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The effects of hydration fluids during prolonged exercise

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THE EFFECTS OF HYDRATION FLUIDS DURING PROLONGED EXERCISE

A Thesis Submitted to the Yale University
School of Medicine in Partial Fulfillment
of the Requirements for the Degree of
Doctor of Medicine

by
Alan Sander Hilibrand
Class of 1990

ERRATA: THE EFFECTS OF HYDRATION FLUIDS...

Abstract - Paragraph #2, sentence #2:

> Core body temperature rose an average of **2.2 ± 0.4 °C.** during CHONa; core temperatures rose **1.6 ± 0.2 °C.** during CHO_{Na}, and **1.7 ± 0.2 °C.** during Placebo.

Section 4.3 - Paragraph #2, sentence #2:

> At 50 minutes, the RQ was significantly greater for the CHONa (0.90 ± 0.01) and the CHO_{Na} (0.91 ± 0.02) trials than for the placebo trial **(0.76 ± 0.03)**.

Section 4.8 - Paragraph #2, sentence #2:

> At t = 30 minutes the **elevation in** plasma sodium levels was significantly higher in the **CHONa** group (2.9 ± 1.2) than in the **CHO_{Na}** group (1.3 ± 0.6) ($p < 0.05$).

Table 4.3a - Time = 50 minutes, Placebo group

> **MEAN ± SEM = 0.76 ± 0.03**

ABSTRACT

THE EFFECTS OF HYDRATION FLUIDS DURING PROLONGED EXERCISE

Alan Sander Hilibrand
Yale University School of Medicine
1990

We tested the hypothesis that drinking fluids supplemented with carbohydrate and sodium during prolonged exercise 1) prolongs the time to fatigue, 2) maintains thermoregulation, and 3) reduces the loss of plasma volume, relative to water. Four volunteers exercised at 70-75% of their maximal aerobic power for three hours or until exhaustion in a warm environment (18 °C., <30% rh). In three separate trials, participants drank either i) placebo (P), ii) 5% glucose polymer / 2% fructose drink in 0.22% NaCl (CHO_{Na}), or iii) the carbohydrate drink in 0.45% NaCl (CHONa) every fifteen minutes.

During $CHO_{Na}$and CHONa trials, volunteers maintained blood glucose levels at ~100 mg/dL for 150 minutes, and exercised for an average of 163 ± 16 minutes; during P, blood glucose levels were significantly lower beyond 30 minutes of exercise, and volunteers exercised for an average of 147 ± 8 minutes. Core body temperature rose an average of 2.5 ± 0.4 °C. during CHONa; core temperatures rose 1.7 ± 0.3 °C. during both CHO_{Na} and P. Plasma volume decreased by 10-12%, without any significant differences between the three trial conditions. Plasma osmolality was significantly higher during CHO_{Na} than during P; plasma [Na^+] was significantly higher by the end of CHONa trial, relative to P.

We concluded that during three hours of moderate intensity exercise, carbohydrate-supplemented fluids prolonged the time to fatigue, relative to plain water. Addition of sodium to these fluids, however, did not reduce the decrease in plasma volume that occurs during exercise, and diminished the body's ability to dissipate heat effectively. We suggest that elevated plasma $[Na^+]$ and plasma osmolality levels in the CHONa test group may have reduced sweat rates and elevated body temperatures.

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CHAPTER 1

REVIEW OF LITERATURE

1.1 INTRODUCTION

Physiologists have long recognized the need for hydration during prolonged exercise[1]. By drinking during exercise, the athlete can maintain muscle perfusion and circulatory volume by replacing evaporative losses. During exercise in the heat, fluid intake also allows sufficient sweating to prevent hyperthermia [36,49,68].

Over 20 years ago, Ahlborg et al[2] demonstrated that a reduction in muscle glycogen is associated with fatigue during prolonged exercise. As a result, many sports drink manufacturers have produced hydration fluids supplemented with carbohydrate. Several authors have shown that these drinks maintain or increase blood glucose levels without decreasing the rate of gastric emptying[16,32,71]. Recent studies have demonstrated that these solutions can prolong time to fatigue during exercise of three hours or more [20,21,47], although Felig et al[25] found no consistent improvement in their subjects. Owen et al[80] suggested that subjects drinking carbohydrate had a greater decrease in plasma volume relative to drinking water. This is important, as it was shown 20 years ago that plasma volume is a major determinant of aerobic capacity[22].

Recently, there has been interest in the effects of sodium supplementation of hydration fluids on the maintenance of plasma volume

during exercise. Nose et al[74] demonstrated faster recovery of intravascular volume after exercise when drinking saline instead of water. They hypothesized that by increasing plasma sodium, subjects' plasma remained hyperosmolar, pulling more free water from the surrounding tissues, and maintaining the CNS drinking stimulus.

We designed the present studies to assess the effects of carbohydrate and sodium supplementation of hydration fluids consumed during prolonged exercise. We measured changes in blood glucose, respiratory quotient, plasma volume, core body temperature, plasma sodium, plasma osmolality, and time to fatigue in subjects exercising for three hours at 70-75% of their maximal aerobic power on a cycle ergometer. We tested the hypothesis that carbohydrate supplementation during prolonged exercise would increase the time to fatigue, and that sodium supplementation would diminish the reduction in plasma volume seen during exercise.

1.2 THE PHYSIOLOGY OF EXERCISE

In his Textbook of Medical Physiology, Arthur C. Guyton introduces the final chapter, Sports Physiology, by highlighting the unusual stresses faced by the human body during physical exertion:

> '...there are no normal stresses to which the body is exposed that even nearly approach the extreme stresses of heavy exercise...if some of [these] were continued for even slightly prolonged periods of time, they might easily be lethal...[41]'

I will discuss five ways in which the body adjusts to exercise stress: 1) *Metabolic* --rapidly making sources of chemical energy available to the contracting muscle cells; 2) *Respiratory*--augmentation of pulmonary

ventilation and perfusion to meet increased oxygen demands; 3) *Cardiovascular*--rapid increases in cardiac output deliver oxygen to contracting muscles; 4) *Thermoregulation*--dissipation of heat produced in the muscles through cutaneous vascular beds and sweating; and 5) *Fluid Balance*--retrieval of water, which is initially forced into the interstitium by increased hydrostatic pressures, from the interstitial and intracellular spaces to maintain plasma volume. This section will conclude with a discussion of how the body adapts to these stresses with training.

1.2.1. METABOLIC SOURCES OF ENERGY

The muscle converts chemical energy, in the form of a high energy phosphate bond, into mechanical energy during contraction. This energy conversion requires Ca^{++} ions and contractile proteins such as actin and myosin, which mediate contraction by the "sliding filament mechanism", described elsewhere[41]. Three sources of chemical energy are available for muscular contraction: muscle phosphagen, anaerobic glycolysis of monosaccharides, and aerobic metabolism of carbohydrates and lipids.

Energy is stored in muscle in two readily available forms; adenosine triphosphate (ATP) and phosphocreatine (see Figure 1.1). Cleavage of each of the two phosphate-phosphate bonds in ATP releases ~11 kcal of energy. Phosphocreatine contains a high energy bond between the phosphate and creatine moieties; cleavage of this bond releases greater than 11 kcal of chemical energy. As a result, while muscle ATP can provide for only a few seconds of heavy exercise, the high energy phosphocreatine bond can immediately replenish exhausted muscle ATP, providing for an additional 10-15 seconds of heavy exertion.

During exercise of any duration, the muscle relies on metabolic production of ATP to maintain energy stores. Muscle cells contain substantial quantities of glycogen, which they can degrade into individual units of glucose. Glucose is also supplied to muscle from liver glycogen via the bloodstream. Muscle cells contain glycolytic enzymes which rapidly catabolize glucose into pyruvate, producing 2 molecules of ATP per glucose molecule. In the absence of oxygen, pyruvate is reduced to lactic acid, and anaerobic metabolism is completed. If oxygen is present, then pyruvate can be completely oxidized to carbon dioxide and water via the citric acid cycle and oxidative phosphorylation. Aerobic metabolism occurs in the mitochondria, and produces 36 moles of ATP per mole of glucose oxidized. Free fatty acids, liberated from triglycerides in adipose tissue, are another primary source of substrate for aerobic metabolism; two carbon units feed directly into the citric acid cycle as acetyl CoA (Figure 1.1).

Aerobic, anaerobic, and phosphagen systems play different roles in providing for muscular contraction. Although the phosphagen system can be rapidly exhausted during heavy exercise, its energy can be generated four times as rapidly as the energy from aerobic metabolism. Aerobic metabolism provides energy at a slower rate for as long as nutrient stores last. Although the nutrient energy from lipid stores could support exercise for several days, exercise duration is limited by carbohydrate stores, which can provide for a few hours of exercise in the average individual. The intensity of exercise which can be supported by aerobic metabolism is highly dependent upon the body's ability to effectively assimilate oxygen into hemoglobin and efficiently deliver it to exercising muscle. As a result, the respiratory and cardiovascular systems play an important role in providing substrates for metabolism.

1.2.2. RESPIRATORY CHANGES WITH EXERCISE

As exercise begins, muscles require oxygen at a greater rate than it can be delivered. This causes an oxygen "deficit" (Fig 1.2), in which muscles must use their own ATP and oxygen stores, and generate energy by the anaerobic metabolism of glucose. After a short period of time, however, the oxygen transport systems adjust to this increased demand, achieving a "steady state" in which oxygen supply matches demand. After the cessation of exercise, however, oxygen transport must remain at an elevated level in order to "repay" the oxygen "debt" and metabolize products of anaerobic glycolysis.

The most commonly used measure of the body's ability to maintain aerobic metabolism at a given level of exercise are the maximal oxygen uptake (designated $VO_{2\ max}$), and the power output at which the $VO_{2\ max}$ is attained, the maximal aerobic power. When exercise is performed at a rate greater than the maximal aerobic power, the additional energy must be provided by anaerobic metabolism (see Fig 1.3). This "burst" of energy can only be maintained for a short period of time due to the fatigue induced by elevated levels of lactate and hydrogen ions in muscle.

There are several pulmonary factors which influence the $VO_{2\ max}$. The lungs must increase oxygen consumption up to 20 times normal levels. Diffusion capacity of oxygen from the alveoli to the bloodstream must increase as well. However, the efficiency of the oxygen transport systems--determined primarily by hemoglobin (Hb) content and blood volume--exerts the greatest influence on $VO_{2\ max}$. This is because oxygen tension in the lungs exceeds the oxygen tension in arterial blood. As a result, an increase in Hb would provide a greater oxygen carrying capacity, increasing $VO_{2\ max}$. Supplementation of

blood volume allows greater perfusion of muscle and delivery of oxygen, as discussed below.

1.2.3. CARDIOVASCULAR CHANGES WITH EXERCISE

The onset of exercise causes rapid changes in circulatory dynamics. Exercising muscles require a large increase in perfusion to provide for increased oxygen demand over time. This is accomplished by local vasodilitation and by supplementation of the cardiac output.

When exercise begins, muscle perfusion is insufficient to sustain aerobic metabolism. As a result, anaerobic metabolism produces H+ and heat, causing a right-shift in the oxygen dissociation curve of Hb by Bohr's Effect (Fig 1.4), and unloading oxygen into the active muscle bed. Along with increases in local K^+, these metabolites also reduce local vascular resistance, increasing local blood flow.

At the level of the heart, the onset of exercise heralds an increase in heart rate through neural stimuli. As muscle vascular resistance drops, central arterial pressures fall. This activates the baroreceptor reflex to reduce splanchnic blood flow and increase the heart rate. Rhythmic contractions of exercising muscle ("the muscle pump") as well as autonomic-mediated venoconstriction increase central venous pressure and cardiac filling, augmenting stroke volume by Starling's Law. As heart rate and stroke volume increase, cardiac output (CO = HR x SV) rapidly increases to four-sixfold resting values.

1.2.4. THERMOREGULATION DURING EXERCISE

One of the more worrisome aspects of exercise is the amount of heat produced with exertion. Since less than 25% of nutrient energy can be converted into mechanical energy, the vast majority is converted into heat during metabolism. In addition, as muscles overcome resistance in tissues and joints, additional heat is produced as friction. The overall thermal load to the body is a function of exercise intensity and ambient temperature. As a result, on an especially hot and humid day or at high exercise intensities, efficient thermoregulation is essential to maintain exercise of any duration[68].

Body temperature is regulated by neural feedback at the level of the hypothalamus. As core temperature rises during exercise, two cooling mechanisms attempt to dissipate the additional heat. First, cutaneous vascular beds dilate, increasing heat transfer capacity up to eightfold. Second, the sweat rate rises, removing up to 100 calories of heat per second (based on a maximal sweat rate of two liters per hour). Although these mechanisms are very effective at controlling core temperature under most conditions, they require maintenance of adequate circulatory volume in order to perfuse cutaneous vessels and provide transudate for sweating.

1.2.5 FLUID BALANCE DURING EXERCISE

As a result of transudative, evaporative, and respiratory losses, fluid balance plays a key role in maintaining adequate circulatory volume. As exercise commences, there is a rapid increase in capillary hydrostatic pressures, resulting in the transudation of intravascular fluid into the interstitial spaces. The loss of intravascular volume is further exacerbated by

evaporation of sweat (the result of transudation into eccrine sweat glands); renal and respiratory losses also account for a small amount of intravascular fluid losses.

The body attempts to minimize these losses by maintaining fluid balance between the intravascular, interstitial, and intracellular spaces (Fig 1.6). Since the fluid lost in sweat has a lower $[Na^+]$ relative to plasma, the plasma $[Na^+]$ increases relative to the interstitial and intracellular spaces. As a result, free water is drawn from these spaces into the bloodstream. As sweating continues, plasma $[Na^+]$ and plasma osmolality continue to rise, activating the human drinking response. If fluids are not available, however, the progressive loss of intravascular volume will ultimately cause a fall in central arterial pressures and perfusion of vital organs. In the short term, the body compensates by increasing the heart rate. If losses are not replaced and exercise persists, however, the body must eventually override thermoregulation and constrict cutaneous vessels in order to maintain central circulatory volume and cerebral perfusion.

1.2.6. ADAPTATIONS WITH TRAINING

Over a period of weeks to months, the human body adapts to the stresses of exercise. Krzentowski et al[53] showed that subjects could increase $VO_{2\ max}$ by 29% after six weeks of light-moderate exercise of one hour's duration, five days per week. This increase in $VO_{2\ max}$ is primarily the result of improvements in oxygen delivery, substrate metabolism, and heat transfer which occur with training.

Efficiency oxygen delivery depends upon the ability of the cardiovascular system to rapidly transport oxygen to exercising muscles[67].

Twenty years ago, Ekblom et al[22] demonstrated that training increases maximal cardiac output by increasing the maximal cardiac stroke volume generated. Convertino[10] and others have shown that endurance training stimulates an expansion of blood volume which elevates cardiac filling pressuresand increases maximal stroke volume by Starling's law. As stroke volume increases, baroreceptor reflexes are thought to increase vagal tone, producing a given cardiac output at a lower heart rate. This may explain why athletes tend to have low resting heart rates.

Training also induces rheologic changes which reduce cardiac afterload. Athletes tend to have a lower [Hb] than nonathletes (although they have a greater total amount of Hb in the blood due to an increase in total blood volume). The lower [Hb] reduces blood viscosity, thereby decreasing resistance to flow in the bloodstream[67].

Oxygen delivery to muscles is also augmented by increased perfusion of muscle beds with training. Saltin and Rowell[88] reported a 60% increase in capillary number per muscle fiber after training. Increasing the number of capillaries in parallel reduces vascular resistance, allowing greater muscle perfusion. Increasing capillary density also reduces the diffusion distance from blood to muscle. The net effect of these changes is a vast improvement in oxygen delivery to muscles, and an increase in whole body VO_2 max.

Intracellular metabolism also adapts to training. Holloszy[43] demonstrated that trained athletes had elevated levels of mitochondrial enzymes involved in the citric acid cycle, fatty acid metabolism, and oxidative phosphorylation, as well as increases in mitochondrial size and number. Saltin and Rowell[88] suggested that this may contribute to the higher VO_2 max in athletes, although Barclay and Stainsby[5] have demonstrated a close relationship between blood flow and maximal metabolic rate in dogs.

Many authors have shown that training reduces the use of monosaccharides and increases the use of fatty acids as metabolic fuel during exercise[53,82]. Koivisto et al[51] demonstrated that trained subjects oxidize a greater proportion of fatty acids to monosaccharides, use muscle glycogen at a slower rate, and maintain higher plasma glucose levels over three hours of exercise. Greater oxidation of fats should spare carbohydrate reserves and increase exercise capacity if exercise performance is related to the absolute amount of stored muscle glycogen, as demonstrated by Karlsson and Saltin[48].

Adaptations in thermoregulation also occur with training. Nadel et al[70] demonstrated that physical training sensitizes the response of sweat glands to elevations in core body temperature, lowering the threshold temperature for sweating. Kirby and Convertino[50] have shown that training in the heat also reduces the $[Na^+]$ lost in sweat. By measuring electrolyte and water balance between compartments, Nose et al[76] have concluded that reducing sweat $[Na^+]$ increases extracellular fluid osmolality, drawing free water from the intracellular space and helping to preserve blood volume.

As mentioned in section 1.2.4., heat transfer is highly dependent upon blood volume, which increases with training. Several studies by Fortney et al[26-30] demonstrated this relationship between absolute blood volume and heat transfer capacity. They explained that increasing blood volume increases cardiac output, augmenting whole body perfusion and increasing thermoregulatory capacity. As a result, supplementation of blood volume is probably the most important physiological adaptation to physical training[67].

