic activation (Terjung,1979;Galbo et al,1973). The dependence on intramuscular glycogen is increased accordingly (Gollnick and Hermansen, 1973).

Pyruvate production at this intensity is greatly enhanced as a result of increased glycogenclysis and the reduced cytosolic ATP levels (Newsholme and Start,1976). Much of the pyruvate will be converted to lactate as a consequence of the LDH isozyme activity of the recruited FT fibers. Dise-

quilibrium of lactate release from muscle and its metabolism cause blood lactate levels to rise. At approximately 4mmol La/L blood, the buffer capacity of the blood becomes saturated (Mader et al,1976). Now free H+ ions are present in the circulation, causing the hydrogen ion concentration to rise.

Continuing lactate influx causes an exponential increase in blood lactate and a significant drop in blood pH. This work intensity corresponds to the 'threshold of decompensated metabolic acidosis' (Reinhard et al,1979) and is indicative of the body's ability to compensate effectively for metabolic acidosis.

The free H+ ions provide an additional drive to ventilation (Sutton and Jones,1979) which now increases out of proportion to CO2 flux. Ventilatory drive may be further enhanced by the increased nerve impulse flow associated with F^T fiber stimulation (Mahler,1979).

Inside the cell, the increased lactate production causes a decrease in intracellular pH which is much larger than that seen extracellularly (Sahlin,1977). Lactate production is in this way self-limiting since declining pH inhibits the reaction velocity of PFK (Danforth,1965) and initiates changes in the ionic form of glycolytic substrates and products (Sahlin,1977). Glycolytic flux is retarded accordingly and the rate of ATP production is slowed.

Muscle acidity has other effects which may interfere with the muscles' ability to contract. Wenger and Reed (1976) listed 2 of these. An H+ mediated decrease in the permeability of the membrane to Na and K+ could result in a hyperpolarized state and impairment of depolarization required for contraction . Further, H+ ions could actively compete with Ca2+ for the binding sites on actomyosin (Katz,1970) and inhibit contraction in this manner.

Apparently then, at work intensities above the TDMA, the work time is limited by the accumulation of intracellular and extracellular lactate and its effect on acidity in those compartments.

2.5 COMPARISON OF THE RESPONSE OF TRAINED AND UNTRAINED INDIVIDUALS

Endurance training has been shown to produce changes in the relative contribution of the aerobic and anaerobic energy supply systems at absolute and relative submaximal work intensities (Saltin and Karlsson, 1971). It has also been shown to be important in determining the use of carbohydrates and fats as substrates during work (Hultmen et al, 1967; Holloszy, 1976). The general response to training is a movement towards a higher contribution of the aerobic energy systems and a greater use of fats as opposed to carbohydrates.

Table 3 presents a comparison of the response of trained and untrained subjects to submaximal work.

Endurance training increases the ability to oxidize fat and carbohydrate substrates including FFA's and the end-products of glycolysis - pyruvate and lactate (Morgan et al, 1971; Mole et al, 1973; Essen et al, 1975; Holloszy, 1976). This ability is linked to an increased provision of substrates and an increase in the activity of enzymes necessary for oxidative metabolism.

PARAMETER	RESPONSE trained vs untrained	AUTHORS
Fat Oxidation	>	Holloszy, 1976
Pyruvate Oxidation	>	Morgan et al, 1971
		Mole et al, 1973
Pyruvate Transamination	>	Mole et al, 1973
Lactate Production	<	Saltin and Karlsson, 1971
Lactate Oxidation	>	Essen, 1975
Standard Bicarbonate	=	Keul et al, 1966
Physiological Landmarks		
Lactate T-Hold	>	Wasserman et al, 1973
		Davis et al, 1979
TDMA	>	Mader et al, 1976
		Kindermann et al, 1979

Table 3: A comparison of the response of trained and untrained subjects to submaximal work.

More FFA's are made available to the mitochondria by virtue of an increased intracellular triglyceride content (Howald et al,1978;Holloszy,1973) and enhanced activity in the enzymes required for the activation, transport and beta-oxidation of fatty acids (Mole et al,1971;Holloszy ,1973). Although the glycogen content of muscle also tends to rise in the trained state (Taylor et al,1972a;Taylor et al,1972b; Taylor et al,1978; Gollnick et al,1972) the actual utilization of glycogen is decreased with training (Saltin and Karlsson,1971a and b).

The augmentation of the activity of the oxidative enzymes is the second major adaptation seen with endurance training. The affected systems include: (1) the enzymes of the Kreb's cycle (Holloszy et al,1970;Dohm et al,1973), (2) the electron transport chain activity (Barnard and Peter,1971;Morgan et al,1973;Gollnick et al,1973) and, (3) the malate-aspartate shuttle mechanism (Mole et al,1973). The mechanism of the increased oxidative activity appears to be related to increased protein synthesis and proliferation of mitochondria within the muscle (Morgan et al,1973;Hoppeller et al,1973).

Even though the capacities for both fat and pyruvate oxidation are enhanced with training (Holloszy,1976), the increased oxidative energy provision as a result of chronic exercise is almost entirely due to an augmentation of fat oxidation (Holloszy et al,1977; Hermansen et al,1976). This is most likely the result of the inhibition of glycolysis during increased oxidation of fats (Newsholme and Randle,1964;Neely and Morgan,1974;Rennie,Winder and Holloszy,1976). Glycolytic inhibition is mediated through the accumulation of citrate which acts as an allosteric modulator of PFK activity. The declining glycolytic flux causes an accumulation of G-6-P and the inhibition of hexokinase activity.

Lactate production and appearance in the blood at absolute and relative submaximal workloads is reduced in the trained state even at similar rates of glycolysis (Saltin and Karlsson,1971a). While part of the reason for this decrease is an enhanced pyruvate oxidation (Mole et al,1973) ,Skinner and McLellan (1980) have attributed part of the difference to a change in the LDH isozyme activity and alanine transamination.

Pyruvate is converted to lactate by the action of the M-LDH isozyme while the reverse reaction is catalysed by H-LDH. Karlsson et al (1975) have demonstrated a decrease in the total LDH activity with endurance training but a shift towards the H-LDH isozyme. Meanwhile, Sjodin (1976) and Sjodin et al (1976) reported that the relative activity of the H-LDH isozyme was enhanced in both FT and ST fibers following an endurance training regime. As a result, slower lactate production may be expected along with an improvement in the ability of the muscle to uptake (Saltin et al,1976) and oxidize lactate (Jorfeldt,1970).

An alternate pathway for the removal of pyruvate is its transamination to alanine. Since alanine aminotransferase activity has been demonstrated to increase with endurance training (Mole et al,1973) it is possible that alanine production may attenuate lactate accumulation in the muscle.

The decreased production and enhanced utilization of lactate results eventually in a lesser accumulation of lactate intramuscularly and in the blood at submaximal workloads (Saltin and Karlsson,1971a). The ability to deal with the blood lactate will affect the appearance of the aerobic/anaerobic transition on the basis of blood parameters.

Training appears to have little effect on the resting concentration of standard bicarbonate i.e. those alkalies bound as bicarbonate at a pCO2 of 40mmHg, 37degrees C and completely O2 saturated hemoglobin (Kaul et al,1966). Be-

cause the level of standard bicarbonate is independent of the pCO2, it will be influenced mainly by the non-volatile acids (lactic and pyruvic) in the blood thereby providing the power for respiratory compensation of the metabolic acidosis. However no additional buffering capacity is indicated through this mechanism.

As a consequence of the increased oxidative capacity, decreased lactate production and increased removal, and equivalent buffering for individuals in the trained state, it would appear that the physiological landmarks under study (VO2max, lactate threshold, threshold of decompensated metabolic acidosis), will differ from the untrained state.

Both longitudinal (Davis, et al,1979;Saltin and Karlsson,1971) and cross-sectional studies (Hermansen and Saltin,1967;Williams et al,1968) have demonstrated that the LT occurs at a greater relative proportion of the maximal oxidative capacity in subjects in the trained state. As a result, the onset of the metabolic transition during incremental work is delayed in these subjects.

The enhanced capacity of trained skeletal muscle for the oxidation of fat substrates, in conjunction with the increased ability to metabolize lactate in skeletal, cardiac and hepatic tissue, may be expected to create a blood lactate equilibrium at a higher relative workload following chronic endurance exercise. Consequently, the buffer system is relieved of some of its stress and the appearance of TDMA is delayed.

It is therefore expected that the transitional phase from aerobic to anaerobic metabolism during incremental work will occur not only at a higher proportion of the maximal oxidative capacity in the trained subjects, but also encompass a larger continuum of workloads than in the untrained state. will differ from the untrained individual.

Chapter III
METHODOLOGY

3.1 SUBJECTS

The subjects in this study were 18 young, healthy, male volunteers between the ages of 20 and 30 who were asymptomatic for any disease and had no history of difficulty during exertion. Body fat estimations were performed to ensure that all volunteers are non-obese i.e., not above the average body fat percentage for age and sex by more than 10%. All procedures were explained in full and the subjects were encouraged to ask questions pertaining to the protocol prior to the obtainment of consent in writing, in accordance with the American College of Sportsmedicine's guidelines for human research models (1975).

Half of the subjects (n=9) were considered to be untrained i.e., not involved in any systematic endurance training for a period of at least 6 months prior to the onset of experimentation. The rest of the subjects (n=9) were considered as endurance trained i.e., they had been involved in a training regimen for at least 6 months prior to the onset of experimentation requiring at least 10 hours of cross-country ski training per week.

3.2 EXERCISE PROCEDURES

The testing required that each subject visit the laboratory on two separate occasions. The visits were separated by at least one day with each subject being tested at the same time of day (+ or - 90 minutes) to minimize any diurnal effects.

3.2.1 Day one

On the first day of testing, the subject reported to the laboratory for an orientation session. Following a description and a demonstration of the testing procedures, consent were obtained in writing.

During this visit, the subject were aquainted with the gas collection apparatus and the Monark cycle ergometer to be used during testing was adjusted to suit the subject (seat height = 109% of the inseam length). In addition, a resting 12 - lead electrocardiogram tracing was obtained and an estimation of the subject's body density was made based on underwater weights.

