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Effects of Oral Glucose on Exercise Thermoregulation in Men After Water Immersion

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13. ABSTRACT (Maximum 200 words) To test the hypothesis that elevated blood glucose would attenuate the rise in exercise rectal temperature, six men age 35 ± S. D. 7 years participated in each of three trials preceded by 4-hr water immersion to the neck: (1) 2.0 g/kg body wt of oral glucose (33.8% wt./vol.) was consumed followed by 80 min controlled rest (Glu/Rest), and 70 min horizontal supine cycle exercise at 62.8% ± S.E. 0.5% (1.97 ± 0.02 L/min) of peak O ₂ uptake followed by 10 min recovery (2) with (Glu/Ex) and (3) without prior glucose (No Glu/Ex). Blood samples were taken at -25, 0, 15, 45, and 68 min of exercise and after +10 min of recovery for measurement of hemoglobin, hematocrit, and blood glucose. Both mean skin (\bar{T}_{sk}) (from six sites) and rectal temperatures (T_{re}) were monitored continuously. Sweat rate was measured by resistance hygrometry. The mean % ΔPV for the exercise trials was -12.2 ± 2.1%. Mean blood glucose for the Glu/Ex trial was higher than that of the No Glu/Ex trial (108.4 ± 3.9 and 85.6 ± 1.6 mg/dl, respectively, P < 0.05). At the end of exercise, T_{sk} for the Glu/Ex trial was lower than for No Glu/Ex (32.0 ± 0.3 and 32.4 ± 0.2°C, respectively, P < 0.05); T_{re} for the Glu/Ex trial was lower than for No Glu/Ex (38.22 ± 0.17 and 38.60 ± 0.11°C, respectively, P < 0.05); and forearm sweat rate for the Glu/Ex trial was lower than for No Glu/Ex (0.34 ± 0.04 and 0.43 ± 0.04 g/cm ² , respectively, P < 0.05). These data suggest that elevation of blood glucose prior to horizontal exercise following hypohydration attenuates the increase in body temperature without altering heat production or exercise hypovolemia.			
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Summary

To test the hypothesis that elevated blood glucose would attenuate the rise in exercise rectal temperature, six men age $35 \pm S. D. 7$ years participated in each of three trials preceded by 4-hr water immersion to the neck: (1) 2.0 g/kg body wt of oral glucose (33.8% wt./vol.) was consumed followed by 80 min controlled rest (Glu/Rest), and 70 min horizontal supine cycle exercise at $62.8\% \pm S.E. 0.5\%$ (1.97 ± 0.02 L/min) of peak O_2 uptake followed by 10 min recovery (2) with (Glu/Ex) and (3) without prior glucose (No Glu/Ex). Blood samples were taken at -25, at 0, 15, 45, and 68 min of exercise and after +10 min of recovery for measurement of hemoglobin, hematocrit, and blood glucose. Both mean skin (\bar{T}_{sk}) (from six sites) and rectal temperatures (T_{re}) were monitored continuously. Sweat rate was measured by resistance hygrometry. The mean % ΔPV for the exercise trials was $-12.2 \pm 2.1\%$. Mean blood glucose for the Glu/Ex trial was higher than that of the No Glu/Ex trial (108.4 ± 3.9 and 85.6 ± 1.6 mg/dl, respectively, $P < 0.05$). At the end of exercise, \bar{T}_{sk} for the Glu/Ex trial was lower than for No Glu/Ex (32.0 ± 0.3 and $32.4 \pm 0.2^\circ C$, respectively, $P < 0.05$); T_{re} for the Glu/Ex trial was lower than for No Glu/Ex (38.22 ± 0.17 and $38.60 \pm 0.11^\circ C$, respectively, $P < 0.05$); and forearm sweat rate for the Glu/Ex trial was lower than for No Glu/Ex (0.34 ± 0.04 and 0.43 ± 0.04 g/cm², respectively, $P < 0.05$). These data suggest that elevation of blood glucose prior to horizontal exercise following hypohydration attenuates the increase in body temperature without altering heat production or exercise hypovolemia.

Introduction

Before examining the effects of a particular perturbation on a system, whether mechanical or biological, it is important to consider what the normal or predictable responses to a primary stimulus are. Following this, one

may consider the application and probable result of a second stimulus delivered with the first; so it is with work/exercise experimentation on humans. The first part of the following work is focused on reviewing pertinent physiological responses to exercise stress under controlled environmental conditions. Several body systems interact during exercise to maintain homeostasis and this integration will be emphasized. Within this will be some discussion of the effects of drinking prior to and during exercise of carbohydrate beverages on thermoregulatory and cardiovascular responses. The remainder of this paper contains sections on the proposed test procedure, the results of those experiments, and finally a discussion of the significant results.

Review of Literature

Introduction

Many body regulatory functions are challenged to maintain homeostasis while optimizing efficiency during extended periods of exercise. Two functions so affected are metabolism and thermoregulation which are distinct yet interactive. For example, as exercise intensity increases, metabolism must also increase to meet skeletal muscle substrate needs. As metabolism increases, so does the production of metabolic heat. Heat may be transferred to the environment via four pathways: radiation, convection, conduction, and evaporation. The first two are continuous and non-regulated by the body but may be affected by clothing; conduction and evaporation are mediated by changes in skin blood flow, to conduct heat from working muscles to the skin and respiratory system, and by sweating, respectively. Greater emphasis is placed on evaporation to moderate increases in core temperature as the environmental temperature increases. The heat loss possible via sweating is about 2,426 J/g (Wenger, 1972).

Exercise induces an increase in core temperature which is proportional to the exercise load (Nielsen, 1938; Robinson, 1949; Nielsen and Nielsen, 1962). Furthermore, the core temperature response is more predictable when related to the relative intensity of work, or percent

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reduced, and this should reduce the role of evaporation for regulating temperature in hypohydrated individuals. The reduction in both total body and local sweat rate at a given core temperature during exercise is progressive as the level of hypohydration increases (Sawka et al., 1985, 1989; Sawka, 1992).

Regulation of Plasma Volume

The physiological mechanism by which hypohydration directly or indirectly mediates a reduction in sweat rate has yet to be proven, but it is probably related to the way in which exercise and thermoregulatory reflexes affect the distribution of available blood volume, as well as the effects of exercise on plasma volume and plasma tonicity. Local regulation of capillary filtration and absorption is considered to be governed by the balance of colloid osmotic and hydrostatic pressures between the intravascular and interstitial spaces (Starling, 1896; Landis and Pappenheimer, 1963). The Starling formula in its simplest form expresses this equilibrium:

$$\text{Rate of filtration} = k_f \cdot (\bar{P}_c - \bar{\Pi}_c), \text{ where}$$

k_f	=	capillary filtration coefficient
\bar{P}_c	=	effective hydrostatic mean transcapillary pressure
$\bar{\Pi}_c$	=	effective colloid osmotic mean transcapillary pressure

Working with these local "Starling Forces" is the more complex ability of the body to modulate regional blood flow through alterations in vascular smooth muscle tone. This will have a net effect on capillary blood flow, either increasing or decreasing capillary hydrostatic pressure and thereby favoring local and regional vascular filtration or absorption, respectively (Mellander and Johansson, 1968; Mellander, 1978). Furthermore, Cohn (1966) showed, with pharmacological manipulation, that systemic changes in the capillary pressure index were inversely related to plasma volume (PV).

The exercise posture (supine; sitting; standing) is a major consideration when discussing fluid balance because moving from sitting to supine and standing postures produces isosmotic hemodilution and hemoconcentration, respectively (Thompson et al., 1928; Waterfield, 1931a; Fawcett and Wynn, 1960; Eisenberg, 1963). The change of PV, approximately 10–15%, is relatively stable after 20 min in the new posture (Thompson et al., 1928; Tan et al., 1973). Although hemoconcentration and hemodilution approach stability by 20 min, complete stabilization of PV and its constituents may take 40 to 60 min (Hagan et al., 1978).

The mechanism by which upright posture hemoconcentration occurs is most likely related to changes in hydrostatic pressure in the lower limb capillary beds (Waterfield, 1931b). When one assumes an upright posture the increase in blood accumulation in the limbs, approximately 500 ml (Gauer and Thron, 1965), initiates a series of baroreceptor-mediated cardiovascular adjustments designed to maintain venous return to the heart. These adjustments result in tachycardia and vasoconstriction with no change in venous tone (Rowell, 1983). Because of the vasoconstriction there is reduced flow into the limb capillary beds; but without venoconstriction, the capillaries are exposed to venous back-pressure resulting in increased hydrostatic pressure, plasma filtration, and hemoconcentration (Hagan et al., 1978; Rowell, 1983). This situation is reversed after the body returns to the original posture, presumably by reduction in venous pressure and thereby a reduction in capillary hydrostatic pressure which favors absorption. Unless a stable baseline posture is established, conclusions drawn concerning the effects of environmental or exercise stress on plasma volume or constituents could be erroneous and more accurately reflecting a combination of postural responses and experimental stresses. The time required for plasma equilibration must also be considered.

When posture is controlled, within the first 10 min of cycle ergometer exercise there is hemoconcentration related almost solely to a decrease in PV (Kaltreider and Meneely, 1940; Harrison et al., 1975; Greenleaf et al., 1979a,b; Beaumont et al., 1981). The volume of plasma filtered (typically 10–15%) is related to the relative intensity of cycling (Diaz et al., 1979; Greenleaf et al., 1979a,b; Senay et al., 1980). The initial loss of PV is proportional to mean arterial pressure (MAP) which is directly related to relative exercise intensity (Miles et al., 1983). This relationship of PV and MAP during exercise is predictable from the Starling model and cardiovascular control mechanisms.

Cardiovascular Regulation During Exercise

With initiation of exercise there is a large decrease in vascular resistance in the working muscles; there is also systemic sympathetic stimulation and parasympathetic withdrawal (Guyton et al., 1973; Sagawa et al., 1974). Vasodilatation within the active muscle may lead to a 15-fold increase in blood flow which will occur with the nerve input from the muscle area blocked (Barcroft and Swan, 1953; Bevegard and Shepherd, 1967; Shepherd, 1967). Further, the level of vasodilatation, and therefore the level of blood flow, is related to the intensity of work (oxygen consumption) (Ekelund and Holmgren, 1967; Hermansen, 1973); local concentration increases of K^+ ,

H⁺, lactate, nucleotide breakdown products, or oxygen deficiency might be involved (Skinner and Powell, 1967; Mohrman and Sparks, 1973; Mellander, 1974).

Sympathetic stimulation affects the heart and peripheral circulation; the combination of vagal withdrawal and sympathetic stimulation increases heart rate and myocardial contractility (Guyton, 1955; Sarnoff, 1955; Braunwald et al., 1967; Cowley and Guyton, 1971). The peripheral effects of sympathetic stimulation are constriction of both arterial and capacitance vessels, and this increase in tone is proportional to the intensity of exercise (Duggan et al., 1953; Merrit and Weissler, 1959; Bevegard and Shepherd, 1967; Shepherd, 1967). These peripheral effects provide an approximately eight-fold increase in arteriolar resistance and expel approximately 40% of the blood contained in capacitance vessels (Mellander, 1960). Two areas affected by vaso- and venoconstriction are the skin and the splanchnic region. Resistance to skin blood flow is initially increased, but as a heat load develops with continued exercise this situation is reversed (Bevegard and Shepherd, 1967; Shepherd, 1967). This will be discussed later in more detail. Blood flow to the kidney, spleen, liver, and intestines is markedly reduced with exercise and may fall to 30% of control (Radigan and Robinson, 1949; Rowell et al., 1966; Castenfors and Piscator, 1967; Rowell, 1973; Clausen et al., 1973; Clausen and Trap-Jensen, 1974). Again, the increase in resistance and decrease in capacitance in these organs is proportional to the relative intensity of exercise (Rowell, 1974). These peripheral factors have a profound effect on maintaining mean circulatory pressure, the main driving force returning blood from the periphery to the heart (Guyton et al., 1973), which exceeds the arterial pressure decrease that would accompany the vasodilatation in working muscles (Donald, 1967; Donald et al., 1968; Bassenge et al., 1972, 1973).

Thus, sympathetic stimulation improves cardiac function and mean circulatory pressure which promotes venous return to the heart, and local vasodilatation in working muscles reduces resistance to venous return. These factors together can increase cardiac output four to six-times normal during exercise, while modifications of these factors singly would produce only modest improvements in cardiac output (Guyton, 1955). Cardiac output usually appears to approach a plateau in less than a minute, and this plateau level is related to the intensity of exercise.