1.3 THE NEED FOR HYDRATION

Since plasma volume is the key to aerobic capacity and thermoregulatory capacity, the drop in intravascular volume during exercise is dctrimental to long term performance. Transudation into the interstitial space and sweating into the environment account for most of these losses. This section will explore the extent of these "losses", and review studies of hydration before, during, and after exercise.

1.3.1 INTERSTITIAL FLUID LOSSES DURING EXERCISE

Although body fluid balance is classically described by evaluating changes in the extracellular and intracellular spaces, we must subdivide the extracellular space into interstitial and intravascular spaces For the purposes of exercise physiology, we must consider three fluid spaces: intracellular, interstitial, and intravascular (see Figure 1.5). Much of the fall in intravascular volume is fluid that has been forced into the interstitial space by incrcased hydrostatic pressures which accompany exercise. In 1972, Lundvall et al[55] found that exercise caused a fluid shift in muscle from the capillaries to the interstitium proportional to excrcise intensity. They demonstrated transudation of over one liter of intravascular fluid into active muscle during 6 minutes of heavy exercise. They noted that the total loss in intravascular volume was only 600 cc; they attributed this discrepancy to an increased plasma osmolality causing resorption of free water from inactive tissues.

Estimating muscle water content by ^{3}H-inulin distribution during heavy exercise of short duration, Sjoggard and Saltin[97] demonstrated an

increase in the water content of exercising muscles. They found that most of this additional muscle water was extracellular, although extracellular fluid comprises less than one third of total muscle water. They attributed this increase in extracellular water to elevated hydrostatic pressures in capillaries within active muscles forcing intravascular fluid into the interstitium.

More recent studies have attempted to delineate the forces governing transudation of intravascular fluid into the interstitium. In 1984, Mohsenin and Gonzalez[59] demonstrated a 17% reduction in plasma volume and an increase in plasma osmolality from 283-299 mosm/kg after two minutes of exercise at 105% of $VO_{2\ max}$. They correlated these findings with increases in colloid osmotic pressure (from 25 to 31 mm Hg) and interstitial fluid pressure (from -1.0 to +1.5 mm Hg) after exercise. They concluded that elevations in colloid osmotic pressure and interstitial hydrostatic pressure oppose elevated hydrostatic pressures, preventing further reductions in plasma volume with maximal exertion.

Nadel et al[69] recently reviewed the forces regulating fluid balance during exercise, as shown in Figure 1.6. These can be explained by the following sequence of events during exercise: 1) Exercise commences, causing large increases in the hydrostatic pressure in capillary beds of exercising muscle, as the circulation attempts to deliver more oxygen to active tissues; 2) Heat produced by exercising muscle is dissipated from the body by evaporation of sweat delivered to the body surface; 3) Because sweat is hypotonic with respect to the intravascular space, plasma osmolality rises, pulling free water from the interstitial space into the intravascular space; 4) As free water leaves the interstitial space, interstitial osmolality rises, drawing free water from the intracellular space. Convertino et al[12] demonstrated the presence of these osmotic and hydrostatic changes at exercise intensities above 40% VO_2

$\dot{V}O_{2max}$. As demonstrated by Lundvall et al[55], these Starling forces increase in proportion to exercise intensity.

1.3.2 FLUID LOSSES IN SWEAT

Sweat losses are an important component of the reduction in plasma volume during prolonged exercise in the heat. Sweating increases with the duration and intensity of exercise as a result of greater heat production within the body. Increases in ambient temperature result in greater reductions of plasma volume during exercise: a hotter environment reduces convective cooling, and greater cutaneous vasodilation allows greater extravasation of fluid into subcutaneous tissues. These losses compromise aerobic and thermoregulatory capacity during exercise, limiting performance. However, there are osmotic factors which help compensate for intravascular losses due to sweating.

Recent studies have shown a correlation between elevations in external temperature and reductions in plasma volume during exercise. Owen et al[80] found a significantly greater decrease in plasma volume during exercise bouts of 2 hours at a temperature of 35 °C. compared to bouts at a temperature of 25 °C. Similarly, Nose et al[77] demonstrated a greater upward drift in heart rate during exercise in a warm (30 °C.) versus a cool (22 °C.) environment. These studies suggest that exercise in the heat places additional strain upon the heart and circulation.

A number of studies by Fortney et al demonstrated the effects of dehydration on exercise performance. In three studies[26,28,30] they showed that reducing absolute blood volume caused an elevation in heart rate, compensating for diminished cardiac stroke volume. These findings have

been confirmed by numerous other studies involving dehydration, hypohydration, or hyperhydration and exercise[33,36,66,72,87,92]. In two other studies[27,29], Fortney et al demonstrated that dehydration compromises thermoregulatory mechanisms during exercise. They observed elevations in the threshold temperature at which sweating mechanisms are activated and reductions in the sweat rate during exercise after dehydration. These changes were attributed to attempts to maintain cardiac filling pressures as cardiac output dropped at the expense of cutaneous blood flow and heat transfer. As a result, exercise would be substantially compromised in a dehydrated state.

The body can compensate for reductions in intravascular volume caused by sweating during exercise. Although sweat is essentially a transudate of extracellular fluid, Nose et al[76] found that the total sweat losses during exercise are much greater than the reduction in extracellular volume during exercise. Nose and his coworkers have studied changes in fluid balance in both rats[78] and humans[76] following exercise-induced dehydration. They explained that because sweat [Na^+] is lower than plasma and interstitial [Na^+], sweating results in elevation of plasma and interstitial osmolality. This draws free water from the intracellular space into the interstitial and intravascular spaces, replacing a portion of the plasma volume lost as sweat (see Figure 1.6). Kirby and Convertino[50] showed that sweat [Na^+] diminishes as subjects become acclimated to exercise and heat. Based upon this finding, Nose et al concluded that by reducing sweat [Na^+], heat-acclimated and/or trained subjects can mobilize greater amounts of free water from the intracellular space by osmotic forces, and are better equipped to maintain plasma volume during exercise in the heat.

1.3.3 EFFECTS OF HYDRATION

Since maintainance of plasma volume is essential for maintaining aerobic power and thermoregulation, it would seem logical to hydrate athletes during competition. Unfortunately, many coaches still believe that fluid supplementation is not needed for optimal performance, and that witholding fluids improves heat acclimation[62]. However, studies have demonstrated the substantial benefits afforded the exercising athlete who drinks fluids before or during exercise.

1.3.3.1 - Hydration Before Exercise

Improvements in exercise capacity have been shown with hydration prior to exercise. In 1965, Moroff and Bass[61] showed that giving two liters of free water before a treadmill walk increased sweat rates and reduced core temperatures and heart rates. Other studies involving pre-exercise hydration or diuresis have produced similar results. In 1971, Nielsen et al[72] found that overhydrating subjects prior to exercise enabled them to maintain a lower core body temperature; the opposite was true for hypohydrated subjects. Nadel et al[66] compared changes in plasma volume and sweat threshold temperatures in dehydrated (by administration of diuretic), overhydrated (by injection of ADH and consumption of two liters of free water), and euhydrated subjects. After 30 minutes of exercise at 55% $VO_{2\ max}$, dehydrated subjects had 700 ml less plasma volume than in the euhydrated state; overhydration resulted in only a small increase in plasma volume, however. The diminished plasma volume in the dehydrated subjects was accompanied by significant increases in core body temperature and sweating threshold temperature. Additionally,

there were reductions in stroke volume and maximum forearm blood flow in dehydrated subjects, causing compensatory increases in heart rate. In 1985, Armstrong et al[3] showed that a diuretic-induced dehydration of approximately 10% of total plasma volume prolonged the time required to complete a foot race and caused earlier exhaustion. No changes were noted in the $VO_{2\ max}$, however. The studies of Fortney et al[26-30] also associated an increased hydration state with the ability to maintain plasma volume, a lower heart rate, and increased cutaneous blood flow, thereby improving body cooling capacity.

1.3.3.2 - Hydration During Exercise

The capacity for hydration fluids consumed during exercise to maintain plasma volume and improve body cooling has been known for many years. In 1970, Costill et al[19] found that over two hours of exercise, fluid consumption lowered core body temperatures. The study was not blinded, however, and there were substantial interindividual variations. In 1979, Francis[33] demonstrated that during two hours of exercise at 50% $VO_{2\ max}$ in a warm environment, heart rate was elevated by 18% when fluids were withheld, compared with ingestion of water or a carbohydrate drink.

More recent studies have shown that hydration during exercise increases plasma volume and improves thermoregulation. None were able to demonstrate any significant differences in $VO_{2\ max}$ during exercise with hydration fluids, however. Brandenberger et al[6] found that subjects who drank water during exercise preserved 4% more total plasma volume compared to no fluid intake. Candas et al[9] demonstrated that during four hours of intermittent exercise at a temperature of 34 °C., witholding fluids resulted in a 3.1% total weight loss and significant elevations in heart rate relative to trials

with fluid intake. They also noted that when subjects drank water, they produced more sweat for a given elevation in core temperature, increasing their "sweat sensitivity." A recent study by Nose et al[77] involving the infusion of saline during exercise also demonstrated a reduction in heart rate and improved heat transfer capacity when intravascular volume was replenished during exercise.

1.3.4 RELATED TOPICS IN HYDRATION PHYSIOLOGY

Based upon the literature, it seems clear that maintaining plasma volume during exercise maintains performance level. However, there should be two concerns of the athlete who drinks during exercise; dilutional hyponatremia and delayed gastric emptying

1.3.4.1 - The Risk of Dilutional Hyponatremia

There are case reports of hypotonic hyponatremia or "water intoxication" in athletes consuming plain water during prolonged exercise (97). For example, Noakes[73] noted four cases of water intoxication in events of greater than 7 hours duration. He attributed the dilution of Na^+ and Cl^- in blood to overzealous hydration with water, in addition to the increased losses of these electrolytes in the sweat of individuals who were unacclimated and untrained . This problem should be associated with "ultraendurance" events only, and can be easily avoided by adding electrolytes to the hydration solution.

1.3.4.2 - Delayed Emptying of Hydration Fluids

Although bloating and fullness are subjective problems which vary with the individual, there have been studies regarding the emptying of hydration fluids during exercise. Most of these will be discussed in Section 1.4, under "factors affecting gastric absorption;" however, a few bear mentioning here as well.

Many people believe that exercise slows gastric emptying. However, Costill and Saltin[15] found that exercise had no effect on gastric emptying unless exercise intensities exceeded 70% $VO_{2\ max}$. Neufer et al[71] actually demonstrated improved gastric emptying after drinking and running at 50-70% $VO_{2\ max}$, compared to drinking and resting. There is also old litcrature[45], based upon empiric studies from the turn of the century, which argues that hypotonic solutions empty more slowly from the gut than isotonic solutions. These issues will be explored in the next section.

1.4 CARBOHYDRATE SUPPLEMENTS IN EXERCISE DRINKS

As explained in section 1.2, carbohydrates are an important source of metabolic energy during exercise. Carbohydrates are more palatable than fats in a drinkable form, and unlike fatty acids, their availability probably limits exercise duration. Therefore, it is not surprising that exercise physiologists have been interested in carbohydrate supplementation during exercise for many years. This section will explore the physiological effects of carbohydrate beverages, their effects on performance and endurance, and their absorption from the gastrointestinal tract.

1.4.1. THE HISTORY OF CARBOHYDRATE SUPPLEMENTATION

Over 20 years ago, Ahlborg et al[2] associated the quantity of muscle glycogen used during exercise with 1) the total energy used during exercise, and 2) the duration of exercise. Since carbohydrates comprise a variable portion of the human diet, scientists studied the effects of a high carbohydrate diet on performance. In 1971, Karlsson and Saltin[47] compared the muscle glycogen levels and the performance in a 30 km road race of subjects consuming a high carbohydrate diet with those consuming a mixed diet. They found that the subjects consuming a high carbohydrate diet doubled their muscle [glycogen] prior to exercise, and had the fastest running times. They also noted that runners in both groups slowed their pace when muscle [glycogen] fell below 3-5 g/kg. They concluded that performance in endurance events may be improved by supplementing the diet with additional carbohydrate prior to competition. In another study from 1971, Pernow and Saltin[83] found that witholding carbohydrate from the diet reduced work capacity and endurance. These studies provide a scientific basis for the practice of "carbo-loading"--consuming a diet high in carbohydrates during the week prior to competition in order to increase muscle glycogen stores and endurance capacity. These studies fostered the development of exercise hydration fluids containing carbohydrate, and numerous studies describing their physiological effects.

1.4.2. THE PHYSIOLOGY OF CARBOHYDRATE SUPPLEMENTATION

There are physiologic variables which can be followed as a means of evaluating metabolism during exercise. When blood glucose levels are elevated, oxidation of glucose relative to fatty acids is increased. As blood glucose falls, more metabolic energy is derived from free fatty acids, which may result in an earlier onset of fatigue[13]. The respiratory quotient (RQ) is another indicator of carbohydrate oxidation. The RQ is the ratio of carbon dioxide produced to oxygen consumed. When the body metabolizes carbohydrate exclusively, the ratio of carbon dioxide produced to oxygen consumed is equal to 1.0; when fats are metabolized for energy, only seven tenths of a mole of carbon dioxide is produced for each mole of oxygen consumed. As a result, the RQ is an indicator of the oxidation of fats relative to carbohydrates during exercise.

1.4.2.1 Blood Glucose and RQ with Carbohydrate Supplementation

Recent studies involving carbohydrate supplementation during exercise have demonstrated an elevation of blood glucose levels as well as RQ throughout the exercise period. In 1985, Fielding et al[26] studied glucose dynamics during exercise, giving carbohydrate in solid form. He found that consumption of 21.5 grams of carbohydrate once per hour elevated blood glucose and RQ for 50 minutes following each dose. The results demonstrated that by increasing glucose availability to muscles, the ratio of carbohydrate to fat metabolized also increased.

Studies of the effects of glucose polymer-supplemented exercise beverages have produced similar results. Owen et al[80] exercised subjects

drinking 10% glucose or water on a treadmill at 65% of $VO_{2\ max}$ for two hours. They found that subjects maintained an elevated blood glucose and RQ throughout the two hours. Coyle et al[20] exercised subjects until exhaustion at 71% of $VO_{2\ max}$ while drinking either plain water or glucose polymer-supplemented fluid. They found that with consumption of plain water, blood glucose fell below 50 mg% prior to fatigue, as the RQ dropped from 0.85 to 0.80. In trials using glucose polymer, however, subjects maintained blood glucose at about 90 mg%, even at the point of exhaustion; the average RQ in these trials remained constant at 0.86.

1.4.2.2 - The Effects of Carbohydrate Supplementation Upon Muscle Glycogen and Endurance

Many studies have empirically demonstrated that when athletes consume carbohydrate beverages instead of plain water during prolonged exercise, the onset of fatigue is delayed. Ivy et al[47] found that giving a glucose polymer drink to subjects walking on a treadmill at 45% $VO_{2\ max}$ prolonged the time to exhaustion by 11.5%. The effects of carbohydrate supplements at higher workloads have been more marked. Coyle et al[20] gave a glucose polymer solution to subjects exercising at 71% $VO_{2\ max}$ until exhaustion. They observed that subjects increased their time to exhaustion by 33%, from three hours to four hours. Placido et al[84] exercised volunteers at 85% of their maximal heart rate. These participants exercised 30% longer when they drank a glucose polymer-supplemented fluid instead of water.

Some studies have shown other improvements in performance with carbohydrate supplements. Fielding et al[26] concluded each of their trials with a sprint to exhaustion; the duration of this "sprint" was longer when subjects consumed glucose every 30 minutes, rather than water. In a recent abstract,

Murray et al[63] reported that it took subjects a shorter time to complete a given amount of work on the cycle ergometer when they consumed a carbohydrate beverage, relative to drinking water. Edwards and Santeusanio[21] studied cyclists competing in three separate 55.2 mile bicycle races consuming either placebo, glucose, or glucose and fructose. Cyclists had faster race times and a lower rating of overall fatigue when they drank the carbohydrate fluids, relative to water.

Not all studies have shown that carbohydrate supplementation of hydration fluids prolongs time to fatigue. The 1982 study by Felig et al[25] could not demonstrate a consistent improvement in exercise duration when glucose was consumed rather than plain water (see Figure 1.7). However, their experiment was poorly designed. Each subject participated in two trials, glucose and water placebo. After completing the first trial, athletes were offered a monetary incentive to outperform their previous performance. This introduced bias into the study. If we assume that a glucose solution can prolong exercise, then subjects who received water the first time would have no difficulty outperforming the first trial, but would probably not *significantly* improve upon the previous time, having already surpassed it. On the other hand, subjects who received glucose in the first trial would be much harder pressed to surpass their previous time. By giving a monetary incentive, however, they might push themselves just a little bit further into exhaustion in order to *just barely* surpass their previous time. As a result, the monetary incentive did not have the same effect on both sets of subjects.

Many scientists have hypothesized that carbohydrate supplementation prolongs the time to exhaustion by sparing muscle glycogen. Ahlborg et al[2] demonstrated that exercise intensity and duration fell with muscle glycogen levels. Pernow and Saltin[83] found that exercising one leg to exhaustion was

accompanied by a drop in muscle [glycogen] from 11.7 to 0.3 g/kg. Other studies have also shown that caffeine ingestion[24] and free fatty acid infusion[42] reduce the depletion of muscle glycogen by stimulating metabolism of free fatty acids. In addition to sparing muscle glycogen, caffeine ingestion was also accompanied by a prolongation of the time to fatigue.