3.2.2 Day two

On the second day of testing the subject appeared in the laboratory in a post-absorptive state for the performance of a continuous incremental work test to exhaustion. All exercise testing was performed with the subject seated in an upright position on a Monark cycle ergometer.

After an initial weighin, the subject remained in a resting state for at least 20 minutes prior to the onset of exercise. During this time the subject was prepared for V5 electrocardiography and a Teflon catheter (Jelco, 20g.,Raritan,N.J.) was placed in a superficial vein on the dorsal surface of the right hand. The catheter was connected to a 3-way stopcock (Monoject,St.Louis) via 10cm. of flexible tubing (Abbott Laboratories, Chicago).

During the test, the subject began pedalling with no resistance at a pedalling frequency of 60 rpms. (The actual number of revolutions was monitored via a microswitch attached to the inside of the ergometer wheel).

The exercise period began with a warmup period during which time the workload was gradually increased to a point that produced a steady-state heart rate of 120 bpm. Subsequently the exercise intensity was increased 180 kpm/min. every 2 minutes until subjective feelings of exhaustion or an inability to maintain the work intensity was noted.

During the exercise the subject breathed through a Collins 'Triple J' low resistance and high velocity valve. The expired air was collected through plastic tubing into a tissot tank. Respiratory gas samples were collected during the final 30 seconds of each workload and the mixed expired samples were analysed for oxygen (FEO2) and carbon dioxide (FECO2) content on a Godart capnograph and oxygen analyser. As well the total expired ventilation (VE) was calculated from the collected gas. Electrocardiogram recordings were made automatically at the onset of each minute.

Minute ventilation (BTPS) was calculated and corrected to STPD and finally used in conjunction with the FEO2 and FECO2 in the computation of VO2 and VCO2. Ventilatory equivalents of oxygen (VEO2) and of carbon dioxide (VECO2) were then calculated as the ratio of VE to VO2 and of VE to VCO2 respectively.

Respiratory gas and venous blood samples were collected at rest, during the final 30 seconds of the warmup period and during the final 30 seconds of each subsequent workload.

3.3 BLOOD SAMPLING AND ANALYSIS

During each blood sample, 1ml of blood was withdrawn and discarded while a further 5ml was collected in a clean syringe. The catheter was kept patent beween samples with sterile, heparinized saline. One ml of the blood sample was immediately deproteinized in ice-cold perchloric acid and then frozen until the enzymatic determination of lactate content (Boehringer Mannheim; accuracy 0.2mM) could be

made. The remaining 4ml of blood was used for the immediate determination of blood pH on a Corning pH/blood gas analyser (model 165; accuracy 0.007 pH units).

LT was determined as the workload at which the first statistically significant increase in blood lactate occured (Ivy et al, 1980). The TDMA was acertained as the workload coinciding with the first significant drop in pH.

3.4 STATISTICAL ANALYSIS

The following statistical techniques were used for the analysis of the data:

1. Descriptive statistics including means and standard deviations.
2. One way analysis of variance with Sheffe post-hoc analysis to determine significant changes in lactate concentration and pH.
3. One way analysis of variance to compare measures of workload, oxygen consumption, % VO2 max utilized and heart rate at the LT and at the TDMA in trained and untrained subjects.
4. Correlational co-efficients to relate the changes in blood parameters to those in ventilation.

Chapter IV
RESULTS AND DISCUSSION

The purpose of this study was twofold; to objectively define criteria for the determination of the transition phase from aerobic to anaerobic metabolism, and to compare the location and duration of the transition phase in untrained and in endurance trained subjects. To this end the results and discussion will be subdivided into 3 sections; (1) physiological characteristics of the subject groups, (2) criteria for the determination of the transition phase, and (3) a comparison of the transition phase in untrained and in endurance trained subjects.

4.1 PHYSIOLOGICAL CHARACTERISTICS OF THE SUBJECT GROUPS

Table 4 provides a summary of the physical characteristics of the trained and untrained subjects. No significant differences were observed with respect to age, height or weight of the subjects. The trained subjects, however, proved to be significantly leaner than their untrained counterparts. This is a common observation in trained subjects since endurance training often leads to a reduction in body fat percentage (Parizkova, 1978).

Maximal values of oxygen consumption, heart rate and blood lactate concentration in trained and untrained subjects are presented in Table 5. No differences were observed in maximum heart rate or in the maximum blood lactate concentration between the two subject groups, indicating that the end points of exercise were similar in relative terms for both trained and untrained subjects. However, trained subjects were characterized by a significantly higher maximal oxygen consumption. A plethora of authors,

PARAMETER	TRAINED	UNTRAINED
Age	21.1	22.7
(Yrs)	3.8	2.2
Height	177	177
(cm)	6	7
Weight	72.5	74.4
(kg)	8.0	7.4
Body Fat	10.3*	13.2
(%)	2.1	3.5

* Significant at 0.05 level

Table 4: Physical characteristics of trained and untrained subjects.

using both longitudinal (Saltin et al, 1969; Williams et al, 1967; I.Astrand et al, 1973; Davis et al, 1979) and cross-sectional (Saltin and Grimby, 1968; Astrand and Rodahl, 1977, p. 319-325) designs have reported an increase in maximal oxygen consumption with endurance training. It appears that the trained subjects in this study were, in fact, more endurance trained than the untrained subjects.

4.2 CRITERIA FOR THE DETERMINATION OF THE TRANSITION PHASE

The means of the pH, and lactate values with increasing workloads are presented in Figures 4 and 5. Figure 4 contains information specific to untrained subjects while Figure 5 describes the responses of trained individuals. As

PARAMETER	TRAINED	UNTRAINED
VO2 max	64*	52
(ml/kg/min)	3	5
Heart Rate	193	193
(bpm)	10	9
Blood Lactate	11.7	11.6
(mM)	3.0	2.7

* Significant at 0.05 level

Table 5: Maximal values of oxygen consumption, heart rate and blood lactate concentration in trained and untrained subjects.

expected, blood pH values remained stable for a period of time after blood lactate had started to accumulate, indicating that compensatory mechanisms were in operation.

The pH values recorded during the present experimentation were markedly lower than those described previously (Bouhuys et al, 1966; Reinhard et al, 1979), even at rest. This may be the result of stress response to the catheter insertion.

The summaries of ANOVA for lactate values with increasing workloads in untrained and trained subjects are presented in Tables 6 and 7 respectively. Significance was obtained across workloads at the 0.01 and the 0.05 level respectively. A comparison of means was conducted using Scheffe post-hoc analysis and the results are presented in Tables 8 and 9.

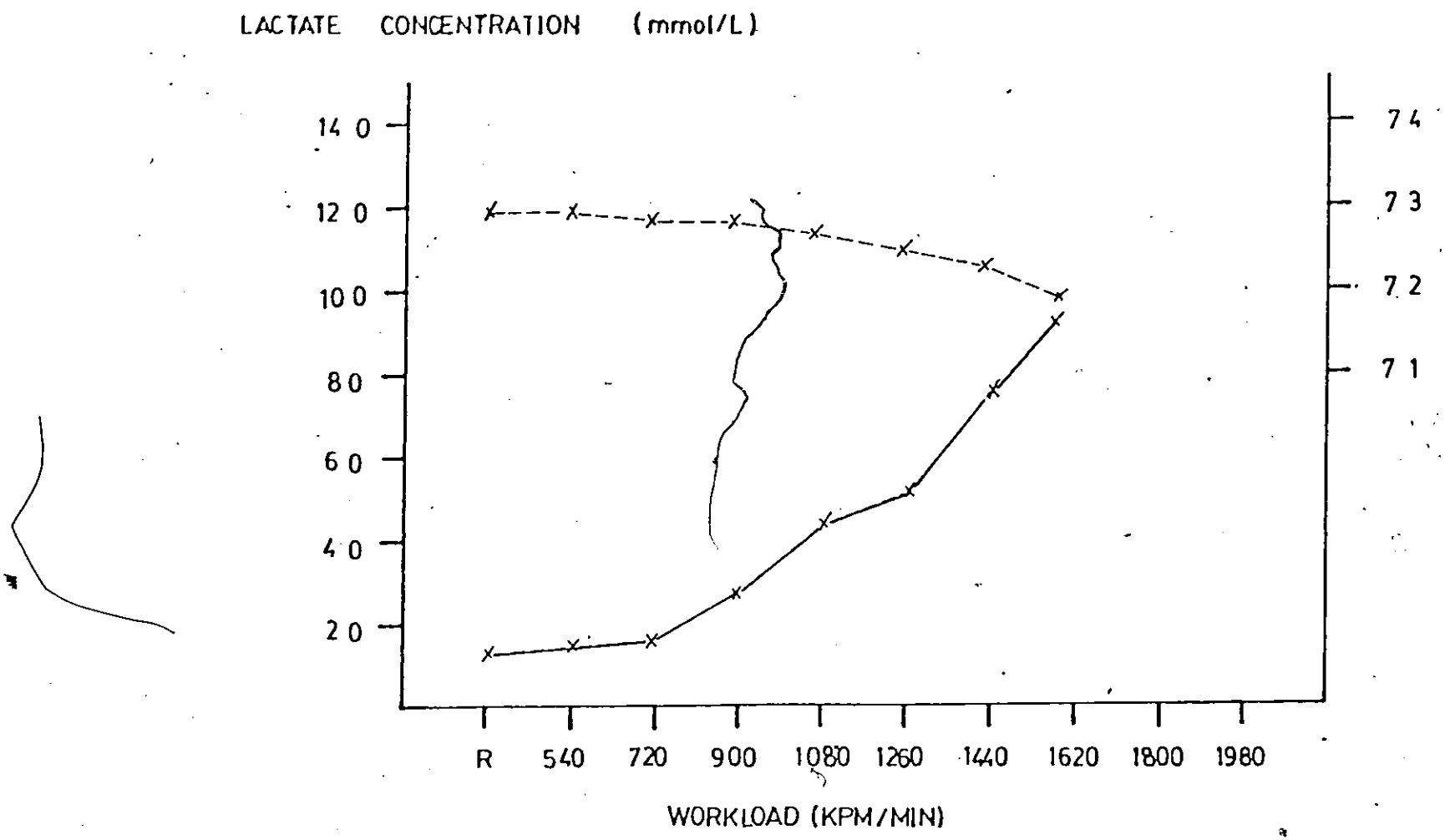


Figure 4: Mean values of pH and lactate concentration with increasing workloads in untrained subjects.