These initial cardiovascular responses to exercise occur rapidly resulting in elevated arterial pressure and decreased vascular resistance within the working muscles; these responses result in increased capillary pressure leading to filtration of plasma into the muscle interstitial space. After 10 min of exercise, the resulting PV plateau

is most likely the result of an increase in interstitial fluid pressure produced by the plasma shift balanced by increased tissue pressure resulting from muscle contraction (Guyton and Coleman, 1968; Smith et al., 1976). Other factors aiding early PV stabilization are elevated plasma osmolality, and fluid absorption from tissue with reduced capillary pressure such as the viscera and non-working muscles (Lundvall et al., 1972; Rowell, 1974; Bennett and Rothe, 1981).

Thermoregulatory Control Mechanisms

As exercise continues the developing heat load engages thermoregulatory reflexes producing vasodilatation (Drappatz and Witzleb, 1970; Johnson et al., 1974; Johnson and Rowell, 1975) which results from stimulation of sympathetic active vasodilator nerves innervating arterioles in nonacral (limbs and trunk) skin. The threshold internal temperature for vasodilatation appears to be related to the relative exercise intensity (Taylor et al., 1988; Mack et al., 1991; Smolander et al., 1991); the variation in threshold from moderate to heavy work is about 0.8°C (Johnson, 1992). The exercise-induced upward shift in threshold temperature for vasodilatation is due solely to a delay in activation of the vasodilator system rather than to blunting of vasodilatation by the elevated vasoconstrictor activity responsible for cutaneous vasoconstriction at the initiation of exercise (Kellogg et al., 1991a,b). The presence of two mechanisms for regulating cutaneous blood flow during exercise evoke questions concerning coordination and control; their existence allows for a more graded and flexible response to differences in demand for blood flow by working muscle while maintaining some level of thermoregulatory control via modulations in skin blood flow.

The vasodilatation induces large increases in skin blood flow (SKBF) in 5–10 min (Johnson, 1992). As internal temperature rises with continued exercise, the rate of increase in SKBF is reduced reflecting only modest increases in cutaneous vasodilatation (Kamon and Belding, 1969; Johnson and Rowell, 1975). Skin blood flow eventually plateaus at approximately 50% of maximal SKBF responses at rest to an equivalent rise in internal temperature (Johnson, 1992). With high environmental temperature and/or humidity, where thermoregulatory steady-state is impossible, there is an abrupt reduction in the rate of increase of SKBF at an internal temperature of about 38°C, and little or no further vasodilatation while internal temperature rises to 39°C (Bregelmann et al., 1977). This apparent upper limit of SKBF during exercise appears to be due to attenuation of increasing active vasodilator activity as opposed to increasing sympathetic vasoconstrictor activity blunting

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responses to increased active vasodilator stimulation (Kenney et al., 1991; Kellogg et al., 1991b). It would appear then that a similar mechanism is involved in controlling both the lower and upper limits for SKBF.

The expected effect of increased skin blood flow on the cardiovascular system, as proposed by Krogh and developed by Rowell, is a shunting of blood away from the "muscle pump" to a region of "great capacitance" resulting in peripheral blood pooling and reduced vascular return to the heart. This response has been termed "cardiovascular drift" and includes declines in arterial and pulmonary pressures, lower central venous pressure, and reduced stroke volume (Krogh, 1912; Ekelund and Holmgren, 1967; Rowell, 1974, 1993). Reduction in ventricular filling pressure leads to altered stimulation of atrial baroreceptors resulting in increased sympathetic outflow, thus producing elevations of heart rate and vasoconstriction in the splanchnic and renal circulations and possibly in active muscle to maintain cardiac output (Rowell, 1974, 1983, 1993). Baroreceptor stimulation may also lead to a reduction in the level of vasodilator tone resulting in a decrease in the rate of rise in SKBF (Kenney et al., 1991; Kellogg et al., 1991a; Rowell, 1993).

There is a moderate progressive decline in plasma volume with continuous exercise beyond the initial loss of ~10% found typically within the first 10 min, and under extreme conditions the upper limit appears to approach 20% (Harrison, 1985). Such a decline in PV in concert with whole-body dehydration will inevitably place greater strain on the distribution of blood between working muscle and skin leading to more greatly impaired SKBF and further reductions in dry heat exchange and consequently a higher internal temperature. Experiments producing isosmotic hypovolemia have shown increased core temperature and a decline in SKBF and/or sweat rate (Nadel et al., 1980; Fortney et al., 1981a,b). Fortney and colleagues (1981b) have proposed that isosmotic hypovolemia could reduce sweat rate via reduced cardiac filling pressure and altered activity of atrial stretch receptors. These receptors have afferent neural projections into the hypothalamus (Gauer et al., 1970). Such modifications could affect the function of hypothalamic neurons associated with the central control of sweating rate.

In addition to progressive hypovolemia, sustained exercise results in progressive hyperosmolality and hypernatremia. The magnitude of rise of plasma osmolality is dependent on the intensity (Costill et al., 1974; Senay et al., 1980) and duration (Kolka et al., 1982) of exercise. The bulk of the plasma hyperosmolality is attributed to the increase in plasma Na^+ ion concentration $[\text{Na}^+]$ (Greenleaf et al., 1977, 1979a; Convertino et al., 1981). Potassium ion con-

centration $[\text{K}^+]$ also increases proportionally more than $[\text{Na}^+]$, reflecting an actual increase in content, probably released from contracting muscle, perhaps as a result of increased glycogenolytic activity (Kozlowski and Saltin, 1964; Kilburn, 1966; Harrison, 1985). Experimentally induced hyperosmolality and hypernatremia have been linked to elevated exercise core temperature beyond that of control groups (Greenleaf et al., 1974, 1976; Fortney et al., 1984).

Since sweat is normally hypotonic to plasma (Kirby and Convertino, 1986), whole body osmotic pressure should increase during extended exercise. It has been shown that hypohydration, whether by exercise or thermally induced, leads to an unequal distribution of fluid loss from the intracellular and extracellular spaces. In the early stages of hypohydration, the majority of the deficit comes from the extracellular space but, as water loss continues, a greater percentage comes from the intracellular space (Costill et al., 1976; Nose et al., 1983; Durkot et al., 1986). Nose and colleagues (1983) examined the distribution of water loss across tissue spaces and organs and found that the majority of fluid redistribution occurs in the intra- and extracellular compartments of muscle and skin. The brain and the liver showed no significant loss in water content. These findings indicate that the areas of greatest perfusion during exercise, namely the skin and muscle, provide the largest water reservoir for fluid loss through sweating; secondly, the principles of osmotic equilibrium are borne out in that fluid movement from the intracellular space becomes an ever larger factor as plasma osmotic pressure increases with continued exercise. Nose and colleagues reiterated that the rise in plasma osmolality provides an osmotic driving force pulling fluid from the intracellular space and defending the plasma volume of hypohydrated subjects (Nose et al., 1988).

It has been proposed that plasma hyperosmolality effects sweating and temperature regulation centrally through changes in tonicity of the extracellular fluid bathing regions of the hypothalamus, the so-called "osmotic sensor" (Senay, 1979; Kozlowski et al., 1980; Silva and Boulant, 1984). It's also possible that interstitial hypertonicity could locally inhibit fluid availability to the eccrine sweat gland (Greenleaf and Castle, 1971; Nielsen et al., 1971; Sawka, 1992). It has been shown experimentally that sweat rate is reduced when plasma osmolality is increased, even when isovolemia is maintained (Nielsen, 1974; Harrison et al., 1978; Fortney et al., 1984). Fortney and colleagues (1984) further indicated that this "... hypertonic effect (is) a shift in the threshold for sweating," and this shift "... may be due to mechanisms similar to those which shift the vasodilatory threshold." From the same study (Fortney et al., 1984) there is some evidence that cutaneous blood flow is reduced across

Carbohydrate Ingestion and Thermoregulation

Besides the performance enhancing effects of carbohydrate ingestion before and during exercise, recent animal research has suggested a thermic effect as well. With dogs exercising on a treadmill, restriction of glucose as a metabolite via insulin induced hypoglycemia and inhibition of glucose utilization by 2-deoxy-d-glucose led to increases in the change of rectal temperature (ΔT_{re}) beyond that of control (Turlejska and Nazar, 1977). The authors concluded that since both treatments reduce the availability of glucose for the CNS, metabolism would be enhanced to produce usable metabolic precursors with increased heat production as a by-product. In a follow-up study by Kruk and colleagues (1987), exercising dogs were infused with glucose, soybean oil to elevate free fatty acid (FFA) levels, and saline as control. As in the previous study, indices of metabolism were monitored including T_{re} and muscle temperature (T_m); oxygen uptake and plasma osmotic changes were also studied. Glucose treated dogs showed significantly lower T_{re} and T_m than control; FFA treated dogs showed the largest temperature increases. O_2 uptake was likewise reduced for the glucose treatment. The respiratory exchange ratio (RER) was significantly elevated for the glucose treatment indicative of high carbohydrate utilization; RER declined for the FFA treatment and control indicative of reduced glucose availability for metabolism and greater emphasis on FFA. Plasma osmolality rose moderately over the course of exercise with no difference between the treatments. The researchers concluded that high glucose availability led to reduced metabolism and lower heat production. Since previous work in the same laboratory indicated that high glucose availability led to reduced catecholamine concentrations during exercise (Kozlowski et al., 1981, 1983), one suggested cause for the observed decline in metabolic rate was a probable reduction in the secretion of catecholamines during the glucose treatment. A similar relationship between glucose and catecholamine concentrations has been observed recently (Hamilton et al., 1991).

From this review it should be evident that a complex interaction exists between whole-body water volume, plasma volume and plasma tonicity in maintaining optimal thermoregulation and their impact on sweat rate and

skin blood flow. Animal data imply that there may be a metabolic factor as well, perhaps relating to changes in substrate availability and how this may affect sympathetic tone, heat production, and possibly the central control of temperature regulation. Therefore, the purpose of this study will be to determine the effect of elevated blood glucose, through the consumption of a concentrated glucose-containing beverage, on thermal responses to exercise in hypohydrated human subjects. Skin and core temperature changes will be of greatest interest, with additional attention given to possible alterations in sweat rate and skin blood flow. Metabolism will also be indirectly monitored via on-line respiratory sampling, as well as blood-borne constituents, to observe any variations produced by glucose consumption.

Material and Methods

Subjects

The subjects for this study were 6 normal healthy male volunteers age $35 \pm SD 7$ years (table 1) who were paid for their participation. After obtaining their informed consent, each subject received a complete physical examination including a medical history, standard lab tests, and an electrocardiogram-monitored treadmill stress test at the Palo Alto Medical Clinic. All experimental testing was conducted in the Laboratory for Human Environmental Physiology and Water Immersion Facility at Ames Research Center by the primary investigator and trained staff.

Procedure

After receiving medical clearance, the subjects took a standard oral glucose tolerance test (OGTT) to screen for pre-diabetic sensitivity to glucose; all were normal. Then they performed one submaximal and two maximal short duration exercise tests to determine their peak oxygen uptake (peak $\dot{V}O_2$, L/min). The highest mean value for the two maximal trials was used to estimate the absolute exercise load necessary to produce 60% of the peak $\dot{V}O_2$. This load was then used for the two 70 min exercise bouts in the experimental phase.

Table 1. Subject anthropometry and physiological baseline data (mean \pm SD)

Age, yr	Ht, cm	Wt, kg	Peak oxygen uptake, supine		Plasma volume	
			L \cdot min ⁻¹	mL \cdot kg ⁻¹ \cdot min ⁻¹	mL	mL \cdot kg ⁻¹
35 \pm 7	1782 \pm 5.9	78.5 \pm 6.0	3.13 \pm 0.19	40.8 \pm 5.5	3385 \pm 545	43 \pm 6

The experimental phase consisted of three 8-hr blocks (fig. 1). Subjects arrived at 0645 hr in a fasted state. Each had been asked to eat an evening meal on the previous day (before 2200 hr) that was high in carbohydrate and low in fat and protein (no red meat). Each subject urinated and then was weighed. The composition of their breakfast was approximately 2.0 g/kg body wt carbohydrate (CHO) and 0.0 g/kg fat. The meal (tables 2 and 3) consisted of 237 ml fruit juice (Dole), 5–6 slices whole wheat bread (The Original Oatmeal Baking Co.; Portland, OR 97209),

and whole fruit preserves (Sorrel Ridge 100% Fruit; Sorrel Ridge Farm; Port Reading, NJ 07064). The subject ate all of his food allocation by 0730 hr, and was allowed to relax.