Recent studies, however, have questioned whether carbohydrates increase time to exhaustion by sparing muscle glycogen. Although Fielding et al[26] found prolonged sprint times in trials with carbohydrate, there was no difference in muscle glycogen content between water and carbohydrate test groups. Coyle et al[20] also demonstrated prolonged exercise times with carbohydrate supplements, but did not find any differences in muscle glycogen content, either. They suggested that the extra hour of exercise in the carbohydrate test group was supported by the oxidation of glucose from sources other than muscle glycogen. This seems unlikely, however, since the circulating levels of glucose and free fatty acids which they reported would not have been sufficient to account for all of the metabolic substrate needed during the extra hour of exercise.

We therefore return to the question of which factors influence fatigue during prolonged exercise. Several studies[20,25,47,84] have demonstrated that blood glucose levels remain elevated at exhaustion when subjects drink carbohydrate beverages; this argues against a relationship between falling blood glucose levels and the onset of fatigue. Other theories have implicated CNS dysfunction as the cause of fatigue and termination of performance. However, Ivy et al[47] found no differences in the performance of psychomotor tests in subjects before or after exercise to exhaustion. Nevertheless, there probably is a CNS role in the termination of exercise which relates to the

perccption of fatigue, nearncss to completion of the assigned task, and othcr factors as yet undefincd.

1.4.3 CARBOHYDRATES USED IN EXERCISE DRINKS

There is some variation in the sugars used in carbohydrate supplements. The most commonly used forms of carbohydrate are glucose, fructose, sucrose, and polymers of glucose. The rationale for including each of these carbohydrates in an exercise drink will be discussed briefly in this section; the gastric emptying and intestinal absorption of these fluids will be considered in the next section.

Glucose is the substrate for glycolysis and aerobic metabolism; other monosaccharides must be converted into glucose in order to enter the respiratory chain. As a result, glucose is almost always included in exercise fluids, either in monomer form, or in small chains (oligosaccharides or glucose polymers, to be dcscribed below). As the substrate for acrobic and anacrobic metabolism, blood glucose is closely regulated by the body, and can be rapidly absobed and metabolized by exercising muscle cells.

Fructose is an isomer of glucose which requires structural modification prior to oxidation. Its metabolic energy is less readily available to the exercising muscle than that of glucose. Although some athletes report a subjcctive feeling of nausea when drinking fructose, Edwards and Santeusanio[21] found that subjects perceived significantly less exertion when a glucose polymer solution was supplemented with fructose.

Sucrose, a disaccharide composed of glucose + fructose, is also in some exercise beverages. Its absorption by the gut may be delayed because it must be hydrolyzed by a disaccharidase in the intestinal brush border. On the othcr

hand, it may produce less perceived exertion than maltose (glucose + glucose) due to the presence of fructose.

Glucose polymer solutions are a popular form of carbohydrate supplement. These solutions are produced by the controlled hydrolysis of corn starch into glucose chains of 3-7 units in length. In the stomach, these chains have about one-fifth the osmolality of glucose, but the same caloric content. In the intestine, they are rapidly hydrolyzed to glucose monomers and absorbed. Delivery of carbohydrate in this form may produce less of a delay in the emptying of gastric contents, as described in the next section.

1.4.4 GASTROINTESTINAL ABSORPTION OF CARBOHYDRATE SUPPLEMENTS

Nearly 30 years ago, Hunt[44,45] showed radiographically that glucose and starch of equal energy densities were emptied from the stomach at similar rates. This suggested that osmotic receptors, if they existed, were located distal to the pyloric sphincter. Fifteen years ago, Costill and Saltin[15] observed that glucose fluids emptied from the stomach in inverse proportion to their concentration. They suggested that glucose concentrations in hydration fluids should be kept low to allow passage to the intestine for absorption. These earlier studies indicated that the caloric content of gastric fluids determined the rate of gastric emptying.

More recently, however, Foster et al[32] demonstrated a more rapid rate of gastric emptying when carbohydrate was delivered in polymer form, compared to monomer form. This suggested that gastric osmolality may also play a role in determining the rate of gastric emptying, a view shared by Shafer et al[95]. Furthermore, Seiple et al[91] found that there were no

significant differences between the gastric emptying rates of a 5% polymer / 2% fructose solution and plain water.

Others have attempted to delineate the relative contributions of different factors to the rate of gastric emptying. Brener et al[7] compared the factors limiting gastric emptying for saline and glucose. They noted that saline emptied rapidly and exponentially, implicating a volume dependent mechanism. Glucose, on the other hand, emptied at a slower rate which they related to a caloric flow of 2.13 kcal of glucose per minute for all concentrations. This seems good evidence that gastric emptying of glucose is regulated by the caloric, or energy content of the stomach. By contrast, a recent study by Hunt et al[46] found that as gastric volumes and/or energy density increased, the rate of energy delivery to the intestine also increased. Furthermore, Mitchell et al[58] found that when there were no significant differences in gastric residue when subjects drank either a glucose polymer solution or water during two hours of cycling.

Collectively, the literature on gastric emptying seems to indicate that the caloric content of the gut is the primary determinant of the rate of gastric emptying. However, gastric emptying is probably also stimulated by increases in gastric volume. As a result, a stomach full of glucose may empty as quickly as water, overriding the effects of the caloric load. Gastric osmolality probably plays a minor role in gastric emptying rates, as well.

Rapid intestinal absorption of carbohydrate beverages is also important. A recent study by Wheeler and Banwell[99] compared the rates of intestinal absorption of glucose polymer, sucrose, and water by delivering these fluids through a jejunal tube placed distal to the Ligament of Treitz. They found that the glucose polymer was absorbed as quickly as water, but that sucrose absorption was significantly slower. Saunders and Sillery[89] also found that

sucrose was absorbed much more slowly than glucose or glucose polymers. They also noted greater net absorption of sodium with a glucose polymer solution. The importance of increasing sodium absorption into the blood stream will be discussed in the next section.

1.5 ELECTROLYTE SUPPLEMENTS AND HYDRATION FLUIDS

Most carbohydrate drinks contain small amounts of many electrolytes. In the view of some physiologists such as Fink[35], these electrolytes are useful only in cases of extremely prolonged exercise, when there is a risk of dilutional hyponatremia from drinking plain water[73]. In less demanding events, the theory goes, the body is capable of reabsorbing sufficient Na^+ and K^+ at the kidney to maintain extracellular and intracellular fluid balance, since losses of these ions in sweat are only a small fraction of the total body Na^+ and K^+ stores.

Recent studies, however, suggest that the inclusion of substantial electrolyte in hydration fluids may prevent the phenomenon of "voluntary dehydration." Because the human brain is not very sensitive to reductions in plasma volume, there is an obligatory reduction in plasma volume of 5-10% before the dipsogenic drive is activated. This delay in the onset of thirst during exercise causes"voluntary" dehydration, since the brain "chooses" not to seek fluid replacement despite diminishing plasma volume. Since thirst is activated when plasma osmolality increases, these recent experiments have found that drinking electrolyte beverages after exercise can maintain the drinking drive and replace more of the fluids lost during exercise. This section will discuss electrolyte balance, summarize the literature on the topic

of voluntary dehydration, and review experiments designed to replace total body water loss during exercise.

1.5.1 ELECTROLYTE BALANCE

The distribution of electrolytes amongst the body fluid compartments creates osmotic pressure. Osmosis is defined as the passage of water through a selectively permeable membrane towards the side with a greater concentration of solute. Osmotic pressure is defined as the pressure which must be exerted in an opposite direction in order to oppose the osmotic movements of water molecules. Mathematically, osmotic pressure equals the product of the osmolality of a solution and 19.3 $\frac{kg \times mmHg}{mosm}$. As a result, the total plasma osmolality of 282.6 mosm/kg water exerts an osmotic pressure of 5450 mm Hg!

The major ions which create osmotic pressures in the body are Na^+, K^+, and Cl^-; their distributions among the intravascular, interstitial, and intracellular spaces are summarized in Figure 1.8. By multiplying the total osmolality of each compartment by 19.3 $\frac{kg \times mmHg}{mosm}$, we can determine the osmotic pressure exerted by each fluid compartment. The osmotic pressure of the intravascular space is 23 mm Hg greater than that of the interstitial and intracellular spaces. This force drawing water into the intravascular space is opposed by hydrostatic pressure which forces fluid out of the intravascular space.

Osmotic equilibrium is established across the vascular and cellular membranes by the forces shown in Figure 1.6. Because water moves across these borders very rapidly, osmotic equilibrium is established almost instantaneously. If one space has a higher concentration of solute, then it is

hypertonic relative to the other space, and water rapidly moves into the hypertonic space. The opposite is true for hypotonic spaces, which have a lower concentration of solute.

There are many changes in fluid balance which occur during exercise; these were discussed in Section 1.2 (and Figure 1.6), and are summarized below:

1) Increased hydrostatic pressures force fluids out of the intravascular space, into the interstitial space

2) Sweat losses result in a greater loss of free water than Na^+ from the intravascular and interstitial spaces than the intracellular spaces[50]

3) Sweat losses result in a rising plasma osmolality and plasma $[Na^+]$, causing the movement of free water from the intracellular space into the interstitial and intravascular spaces, partially compensating for lost volume[76,78]

4) The brain senses fluid losses from the body by the rising plasma osmolality and plasma $[Na^+]$as well as the reduction in intravascular volume at baroreceptors, which stimulates drinking[38,40].

5) Intake of plain water replaces some of the lost volume and reduces plasma osmolality and sodium such that the drinking stimulus is removed (i.e., voluntary dehydration--see below)

6) If exercise continues for long enough and the athlete drinks plain water, the losses in electrolytes may lead to dilutional hyponatremia[73].

Thus, although fluid shifts can partially compensate for intravascular volume losses, complete replacement of total body water is limited by the removal of the drinking stimulus when drinking plain water. As a result, we must determine how the factors which affect thirst can be manipulated in order to overcome the phenomenon of voluntary dehydration.

1.5.2 VOLUNTARY DEHYDRATION

In the 1947 text, The Physiology of Man in the Desert, Rothstein et al[86] noted that man was unable to replace all water lost in sweat despite the availability of adequate supplies. They saw obligatory losses of as much as 2-5% of total body water in these subjects--losses sufficient to limit performance. From this observation, they defined "voluntary dehydration" as the tendancy of man to become dehydrated under thermal stresses despite the availability of adequate water.

Recently, Greenleaf[38] reviewed the literature on factors affecting the human drinking response. He suggested a model of two additive but not interactive paths towards dehydration-induced drinking, based on the work of Oatley, shown in Figure 1.9. One pathway is activated when a drop in the extracellular fluid level stimulates the renin-angiotensin-aldosterone system at the renal juxtaglomerular apparatus. This results in the production of angiotensin II which stimulates the thirst center of the brain. The second pathway is activated when an increase in plasma osmolality stimulates the osmoreceptors of the hypothalamus, which relay this information to the thirst center of the brain.

In another article, Greenleaf et al[40] considered the teleological significance of these pathways. They argued that voluntary dehydration may

have developed in humans because of stimulation of the renin-angiotensin-aldosterone system by the upright posture (the volume argument), or because of the human ability to concentrate plasma through sweating (the osmolality argument). Experimentally, they found that drinking was most closely related to the sweat rate during exercise. Since increases in the sweat rate reduce plasma volume *and* increase plasma osmolality, this does not imply a greater role for one factor or the other.

A recent study by Seckl et al[90] questioned the influence of elevated plasma osmolality upon the drinking. Subjects were dehydrated over 24 hours (during which time they were also given two salt pills), then rehydrated with either water or hypertonic saline. They found that plasma osmolality returned to normal 30-60 minutes after drinking plain water, but remained elevated after drinking hypertonic saline. Because all subjects who drank hypertonic saline reported diminished thirst, the authors concluded that the sensation of thirst did not correlate with plasma osmolality. However, they did not observe water-seeking behavior beyond one hour. Furthermore, these observations were made in subjects at rest; during exercise, changes in the Starling forces may alter the role of plasma volume and plasma osmolality in stimulating thirst and drinking.

1.5.3 ATTEMPTS TO PREVENT OF VOLUNTARY DEHYDRATION

In 1985, Nose et al[79] studied voluntary dehydration in rats. After a dehydration of 7% of body weight in the heat, rats were rehydrated with either deionized water, 0.45% NaCl, or 0.9% NaCl over six to twelve hours. They found that when rats drank deionized water, they replaced only half of their water losses; when rats drank a saline solution, they replaced almost all of

their water losses. Additionally, when rats drank deionized water, they lost Na^+; when they drank saline they gained Na^+. The authors concluded that voluntary dehydration was due to dilutional inhibition of the osmotic effects of Na^+ when drinking plain water.

A recent series of studies by Nose et al[73-75] tested how the sodium content of ingested fluids affects rehydration following dehydration in humans. Subjects were dehydrated over 90-110 minutes by exercising at 40% of $VO_{2\ max}$ in the heat, and then rehydrated ad libitum with either plain water or 0.45% NaCl. After three hours, subjects who drank saline had restored 71% of their total body water losses and 174% of their plasma volume losses, while subjects who drank plain water had replaced only 51 % of total body water losses and 78% of their plasma volume losses. Plasma osmolality remained elevated after three hours with saline rehydration, but returned to normal after 30 minutes with water rehydration. The authors also found that as plasma volume was restored, the hormonal drive to retain Na^+ was removed.

Nose et al concluded that less of the total body water losses were replaced with plain water due to the removal of the osmotic drinking drive. When plasma became isoosmotic, fluid intake was limited by an increase in free water clearance and a decrease in Na^+ retention by the kidney. By consuming saline, however, subjects could reach intravascular euvolemia, yet maintain the drive to drink by virtue of an elevated plasma osmolality. Na^+ losses in the urine due to euvolemic inhibition of the renin-angiotensin-aldosterone system were overcome by continued sodium intake, allowing *expansion* of plasma volume. In summary, the authors found that osmolality continues to play a role in the regulation of thirst even after the removal of a volume stimulus.

Nadel et al[69] recently reviewed the fluid replacement literature, drawing broader conclusions. They surmised that during rehydration, there is a preferential replacement of intravascular losses before interstitial or intracellular losses. Once euvolemia is reached, consumption of plain water dilutes the plasma, increasing free water clearance at the kidneys. On the other hand, consumption of saline would maintain the elevated plasma osmolality achieved with dehydration, stimulating thirst, and resulting in the recovery of a greater percentage of total body water losses. They observed that since the degree of rehydration in each compartment depends upon the recovery of the predominant cation in that compartment, hydration fluids should include sufficient Na^+ to restore total body losses of Na^+ rather than plasma volume losses alone.

1.6 CONCLUSIONS OF LITERATURE REVIEW

We have established that hydration during prolonged exercise replaces fluid losses, maintains cardiac output, and allows thermoregulation. If exercise will last for two hours or longer, then the hydration beverage should include carbohydrate in order to supplement endogenous stores of glucose[13]. Glucose has the best availability for metabolism, but may be emptied more quickly from the stomach when included in polymer form. The addition of fructose allows more rapid absorption in monkeys[60], and it may reduce the level of perceived exertion during exercise[21]. The fluid should also be suplemented with Na^+ in order to maintain an elevated plasma osmolality and maintain the drinking drive to replace total body water losses. Sodium supplementation may also speed the absorption of glucose in the intestine.

Some issues relating to the effects of exercise hydration beverages still remain unresolved, however.

1) We have not yet isolated which element of carbohydrate supplementation is responsible for the prolonged time to fatigue seen with consumption of these beverages.

2) If carbohydrate solutions have a slower rate of gastric emptying than water, is this slowing significant during *prolonged* exercise?

3) What are the most important factors affecting the drinking response *during* exercise?

4) Will increasing the Na^+ content of hydration fluids reduce plasma volume losses *during* exercise?

CHAPTER 2

HYPOTHESES

These experiments were designed to test the following hypotheses:

1) By consuming a 5% glucose polymer / 2% fructose solution, subjects would maintain elevated levels of plasma glucose and raise the respiratory quotient relative to drinking plain water.

2) By supplying exogenous glucose with this carbohydrate beverage, subjects would prolong their time until exhaustion, relative to drinking plain water.

3) By raising the Na concentration of the carbohydrate beverage to 0.45% NaCl, subjects would reduce their plasma volume losses during exercise without compromising thermoregulatory capacity.

CHAPTER 3

EXPERIMENTAL DESIGN

The following procedure was approved by the Yale University Human Investigation Committee (protocol #4272).

3.1 SELECTION OF VOLUNTEERS

Fifteen healthy volunteers, twelve male and three female, engaging in regular vigorous activity applied to participate in this study. Each volunteer first passed a physical examination which included assessment of cardiac function by auscultation and electrocardiogram. We then measured the maximal oxygen uptake ($VO_{2\ max}$) of each volunteer in an incremental exercise test on the cycle ergometer (see section 3.4). This test screened out applicants who would be unlikely to complete the three hour trials, since the greater the capacity for oxygen delivery, the greater the ability to maintain aerobic metabolism over a prolonged period time (see section 1.2.6). Five volunteers, four male and one female, surpassed the $VO_{2\ max}$ criterion of ≥55 milliliters O_2 per minute per kg body weight, and were accepted into the study after giving informed consent. Their physical characteristics are summarized in Table 3.1.

