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Comparison of fructose and glucose ingestion before and during endurance cycling to exhaustion

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A Comparison of Fructose and Glucose Ingestion Before and During Endurance Cycling to Exhaustion

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By

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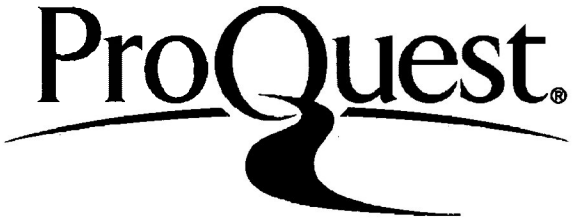

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Sandy Brundle

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Abstract

The aim of this study was to compare the effect of pre-exercise and exercise ingestion of fructose and glucose during prolonged cycling exercise. The primary purpose was to determine if ingesting fructose before and during exercise was as beneficial or more beneficial than glucose ingestion. Seventeen trained subjects performed a control cycle to exhaustion. At least one week later, each subject performed a second ride to exhaustion ingesting either fructose or glucose before and during exercise. Blood was drawn before and at timed intervals during exercise to determine blood glucose, lactate and free fatty acid (FFA) levels for all three conditions (control, fructose, glucose). Gas measurements (Beckman Metabolic Measurement Cart) were taken at approximately 10 minute intervals, to ensure each subject was cycling at 75% VO_2 max. and to determine respiratory exchange ratio (RER).

Exercise time to exhaustion for the control group was significantly less ($\propto = .05$) than either the fructose ($p < .02$) or glucose ($p < .001$) group, but the fructose and glucose groups were not significantly different from each other. Blood glucose levels in the fructose group remained more stable than the glucose group and actually increased throughout the exercise test to exhaustion. Prior to the onset of exercise, the blood lactate level of the control group was significantly ($\propto = .05$) lower than either the fructose ($p < .002$) or the glucose ($p < .01$) group. The fructose and glucose groups did not show any significant differences in blood lactate over time. There were no significant differences in blood FFA between the treatment groups during the exercise test to exhaustion, but the control group FFA level was significantly ($\propto = .05$) higher than that of the fructose group ($p < .02$) prior to the onset of exercise. All three groups demonstrated gradual declines in RER throughout the exercise test to exhaustion.

In this study it was established that fructose and glucose are of equal value in prolonging exercise time to exhaustion in endurance cycling performance. Ingesting fructose before and during exercise allowed for a more constant supply of glucose to be available to the working muscles than glucose ingestion. The more stable blood glucose levels with fructose ingestion may be beneficial in reducing perceived exhaustion, increasing mental alertness and postponing the athletes' perception of 'hitting the wall', thereby allowing for an enhancement in exercise performance.

Chapter 1

INTRODUCTION

Purpose

Seventeen endurance athletes were studied to compare the effect of pre-exercise and exercise ingestion of fructose and glucose during prolonged cycling exercise. The primary purpose of this experiment was to determine if ingesting fructose before and during exercise is as beneficial or more beneficial than glucose ingestion before and during exercise. A control condition was included to establish a baseline. Exercise time to exhaustion as well as other dependent variables were measured to compare the effectiveness of these dietary manipulations.

Significance of Study

Ingesting glucose before an endurance event is a method utilized by many athletes. Many problems are evident with this regimen. Ingesting glucose before an endurance event results in the stimulation of an insulin response, thereby producing hyperinsulinemia (Hasson & Barnes, 1987). This overproduction of insulin retards the process of glycogenolysis, inhibits free fatty acid mobilization and may result in an insulin-induced hypoglycemic condition. The actively contracting skeletal muscle will quickly become depleted of muscle glycogen, commonly reducing performance (Costill, Coyle, Dalsky, Evans, Fink & Hoopes, 1977; Foster, Costill & Fink, 1979).

Various studies (Fielding et al. 1985; Murray et al. 1987; Okano et al. 1988) have shown fructose ingestion to be of benefit during endurance events. Fructose ingestion may overcome some of the adverse side effects observed following ingestion of a large dose of glucose (Hasson & Barnes, 1987). Fructose does not require insulin to enter the cell (Hasson & Barnes, 1987; Schwarz et al. 1989), therefore hypoglycemia does not occur. Furthermore, fructose ingestion has been shown to increase free fatty acid (FFA) mobilization (Addington & Grunewald, 1987; Guezennec et al. 1989; Hargreaves, Costill, Katz & Fink, 1985) thereby offering an alternative energy source to the working muscles, possibly postponing fatigue. Some studies (Hargreaves et al. 1985; Koivisto, Karonen & Nikkila, 1981; Levine, Evans, Cadarette, Fisher & Bullen, 1983) also show glycogen sparing with fructose ingestion.

The advantages of fructose ingestion may suggest endurance performance enhancement and therefore warrant further investigation. To date, it would not appear that the effects of fructose ingestion have been directly compared to the effects of glucose ingestion under the procedure outlined in the present investigation. Questions pertaining to fructose ingestion as an ergogenic aid can be more clearly answered in an experiment comparing the effects of fructose ingestion to glucose ingestion on endurance exercise performance.

Delimitations

1. - the subjects consisted of 17 trained endurance athletes (mean VO_2 max =

61 ml/kg) with an average age of 23 years.

2. - the independent variables include the dietary manipulation before and during prolonged cycling exercise by means of glucose ingestion, fructose ingestion or the ingestion of an artificially sweetened placebo.

3. - the dependent measures include the performance variable of exercise time to exhaustion, blood levels of glucose, lactate, free fatty acids (FFA), and gas measurements of respiratory exchange ratio (RER).

4. - an alpha (α) level of .05 was used for the statistical analysis of the various measured parameters.

5. - subjects were aware of the methodology of the experiment, however the subjects were not informed of the experimenter's hypothesis, nor were they aware of which supplement they ingested.

6. - verbal encouragement was equally given to all subjects, although the only indicator used for assessing maximal work efficiency was exercise time to exhaustion for each subject.

Limitations

1. - genetic endowment and psychological components (ie. motivation, competitiveness) cannot be controlled in this study.

2. - diet was not controlled in the present study. All subjects were advised to continue their normal dietary habits. Subjects were required to keep a detailed dietary diary for the seven days preceding each cycling ride to exhaustion in order to monitor individual diets as precisely as possible.

3. - individual exercise programs were unable to be controlled as many of the subjects were highly trained endurance athletes, competing at provincial and national levels. The subjects were required to keep an exercise diary for the duration of the study and were asked to refrain from physical activity for 24 hours preceding the cycling ride to exhaustion.

4. - a learning effect may have occurred during the second exercise test to exhaustion. Subjects were not informed of the duration of their first cycle to exhaustion, nor were they permitted to record exercise duration.

5. - respiratory exchange ratio cannot be statistically analysed since measurements were not taken at predetermined intervals.

Definitions

Absorption. The movement of a particular substance through a cellular wall.

Anaerobic Threshold (AT). The point at which the metabolic demands of exercise can no longer be met by available aerobic sources and at which an increase in anaerobic metabolism occurs, reflected by an increase in blood lactate concentration.

Cori Cycle. The process by which liver and muscle glycogen contribute to the increase in blood sugar brought about by epinephrine.

Gluconeogenesis. The metabolic process by which glucose is formed from non-carbohydrate precursors, which include lactate, pyruvate, glycerol and the amino acids. It is a specialized function of the liver and kidneys and involves the Cori and the Glucose-Alanine Cycles.

Glycogenolysis. The metabolic breakdown of glycogen.

Glycogen Synthetase. The rate limiting enzyme for glycogen synthesis, responsible for the addition of one molecule of glucose to the glycogen chain.

Glycolysis. The metabolic pathway of glucose breakdown in mammalian cells that proceeds by a specific route, involving specific steps (intermediate products), in which each step is catalyzed and regulated by a specific enzyme.

Lactate Threshold (T_{lact}). The point where lactic acid metabolization cannot keep up to lactic acid production, so a non-linear increase in blood lactate occurs.

Metabolism. All of the chemical reactions that occur within a living organism.

Onset of Blood Lactate Accumulation (OBLA). The exercise intensity that elicits a blood lactate concentration of 4 mM. It is a good means of predicting performance in various forms of endurance exercise.

Chapter 2

REVIEW OF LITERATURE

Introduction

Fructose has been a human dietary food from the time when prehistoric humans first tasted honey and found enjoyment in the sweet substance. Since then, sugars in one form or another have become an increasing component of the human diet (Chen & Whistler, 1977). Recent changes in the use of commercial sweeteners has increased the fructose levels in manufactured foods and has increased the availability of fructose or fructose-containing sweeteners for home use (Crapo & Kolterman, 1984). This is due to recent commercial availability of pure crystalline fructose and the increased commercial use of high fructose corn syrups.

The major sources of natural fructose are fruits and honey. Dried figs, dates, prunes and grapes contain the largest amounts of fructose (Ravich, Bayless & Thomas, 1983). In recent years, fructose has been produced and offered not only as a very sweet sugar but as a beneficial sweetening agent for people with certain metabolic disorders. Fructose is also beneficial due to its ease of metabolism. Many athletes claim it provides a quick source of energy (Chen & Whistler, 1977). Numerous scientific articles (Guezennec et al. 1989; Hargreaves et al. 1985; Koivisto et al. 1981; Levine et al. 1983) have documented the beneficial effects of fructose in endurance activities.

A Comparison of Glucose and Fructose

Fructose is a six-carbon monosaccharide and is the sweetest of all natural sugars (Niewoehner, Gilobe, Nuttal & Nuttal, 1984). Fructose is an isomer of glucose, having the same chemical formula ($C_6 H_{12} O_6$), but a different structure. The differences in these related molecules are enough that fructose ingestion does not initiate an insulin response from the pancreas (Bohannon, Karam & Forsham, 1980; Koivisto et al. 1981; MacDonald, Keyser & Pacy, 1978), however fructose is readily converted to glucose in the liver (Chen & Whistler, 1977; Nilsson & Hultman, 1974). Since fructose does not initiate an insulin response, glycogenolysis of liver glycogen can occur to meet the energy requirements during exercise when blood glucose levels decline. This allows blood glucose to become available to the exercising skeletal muscles. Ingesting fructose may overcome some of the adverse side effects (ie. hypoglycemia) observed following ingestion of a large dose of glucose (Hasson & Barnes, 1987). These unique characteristics (ie. fructose uptake into skeletal muscle tissue is insulin independent, and can be utilized by skeletal muscle tissue and metabolized similarly to glucose) provide a basis for fructose utilization as an ergogenic aid (Chen & Whistler, 1977; Gammeltoft, Kruhohher & Lundsgaard, 1944; Hasson & Barnes, 1987; Nilsson & Hultman, 1974).

When blood circulates past the liver, fructose is taken up by liver cells, where enzymes rearrange the carbon, hydrogen and oxygen atoms to make compounds similar to those derived from glucose and also to make glucose

itself (Coggan & Swanson, 1992; Whitney & Hamilton, 1987). When glucose enters the liver cell it is converted to glucose-6-phosphate, with the aid of the enzyme glucokinase, and enters the glycolytic pathway where it is ultimately converted to glycogen (Van den Berghe, 1986). Fructose, on the other hand, is converted to fructose-1-phosphate by the enzyme fructokinase when it enters the liver cell. With the help of fructose bisphosphate aldolase, fructose-1-phosphate is converted into two triose molecules prior to conversion to glucose-6-phosphate and then enters the glycolytic pathway with glucose (Nuttall, Gilboe, Gannon, Niewoehner & Tan, 1988). When compared with glucose, fructose is more rapidly metabolized by the liver (Chen & Whistler, 1977; Heinz, Lamprecht & Kirsch, 1968;) through the specific fructose-1-phosphate pathway (Heinz et al. 1968; Van den Berghe, 1986).

Fructose and glucose are not used by the body in exactly the same manner. A problem with ingesting glucose before an endurance event is that increased blood glucose concentrations can stimulate an insulin response from the pancreas, resulting in hyperinsulinemia (Hasson & Barnes, 1987). An overproduction of insulin retards the process of glycogenolysis, inhibits free fatty acid (FFA) mobilization, and ultimately may result in an insulin-induced hypoglycemic condition (Hasson and Barnes, 1987). The actively contracting skeletal muscle will quickly become depleted of muscle glycogen, commonly

As discussed, fructose does not stimulate insulin secretion nor require

the presence of insulin to gain access to the intracellular compartment (Schwarz et al. 1989). Consequently, fructose does not produce the hyperinsulinemic effect found with glucose.

During endurance events, blood glucose is increasingly utilized as the primary fuel source (Hultman, 1967). Following glucose ingestion, blood glucose concentration is initially elevated, but falls rapidly below normal levels due to an exponential over-compensation of insulin production. Following the ingestion of fructose, blood glucose concentration is initially elevated and remains elevated during exercise through glycogenolysis. Therefore, a greater supply of blood glucose will be available during the critical time frame when both exercising skeletal muscle and brain tissue compete for available carbohydrate fuel sources. As a result, fructose ingestion might eliminate many symptoms of fatigue (weakness, dizziness and disorientation) observed during endurance exercise activities (Hasson & Barnes, 1987).

Blood Glucose Response to Exercise

Exercise alters circulating levels of blood glucose (Brooks & Fahey, 1984). In short duration, high intensity exercise, blood glucose rises above resting levels due to the stimulation of hepatic glycogenolysis by the autonomic nervous system (Brooks & Fahey, 1984). The ability of the liver to maintain a high rate of glucose release during exercise is limited by the amount of stored glycogen and by the activities of glycogenolytic and gluconeogenic enzymes (Brooks & Fahey, 1984).

During prolonged exercise, glucose production may be limited because of glycogen depletion, resulting in a reduced availability of blood glucose for the working muscles. The glucose that is available is directed to essential tissues, such as the brain and the central nervous system (CNS). When blood glucose levels fall, the exercise becomes more difficult due to CNS starvation and a lack of energy sources to the exercising muscles (Brooks & Fahey, 1984).

Absorption and Metabolism of Fructose and Glucose

Taken orally, fructose is absorbed by the small intestine at rates that are roughly half of those of other monosaccharides such as glucose or galactose (Chen & Whistler, 1977; Dencker, Lunderquist, Meeuwisse, Norryd & Tranberg, 1972). Since fructose is absorbed slowly from the small intestine, it does not cause abrupt changes in the serum levels of carbohydrates, resulting in little, if any, effect on insulin secretion.

The pathway of fructose absorption into the small intestine differs from that of glucose. Glucose is actively transported across the intestinal epithelium, whereas fructose is absorbed via facilitated diffusion (Van den Berghe, 1986). As a result, fructose is absorbed from the proximal small intestine at a rate slower than that of glucose, resulting in comparatively slower fluid absorption rates (Coggan & Swanson, 1992; Holdsworth & Dawson, 1964). This slower rate of fructose absorption is considered to be the cause of the gastrointestinal distress and diarrhea that often accompanies the ingestion of large amounts of this sugar (Coggan & Swanson, 1992; Ravich et

al. 1983).

Fructose is transported to the liver from the small intestine by way of the hepatic portal system. In healthy individuals, 70 to 90% of ingested fructose enters the portal circulation as fructose (Levine et al. 1983). Similarly, in a fasted state, most of the glucose formed in the liver is converted to glycogen and consequently there is no significant rise in plasma glucose or insulin levels. The liver is the principal site of fructose metabolism (Chen & Whistler, 1977).

From the circulation, fructose is taken up by the liver (Van den Berghe, 1986). Up to 85% of orally administered fructose undergoes metabolism in the liver (Adelman, Spolter & Weinhouse, 1966). The metabolism of fructose begins when the molecule is acted upon by enzymes. When fructose is metabolized in the liver, the first step involves a phosphorylation to fructose 1-phosphate by fructokinase (Cori, Ochoa, Skein & Cori, 1951; Hers & Kusaka, 1953; Newsholme & Leech, 1983). This enzyme is about ten times more active than the combined activities of the two enzymes, glucokinase and hexokinase, necessary for glucose phosphorylation (Mayer & Laker, 1986). Fructose metabolism also bypasses the first regulatory enzyme of the glycolytic pathway (phosphofructokinase), therefore metabolizing fructose faster than glucose, as well as providing lactate, a precursor for glycolysis and gluconeogenesis (Van den Berghe, 1986).

Following phosphorylation, fructose-1-phosphate is split by fructose-

bisphosphate aldolase into two triose molecules, glyceraldehyde and dihydroxyacetone phosphate (Hers & Kusaka, 1953). Glyceraldehyde is phosphorylated to glyceraldehyde 3-phosphate by the enzyme triokinase. The activity of these enzymes is subject to dietary composition and hormonal control. After 48 to 72 hours of fasting, fructokinase, fructose-bisphosphate aldolase and triokinase decrease to at least half their normal activity but are restored to normal after 24 hours upon fructose administration. Adelman et al. (1966) found that long term feeding of fructose resulted in the maintenance of a considerably higher level of all three enzymes, an effect also seen with rats maintained on a high fat or high protein diet. Depending on the hormonal control of the pathways, the triose phosphates are further metabolized to glucose (gluconeogenesis) or to pyruvate (glycolysis) (Newsholme & Leech, 1983).