At 0755 hr the subject voided, was weighed in exercise shorts, and escorted to the water immersion tank. By 0810 hr he was immersed to the neck in thermoneutral (34.5°C) water, positioned supine and feet-down on a submerged plinth, and secured loosely by chest and ankle

Treatments

- Glucose/Exercise
- no Glucose/Exercise

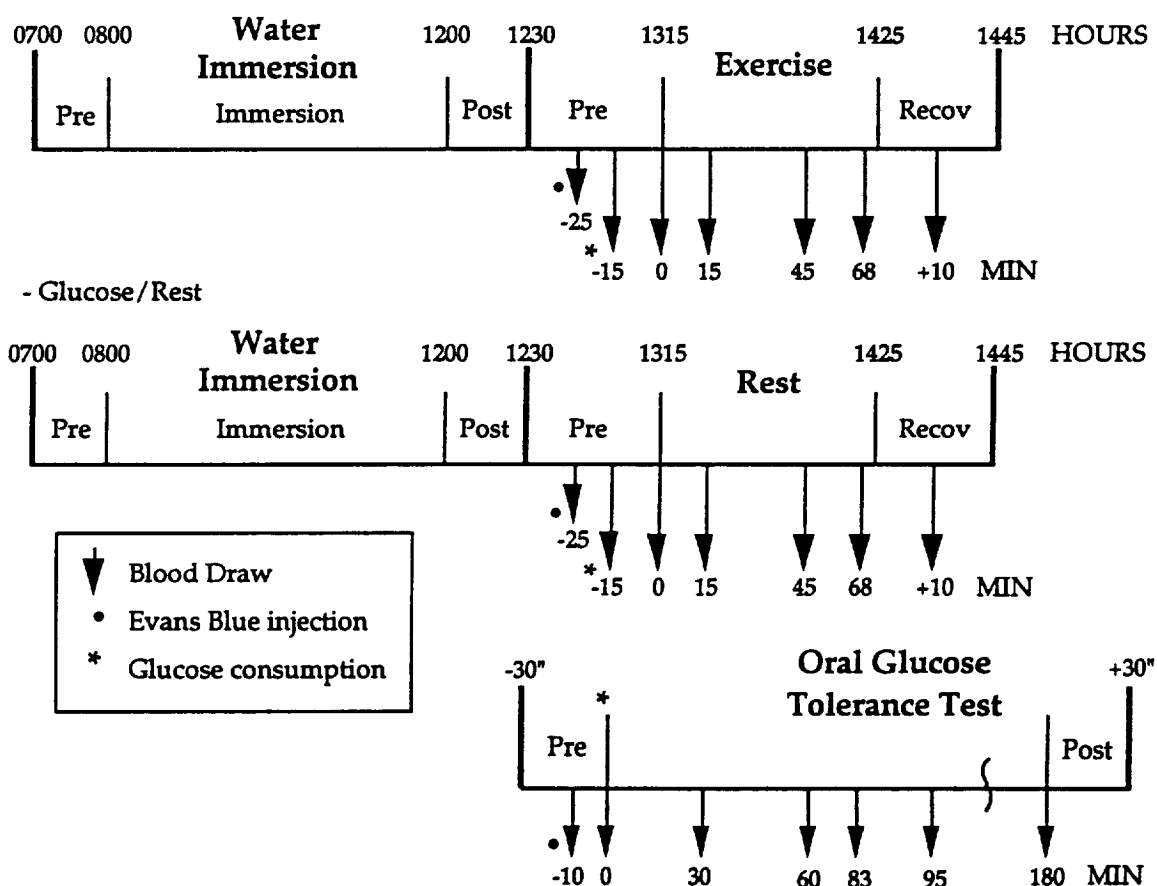


Figure 1. Test protocols.

Table 2. Pre-experimental meal and glucose beverage (Dolce C) composition

	Juice, ml	Bread, slice	Preserves, g	Dolce C, ml
Carbohydrate, g	0.1	20.0	0.5	0.3
Protein, g	0	4.0	0	0
Kcal	0.6	100.0	2.2	1.4

Table 3. Mean fuel intake supplied by the pre-experimental meal and the glucose beverage (mean \pm SD)

	Meal			Dolce C			
	Glu/Rest	No Glu/Ex	Glu/Ex	Glu/Rest	Glu/Ex	OGTT ^a	OGTT ^b
Carbohydrate, g	161.0 \pm 13.1	158.4 \pm 11.9	158.5 \pm 13.7	155.3 \pm 12.1	155.0 \pm 12.1	75.8 \pm 6.9	161.7 \pm 11.2
Protein, g	21.1 \pm 2.9	20.0 \pm 1.3	20.5 \pm 3.1	none	none	none	none
Volume, ml	none	none	none	459.6 \pm 35.7	458.2 \pm 38.8	224.3 \pm 20.5	478.5 \pm 33.2
Kcal	773.6 \pm 63.4	757.8 \pm 51.2	760.8 \pm 71.8	636.7 \pm 49.5	633.9 \pm 54.2	310.6 \pm 28.4	662.8 \pm 46.0

^aOGTT trial utilizing 1 g/kg body wt. glucose.

^bOGTT trial utilizing 2 g/kg body wt. glucose.

straps. A heating element suspended above the tank was adjusted for comfort. A television and VCR were available for entertainment. The subjects remained in the tank for four hr and stood just out of the water to void. Sequential urine volumes were pooled to determine total urinary loss during immersion.

At approximately 1200 hr the subject voided a final time, and then inserted a rectal probe thermistor to a depth of 12 cm. He was dried rapidly and lay on a gurney for transport to the exercise laboratory in an adjoining building where he was again weighed and returned to the gurney. This pre-exercise weight was used for determining the volume of glucose consumed by the subject prior to exercise in the H₂O/Glu/Rest and H₂O/Glu/Ex trials. The subject rested supine on the gurney for at least 30 min prior to the plasma volume determination (Hagan et al., 1978).

After returning to the gurney, an 18-gauge flexible nylon catheter was inserted into a major vein in the antecubital region of the subject's right arm by an experienced nurse. All blood withdrawals and Evans blue dye injections were made through this catheter. Then the subject was fitted with six skin thermistors, a laser Doppler probe, ECG electrodes, and three sweat measurement capsules. A thermistor was also inserted into the ear canal as an auxiliary measure of core temperature to that of the previously inserted rectal probe.

At 1245 hr environmental measurements including dry and wet bulb temperature, barometric pressure, and humidity using a psychrometer were made. At approximately 1250 hr the preliminary (pre) blood draw was taken and 2.5 ml of Evans blue dye was injected for blood volume determination. After a 10-min equilibration period the post-Evans blue (post-E.B.) dye blood draw was taken. If the experiment called for glucose he was assisted to a sitting position and drank the beverage as rapidly as possible (table 3). After two-thirds of the original volume had been consumed, a 15-min timer was started (T-15). At T-10 baseline heart rate (HR), blood pressure (BP), skin (T_{sk}) and rectal (T_{re}) temperature, subcutaneous blood flow volume and velocity, and pre-exercise sweat rate

data were recorded. At T-5 measurement of respiratory gases and ventilation was initiated. At T0 the pre-exercise baseline blood sample was taken and values for HR, BP, T_{sk}, T_{re}, Laser Doppler parameters, and sweat rate were recorded.

Then the subject began to exercise at approximately 60% of their peak $\dot{V}O_2$. Exercise was maintained for 70 min with continuous monitoring of HR, T_{sk}, T_{re}, subcutaneous vascular changes, and sweat rate. Oxygen uptake was monitored during the first 20 min and final 25 min of exercise. Blood samples were taken at 15, 45, and 68 min of exercise, and after 10 min of recovery (Rec) while still supine. Heart rate and BP were recorded at 10 min intervals. Systolic (SBP) and diastolic (DBP) pressure readings were used to calculate pulse pressure (PP) and mean arterial pressure (MAP) by standard formulae: PP = SBP - DBP; MAP = DBP + 1/3 PP.

The catheter was withdrawn after the Rec blood sample. After Rec measurements had been recorded, the subject was towel dried, weighed, offered water, asked how he felt, rested awhile, and then excused from the facility.

Oral Glucose Tolerance Test

Preliminary glucose tolerance testing of the subjects preceded their participation in the experimental trials. The protocol followed was a modification of a standard OGTT (Anonymous: 1969) (fig. 1). Each subject consumed 2.0 g/kg body weight of the beverage (33.8% glucose, wt./vol.), Dolce C; Hopping Bottling Co., Inc.; Sunnyvale, CA 94086) (table 3). The original glucose quantity ingested was 1.0 g/kg body weight, but results from four subjects showed that this quantity would not produce sustained elevation of blood glucose in resting, aerobically-trained individuals. A number of investigators found an attenuation in blood glucose elevation after glucose consumption in trained subjects (Bjorntorp et al., 1979; Le Blanc et al., 1979; Heath et al., 1983; Seals et al., 1984). The design of this study required significantly elevated blood glucose during exercise in the Glu/Ex

group over that of the No Glu/Ex group. Therefore, the dosage of glucose in the OGTT and experimental trials was increased to 2.0 g/kg. After beverage consumption the blood glucose levels were monitored over a 3 hr period.

Each subject arrived at the facility at least 6 hr postprandial. The subject was weighed and then placed on a gurney in a horizontal supine posture. After a 30 min equilibration period a teflon catheter was inserted into an antecubital vein. A blood sample was taken and then 2.5 ml of Evans blue dye was injected. After 10 min a second sample was taken. This dye-labeled sample was used to determine the subjects' ambulatory plasma volume, the pre-immersion baseline value.

The subject was assisted to a sitting posture and asked to drink the beverage as quickly as possible. After two-thirds of the volume had been consumed, the clock was started. Blood samples were taken at 30, 60, 83, 95, and 180 min after drinking. The first four sample times were selected to coincide with blood draws during the Exercise Phase of the experimental trials, and the 180 min draw was part of the clinical OGTT protocol (fig. 1). After completion of the final draw, the catheter was removed and the subject was excused.

Preliminary Exercise Testing

In most cases the subjects came to the laboratory on three separate occasions prior to the study for initial submaximal cycle ergometer familiarization and two peak $\dot{V}O_2$ test sessions. All exercise was done on a Quinton Imaging/Ergometer Table (Quinton Instruments Co.; Seattle, WA 98121) with the subjects in a horizontal, supine posture. They were instructed on efficient peddling to minimize discomfort in the legs. Ventilation and expired respiratory gas concentrations were monitored by open-circuit, indirect calorimetry employing an on-line analysis system. Expired gas flowed through a Rudolph valve with an attached model S-301 Spirometer (Pneumoscan), its composition measured with a model N-22 O_2 sensor and model S-3A1 O_2 analyzer, model P-61B CO_2 sensor and model CD-3A CO_2 analyzer (Ametek Applied Electrochemistry; Pittsburgh, PA 15238), and oxygen uptake calculated with a Vista computer interface and software (Vacumed; Ventura, CA 93003), and an IBM (model AT) PC. The gas analyzers were calibrated with standard laboratory gas prior to each data collection period. Heart rate was monitored with a three-lead ECG using a Hewlett Packard cardi tachometer (model 78905A) and ECG module (model 78203C; Hewlett Packard; Medical Products Group; Waltham, MA 02154). Blood pressure was monitored by the auscultatory method using a Riva-Rocci cuff and sphygmomanometer.

Sub-maximal and maximal test protocols began with a five min monitored rest period. The subject exercised at a load of 400 kpm for five min at or above 70 rpm which he could monitor via a display positioned at eye level. At the beginning of the fifth minute blood pressure was taken and heart rate recorded. During the submaximal test, the load was then increased to 900 kpm to elicit an O_2 uptake of approximately 50% of their peak. Since the subject's peak $\dot{V}O_2$ was unknown during the submaximal familiarization phase, his age predicted maximum heart rate and heart rate reserve were used for determining the 60% of peak ceiling for that protocol (Fletcher et al., 1990):

$$\text{Max HR, 60\%} = ((220 - \text{age}) - \text{rest HR}) \times 0.6 + \text{rest HR}$$

The subject exercised at this load for 2 min with BP and HR measured during the second minute. The load was then increased by 100 or 200 kpm to produce a HR of roughly 60% of their predicted maximum. This load was maintained for 2 min with BP and HR measured during the final minute. The load was then lowered to 400 kpm allowing the subject to cool down until his heart rate reached or fell below 120 beats/min.