3.2 DOUBLE-BLIND CROSS-OVER PROTOCOL

Four of the five volunteers participated in all three trials in a randomly determined sequence, as outlined in Table 3.2. The fifth volunteer (M.M.) was unable to tolerate the experimental design and did not complete any of the trials. The three trials were scheduled over a period of two months, with at least ten days off between trials for each participant. In Trial A (Placebo), volunteers drank 250 ml of flavored/colored water every fifteen minutes throughout the experiment. In Trial B (CHO_{Na}), volunteers drank 250 ml of a 5% glucose polymer / 2% fructose supplement (Exceed™) every fifteen minutes. In Trial C (CHONa), volunteers drank 250 ml of Exceed™ with extra Na^+ added to constitute a 0.45% NaCl solution. The carbohydrate and electrolyte components of each drink are outlined in Table 3.3. The drinks were indistinguishable by taste to the volunteers. The trials were randomized so that neither the volunteers nor the experimenters knew which drink was being given in any trial.

Prior to each trial, volunteers rested in a cool environment (18° C.) in the recumbent position for one hour. After emptying his bladder, the participant was weighed; using this weight, we calculated the load which corresponded to 60% of his experimentally determined $VO_{2\ max}$ at a cycling frequency of 60 revolutions per minute (see section 3.4). Volunteers consumed the trial beverage every fifteen minutes throughout the procedure, as outlined above. At t = 20, 50, 80, 110, and 140 minutes, expired air was collected over a three minute period for calculation of the respiratory quotient. At t = 0, 15, 30, 60, 90, 120, and 150 minutes, 10 ml of blood was removed from a Teflon catheter placed in an antecubital vein for

measurement of [glucose], hemoglobin and hematocrit, [Na^+], and osmolality. The catheter was kept patent by flushing with sterile heparinized saline after each sample.

3.3 MEASUREMENTS

3.3.1. REAL-TIME MONITORING

In order to insure a steady power output during the experiment, a cyclometer with an LCD display visible to the participant was mounted to the cycle ergometer frame during each trial. Both the instantaneous rate and the cumulative number of revolutions were monitored to assure constant power output throughout the three hour trials.

We monitored heart rate using a Hewlett-Packard Model 1500B electrocardiograph. Each volunteer wore limb leads throughout the experiment, one attached at each shoulder and one on each side of the waist. Heart rate was recorded over the first 15 minutes to insure adequate workload, and then every 15 to 30 minutes thereafter.

We monitored core body temperature using an esophageal thermocouple inserted into the proximal third of the esophagus, at the level of the great vessels. This device was calibrated by placing the probe in warmed water at 35° and 40° C. A Honeywell Electronik Model 195 temperature sensor continuously displayed core body temperature throughout the experiment.

3.3.2. MEASUREMENT OF THE RESPIRATORY QUOTIENT

The respiratory quotient (RQ) was calculated from measurments of O_2 and CO_2 in the inspired and expired air, as explained in section 3.4. At half-hour intervals beginning at 20 minutes, we collected expired air samples over a three minute period. Volunteers breathed through a Daniel's valve; the expired air volume was measured by a Carl Poe Co. dry gas meter, and the O_2 and CO_2 levels in the expired air were analyzed by an Applied Electrochemistry Model S-3A oxygen analyzer and a Beckman Model LB-2 Medical Gas Analyzer, respectively. These instruments were calibrated using room air concentrations of O_2 (20.93%) and CO_2 (0.03%), as well as a prepared standard of 15.96% O_2 and 2.82% CO_2.

3.3.3. BLOOD MEASUREMENTS

Each blood sample was apportioned for the measurement of blood glucose, changes in plasma volume, plasma osmolality, and plasma sodium. Immediately after drawing, three 10 µl samples of whole blood were placed in a Beckman Model 2 Glucose Analyzer for measurement of blood glucose. The autoanalyzer was calibrated with a 150 mg% glucose standard prior to each sample measurement.

During the trial, drawn blood was also apportioned for the measurement of changes in plasma volume, calculated from changes in hematocrit and [hemoglobin] as described in section 3.4. Three microcapillary tubes were filled with approximately 50 µl of whole blood. At the conclusion of the trial, all tubes were placed in an IEC MB Centrifuge at low speed for three minutes, the hematocrit was determined on an IEC Micro-Capillary

Reader. Hemoglobin concentration was determined using the cyanomethemoglobin method. 20 µl of whole blood was added to each of three tubes containing 5 ml of cyanomethemoglobin reagent and centrifuged in an IEC Model UV Centrifuge at medium speed. The absorbance of each sample at a wavelength of 540 nm was measured in a Coleman Junior II spectrophotometer. The hemoglobin concentration of the sample was then interpolated from a standard curve relating absorbance at 540 nm to cyanomethemoglobin concentration.

The remaining 9 ml of blood from each sample was centrifuged in the IEC MB Centrifuge; the plasma layer was extracted and frozen for later measurement of plasma osmolality and $[Na^+]$. Plasma osmolality was determined by the freezing point depression method, using an Advanced Instruments Model 3DII osmometer; this machine was calibrated with standard solutions of 100 and 500 mosm/kg prior to analyzing each series of samples. Plasma sodium levels were measured by flame photometry, using an International Laboratory Model 943 flame photometer, and calibrated with 100 and 140 mEq/L sodium standards.

3.4 CALCULATIONS

3.4.1. MAXIMAL OXYGEN UPTAKE / MAXIMAL AEROBIC POWER

We defined the maximal oxygen uptake ($VO_{2\ max}$) of each volunteer as the maximum amount of oxygen which can be used per minute of exercise, relative to the total body weight in kilograms. This value was calculated from the difference between the oxygen content of room air and the oxygen

content of expired air during exercise of maximal intensity. We defined the maximal aerobic power as the power output at which the $VO_{2\ max}$ is achieved.

These values were experimentally determined during an incremental exercise test on a cycle ergometer. The oxygen content of expired air samples was measured while volunteers cycled against a steadily increasing load. The test ended when subjects could not maintain a constant cycling rate despite strong encouragement. The total power output was calculated as shown in equation 3.4.1 below:

$$\text{Power} = \frac{[\text{flywheel circumference(m/rev)}](\text{rev/min})(\text{load(kg)})(9.8\text{N})}{(60\text{sec/min})(\text{body weight in kg})}$$

$$= \text{power in (N·m/sec), or Watts} \qquad \text{(equation 3.4.1)}$$

Using this calculation, the oxygen uptake (in ml/min/kg) was graphed as a function of the total power output, as shown in Figure 1.3. In this example (T.Z.), the $VO_{2\ max}$ of 61 ml O_2/min/kg corresponded to a maximal aerobic power of 5 Watt/kg. From this, 60% of the maximal aerobic power can be calculated as 3 Watt/kg. Equation 3.4.1 is then rearranged, substituting a power of 3 Watt/kg, to calculate the load against which T.Z. must pedal to work at 60% of his $VO_{2\ max}$.

3.4.2. THE RESPIRATORY QUOTIENT

The respiratory quotient (RQ) is defined as the ratio of CO_2 production to O_2 consumption. It can be calculated using the expired ($\%O_{2_e}$

and $\%CO2_e$) and inspired ($\%O2_i$ and $\%CO2_i$) gas concentrations as well as the expiratory and inspiratory volumes (V_E and V_I), as in equation 3.4.2.1, below:

$$RQ = \frac{(V_E)(\%CO2_e) - (V_I)(\%CO2_i)}{(V_I)(\%O2_i) - (V_E)(\%O2_e)}$$

(Equation 3.4.2.1)

$$= \frac{V_{CO_2}}{V_{O_2}}$$

$$\text{where } V_I = V_E \cdot \frac{(1 - \%O2_e - \%CO2_e)}{0.7904}$$

(Equation 3.4.2.2)

These calculations assume that all gases are at the same temperature and pressure. All variables in these calculations were then obtained from the dry gas recording equipment during each three minute collection.

3.4.3. CHANGES IN PLASMA VOLUME

The change in plasma volume with exercise was determined by serial comparisons of the [hemoglobin] and the hematocrit of each sample with the sample drawn at t = 0. "Initial" (Hb_i, Hct_i) samples are those taken at t = 0; "final" (Hb_f, Hct_f) samples are those taken during the experiment. Using the changes in hemoglobin and hematocrit, the change in plasma volume can be calculated as the ratio of the final values ($\frac{1-Hct_f}{Hb_f}$) to the initial values ($\frac{1-Hct_i}{Hb_i}$). Using this ratio, the % change can be calculated using equation 3.4.3, below:

$$\% \Delta PV = 100 \frac{[(Hb_i)/(Hb_f)][(1-Hct_f)]}{[(1-Hct_i)]} - 100$$

(Equation 3.4.3)

This equation assumes that there is no change in red cell mass over the observed range of plasma volume.

3.5 ANALYSIS

Differences in each form of data between trials for each subject were analyzed using a paired t-test. Values of $p<0.05$ were considered significant; values of $p<0.001$ were considered highly significant. Group differences between the trials were assessed using the Students t-test for time to fatigue data in Section 4.1.

CHAPTER 4

RESULTS

4.1 AVERAGE TIME TO FATIGUE

Table 4.1 contains the exercise times of the four volunteers for all three trials. The volunteers exercised for an average period of 169 ± 14 minutes when they drank CHONa. Participants exercised for an average of 157 ± 18 minutes when drinking CHO_{Na}, and for an average of 147 ± 8 minutes when drinking Placebo. Exercise times for the CHONa test group were significantly greater than those for the Placebo test group ($p < 0.05$). There was no statistically significant difference between the CHO_{Na} and CHONa groups.

The only three trials which were stopped at 180 minutes involved CHO_{Na} or CHONa consumption. As a result, the difference between Placebo and CHO_{Na}, or between CHO_{Na} and CHONa trials might have reached significance if these trials had proceeded to exhaustion.

4.2 CHANGES IN BLOOD GLUCOSE WITH EXERCISE

Blood glucose levels were measured at 0, 15, 30, 60, 90, 120, and 150 minutes of exercise (see Section 3.3.3). The changes in blood glucose for each trial are compiled in Table 4.2. As shown in Figure 4.2, blood glucose levels were between 80-90 mg% at the onset of exercise. In the CHO_{Na} and CHONa trials, blood glucose levels rose to 100-110 mg% during the first half hour of

exercise, then remained between 90-100 mg% for the duration of the trial. In the Placebo trials, blood glucose levels steadily declined to less than 70 mg% at the time of exhaustion.

As shown in Figure 4.2, blood glucose levels in the $CHONa$ test group were significantly higher than in the Placebo test group at 60, 120, and 150 minutes. Blood glucose levels in the CHO_{Na} test group were significantly greater than in the placebo test group at 30, 120, and 150 minutes. There were no significant differences in blood glucose levels between the CHO_{Na} and $CHONa$ test groups at any point during the trials.

4.3 CHANGES IN RESPIRATORY QUOTIENT DURING EXERCISE

The RQ data for each trial is listed in Table 4.3. The respiratory quotients of volunteer N.S. were less than 0.7 (the theoretical value at which the body is *only* metabolizing fatty acids) in the latter portion of Placebo and CHO_{Na} trials. In addition, two out of five Placebo measurements, four out of five CHO_{Na} measurements, and two out of five $CHONa$ measurements for N.S. were outside of two standard deviations (shown within parentheses). Because of these unusual values, his data was not included in Table 4.3a or Figure 4.3.

As shown in Figure 4.3, the RQ was lower during the first hour of exercise for the Placebo test group. At 50 minutes, the RQ was significantly greater for the $CHONa$ (0.90 ± 0.01) and the CHO_{Na} (0.91 ± 0.02) trials than for the Placebo trials (0.76 ± 0.05). There were no other significant differences between any of the test groups during the remainder of the exercise period. However, considerable interindividual variability confounded interpretation of the RQ data (see Tables 4.3 and 4.3a).

4.4 CHANGES IN PLASMA VOLUME WITH EXERCISE

As shown in Figure 4.4, the amount of plasma volume dropped during the first hour of exercise, then stabilized at approximately 10% of its resting level. Neither the CHO_{Na} nor CHONa protocols altered the amount of plasma volume reduction during these trials, relative to the water Placebo.

In the Placebo test group, however, there was a significantly slower rate of plasma volume reduction during the first hour, relative to the carbohydrate beverage test groups. At t = 15 minutes, the CHO_{Na} and CHONa trials produced a significantly greater reduction in plasma volume, relative to Placebo ($p < 0.02$). At t = 30 minutes, the differences were no longer statistically significant; by 60 minutes of exercise, the values were virtually identical. Plasma volume changes for all subjects are shown in Table 4.4.

4.5 CHANGES IN HEART RATE WITH EXERCISE

Reductions in plasma volume cause an increase in heart rate via the baroreceptor reflex. We recorded each volunteer's heart rate in Table 4.5 to determine whether *insignificant* differences in lost plasma volume between the three groups caused any *significant* differences in heart rate. As can be seen, heart rate values were relatively consistent between individuals and groups.

As shown in Figure 4.5, the average heart rate varied from 156 ± 9 bpm at 30 minutes to 169 ± 7 bpm at 120 minutes of exercise in the Placebo trials. In the CHO_{Na} and CHONa trials, average heart rate varied from 158 ±12 and 156 ± 6

bpm at 30 minutes, to 162 ±11 and 165 ±7 bpm at 120 minutes, respectively. There were no significant differences within test groups or between the test groups over time.

4.6 CHANGES IN CORE BODY TEMPERATURE WITH EXERCISE

Changes in core body temperature are shown in Table 4.6.. There was considerable interindividual variability. The body temperatures of volunteer A.P. varied little throughout the three hour studies; however, only a few of his values (shown within parentheses) fell outside of two standard measurements from the mean. As a result, all of his data was included in the statistical analysis shown in Table 4.6 and Figure 4.6.

During the first 30 minutes of exercise, all three groups experienced a rise in core body temperature of approximately 1.5° C. During the second and third hours of exercise, participants stabilized their core temperatures while consuming CHO_{Na} or water Placebo. When volunteers drank CHONa, however, their core temperatures continued to rise. After 150 minutes of exercise, the change in core temperature in the CHONa test group averaged +2.2 ± 0.4° C., while the changes in core temperature in the CHO_{Na} and Placebo test groups were +1.6 ± 0.2° C. and +1.7 ± 0.2° C., respectively. These differences were not statistically significant ($0.05 < p < 0.10$).

4.7 CHANGES IN PLASMA OSMOLALITY WITH EXERCISE

All plasma osmolality data is expressed as the change from resting plasma osmolality, as shown in Table 4.7. As shown in Figure 4.7, there was an

increase in plasma osmolality of 10 to 12 mosm/kg when volunteers consumed CHO_{Na}. In the CHONa test group, the average rise in plasma osmolality was 6 to 8 mosm/kg, while in the Placebo group, the average rise in plasma osmolality ranged from 3 to 6 mosm/kg. The differences between the CHO_{Na} and Placebo groups were statistically significant at t = 30, 60, 90, and 120 minutes of exercise ($p < 0.05$). There were no significant differences between CHO_{Na} and CHONa, or between CHONa and Placebo groups.

4.8 CHANGES IN PLASMA SODIUM WITH EXERCISE

The change in plasma sodium from the t = 0 value for each volunteer is shown in Table 4.8. The data of subject T.Z was rejected because of large variations in serial measurements which placed three out of five of the CHO_{Na} measurements and three out of five of the CHONa measurements outside of two standard measurements The data was recalculated for n = 3 in Table 4.8a.

The average change in sodium during exercise for each test group is shown in Figure 4.8. At t = 30 minutes, the plasma sodium levels were significantly higher in the CHO_{Na} group than in the Placebo group ($p < 0.05$). At t = 120 minutes, plasma sodium levels were significantly higher in the CHONa group than in the Placebo group ($p < 0.05$). There were no other significant differences between the test groups.

CHAPTER 5

DISCUSSION

5.1 EFFECTS OF CARBOHYDRATE SUPPLEMENTS ON EXERCISE

In these trials, we confirmed previously observed physiological effects of carbohydrate-supplemented beverages. Volunteers maintained significantly higher blood glucose levels when they consumed carbohydrate-supplemented fluids than when they consumed flavored water. Blood glucose fell prior to exhaustion in the Placebo trials, while blood glucose levels remained elevated at the end of all CHO_{Na} trials. When volunteers drank CHO_{Na} or CHONa, they obtained a greater fraction of their nutrient energy from carbohydrate, as indicated by the significantly elevated RQ noted at 50 minutes. This metabolic preference for carbohydrates diminished during the three hours of exercise.

To determine whether carbohydrate supplementation could improve exercise performance would require measuring the level of perceived exertion during exercise. This was not attempted in the present study. However, we did observe a significantly prolonged time to fatigue when volunteers drank the CHONa beverage, compared to the Placebo. Additionally, volunteers had consumed carbohydrate in *all* trials which ran for three hours.

Our findings are consistent with those of many other authors. Previous studies have demonstrated elevation of blood glucose and RQ during exercise with glucose or glucose polymer hydration fluids[20,25,26,47,57]. Many authors have also observed longer exercise times when athletes consumed carbohydrate beverages. Our experimental design is probably most similar to that of Coyle et al[20], who found that the CHO_{Na} test group could exercise for one hour longer than controls at 71% of VO2 max. Similar studies of exercise at lower[47] and higher[84] intensities have also found longer exercise times when subjects consumed a glucose polymer-electrolyte beverage instead of water during exercise.