Glyceraldehyde is then usually metabolized to lactic acid, whereas dihydroxyacetone phosphate is typically metabolized in the Citric Acid Cycle to produce carbon dioxide and water (Hers & Kusaka, 1953).

Fructose is taken up directly in muscles (Bergstrom & Hultman, 1967) and adipose tissue (Froesch & Ginsberg, 1962). In humans, the uptake of administered fructose into the muscles occurs directly from the blood stream, whereas administered glucose will not pass the membrane barriers from blood to muscle. Bergstrom et al. (1972) proposed that fructose is taken up by skeletal muscle tissue and used without first being metabolized in the liver or

other tissues. Various studies (Bergstrom & Hultman, 1967; Miller, Drucker, Owens, Craig & Woodward, 1952; Weichselbaum, Elman & Lund, 1950) have revealed that fructose is more rapidly metabolized, resulting in a lower total sugar concentration in the blood than when an equal amount of glucose is given. Fructose has been reported (Thoren, 1964) to have a less irritant effect on peripheral veins than glucose, implying that fructose solutions for intravenous use can be given in higher concentrations.

Crapo and Kolterman (1984) studied the metabolic effects of a 2-week feeding of fructose (63 to 99 grams/day) and found that large amounts of fructose are rapidly taken up by the liver and are converted to lactate and pyruvate, which are subsequently released into the peripheral circulation. This enhanced lactate response is probably due to the substrate flux exceeding the capacity of pyruvate dehydrogenase to oxidize pyruvate to acetyl-CoA (Schwarz et al. 1989).

Froesch (1972) studied the metabolism of fructose in adipose tissue and concluded that fructose is transported by a different mechanism than that of glucose and by a system that is not insulin-dependent. As in the liver, adipose tissue metabolism of fructose is rapid and is accomplished with the participation of fructokinase (Adelman et al. 1966) and a non-specific hexokinase (Froesch & Ginsberg, 1962; Gromova, 1965).

Decombaz et al. (1985) discovered that after fructose ingestion, some fructose is absorbed in the blood since the concentration of blood fructose

increased fourfold. This indicated that fructose is utilized for energy as efficiently as glucose and contributed significantly to the energy supply.

The stimulation of the insulin release with glucose ingestion has an inhibitory effect on lipolysis (Carlstrom, 1969; Galbo, Holst & Christensen, 1979). This inhibitory effect decreases the utilization of free fatty acids (FFA) as an energy source, thereby further depleting carbohydrate stores. Furthermore, a hyperinsulinemic decline of blood glucose will not initiate glycogenolysis because high concentrations of insulin retard the release of glucagon from the pancreas (Bohannon et al. 1980). As stated previously, fructose ingestion does not result in an increased insulin secretion as does glucose (Koivisto et al. 1981). It therefore follows that the anti-lipolytic effect observed with glucose feedings should not occur with fructose feedings. In a recent study on rats (Addington & Grunewald, 1987), the fructose fed animals had the greatest increase in circulating FFA compared to rats fed glucose or sucrose. The results of two studies (Koivisto et al. 1985; McMurray, Wilson & Kitchell, 1983) found that fructose ingestion did not reduce the levels of circulating FFA as dramatically as glucose ingestion. In fact, free fatty acid utilization was actually enhanced following fructose ingestion. Glycogen sparing, attributable to enhanced FFA mobilization and utilization, exerts a beneficial effect on endurance performance (Hickson, Rennie, Conlee, Winder & Holloszy, 1977; Ivy, Costill, Fink & Lower, 1978; Rennie, Winder & Holloszy, 1976).

Bergstrom and Hultman (1967) reported that during fructose infusion, splanchnic lactate output may be converted to lactic acid in the liver. However, in the four experiments performed by Bergstrom and Hultman (1967), the lactate production was much less than the fructose uptake, suggesting that a large part of the fructose supplied to the splanchnic region is stored in the liver as glycogen, or converted in some other way. Previously, Mendeloff and Weichselbaum (1953) reported similar results.

The relationship between administered fructose and lactate may be explained as follows. Fructose is transported by a specific carrier into the absorptive cells of the intestine, where it may be metabolized to lactate in the epithelial cells, or enter the hepatic portal circulation as fructose (Newsholme & Leech, 1983). The results presented by Decombaz and coworkers (1985) confirm that lactate is released into the circulation after fructose ingestion. Fructose administration has also been associated with lactic acidosis (Woods & Alberti, 1972).

Insulin and Glucagon Response to Exercise

In order to understand the mechanism by which exogenous carbohydrate is used as an energy source during prolonged exercise, the response of insulin and glucagon should be discussed. Insulin and glucagon are protein hormones which provide the immediate control of blood glucose levels. Insulin is secreted by the Islets of Langerhans (beta cells) that stimulate glucose uptake by many cells, of which muscle and adipose tissue

are most important (Brooks & Fahey, 1984). The alpha cells of the pancreas secrete glucagon. When blood glucose levels are high, insulin is secreted, promoting the removal of glucose from the blood, whereas glucagon is secreted when blood glucose levels are low, acting to raise blood glucose levels. Glucagon has two effects on hepatic metabolism: 1) enhanced glycogenolysis and 2) increased gluconeogenesis (Brooks & Fahey, 1984).

Brain cells and erythrocytes depend on glucose for fuel, however they do not depend on insulin for glucose uptake. Increased glucose uptake usually stimulates glycogen synthesis in muscle, and fat synthesis in adipose tissue. Glucose uptake from blood causes a reduction in blood glucose levels (Brooks & Fahey, 1984).

Insulin is primarily affected by the time at which glucose is ingested. In an attempt to provide carbohydrates to contracting muscles, it has been observed that glucose ingestion 30 to 60 minutes before exercise causes an increased blood glucose concentration, resulting in an increased insulin secretion (Foster et al. 1979; Koivisto et al. 1981). This hyperinsulinemia is followed by a rapid exercise- and insulin-induced decrease in blood glucose concentration and greater depletion of muscle glycogen (Newsholme, 1979). The stimulation of the insulin release has an inhibitory effect on lipolysis (Galbo et al. 1979). With glucose ingestion, this inhibitory effect on lipolysis decreases the utilization of FFAs as an energy source, thereby further depleting carbohydrate stores and hindering endurance performance.

When glucose is ingested during exercise, the insulin response is different. Exercise leads to a decrease in plasma insulin levels, in preparation for the increased glucose needs of the exercising muscles (Coyle & Coggan, 1984). Coyle and Coggan (1984) concluded that hyperglycemia and hyperinsulinemia following carbohydrate ingestion is prevented if the carbohydrate is given during rather than 30 minutes before exercise.

Requirements for glucose in muscle during even moderate intensity exercise tend to cause a decline in blood glucose. This decline is compensated, at least partly, by the release of glucose from the liver and also from the kidney. During exercise, blood glucose levels may actually rise as a result of this accelerated release. Due to the increased glucose needs during exercise, glucose uptake eventually exceeds release and blood glucose levels fall, with a similar decline in insulin levels (Brooks & Fahey, 1984).

The decline in blood glucose and insulin levels helps minimize glucose uptake by non-active tissue, thereby sparing blood glucose for active muscle and brain. Falling glucose and insulin levels help to spare blood glucose and muscle glycogen by enhancing lipolysis and making FFA available in the circulation for both active and non-active tissues (Brooks & Fahey, 1984)

Endurance training affects the secretion of various hormones (Brooks & Fahey, 1984). The hormonal response is reduced during exercise. Glucoregulatory hormones released during exercise (ie. insulin, glucagon and catecholamines) are released to a lesser extent in trained individuals. During

exercise, insulin does not fall as far as in the untrained and results in higher insulin levels in trained athletes during exercise (Brooks & Fahey, 1984). In trained athletes, the increase in FFA utilization and gluconeogenesis results in better control of blood glucose levels (Brooks & Fahey, 1984)

During prolonged exercise, the blood glucagon level rises as glucose and insulin levels fall (Brooks & Fahey, 1984). In trained athletes, the plasma glucagon levels are greatly reduced, allowing blood glucose levels to be maintained at a more constant level throughout the duration of exercise. Therefore, both the insulin and glucagon responses help to maintain blood glucose homeostasis (Brooks & Fahey, 1984).

Fructose Ingestion and Endurance Performance

Numerous studies have examined carbohydrate ingestion and endurance performance. Fructose ingestion may prove beneficial during prolonged intense physical activity. The reduced insulin response (Hasson & Barnes, 1987; Schwarz et al. 1989), elevated blood glucose levels (Koivisto et al. 1981), increased availability of FFAs as an energy source (Addington & Grunewald, 1987; Guezennec et al. 1989; Hargreaves et al. 1985; Koivisto et al. 1981), and lower muscle glycogen depletion (Hargreaves et al. 1985; Koivisto et al. 1981; Levine et al. 1983) all point to the possibility that fructose may be a preferred carbohydrate source during prolonged exercise.

Positive Results with Fructose Ingestion

Hargreaves et al. (1985) examined the effects of pre-exercise glucose and

fructose ingestion on muscle glycogen usage during exercise. The exercise consisted of 30 minutes of cycling exercise at 75% VO_2 max. The results revealed a trend for muscle glycogen use to be lower during fructose rather than glucose ingestion. They concluded that the adverse effects of pre-exercise glucose ingestion do not appear to be observed with fructose ingestion. Due to the blunted glucose and insulin responses with fructose, this carbohydrate may be suitable for pre-exercise ingestion.

Perhaps the major benefit of fructose feeding is the maintenance/ supplementation of liver carbohydrate stores (Hargreaves et al. 1985). Therefore, fructose may be of benefit prior to prolonged exercise by providing a carbohydrate source for later use, without stimulating muscle glycogenolysis during the early stages of exercise. The authors (Hargreaves et al. 1985) concluded that the relationship between fructose ingestion, muscle glycogen use and prolonged exercise performance deserves further investigation.

Levine and coworkers (1983) compared the effects of pre-exercise glucose, fructose and placebo ingestion on 30 minutes of treadmill running at 75% VO_2 max. Each test was preceded by 3 days of a high carbohydrate diet. Muscle glycogen depletion, as determined by pre- and post-exercise muscle biopsies, was significantly less during the fructose trial than during the glucose or placebo trials (Levine et al. 1983). This glycogen sparing during the fructose trial occurred while similar levels of carbohydrate oxidation appeared to occur in both fructose and glucose trials, as evidenced by respiratory

exchange ratio (RER) values. The authors state that fructose ingested 45 minutes before a 30 minute bout of submaximal exercise will maintain stable blood glucose and insulin concentrations, which may lead to the observed sparing of muscle glycogen. Levine et al. (1983) suggested that the mechanism for the observed glycogen sparing, as well as the extent to which this sparing would continue during more prolonged (1 hour +) exercise (ie. when glycogen reserves become critical) deserves further investigation.

Pre-exercise glucose, fructose and a placebo were compared during 30 minutes of cycling exercise at 75% VO_2 max (Koivisto et al. 1981). Glucose ingestion prior to exercise resulted in hypoglycemia during exercise, causing a depletion of muscle glycogen stores. Conversely, fructose ingestion was associated with only a modest rise in plasma insulin and hypoglycemia did not occur during exercise. After fructose ingestion and before exercise, the rise in plasma insulin was only one-third of that observed after the ingestion of glucose (Koivisto et al. 1981). The fall in blood glucose during exercise in the fructose group was less than one-fifth of that after glucose feeding. These findings emphasize that elevated insulin levels can cause a decline in blood glucose during exercise.

In the study by Koivisto et al. (1981), it was demonstrated that plasma FFA levels were lower after glucose ingestion when compared to ingestion of fructose or a placebo. Since FFA uptake by the working muscle is dependent on substrate availability (Ahlborg & Felig, 1977; Ahlborg, Felig, Hagenfeldt,

Hendler & Warren, 1974), decreased FFA concentrations after glucose ingestion may result in decreased FFA utilization (Randle, Garland, Hales & Newsholme, 1963) and enhanced glucose uptake during exercise. This increased glucose uptake could possibly result in earlier depletion of muscle glycogen, thereby decreasing exercise time to exhaustion.

Guezennec et al. (1989) examined the oxidation of corn starch, glucose and fructose ingested 60 minutes before cycling exercise at 60% VO_2 max for 120 minutes. The plasma glucose and insulin concentration significantly increased in response to glucose and corn starch feedings. These high plasma insulin values resulted in a significant transient reduction in plasma glucose in the first hour of exercise and blunted plasma FFA and glycerol concentrations when compared to the values observed with fructose ingestion. Fructose did not modify plasma glucose or insulin concentrations. This study demonstrated higher FFA utilization during the last hour of exercise with fructose and also reflected higher glycerol levels during the last 1.5 hours with fructose as compared to glucose and corn starch. Furthermore, during the final 30 minutes of exercise, the amount of substrate oxidation with fructose was significantly less than with corn starch or glucose. The lower rate of exogenous fructose utilization could be associated with an increased fat utilization (Bjorkman, Sahlin, Hagenfeldt & Wahren, 1984; Hargreaves et al. 1985) resulting from enhanced lipolysis due to the low plasma insulin level (Ahlborg & Felig, 1977) and/or to a reduction of glycerol conversion into

glucose (Hodges & Krehl, 1965). The enhanced plasma FFA and glycerol levels associated with pre-exercise fructose feedings in the study by Guezennec et al. (1989) suggest an increased fat mobilization.

Other researchers (Okano et al. 1988) compared pre-exercise fructose ingestion to a placebo during cycling exercise to exhaustion with 12 trained male subjects. For all subjects, exercise began 60 minutes after the ingestion of 60 or 85 grams of fructose or a sweet placebo at an intensity that required 62% VO_2 max. At 90 minutes into the exercise, the intensity was increased to 72%, then 81% of VO_2 max at 120 minutes. Exercise time to exhaustion was significantly increased after fructose ingestion compared to the sweet placebo (Okano et al. 1988). The results also illustrated an increase in exercise time to exhaustion of the 85 gram fructose group over the 60 gram group. They concluded that fructose ingestion is of benefit before prolonged exercise because it provides a carbohydrate source to contracting muscles without temporary hypoglycemia and a depression in fat utilization, thereby delaying fatigue.

Fasted rats were studied to determine the effects of pre-exercise feedings of glucose, fructose, sucrose or water on substrate depletion (Addington & Grunewald, 1987). The water fed rats had the highest increase in FFA (215.4%) followed by fructose (120.8%), sucrose (69.2%) and glucose (57.5%). The fructose fed rats showed the greatest depletion of liver glycogen and the smallest decline in soleus and vastus lateralis muscle glycogen compared to

the rats fed other carbohydrates. This indicates that exercise-induced changes in substrate levels can be modified by the type of carbohydrate given before exercise. Utilization of muscle glycogen can be altered by the type of carbohydrate fed before exercise (Addington & Grunewald, 1987). As stated previously, the fructose fed rats demonstrated a smaller decline in soleus and vastus lateralis glycogen concentrations than those fed glucose or sucrose. The sparing of muscle glycogen in the fructose fed rats may be attributed to an increased utilization of alternative energy sources (ie. liver glycogen and FFAs) during exercise of this intensity (18 meters/min for 2 hours).

Hasson and Barnes (1987) studied the effects of pre-exercise glucose, fructose and placebo ingestion during rest versus 30 minutes of cycling exercise at 80% VO_2 max. Following the fructose exercise trial, blood glucose declined initially in the first 10 minutes, then increased significantly as the exercise continued. This increase in blood glucose concentration, resulting from the combined effect of fructose ingestion and exercise may be attributable to liver glycogenolysis (Hasson & Barnes, 1987). Fructose ingestion does not initiate an insulin response. Therefore, during exercise-induced declines in blood glucose, glycogenolysis of liver glycogen can occur. This will allow blood glucose to become available during the critical period when both exercising skeletal muscle and brain tissue compete for available carbohydrate fuel sources.

Murray et al. (1987) studied the effect of various ingested carbohydrate

solutions (5% glucose polymer, 6% sucrose/glucose, 7% glucose polymer/fructose, placebo) during the performance of intermittent submaximal (55 to 65% VO_2 max) cycling, followed by a sprint bout. The mean time to complete the 480 pedal revolutions (sprint trial) was significantly faster for the glucose polymer/fructose trial as compared to the glucose polymer trial, suggesting that the fructose may have been responsible for the faster performance bout at the end of 1.6 hours of intermittent cycling.

Although much of the scientific literature supports the superiority of fructose ingestion on endurance performance, some of the research literature proves to be contradictory.