During the first peak test the initial 400 kpm load was followed by the load which had elicited 60% of the predicted maximum heart rate during the submaximal familiarization ride. This load was maintained for 2 min and was followed by an increase of 200 kpm which was again maintained for 2 min. A third load increase of 200 kpm followed and, in most cases, the subjects failed to maintain at least 60 rpm for the full 2 min and ceased pedaling. If a subject completed this third load, a fourth 200 kpm increase ensued (Greenleaf et al., 1989). Blood pressure and HR were monitored during the 2nd min of each load. A second peak test was done some days later to verify the results of the first.

Blood Sampling, Analysis, and Requirements

Blood sampling was done via an 18-gauge intravascular teflon catheter (Quik-Cath; Baxter Healthcare Corp.; Deerfield, IL 60015) in an antecubital vein inserted by an experienced nurse (NursesNetwork, San Jose, Calif.). The catheter was kept patent with 2 cc of 100 units/ml heparinized saline infused between blood draws. The sequence was withdrawal of 2.5 ml which was discarded, drawing the appropriate sample volume, and then the infusion of the heparinized saline. During the OGTT protocol the -10 min draw was 8 ml and the 0 min draw was 6 ml. The remaining samples were approximately 2 ml. Total blood required was approximately 24 ml. The pre draw of the Exercise Phase was 13 ml, and the post-E.B. volume was six ml. The 0 min, Exercise, and Rec volumes were seven ml. Total blood required for each

experimental trial was 54 ml, and total blood for the study was 186 ml/subject.

Six ml of blood from the Pre-E.B. sample and the entire Post-E.B. sample were placed in lithium heparin tubes and spun in a Sorvall, model RC2-B, refrigerated centrifuge at 2,500 rpm for 20 min. The plasma was drawn off and frozen for later determination of plasma volume. For all draws, except the Post-E.B. sample, 1.5 ml whole blood were placed in a tube with potassium oxalate and sodium fluoride (glycolytic inhibitors), spun at 2,500 rpm for 20 min, and the resulting plasma was analyzed for glucose using a Cobas Mira analyzer (Roche Diagnostic Systems, Inc.; Nutley, NJ 07110-1199); hexokinase coupled with glucose-6-phosphate dehydrogenase produced NADH which indicated the concentration of glucose (Barthelmai and Czok, 1962; Anonymous, 1976).

One ml of blood from each sample was placed in an EDTA tube, gently tilted to minimize lysis, and analyzed for hemoglobin (Hb) and hematocrit (Hct). Blood Hb was measured using the Coulter Diluter II and Hemoglobi-nometer (Coulter Electronics; Hialeah, FL 33010), and Hct by the microcapillary technique using an International Microcapillary Reader (model CR; International Equip-ment Co.; Needham Heights, MA 02194). Calculations of percent change in plasma volume were made using the method of Dill and Costill (1974).

Three ml of blood were allowed to clot. The clot was swept and the tube spun at 2,500 rpm for 20 min. Serum was withdrawn and frozen in cryogenic tubes for later analysis of sodium and potassium concentration using ion-specific electrodes (Beckmann), and osmolality by freeze-point depression (Advanced Digimatic Osmometer Model 3DII, Advanced Instruments, Inc., Needham Heights, MS 02194).

Plasma Volume Determination

Plasma volume (PV) was measured post-immersion and again prior to the OGTT utilizing the Evans blue dye (T-1824; David Bull Laboratories; New World Trading Corp.; Longwood, FL 32750) dilution technique (Young et al., 1973). A six ml pre sample was used as the plasma blank. Then 2.5 ml of a 0.1% dye solution (T-1824 in iso-tonic saline) was injected. After a 10-min equilibration period, six ml of blood were drawn. The pre- and post-injection samples were spun, their plasma removed, and the dye subsequently recovered from the plasma by chro-matography (O'Brien et al., 1968) using custom-blown columns containing wood cellulose (Solka Floc; James River Corp.; Berlin-Gorham Group; Berlin, NH 03570) as the ion-exchange medium. Spectrophotometric analysis

yielded the optical density of test solutions allowing cal-culation of PV by application of the Beer-Lambert law:

$$\text{Plasma Volume} = \frac{V \cdot St}{T \cdot D \cdot 1.03}$$

where:

- V = Volume T-1824 injected (ml)
- D = Dilution of standard (typically 1:250)
- St = Absorbance of standard (O.D.)
- T = Absorbance of test; subtract plasma blank (O.D.)
- 1.03 = Factor introduced to correct for slow dye uptake by the tissues (dimensionless)

Thermoregulation Variables

Body temperatures were recorded using series 400 ther-mistors (Yellow Springs Instruments Co., Yellow Springs, OH 45387). Skin temperature was monitored at six sites: chest, back, upper arm, forearm, thigh and calf; the sen-sors were attached to the skin with prototype optimum air-flow holders (Greenleaf, 1974). Core temperature was measured as rectal temperature (T_{re}) at a depth of 12 cm (Nielsen and Nielsen, 1962). A multisite data logger, model SQ32-2YS/8YS/1V/HR Squirrel (Science/ Electronics Inc., Miamisburg, OH 45342), was used for continuous monitoring of sensor inputs. Mean skin temperature (\bar{T}_{sk}) (Hardy and DuBois, 1938; Greenleaf and Castle, 1972) was calculated:

$$\bar{T}_{sk} = \text{chest}(0.19) + \text{back}(0.20) + \text{U. arm}(0.06) + \text{F. arm}(0.13) + \text{calf}(0.21) + \text{thigh}(0.21)$$

Sweat rate was measured at three sites: arm, forearm, and calf. Capsules at these sites were attached via vacuum lines to a resistance hygrometer (Spaul, 1983) with sen-sors from Thunder Scientific, Albuquerque, NM. Room air was used as a reference. Relative humidity and tem-perature were measured at each site. The specific volume of air (SVA, L/g dry air) was estimated, with relative humidity and temperature values from the reference line, from a psychrometric chart (Chambers, 1970). Sweat rate (\dot{M}_{sw}) at the three sites was calculated:

$$\dot{M}_{sw} = \frac{V_a (W_{out} - W_{in})}{(A_{sw})(SVA)}$$

$$\dot{M}_{sw} = \text{sweat rate, g} \cdot \text{cm}^{-2} \cdot \text{min}^{-1}$$

$$V_a = \text{volume flow rate, L/min}$$

W_{out} = absolute humidity ratio leaving capsule, lb H_2O /lb dry air
 W_{in} = absolute humidity ratio of control, lb H_2O /lb dry air
 A_{sw} = area of collection capsule (3.14 cm^2)
SVA = specific volume of air, L/g dry air

Peripheral blood flow was measured with a Laser Flo blood perfusion monitor (model BPM 403A, TSI Inc., St Paul, MN 55164); the probe was attached to the subject's temple and secured with surgical tape. Monitored parameters were blood velocity ($\text{Hz} \cdot 10^2$), blood volume ($\text{Hz} \cdot 10^2$), and blood flow ($\text{ml} \cdot \text{min}^{-1} \cdot 100\text{g}^{-1}$ tissue).

Statistical Analysis

The data were analyzed using a two-way (treatment \times time) analysis of variance (ANOVA) with repeated measures. Separate ANOVAs were calculated for each dependent variable. The conservative Greenhouse-Geisser adjustment factor was used to counter the inherent correlation of repeated measurements. Significant effects between treatments and at individual time intervals were determined by contrast analysis (SuperANOVA, Abacus Concepts, Berkeley, Calif.). Data are expressed as mean \pm SE. Significance was set at $P < 0.05$.

Results

Oxygen Uptake, RER, and Blood Glucose Responses

Oxygen uptake was not significantly different between the two exercise groups (fig. 2, upper panel). At 14 min of exercise $\dot{V}O_2$ was 1.95 ± 0.08 (No Glu/Ex) and 1.93 ± 0.03 L/min (Glu/Ex) (62.2 ± 1.8 and $61.8 \pm 1.1\%$ of $\dot{V}O_2$ max, respectively), and remained relatively constant for the remainder of exercise ending with values of 2.02 ± 0.05 and 2.00 ± 0.05 L/min (64.6 ± 1.8 and $63.9 \pm 1.1\%$ of $\dot{V}O_2$ max, respectively).

The respiratory exchange ratio was not different between the two groups during exercise (fig. 2, middle panel). At 0 min the RER for the Glu/Ex group was 0.84 ± 0.03 , while for the No Glu/Ex and Glu/Rest groups it was increased ($P < 0.05$) to 0.91 ± 0.02 and to 0.90 ± 0.03 , respectively. The RER for the two exercise groups then rose to an identical value of 1.00 ± 0.01 at 14 min of exercise ($P < 0.05$), and then remained elevated and parallel for the remainder of exercise with the No Glu/Ex group showing a slightly greater depression at 70 min. The Glu/Rest RER showed a significant ($P < 0.05$), linear rise to 1.03 ± 0.03 at 70 min.

Blood glucose (fig. 2, lower panel) was different between the exercise groups; at -25 min there was no difference between the groups, but by 0 min the Glu/Rest and Glu/Ex values were both elevated significantly ($P < 0.05$) above their control values (105 ± 5 and 118 ± 5 mg/dl, respectively), and the No Glu/Ex concentration was significantly ($P < 0.05$) lower than the other two at 92 ± 2 mg/dl. Blood glucose for the No Glu/Ex group remained significantly lower than that of the Glu/Ex for the entire exercise period ($P < 0.05$); end exercise values were 81 ± 3 and 99 ± 4 mg/dl, respectively. There was a significant ($P < 0.05$) decline in No Glu/Ex blood glucose over the exercise period with return to control (91 ± 4 mg/dl) after 10 min of recovery. The Glu/Rest and Glu/Ex groups had similar glucose curves over the 70 min exercise period; however, after 10 min of recovery the blood glucose values were very different (101 ± 13 and 135 ± 7 mg/dl, respectively).

Cardiovascular Responses

Heart rate was similar for the two exercise groups (fig. 3, upper panel). In addition to a rapid rise by 10 min, both curves exhibited a continued linear increase during exercise: from the 10 min point the No Glu/Ex rate had risen by ~ 30 beats/min, and the Glu/Ex rate by ~ 21 beats/min by the end of exercise. At Rec, both groups' HR had decreased similarly, yet were still elevated significantly ($P < 0.05$), by 23–29 b/min, above control.

Systolic and diastolic blood pressure responses were not significantly different between the two exercise groups (table 4). Systolic pressures increased significantly ($P < 0.05$), peaked at 20 min (173 ± 8 and 174 ± 7 mmHg, No Glu/Ex and Glu/Ex, respectively), and were relatively stable for the remainder of exercise. Diastolic pressures rose similarly, but then declined significantly ($P < 0.05$) to below control values for both groups during exercise. Diastolic pressure for the No Glu/Ex group at R + 10 was still reduced below the 0 min value. Glu/Rest group systolic and diastolic pressures were relatively constant. Pulse pressure rose significantly ($P < 0.05$) with the initiation of exercise and was followed by an extended plateau for the duration of exercise in both groups. Pulse pressure did not vary significantly over the Glu/Rest group.

Mean arterial pressure (fig. 3, lower panel) for the two exercise groups increased significantly ($P < 0.05$) by 10 min of exercise, then declined steadily to a level ~ 10 mmHg above the 0 min value by the end of exercise. At R + 10 the Glu/Ex MAP was lower ($P < 0.05$) than the 0 min value, and was also lower ($P < 0.05$) than the MAP for the Glu/Rest and Glu/Ex groups.