Although several studies have found that carbohydrate fluids can prolong exercise times, relative to water, the proposed mechanism of sparing muscle glycogen is still only theoretical. In 1967, Ahlborg et al[2] related the amount of muscle glycogen used with total energy and duration of exercise, establishing an association between muscle glycogen levels and endurance. Other studies in this area[48,83] confirmed this association, implying that carbohydrate loading before exercise could increase muscle glycogen stores, prolonging the duration of exercise.

Recently, Coyle et al[20] tested the hypothesis that the increased time to fatigue seen in athletes consuming carbohydrate beverages resulted from the direct sparing of muscle glycogen. Subjects exercised over one hour longer when consuming a carbohydrate beverage relative to water placebo. However, biopsies of the quadriceps muscle during the trials did not demonstrate any significant differences in muscle glycogen depletion between the carbohydrate and water test groups. The authors accounted for the prolonged time to fatigue by the oxidation of exogenous glucose and circulating free fatty acids during the last hour of exercise.

It is possible (as suggested by Coyle et al) that carbohydrate supplements do not spare muscle glycogen. By raising blood glucose levels, exogenous glucose also raises the respiratory quotient. If the RQ is raised enough, then each oxidized molecule of exogenous glucose may spare an energetically equivalent amount of free fatty acids. The slow exhaustion of muscle glycogen would therefore not be affected by consumption of carbohydrate during exercise. Future studies should attempt to answer this possibility using newer technologies now available in medicine. New techniques for measuring muscle glycogen, such as NMR spectroscopy[4], should avoid the variable and invasive nature of muscle biopsy studies. Labelling of glucose in a carbohydrate beverage would permit careful accounting of the relative contributions of exogenous (labelled) glucose versus endogenous (muscle and liver) glycogen. Comparison of radionuclide levels in the blood and expired gases of the CHO_{Na} group with the RQ and blood glucose levels of the water placebo group would indicate whether inclusion of a carbohydrate reduced the oxidation of endogenous glucose stores.

Athletes who must exercise for prolonged periods must also worry about beverage absorption. In the present study we found that during the first hour of exercise, plasma volume dropped much more rapidly when subjects consumed CHO_{Na} or CHONa instead of water placebo. At t = 15 minutes, plasma volume was lower than at any other point during the three hour experiment for the CHO_{Na} and CHONa test groups. However, these differences were no longer present after one hour of exercise.

An explanation for this observation may be found in the literature on carbohydrate absorption. Several studies of GI physiology[7,15,46,94] have demonstrated the dependence of gastric emptying on the energy content of the stomach. As a result, we may hypothesize that the first drink (at t = 10

minutes) was emptied from the stomach and absorbed into the bloodstream when water was consumed, but was delayed in the stomach when volunteers drank the CHO_{Na} or CHONa beverages.

On the other hand, many authors have shown that during *endurance* events, carbohydrate beverages are well-absorbed, with no significant differences in gastric residue after exercise between the CHO_{Na} and water groups[54,58]. In support of these findings, some studies have demonstrated a volume-dependent mechanism for gastric emptying as well as a caloric mechanism[7,15,46]. By the end of endurance events, the volume dependent mechanism may become the primary determinant of gastric emptying rate.

In the present study, none of the participants became bloated or nauseous with consumption of the CHO_{Na} or CHONa beverages. We also found that by one hour of exercise, plasma volume levels had returned from the minimum values at 15 minutes to equal those of the Placebo group. This suggests that during prolonged exercise, there is an initial delay in the gastric emptying of carbohydrate fluids due to the elevated energy content of the stomach; as the stomach fills and as exercise continues, however, a volume-dependent mechanism for the emptying of gastric contents causes carbohydrate fluids to empty at sufficient rates to prevent bloating.

5.2 EFFECTS OF SODIUM SUPPLEMENTS DURING EXERCISE

Previous work in this laboratory by Nose et al[74,75,76] demonstrated that inclusion of sodium in a rehydration beverage increased the replacement of total body water losses following exercise in the heat. They found that volunteers were able to replace 174% of their lost plasma volume when

consuming a 0.45% NaCl solution, but only 78% of their lost plasma volume when consuming plain water. The authors attributed these findings to a greater ad libitum intake of 0.45% NaCl than plain water. They hypothesized that the increase in plasma volume was due to an increased plasma osmolality reducing free water clearance at the kidney and maintaining the dipsogenic drive.

In the present study, we tested the hypothesis that inclusion of additional Na^+ in a carbohydrate beverage would diminish the reduction in plasma volume during exercise, without compromising body cooling. Our results indicated that the reduction in plasma volume was not significantly different between the three test groups. Body temperatures were higher for three of the four subjects when CHONa was consumed, relative to CHO_{Na} or water placebo; however, the calculated differences between these groups were not statistically significant ($0.05 < p < 0.10$).

Because the regulation of plasma volume and fluid balance is related to plasma osmolality and / or plasma sodium levels, these were also measured in this study. The plasma osmolalites of the CHO_{Na} test group were significantly higher than the Placebo group; the calculated differences in plasma osmolality between the CHONa and Placebo groups were not statistically significant by paired t-test. Plasma sodium levels were significantly higher in the CHONa group than in the Placebo group by 120 minutes of exercise.

The differences between the results of this study and the previous work of Nose et al are probably due to differences in the experimental design. Nose et al studied rehydration *after* exercise, whereas our study examined the effects of hydration *during* exercise. The Starling forces affecting filtration and resorption across the capillary wall in muscle change with exercise. There is a large increase in the hydrostatic pressure during exercise which

may counterbalance osmotic forces and permit an elevated plasma osmolality (see Figure 1.5).

This hypothesis is supported by the previous work of other authors. Lundvall et al[55] demonstrated a transcapillary fluid loss in proportion to the intensity of exercise which elevated plasma osmolality. Convertino et al[12] specifically demonstrated that at work intensities above 40% VO_{2max}, plasma osmolality and plasma sodium levels were significantly elevated. These elevations were also directly proportional to the intensity of the exercise. These studies support the hypothesis that exercise at 70% $VO_{2\ max}$ changes the Starling forces across the capillary walls in active muscle. Elevated hydrostatic pressures would permit plasma to remain hyperosmolal relative to the fluid in the interstitial and intracellular spaces.

Inclusion of additional sodium in the carbohydrate beverage did not cause a significant elevation in core body temperature, although three out of four subjects showed a significant increase in body temperature when drinking CHONa relative to drinking CHO_{Na}.or placebo. Loss of thermoregulation usually occurs only when plasma volume reductions approach 20%. However, the body's thermoregulatory center may sense reductions in plasma volume as elevations in plasma osmolality or sodium. In the CHONa group, elevations in plasma osmolality may have been sensed by the thermoregulatory centers, adversely affecting body cooling.

Support for this hypothesis may also be found in the literature. Nielson et al[72] observed that plasma osmolality and body temperature rose together in subjects exercising at 50% $VO_{2\ max}$ for one hour. They hypothesized that cooling capacity was reduced either by the influence of elevated plasma osmolality at the thermoregulatory center of the brain or by the influence of increased interstitial fluid osmolality at peripheral sweat glands. Fortney et

al[27] found that elevations in plasma osmolality raised the threshold body temperature for vasodilitation and sweating. In a review article on thermoregulation, Senay[93] speculated that a higher body temperature in the hypohydrated state is due to the inhibitory actions of elevated plasma osmolality and plasma sodium on the hypothalamus.

Although these hypotheses are reasonable, the osmolality and sodium data obtained in our study were confusing. Plasma osmolality was greatest in the CHO_{Na} test group, whereas we had expected the greatest plasma osmolality in the CHONa group. On the other hand, plasma sodium *was* higher in the CHONa group. In both sets of data, variability between individuals highlighted the greatest weakness of these studies--their small sample size.

5.3 LIMITATIONS OF THE EXPERIMENTAL DESIGN

Because of the difficult physical nature of this study, it was flawed from the outset by the small number of people who were adequately conditioned to complete it. Of the four volunteers who were sufficiently conditioned to complete the study, two trained as members of Yale's varsity crew team, one trained exclusively by running, and one trained by running and cycling. As a result, each probably adapted to the mode of training inherent to each sport, magnifying the degree of interindividual variability within this small group.

Another point of variability in this experiment was the amount of beverage consumed by the participants . Each was required to drink 250 ml of fluid every fifteen minutes, regardless of body size. D.S., who weighed only 55 kg, consumed as much beverage as N.S., who weighed 85 kg. As a result, the carbohydrate drink replaced a much greater proportion of D.S.'s fluid and

carbohydrate losses than for N.S. This led to much interindividual variability. Future studies should be designed to give each subject an equivalent amount of drink relative to his or her body weight.

Future studies should also examine the role of K^+ in hydration and rehydration. As suggested by Nose et al[75], since K^+ is the major intracellular ion, its inclusion in rehydration beverages should improve the replacement of total body water losses by drawing more fluid into the intracellular space. The K^+ content of major commercial drinks is shown in Table 6.1.

CHAPTER 6

CONCLUSIONS

6.1 SUMMARY

We drew the following conclusions from the present study:

1) Drinking fluids containing 7% carbohydrate during exercise i) maintained increased levels of blood glucose, ii) caused preferential oxidation of glucose over fatty acids, and iii) increased the time to fatigue during prolonged exercise.

2) During the first half-hour of exercise, there was a greater decrease in plasma volume with ingestion of carbohydrate, relative to water. This was most likely due to an initial delay in gastric emptying related to the caloric content of the carbohydrate drinks.

3) There was no attenuation of the reduction in plasma volume seen during exercise when drinking carbohydrate in a 0.215% or 0.45% NaCl solution.

4) Drinking carbohydrate in a 0.45% NaCl solution may compromise thermoregulatory capacity. In our study, differences between CHO$_{Na}$ and CHO$_{Na}$ or Placebo were not statistically significant.

We hypothesized that the ingestion of additional sodium might cause an elevation in plasma osmolality and sodium which would inhibit body cooling. However, our osmolality and sodium data could not conclusively support this hypothesis.

6.2 RECOMMENDATIONS

Based upon the results of this study and the literature, we can make the following recommendations regarding the consumption of carbohydrate and electrolyte supplemented fluids during exercise.

1) Hydration during exercise of any duration is important, especially in a warm environment.

2) During exercise of less than two hours' duration, there is probably no advantage to the consumption of any drink other than plain water.

3) During exercise of over two hours' duration, consumption of carbohydrate beverages can prolong the time to fatigue.

4) Carbohydrate beverages should be relatively low in Na^+ to prevent any interference with thermoregulation.

5) *Rehydration* beverages consumed after exercise should contain higher amounts of Na^+ and K^+ to more rapidly and completely replace total body water losses by maintaining the dipsogenic drive.

The carbohydrate, sodium, and potassium composition of some popular exercise drinks are shown in Table 6.1. Good luck with your training program!

CHAPTER 7

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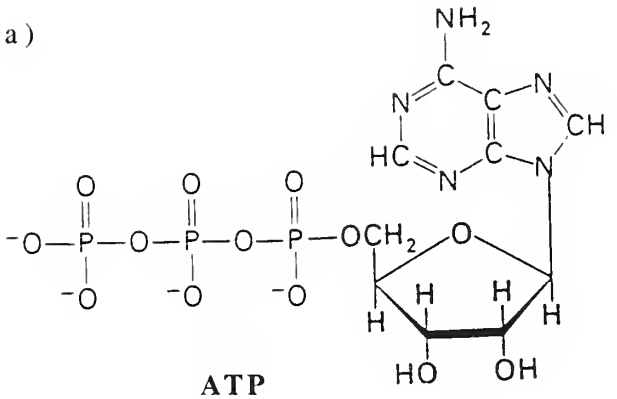
CHAPTER 8

TABLES AND FIGURES

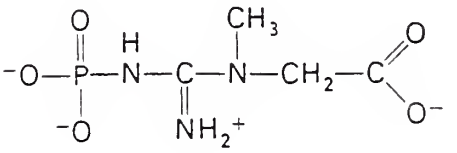
FIGURE 1.1 - Elements of Human Metabolism

a)



ATP

b)



Creatine Phosphate

c)

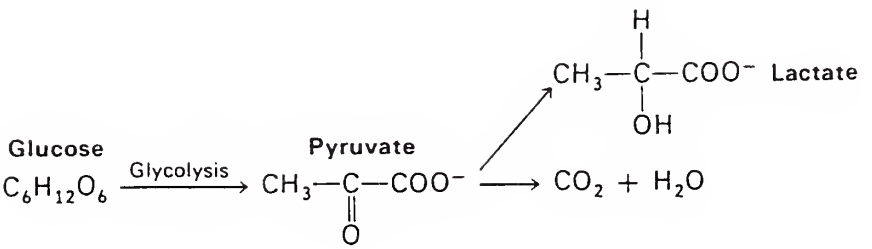


Figure 1.1c: A simplified drawing of the anaerobic (upper) and the aerobic (lower) pathways for glucose oxidation (Reprinted from Stryer, L. Biochemistry, with permission.)

d)

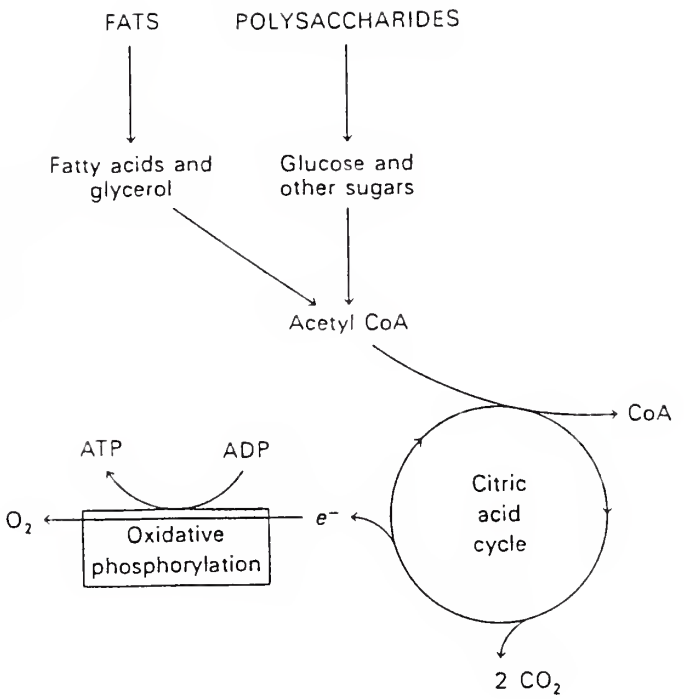


Figure 1.1d: Aerobic metabolism of fats and carbohydrates. A molecule of glycerol or a fatty acid turns the citric acid cycle once; a molecule of glucose turns it twice. (Reprinted from Stryer, L.Biochemistry, by permission.)

Figure 1.2 - Oxygen Uptake During Exercise

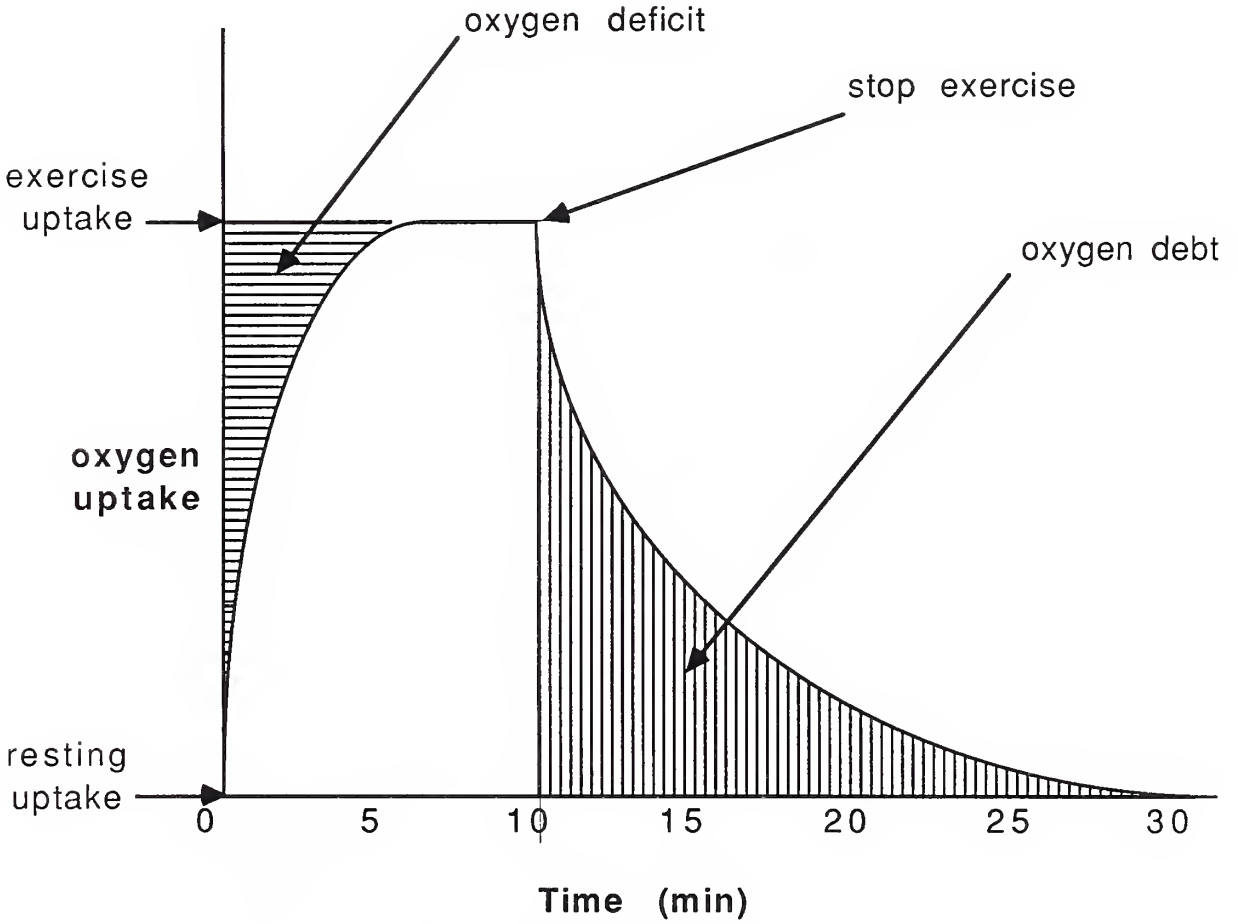


Figure 1.2: Drawing of oxygen uptake during ten minutes of submaximal exercise. The oxygen deficit is the oxygen needed at the onset of exercise, but is not yet available to exercising muscles. The oxygen debt is the extra oxygen carried to and used by the exercised muscles to repay the oxygen deficit.