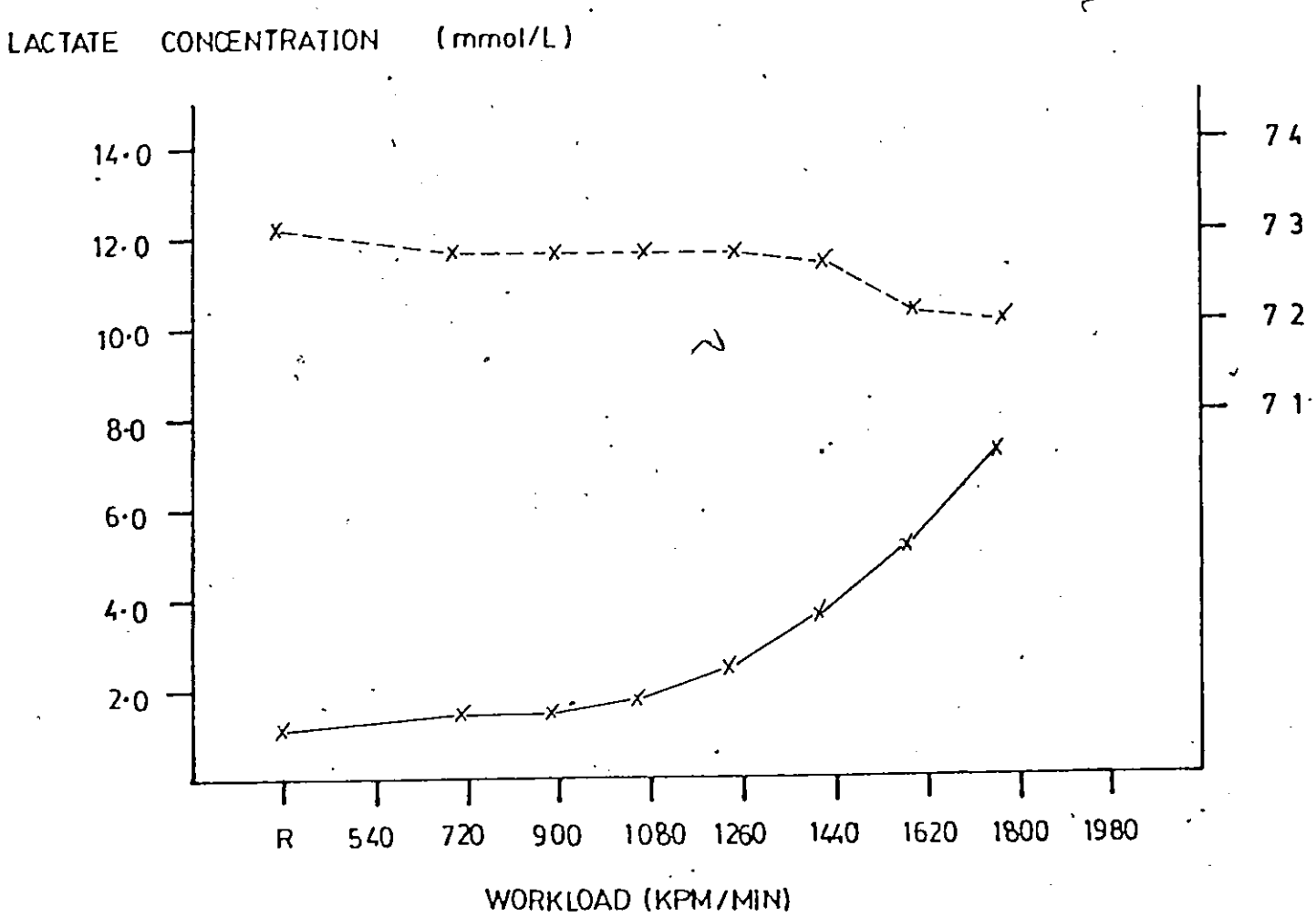


Figure 5: Mean values of pH and lactate concentration with incresing workloads in trained subjects.

SOURCE OF VARIATION	SS	df	MS	F
Between Subjects	6.5x10	7	9.3x10	9.43*
Within Subjects	5.1x10	52	9.8x10	

*Significant at 0.01 level

Table 6: Summary of ANOVA comparing blood lactate values with increasing workloads in untrained subjects.

The critical difference required for significance in the Scheffe test was determined to be 1.1 mM in the untrained subjects and 0.9 mM in the trained subjects. These values were added to the resting lactate values for each subject in their respective groups, to ascertain where a significant increase in blood lactate had occured. LT was defined by the workload just prior to the first significant accumulation of blood lactate.

SOURCE OF VARIATION	SS	df	MS	F
Between Subjects	9.1x10	8	1.1x10	6.14*
Within Subjects	1.1x10	58	1.9x10	

* Significant at 0.05 level

Table 7: Summary of ANOVA comparing lactate concentration with increasing workloads in trained subjects.

The summaries of ANOVA comparing blood acidity measures (pH) with increasing workloads in untrained and trained subject are presented in Tables 10 and 11, respectively. Significance was obtained across the workloads in both subject groups. Scheffe post-hoc analysis was utilized to compare the individual workload means. These results are summarized in Tables 12 and 13.

The critical change in pH required for significance in the Scheffe test was determined to be 0.08 pH units in the untrained subjects and .11 pH units in the trained subjects. These values were subtracted from the resting value for each subject in their respective groups to determine where a significant decrease in blood pH had occured.

SAMPLE	Rest	2	3	4	5	6	7	8
Mean La conc. (mM)	1.3	1.5	1.6	2.6	4.4	5.0	7.7	9.4
Rest	1.3	0.2	0.3	1.3*	3.1*	3.8*	6.4*	8.1*
2	1.5		0.1	1.1*	2.9*	3.5*	6.2*	7.9*
3	1.6			1.0	2.8*	3.4*	6.1*	7.8*
4	2.6				1.8*	2.4*	5.1*	6.8*
5	4.4					0.6	3.3*	5.0*
6	5.0						2.7*	4.4*
7	7.7							1.7*

* Significant at 0.05 level; S (.05) = 1.1

Table 8: Post-hoc comparison of mean blood lactate values with increasing workloads in untrained subjects for the determination of criterion difference in lactate required for the LT.

The TDMA was defined as the workload just prior to the first significant decrease in blood pH in comparison to resting values.

A comparison of the mean blood lactate concentrations at LT and at TDMA for the trained and untrained subjects is provided in Table 14. No significant differences were observed at the .05 level of significance at either threshold

SAMPLE		Rest	2	3	4	5	6	7	8	9
Mean La conc. (mM)		1.0	1.3	1.3	1.5	2.2	3.4	4.9	7.1	6.6
Rest	1.0		0.3	0.3	0.5	1.2*	2.4*	3.9*	6.1*	5.6*
2	1.3			0	0.2	0.9*	2.1*	3.6*	5.8*	5.3*
3	1.3				0.2	0.9*	2.1*	3.6*	5.8*	5.3*
4	1.5					0.7	1.9*	3.4*	5.6*	5.1*
5	2.2						1.2*	2.7*	4.9*	4.4*
6	3.4							1.5*	3.7*	3.2*
7	4.9								2.2*	1.7*
8	7.1									0.5

* Significant at 0.05 level; S (.05)= 0.9

Table 9: Post-hoc comparison of mean blood lactate values with increasing workloads in trained subjects for the determination of criterion difference in lactate required for the LT.

SOURCE OF VARIATION	SS	df	MS	F
Between Subjects	390.2	7	55.7	21.2*
Within Subjects	129.0	52	2.6	

* Significant at 0.01 level

Table 10: Summary of ANOVA comparing the measures of blood pH with increasing workloads in untrained subjects.

point. However, a large standard deviation of blood lactate concentrations was noted at the TDMA. This indicates that an absolute lactate value of 4mM as suggested by Kindermann et al (1979) may not adequately describe the same point in different subjects.

Correlational co-efficients relating the percentage VO2 maximum observed at the LT, the TDMA, the first non-linear increase in VE (STPD) and the minimum value of VECO2 for untrained and trained subjects are described in Tables 15 and 16 respectively.

Previous investigations had suggested that the LT - as determined from blood lactate measurements - would be highly

SOURCE OF VARIATION	SS	df	MS	F
Between Subjects	290.0	8	36.3	11.6*
Within Subjects	177.7	58	3.1	

* Significant at 0.01 level

Table 11: Summary of ANOVA comparing the measures of blood pH with increasing workloads in trained subjects.

correlated with the first non-linear increase in VE (STPD) (Wasserman et al, 1973; Davis et al, 1976; Reinhard et al, 1979). Likewise, the TDMA has been reported to correspond to the minimum value of VECO2 (Reinhard et al, 1979; Gutin and Young, 1980) although this relationship is somewhat weaker.

In the present study, no significant correlations existed between these parameters. Possible reasons for these discrepancies include: a difference in exercise protocols (1 minute versus 2 minute workloads), differences in the location of blood sampling and differences in the statistical criteria used to denote threshold points. In addition, the ventilatory responses to exercise may differ between trained and untrained individuals (Byrne-Quinn et al, 1971, Stegemann et al, 1975)

SAMPLE		Rest	2	3	4	5	6	7	8
Mean pH		7.30	7.30	7.29	7.29	7.27	7.25	7.23	7.19
Rest	7.30		0	.01	.01	.03	.05	.07	.11*
2	7.30			.01	.01	.03	.05	.07	.11*
3	7.29				0	.02	.04	.06	.10*
4	7.29					.02	.04	.06	.10*
5	7.27						.02	.04	.08*
6	7.25							.02	.06
7	7.23								.04

* Significant at .05 level; S (.05)= .08

Table 12: Post-hoc comparison of mean blood pH values with increasing workloads in untrained subjects for the determination of criterion difference in pH required for the TDMA.