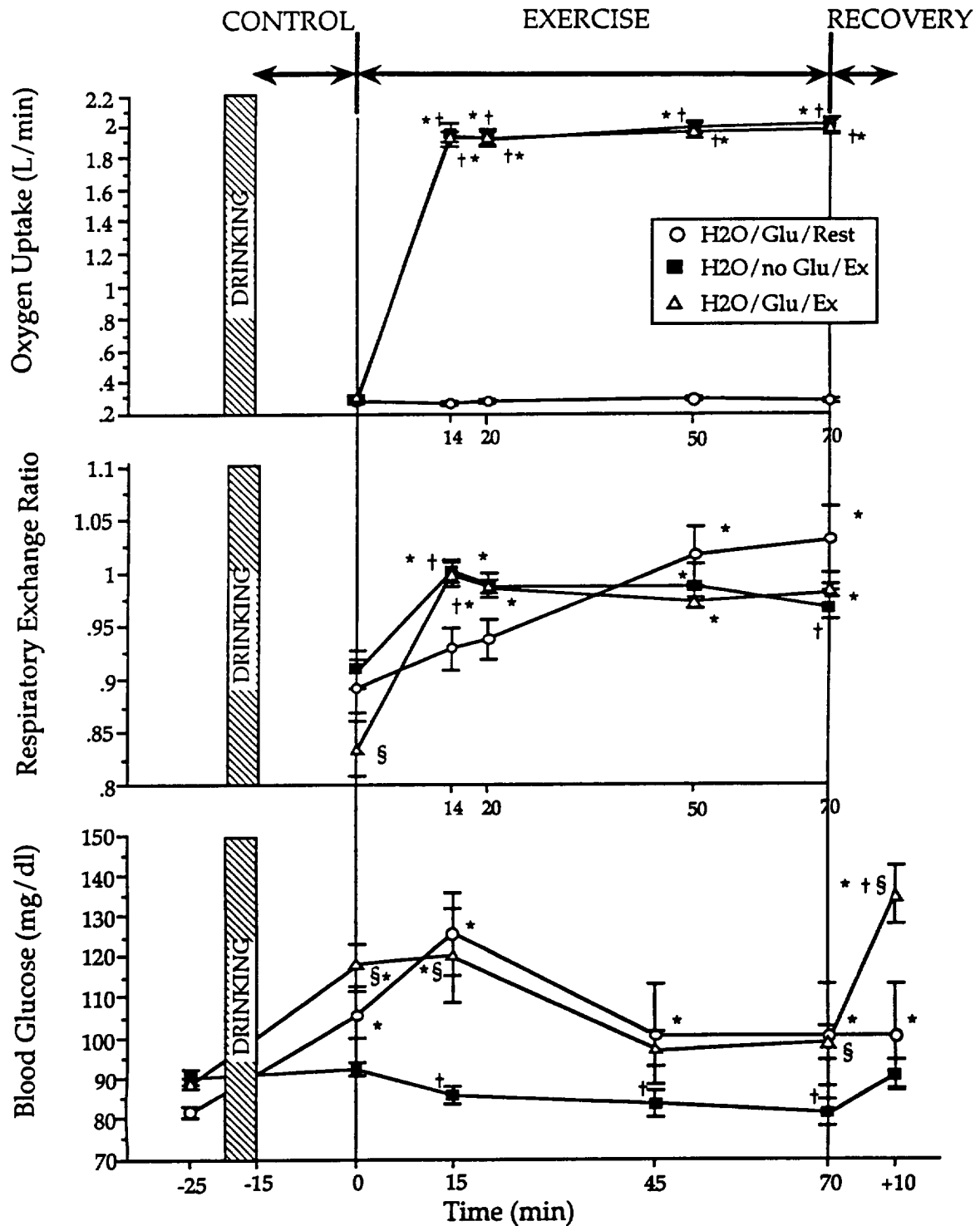


Figure 2. $\dot{V}O_2$, Respiratory exchange ratio, and blood glucose (mean \pm SE) during control, 70 min of exercise, and after 10 min recovery with subjects ingesting glucose beverage or not, and at rest after glucose ingestion, all following 4 hr water immersion. §No Glucose is significantly different from Glucose at this corresponding time ($P < 0.05$). †Significantly different from Rest at this corresponding time ($P < 0.05$). *Significantly different from initial value (-25 or 0) for that trial ($P < 0.05$).

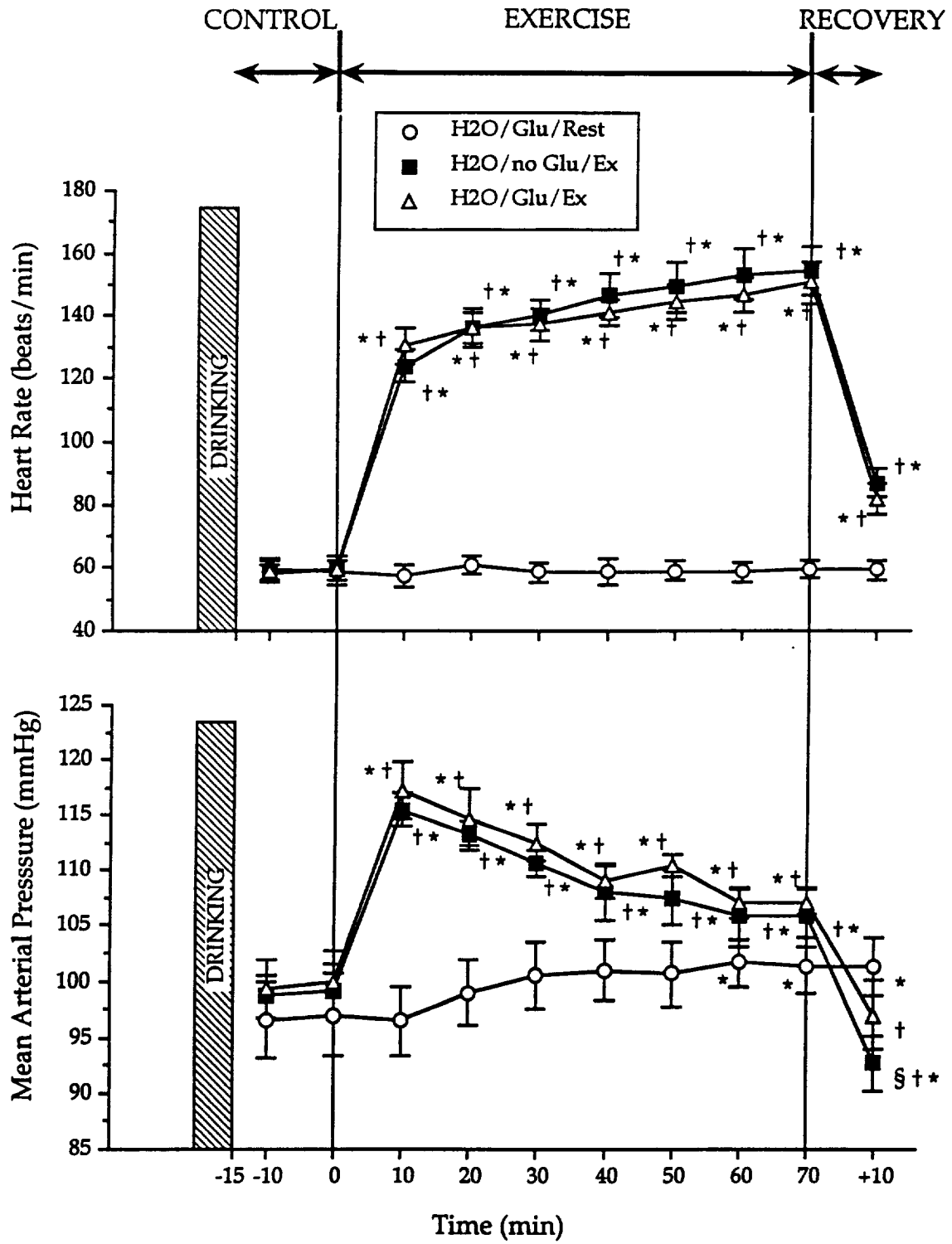


Figure 3. Heart rate and mean arterial pressure (mean \pm SE) during control, 70 min of exercise, and after 10 min recovery with subjects ingesting glucose beverage or not, and at rest after glucose ingestion, all following 4 hr water immersion. \S No Glucose is significantly different from Glucose at this corresponding time ($P < 0.05$). \dagger Significantly different from Rest at this corresponding time ($P < 0.05$). \ast Significantly different from initial value (0) for that trial ($P < 0.05$).

Table 4. Systolic, diastolic, pulse, and mean arterial pressures during control, 70 min of exercise, and recovery for the three treatments (mean \pm SE)

Treatment	Time, min									
	-10	0	10	20	30	40	50	60	70	+10
	Systolic pressure, mmHg									
Glu/Rest	124 \pm 2	125 \pm 2	127 \pm 2	129 \pm 3	129 \pm 2	128 \pm 2	129 \pm 2	130 \pm 2	128 \pm 2	129 \pm 2
No Glu/Ex	128 \pm 2	182 \pm 2	171 \pm 7 ^{ab}	173 \pm 8 ^{ab}	166 \pm 7 ^{ab}	166 \pm 9 ^{ab}	165 \pm 7 ^{ab}	163 \pm 8 ^{ab}	163 \pm 8 ^{ab}	118 \pm 3
Glu/Ex	128 \pm 2	182 \pm 2	179 \pm 9 ^{ab}	174 \pm 7 ^{ab}	172 \pm 7 ^{ab}	170 \pm 7 ^{ab}	172 \pm 7 ^{ab}	168 \pm 6 ^{ab}	162 \pm 7 ^{ab}	122 \pm 2
	Diastolic pressure, mmHg									
Glu/Rest	82 \pm 4	82 \pm 6	81 \pm 5	84 \pm 5	86 \pm 5	87 \pm 5	86 \pm 5	88 \pm 4	88 \pm 4	87 \pm 4
No Glu/Ex	84 \pm 3	85 \pm 4	88 \pm 3 ^b	84 \pm 3	83 \pm 3	79 \pm 3 ^{ab}	79 \pm 4 ^{ab}	77 \pm 5 ^{ab}	77 \pm 5 ^{ab}	80 \pm 3 ^b
Glu/Ex	85 \pm 4	86 \pm 4	90 \pm 5 ^b	85 \pm 5	83 \pm 5	79 \pm 3 ^{ab}	80 \pm 4 ^{ab}	77 \pm 3 ^{ab}	80 \pm 4 ^{ab}	85 \pm 4
	Pressure pressure, mmHg									
Glu/Rest	42 \pm 3	43 \pm 6	47 \pm 6	45 \pm 7	44 \pm 6	41 \pm 6	43 \pm 6	43 \pm 6	41 \pm 4	42 \pm 4
No Glu/Ex	44 \pm 4	43 \pm 5	83 \pm 10 ^{ab}	89 \pm 11 ^{ab}	83 \pm 10 ^{ab}	87 \pm 11 ^{ab}	86 \pm 10 ^{ab}	86 \pm 11 ^{ab}	86 \pm 11 ^{ab}	38 \pm 3
Glu/Ex	42 \pm 5	42 \pm 5	83 \pm 13 ^{ab}	89 \pm 11 ^{ab}	90 \pm 12 ^{ab}	91 \pm 10 ^{ab}	92 \pm 10 ^{ab}	91 \pm 9 ^{ab}	82 \pm 11 ^{ab}	37 \pm 4
	Mean arterial pressure, mmHg									
Glu/Rest	96 \pm 3	97 \pm 4	96 \pm 3	99 \pm 3	100 \pm 3	101 \pm 3	101 \pm 3	102 \pm 2	101 \pm 3	101 \pm 3
No Glu/Ex	99 \pm 2	99 \pm 2	116 \pm 1 ^{ab}	113 \pm 1 ^{ab}	110 \pm 1 ^{ab}	108 \pm 3 ^{ab}	108 \pm 3 ^{ab}	106 \pm 3 ^{ab}	106 \pm 3 ^{ab}	93 \pm 3 ^{abc}
Glu/Ex	99 \pm 3	100 \pm 3	117 \pm 3 ^{ab}	115 \pm 3 ^{ab}	113 \pm 2 ^{ab}	109 \pm 4 ^{ab}	110 \pm 1 ^{ab}	107 \pm 1 ^{ab}	107 \pm 1 ^{ab}	107 \pm 1 ^b

^aSignificantly different from initial value (O) for that trial (P < 0.05).

^bSignificantly different from rest at this corresponding time (P < 0.05).

^cNo Glu/Ex is significantly different from glu/ex at this corresponding time (P < 0.05).