Figure 1.3 - Test of Maximal Aerobic Power

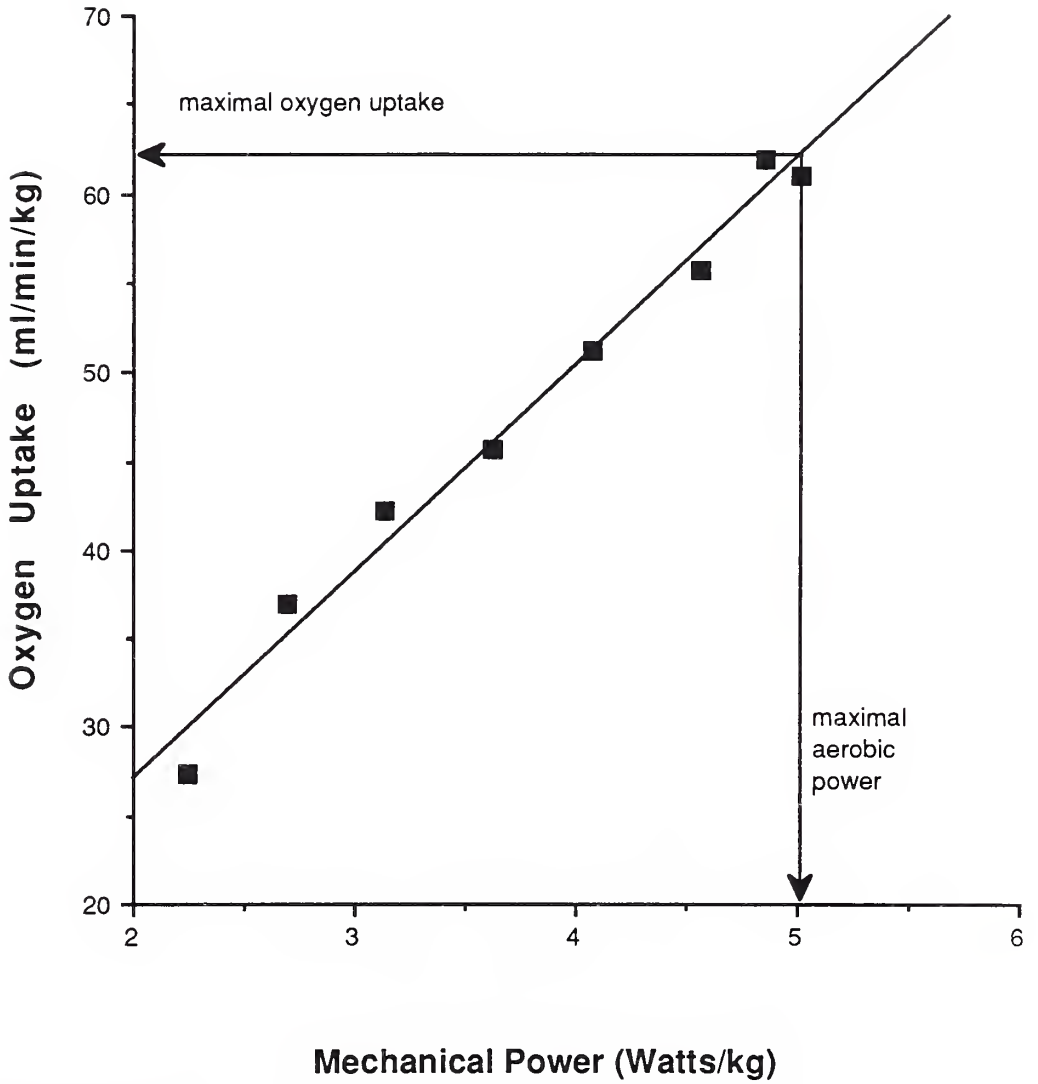


Figure 1.3: Results of maximal aerobic capacity test for volunteer T.Z. As he reaches his maximal oxygen uptake, additional power can be generated only through anaerobic processes.

Figure 1.4 - Bohr's Effect

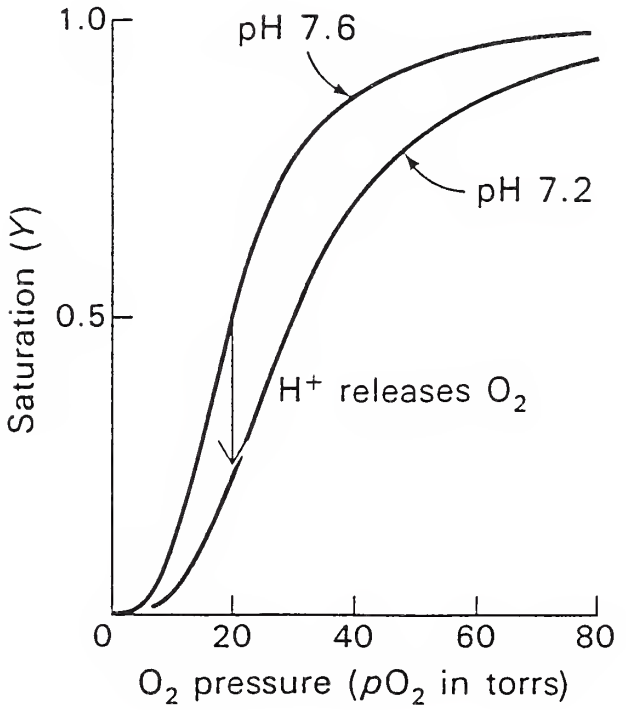


Figure 1.4: An illustration of Bohr's effect. As the plasma [H^+] rises (and pH falls), the O2 carrying capacity is reduced by the competition of H+ for O2 binding positions. This results in the release of greater amounts of O2 in acidotic, exercising muscles (Reprinted from Stryer, L. Biochemistry, with permission).

Figure 1.5 - Total Body Water By Fluid Compartment

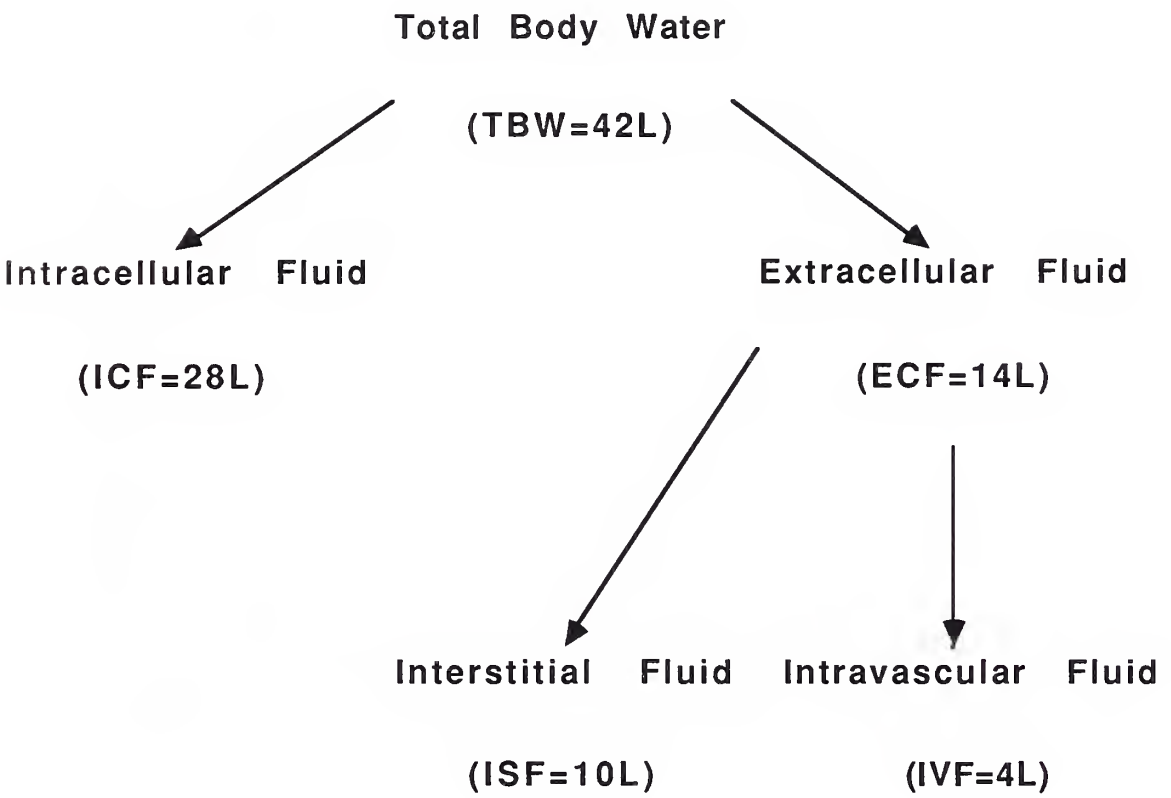


Figure 1.5: The division of body fluids by compartment for a 70 kg male. Note that the intravascular volume is only 10% of total body water, yet changes in this compartment are monitored by the brain to determine overall hydration status.

Figure 1.6 - Forces Affecting Fluid Balance During Exercise

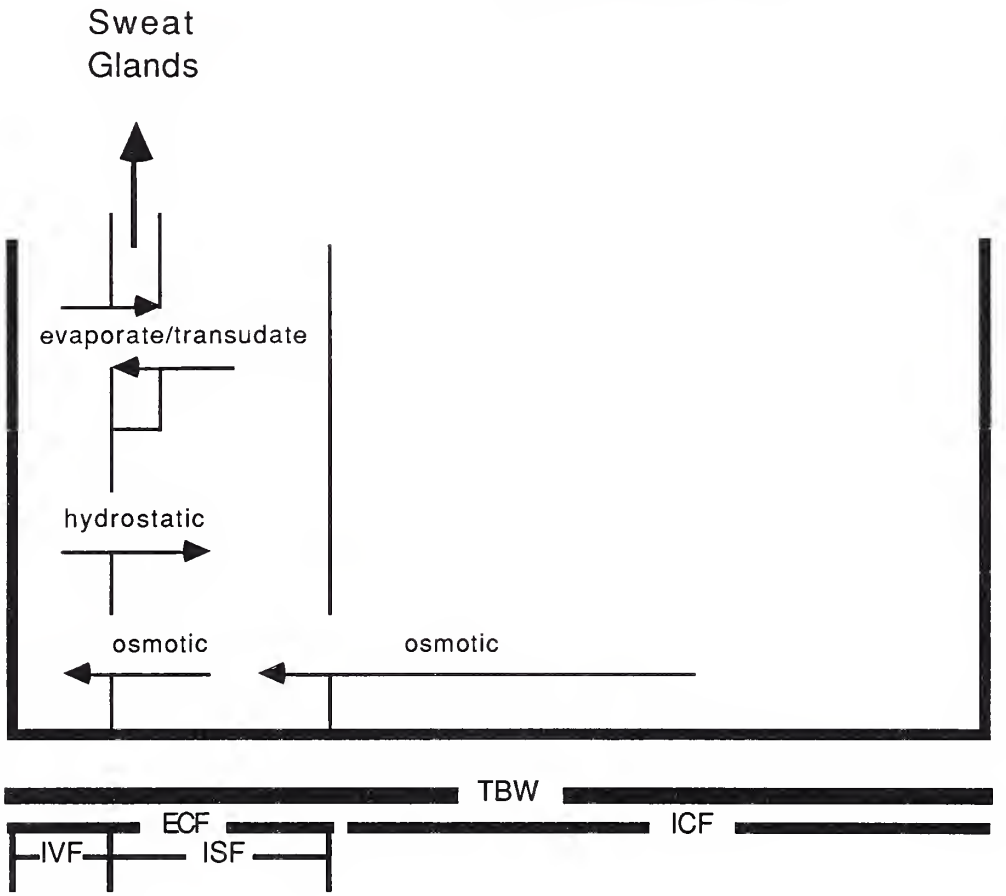
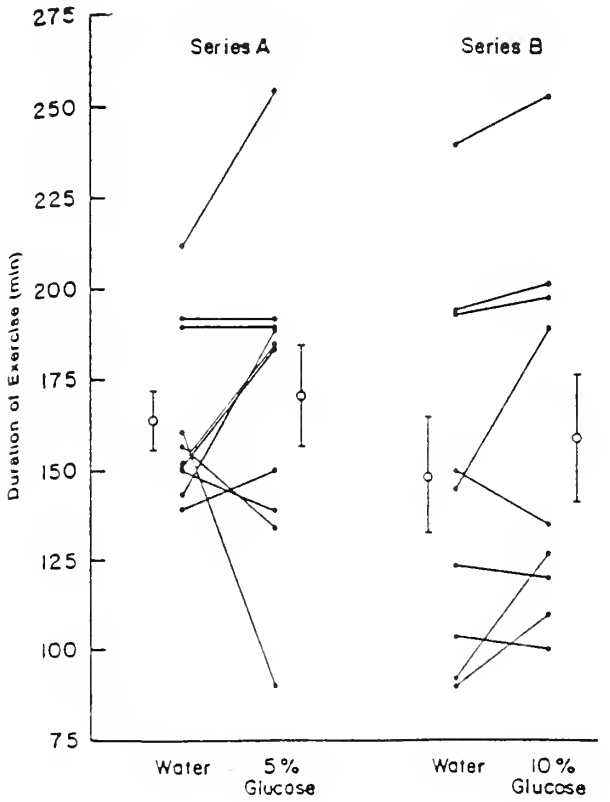


Figure 1.6: Schematic depiction of forces between body fluid compartments during exercise. Note that the sweat glands lie "between the IVF and ISF; its hypotonic secretions are derived from both compartments.

Figure 1.7 - Data from Felig et al

(see Section 1.4.2.2)



Duration of Exercise during Ingestion of Water, 5 per Cent Glucose (Series A), and 10 per Cent Glucose (Series B).

The value obtained for each subject during the water study is connected by a line with the value observed for the same subject in the glucose study. The horizontal and vertical lines adjacent to the individual values represent the mean ±S.E.M. The mean duration of exercise with glucose ingestion was not significantly different from that observed with water ingestion in either Series A or Series B.

Figure 1.8 - Electrolyte Levels In Body Fluids

SOLUTE	PLASMA (mEq/L)	ISF (mEq/L)	ICF (mEq/L)
Sodium	142	145	10
Potassium	4	4.1	159
Chloride	104	117	3
Bicarbonate	24	27	7
Proteins	14	<0.1	45
Glucose	4.7	5	---

Figure 1.9 - Theories of the Dipsogenic Stimulus

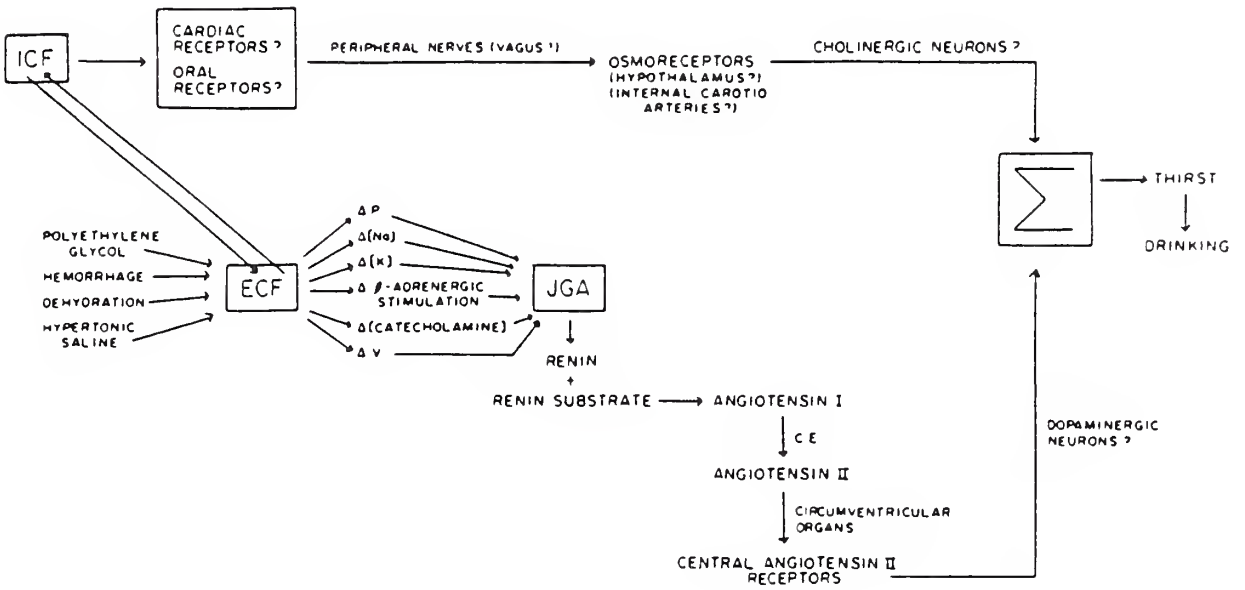


Figure 1.9: model illustrating two major pathways—osmoreceptors (above) and angiotensin (below), and associated factors for induction of fluid intake. Synthesized from Oatley, K. Simulation and theory of thirst. Epstein, A. N.; Kissileff, H. R.; Stellar, E., eds. *The neuropsychology of thirst: new findings and advances in concepts.* Washington, DC: Winston & Sons; 1973: 199–223.