SAMPLE		Rest	2	3	4	5	6	7	8	9
Mean pH		7.30	7.28	7.28	7.28	7.28	7.27	7.22	7.20	7.18
Rest	7.30		.02	.02	.02	.02	.03	.08	.10*	.12*
2	7.28			0	0	0	.01	.06	.08	.10
3	7.28				0	0	.01	.06	.08	.10
4	7.28					0	.01	.06	.08	.10
5	7.28						.01	.06	.08	.10
6	7.27							.05	.07	.09
7	7.22								.02	.04
8	7.20									.02

* Significant at .05 level; S (.05) = .11

Table 13: Post-hoc comparison of mean blood pH values with increasing workloads in trained subjects for the determination of criterion difference in pH required for the TDMA.

PARAMETER	TRAINED	UNTRAINED
Lactate conc. at LT (mM)	1.6 .3	1.7 .3
Lactate conc. at TDMA (mM)	4.7 2.3	5.4 2.0

* Significant at .05 level.

Table 14: Comparison of mean lactate concentration at the LT and at the TDMA in trained and untrained subjects.

4.3 THE TRANSITION PHASE IN TRAINED AND UNTRAINED SUBJECTS

Table 17 provides a comparison of the LT and the TDMA as observed in trained and untrained subjects.

LT was found to occur at a significantly higher absolute workload (both in terms of kpm/min. and in VO2) in trained subjects in comparison to untrained subjects. This difference also remained when workload was expressed relative to the individual's VO2 max. This group also demonstrated a higher mean heart rate at this point.

The TDMA also occured at a significantly higher absolute workload in the trained subjects in comparison to those in the untrained group. Again this difference remained when workload was expressed relative to the individuals' VO2 max.

Table 18 provides a comparison of the relative and absolute work capacity encompassed by the aerobic-anaerobic transition phase in trained and untrained subjects.

	LT	TDMA	Non-linear increase in VE (STPD)	Minimum value of VECO2
LT		-.04	.11	-.39
TDMA			.57	.43
Non-linear increase in VE (STPD)				.54

* Significant at .05 level; Critical value = .602

Table 15: Correlational co-efficients of % VO2 max observed at the LT, the TDMA, the first non-linear increase in VE and the minimum value of VECO2 in untrained subjects.

No significant differences were observed between trained and untrained subjects in terms of the workload, the percentage VO2 max or the VO2 values between the LT and the TDMA. It appears, then, that the trained subjects have a transition phase which occurs at a higher relative proportion of the maximal oxidative capacity.

The LT has been shown, previously, to be elevated in endurance trained subjects. (Hermansen and Saltin, 1967; Williams et al, 1968; Costill, 1970; Davis et al, 1979). Lactate production and its appearance in the blood at absolute

	LT*	TDMA	Non-linear increase in VE	Minimum value of VECO2
LT		.28	-.21	-.38
TDMA			.04	.25
Non-linear increase in VE (STPD)				.34

* Significant at .05 level; Critical value = .602

Table 16: Correlational co-efficient of % VO2 max observed at the LT, the TDMA, the first non-linear increase in VE and the minimum value of VECO2 in trained subjects.

and relative submaximal workloads is reduced in the trained state even at similar rates of glycolysis (Saltin and Karlsson, 1971).

The elevation of the LT is believed to be the result of several mechanisms. Training results in an increased ability to oxidize fats (Holloszy et al, 1977; Hermansen et al, 1976) causing an inhibition of glycolysis (Newshclme and Randle, 1964; Neely and Morgan, 1974; Rennie et al, 1976). At the same time, the ability to oxidize pyruvate, is also increased (Holloszy, 1976) and alternate pathways favoring the transamination of pyruvate to alanine increase their activity (Mole et al, 1973). The net result is a decreased production of lactate.

PARAMETER	TRAINED	UNTRAINED
LACTATE THRESHOLD		
Workload	1269*	1020
(kgm/min)	156	201
VO2	46*	32
(ml/kg/min)	7	4
% VO2 max	72*	62
	10	8
Heart Rate	155*	144
(bpm)	11	10
THRESHOLD OF DECOMPENSATED METABOLIC ACIDOSIS		
Workload	1600*	1350
(kgm/min)	1	167
VO2	57*	43
(ml/kg/min)	4	5
% VO2 max	89*	83
	6	7
Heart Rate	177	173
(bpm)	8	9

* Significant at .05 level

Table 17: A comparison of the workload, oxygen consumption, and heart rate at the LT and at the TDMA in trained and untrained subjects.

PARAMETER	TRAINED	UNTRAINED
Workload	340	330
(kgm/min)	210	168
VO2	11	12
(ml/kg/min)	8	5
% VO2 max	18	21
	13	10
Heart Rate	23	29
(bpm)	12	4

* Significant at the .05 level

Table 18: The workloads, oxygen consumptions and heart rates measured between the LT and the TDMA in trained and untrained subjects.

Ivy et al (1980) have recently demonstrated a significant correlation between the LT and the percentage of ST fibers in biopsy samples. Well trained endurance athletes tend to have higher percentages of ST fibers (Bergh et al, 1978; Costill et al, 1976a; Costill et al, 1976b; Gollnick et al, 1972; Saltin et al, 1977) and a preferential H-LDH isozyme pattern (Karlsson et al, 1975; Sjodin et al, 1976). The ST fibers would, therefore, have the ability to oxidize the lactate being produced in adjacent fibers, preventing some lactate release into the circulation.

Blood lactate values are dependent not only on lactate production, but also its release and metabolism.

Lactate release into the blood is governed by the perfusion of the involved muscle fibers (Graham, 1978) and also by the pH gradient against which the diffusion is occurring (Mainwood and Worseley - Brown, 1975). Lactate release is facilitated by a high extracellular pH and inhibited by a low extracellular pH. As may be noted from Figure 4, values of blood pH at LT are similar in trained and untrained subjects. Hence lactate release does not appear to be an important factor at this point.

The catabolism of lactate occurs largely in muscle still operating aerobically during exercise. This includes both skeletal (Essen et al, 1975; Ahlborg et al, 1975) and cardiac muscle (Keul et al, 1966). In addition lactate may act as a gluconeogenic precursor in the liver (Wahren, 1977). Several chronic adaptations with exercise may enhance the ability of trained subjects to remove lactate from the blood.

As mentioned previously, skeletal muscle of endurance trained subjects is characterized by a lower total LDH activity but a shift towards the H-LDH subgroup (Karlsson et al, 1975). This adaptation apparently occurs in both ST and FT fibers (Sjodin, 1976; Sjodin et al,1976). Aerobically operating fibers thus demonstrate the ability to oxidize greater amounts of the lactate produced by more active lactate producing fibers. This lactate-oxidizing function of non-working musculature may be facilitated by a decreased blood flow to the working musculature and a concomitant increase in the blood to less active musculature (Rowell, 1974; Clausen, 1976).

The rate of splanchnic uptake of lactate appears to be proportional to its blood concentration and the blood flow

to this area (Hultman, 1967; Rowell, 1974). Training results in a redistribution of blood flow of which more is directed to the hepatic tissues (Rowell, 1974; Clausen, 1976).

The increased "lactate washout" seen with training has an effect on the appearance of the LT.

The mechanism of the elevation of the TDMA witnessed may also be multi-faceted. The appearance of a significant drop in blood pH is dependent mainly on: (1) the degree of exercise-induced acidosis finding its way into the blood, (2) the compensatory capacity of the blood i.e., the buffer systems, and (3) the ability to remove H+ from the circulation.

The trained subjects in this study apparently had a reduced acid stress affecting the circulatory system. The reasons for a decline in lactate following training have been outlined above. No differences in the blood lactate concentration at the TDMA were noted in a comparison between trained and untrained subjects even though the TDMA occurred at a higher relative workload in trained subjects.

The trained subjects appear to have no significant advantage over their untrained counterparts in terms of the compensatory capacity of the circulatory system for acid stress. The amount of absolute or relative work performed during the transition stage was not different between the subject groups. This is in good agreement with the work of Robinson and Harmon (1941) and Keul et al (1966) who found no difference, with training, in the level of standard bicarbonate - the primary buffer of lactate in the blood (Keul et al, 1972).

The standard bicarbonate level is related to pH through the Henderson Hasselbach equation: $pH = pKa + \log [HCO3]/pCO2]$. H+ ion entering the circulation is buffered in the bicarbonate system. In order for the pH to remain

constant with an increase in H+ ion concentration and in the saturation of the available bicarbonate, the CO2 content of blood must decrease in proportion to the saturation of HCO3-. This system is effective during the transition phase but as the workload intensity increases the acidosis becomes saturating to this buffer system and pH declines despite a significant reduction in pCO2 (Whipp, 1977).

One of the basic principles of exercise physiology is that of progressive overload. According to this axiom, as an individual becomes more trained, the absolute workload against which he is working must be increased in order to provide the same overload to the metabolic systems (de Vries, 1980). In the present study it was demonstrated that the transition phase of metabolism, as delineated by the appearance of the LT and the TDMA occurs at a higher proportion of the maximal oxidative capacity in trained subjects in comparison to untrained individuals. This indicates that following endurance training, not only does the absolute training workload have to be increased, but also the workload relative to the individual's maximal capacity must also be increased.

By elevating the location of the transition phase within the oxidative capacity, the potential perfcrmance in prolonged events is increased with or without changes in the maximal oxidative capacity. For this reason, VO2 max is not an especially good predictor of endurance performance in individuals of similar capacities.

Chapter V
CONCLUSIONS AND RECOMMENDATIONS

The results of the present study implicate the following conclusions:

(1) The LT may be defined by an increase in blood lactate from resting values of 1.10 mM in untrained subjects and 0.90 mM in trained subjects.

(2) The TDMA may be defined by a decrease in blood pH from resting valus of 0.08 units in untrained subjects and 0.11 units in trained subjects.

(3) Neither of these points are significantly related to a non-linear rise in VE (STPD) or the minimum value of VECO2 in these subject groups.