Similar Results with Fructose and Glucose Ingestion

Hargreaves, Costill, Fink, King and Fielding (1987) examined the effects of pre-exercise carbohydrate feedings on a cycle ride to exhaustion at 75% VO_2 max. Forty-five minutes before exercise, the subjects ingested 75 grams of glucose, fructose or a sweet placebo, all in liquid form. No significant differences were observed between treatments for oxygen uptake, RER, heart rate or exercise time to exhaustion (Hargreaves et al. 1987). Muscle glycogen use during the first 30 minutes of exercise and total glycogen use were similar in the three trials. Despite more stable blood glucose and insulin levels with fructose compared to glucose, no advantage to endurance performance or muscle glycogen utilization during prolonged exercise was provided (Hargreaves et al. 1987). Furthermore, subjects in the exhausted state had as

much as 50 to 55 mmol/kg wet weight of glycogen remaining in their muscles which supports the view that factors other than glycogen depletion may have contributed to fatigue. Since endurance exercise of this type predominately depletes the slow twitch fibres of glycogen (Gollnick, Piehl & Saltin, 1974), it is possible that the remaining glycogen may have been present in the relatively non-depleted fast twitch fibres.

Decombaz et al. (1985) studied the effect of 1 g/kg fructose versus glucose ingestion, one hour before exercise. Ten trained subjects exercised on a cycle ergometer at 61% VO_2 max for 45 minutes, followed by 15 minutes of all out effort (100% VO_2 max). During the rest hour, blood glucose and insulin were lower and RER and blood lactate higher after fructose ingestion. During the exercise trial, the differences disappeared aside from a brief but moderate hypoglycemia after glucose compared to fructose ingestion. During exercise, no differences were observed for uric acid, glycerol, FFA or glucagon between glucose and fructose as well as no glycogen differences in the vastus lateralis (Decombaz et al. 1985). Although the findings do not suggest more beneficial results with fructose over glucose, fructose ingestion prior to exercise allowed a more stable glycemia although it did not increase performance.

Furthermore, Decombaz et al. (1985) reported higher blood lactate values at rest with fructose ingestion. Lactate was released into the circulation after fructose ingestion since blood fructose concentration increased four fold. One cause of exhaustion during strenuous activity is thought to be lactic

acidosis produced by anaerobic work (Hermansen, 1981). Since a rise in blood lactate is well documented after fructose ingestion (Chen & Whistler, 1977; Koivisto et al. 1981), the question arises as to whether fructose intake encourages earlier exhaustion, thereby reducing work output. Although lactate levels were elevated at rest, there was no sign of combined action between fructose-induced and exercise-induced lactacidemia (Decombaz et al. 1985). Since the workload remained predominately aerobic, it is possible that the circulating lactate served as a fuel for the working muscles (Ahlborg & Felig, 1977). The risk of earlier onset of fatigue due to fructose-induced lactacidemia in conjunction with anaerobic acidosis seems unlikely.

Two studies (Chen & Whistler, 1977; Moran & McHugh, 1981) have indicated that large doses of fructose may cause osmotic diarrhea due to a faster gastric release and slower intestinal absorption than glucose. These problems were not observed in the study by Decombaz et al. (1985) and the authors state that individuals not unusually sensitive should be able to ingest up to 0.8 g/kg body weight of fructose without gastrointestinal problems.

In 1987, Fielding and coworkers studied the effect of pre-exercise carbohydrate feedings on muscle glycogen use during 30 minutes of treadmill running at 70% VO_2 max in six well-trained runners. Thirty minutes prior to exercise, each runner ingested either 75 grams of glucose, fructose or a sweetened placebo. During exercise no differences were reported in oxygen uptake, heart rate or perceived exertion (Fielding et al. 1987). Muscle glycogen

utilization in the first 15 minutes of exercise was similar as was glycogen use in all three groups. The results suggest that feedings of glucose or fructose prior to 30 minutes of treadmill running do not effect the rate of muscle glycogen utilization. The most significant finding was that the rate of muscle glycogen utilization was not affected by glucose or fructose feedings, despite the rapid drop in serum glucose during the first 15 minutes of exercise in the glucose trial.

Slama and associates (1989) recently compared oral administration of 50 grams of glucose or fructose in six healthy subjects during 90 minutes of exercise at 50% VO_2 max. Fructose was oxidized to approximately the same overall extent as glucose, yet with a significant difference in the kinetics of utilization. This faster rate of glucose utilization may be explained in several ways. Firstly, in rats (Niewoehner et al. 1984) and in humans (Ravich et al. 1983), the speed of fructose absorption by the gut is known to be only half that of glucose absorption. Secondly, skeletal muscle lacks the specific enzymes (fructokinase, aldolase B and triose kinase) required for fructose oxidation (Niewoehner, 1986). Since exercise promotes fuel consumption in muscle, it may favour glucose over fructose utilization (Slama et al. 1989). Thirdly, the main fate of ingested fructose may be glycogen synthesis rather than glycogen combustion (breakdown), as fructose has been shown to be superior to glucose as a glycogen precursor in man (Nilsson & Hultman, 1974).

Negative Results with Fructose Ingestion

Some of the studies in the literature dealing with the influence of fructose ingestion on endurance performance have reported negative results.

Koivisto et al. (1985) examined glycogen depletion during 2 hours of cycling exercise at 55% VO_2 max in eight healthy males. Seventy-five grams of glucose, fructose or placebo were given orally, 45 minutes before the commencement of exercise. Serum FFA levels were 1.5 to 2 folds higher after the placebo compared to the glucose or fructose ingestion. In the same study, quadriceps femoris concentration of muscle glycogen fell by 60 to 65% during exercise in all three groups. These findings appear to indicate that fructose ingestion was no more effective than glucose or the placebo in sparing glycogen during long term exercise.

An important phenomenon discovered by Koivisto et al. (1985) was that after fructose ingestion, FFA levels were reduced. It was speculated (Koivisto et al. 1985) that this may be the result of a small (two-fold) rise in insulin. Furthermore, it is possible that the increased availability of fructose's three carbon metabolites, such as alpha-glycerophosphate, may have facilitated FFA re-esterification (Huttunen, 1971). As a result, glucose may have been used as an energy source more than FFAs. Since the placebo group did not have the carbohydrate supply to rely on, the level of FFAs increased to meet the energy requirements (Koivisto et al. 1985); therefore the placebo group utilized more FFA and the glucose and fructose groups utilized more carbohydrate. Hence,

it is probable that the exercising muscle is able to utilize either carbohydrate or fat as an energy source, depending on both substrate availability and exercise intensity.

Massicotte, Peronnet, Brisson, Bakkouch and Hillaire-Marcel (1989) compared the oxidation of glucose, glucose polymer, fructose and a water placebo during 120 minutes of cycling exercise at 53% VO_2 max. Six healthy males ingested a total of 1.4 litres of a 7% carbohydrate solution at 6 intervals throughout the exercise. The oxidation of exogenous glucose and glucose polymer were similar and significantly greater than exogenous fructose oxidation. Endogenous carbohydrate utilization was significantly lower with glucose, glucose polymer and fructose than with water (Massicotte et al. 1989). Exogenous fructose appeared to be less readily available for oxidation than glucose or glucose polymer and provided only 13% of the total energy requirements. This is most likely the result of the slow conversion of fructose into glucose by the liver before peripheral oxidation of fructose occurs.

The plasma insulin levels were similar with glucose and glucose polymer ingestions and significantly higher than with water or fructose ingestions despite similar peripheral plasma glucose values (Massicotte et al. 1989). This could be due to the fact that gastrointestinal and/or portal gluco-receptors appear to be less sensitive to fructose than to glucose (Mei, 1985).

Despite the differences between plasma insulin responses to exercise with fructose versus glucose or glucose polymer, no significant differences were

observed in fat utilization (Massicotte et al. 1989). The only evident difference in substrate utilization was a greater use of endogenous carbohydrate stores with fructose than with glucose or glucose polymer ingestions. This may have been related to the lower rate of exogenous fructose utilization, compared with the other two exogenous carbohydrates (Massicotte et al. 1989). To summarize, the results seem to suggest that fructose ingested during exercise is less readily available for oxidation than glucose and glucose polymer ingestion over 2 hours of cycling exercise at 53% VO_2 max.

The influence of glucose and fructose ingestion on the capacity for long-term exercise was studied in eight well-trained men (Bjorkman et al. 1984). The subjects exercised on a cycle ergometer at 68% VO_2 max until exhaustion on three separate occasions, ingesting 250 ml of a 7% glucose, fructose or water solution every 20 minutes. Total work time to exhaustion was significantly longer with glucose (137 minutes) than with fructose (114 minutes) or water (116 minutes) ingestion. Glucose, but not fructose, postponed fatigue during heavy exercise by 20% compared to water ingestion. Also, the rate of glycogen depletion was significantly lower with glucose than with fructose ingestion. It was concluded that intermittent glucose ingestion during prolonged cycling at about 68% VO_2 max postponed exhaustion and exerted a glycogen-conserving effect in the active skeletal musculature. Fructose ingestion during exercise, in contrast, maintained the glucose concentration at the basal level but failed to influence either muscle glycogen

degradation or endurance performance (Bjorkman et al. 1984).

Another study which did not demonstrate positive results with fructose ingestion was conducted in 1989 by Murray, Paul, Seifert, Eddy and Halaby. The physiological, sensory and exercise performance responses were compared for 6% glucose, fructose or sucrose solutions during 115 minutes of intermittent cycling exercise at 65 to 80% VO_2 max. The intermittent cycling exercise was followed by a timed bout requiring the completion of 600 pedal revolutions. The test solutions were consumed during each of the five 4 minute rest periods. The fructose fed group experienced lower plasma glucose and serum insulin, a larger loss of plasma volume, greater gastrointestinal distress (slower absorption) and higher perceived exertion ratings than the other carbohydrate beverages. Higher plasma and serum concentrations of FFAs, fructose and cortisol values were found in the fructose group during the performance bout than in either the glucose or sucrose groups. The average time required to complete the 600 pedal revolutions was significantly slower for fructose (488 seconds) than for glucose (424 seconds) or sucrose (419 seconds) ingestion (Murray et al. 1989).

In addition, Murray et al. (1989) reported that RER values remained similar for all trials, thereby revealing little evidence of a shift to FFA oxidation with fructose feeding. Previously, Ravussin and coworkers (1986) suggested that the increase in FFA levels with fructose feeding may not be large enough to substantially increase the contribution of fat to energy metabolism.

Production and Utilization of Lactate

In order to discuss the mechanism by which lactate can be utilized as an energy source, the production of lactate must first be reviewed. Under anaerobic conditions, no oxygen is available to accept electrons in the cytochrome c oxidase reaction and the electron carriers in the electron transfer chain become almost totally reduced (Newsholme & Leech, 1983). As a result, cytosolic NADH cannot be oxidized in the mitochondria and glycolysis must proceed because it is the only pathway capable of generating energy under these conditions (Newsholme & Leech, 1983). For glycolysis to continue, the NAD+/NADH ratio must be maintained at the high values characteristic of the cytosol. The most important process for reoxidation of NADH is the reduction of pyruvate to lactate in the reaction catalyzed by lactate dehydrogenase (pyruvate + NADH + H+ ----> L-lactate + NAD+) (Newsholme & Leech, 1983). This reduction reaction keeps the concentration of NAD+ higher than that of NADH, allowing glycolysis to proceed and thereby permitting exercise to continue.

A second reaction that plays a role in this re-oxidation is the cytosolic glycerol-3-phosphate dehydrogenase reaction (Newsholme & Leech, 1983). Dihydroxyacetone phosphate is reduced to glycerol 3-phosphate (dihydroxyacetone phosphate + NADH + H+ ----> glycerol 3-phosphate + NAD+). It is possible that this reaction plays a significant role in the re-oxidation of NADH in the initial stages of anaerobiosis.

It follows that the concentration of glycerol 3-phosphate and lactate increase in the muscle during anaerobic conditions. Since lactate is released from the muscle into the bloodstream, its production is continuous. Conversely, glycerol 3-phosphate cannot cross the cell membrane so it increases rapidly to a high concentration which remains within the muscle (Newsholme & Leech, 1983). However, once oxygen is available (aerobic exercise), the concentration of glycerol 3-phosphate decreases. This is most likely due to its oxidation via pyruvate conversion. The lactate that diffuses into the bloodstream is carried to the liver where it is taken up and is reconverted to glucose, a process known as gluconeogenesis and is accomplished via the Cori Cycle, under aerobic conditions (Newsholme & Leech, 1983).

Lactate as Energy

The primary substrate for lactate production in muscle is the glucosyl units derived from the local glycogen stores (Gollnick, Bayly & Hodgson, 1986). Glycogenolysis supplies most of the glucosyl residues of the glycolytic pathway in muscle during heavy exercise (Brooks & Fahey, 1987). The net production of ATP from the breakdown of glucosyl units to lactate releases only about 10% of the total energy stored in the glucose molecule (Brooks, 1988). Although this percentage appears small, it can mean the difference between average and elite performance. Lactate is produced as an emergency source of ATP or to supplement the normal aerobic production of ATP when the oxygen uptake of

the body is near maximum (Gollnick et al. 1986).

Lactate can increase in the cell by one of two mechanisms. Firstly, when glycolysis increases so rapidly that the mitochondria cannot utilize pyruvate fast enough to prevent its elevation in the cytosol (low mitochondrial/glycolytic capacity), the amount of lactate increases by mass action, without a change in the lactate/pyruvate ratio (Wasserman et al. 1985). The second way lactate can increase in the cell is by way of the mitochondrial membrane proton shuttle. This shuttle normally oxidizes cytosolic NADH + H+ as it transfers protons and electrons to mitochondrial oxygen. If the system is too slow to reoxidize the reduced cytosolic NAD+, pyruvate is converted to lactate with a resultant change in the lactate/pyruvate ratio, as illustrated by the altered redox state (Wasserman et al. 1985).

Lactic acid can be formed under fully aerobic conditions or as part of the Cori Cycle mechanism (Brooks, 1988). Lactic acid is actively and continually formed during submaximal exercise, and is removed as exercise continues. Even during steady state exercise that elevates blood lactate several times above rest values, almost all of the lactate is removed by direct oxidation and the lactate shuttle mechanism during exercise itself (Brooks & Gaesser, 1980). Lactate production permits the release of some of the energy incorporated in the glucose molecule and transfers this energy to ADP for the production of ATP (Gollnick et al. 1986).

The lactate produced during exercise is not necessarily a hinderance to

the athlete. During mild exercise, lactate can be utilized as a fuel (Gollnick et al. 1986). "During exercise, lactate represents a fuel source which is quantitatively more important than blood glucose" (Brooks, 1988, p. 2). At intensities ranging from 40 to 75% VO_2 max, approximately 85% of lactate formed is oxidized, whereas only about 15% undergoes gluconeogenesis. Close to 50% of the lactate is removed by oxidation within the active muscle tissue, while the heart and inactive skeletal muscle account for the remainder of lactate removal by oxidation (Brooks, 1988).

Blood and Muscle Lactate Changes During Exercise

Generally, as the intensity of exercise increases, VO_2 increases linearly. Conversely, changes in blood lactate levels are very slight until approximately 60% of VO_2 max is reached (Brooks & Fahey, 1987), at which point, blood lactate increases nonlinearly. This inflection point on the blood lactate curve has been given many names including lactate threshold (T_{lact}), anaerobic threshold (AT) and the onset of blood lactate accumulation (OBLA) (Brooks, 1988, Gollnick et al. 1986, Brooks & Fahey, 1987). Changes in blood lactate concentration cannot be taken as truly reflective changes in muscle lactate production for a number of reasons (Brooks & Fahey, 1987). Lactate is produced in the muscles and enters the blood to be oxidized. At rest and during exercise, the lactate concentration in muscle is higher than in the blood (Diamant, Karlsson & Saltin, 1968; Stanley, Gertz, Wisneski, Neese & Brooks, 1985). At the cessation of exercise, lactate levels in the blood rise, as the

lactate is shunted from muscle to the blood (Hermansen & Osnes, 1972). These findings suggest that the lactate moves from the muscles into the blood by a mechanism of facilitated transport (Deuticke, Beyer & Forst, 1982; Newsholme & Leech, 1983; Gollnick et al. 1986).

A sudden rise in blood lactate can signify a rapid rate of muscle glycogenolysis. When glycogenolysis is accelerated during exercise, glycogen depletion and muscle fatigue may result (Brooks & Fahey, 1987; Brooks, 1988). A rise in blood lactate concentration during exercise suggests that lactate enters the blood faster than it can be removed. The failure to contend with lactate production during exercise results in blood acidosis and muscle fatigue (Brooks & Fahey, 1987). It has been suggested that complete fatigue may occur when lactate concentrations of between 20 and 25 mmol/kg wet tissue are obtained in muscle (Mainwood & Renaud, 1985), although Hermansen and Stensvold (1972) and Hermansen and Vaage (1977) reported blood lactate concentrations above 30 mmol/litre following multiple bouts of dynamic exercise in humans.