Table 3.1 - Characteristics of Volunteers

Name	Age	Sex	Weight (kg)	VO2 Max (ml/min/kg)
T.Z.	23	M	66.7	61.9
D.S.	23	M	59.8	56.4
N.S.	21	M	87	61.2
A.P.	21	M	78.8	54.6
M.M.	22	F	43.6	57.3

Table 3.2 - Drink Sequence for Each Volunteer

Volunteer	Trial #1	Trial #2	Trial #3
T.Z.	Placebo	CHO/Na	CHO
D.S.	CHO	Placebo	CHO/Na
N.S.	Placebo	CHO/Na	CHO
A.P.	CHO	CHO/Na	Placebo

Table 3.3 - Composition of Trial Beverages

Beverage	Sweetener	% Sodium	% Potassium
Placebo	aspartame	0.00%	0%
CHO	5% GP / 2% fructose	0.22%	0.19%
CHO/Na	5% GP / 2% fructose	0.45%	0.19%

Table 4.1 - Time to Fatigue (min)

Volunteer	Placebo	CHO/.22% NaCl	CHO/.45% NaCl
T.Z.	137	150	180
D.S.	156	138	180
N.S.	150	160	165
A.P.	144	180	150
MEAN ± SD	147±8	157±18	169±14

Time to Fatigue (All Placebo Trials)		Time to Fatigue (All CHO Trials)	
MEAN	147	MEAN	163
SD	8	SD	16

Figure 4.2 - Changes in Blood Glucose with Exercise

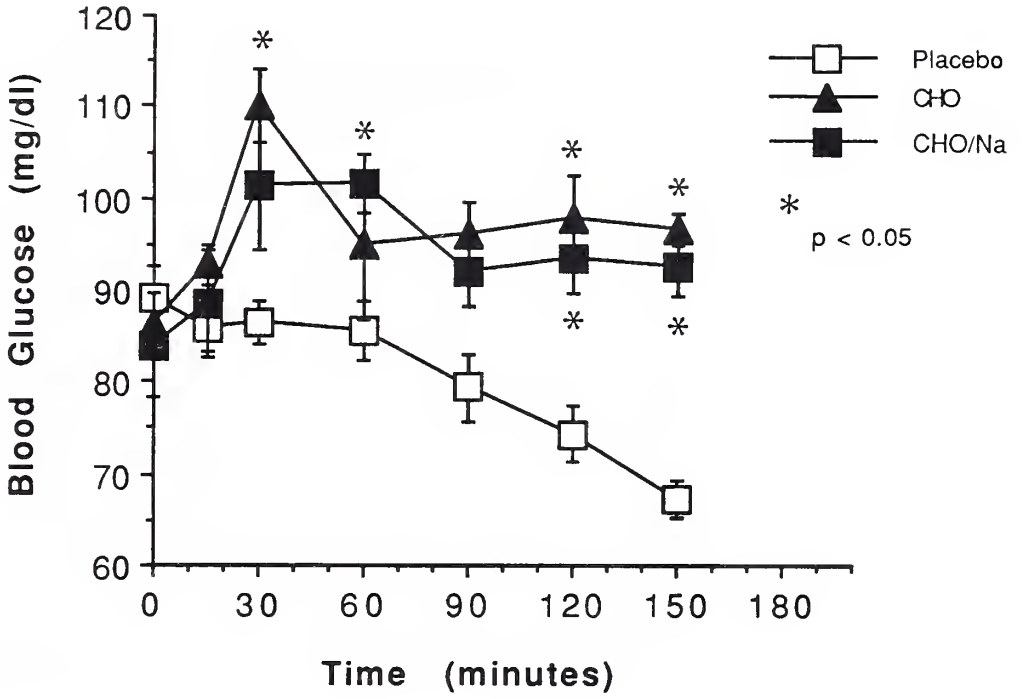


Figure 4.2: Blood was drawn from an antecubital vein catheter at regular intervals and glucose concentration was measured on a glucose analyzer.

Table 4.2 - Blood Glucose Data (mg/dL)

Time (min)	0	15	30	60	90	120	150
PLACEBO							
T.Z. 1	92	84	87	88	77	70	70
D.S. 2	81	80	80	77	70	70	64
N.S. 1	97	92	90	90	86	83	72
A.P. 3	87	88	89	89	84	76	65
MEAN ± SEM	89±3	86±3	87±2	86±3	79±4	74±3	68±2
CHO/0.22% NaCl							
T.Z. 3	90	92	101	106	96	93	94
D.S. 1	89	89	119	77	100	111	101
N.S. 3	91	99	107	111	103	97	98
A.P. 1	76	92	114	86	86	90	95
MEAN ± SEM	86±4	93±2	110±4	95±8	96±4	98±5	97±2
CHO/0.45% NaCl							
T.Z. 2	98	97	104	108	101	91	96
D.S. 3	71	72	81	92	83	85	88
N.S. 2	81	95	115	105	90	96	87
A.P. 2	86	91	107	102	94	102	101
MEAN ± SEM	84±6	89±6	102±7	102±3	92±4	93±4	93±3

Table 4.3 - Respiratory Quotient Data

Time (min)	20	50	80	110	140
PLACEBO					
T.Z. 1	0.84	0.71	0.70	0.75	
D.S. 2	0.93	0.80	0.90	0.92	0.86
N.S. 1	0.80	0.77	0.76	(0.69)	(0.68)
A.P. 3	0.86	0.77	0.85	0.82	0.79
MEAN ± SEM	0.86±0.03	0.76±0.02	0.80±0.04	0.79±0.05	0.78±0.05
CHO					
T.Z. 3	0.99	0.92	0.91	0.86	0.73
D.S. 1	0.95	0.93	0.93	0.92	
N.S. 3	(0.74)	(0.74)	(0.71)	(0.68)	0.68
A.P. 1	0.90	0.89	0.87	0.83	0.82
MEAN ± SEM	0.89±0.06	0.87±0.04	0.85±0.05	0.82±0.05	0.74±0.04
CHO/NA					
T.Z. 2	0.96	0.90	0.85	0.84	0.83
D.S. 3	0.95	0.91	0.87	0.82	0.84
N.S. 2	(0.84)	(0.84)	0.79	0.80	0.76
A.P. 2	0.90	0.89	0.78	0.74	0.74
MEAN ± SEM	0.91±0.03	0.89±0.02	0.82±0.02	0.80±0.02	0.79±0.02

Figure 4.3 - Changes in Respiratory Quotient

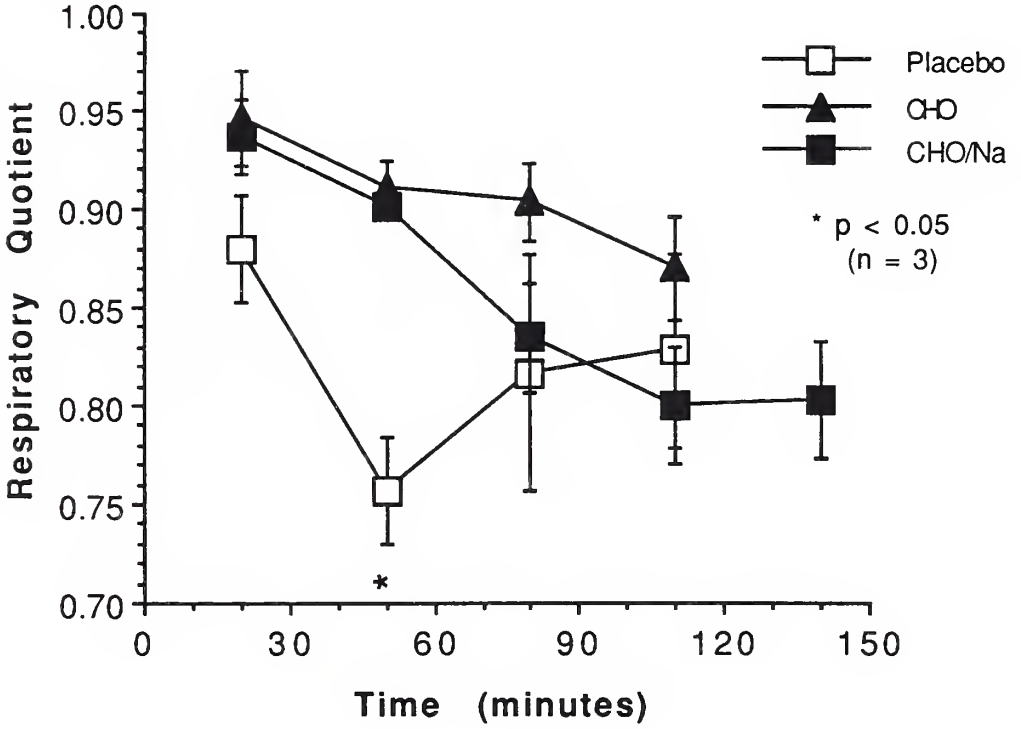


Figure 4.3: Respiratory quotient was determined by measurement of expired oxygen and carbon dioxide, as described in section 3.3.2 of the text.

Table 4.3a - Respiratory Quotient Data (n = 3)

Time (min)	20	50	80	110	140
PLACEBO					
T.Z. 1	0.84	0.71	0.70	0.75	
D.S. 2	0.93	0.80	0.90	0.92	0.86
A.P. 3	0.86	0.77	0.85	0.82	0.79
MEAN ± SEM	0.88±0.05	0.76±0.05	0.82±0.10	0.83±0.09	0.82±0.05
CHO					
T.Z. 3	0.99	0.92	0.91	0.86	0.73
D.S. 1	0.95	0.93	0.93	0.92	
A.P. 1	0.90	0.89	0.87	0.83	0.82
MEAN ± SEM	0.95±0.04	0.91±0.02	0.90±0.03	0.87±0.05	0.77±0.07
CHO/NA					
T.Z. 2	0.96	0.90	0.85	0.84	0.83
D.S. 3	0.95	0.91	0.87	0.82	0.84
A.P. 2	0.90	0.89	0.78	0.74	0.74
MEAN ± SEM	0.94±0.03	0.90±0.01	0.83±0.05	0.80±0.05	0.80±0.05

Figure 4.4 - Reduction in Plasma Volume

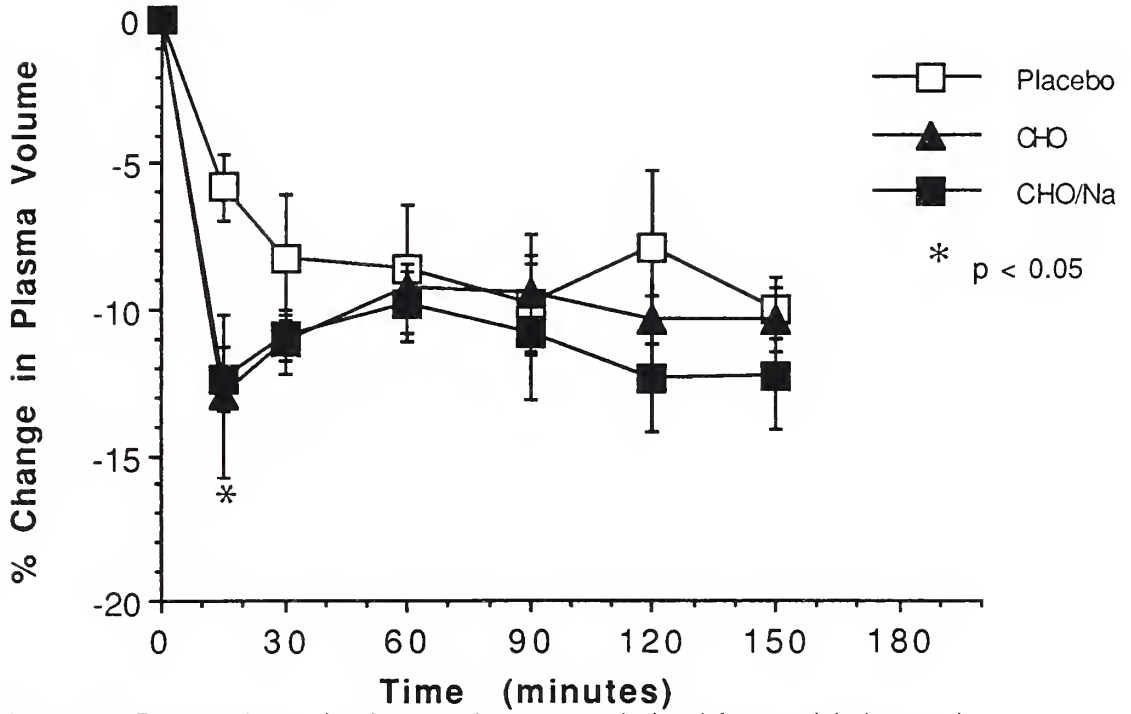


Figure 4.4: Percent change in plasma volume was calculated from serial changes in hematocrit and hemoglobin during exercise (see section 3.4.3 of the text)

Table 4.4 - Plasma Volume Data (% Change)

Time (min)	t = 0 (Hb)	t = 0 (Hct)	15	30	60	90	120	150
PLACEBO								
T.Z. 1	0.47	16.68	-5.6	-1.9	-3.3	-6.3	-5.1	-7.8
D.S. 2	0.44	15.00	-10.3	-10.9	-10.5	-8.6	-6.7	-9.0
N.S. 1	0.43	14.93	-3.6	-10.7	-13.4	-14.3	-15.9	-12.4
A.P. 3	0.44	14.54	-3.8	-9.5	-7.2	-10.2	-4.0	-10.9
MEAN ± SEM	0.45±0.01	15.29±0.48	5.8±1.6	8.2±2.1	8.6±2.2	9.9±1.7	7.9±2.7	10.0±1.0
CHO								
T.Z. 3	0.46	13.86	-14.5	-10.2	-9.6	-12.8	-11.8	-12.9
D.S. 1	0.43	15.56	-19.9	-14.0	-9.9	-3.6	-8.0	-7.6
N.S. 3	0.42	14.31	-10.5	-11.5	-9.9	-11.5	-10.8	-10.5
A.P. 1	0.44	15.16	-7.0	-8.6	-7.6	-9.9	-10.8	-10.5
MEAN ± SEM	0.44±0.01	14.72±0.39	13.0±2.8	11.1±1.1	9.2±0.6	9.4±2.0	10.4±0.8	10.4±1.1
CHO/NA								
T.Z. 2	0.45	15.89	-11.0	-11.0	-9.0	-10.4	-8.6	-11.2
D.S. 3	0.44	14.88	-14.5	-13.7	-6.4	-5.0	-10.8	-10.8
N.S. 2	0.44	16.11	-10.0	-10.0	-10.2	-11.6	-13.3	-9.3
A.P. 2	0.44	15.66	-14.0	-11.4	-12.8	-16.2	-17.0	-17.8
MEAN ± SEM	0.44±0.00	15.64±0.27	12.4±1.1	11.5±0.8	9.6±1.3	10.8±2.3	12.4±1.8	12.3±1.9

Figure 4.5 - Changes in Heart Rate

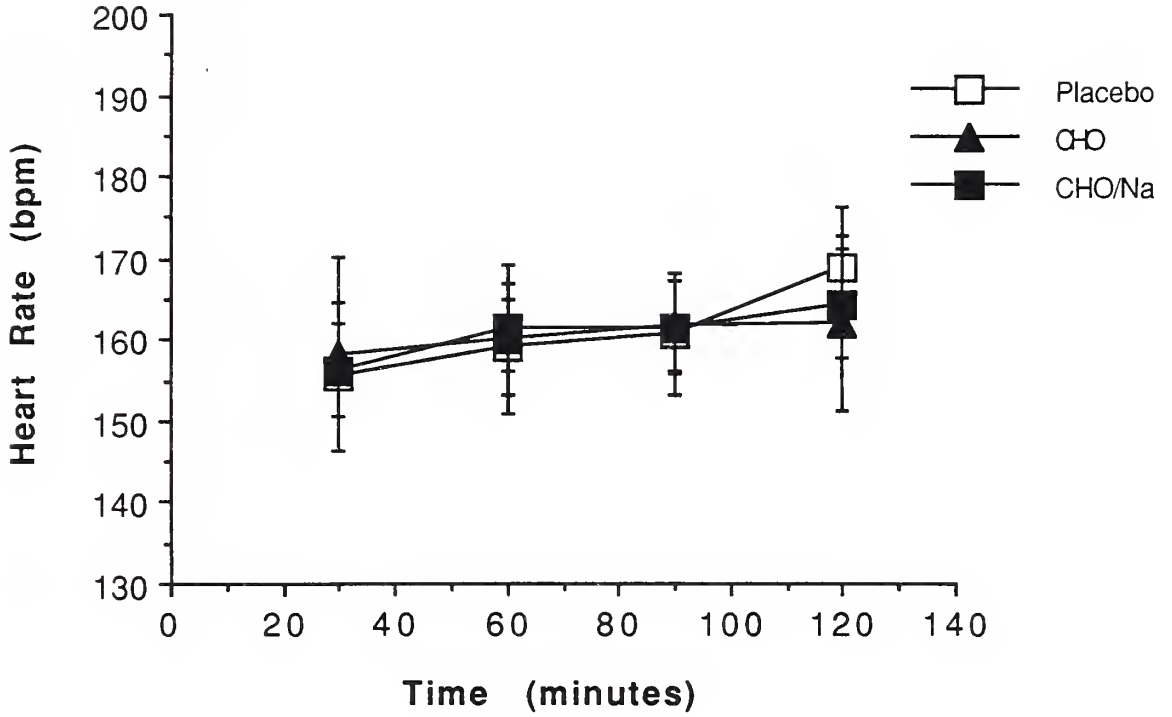


Figure 4.5: Heart rate was measured every 30 minutes by electrocardiographic analysis of lead II.