(4) The transition phase in trained subjects occurs at a greater relative proportion of the maximal oxidative capacity in comparison to untrained subjects. This shift is the result of a significantly elevated LT and a significantly higher TDMA. The total oxidative capacity located within the transition phase is independent of the training state.

Based on these conclusions the following recommendations seem warranted;

(1) The mechanisms resulting in an elevation of the TDMA should be ascertained. These studies should concentrate on

the regulation of respiratory compensation and the metabolic removal of acid metabolites. To this end, measurement of pCO_2, Hb concentration and standard bicarbonate would be helpful in more fully describing the acid/base status of the blood.

(2) The correlation of the TDMA with performance capacity is still unknown. This understanding is critical for the practical application of the transition phase to training.

(3) Longitudinal training studies are required to identify the most efficient methods of influencing these points.

(4) The transition phase should also be explored using alternate protocols. Smaller increments would surely help refine the delineation of the transition phase. Longer workloads would help to ensure that blood lactate concentrations were truly representative, particularly at the higher workloads.

References

1. Ahlborg, G., Hagenfeldt, L., Wahren, J. Influence of lactate infusion on glucose and free fatty acid metabolism in man. CLIN.SCI.MOL.MED.48(2):139-145, 1975

2. Armstrong, R.B. Biochemistry: Energy liberation and use. In:Strauss, R.H. (ed):SPORTSMEDICINE AND PHYSIOLOGY. Saunders:Phila., 1979 pp.3-28.

3. Astrand, I., Astrand, P.O., Hallback, I., Kilbom, A. Reduction in maximal oxygen uptake with age. J. APPL.PHYSIOL. 35:649, 1973.

4. Astrand, P.O., Rodahl, K. TEXTBOOK OF WORK PHYSIOLOGY. McLellan: Toronto, 1977, pp.345-400.

5. Baldwin, K.M., Winder, W.W., Terjung, R.L. et al. Glycolytic enzymes in different types of skeletal muscle : adaptations to exercise. AM.J.PHYSIOL.225:962-966, 1973.

6. Barnard, R.J., Peter, J.B. Effects of exercise on skeletal muscle III cytochrome changes. AM.J.PHYSIOL.31:904-908.

7. Berger, M., Hagg, S., Goodman, M., Ruderman, N. Glucose metabolism in perfused skeletal muscle. Effects of starvation, diabetes, fatty acids, acetoacetate, insulin and exercise on glucose uptake and disposition. BIOCHEM.J.158:191-202, 1976.

8. Bouhuys, A., Pool, J., Binkhorst, R., van Leeuwen, P. Metabolic acidosis of exercise in healthy males. J.APPL.PHYSIOL.21:1040-1046, 1966.

9. Byrne-Quinn, E. Weil, J.V., Sodal, I.E. et al. Ventilatory control in the athlete. J. APPL. PHYSIOL. 30:91-97, 1971.

10. Carlson, L.A., Ekelund, L., Froberg, S.O. Concentration of triglyceride, phospholipids and glycogen in skeletal muscle and of free fatty acids and beta-hydroybutarate in blood in man in response to exercise. EUR.J.CLIN.INVEST.1:248-254, 1971.

11. Clausen, J.P., KlausenmK., Rasmussen, B. et al. Central and peripheral circulatory changes after training of the arms or the legs. AM.J.PHYSIOL.225:675, 1973.

12. Clausen, J.P. Circulatory adjustments to dynamic exercise and the effect of physical training in normal subjects and in patients with coronary artery disease. PROG.CARDIOVASC.DIS.18:459-495, 1976.

13. Clausen, J. Effects of training on cardiovascular adjustments to exercise in man. PHYSIOL.REV.57:779-815, 1977.

14. Clode, M., Campbell, E. The relationship between gas exchange and changes in blood lactate concentrations during exercise. CLIN.SCI.37:263-272, 1969.

15. Comroe, J. PHYSIOLOGY OF RESPIRATION. Year Book Medical Publishers: Chicago, 1968, pp.170-178.

16. Costill, D. Metabolic responses during distance running J.APPL.PHYSIOL.28:251-255, 1970.

17. Costill,D.,Thomason,H.,Roberts,E. Fractional utilization of the aerobic capacity during distance running. MED.SCI.SPORTS 5:248-252,1973.

18. Costill,D.L.,Miller,J.M. Nutrition for endurance sport: Carbohydrate and fluid balance. INT.J.SPORTS MEDICINE 1:2-14,1980.

19. Danforth,W.H. Control of energy metabolism activation of glycolytic pathway in muscle. In . CONTROL OF ENERGY METABOLISM. B.Chance (ed), New York: Academic Press,1965,pp.287-297.

20. Davenport,H.W. THE ABC OF ACID-BASE CHEMISTRY. University of Chicago Press:Chicago,1971,p.92-94.

21. Davies,C.T.M.,Knibles,A.V.,Musgrove,J. The rate of lactic acid removal in relationship to different baselines of recovery exercise. INT.Z.ANGEW.PHYSIOL.28:155-161,1970.

22. Davis, J.E.,Brewer, N. Effect of physical training on blood volume, hemoglobin, alkali reserve, and osmotic resistance of erythrocytes. AM.J.PHYSIOL.113:586-591, 1935

23. Davis,J.,Vodak,P.,Wilmore,J. et al. Anaerobic threshold and maximal aerobic power for three modes of exercise. J.APPL.PHYSIOL.41:544-550,1976.

24. Davis,J. et al Anaerobic threshold alterations caused by endurance training in middle-aged men. J.APPL.PHYSIOL.46:1039-1046,1979.

25. Dehn,M.M.,Mitchell,J. The circulatory system. In: Strauss,R.H.(ed):SPORTSMEDICINE AND PHYSIOLOGY. Saunders:Phila.,1979 p. 77-93

26. de Vries, H. PHYSIOLOGY OF EXERCISE FOR PHYSICAL EDUCATION AND ATHLETICS. 3rd ed. Dubuque, Iowa: Wm. C. Brown Co. Publishing, 1980.

27. Dill, D.B.,Braithwaite, K.,Adams, W.C.,Bernaur, W.M. Blood volume of middle distance runners; effect of 2300 m altitude and comparison with non-athletes. MED.SCI.SPORTS 6:1 -7, 1974.

28. Dohm,G.L.,Huston,M.L.Askew,E.W. et al. Effects of exercise, training and diet on muscle citric acid cycle enzyme activity. CAN.J.BIOCHEM 51:849-854,1973.

29. Edgerton,V.R.,Essen,B.,Saltin,B. et al. Glycogen depletion in specific types of human skeletal muscle fibers in intermittent and continuous exercise. In H.Howald and J.Poortsman (eds): METABOLIC ADAPTATION TO PROLONGED PHYSICAL EXERCISE. Birkhauser Verlag Bagel Lausanne, pp.402-415.

30. Edington,D.W. Pyridine nucleotide oxidized to reduced ratio as a regulator of muscular performance. EXPERIENTIA 26:601-602,1970.

31. Essen,B.,Jansson,E.,Henriksson,J., et al. Metabolic characterisics of fiber types in human skeletal muscle. ACTA PHYSIOL.SCAND.95:153-165,1975.

32. Essen,B. Intramuscular substrate utilization during prolonged exercise. ANN.N.Y.ACAD.SCI.301:30-44,1977.

33. Essen,B. Glycogen depletion of different fiber types in human skeletal muscle during intermittent and continuous exercise. ACTA PHYSIOL.SCAND.103:446-455,1978.

34. Felig,P.,Pozefsky,T.,Marliss,E.,Cahill,G.F.Jr. Alanine: key role in gluconeogenesis. SCIENCE.167:1003,1970.

35. Galbo,H.,Holst,J.J.,Christensen,N.J. Glucagon and plasma catacholamine responses to graded and prolonged exercise in man. J.APPL.PHYSIOL.38:70-76,1975.

36. Galbo,H.,Richter,E.A.,Hilsted,J., et al. Hormonal regulation during prolonged exercise. ANN.N.Y.ACAD.SCI.301:67-75,1977.

37. Gollnick,P.D.,Hermansen,L. Biochemical adaptations to exercise: Anaerobic metabolism. EX.SPORTS SCI.REV.1:1-43,1973.

38. Gollnick,P.D. Delivery and uptake of substrates. In F.Landry and W.A.R.Orban (eds): 3rd INTERNATIONAL SYPOSIUM ON THE BIOCHEMISTRY OF EXERCISE.Book 3, Symposia Specialists:Miami,1978

39. Gollnick,P.D.,Armstrong,R.B.,Saubert,C.W. et al. Enzyme activity and fiber composition in skeletal muscle of trained and untrained men. J.APPL.PHYSIOL.33:312-319,1972.

40. Gollnick,P.D.,Armstrong,R.B.,Sembrowich,W.L.et al. Glycogen depletion pattern in human skeletal muscle fibers after heavy exercise. J.APPL.PHYSIOL.34:615-618,1973.

41. Gollnick,P.D.,Piehl,K.,Karlsson,J.,Saltin,B. Glycogen depletion patterns in human skeletal muscle fibers after varying types and intensities of exercise. In H.Howald and J.Poortsman (eds): METABOLIC ADAPTATION TO PROLONGED PHYSICAL EXERCISE. Birkhauser Verlag Bagel Lausanne,1975, p.416-421.

42. Graham,T.E.,Sinclair,D.G.,Chapler,C.K. Metabolic intermediates and lactate diffusion in active dog skeletal muscle. AM.J.PHYSIOL.231:766-771,1976.

43. Graham,T.E. Oxygen delivery and blood and muscle lactate changes during muscular activity. CAN.J.APPL.SPORTS SCI.3:153-159,1978.

44. Haggendahl,J.,Hartley,L.H.,Saltin,B. Arterial noradrenaline concentration during exercise in relation to the relative work levels. SCAND.J.CLIN.LAB.INVEST.26:337-347,1970.

45. Hartley,L.H.,Mason,J.W.,Hogan,R.P. et al. Multiple hormonal reponses to graded exercises in response to physical training. J.APPL.PHYSIOL.33:602-606,1972a.

46. Hartley,L.H.,Mason,J.W.,Hogan,R.P., et al. Multiple hormanal responses to prolonged exercise in relation to physical training. J.APPL.PHYSIOL.33:607-610,1972b.