Fructose Ingestion and Lactate Production

The results presented by Decombaz and colleagues (1985) verify that lactate is released into the circulation after fructose ingestion. Fructose administration has also been associated with lactic acidosis (Woods & Alberti, 1972).

As forementioned, fructose ingestion has been found to increase free

fatty acid mobilization (Addington & Grunewald, 1987; Guezennec et al. 1989; Hargreaves et al. 1985), thereby offering an alternative energy source to the working muscles and may result in postponed fatigue. However when the lactate concentration of the blood increases (pH decreases), the mobilization of free fatty acids (FFA) is reduced (Bagby, Green, Katsuta & Gollnick, 1978; Boyd, Gianber, Mager & Lebovitz, 1974; Green, Houston, Thomson, Sutton & Gollnick, 1979). Fructose ingestion results in an increase in FFA mobilization as well as an increase in lactate production. At present, it is not clear whether the FFA or lactate demonstrates a larger influence when fructose is ingested during exercise.

Respiratory Exchange Ratio Changes During Exercise

Respiratory exchange ratio (RER) analyses the ratio of carbon dioxide produced to oxygen consumed (VCO_2/VO_2) and provides an indication of the fuel being metabolized during exercise (Brooks & Fahey, 1984). During high intensity exercise, an individual's RER approaches 1.0. During prolonged periods of submaximal exercise, the RER goes down steadily towards 0.7, indicating the increased reliance upon fat as a fuel source.

During high intensity exercise, the amount of oxygen an individual can consume may be limited, CO_2 expended will be higher, resulting in a higher RER, and thereby oxidizing carbohydrate more than fat (Brooks & Fahey, 1984). During prolonged periods of submaximal exercise, more oxygen can be utilized. Therefore, the RER will be lower than 1.0, indicating the metabolism

of fat as a fuel source.

Endurance trained individuals have lower respiratory exchange ratio values than untrained at comparable percentages of their VO_2 max, during submaximal exercise. Trained persons are able to derive a greater percentage of their fuel sources from fat and less from carbohydrate than do sedentary individuals. Furthermore, during prolonged exercise to exhaustion, RER values gradually decline for both trained and untrained subjects, illustrating an increased reliance on fat as submaximal exercise continues (Hermansen, Hultman & Saltin, 1967).

Since the ingestion of fructose has been found to increase FFA mobilization (Addington & Grunewald, 1987; Guezennec et al. 1989; Hargreaves et al. 1985) it follows that lower RER values may be observed following fructose ingestion, when compared to the ingestion of glucose or a control solution.

Gastric Emptying

It has been demonstrated that one consequence of ingesting large doses of fructose may be gastrointestinal distress and diarrhea (Coggan & Swanson, 1992; Murray et al. 1989; Ravich et al. 1983). In order to utilize fructose as an ergogenic aid during endurance exercise, a dose must be prescribed that will not cause distress in the athlete. The effectiveness of hydration and supplementation is dependent upon transit time and absorption in the gastrointestinal tract (Rehrer, Beckers, Brouns, Ten Hoor & Saris, 1989). The

rate of gastric emptying is one of the factors limiting the effectiveness of drinking a nutrient containing fluid during endurance activities (Costill, Kammer & Fisher, 1970). It is therefore important to ingest a solution that will not inhibit gastric emptying. The efficacy of a given drink is limited by the rate of absorption, which is in turn limited by gastric emptying (Rehrer et al. 1989).

Various factors affect gastric emptying. The caloric content appears to be the primary determinant of the gastric emptying rate (Brener, Hendrix & McHugh, 1983; Case, Phillips, Lewis & Connolly, 1981a; Case, Lewis, Phillips & Clark, 1981b). Murray et al. (1987) observed that gastric emptying slows as the glucose concentration (energy density) of the ingested solution increases. Previously, glucose solutions greater than 2.5% carbohydrate have been shown to empty more slowly than water as a function of concentration (Costill & Saltin, 1974). Ryan, Bleiler, Carter and Gisolfi (1989) concluded that ingesting 350 ml of a 5% carbohydrate solution every 20 minutes at 60% VO_2 max resulted in over 90% of the consumed beverage being emptied by the end of the three hour cycling exercise bout. Another study has shown that a 6 to 8% carbohydrate solution is beneficial (Sherman, Costill, Fink & Miller, 1981). It is proposed that when exercise continues for more than two hours, a dietary supplement is required during exercise. The gastric emptying rate was also dependent on time. Calories appear to be emptied from the stomach at a significantly faster rate from 0 to 30 minutes (4.5 kcal/min), than from 30 to 120 minutes (2.6 kcal/min) (Sherman et al. 1981).

Gastric emptying is also related to the volume of beverage ingested. The rate is related to the pressure exerted on the stomach (Rehrer et al. 1989). A linear increase in amount emptied has been shown with an increase in gastric content (Hunt & Spurrel, 1951) up to a maximum of 600 ml of ingestate (Costill & Saltin, 1974).

Five to 25% glucose solutions are emptied from the stomach in two phases (Brener et al. 1983): 1) an initial, rapid phase primarily dependent upon volume or intragastric pressure and 2) a slower, relatively constant phase primarily dependent upon caloric content and presumably due to feedback from duodenal receptors responding to glucose (Brener et al. 1983).

The temperature of the ingested beverage also affects gastric emptying. A cold beverage tends to leave the stomach more quickly than a warm one (Costill & Saltin, 1974; Gershon-Cohen, Shay & Fels, 1940).

Exercise intensity plays a role in gastric emptying. Exercise below 65% VO_2 max had no significant influence on either gastric emptying or intestinal absorption of glucose, fluid or electrolytes (Costill & Saltin, 1974). Fordtran and Saltin (1967) found that exercise at a high intensity level (70% VO_2 max +) may inhibit gastric emptying.

The type of exercise also affects gastric emptying. Exercise induced influences on gastrointestinal function and regulation may differ due to different types of body movements (Brouns, Saris & Rehrer, 1987). It would appear that most studies on gastric emptying have been conducted with

cycling exercise (Costill & Saltin, 1974; Fordtran & Saltin, 1967). During running, the movement of fluid in the stomach may increase gastric emptying (Murray et al. 1987). This possibility makes generalizations from cycling to running questionable.

The type of solution consumed may affect gastric emptying as well. Fructose solutions have been shown to empty from the stomach at faster rates than equimolar glucose solutions in resting humans (Elias, Gibson, Greenwood, Hunt & Tripp, 1968). As discussed, fructose is absorbed by way of facilitated diffusion, a process not associated with glucose transport and unaffected by sodium or other electrolytes (Holdsworth & Dawson, 1964). The activity of a separate facilitated diffusion mechanism for fructose uptake across the duodenal villae, which increases linearly with increasing fructose concentration in the ingested solution, might explain the increased gastric emptying effect (Crane, 1968; Fordtran & Ingelfinger, 1968). Therefore, fructose stimulates somewhat less water absorption than equimolar glucose absorption (Sladen, 1972).

From the information presented, an ideal carbohydrate solution can be designed that will maximize gastric emptying. This will allow the athlete to utilize the ingested carbohydrate and also maintain proper hydration for the duration of exercise. The solution should be between 6 and 8% (Sherman et al. 1981) of a cold (Costill & Saltin, 1974; Gershon-Cohen et al. 1940) fructose solution, administered during cycling exercise at an exercise intensity of no

greater than 70 to 75% VO_2 max. (Fordtran & Saltin, 1967).

Chapter 3

METHODS AND PROCEDURES

Subjects

The subjects consisted of 17 trained endurance athletes who volunteered to participate in the study. All subjects were residents of the Thunder Bay area. The experimental treatments included glucose and fructose trials. A control condition was included to establish baseline data on the various dependent measures and to match subjects on exercise time to exhaustion. All subjects were informed of the methodology of the experiment and gave full consent to participate. None of the subjects had a history of glucose or fructose intolerance and none of the subjects were diabetic.

Research Design

The research design for the present study involved a true experiment with no random selection, as the subjects were volunteers. The treatment period involved the dietary manipulation (ie. fructose ingestion, glucose ingestion, control). The posttest included the measurement of the various dependent measures.

Procedures

The VO_2 max test, the exercise test to exhaustion and the various experimental procedures were approved by the Senate Ethics Committee on Human Testing at Lakehead University. At least one week before the dietary

manipulation was to begin, each subject underwent a VO_2 max test in order to determine the workload to be maintained for each of the experimental sessions. The exercise tests were conducted on a calibrated Monarch Bicycle Ergometer, model 868 (Monarch, Stockholm, Sweden).

At least one week after the VO_2 max test, all subjects performed the cycling exercise to exhaustion under the control condition. The control condition involved the ingestion of a sweetened placebo before and during the exercise session. All subjects in the control condition ingested 80 mg of saccharine in a 500 ml solution (Fielding et al. 1987) and 250 ml of the same saccharine solution at 20, 50 and 90 minutes during exercise. The results of the control condition were ordered from longest to shortest on the dependent measure of exercise time to exhaustion. All subjects were matched and placed into either the fructose or the glucose group. This procedure allowed the subjects to be balanced on the dependent variable of exercise time to exhaustion.

The investigator met with each subject to discuss his or her role in the next part of the study. In both the fructose and glucose treatment groups, all subjects were instructed that they would take part in a second cycling test to exhaustion. The investigator ensured that the test was scheduled at least one week after the control test and at the same time of day. Subjects in the fructose and glucose treatment groups ingested 1 gram per kg body weight (Decombaz et al. 1985) of fructose or glucose in 500 ml of water one hour

before exercise and 0.4 grams per kg body weight (Decombaz et al. 1985) in 250 ml water at 20, 50 and 90 minutes during exercise.

Prior to the second exercise test, the subjects were instructed to follow similar dietary patterns and exercise participation patterns as during the first test. By keeping a detailed list of all foods consumed, the percentage of carbohydrate, protein and fat in each subjects' diet could be determined. This dietary analysis was conducted using the software programme Mosby Diet Simple (N-Squared Incorporated, 1989). During the experimental exercise trials, the beverages were ingested before and during the exercise test to exhaustion.

All three trials involved cycling exercise at a workload to elicit 75% of each subject's VO_2 max until exhaustion. The subjects were instructed to ride at 80 rpm. Exhaustion was defined as the time when they could no longer maintain 70 rpm (Hargreaves et al. 1987). Cycling cadence was continually monitored by the investigator to ensure each subject was riding at 80 rpm. The subject was told to correct their cadence if it was above 90 or below 75 rpm. All subjects were instructed to exercise to total exhaustion and were motivated to the same extent by the investigator.

Prior to the onset of the exercise tests to exhaustion, an indwelling catheter was inserted into the median cubital vein of each subject by a registered nurse or a trained technician. Blood was drawn from the catheter at rest, at 30, 60 and 90 minutes of exercise and immediately post exercise (T =

Exh.). The blood was slowly injected into three different vacutubes for future analysis. The amount of blood drawn from each subject during each exercise test to exhaustion was approximately 93 mls. The blood sampling guidelines and procedures are discussed in Appendix B.

The subjects were connected to the Beckman Metabolic Measurement Cart (MMC Horizon Systems) at approximately 10 minute intervals for measurement of oxygen and carbon dioxide levels. Each subject informed the investigator when he or she was approaching exhaustion to ensure a gas sample was taken within one minute of exhaustion.

Measures

The independent variables were dietary manipulation before and during exercise. Condition A was fructose ingestion and condition B was the ingestion of glucose.

Various measures were taken before and during the experimental exercise sessions. These dependent measures included exercise time to exhaustion, glucose, lactate and free fatty acid (FFA) concentrations and respiratory exchange ratio (RER). Plasma glucose and lactate were determined colorimetrically at a wave length of 540 nm employing the Kodak Ektachem (E700). Serum free fatty acids were measured colorimetrically at a wave length of 436 nm (Laurell & Tibbling, 1967; Noma, Okabe & Kita, 1973), as described in Appendix E.

Blood was drawn with an indwelling catheter from the median cubital

vein 5 minutes before the commencement of exercise (rest), at 30, 60 and 90 minutes during exercise, with a final blood sample taken immediately post exercise (exhaustion). In all trials, the final solution was ingested after the 90 minute blood sample. The dependent measures observed from blood sampling included glucose, lactate and free fatty acid concentrations.

Gas measurements (Beckman MMC) were taken at various intervals during the exercise session. This permitted the analysis of RER, thereby illustrating the predominance of carbohydrate or fat as a fuel source utilized throughout each of the experimental trials.

Data Analysis

The independent and dependent variables were analyzed and presented in a variety of ways. Exercise time to exhaustion was represented by way of a bar graph comparing the duration of exercise for fructose ingestion, glucose ingestion, and the ingestion of a control solution. Blood glucose, blood lactate, blood free fatty acids and respiratory exchange ratio (RER) were depicted by line graphs comparing the three dietary measures.

Exercise time to exhaustion was statistically analyzed via a paired t-test to determine if a significant difference existed between the dietary manipulations. The remainder of the dependent parameters were analyzed using an analysis of variance (ANOVA). Each set of data points were analyzed independently (treatment, time), allowing for the location of significant differences. All statistical analyses were completed using the statistical

analysis package in Microsoft Excel, version 4.0a.

Chapter 4

RESULTS

Physical Characteristics of Subjects

The mean age (23.8 years, ±4.7), height (177.3 cm, ±9.2), weight (70.7 kg, ±9.9) and VO_2 max (60.65 ml/kg, ±8.1) are listed in Table 1. Fifteen subjects were male and two were female.

Composition of Subject Diets

The dietary composition of the subjects for the two, one week sessions preceding the exercise tests to exhaustion were analysed for 16 of the 17 subjects. The average diet of the subjects consisted of 52% (±8%) carbohydrate, 15% (±2.5%) protein and 33% (±8.1%) fat (Mosby Diet Simple, N-Squared Inc. 1989) and is listed in Table 2.

Exercise Time to Exhaustion

The mean exercise time to exhaustion for the control trial (122.8 minutes, ±26), the fructose trial (167.7 minutes, ±46.3) and the glucose trial (162.8 minutes, ±21.7) is listed in Table 3 and depicted in Figure 1.

The exercise time to exhaustion for the control group was significantly less ($\propto = .05$) than both the fructose ($p < .02$) and glucose ($p < .001$) groups. Furthermore, the exercise time to exhaustion for the fructose group was not significantly different from the time for the glucose group.

Table 1: Physical Characteristics of Subjects
(n = 17)

Variable	Mean	S.D.	Minimum	Maximum
Age	23.80 years	±4.65	18.0	31.0
Height	177.30 cm.	±9.20	155.2	195.2
Weight	70.64 kg.	±9.86	51.0	84.8
VO_2 max.	60.65 ml/kg	±8.10	51.0	82.9

Table 2: Composition of Subject Diets
(n = 16)

Variable	Mean	S.D.	Minimum	Maximum
Carbohydrate	52 %	±8.05	41	65
Protein	15 %	±2.53	12	19
Fat	33 %	±8.13	20	44

(Mosby Diet Simple, N-Squared Inc. 1989)

Table 3: Exercise Time to Exhaustion

Variable	Mean	S.D.	Minimum	Maximum
Control (n = 17)	122.82 min.	±25.95	93	180
Fructose (n = 9)	167.72 min.	±46.31	116	245
Glucose (n = 8)	162.75 min.	±21.69	120	193

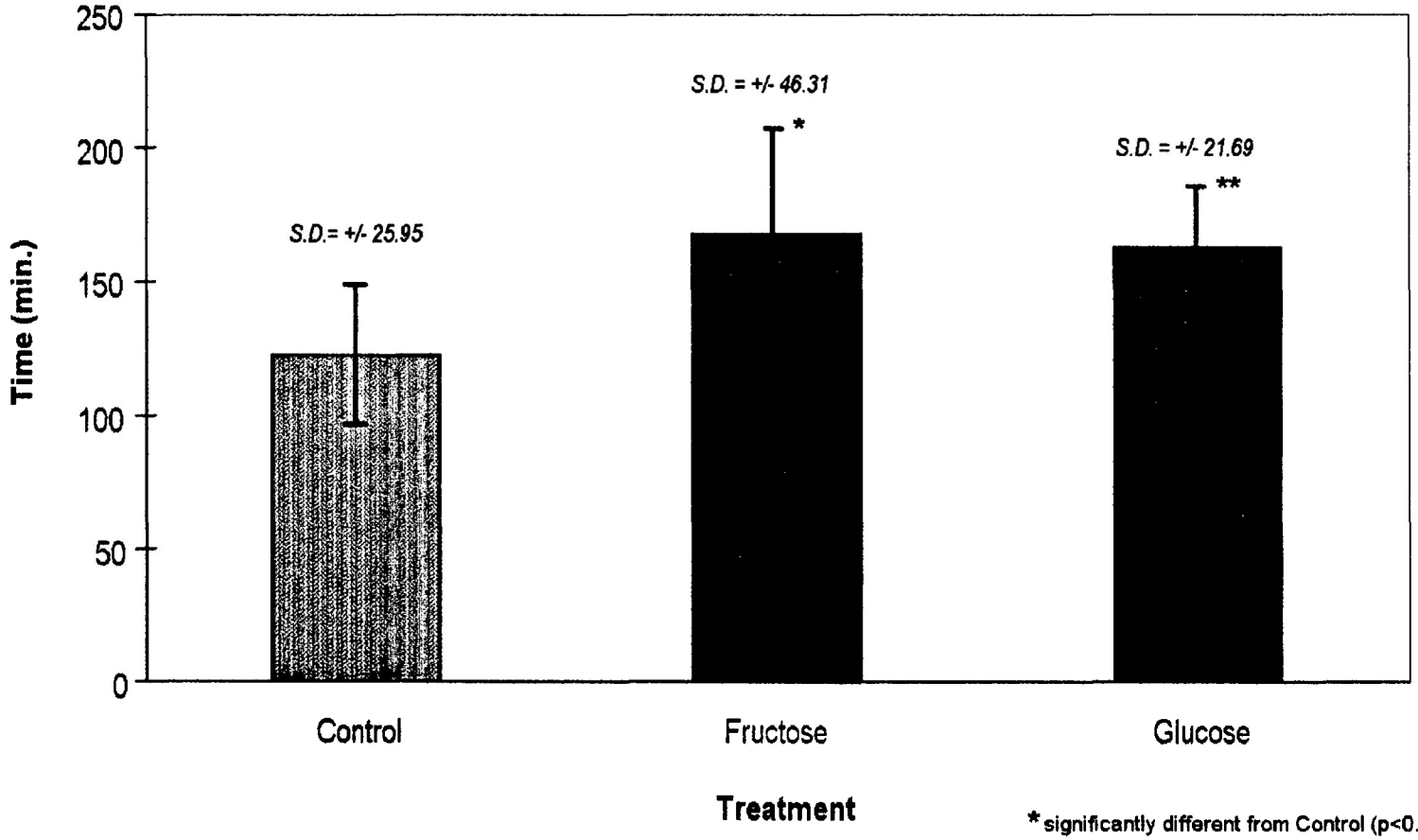

Figure 1: Exercise Time to Exhaustion

Blood Values During Exercise Test To Exhaustion

Blood Glucose - There was a significant difference ($\propto$ = .05) between treatments with the blood glucose levels of the fructose condition remaining more stable and actually increasing throughout the exercise test to exhaustion.