Water Balance

Body weight changes occurring as a result of water immersion and glucose consumption followed by exercise or rest, reflect changes in total body water. Pre and post-immersion body weights did not differ significantly for the three groups over time (table 5). There was a difference ($P < 0.05$) in body weight between the two conditions for each of the groups. Urine volume during the 4-hr water immersion was not significantly different between the three groups. After correcting post-exercise body weight of Glu/Rest and Glu/Ex groups for the volume of glucose consumed, there was no difference in post-exercise body weight between No Glu/Ex and Glu/Ex. Loss of weight during exercise for the two exercise groups was significant ($P < 0.05$). The corrected change in body weight of -1.30 ± 0.04 kg for No Glu/Ex, and -1.37 ± 0.17 kg for Glu/Ex corresponded to body weight losses of 1.7 and 1.8%, respectively.

Hemoglobin, Hematocrit and Plasma Volume

Hemoglobin concentration did not differ between the exercise groups (table 6). Within the first 15 min of exercise there was an increase ($P < 0.05$) in Hb, and no change over the following 55 min of exercise. There was a slight increase ($P < 0.05$) in Hb for No Glu/Ex between -25 min and 0 min over that of the Glu/Rest group. There was a similar increase ($P < 0.05$) in Hb for the Glu/Ex group during the same pre-exercise period. Both exercise groups were still above ($P < 0.05$) control values after 10 min of recovery, and significantly different ($P < 0.05$) from Glu/Rest.

Hematocrit was significantly different ($P < 0.05$) between the two exercise groups at 15 min and 45 min (table 6). After rising significantly within the first 15 min of exercise, Hct was unchanged over the remainder of exercise for both exercise groups. At R + 10, both exercise groups'

Hct remained elevated ($P < 0.05$) above their 0 min levels. All three groups showed a small increase in Hct during the -25 to 0 min interval; the rise in Glu/Ex was significant ($P < 0.05$).

The calculated changes in plasma volume (% Δ PV) were not significantly different between the two exercise groups when the 0 min value was used as reference (fig. 4). After 15 min of exercise a difference ($P < 0.05$) in PV was evident between the exercise groups (-10.6 ± 1.9 and $-7.0 \pm 1.1\%$ for No Glu/Ex and Glu/Ex, respectively). There was no significant difference during the remainder of exercise as the No Glu/Ex PV more or less stabilized, while that of Glu/Ex continued to decline. At 70 min the No Glu/Ex and Glu/Ex PV were not different (-12.3 ± 2.2 and $-12.1 \pm 2.1\%$), respectively; at R + 10 both groups' PV were still below their respective 0 min values (-4.9 ± 1.6 and $-4.5 \pm 1.9\%$, respectively). The Glu/Rest PV showed a slight initial increase (NS), followed by a return to baseline. Prior to exercise all three groups experienced a decline in PV; that for Glu/Ex was significant ($P < 0.05$), and it began at a more hemodiluted level than those for Glu/Rest or No Glu/Ex.

Plasma Electrolytes

Sodium concentration did not differ between the two exercise groups at rest or during exercise (fig. 5). Within the first 15 min of exercise [Na^+] rose moderately ($P < 0.05$) in both groups, but did not rise above the corresponding level for Glu/Rest. For the remainder of exercise both exercise groups showed small increases in Na^+ the increases for No Glu/Ex were greater than the corresponding Glu/Rest values at 45 and 70 min. Sodium returned to the 0 min levels at R + 10 for both exercise groups. Sodium concentration for Glu/Rest showed little change during the experiment.

Table 5. Body weight changes over the course of water immersion and exercise or rest, with and without glucose beverage (mean \pm SE)

Treatment	Preimmersion body wt, kg	Postimmersion body wt, kg	Immersion urine volume, liters/4 hr	Postexercise body wt, kg	Beverage volume, liters	Δ Body wt, exercise, kg ^a
Glu/Rest	78.43 \pm 2.96	77.48 \pm 2.85	0.99 \pm 0.16	77.88 \pm 2.86	0.46 \pm 0.01	-0.06 \pm 0.02
No Glu/Ex	78.15 \pm 2.91	76.96 \pm 2.88 ^a	1.27 \pm 0.18	76.66 \pm 2.89 ^{ab}	none	-1.30 \pm 0.04 ^{bc}
Glu/Ex	78.35 \pm 2.96	77.31 \pm 2.96 ^a	1.08 \pm 0.18	76.39 \pm 2.92 ^{ab}	0.46 \pm 0.02	-1.37 \pm 0.17 ^{bc}

^aBody wt. exercise values were calculated by finding the difference between the postimmersion and postexercise body weights and then correcting the Glu/Rest and Glu/Ex values for the volume of glucose beverage consumed.

^bSignificantly different from initial value for that trial ($P < 0.05$).

^cSignificantly different from rest at this corresponding time ($P < 0.05$).

Table 6. Hemoglobin and hematocrit during control, 70 min of exercise, and recovery for the three treatments (mean \pm SE)

Treatment	Time, min					
	-25	0	15	45	70	+10
Hemoglobin, mg/dl						
Glu/Rest	15.4 \pm 0.7	15.5 \pm 0.5	15.4 \pm 0.5	15.5 \pm 0.7	15.7 \pm 0.6	15.5 \pm 0.5
No Glu/Ex	15.8 \pm 0.6	16.0 \pm 0.5 ^b	17.0 \pm 0.5 ^{ab}	17.1 \pm 0.4 ^{ab}	17.3 \pm 0.4 ^{ab}	16.5 \pm 0.4 ^{ab}
Glu/Ex	15.5 \pm 0.4	16.0 \pm 0.4 ^b	16.7 \pm 0.4 ^{ab}	17.1 \pm 0.4 ^{ab}	17.5 \pm 0.5 ^{ab}	16.6 \pm 0.5 ^{ab}
Hematocrit, %						
Glu/Rest	44.8 \pm 1.4	45.4 \pm 1.4	45.0 \pm 1.4	45.1 \pm 1.5	45.3 \pm 1.5	45.2 \pm 1.5
No Glu/Ex	45.1 \pm 1.4	45.6 \pm 1.3	48.1 \pm 1.3 ^{abc}	48.0 \pm 1.3 ^{cbc}	48.2 \pm 1.3 ^{ab}	46.6 \pm 1.3 ^a
Glu/Ex	44.8 \pm 1.1	45.6 \pm 1.1 ^a	47.2 \pm 1.1 ^{ab}	47.4 \pm 1.2 ^{ab}	47.9 \pm 1.2 ^{ab}	46.2 \pm 1.1 ^a

^aSignificantly different from initial value (0) for that trial ($P < 0.05$).

^bSignificantly different from Rest at this corresponding time ($P < 0.05$).

^cNo Glu/Ex is significantly different from Glu/Ex at this corresponding time ($P < 0.05$).

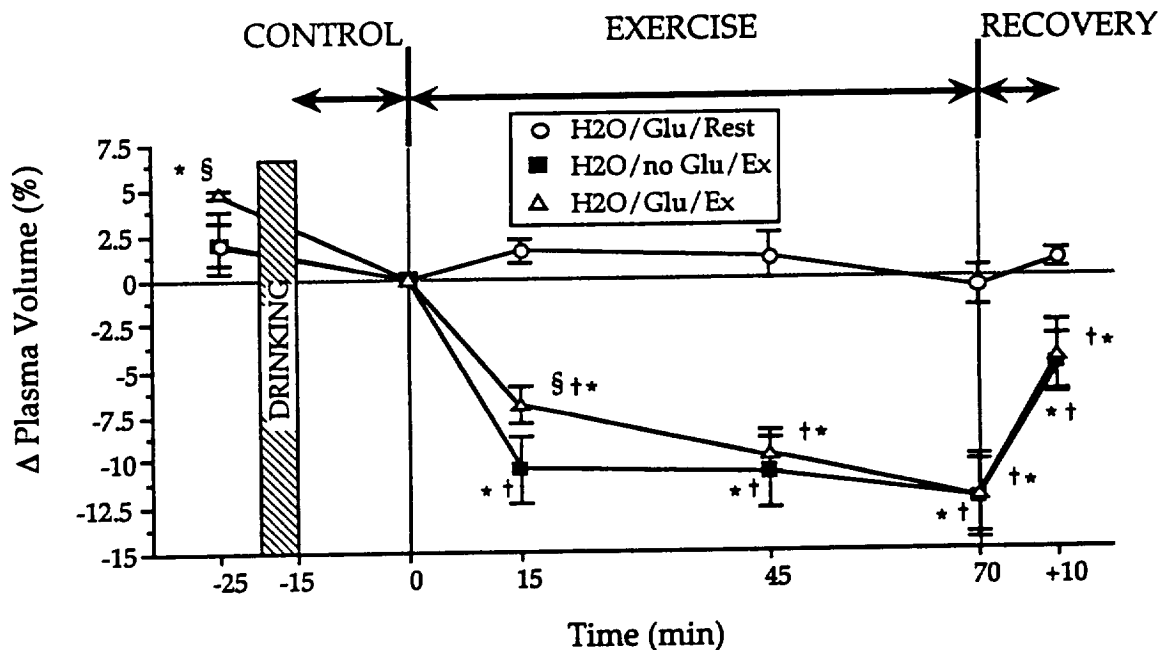


Figure 4. % Δ Plasma volume (\pm SE) during control, 70 min of exercise, and after 10 min recovery with subjects ingesting glucose beverage or not, and at rest after glucose ingestion, all following 4 hr water immersion. [§]No Glucose is significantly different from Glucose at this corresponding time ($P < 0.05$). [†]Significantly different from Rest at this corresponding time ($P < 0.05$). ^{*}Significantly different from initial value (0) for that trial ($P < 0.05$).

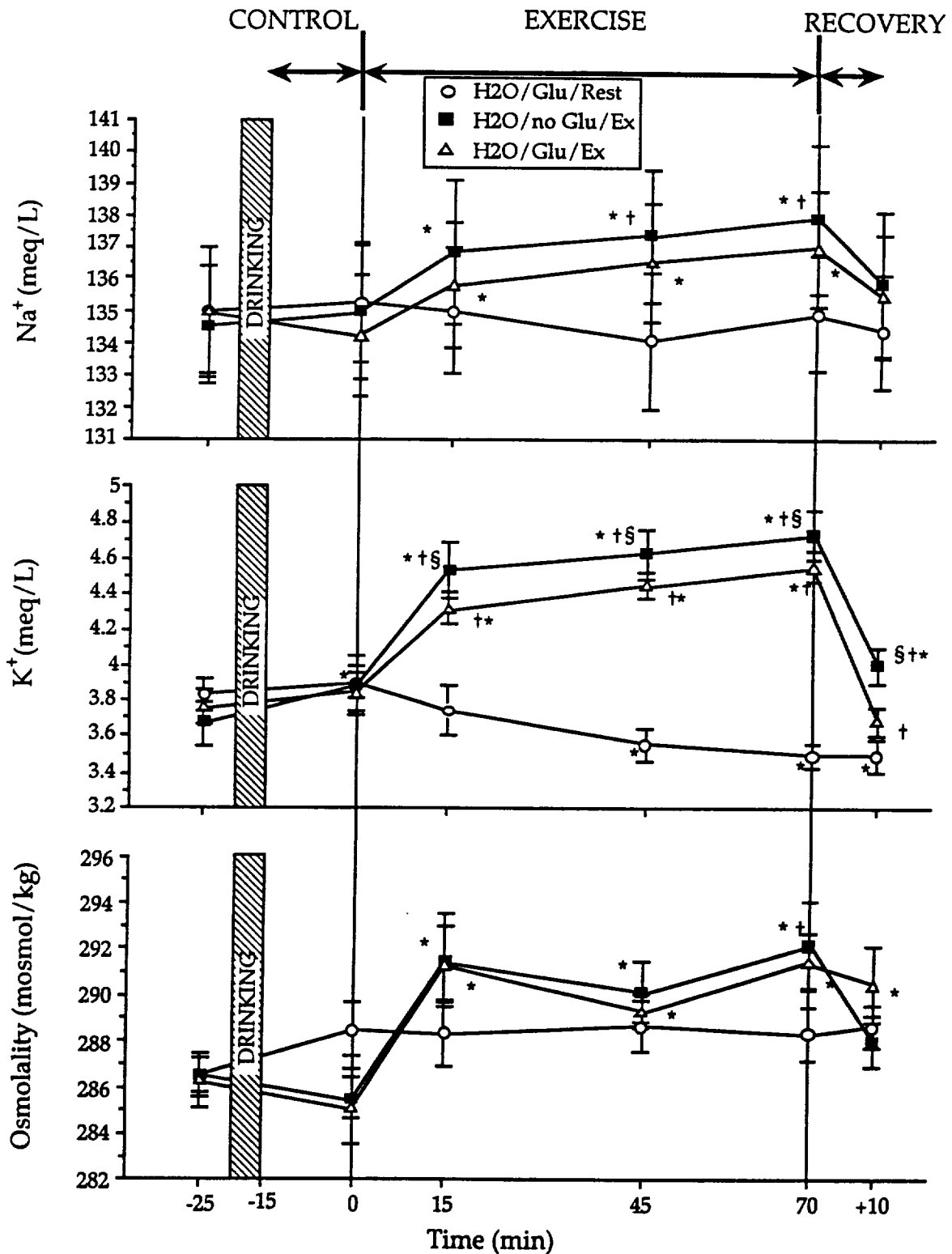


Figure 5. Changes in serum electrolytes and osmolality (\pm SE) during control, 70 min of exercise, and after 10 min recovery with subjects ingesting glucose beverage or not, and at rest after glucose ingestion, all following 4 hr water immersion. § No Glucose is significantly different from Glucose at this corresponding time ($P < 0.05$). † Significantly different from Rest at this corresponding time ($P < 0.05$). * Significantly different from initial value (0) for that trial ($P < 0.05$).