47. Heisler,N.,Piiper,J. Determination of intracellular buffering properties in rat diaphram muscle. AM.J.PHYSIOL.222:747-753,1972.

48. Henriksson,J. Training induced adaptation of skeletal muscle and metabolism during submaximal exercise. J.PHYSIOL.(London) 270:661-675,1977.

49. Hermansen,L.,Hultman,E.,Saltin,B. Muscle glycogen during prolonged severe exercise. ACTA.PHYSIOL.SCAND.71:129-139,1967.

50. Hermansen,L.,Saltin,B. Blood lactate concentration during exercise at acute exposure to altitude. In: EXERCISE AT ALTITUDE., edited by R. Margaria, Amsterdam:Excerpta Medica Foundation, 1967, p.48-53.

51. Hermansen,L.,Maehlum,S.,Pruett,E.D.R. Lactate removal at rest and during exercise. In H.Howald and J.Poortsman (eds): METABOLIC ADAPTATION TO PROLONGED PHYSICAL EXERCISE. Birkhauser Verlag Bagel Lausanne, p.101-105

52. Hjemdahl,P.,Fredholm,B. Comparison of the lipolytic activity of circulating and locally released noradrenaline during exercise. ACTA PHYSIOL.SCAND.92:1-11,1974.

53. Hochachka,P.,French,C.,Guppy,M. When and how the Alpha-glycerophosphate cycle works. In: F.Landry and W.A.R.Orban (eds.): 3RD INTERNATIONAL SYMPOSIUM ON THE BIOCHEMISTRY OF EXERCISE. Book 3, Symposia Specialists:Miami,1978, p.29-42.

54. Holloszy,J.O.,Winder,W.W.,Fitts,R.H., et al. Energy production during exercise. In F.Landry and W.A.R.Orban (eds): 3rd INTERNATIONAL SYPOSIUM ON THE BIOCHEMISTRY OF EXERCISE.Boo Symposia Specialists:Miami,1978,

55. Holloszy,J.O. Adaptations of muscular tissue to training. PROG.CARDIOVASC.DIS.18:445-458,1976.

56. Holloszy,J.O. Adaptations of skeletal muscle to endurance training. MED.SCI.SPORTS 7:155-164,1975.

57. Hoppeller,H.,Luthi,P.,Claassen,H., et al. The ultrastructure of the normal human skeletal muscle. A morphometric analysis of untrained men, women and well-trained orienteers. PFLUGERS ARCH.344:217-232,1973.

58. Howald,H.,von Glutz,G.,Billeter,R. Energy stores and substrate utilization in muscle during exercise. In F.Landry and W.A.R.Orban (eds): 3rd INTERNATIONAL SYPOSIUM ON THE BIOCHEMISTRY OF EXERCISE.Book 3, Symposia Specialists:Miami,1978,

59. Hubbard,J.L. The effect of exercise on lactate metabolism. J.PHYSIOL.231:1-18,1973.

60. Hughson,R.L. Ventilatory CO2 response in endurance trained rats. EUR.J>APPL.PHYSIOL.45:103-1 009,1980.

61. Hultman,E.,Bergstrom,J. Local energy supplying substrates as limiting factors in different types of leg muscle work in man. In Keul,J. (ed): LIMITING FACTORS OF PHYSICAL PERFORMANCE. Stuttgart: Georg Thieme Publishers, 1973, pp.113-125.

62. Hultman,E. Studies on muscle metabolism of glycogen and active phosphate in man with special reference to exercise and diet. SCAND.J.CLIN.LAB.INVEST.19:Suppl.94,39-40,1967.

63. Issekutz,B.,Miller,H.I.,Rodahl,K. Lipid and carbohydrate metabolism during exercise. FED.PROC.25:1415-1420,1966.

64. Ivy,J.L.,Costill,D.L.,Essig,D.A., et al. The relationship of blood lactate to the anaerobic threshold and hyperventilation. (Abstract) MED.SCI.SPORTS 11:96, 1979.

65. Ivy,J.L.,Withers,R.T.,VanHandel,P.J., et al. Muscle respiratory capacity and fiber type as determinants of the LT. J.APPL.PHYSIOL.48:523-527,1980.

66. Jobsis,F.F.,Stainsby,W.N. Oxidation of NADH during contractions of circulated mammalian skeletal muscle. RESP.PHYSIOL.4:292-300,1968.

67. Jorfeldt,L. Metabolism of L-Lactate in human skeletal muscle during exercise. ACTA PHYSIOL.SCAND.Suppl.338,1970.

68. Jorfeldt,L.,Juhlin-Dannfelt,A.,Karlsson,J. Lactate release in relation to tissue lactate in human skeletal muscle during exercise. J.APPL.PHYSIOL.44:350-352,1978.

69. Karlsson,J. Lactate and phosphagen concentrations in working muscle of man. ACTA.PHYSIOL.SCAND. Suppl. 358, 1971.

70. Karlsson,J.,Saltin,B. Lactate, ATP and CP in working muscles during exhaustive exercise in man. J.APPL.PHYSIOL.29:598-602,1970.

71. Karlsson,J.,Sjodin,B.,Thorstensson,A., et al. LDH isozymes in skeletal muscle of endurance and strength trained athletes. ACTA PHYSIOL.SCAND.93:150-156,1975.

72. Karlsson,J.,Nordesjo,L.O.,Saltin,B. Muscle glycogen utilization during exercise after physical training. ACTA PHYSIOL.SCAND.90:210-217,1974.

73. Katch,V.,Weltman,A.,Sady,S.,Freedson,P. Validity of the relative percent concept for equating training intensity. EUR.J.APPL.PHYSIOL.39:219-227,1978.

74. Katz,A.M. Contractile proteins of the heart. PHYSIOL.REV.50:63-158, 1970.

75. Keul,J.,Keppler,D.,Doll,E. Beziehungen zwischen standardbikarbonat, pH-wert, und Lactat-und Pyruvatkonzentrationen im Blut wahrend und nach korperlicher Arbeit. DTSCH.MED.WSCHR.92:66,1967.

76. Keul,J.,Doll,E.,Keppler,D. Energy metabolism of human muscle. MED.and SPORT. Vol.7, Basel: Karger, 1972.

77. Kindermann,W.,Simon,G.,Keul,J. The significance of the aerobic-anaerobic transition for the determination of workload intensities during endurance training. EUR.J.APPL.PHYSIOL.42:25-34,1979.

78. Kjellberg, S.R.,Rudhe, V.,Sjostrand, T. Increase in the amount of hemoglobin and blood volume in connection with physical training. ACTA.PHYSIOL.SCAND.19:146-151, 1949.

79. Klausen,K.,Sjogaard,G. Glycogen stores and lactate accumulation in skeletal muscle of man during intense bicycle exercise. SCAND.J.SPORTS.SCI.2:7-12,1980.

80. Koyal,S.N.,Whipp,B.J.,Huntsman,D., et al. Ventilatory equivalent Ventilatory responses to the metabolic acidosis of treadmill and cycle ergometry. J.APPL.PHYSIOL.40:864-867,1976.

81. Lehninger,A.L. BIOCHEMISTRY. Worth Publishers:New York, 1975.

82. MacDougall,D. The anaerobic threshold: Its significance for the endurance athelete. CAN.J.APPL.SPORTS SCI.2:137-140,1977.

83. Mader,A.,Liesen,H.,Heck,H.,et al. Zur Beurteilung der sportartspezifischen Aurdauerleistungsfahigkeit im labor. SPORTARZT UND SPORTMEDIZIN 110-112, 1976.

84. Mahler,M. Neural and humoral signals for pulmonary ventilation arising in exercising muscle. MED.SCI.SPORTS 11:191-197,1979.

85. Mainwood,G.W.,Worsley-Brown,P. The effects of extracellular pH and buffer concentration on the efflux of lactate from frog sartorius muscle. J.PHYSIOL.(London).250:1-22,1975.

86. Martin,B.J.,Weil,J.V. CO2 and exercise tidal volume. J.APPL.PHYSIOL.46:322-325,1979.

87. Masaro,E.J.,Rowell,L.B.,Steinart,B.,MacDonald,R.M. Skeletal muscle lipids. Nonutilization of intracellular lipids as an energy source for contracile activity. J.BIOL.CHEM.241:2626-2634,1966.

88. McGilvery,R.W. The use of fuels for muscular work. In H.Howald and J.Poortsman (eds): METABOLIC ADAPTATION TO PROLONGED PHYSICAL EXERCISE. Birkhauser Verlag Bagel Lausanne, p.12-30. p.1-34.

89. McMurray,W.C. ESSENTIALS OF HUMAN METABOLISM. Harper and Row, Hagarstown,1977.

90. Mole,P.A.,Baldwin,K.M.,Terjung,R.L.,Holloszy,J.O. Enzymatic pathways of pyruvate metabolism in skeletal muscle: adaptation to exercise. AM.J.PHYSIOL.224:50-54,1974.

91. Mole,P.A.,Oscai,L.B.,Holloszy,J.O. Adaptation of muscle to exercise: increase in the levels of palmityl Co A, carnitne palmityltransferase and palmityl Co A dehydrogenase and in the capacity to oxidize FFA's. J.CLIN.INVEST.50:2323-2330,1971.

92. Morgan,T.E.,Short,F.A.,Cobb,L.A. Alterations in human skeletal muscle lipid composition and metabolism induced by physical conditioning. In: Poortsman,J.R. (ed), Biochemistry of exercise. MED and SPORT 3, Basel:karger,1969,p.116-121.

93. Newsholme,E.A. Control of energy provision and utilization in muscle in relation to sustained exercise. In: F.Landry and W.A.R.Orban (eds): 3rd INTERNATIONAL SYPOSIUM ON THE BIOCHEMISTRY OF EXERCISE.Book 3, 1978,p. 3-27.

94. Newshclme,E.A. The regulation of intracellular and extracellular fuel supply during sustained exercise. ANN.N.Y.ACAD.SCI.301:81-91,1977.