Prior to the onset of exercise (T = 0), the blood glucose levels in the glucose treatment group were significantly higher ($p < .04$) than the control group. The blood glucose levels of the glucose treatment group continued to show dramatic shifts throughout the duration of the exercise sessions (see Figure 2), including a significant decrease ($p < .02$) at 90 minutes of exercise when compared to the fructose treatment group. The blood glucose level of the fructose treatment group was also significantly higher ($p < .0005$) than the control group at 90 minutes of exercise.

Significant differences in blood glucose levels were also noted over time ($\propto$ = .05). In the control group, the highest levels of blood glucose were observed at 30 minutes of exercise (T = 30) and were significantly higher than T = 0 ($p < .03$), T = 90 ($p < .00005$) and T = Exh. ($p < .0002$). The blood glucose levels in the control group increased from the onset of exercise to peak at 30 minutes (5.2 mmol/l), then declined to exhaustion (4.4 mmol/l).

The fructose treatment allowed for a more constant supply of glucose to the blood. As stated, in the fructose treatment group, the blood glucose levels increased gradually from the onset of exercise, peaked at 90 minutes (5.1 mmol/l) and gradually declined at exhaustion (4.9 mmol/l). No significant

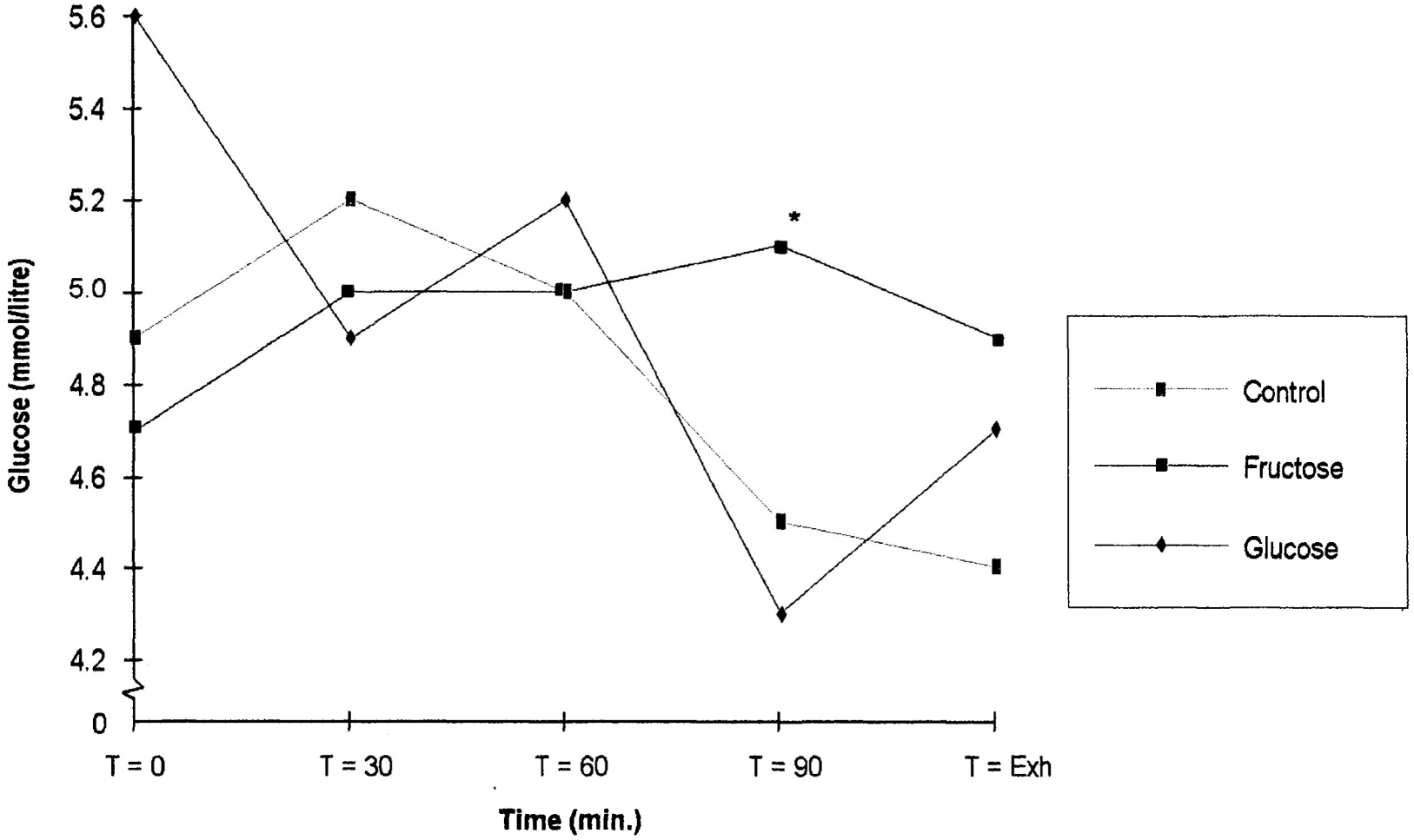

Figure 2: Blood Glucose vs. Time

* significantly different from Control ($p<0.0005$) and Glucose ($p<0.02$)

differences were observed over time.

The blood glucose levels of the glucose treatment group demonstrated significant ($\propto$ = .05) shifts throughout the exercise test to exhaustion. The blood glucose levels were highest at T = 0 (5.6 mmol/l) and were significantly higher ($p < .04$) than the blood glucose level at T = 90 (4.3 mmol/l).

Blood Lactate - The blood lactate response during exercise illustrated an increase for all conditions at T = 30, decreasing to just over resting values at T = 60 and showing very gradual increases to exhaustion (see Figure 3).

A significant difference ($\propto$ = .05) between treatment groups was noted at T = 0. The blood lactate level in the control group was significantly lower than either the fructose ($p < .002$) or the glucose treatment groups ($p < .01$).

Significant differences in blood lactate levels were noted over time ($\propto$ = .05) for the control group. Blood lactate levels peaked in the control group at 30 minutes of exercise (4.8 mmol/l) and were significantly higher than at the onset of exercise ($p < .00002$), T = 60 ($p < .02$), T = 90 ($p < .007$) and T = Exh. ($p < .03$).

The fructose and glucose treatment groups did not show any significant differences in blood lactate levels over time.

Blood Free Fatty Acids (FFA) - Prior to the onset of exercise (T = 0), blood FFA levels in the control group were significantly higher ($p < .02$) than the fructose treatment group. No other significant differences between treatment groups were noted with respect to blood FFA levels.

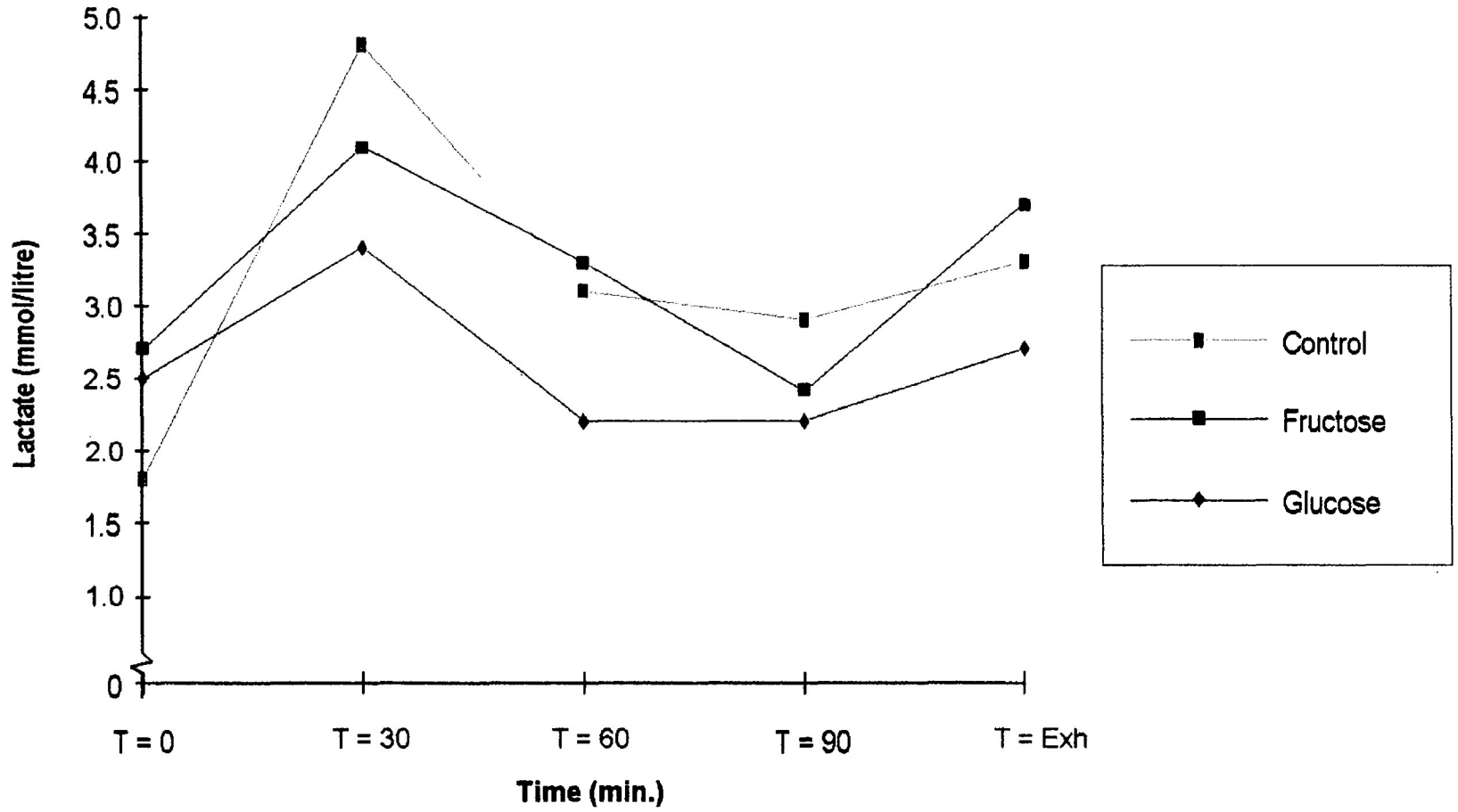

Figure 3: Blood Lactate vs. Time

Significant differences in blood FFA levels were noted over time ($\propto$ = .05) (see Figure 4). The fructose and glucose treatment groups showed gradual increases in blood FFA levels throughout the duration of the exercise test to exhaustion. The fructose treatment group showed significant increases in blood FFA at T = 90 ($p < .01$) and T = Exh. ($p < .01$) when compared to the FFA levels prior to the onset of exercise. The glucose treatment group showed a significant increase in blood FFA at T = Exh. ($p < .01$) over the FFA level at T = 0. The control group showed gradual decreases in blood FFA over the duration of the exercise test with a very gradual increase at exhaustion, although no significant differences in the control group were noted.

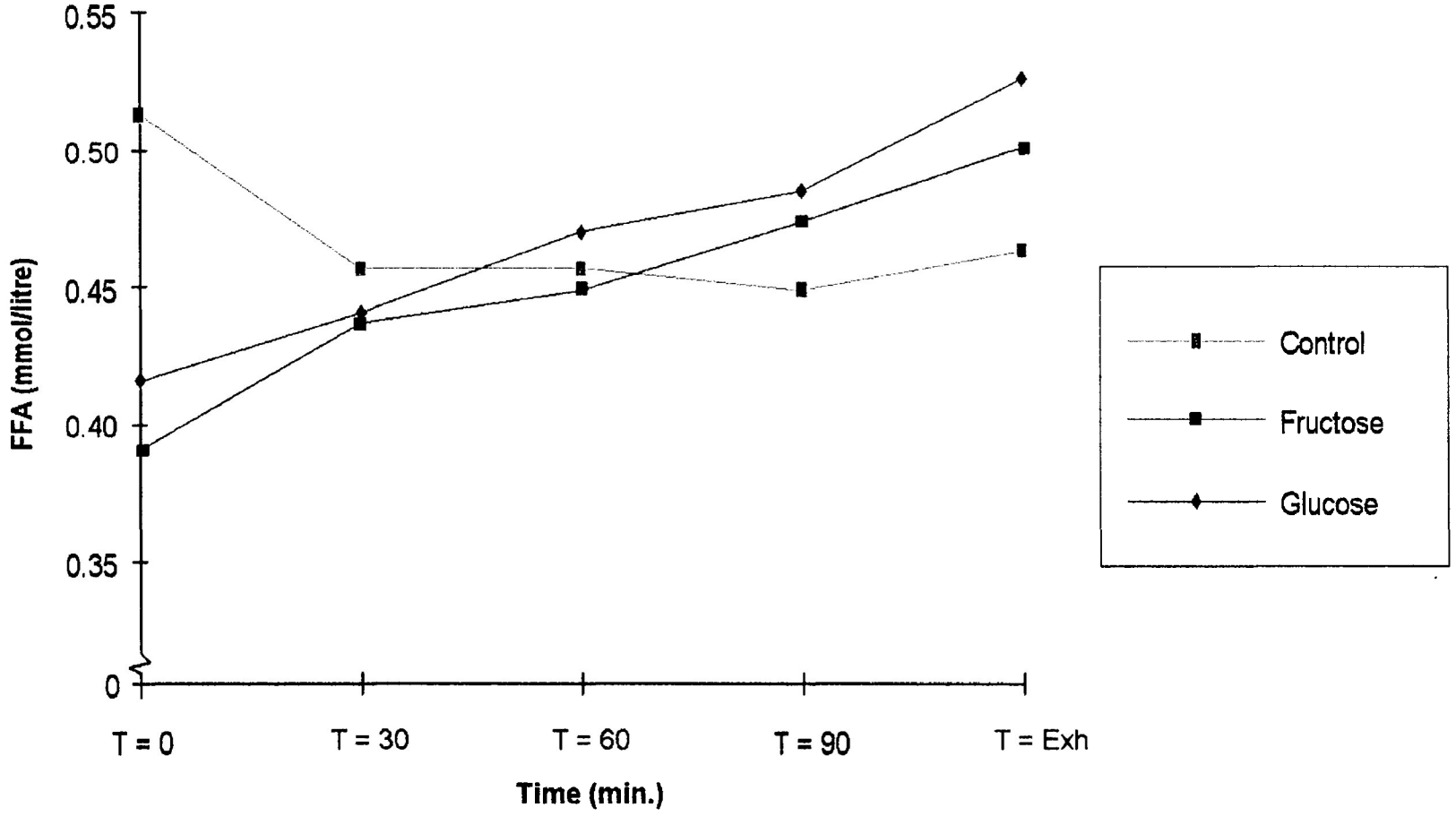

Figure 4: Blood Free Fatty Acids vs. Time

Chapter 5

DISCUSSION

Many studies support the belief that fructose may be of benefit during endurance activities (Addington & Grunewald, 1987; Guezennec et al. 1989; Hargreaves et al. 1985; Koivisto et al. 1981; Levine et al. 1983). In the present study, the ingestion of a fructose solution before and during endurance cycling performance allowed for the postponement of fatigue over a control solution, but did not demonstrate a significant difference from a glucose solution on the dependent variable of exercise time to exhaustion.