Potassium concentration in No Glu/Ex showed a small increase ($P < 0.05$) between -25 and 0 min (fig. 5). Potassium was significantly different ($P < 0.05$) between the exercise groups for the duration of exercise. There was no difference between the three experimental groups at 0 min, but by 15 min the two exercise groups had increased concentrations with No Glu/Ex $[K^+]$ rising significantly higher ($P < 0.05$) than that for Glu/Ex. For the remainder of exercise both exercise groups' $[K^+]$ remained elevated above the corresponding Glu/Rest values and they were significantly different ($P < 0.05$) from each other. Both groups showed marked drops in $[K^+]$ at $R + 10$, with No Glu/Ex remaining elevated ($P < 0.05$) above Glu/Ex, Glu/Rest, and its' own 0 min value. The Glu/Ex $[K^+]$ returned to control level at $R + 10$. Potassium concentration declined steadily during Glu/Rest and was significant ($P < 0.05$) after 45 , 70 , and $+10$ min.

Plasma osmolality for the exercise groups did not differ during the exercise period. Both osmolalities rose ($P < 0.05$) within the first 15 min of exercise, and then remained relatively constant for the remainder of exercise. At 70 min the No Glu/Ex osmolality was higher ($P < 0.05$) than the corresponding value for Glu/Rest. At $R + 10$ both groups' values dropped with Glu/Ex osmolality remaining elevated ($P < 0.05$), and that for No Glu/Ex returning to the control level. Osmolality for the Glu/Rest group remained unchanged during the experiment.

Rectal and Skin Temperatures

There was no significant difference in mean rectal temperatures between the two exercise groups (fig. 6, upper panel). At 0 min there was no difference between the three groups: values for Glu/Rest, No Glu/Ex, and Glu/Ex were 36.86 ± 0.09 , 36.82 ± 0.05 , and 36.71 ± 0.05 °C, respectively. After 10 min of exercise both exercise groups' T_{re} had risen ($P < 0.05$) above their respective 0 min values, and by 20 min were higher ($P < 0.05$) than the corresponding Glu/Rest value. The two T_{re} continued to increase in a linear manner for the duration of exercise and, at 50 min, Glu/Ex group showed an attenuation in the rate of increase in rectal temperature ($P < 0.05$). This attenuation was maintained for the remainder of exercise giving final T_{re} values ($P < 0.05$) of 38.60 ± 0.11 and 38.22 ± 0.17 °C for No Glu/Ex and Glu/Ex, respectively. Both exercise groups' T_{re} decreased at $R + 10$; Glu/Ex declined ($P < 0.05$) more than No Glu/Ex (to 37.81 ± 0.21 and to 38.29 ± 0.11 °C, respectively). Rectal temperature with Glu/Rest declined linearly over the entire period becoming significant at 40 min ($P < 0.05$), and reaching a final temperature of 36.57 ± 0.12 °C at $R + 10$.

Similar responses in the change in rectal temperature occurred as with the absolute temperature responses (fig. 6, lower panel); there was no difference in ΔT_{re} between the two groups during exercise, but at $R + 10$ there was a significant difference ($P < 0.05$) in ΔT_{re} in the two exercise groups.

Mean skin temperature overall was not significantly different between the exercise groups (fig. 7, upper panel). The -10 , 0 , and 10 min exercise values were higher ($P < 0.05$) for No Glu/Ex than for Glu/Ex. The -10 and 0 min values of No Glu/Ex were also higher than Glu/Rest group at those corresponding points ($P < 0.05$). Both exercise groups' \bar{T}_{sk} rose rapidly for the first 20 min of exercise and then increased more slowly for the remainder of the exercise bout. From 50 min until the end of exercise No Glu/Ex \bar{T}_{sk} remained higher ($P < 0.05$) than that for Glu/Ex. End exercise mean skin temperatures were 32.40 ± 0.20 and 31.98 ± 0.28 °C for No Glu/Ex and Glu/Ex, respectively. Glu/Ex $R + 10$ mean skin temperature fell to 31.48 ± 0.39 °C ($P < 0.05$), but No Glu/Ex \bar{T}_{sk} was unchanged at 31.98 °C. Glu/Rest mean skin temperature was unchanged throughout the experiment.

There was no significant difference in Δ mean skin temperature between the two exercise groups (fig. 7, lower panel). Both increased rapidly ($P < 0.05$) over the first 20 min of exercise ($P < 0.05$) and then increased more slowly thereafter. End exercise $\Delta \bar{T}_{sk}$ were 1.57 ± 0.20 and 1.83 ± 0.10 °C for No Glu/Ex and Glu/Ex, respectively. At $R + 10$ No Glu/Ex $\Delta \bar{T}_{sk}$ remained at the 70 min level, 1.57 ± 0.30 °C, while that for Glu/Ex decreased to 1.32 ± 0.30 °C. Glu/Rest $\Delta \bar{T}_{sk}$ was unchanged throughout the experiment.

Calf, Arm, and Forearm Sweat Rates

The rate of increase in mean calf sweat rate was not different during exercise in the exercise groups (fig. 8, upper panel). By 15 min of exercise calf sweating had risen significantly ($P < 0.05$) and both rates were greater ($P < 0.05$) than the corresponding value for Glu/Rest. Both rates continued to increase throughout exercise with an apparent leveling off at 65 min; end exercise calf sweat rates were 0.07 ± 0.01 g · cm⁻² · min⁻¹ for both groups. Glu/Rest calf sweat rate was unchanged over the 70 min period.

Mean arm sweat rate was not different between the two exercise groups (fig. 8, middle panel); both rates rose ($P < 0.05$) throughout exercise. After 15 min of exercise both rates had risen ($P < 0.05$) above their 0 min levels which were also higher ($P < 0.05$) than the corresponding rate for Glu/Rest. By 65 min of exercise both rates reached steady state at 0.09 ± 0.01 and

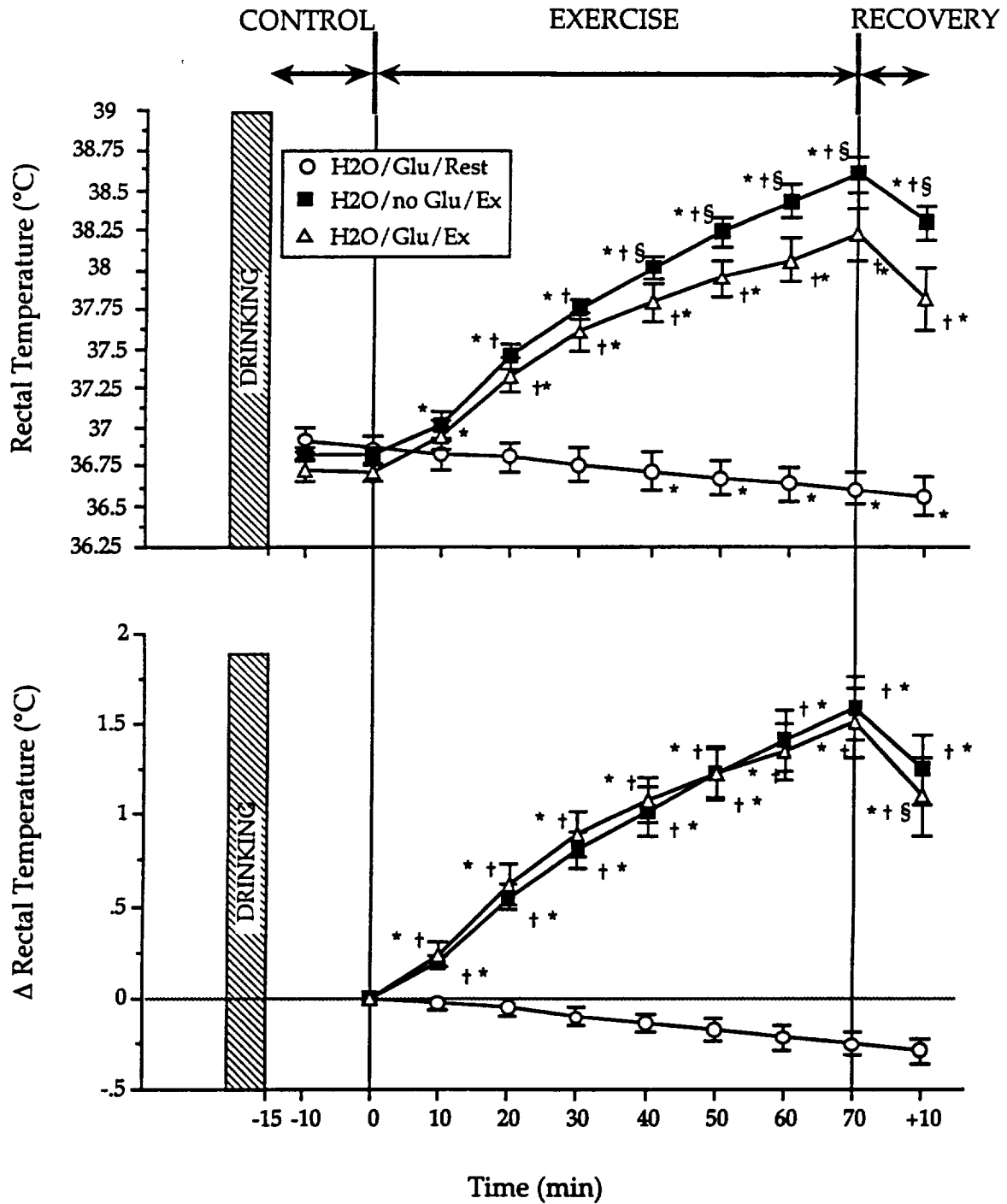


Figure 6. Rectal and Δ rectal temperature (mean \pm SE) during control, 70 min of exercise, and after 10 min recovery with subjects ingesting glucose beverage or not, and at rest after glucose ingestion, all following 4 hr water immersion. [§]No Glucose is significantly different from Glucose at this corresponding time ($P < 0.05$). [†]Significantly different from Rest at this corresponding time ($P < 0.05$). ^{*}Significantly different from initial value (0) for that trial ($P < 0.05$).