95. Newsholme,E.A.,Start,C. REGULATION IN METABOLISM. J.Wiley and Sons,1976.

96. Parizkova, J. NUTRITION, PHYSICAL FITNESS, AND HEALTH. Baltimore: University Park Press, 1978.

97. Paul,P. Effects of long physical exercise and training on lipid metabolism. In: H.Howald and J.Poortsman (eds): METABOLIC ADAPTATION TO PROLONGED PHYSICAL EXERCISE. Birkhauser Verlag Bagel p.156-193.

98. Pernow,B.,Saltin,B. Availability of substrates and capacity for prolonged heavy exercise in man. J.APPL.PHYSIOL.31:416-422,1971.

99. Pette,D. Mitochondrial enzyme activities. In: Tager,J.M.,Papa,S.,Quagliariello,E. and Seater,E.C. (eds.) REGULATION OF METABOLIC PROCESSES IN MITOCHONDRIA. Amsterdam:Elsevier, 1966,p.28-49.

100. Reinhard,U.,Muller,P.H.,Schmulling,R.M. Determination of anaerobic threshold by the ventilation equivalent in normal individuals. RESPIRATION 38:36-42,1979.

101. Reitman,J.,Baldwin,K.M.,Holloszy,J.O. Intramuscular triglyceride utilization by red, white and intermediate skeletal muscle and heart during exhausting exercise. PROC.SOC.EXP.BIOL.MED.142:628-631,1973.

102. Rennie,M.J.,Winder,W.W.,Holloszy,J.O. A sparing effect of increased plasma fatty acids on muscle and liver glycogen content in the exercising rat. BIOCHEM.J.156:647-655,1976.

103. Robinson, S.,Harmon, P.M. The lactic acid mechanism and certain properties of the blood in relation to training. AM.J.PHYSIOL.132:757, 1941.

104. Rowell,L.B.,Kraning,K.K.,Evans,T.O.,et al. Sphlanchnic removal of lactate and pyruvate during prolonged exercise in man. J.APPL.PHYSIOL.21:1773-1783,1966.

105. Rowell,L.B. Human cardiovascular adjustments to exercise and thermal stress. PHYSIOL.REV.54:75-159,1974.

106. Sahlin,K. Intracellular pH and energy metabolism in skeletal muscle of man. ACTA PHYSIOL.SCAND.Suppl.455,1978.

107. Saltin, B., Haretley, H., Kilbom, A., Astrand, I. Physical training in sedentary middle aged and older men. SCAND. J. CLIN. LAB. INVEST.24: 323, 1969.

108. Saltin,B.,Karlsson,J. Muscle ATP, CP and lactate during exercise after physical conditioning. In: B. Pernow and B. Saltin (eds.): MUSCLE METABOLISM DURING EXERCISE. New York:Plenum Press, 1971a, p.395-399.

109. Saltin,B.,Karlsson,J. Muscle glycogen utilization during work at different intensities. In: B. Pernow and B. Saltin (eds.): MUSCLE METABOLISM DURING EXERCISE. New York:Plenum Press, 1971b, p.289-299.

110. Saltin,B.,Hartley,L.H.,Kilbom,A.,Astrand,I. Physical training in sedentary and middle-aged and older men. II Oxygen uptake, heart rate and blood lactate concentration at submaximal and maximal exercise. SCAND.J.CLIN.INVEST.24:323-334,1969.

111. Saltin,B.,Henriksson,J.,Nygaard,E., et al. Fiber types and metabolic potentials of skeletal muscle in sedentary man and endurance runners. ANN.N.Y.ACAD.SCI.301:3-29,1977.

112. Schmalbruch,H. Die quergestreiften Muskelfasern des Menschen. Ergebnisse der Anatomie und Entwicklungsgeschichte. Band 43, Heft I, Berlin: Springer Verlag, 1970.

113.

114. Siggaard-Anderson, O. THE ACID-BASE STATUS OF THE BLOOD. Copenhagen: Munksgaard, 1974.

Sjodin,B.,Thorstensson,A.,Frith,K.,Karlsson,J. Effect of physical training on LDH activity and LDH isozyme pattern in human skeletal muscle. ACTA PHYSIOL.SCAND.97:150-157,1976.

116. Sjodin,B. Lactate dehydrogenase in human skeletal muscle. ACTA PHYSIOL.SCAND.Suppl.436, 1976.

116. Simon,J.,Gutin,B.,Young,J.L.,Blood,D.L. Lactate accumulation during constant load work just below and just above the anaerobic and respiratory compensation thresholds. (Abstract) MED.SCI.SPORTS 12:126,1980.

117. Skinner,J.S.,McLellan,T.H. The transition from aerobi to anaerobic metabolism. RESEARCH Q.EX.SPORTS 51:234-238, 1980.

118. Skinner,S.,Powell,J. Regulation of skeletal muscle blood flow during exercise. CIRCULATION RES.21:Suppl 1, 1967.

119. Smith,E.,Guyton,A.,Manning,D.,White,R.J. Integrated mechanisms of cardiovascular response and control during exercise in the normal human. PROG.CARDIO.DIS. 18:421-444,1976.

120. Stegemann, J. Mathematical model of the ventilatory control system to carbon dioxide with special reference to athletes and non-athletes. PFLUEGER'S ARCH. 356(3):223-236, 1975.

121. Sutton,J.R.,Jones,N.L. Control of the pulmonary ventilation during exercise and mediators in the blood CO2 and hydrogen ion. MED.SCI.SPORTS 11: 198-203,1979.

122. Swanson,G.D. Overview of ventilatory control during exercise. MED.SCI.SPORTS 11:221-226,1979.

123. Taylor,A.W.,Thayer,R.,Rao,S. Human skeletal muscle glycogen synthetase activities with exercise and training. CAN.J.PHYSIOL.PHARM.50: 411-415, 1972.

124. Taylor,A.W.,Booth,M.A.,Rao,S. Human skeletal muscle glycogen phosphorylase acivities with exercise and training. CAN.J.PHYSIOL.PHARM. 50:1038-1042, 1972.

125. Taylor,A.W.,Lavoie,S.,Lemieux,G., et al. Effects of endurance training on the fiber area and enzyme activities of skeletal muscle of French-Canadians. In: F.Landry and W.A.R.Orban (eds): 3rd INTERNATIONAL SYPOSIUM ON THE BIOCHEMISTRY OF EXERCISE.Book 3, Symposia Specialists:Miami,1978, p.267-278.

126. Terjung,R. Endocrine systems. In: Strauss,R.H.(ed):SPORTSMEDICINE AND PHYSIOLOGY. Saunders:Phila.,1979

127. Tesch,P.,Sjodin,B.,Thorstensson,A. Relationship between lactate accumulation, LDH activity, LDH isozyme and fiber distribution in human skeletal muscle. ACTA PHYSIOL.SCAND.103:40-46,1978.

128. Van Dam,K.,Meyer,A.J. Oxidation and energy conservation by mitochondria. ANN.REV.BIOCHEM.40:115-160,1971.

129. Wahren, J. Glucose turnover during exercise in man. ANN.N.Y.ACAD.SCI.301:45-55, 1977.

130. Wasserman,K.,Whipp,B.J.,Koyal,S.N.,Beaver,W.L. Anerobic threshold and repiratiry gas exchange during exercise. J.APPL.PHYSIOL.35:236-243,1973.

131. Wasserman,K.,Whipp,B.J.,Casaburi,R., et al. Ventilatory control during exercise in man. BULL.EUROP.PHYSIOPATH.RESP.15:27-47,1979.

132. Weiser,P.C.,Norton,C.H.,Krogh,L.A. Anaerobic threshold and running speed for 3.2 km. MED.SCI.SPORTS 10:43-48,1978.

133. Wendt,I.R.,Chapman,J.B. Flurometric studies of recovery metabolism of rat fast- and slow-twitch muscles. AM.J.PHYSIOL.230:1644-1649,1976.

134. Wenger,H.A.,Reed,A.T. Metabolic factors associated with muscular fatigue during aerobic and anaerobic work. CAN.J.APPL.SPORTS SCI.1:43-47,1976.

135. Whipp,B.J. The hyperpnea of dynamic muscular exercise. EX.SPORTS SCI.REV.5:295-311,1977.

136. Whipp,B.J.,Davis,J.A. Peripheral chemoreceptors and exercise hyperpnea. MED.SCI SPORTS 11:204-212,1979.

137. Williams, C.G., Wyndham,C.H., Kok, R., von Rahden, M.J.E. Effect of training on maximum oxygen uptake and on anaerobic metabolism in man. INT.Z ANGEW.PHYSIOL.EINSCHL.ARBEITSPHYSIOL.24:18, 1967.

APPENDICES

APPENDIX A

Physical Characteristics of Subject Groups

Subject Number	Age (yr)	Height (cm)	Weight (Kg)	Body Fat %
TRAINED SUBJECTS				
1.	18	173	67.0	9.0
2.	18	164	62.1	8.0
3.	21	184	70.5	8.9
4.	18	175	69.4	7.3
5.	29	166	67.8	13.0
6.	19	173	68.0	12.9
7.	25	181	76.9	11.5
8.	22	176	78.9	13.0
9.	20	175	69.4	11.0
$\bar{X}$	21.1	177	72.5	10.3
UNTRAINED SUBJECTS				
1.	21	190	87.2	10.9
2.	25	179	73.1	18.0
3.	24	186	85.6	13.0
4.	19	180	82.1	13.0
5.	24	175	76.2	17.0
6.	23	176	81.9	14.0
7.	25	176	61.2	8.0
8.	23	185	73.5	9.0
9.	23	173	71.5	14.5
$\bar{X}$	22.7	177	74.4	13.2

APPENDIX B

Maximal Values of Oxygen Consumption, Heart Rate, and Blood Lactate Observed in Trained and Untrained Subjects.