As was discussed in the Review of Literature, many studies have been conducted to examine the effect of fructose ingestion on exercise performance, but none have followed the protocol of the current study. Some studies (Decombaz et al. 1985; Guezennec et al. 1989; Hasson & Barnes, 1987; Koivisto et al. 1985; Koivisto et al. 1981; Massicotte et al. 1989; Okano et al. 1988) have examined fructose utilization during cycling exercise of a certain duration (ie. 30, 60 minutes). Other studies have analyzed fructose utilization with treadmill running (Fielding et al. 1987; Levine et al. 1983), which cannot be directly compared to cycling due to the increased upper body movement with running. Exercise intensities have also varied in the examination of fructose utilization. Some studies (Decombaz et al. 1985; Murray et al. 1989; Murray et al. 1987; Okano et al. 1988) have examined exercise performance

above or below the anaerobic threshold, which will influence substrate utilization.

These different protocols make it difficult, and even impossible, to compare past findings to the present study. To this researcher's knowledge, there have not been any studies conducted following the protocol of the present experiment. Therefore, this is the first study of its kind to examine exercise time to exhaustion with an analysis of substrate utilization, upon the ingestion of fructose and glucose solutions.

Exercise Time To Exhaustion

The results of the present study show that both glucose and fructose solutions were equally more effective than a control solution in postponing fatigue in an exercise test to exhaustion.

There are two possible explanations for these results. First, it is possible that both glucose and fructose were similar in their effectiveness in prolonging exercise time to exhaustion. It has been demonstrated that blood glucose oxidation can reach very high levels late in prolonged, moderately intense exercise when muscle and liver glycogen levels are low, but blood glucose is maintained by exogenous supplementation (Burgess, Robertson, Davis & Norris, 1991). Although the test protocols were not identical to the present study, some researchers (Decombaz et al. 1985; Fielding et al. 1987; Hargreaves et al. 1987) have found fructose and glucose to be of equal benefit as an aid for prolonged exercise performance.

Secondly, it is possible, although unlikely, that the subjects underwent a learning effect. Each subject participated in a control ride to exhaustion prior to the treatment (glucose, fructose) trial. This may have allowed the subjects to be more comfortable on the second ride, as they knew more of what to expect. During the second ride, they may have been better able to focus on the task at hand. Although the subjects were not informed of the duration of their first cycle to exhaustion, they would have a good idea of how long they have been participating in the experiment. As discussed, all of the subjects were trained endurance athletes, with the motivation to better subsequent performances.

Blood Values During Exercise Test to Exhaustion

1) Blood Glucose

It has been demonstrated that following glucose ingestion, the concentration of glucose in the blood is elevated (Nishibata, Sadamoto, Mutoh & Miyashita, 1993), but falls rapidly below normal levels due to an exponential over-compensation of insulin production (Hultman, 1967). As is evident in Figure 2, this insulin effect with glucose ingestion led to dramatic blood glucose shifts throughout the exercise test to exhaustion. However, fructose does not require insulin to enter the cell (Hasson & Barnes, 1987; Schwarz et al. 1989), and thereby allows the blood glucose to remain at a more constant level throughout the exercise test to exhaustion. The blood glucose levels remained more stable and actually increased throughout the exercise test to

exhaustion. Therefore, fructose allowed for a more constant supply of glucose to be available to the working muscles throughout the exercise test.

Several researchers have shown that the maintenance of blood glucose can be a critical factor in delaying the onset of fatigue during prolonged exercise (Davis, Burgess, Slenty, Bartoli & Pate, 1988a; Davis et al. 1988b). In the present study, blood glucose levels in the glucose treatment group fell dramatically between 60 to 90 minutes of exercise, but following glucose ingestion at 90 minutes blood glucose levels steadily increased until exhaustion was reached. It is therefore surprising that the more stable glucose levels in the fructose treatment group did not produce significant differences in performance time to exhaustion. Perhaps the blood glucose levels in the glucose treatment group remained sufficiently high to maintain adequate glucose uptake to the working muscles. Recently, McConell, Fabris, Proietto and Hargreaves (1994) demonstrated that glucose ingestion during prolonged exercise resulted in a suppression of hepatic glucose production and increased glucose uptake mediated mainly by increased plasma glucose and insulin levels.

It has been explained in the literature (Chen & Whistler, 1977) that fructose allows for glycogenolysis of liver glycogen to occur. This process of glycogen breakdown may have helped to keep blood glucose levels elevated in the fructose treatment group. An alternative possibility is that the delay in the onset of fatigue, late in prolonged exercise, is largely due to the oxidation of

blood-borne glucose and not necessarily the sparing of muscle glycogen (Burgess et al. 1991).

The control group began within normal blood glucose levels, increased at 30 minutes of exercise, steadily declined at 90 minutes and gradually decreased at exhaustion. This pattern demonstrated a normal exercise response. Throughout the first 30 minutes, the body makes glucose available to the working muscles. As exercise continues, this supply of blood glucose is reduced, as no external energy sources are administered. It is interesting to note that muscle and liver glycogen did not appear to be broken down, which would have allowed for a more constant supply of blood glucose to be available to the working muscles. Brooks and Fahey (1984) have illustrated that during prolonged endurance exercise, muscle and liver glycogen are converted into blood glucose, and thereby allow an energy source to be available to the working muscles. The blood glucose level in the control group did not appear to follow this trend, as it fell quite rapidly throughout the exercise test to exhaustion.

2) Blood Lactate

As is evident in Figure 3, all trials demonstrated an elevation in blood lactate during the first 30 minutes of exercise. At the onset of exercise, lactate production exceeds lactate removal (Brooks & Fahey, 1984), thereby causing lactate to accumulate in the blood. Houston, Waugh, Green and Noble (1976) found similar results in that the major increases in blood concentrations of

lactate occur early in exercise.

Recently, Burgess and coworkers (1991) demonstrated, in both a control and glucose fed group, a steady decline in plasma lactate concentration with prolonged endurance exercise. However, no significant differences between conditions were observed. In the present study, after 30 minutes of exercise, the concentration of lactate in the blood declined steadily and achieved a steady state of lactate production and lactate removal. In this experiment, there were no significant differences between the fructose and glucose treatment groups, although the fructose treatment group showed higher blood lactate values at each sample time. It is possible that the subjects in the fructose treatment group were better able to utilize the lactate as an energy source. Studies (Brooks, 1988; Gollnick et al. 1986) have shown that lactate can be used as an energy source during exercise, a fuel that may be of more importance than blood glucose.

3) Blood Free Fatty Acids (FFA)

In the control group, the pre-exercise FFA levels were significantly higher than both treatment groups, but dropped quickly at 30 minutes of exercise and remained stable throughout the exercise test to exhaustion. Both the fructose and glucose treatment groups showed gradual increases in blood FFA levels throughout the duration of the exercise test to exhaustion (see Figure 4). Significant increases in blood FFA were observed in the fructose treatment group at 90 minutes of exercise and at exhaustion, whereas the glucose

treatment group had significant increases in blood FFA at exhaustion.

Both the fructose and glucose treatment groups had similar FFA levels throughout the exercise test to exhaustion. The inhibitory effect on lipolysis following glucose ingestion (Carlstrom, 1969; Galbo et al. 1979) did not appear to occur in the present study. Nishibata et al. (1993) found FFA levels to be significantly higher during endurance exercise with the ingestion of a placebo over the ingestion of a glucose solution. Similarly, Deuster, Singh, Hofmann, Moses & Chrousos (1992) reported that the mobilization of FFA was reduced with carbohydrate ingestion before and during prolonged exercise.

Although studies have shown that fructose ingestion allows for an increase in FFA mobilization (Addington & Grunewald, 1987; Guezennec et al. 1989; Hargreaves et al. 1985), thereby offering an alternative energy source to the working muscles, possibly postponing fatigue, this increase was not significant in the present study. It should be noted that although the levels were not significantly different from the control group, both the fructose and glucose treatment groups increased throughout the exercise test to exhaustion. This increase in blood levels of FFA possibly allowed FFA to be used as an energy source to the working muscles and aided in the postponement of fatigue. However, it is more likely that the postponement of fatigue was largely due to the maintenance of blood glucose in the fructose treatment group and the RER values lend support to this contention.

Respiratory Exchange Ratio

As mentioned in Chapter 3 (Methods and Procedures), gas readings for each subject were recorded on the Beckman Metabolic Measurement Cart (MMC) at approximately 10 minute intervals for measurement of oxygen and carbon dioxide levels, during the exercise test to exhaustion. Since this analysis was not conducted at predetermined intervals, a statictical analysis of the values was not possible. Trends in the exercise tests will be addressed.

The respiratory exchange ratio (RER) values are illustrated in Figure 5. All three groups (control, fructose, glucose) demonstrated gradual declines in RER throughout the exercise test to exhaustion, depicting a reliance on both fat oxidation as well as carbohydrate oxidation during endurance cycling exercise. This gradual decline in RER throughout the exercise test to exhaustion has been supported in the literature. Hermansen et al. (1967) found that during prolonged periods of submaximal exercise, the RER decreases towards 0.7, indicating the increased reliance on fat as a fuel source.

The only observable difference between the three groups occurred prior to the onset of exercise. The fructose and glucose treatment groups had RER values greater than 1.0 at the onset of exercise due to the ingestion of fructose or glucose one hour prior to the exercise session. Over the first 30 minutes of exercise the RER of the fructose and glucose treatment groups dropped below 1.0 and demonstrated similar fuel utilization as the control group throughout

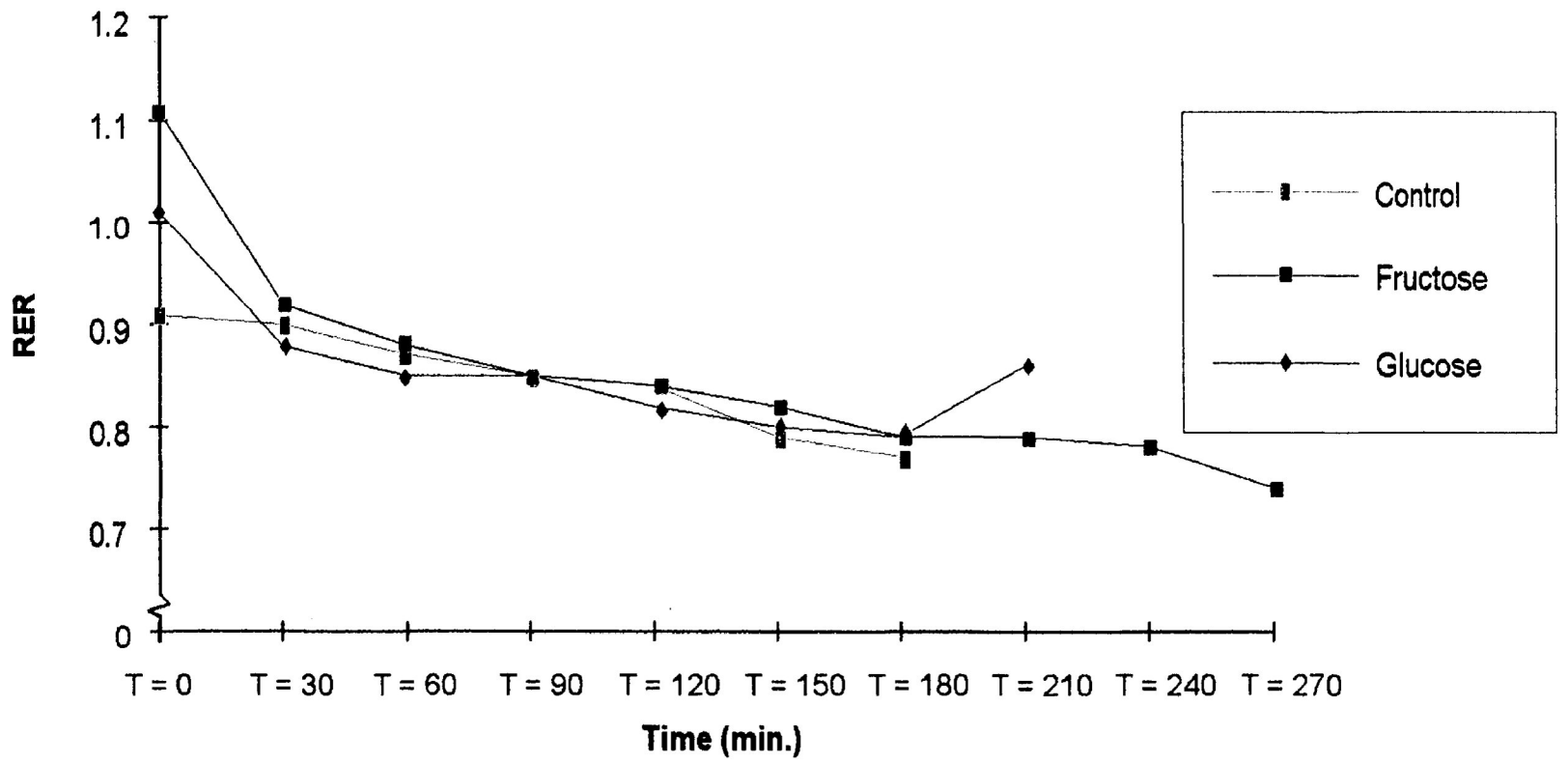

Figure 5: Respiratory Exchange Ratio (RER) vs. Time

the remainder of the exercise test to exhaustion (see Figure 5). Similar findings were reported by Nishibata et al. (1993) who found no significant differences in respiratory exchange ratio values between a glucose and a control group during endurance cycling exercise.

The RER values revealed that the fructose group did not demonstrate an increase in FFA mobilization or utilization. Therefore, an increased reliance on fat as a fuel source did not occur in the present investigation, as was previously reported in various research investigations (Addington & Grunewald, 1987; Guezennec et al. 1989; Hargreaves et al. 1985).

The final data points on the RER graph deserve explanation. By examining Figure 5, it appears that the fructose group had the longest exercise time before exhaustion and the RER of the glucose group appears to increase at exhaustion. In calculating the data points for Figure 5, the average RER value of the group was used at each time interval (30 minutes). As the exercise test to exhaustion continued, fewer data points were available as subjects in each of the groups reached exhaustion. Therefore, at the last data point for the fructose and glucose treatment groups, the value of only one subject was available. This results in unusual RER readings (glucose) and the appearance of the fructose treatment group having the longest exercise time to exhaustion.

Chapter 6

SUMMARY, CONCLUSIONS & RECOMMENDATIONS

Summary

The purpose of the present investigation was to determine if ingesting fructose before and during exercise is as beneficial or more beneficial in increasing exercise time to exhaustion than glucose ingestion before and during exercise. Seventeen endurance athletes from the Thunder Bay area were studied to compare the effects of fructose to glucose ingestion.

Each subject underwent two cycling rides to exhaustion at 75% VO_2 max. The first cycle involved the ingestion of a control solution. At least seven days later, each subject participated in a second ride to exhaustion, ingesting either a glucose or a fructose solution. Blood was sampled at pre-determined intervals to examine glucose, lactate and free fatty acids (FFA). These values were plotted against time, comparing the glucose to fructose ingestions. The subjects were occasionally connected to the Beckman MMC at various intervals to record RER values.

It was established in this study, that fructose and glucose are equally effective in prolonging exhaustion in endurance cycling performance. It was noted that fructose ingestion allowed for a more constant supply of blood glucose to be available to the working muscles. This eliminated the fluctuations in blood glucose, noted with glucose ingestion, that have been demonstrated in the literature (Hultman, 1967).

Conclusions

The ingestion of fructose and glucose postponed fatigue in a cycling ride to exhaustion. However, fructose allowed for a more stable blood glucose response throughout the exercise test to exhaustion. The more stable blood glucose levels attained with fructose ingestion may be beneficial over glucose ingestion in several ways. First, stable blood glucose levels may allow the athlete to perceive less physical exhaustion, thereby increasing his or her exercise performance. Second, higher blood glucose levels may increase mental alertness and precision required in some physical activities (ie. biathlon, triathlon). Also, higher blood glucose levels during endurance exercise activities may postpone athletes' perception of 'hitting the wall', thereby allowing for an increase in exercise performance.