Table 4.5 - Heart Rate Data (bpm)

Time (min)	30	60	90	120
PLACEBO				
T.Z. 1	155	162	163	165
D.S. 2	168	166	170	180
N.S. 1	146	153	152	166
A.P. 3	153	156	158	165
MEAN ± SD	156±9	159±6	161±8	169±7
CHO				
T.Z. 3	153	157	161	156
D.S. 1	176	173	170	178
N.S. 3	154	152	159	158
A.P. 1	150	158	157	156
MEAN ± SD	158±12	160±9	162±6	162±11
CHO/NA				
T.Z. 2	160	168	165	160
D.S. 3	162	155	153	158
N.S. 2	150	162	165	172
A.P. 2	153	161	163	168
MEAN ± SD	156±6	162±5	162±6	165±7

Figure 4.6 - Increase in Core Body Temperature

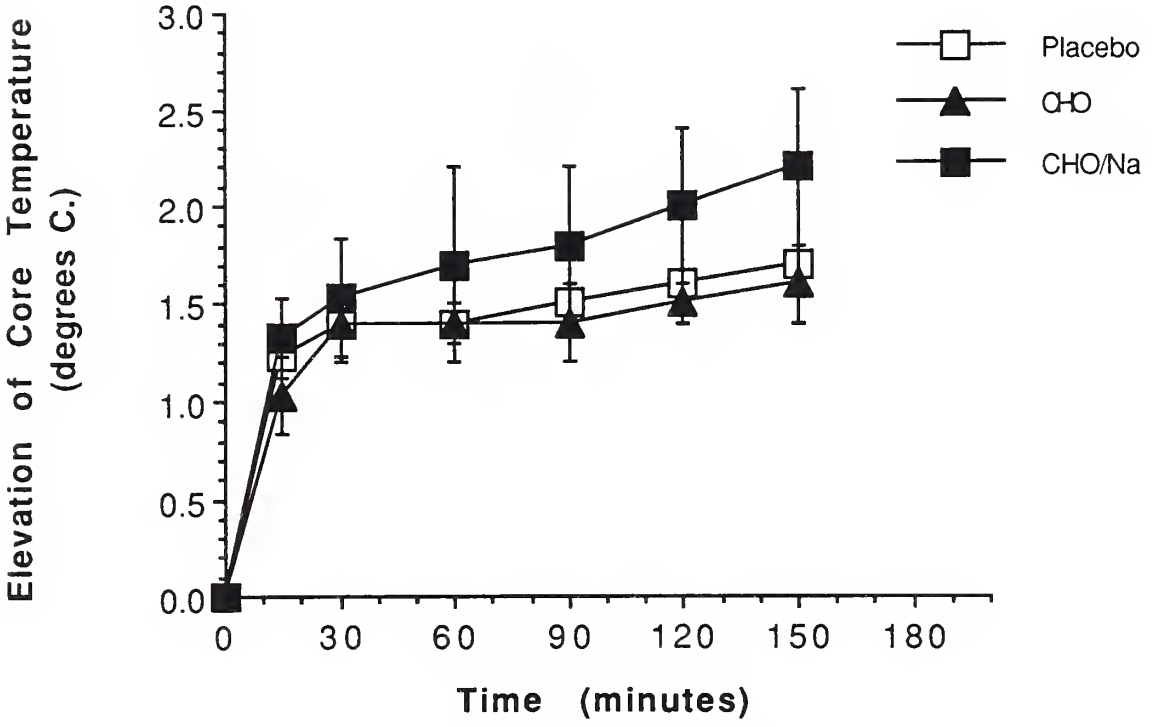


Figure 4.6: Core body temperature was continuously measured using an esophageal thermocouple inserted in the esophagus (see section 3.3.1 of the text).

Table 4.6 - Change in Core Temperature Data

Time (min)	0	15	30	60	90	120	150
PLACEBO							
T.Z. 1	36.7	1.7	1.8	1.8	1.9	1.9	2.0
D.S. 2	36.7	1.1	1.1	1.2	1.1	1.2	1.2
N.S. 1	36.2	0.9	1.4	1.4	1.4	1.7	1.9
A.P. 3	(36.6)	0.9	1.1	1.3	1.5	1.6	1.7
MEAN ± SEM	36.6±0.1	1.2±0.2	1.4±0.2	1.4±0.1	1.5±0.2	1.6±0.1	1.7±0.2
CHO							
T.Z. 3	36.6	1.9	2.1	2.1	2.1	2.1	2.2
D.S. 1	36.7	0.7	1.2	1.0	0.9	1.0	1.1
N.S. 3	36.0	0.5	1.3	1.3	1.4	1.7	1.7
A.P. 1	36.4	0.7	1.0	1.1	1.2	1.2	1.3
MEAN ± SEM	36.4±0.2	1.0±0.3	1.4±0.2	1.4±0.2	1.4±0.3	1.5±0.2	1.6±0.2
CHO/NA							
T.Z. 2	36.6	1.9	2.4	3.1	2.9	3.0	3.2
D.S. 3	36.5	1.1	1.0	1.2	1.5	1.8	1.8
N.S. 2	36.2	1.0	1.2	1.3	1.6	2.0	2.5
A.P. 2	36.6	1.1	1.2	1.2	1.1	(1.2)	(1.3)
MEAN ± SEM	36.5±0.1	1.3±0.2	1.5±0.3	1.7±0.5	1.8±0.4	2.0±0.4	2.2±0.4

Figure 4.7 - Increase in Plasma Osmolality

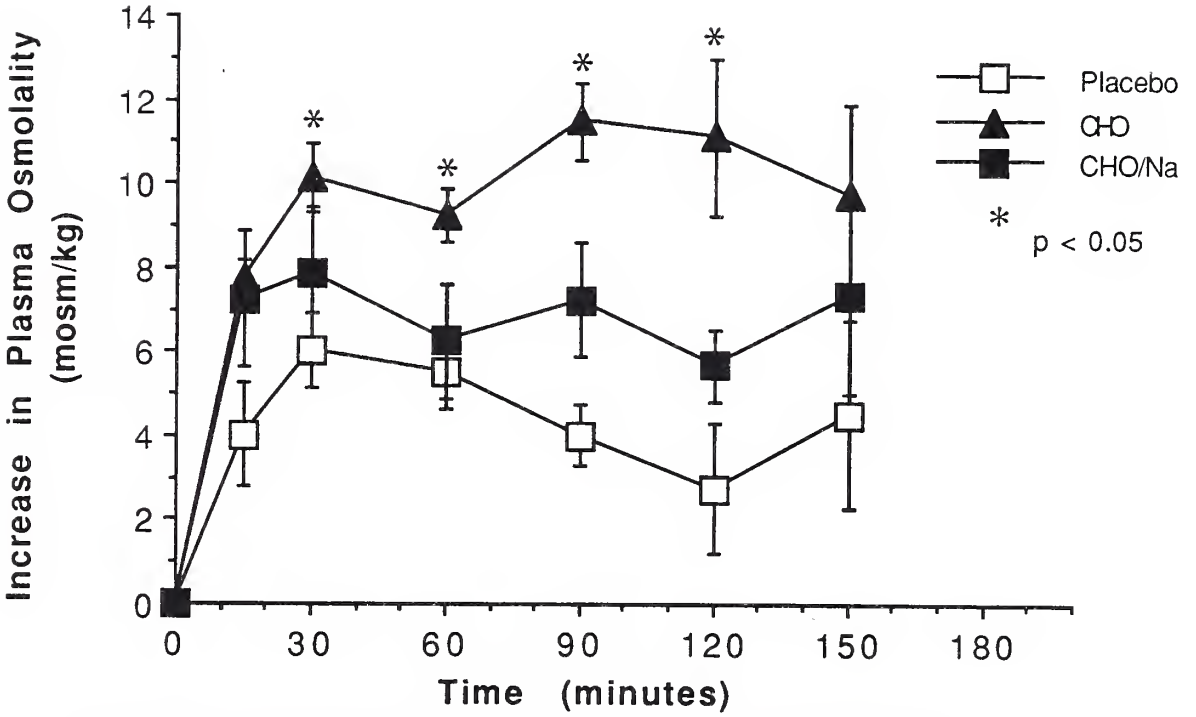


Figure 4.7: Blood was drawn from an antecubital vein at regular intervals; the osmolality of the plasma was determined by freezing point depression (see section 3.3.3 of the text).

Table 4.7 - Change in Plasma Osmolality Data

Time (min)	0	15	30	60	90	120	150
PLACEBO							
T.Z. 1	285.0	3.0	6.0	3.0	3.0	-1.0	-1.0
D.S. 2	284.5	6.5	7.5	6.5	2.5	4.5	8.5
N.S. 1	274.0	1.0	7.0	7.0	5.0	6.0	8.0
A.P. 3	278.5	5.5	3.5	5.5	5.5	1.5	3.0
MEAN±SEM	280.5±2.6	4.0±1.2	6.0±0.9	5.5±0.9	4.0±0.7	2.8±1.6	4.6±2.2
CHO							
T.Z. 3	282.0	6.5	10.5	8.0	10.5	7.5	7.0
D.S. 1	277.0	10.0	12.0	11.0	14.0	12.5	16.0
N.S. 3	279.0	8.0	8.0	9.0	10.0	10.5	9.0
A.P. 1	274.5	7.5	10.0	9.0	11.5	4.0	7.0
MEAN±SEM	278.1±1.6	8.0±0.7	10.1±0.8	9.3±0.6	11.5±0.9	8.6±1.9	9.8±2.1
CHO/NA							
T.Z. 2	278.5	6.0	11.0	9.5	10.0	6.5	8.0
D.S. 3	278.0	5.0	5.0	4.0	6.0	0.0	0.5
N.S. 2	280.0	10.0	10.0	7.5	9.0	6.5	11.0
A.P. 2	280.5	4.5	5.5	4.0	4.0	4.0	3.0
MEAN±SEM	279.3±0.6	6.4±1.2	7.9±1.5	6.3±1.4	7.3±1.4	4.3±1.5	5.6±2.4

Table 4.8 - Change in Plasma Sodium Data

Time (min)	0	30	60	90	120	150
PLACEBO						
T.Z. 1	0.0	3.7	2.1	(1.9)	1.7	0.7
D.S. 2	0.0	2.8	1.8	1.0	1.8	2.4
N.S. 1	0.0	2.8	0.7	0.5	0.5	0.7
A.P. 3	0.0	0.2	0.8	0.9	1.0	1.0
MEAN ± SEM	0.0	2.4±0.8	1.4±0.4	1.1±0.3	1.3±0.3	1.2±0.4
CHO						
T.Z. 3	0.0	(3.9)	(-0.6)	(6.2)	2.8	2.4
D.S. 1	0.0	2.0	4.2	2.1	2.8	3.5
N.S. 3	0.0	1.6	2.0	2.2	1.7	1.8
A.P. 1	0.0	0.2	0.4	0.6	-0.9	0.4
MEAN ± SEM	0.0	1.9±0.8	1.5±1.0	2.8±1.2	1.6±0.9	2.0±0.6
CHO/NA						
T.Z. 2	0.0	4.3	(-5.2)	(-1.1)	(-0.8)	4.1
D.S. 3	0.0	5.2	4.0	2.9	3.9	3.9
N.S. 2	0.0	1.8	2.9	2.3	3.3	3.5
A.P. 2	0.0	1.6	1.4	1.8	0.4	1.0
MEAN ± SEM	0.0	3.2±0.9	0.8±2.1	1.5±0.9	1.7±1.1	3.1±0.7

Figure 4.8 - Changes in Plasma Sodium

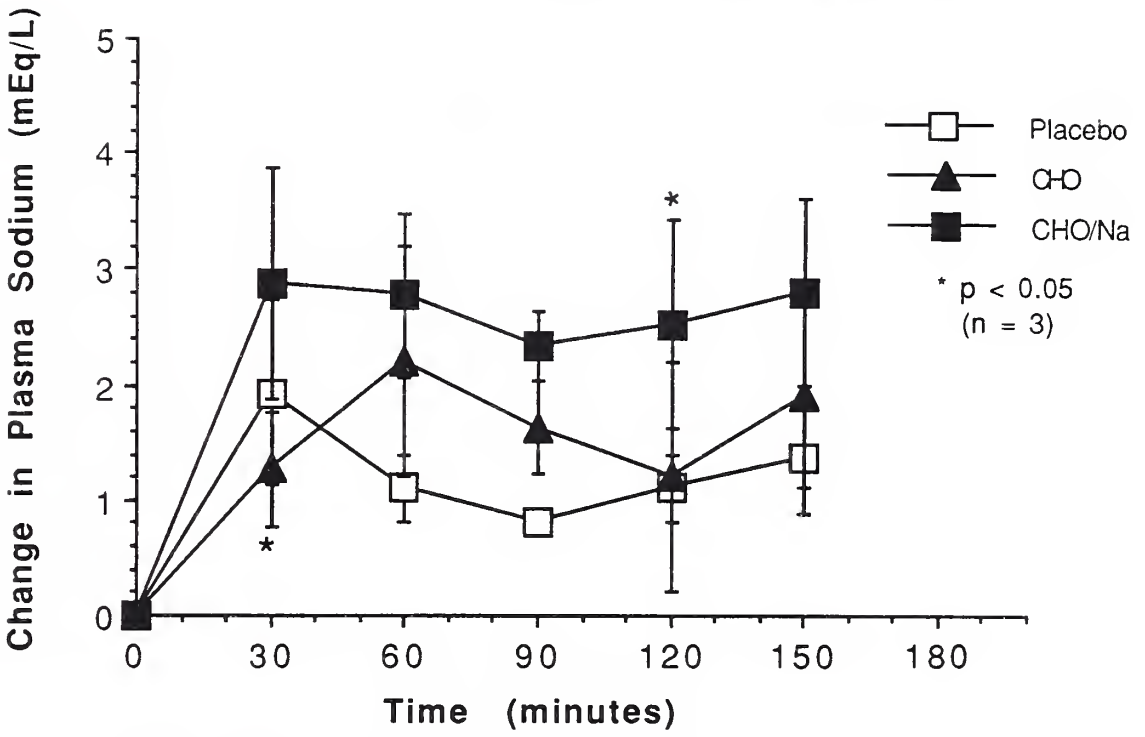


Figure 4.8: Blood was drawn from an antecubital vein at regular intervals; [sodium] of the plasma was measured with a flame photometer (see section 3.3.3 of the text).

Table 4.8a - Change in Plasma Sodium Data (n=3)

Time (min)	0	30	60	90	120	150
PLACEBO						
D.S. 2	0.0	2.8	1.8	1.0	1.8	2.4
N.S. 1	0.0	2.8	0.7	0.5	0.5	0.7
A.P. 3	0.0	0.2	0.8	0.9	1.0	1.0
MEAN ± SEM	0.0	1.9±0.9	1.1±0.4	0.8±0.2	1.1±0.4	1.4±0.5
CHO						
D.S. 1	0.0	2.0	4.2	2.1	2.8	3.5
N.S. 3	0.0	1.6	2.0	2.2	1.7	1.8
A.P. 1	0.0	0.2	0.4	0.6	-0.9	0.4
MEAN ± SEM	0.0	1.3±0.6	2.2±1.1	1.6±0.5	1.2±1.1	1.9±0.9
CHO/NA						
D.S. 3	0.0	5.2	4.0	2.9	3.9	3.9
N.S. 2	0.0	1.8	2.9	2.3	3.3	3.5
A.P. 2	0.0	1.6	1.4	1.8	0.4	1.0
MEAN ± SEM	0.0	2.9±1.2	2.8±0.8	2.3±0.3	2.5±1.1	2.8±0.9

Table 6.1 - Composition of Some Commercial Drinks

	EXCEED	GOOKINAID E.R.G.	GATORADE
CALORIES	295	190	210
CARBOHYDRATE (% BY WEIGHT)	7%	5%	6%
SOURCE	GlcPoly/Fructose	Glucose	Sucrose/Glucose
% SODIUM	0.22%	0.29%	0.46%
% POTASSIUM	0.19%	0.42%	0.10%
OSMOLALITY	250	265	NA

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