Subject Number	Maximal Oxygen Consumption (ml/kg/min)	Maximal Heart Rate (bpm)	Maximal Blood Lactate (mM)
TRAINED SUBJECTS			
1.	61	191	13.9
2.	70	203	11.1
3.	64	195	11.2
4.	61	200	13.3
5.	61	213	17.2
6.	64	196	10.3
7.	60	180	10.6
8.	66	180	15.6
9.	66	190	6.3
$\bar{X}$	64	193	11.7
UNTRAINED SUBJECTS			
1.	56	204	12.6
2.	51	187	13.3
3.	48	194	13.2
4.	51	198	4.3
5.	58	175	10.9
6.	50	190	13.9
7.	42	198	9.6
8.	58	192	14.2
9.	54	196	13.3
$\bar{X}$	52	193	11.6

SUBJECT NUMBER	WORKLOAD (kp's) R	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0	5.5	MAX.
UNTRAINED											
1.	1.7			1.4	2.3	2.3	3.6	5.6	5.7	10.1	12.3
2.	0.7	1.7	1.9	2.1	7.3	7.3	9.0				13.3
3.	1.3	1.6	1.7	2.8	4.7	5.3	6.0	7.6			13.2
4.	1.3	1.3	1.2	1.3	3.0	4.3					8.0
5.	1.0		2.1	2.6	3.4	6.2	9.8	11.4			13.3
6.	1.2		1.4	2.1	1.7	4.8	8.4	12.9	8.6		13.9
7.	1.9	1.6	1.3	6.2	9.6	10.4					8.0
8.	1.3			1.4	3.0	3.8	7.2	9.2	9.0		14.2
9.	1.0	1.4	1.6	2.4	4.8	5.0	7.7				8.4
$\bar{X}$	1.3	1.5	1.6	2.6	4.4	5.0	7.7	9.4			11.6

Blood lactate values in untrained subjects with increasing workloads.

SUBJECT NUMBER	R	2.0	2.5	3.0	3.5	4.0	4.5	5.0	5.5	6.0	MAX.
	WORKLOAD (kp's)										
TRAINED											
1.	0.8		1.0	1.2	1.0	1.8	2.9	6.4	9.2		14.2
2.	1.0	1.2	1.2	1.0	1.9	3.3	6.3				11.0
3.	0.7			2.6	2.3	2.8	5.4	6.4	9.9		11.2
4.	1.2	1.6	2.0	1.6	2.8	3.9	6.3	10.1	10,4		17.2
5.	1.0	1.2	1.2	1.3	3.9	9.9	10.1				13.3
6.	1.4		1.1	2.1	2.2	2.1	3.7	10.3			9.0
7.	1.0		1.1	0.9	1.5	1.5	2.5		2.8		10.6
8.	1.0			1.6	1.9	2.5	2.6	4.2	4.7		8.6
9.	1.0		1.2	0.9	2.0	3.0	4.7	4.9	6.3		12.2
$\bar{X}$	1.0	1.3	1.3	1.5	2.2	3.4	4.9	7.1	6.6		11.7

Blood lactate values in trained subjects with increasing workloads.

APPENDIX E

SUBJECT NUMBER	WORKLOAD (kp's) R	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0	5.5
UNTRAINED										
1.	7.30			7.29	7.30	7.30	7.30	7.31	7.22	7.17
2.	7.31	7.30	7.27	7.28	7.30	7.20	7.19			
3.	7.31	7.28	7.30	7.29	7.27	7.27	7.21	7.15		
4.	7.30	7.32	7.31	7.28	7.20	7.17				
5.	7.28		7.26	7.32	7.27	7.30	7.22	7.19		
6.	7.31		7.33	7.29	7.27	7.28	7.27	7.26	7.22	
7.	7.33	7.27	7.33	7.30	7.30	7.22				
8.	7.28			7.27	7.31	7.25	7.28	7.19	7.14	
9.	7.30	7.28	7.28	7.28	7.27	7.28	7.22			
$\bar{X}$	7.30	7.30	7.29	7.29	7.27	7.25	7.23	7.19		

Blood pH values in untrained subjects with increasing workloads.

SUBJECT NUMBER	R	2.0	2.5	3.0	3.5	4.0	4.5	5.0	5.5
				WORKLOAD (kp's)					
TRAINED									
1.	7.31		7.26	7.29	7.28	7.29	7.28	7.22	7.23
2.	7.25	7.30	7.30	7.25	7.24	7.15	7.12		
3.	7.32			7.26	7.24	7.27	7.26	7.28	7.22
4.	7.30	7.24	7.27	7.27	7.32	7.27	7.15	7.10	
5.	7.33	7.30	7.27	7.29	7.26	7.30	7.26	7.16	
6.	7.31		7.23	7.29	7.28	7.28	7.23	7.19	
7.	7.29		7.26	7.29	7.25	7.27	7.28	7.14	7.15
8.	7.27			7.26	7.28	7.28	7.24	7.22	7.15
9.	7.32		7.36	7.32	7.30	7.34	7.25	7.27	7.17
$\bar{X}$	7.30	7.28	7.28	7.28	7.28	7.27	7.22	7.20	7.18

Blood pH values in trained subjects with increasing workloads.

APPENDIX G

	Lactate at 'LT' (mmol La/l)	Lactate at 'TDMA' (mmol La/l)
TRAINED		
1.	1.8	2.9
2.	1.9	3.3
3.	1.8	6.4
4.	1.6	3.9
5.	1.3	10.1
6.	2.1	3.7
7.	1.5	2.5
8.	1.9	4.2
9.	0.9	4.9
UNTRAINED		
1.	2.3	5.6
2.	1.7	7.3
3.	1.7	5.3
4.	1.3	3.0
5.	2.1	6.2
6.	1.7	8.4
7.	1.3	6.2
8.	1.4	3.8
9.	1.6	2.4

Blood lactate values at Lt and TDMA in trained and untrained subjects.

APPENDIX H

SUBJECT NUMBER	'LT' (% VO_2max)	"TDMA' (% VO_2max)	Non-linear increase in V_E(STPD) (% VO_2max)	Minimum value of $VECO_2$ (% VO_2max)
UNTRAINED				
1.	68	75	75	75
2.	52	90	75	75
3.	56	85	75	75
4.	69	78	69	69
5.	56	87	81	81
6.	73	92	78	73
7.	71	88	71	69
8.	60	74	60	63
9.	57	81	57	76
TRAINED				
1.	80	92	92	75
2.	84	84	68	68
3.	58	91	91	80
4.	67	89	75	75
5.	75	93	75	93
6.	80	95	64	64
7.	78	79	78	78
8.	64	86	70	70
9.	59	95	72	86

Lactate threshold, threshold of decompensated metabolic acidosis, point of non-linear rise in V_E, and the minimum value of $V_E CO_2$

SUBJECT NUMBER	LACTATE THRESHOLD ml/kg	% VO_2max	kpm/min	HR	TDMA ml/kg	% VO_2max	kpm/min	HR
UNTRAINED								
1.	38	67.8	1260	141	42	75.0	1440	170
2.	27	52.4	720	150	46	90.2	1260	181
3.	27	56.3	900	133	41	85.4	1440	167
4.	35	68.6	1260	156	40	78.4	1440	186
5.	30	55.6	900	131	47	87.0	1440	167
6.	37	72.5	1260	160	46	92.0	1530	182
7.	30	71.4	900	141	37	88.0	1080	166
8.	33	56.9	1080	140	47	81.0	1440	167
9.	29	60.4	900	141	34	73.9	1080	168
TRAINED								
1.	49	80.3	1440	152	56	91.8	1620	170
2.	59	84.3	1260	171	59	84.3	1440	189
3.	37	57.8	1080	143	58	90.6	1800	184
4.	41	67.2	1080	138	54	88.5	1440	174
5.	46	75.4	1080	161	57	93.4	1260	184
6.	51	79.7	1440	161	61	95.3	1620	179
7.	47	78.3	1440	162	48	78.7	1620	167
8.	42	63.6	1260	159	57	86.4	1800	168
9.	39	59.1	1260	145	63	95.4	1800	176

APPENDIX J

CONSENT FORM

I_____the undersigned, agreee to participate in the thesis research entitled ' A comparison of the transition from aerobic to anaerobic metabolism in trained and untrained subjects'.

I understand that this will involve my performance of work on a stationary bicycle. During this test, the resistance against which I am pedalling will be increased over a period of about 20 minutes from a very easy effort to a maximum effort. During this test I may expect my heart rate to reach near maximal levels. For the length of the test I will be breathing into a mouthpiece that collects my expired air. During the test blood samples will also be withdrawn from a vein in the back of my hand. This will be accomplished with the use of a venous catheter which will be inserted by qualified medical personnel.

Although I realize that I can stop the test at any time, I understand that certain personal risks are involved with a moderate to maximal work test such as light-headedness, nausea, fainting, chest discomfort, leg cramps, muscle strains and/or sprains, and, in very rare cases, cardiac failure.

I realize that in agreeing to participate in this study I can expect to derive no direct monetary or otherwise material reward. In any case all results will be held confidential by the researchers.

I certify that, to the best of my knowledge, I am free from the sympthoms or treatment of any neuromuscular, pulmonary or circulatory disorder and that I have not in the past suffered difficulty during exertion.

In signing this consent form, I acknowledge that I have had the opportunity to hear the test and any potential risks explained and ask any questions I wanted.

APPENDIX K

INFORMATION FOR SUBJECTS

Now that you have kindly consented to be a subject in this experiment, there are a few things that I would like you to try and keep in mind.

DIET: There are no major dietary restrictions imposed by this study. Try to maintain a normal diet of approximately 60% carbohydrate, 15% protein and 25% fat. I only ask that, when you report to the lab for testing, please ensure that you have eaten no sooner than 4 hours previously. It is also important that you do not cosume any caffeine-containing beverages on the day of the testing (i.e. coffee, tea, cocoa or Coke).

EXERCISE: On the day of the test, all other exercise behaviors must be avoided. If you are training now, avoid high-intensity and prolonged duration exercise on the day previous to the test also.

Your incremental work test will occur at _____on _____ in room 306 of Montpetit Hall. Try to arrive at least one half hour prior to the designated time in order that we may place the catheter and allow you a chance to rest before your test. You should be dressed in shorts and T-shirt and be wearing relatively sturdy training shoes on your feet.

If for any reason you are unable to appear at the designated time, please contact me at 729-5726 during the evening or leave a message at the lab (231-6543).

Thank you for your cooperation

BOB REID