Recommendations

Although fructose ingestion allowed for more stable blood glucose levels throughout the duration of the exercise test to exhaustion, the psychological effects are unclear. It would be interesting to examine psychological characteristics of the subjects during various stages of the test to examine if blood glucose levels influenced their subjective feelings of exertion and fatigue, including weakness, dizziness and disorientation. Due to fructose ingestion maintaining blood glucose at more stable levels than glucose ingestion, fructose may help to eliminate some of these symptoms, as explained by Hasson and Barnes (1987). This may point to beneficial effects of ingesting

fructose during prolonged events requiring mental alertness and focusing (ie. biathalon, triathlon).

Conducting muscle biopsies during exercise would allow for a more accurate picture of what is occurring in the muscle. As has been discussed, blood values are not an accurate indication of what is occuring in the muscle cell. By the time lactate enters the blood, the levels may not be representative of lactate activity in the muscle. Furthermore, as noted in the Review of Literature, the reduction in lactate activity in fast glycolytic muscle with endurance training has been observed (Brooks and Fahey, 1984). Conducting a muscle biopsy would allow for an analysis of skeletal muscle lactate activity and the ability to examine the relationship between substrate utilization and lactate activity. Muscle biopsies would also allow for an analysis of muscle glycogen levels to determine the extent of substrate utilization and furthermore illustrate the depletion of muscle glycogen in Type I versus Type II fibres.

Since this study found that fructose was of equal benefit to glucose in prolonging exercise time to exhaustion, it may be of benefit to diabetic athletes, as an alternative energy source to glucose. As has been discussed, fructose does not require insulin to gain access to the intracellular compartment (Schwarz et al. 1989), and may therefore act as a suitable alternative to glucose ingestion for diabetic athletes.

As with any scientific study, the findings would be more significant with a larger subject sample. This would allow for a more accurate indication of the

effects of the various ingested solutions. A larger subject sample would assist in highlighting areas of significant differences. It is difficult to observe significant differences with samples of only 8 and 9. Also, it would be beneficial for all subjects to undergo each treatment condition, to more accurately compare the effects of the various ingested solutions with each subject.

REFERENCES

Addington, E.E. & Grunewald, K.K. (1987). Preexercise feedings of glucose, fructose or sucrose: effects on substrate depletion in rats. Journal of Nutrition, 117, 593-597.

Adelman, R.C., Spolter, P.D. & Weinhouse, S. (1966). Dietary and hormonal regulation of enzymes of fructose metabolism in rats. Journal of Biology and Chemistry, 241, 5467-5472.

Ahlborg, G., Felig, P., Hagenfeldt, L., Hendler, R. & Warren, J. (1974). Substrate turnover during prolonged exercise in man. Journal of Clinical Investigations, 53, 1080-1090.

Ahlborg, G. & Felig, P. (1977). Substrate utilization during prolonged exercise preceded by ingestion of glucose. American Journal of Physiology, 233 (Endocrinology and Metabolism of Gastrointestinal Physiology), 2, E188-E194.

Bagby, G.J., Green, H.J., Katsuta, S. & Gollnick, P.D. (1978). Glycogen depletion in exercising rats infused with glucose, lactate, or pyruvate. Journal of Applied Physiology, 45, 425-429.

Bergstrom, J., Furst, P., Gallyas, F., Hultman, E., Nilsson, L.H. & Vinnars, E. (1972). Aspects of fructose metabolism in normal man, in Symposium on Clinical and Metabolic Aspects of Fructose, 57-64.

Bergstrom, J. & Hultman, E. (1967). Synthesis of muscle glycogen in man after glucose and fructose infusion. Acta Medica Scandinavica, 182 (1), 93-107.

Bjorkman, O., Sahlin, K., Hagenfeldt, L. & Wahren, J. (1984). Influence of glucose and fructose ingestion on the capacity for long-term exercise in well-trained men. Clinical Physiology, 4, 483-494.

Bohannon, N.V., Karam, J.H. & Forsham, P.H. (1980). Endocrine responses to sugar ingestion in man. Journal of the American Dietetic Association, 76, 555-560.

Boyd, A.E., Gianber, S.R., Mager, M. & Lebovitz, H.E. (1974). Lactate inhibition of lipolysis in exercising man. Metabolism, 23, 531-542.

Brener, W., Hendrix, T.R. & McHugh, P.R. (1983). Regulation of gastric emptying of glucose. Gastroenterology, 85, 76-82.

Brooks, G.A. (1988). Lactate production during exercise: Oxidizable substrate versus fatigue agent. Science Periodical On Research and Technology in Sport, 8 (1), 1-12.

Brooks, G.A. & Fahey, T.D. (1987). Fundamentals of Human Performance. New York: Macmillan Publishing Company.

Brooks, G.A. & Fahey, T.D. (1984). Exercise Physiology: Human Bioenergetics and Its Application. Toronto: John Wiley and Sons.

Brooks, G.A. & Gaesser, G.A. (1980). End points of lactate and glucose metabolism after exhausting exercise. Journal of Applied Physiology: Respiratory Environment in Exercise Physiology, 49, 1057-1069.

Brouns, F.J., Saris, W.H.M. & Rehrer, N.J. (1987). Abdominal complaints and gastro-intestinal function during longlasting exercise. International Journal of Sports Medicine, 8, 175-189.

Burgess, M.L., Robertson, R.J., Davis, J.M. & Norris, J.M. (1991). RPE, blood glucose, and carbohydrate oxidation during exercise: effects of glucose feedings. Medicine and Science in Sport and Exercise, 23(3), 353-359.

Carlstrom, S. (1969). Studies on fatty acid metabolism in diabetes during exercise. VII. Plasma glycerol concentrations in juvenile diabetics during exercise before and after adequate insulin treatment. Acta Medica Scandinavica, 186, 429-432.

Case, G.L., Phillips, R.W., Lewis, L.D. & Connolly, B. (1981a). Effects of osmolality of liquid nutrient diets on plasma equilibrium of water and carbohydrate in Yucatan miniature swine. American Journal of Clinical Nutrition, 34, 1861-1867.

Case, G.L., Lewis, L.D., Phillips, R.W. & Clark, J.L. (1981b). Effects of osmolality of liquid nutrient diets on meal passage and nutrient absorption in Yucatan miniature swine. American Journal of Clinical Nutrition, 34, 1868-1878.

Chen, M. & Whistler, R.L. (1977). Metabolism of D-fructose. Advances in Carbohydrate Chemistry and Biochemistry, 34, 265-343.

Coggan, A.R. & Swanson, S.C. (1992). Nutritional manipulations before and during endurance exercise: effects on performance. Medicine and Science in Sport and Exercise, 24(9) Supplement, S331-S335.

Cori, G.T., Ochoa, S., Slein, M.W. & Cori, C.F. (1951). The metabolism of fructose in liver. Isolation of fructose-1-phosphate and inorganic pyrophosphate. Biochemistry and Biophysics Acta (Amst.), 304.

Costill, D.L., Coyle, E., Dalsky, G., Evans, W., Fink, W. & Hoopes, D. (1977). Effects of elevated plasma FFA and insulin on muscle glycogen usage during exercise. Journal of Applied Physiology: Respiratory Environment in Exercise Physiology, 43 (4), 695-699.

Costill, D.L., Kammer, W.F. & Fisher, A. (1970). Fluid ingestion during distance running. Archives of Environmental Health, 21, 520-525.

Costill, D.L. & Saltin, B. (1974). Factors limiting gastric emptying during rest and exercise. Journal of Applied Physiology, 37, 679-683.

Coyle, E.F. & Coggan, A.R. (1984). Effectiveness of carbohydrate feeding in delaying fatigue during prolonged exercise. Sports Medicine, 1, 446-458.

Crane, R. (1968). Absorption of sugars. In: Handbook of Physiology - Alimentary Canal IV. American Physiological Society, Washington, D.C., 1323-1351.

Crapo, P.A. & Kolterman, O.G. (1984). The metabolic effects of 2-week fructose feeding in normal subjects. American Journal of Clinical Nutrition, 39, 525-534.

Davis, J.M., Burgess, W.A., Slenty, C.A., Bartoli, W.P. & Pate, R.R. (1988a). Effects of ingesting 6% and 12% glucose/electrolyte beverages during prolonged intermittent cycling in the heat. European Journal of Applied Physiology. 57, 563-569.

Davis, J.M., Lamb, D.R., Pate, R.R., Slenty, C.A., Burgess, W.A. & Bartoli, W.P. (1988b). Carbohydrate-electrolyte drinks: effects on endurance cycling in the heat. American Journal of Clinical Nutrition. 48, 1023-1030.

Decombaz, J., Sartori, D., Arnaud, M.J., Thelin, A.L., Schurch, P. & Howald, H. (1985). Oxidation and metabolic effects of fructose or glucose ingested before exercise. International Journal of Sports Medicine, 6, 282-286.

Dencker, H., Lunderquist, A., Meeuwisse, G., Norryd, C. & Tranberg, K.G. (1972). Absorption of fructose as measured by portal catheterization. Scandinavian Journal of Gastroenterology, 7, 701-705.

Deuster, P.A., Singh, A., Hofmann, A., Moses, F.M. & Chrousos, G.C. (1992). Hormonal responses to ingesting water or a carbohydrate beverage during a 2 h run. Medicine and Science in Sport and Exercise, 24(1), 72-79.

Deuticke, B., Beyer, E. & Forst, B. (1982). Discrimination of three parallel pathways of lactate in human erythrocyte membranes by inhibitors and kinetic properties. Biochemistry and Biophysics Acta, 6894, 96-110.

Diamant, B., Karlsson, J. & Saltin, B. (1968). Muscle tissue lactate after maximal exercise in man. Acta Physiologica Scandinavica, 72, 383-384.

Elias, E., Gibson, G.J., Greenwood, L.F., Hunt, J.N. & Tripp, H.J. (1968). The slowing of gastric emptying by monosaccharides and disaccharides in test meals. Journal of Physiology, 194, 317-326.

Fielding, R.A., Costill, D.L., Fink, W.J., King, D.S., Hargreaves, M. & Kovaleski, J.E. (1985). Effect of carbohydrate feeding frequencies and dosage on muscle glycogen use during exercise. Medicine and Science in Sports and Exercise, 17 (4), 472-476.

Fielding, R.A., Costill, D.L., Fink, W.J., King, D.S., Kovaleski, J.E. & Kirwan, J.P. (1987). Effects of pre-exercise carbohydrate feedings on muscle glycogen use during exercise in well-trained runners. European Journal of Applied Physiology, 56, 225-229.

Fordtran, J.S. & Ingelfinger, F.J. (1968). Absorption of water, electrolytes and sugars from the human gut. In: Handbook of Physiology - Alimentary Canal IV. American Physiological Society, Washington, D.C., 1457-1489.

Fordtran, J.S. & Saltin, B. (1967). Gastric emptying and intestinal absorption during prolonged severe exercise. Journal of Applied Physiology, 23, 331-335.

Foster, C., Costill, D.L. & Fink, W.J. (1979). Effects of preexercise feedings on endurance performance. Medicine and Science in Sport, 11 (1), 1-5.

Froesch, E.R. (1972). Fructose metabolism in adipose tissue. Acta Medica Scandinavica Supplement, 542, 37-46.

Froesch, E.R. & Ginsberg, J.L. (1962). Fructose metabolism of adipose tissue. I. Comparison of fructose and glucose metabolism in epididymal adipose tissue of normal rats. Journal of Biological Chemistry, 237, 3317.

Galbo, H., Holst, J.J. & Christensen, N.J. (1979). The effect of different diets and of insulin on the hormonal response to prolonged exercise. Acta Physiologica Scandinavica, 107, 19-32.

Gammeltoft, A., Kruhohher, P. & Lundsgaard, E. (1944). Insulin and the assimilation of fructose. Acta Physiologica Scandinavica, 8, 162-175.

Gershon-Cohen, J., Shay, H. & Fels, S. (1940). The relation of meal temperature to gastric motility and secretion. American Journal of Roentgenology - Radium Therapy in Nuclear Medicine, 43, 237-242.

Gollnick, P.D., Bayly, W.M. & Hodgson, D.R. (1986). Exercise intensity, training, diet, and lactate concentration in muscle and blood. Medicine and Science in Sports and Exercise, 18 (3), 334-340.

Gollnick, P.D., Piehl, K. & Saltin, B. (1974). Selective glycogen depletion patterns in human fibers after exercise of varying intensity and at varying pedalling rates. Journal of Physiology, 241, 45-57.

Green, H.J., Houston, M.E., Thomson, J.A., Sutton, J.R. & Gollnick, P.D. (1979). Metabolic consequences of supramaximal arm work performed during prolonged submaximal leg work. Journal of Applied Physiology, 46, 249-255.

Gromova, K.G. (1965). The utilization of fructose by fat tissue of the epididymis of normal and starving rats and in the presence of insulin. Biokhimiya, 30, 563-566.

Guezennec, C., Satabin, P., Duforez, F., Merino, D., Peronnet, F. & Koziet, J. (1989). Oxidation of corn starch, glucose and fructose ingested before exercise. Medicine and Science in Sport and Exercise, 21 (1), 45-50.

Hargreaves, M., Costill, D.L., Fink, W.J., King, D.S. & Fielding, R.A. (1987). Effect of pre-exercise carbohydrate feedings on endurance cycling performance. Medicine and Science in Sport and Exercise, 19 (1), 33-36.

Hargreaves, M., Costill, D.L., Katz, A. & Fink, W.J. (1985). Effect of fructose ingestion on muscle glycogen usage during exercise. Medicine and Science in Sport and Exercise, 17 (3), 360-363.

Hasson, S.M. & Barnes, W.S. (1987). Blood glucose levels during rest and exercise: influence of fructose and glucose ingestion. Journal of Sports Medicine, 27, 326-332.

Heinz, F., Lamprecht, W. & Kirsch, J. (1968). Enzymes of fructose metabolism in human liver. Journal of Clinical Investigations, 47, 1829-1832.

Hermansen, L. (1981). Muscular fatigue during maximal exercise of short duration, in di Prampero P.E., Poortsmans J. (eds.): Physiological Chemistry of Exercise and Training, vol. 13, Basel, Karger, 45-52.

Hermansen, L., Hultman, E. & Saltin, B. (1967). Muscle glycogen during prolonged severe exercise. Acta Physiologica Scandinavica, 71, 129-139.

Hermansen, L. & Osnes, J.B. (1972). Blood and muscle pH after maximal exercise in man. Journal of Applied Physiology, 32, 304-308.

Hermansen, L. & Stensvold, I. (1972). Production and removal of lactate during exercise in man. Acta Physiologica Scandinavica, 86, 191-201.

Hermansen, L. & Vaage, O. (1977). Lactate disappearance and glycogen synthesis in human muscle after maximal exercise. American Journal of Physiology, 233, E422-E429.

Hers, H.G. & Kusaka, T. (1953). Le metabolisme du fructose-1-phosphate dans le foie. Biochimica et Biophysica Acta (Amst.), 11, 427.

Hickson, R.C., Rennie, M.J., Conlee, R.K., Winder, W.W. & Holloszy, H.O. (1977). Effects of increased plasma free fatty acids on glycogen utilization and endurance. Journal of Applied Physiology: Respiratory Environment in Exercise Physiology, 43, 829-833.

Hodges, R.E. & Krehl, W.A. (1965). The role of carbohydrates in lipid metabolism. American Journal of Clinical Nutrition, 17, 334-346.

Holdsworth, C.D. & Dawson, A.M. (1964). The absorption of monosaccharides in man. Clinical Science, 27, 371-379.

Houston, M.E., Waugh, M.R., Green, H.J. & Noble, E.G. Response of serum enzymes to intermittent work , in: Third International Symposium on Biochemistry of Exercise - Book 3, 1976, 187-192.

Hultman, E. (1967). Studies on muscle metabolism of glycogen and active phosphate in man with special reference to exercise and diet. Scandinavian Journal of Clinical Laboratory Investigations, 19, 94 (Abstract).

Hunt, J.N. & Spurrel, W.R. (1951). The pattern of emptying of the human stomach. Journal of Physiology, 113, 157-168.

Huttunen, J.K. (1971). Fructose in medicine. A review with particular reference to diabetes mellitus. Postgrad Medical Journal, 47, 654-659.

Ivy, J.L., Costill, D.L., Fink, W.J. & Lower, R.W. (1978). Role of caffeine and glucose ingestion on metabolism. Medical Science in Sports, 10, 66 (Abstract).

Koivisto, V.A., Harkonen, M., Karonen, S.L., Groop, P.H., Elovainio, R., Ferrannini, E., Sacca, L. & Defronzo, R.A. (1985). Glycogen depletion during prolonged exercise: influence of glucose, fructose or placebo. Journal of Applied Physiology, 58 (3), 731-737.

Koivisto, V.A., Karonen, S.L. & Nikkila, E.A. (1981). Carbohydrate ingestion before exercise: comparison of glucose, fructose and sweet placebo. Journal of Applied Physiology: Respiratory Environment and Exercise Physiology, 51 (1), 783-787.

Laurell, S. & Tibbling, G. (1967). Colormetric micro-determination of free fatty acids in plasma. Clinica Chimica Acta, 16, 57-62.

Levine, I., Evans, W.J., Cadarette, B.S., Fisher, E.C. & Bullen, B.A. (1983). Fructose and glucose ingestion and muscle glycogen use during submaximal exercise. Journal of Applied Physiology: Respiratory Environment and Exercise Physiology, 55 (6), 1767-1771.

MacDonald, I., Keyser, A. & Pacy, D. (1978). Some effects, in man, of varying the load of glucose, sucrose, fructose, or sorbitol on various metabolites in blood. American Journal of Clinical Nutrition, 31, 1305-1311.

Mainwood, G.W. & Renaud, J.M. (1985). The effect of acid-base on fatigue of skeletal muscle. Canadian Journal of Physiology and Pharmacology, 63, 403-416.

Massicotte, D., Peronnet, F., Brisson, G., Bakkouch, K. & Hillaire-Marcel, C. (1989). Oxidation of a glucose polymer during exercise: comparison with glucose and fructose. Journal of Applied Physiology, 66 (1), 179-183.

Mayer, P.A. & Laker, M.E. (1986). Effects of acute and long-term fructose administration on liver metabolism. Progress in Biochemical Pharmacology, 21, 33-58.

McConell, G., Fabris, S., Proietto, J. & Hargreaves, M. (1994). Effect of carbohydrate ingestion on glucose kinetics during exercise. Journal of Applied Physiology, 77 (3), 1537-1541.

McMurray, R.G., Wilson, J.R. & Kitchell, B.S. (1983). The effects of glucose and fructose on high intensity endurance performance. Research Quarterly for Exercise and Sport, 54, 156-162.

Mei, N. (1985). Intestinal chemosensitivity. Physiological Review, 65, 211-237.

Mendeloff, A.L. & Weichselbaum, T.E. (1953). Role of the human liver in the assimilation of intravenously administered fructose. Metabolism, 2, 450 (Abstract).

Miller, M., Drucker, W.R., Owens, J.E., Craig, J.W. & Woodward, H. (1952). Metabolism of intravenous fructose and glucose in hormal and diabetic subjects. Journal of Clinical Investigations, 31, 115 (Abstract).

Moran, T.H. & McHugh, P.R. (1981). Distinctions among three sugars in their effects on gastric emptying and satiety. American Journal of Physiology, 241, R25-R30.

Murray, R., Eddy, D.E., Murray, T.W., Seifert, J.G., Paul, G.L. & Halaby, G.A. (1987). The effect of fluid and carbohydrate feedings during intermittent cycling exercise. Medicine and Science in Sports and Exercise, 19 (6), 597-604.

Murray, R., Paul, G.L., Seifert, J.G., Eddy, D.E. & Halaby, G.A. (1989). The effects of glucose, fructose and sucrose ingestion during exercise. Medicine and Science in Sports and Exercise, 21 (3), 275-282.

Newsholme, E.A. (1979). The control of fuel utilization by muscle during exercise and starvation. Diabetes, 28, suppl. 1: 1-7.

Newsholme, E.A. & Leech, A.R. (1983). Biochemistry for the Medical Sciences. Toronto: John Wiley and Sons.

Niewoehner, C.B. (1986). Metabolic effects of dietary versus parenteral fructose. Journal of American College of Nutrition, 5, 443-450.

Niewoehner, C.B., Gilobe, D.P., Nuttal, G.A. & Nuttal, F.Q. (1984). Metabolic effects of oral fructose in the liver of fasted rats. American Journal of Physiology, 247, E504-E512.

Nilsson, L.H. & Hultman, E. (1974). Liver and muscle glycogen in man after glucose and fructose infusion. Scandinavian Journal of Clinical Laboratory Investigations, 33, 5-10.

Nishibata, I., Sadamoto, T., Mutoh, Y. & Miyashita, M. (1993). Glucose ingestion before and during exercise does not enhance performance of daily repeated endurance exercise. European Journal of Applied Physiology, 66, 65-69.

Noma, A., Okabe, H. & Kita, M. (1973). A new colormetric microdetermination of free fatty acids in serum. Clinica Chimica Acta, 43, 317-320.

Nuttall, F.Q., Gilboe, D.P., Gannon, M.C.M. Niewoehner, C.B. & Tan, A.W.H. (1988). Regulation of glycogen synthesis in the liver. The American Journal of Medicine, 85 (5A), 77-85.

Okano, G., Takeda, H., Morita, I., Katoh, M., Mu, Z. & Miyake, S. (1988). Effect of pre-exercise fructose ingestion on endurance performance in fed men. Medicine and Science in Sport and Exercise, 20 (2), 105-109.

Randle, P.J., Garland, P.B., Hales, C.N. & Newsholme, E.A. (1963). The glucose-fatty acid cycle. Its role in insulin sensitivity and the metabolic disturbances of diabetes mellitus. Lancet, 1, 785-789.

Ravich, W.J., Bayless, T.M. & Thomas, M. (1983). Fructose: incomplete intestinal absorption in humans. Gastroenterology, 84, 26-29.

Ravussin, E., Bogardus, C., Scheidegger, K., LaGrange, B., Horton, E.D. & Horton, E.S. (1986). Effect of elevated FFA on carbohydrate and lipid oxidation during prolonged exercise in humans. Journal of Applied Physiology, 60 (3), 893-900.

Rehrer, N.J., Beckers, E., Brouns, F., Ten Hoor, F. & Saris, W.H.M. (1989). Exercise and training effects on gastric emptying of carbohydrate beverages. Medicine and Science in Sports and Exercise, 21 (5), 540-549.

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

Ryan, A.J., Bleiler, T.L., Carter, J.E. & Gisolfi, C.V. (1989). Gastric emptying during prolonged cycling exercise in the heat. Medicine and Science in Sports and Exercise, 21 (1), 51-58.

Schwarz, J.M., Schutz, Y., Froidevaux, F., Acheson, K.J., Jeanpretre, N., Schneider, H., Felber, J.P. & Jequier, E. (1989). Thermogenesis in men and women induced by fructose vs glucose added to a meal. American Journal of Clinical Nutrition, 49, 667-674.

Sherman, W.M., Costill, D.L., Fink, W.J. & Miller, J.M. (1981). Effect of exercise-diet manipulation on muscle glycogen and its subsequent utilization during performance. International Journal of Sports Medicine, 2, 114-118.

Sladen, G.E. (1972). A review of water and electrolyte transport. In Burland and Samuels (Eds) Transport Across the Intestine, 14-34, Churchill Livingstone, Edinburgh.

Slama, G., Boillot, J., Hellal, I., Darmaun, D., Rizkalla, S.W., Orvoen-Frija, E., Dore, M.F., Guille, G., Fretault, J. & Coursaget, J. (1989). Fructose is as good a fuel as glucose for exercise in normal subjects. Diabete and Metabolisme, 15, 105-106.

Stanley, W.C., Gertz, E.W., Wisneski, J.A., Neese, R.A. & Brooks, G.A. (1985). Systemic lactate kinetics during graded exercise in man. American Journal of Physiology: Endocrinology and Metabolism, 249 (12), E595-E602.

Thoren, L. (1964). Parenteral nutrition with carbohydrate and alcohol. Acta Chirurgica Scandinavica. Supplement, 325, 75 (Abstract).

Van den Berghe, G. (1986). Fructose: metabolism and short-term effects on carbohydrate and purine metabolic pathways. Progress in Biochemical Pharmacology, 21, 1-32.

Wasserman, L., Beaver, W.L., Davis, J.A., Pu, J.Z., Heber, D. & Whipp, B.J. (1985). Lactate, pyruvate and lactate-to-pyruvate ratio during exercise and recovery. Journal of Applied Physiology, 59 (3), 935-940.

Weichselbaum, T.E., Elman, R. & Lund, R.H. (1950). Comparative utilization of fructose and glucose given intravenously. Proceedings of the Society for Experimental Biology and Medicine (N.Y.), 75, 816 (Abstract).

Whitney, E.N. & Hamilton, E.M.N. (1987). Understanding Nutrition. New York: West Publishing Company, 60-81.

Woods, H.F. & Alberti, K.G.M.M. (1972). Dangers of intravenous fructose. Lancet, 2, 1354-1357.

APPENDIX A

Exercise Test To Exhaustion - Experimental Protocol

1. Subject ingests test solution (500 ml).
2. Subject rests for 1 hour.
3. Prepare bicycle (ie. adjust seat height, calibrate, etc.).
4. Enter subject data into Beckman MMC.
5. Insert indwelling catheter.
6. Blood sample # 1 (T = 0).
7. Begin exercise at 75% VO_2 max.
8. Ingest test solution (T = 20); (250 ml).
9. Blood sample # 2 (T = 30).
10. Ingest test solution (T = 50); (250) ml.
11. Blood sample # 3 (T = 60).
12. Blood sample # 4 (T = 90).
13. Ingest test solution (T = 90); (250 ml).
14. Blood sample # 5 (T = Exh.).

-----> ensure subject is pedalling at 75% VO_2 max
-----> record RER when subject is connected to Beckman
-----> ensure subject feels fine before he or she leaves the test site (ie. ensure food/beverage ingestion)

APPENDIX B

BLOOD SAMPLING GUIDELINES AND PROCEDURES

Blood Sampling

Large green vacutainers containing sodium heparin (7 ml) - FFA
Small green vacutainers containing sodium heparin (4 ml) - glucose and lactate
Small purple vacutainers containing EDTA (3 ml) - hemoglobin (don't spin)

1. Time = 0 - take - 2 large green vacutainers
   1 small green vacutainer
   1 small purple vacutainer

2. Time = 30 - take - 2 large green vacutainers
   1 small green vacutainer

3. Time = 60 - take - 2 large green vacutainers
   1 small green vacutainer

4. Time = 90 - take - 2 large green vacutainers
   1 small green vacutainer

5. Time = Exh. - take - 2 large green vacutainers
   1 small green vacutainer

Blood Sampling Procedures

1. Prior to the onset of exercise, an indwelling catheter was inserted into the median cubital vein of each subject by a registered nurse or a trained technician.

2. At each sample time, approximately 18 mls. of blood were slowly injected into 3 different vacutainers.

3. Prior to the onset of exercise, an additional 3 ml. sample was drawn to determine the hemoglobin level of each subject.

4. The hemoglobin vacutainer was not spun and was kept at room temperature. Hemoglobin analysis was completed at Port Arthur General Hospital by the lab technician (Donna Newhouse) using the Coulter Automated technique.

5. A serum/plasma separator was put into the 7 ml. and the 4 ml. vacutainers.

6. The samples were spun for 10 minutes.

7. The plasma from each 7 ml. vacutainer was put into 2 blue tubes (x2).

8. The 4 blue tubes were immediately put into the freezer for free fatty acid (FFA) analysis. Analysis was completed at Lakehead University by Dr. Bob Thayer. For procedure see Appendix E.

9. The 4 ml. tube was put into the refrigerator (after it was spun) for glucose and lactate analysis. Analysis was completed at Port Arthur General Hospital by the lab technician using the Kodak Ektachem (E700).

APPENDIX C

SUBJECT INFORMATION SHEET - VO_2 MAX TEST

I, _____, have an appointment to undergo a VO_2 max test on the cycle ergometer at _____ on _____. The duration of the test will be about 1/2 hour.

Subject Information Prior to VO_2 Max Test.

1. Refrain from any exercise for 24 hours prior to the test.
2. Refrain from eating 4 hours prior to the test.
3. Refrain from alcoholic beverages 24 hours prior to the test.
4. Consume a normal mixed diet on the day of the test.

If you have any questions about the VO_2 max test, or any other concerns, please do not hesitate to contact me at:

683-8195 - home
or
343-8544 - P.E. Office - to leave a message.

Thank you,

Sandy Brundle

APPENDIX D

INFORMED CONSENT FOR ENDURANCE CYCLING EXERCISE TEST, CARBOHYDRATE INGESTION AND BLOOD SAMPLING

Experimenter: Miss Sandy Brundle

Advisor: Dr. Robert Thayer

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1. All subjects are to be informed that they have the right to withdraw from the study, at any time, if they so choose.

2. All subjects will be given exercise and dietary information pertaining to the study before the commencement of the experimental session.

3. Each subject will be required to participate in an exercise session whereby VO_2 max will be determined.

4. The experimental protocol will involve two weeks of dietary and exercise modification. The specific dates of each session will be arranged to complement each subjects' training and personal schedules.

5. The exercise sessions will involve cycling exercise to exhaustion at 75% of VO_2 max.

6. Each subject will participate in two cycling exercise sessions to exhaustion coinciding with two dietary regimens.

7. Beverages must be consumed during the experimental session, in order to hydrate subjects, at predetermined times.

8. The subjects will be connected to the Beckman MMC (metabolic measurement cart) gas analyzer for very short periods during the exercise sessions.

9. **Risks and Discomforts.** Usually no problems or complications arise after an exercise test to exhaustion. However, there exists the possibility of certain changes occurring during the test (ie. episodes of transient lightheadedness, fainting, abnormal blood pressure, chest discomfort, leg cramps and nausea).

10. **Blood Analysis.** Small samples of blood will be drawn from the median

cubital vein of each subject 60 minutes before the commencement of exercise and at various intervals during exercise until exhaustion. Blood analysis will be performed and monitored by qualified personnel. Blood work will be performed using up-to-date scientific techniques, utilizing the utmost sanitary care. Blood samples may be slightly uncomfortable but are not painful.

11. All subjects will be given a summary of their individual results as well as the results, conclusions and recommendations developed by the experimenter.

12. By participating in this study, the subject has the ability to gain an understanding of how various carbohydrate ingestions affect their athletic performance, thereby offerring training possibilities and potential dietary manipulations to enhance endurance performance.

13. All procedures subjected to are well accepted procedures which will not, in any way, lead to harmful or potentially harmful side effects.

14. **Inquiries.** Any questions about the procedures used in the exercise test, in the blood sampling techniques or in the estimation of VO_2 max are welcome. If you have any concerns or questions, please do not hesitate to ask.

I, _____, have read, understood and completed the Physical Activity Readiness Questionnaire (PAR-Q), and understand the test procedures that I will perform and I agree to participate in the proposed study.

_____

Signature of Subject

_____ _____

Date **Witness**

APPENDIX E

FREE FATTY ACID ANALYSIS - SERUM PROTOCOL

PRINCIPLE:

Lipids exist in the serum in the most part, in the form of neutral fats, phospholipids, cholesterol esters, and free cholesterol. The neutral fats, or triglycerides, may be relieved of their fatty acid component by the action of lipases. The free fatty acid (FFA) concentration is, however, normally very low.

Thus, removing the FFA from their aqueous environment to a solvent in which they may be colorimetrically quantified requires a rather sensitive procedure.

In order to best extract the FFA, methanol is mixed in low concentration with the highly nonpolar solvents choloroform and heptane. This solvent can then be used as an environment where FFA can form copper salts when added to a copper - TEA solution.

The copper salts of the FFA can then form a colored product upon reacting with the sodium salt of diethyldithiocarbamic acid (DDC).

$$FFA + Cu^{++} \text{ ----------> } FFA\text{ -- }Cu$$

$$FFA\text{ -- }Cu + DDC \text{ ----------> colored product}$$

REAGENTS:

Extraction reagent

choloroform	-	heptane	methanol
1	:	1	2%

Copper reagent (fresh biweekly)

10 ml	0.5 M	$Cu(NO_3)_2$
10 ml	1.0 M	TEA pH 8.3
3.5 ml	1.0 N	NaOH

Bring to 100 ml volume with saturated NaCl in H_2O

Color reagent (fresh before use)

sodium diethyldithiocarbamate 22 mg / 10 ml butanol

Standard FFA (palmitate)

1 mM in serial dilutions in CHM reagent

PROCEDURE:

Add 200 ul serum to large diameter capped test tubes.

Add 3 ml extraction reagent, jiggle gently to break up emulsion.

Add one (1) ml copper reagent - shake mechanically for 10 minutes.
DO NOT VORTEX

Centrifuge for 20 minutes @ 3000 rpm

Transfer 2 ml of the upper phase to a clean culture tube
(13 mm x 100 mm or 12 X 75 mm).
DO NOT TOUCH SIDE OF TUBE WITH PIPETTE.

Add 0.5 ml color reagent in a timed sequence and vortex.

Read absorbance @ 436 nm, 10 minutes after addition of color reagent.

CALCULATIONS:

Use the standard serial dilutions to obtain a linear regression equation ($y = ax + b$) and calculate mM concentration of the sample. It might be found that the regression line is not linear, but parabolic. Thus, we suggest that the standard curve be treated by parabolic analysis ($y = a + bx + cx^2$).