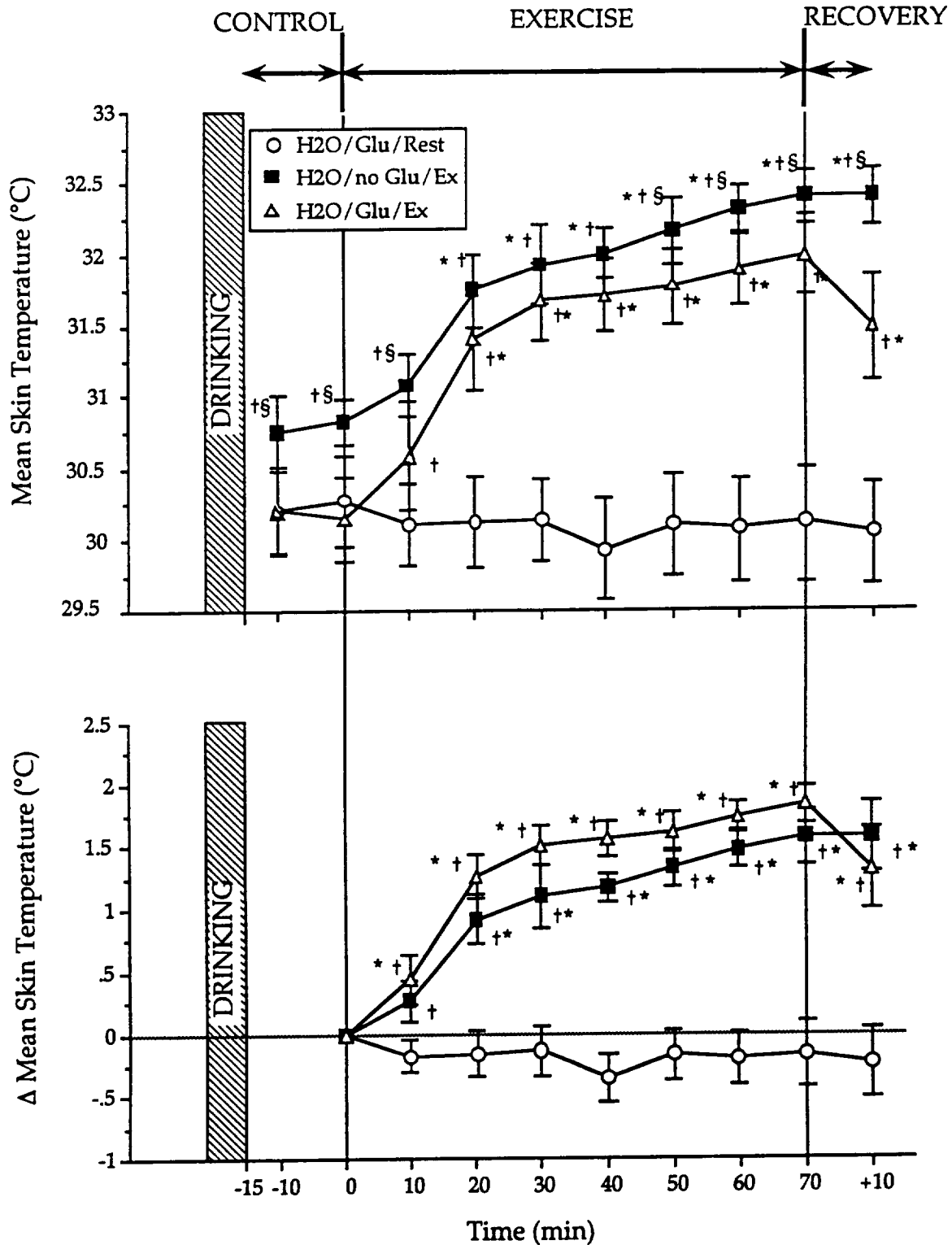


Figure 7. Mean skin and Δ mean skin temperature (mean \pm SE) during control, 70 min of exercise, and after 10 min recovery with subjects ingesting glucose beverage or not, and at rest after glucose ingestion, all following 4 hr water immersion. §No Glucose is significantly different from Glucose at this corresponding time ($P < 0.05$). †Significantly different from Rest at this corresponding time ($P < 0.05$). *Significantly different from initial value (0) for that trial ($P < 0.05$).

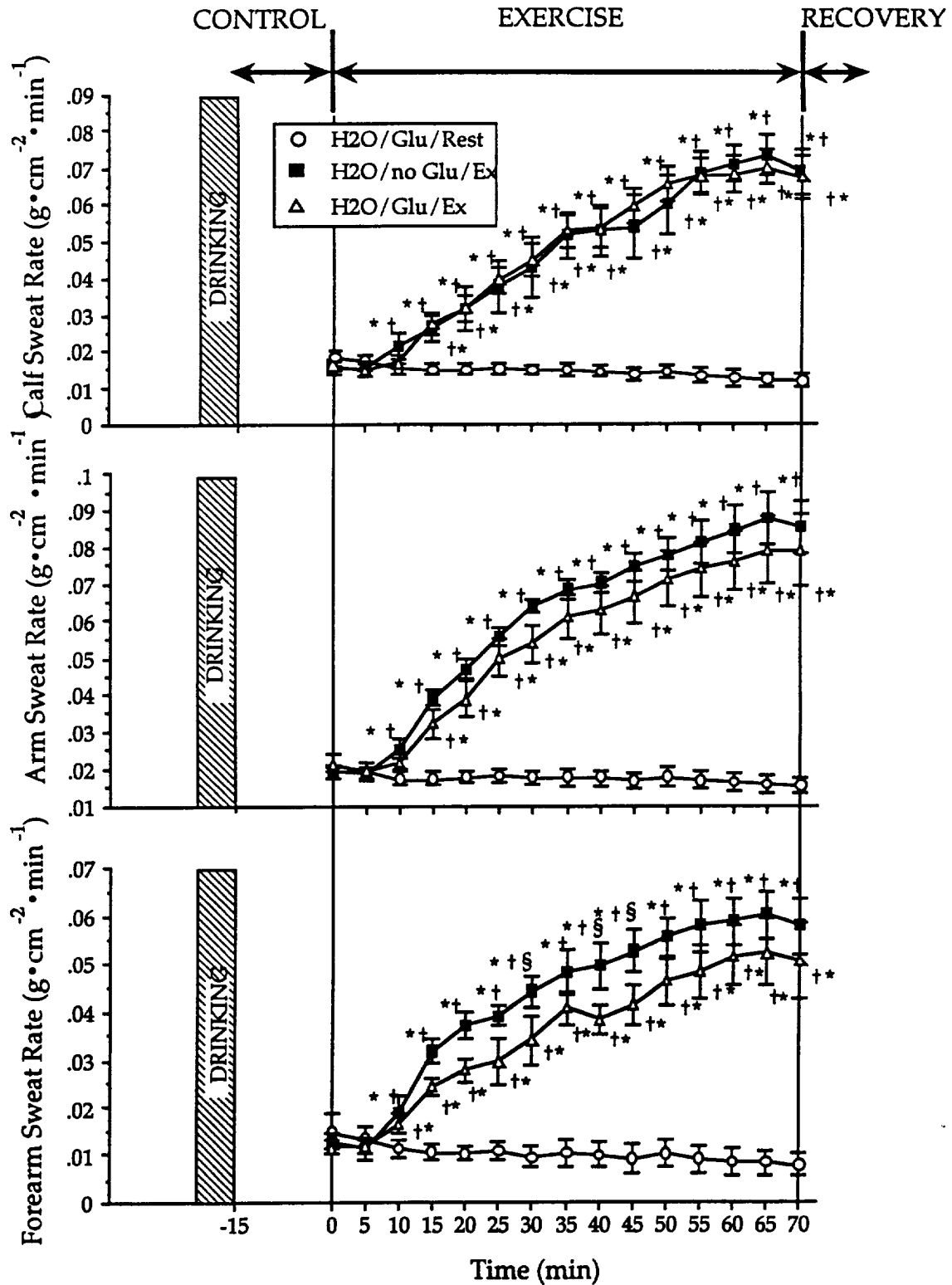


Figure 8. Sweat rate (mean ± SE) during control, 70 min of exercise, and after 10 min recovery with subjects ingesting glucose beverage or not, and at rest after glucose ingestion, all following 4 hr water immersion. [§]No Glucose is significantly different from Glucose at this corresponding time ($P < 0.05$). [†]Significantly different from Rest at this corresponding time ($P < 0.05$). ^{*}Significantly different from initial value for that trial ($P < 0.05$).

$0.08 \pm 0.01 \text{ g} \cdot \text{cm}^{-2} \cdot \text{min}^{-1}$ for No Glu/Ex and Glu/Ex, respectively. Glu/Rest arm sweat rate was unchanged over the 70 min period.

Mean forearm sweat rate was not different between the exercise groups (fig. 8, lower panel), and it also increased during exercise. At 15 min of exercise both rates had increased ($P < 0.05$) above their respective 0 min levels, as well as above ($P < 0.05$) the corresponding value for Glu/Rest. At this point there was attenuation of the Glu/Ex rise and, at 30, 40, and 45 min, the difference from No Glu/Ex was significant ($P < 0.05$). By 65 min, both exercise rates had leveled off at 0.06 ± 0.01 and $0.05 \pm 0.01 \text{ g} \cdot \text{cm}^{-2} \cdot \text{min}^{-1}$ for No Glu/Ex and Glu/Ex, respectively. Again, forearm sweat rate for Glu/Rest was unchanged during the 70 min period.

Peripheral (Temporal) Blood Flow Parameters

Blood velocity was not significantly different between the two exercise groups (fig. 9, upper panel); both increased ($P < 0.05$) by 10 min of exercise and, from 30 min, No Glu/Ex appeared to decline while Glu/Ex remained relatively constant. At 70 min of exercise blood velocity for No Glu/Ex and Glu/Ex had reached 1.51 ± 0.24 and $1.67 \pm 0.21 \text{ Hz} \cdot 10^2$, respectively; both groups showed small decreases ($P < 0.05$) at R + 10. Blood velocity for Glu/Rest was unchanged during the experiment.

Blood volume was not different between the two exercise groups (fig. 9, middle panel); both showed steady increases ($P < 0.05$) during exercise, and from min 50 No Glu/Ex volumes climbed more steeply resulting in 60 and 70 min values significantly higher ($P < 0.05$) than corresponding values for Glu/Ex group. At the end of exercise volume levels were 0.45 ± 0.05 and $0.35 \pm 0.02 \text{ Hz} \cdot 10^2$ ($P < 0.05$) for No Glu/Ex and Glu/Ex, respectively. Both groups' volumes declined by R + 10, yet still remained elevated ($P < 0.05$) over control levels and over the corresponding value for Glu/Rest. Glu/Rest blood volume was also unchanged during the experiment.

Blood flow did not differ significantly between the exercise groups (fig. 9, lower panel); flows increased ($P < 0.05$) within the first 10 min of exercise and after 30 min they both leveled off. After 70 min of exercise blood flows for No Glu/Ex and Glu/Ex were 35.1 ± 5.4 and $33.3 \pm 3.4 \text{ ml} \cdot \text{min}^{-1} \cdot 100 \text{ g}^{-1}$, respectively. At R + 10 both flows remained elevated ($P < 0.05$) above their control levels and above the corresponding value for Glu/Rest. Glu/Rest flow was unchanged during the experiment.

Discussion

The purpose of these experiments was to determine the effect of elevated blood glucose via drinking 2 g/kg body wt. of a concentrated glucose beverage (33%) on thermoregulatory responses (rectal temperature, skin temperature, and sweat rate) to horizontal, supine cycle ergometer exercise (60% of peak $\dot{V}O_2$) of hypohydrated (via water immersion) male subjects. As a control, the same subjects were similarly hypohydrated but were given nothing to drink prior to exercise. Cardiovascular, respiratory, and blood factors were studied to provide additional information for interpreting findings. It appears from the data that the effect of glucose on human exercise thermoregulation is equivocal. Absolute rectal temperature data indicate that glucose might produce an attenuation in the rise of core temperature with exercise. However, when the net change in rectal temperature at the various points was calculated, the two exercise groups were identical in their responses. Absolute and Δ mean skin temperature results also suggested different conclusions. Glucose consumption produced lower skin temperatures prior to exercise, and this pre-exercise differential was maintained for the majority of exercise. When calculated as change in skin temperature with exercise, it was found that there was no difference in skin temperature response with glucose. In a few cases, subject skin temperature was monitored before and during drinking, in addition to that stipulated in the protocol 10 min prior to exercise initiation. The data showed a downward temperature transient. Perhaps glucose consumption or drinking in general, modulates skin temperature possibly through a reduction in skin blood flow as a result of increased splanchnic blood flow (Rowell, 1973, 1993).

The rectal temperature responses seen here are in contrast with the results of Kruk and colleagues (1987). When compared with the control group (24 hr fasted), elevated blood glucose caused a reduction in the exercise-induced rise in both rectal temperature (by $0.9 \pm 0.11^\circ\text{C}$) and more importantly muscle temperature (by $0.9 \pm 0.16^\circ\text{C}$). Furthermore, when hypoglycemia or glucopenia was induced, ΔT_{re} was significantly larger ($1.33 \pm 0.18^\circ\text{C}$ and $1.36 \pm 0.12^\circ\text{C}$, respectively) than that of the control group ($0.94 \pm 0.10^\circ\text{C}$) (Turlejska and Nazar, 1977). It is worth mentioning that the group receiving intravenous glucose in Kruk's study (1987) demonstrated RER values above 1.0 during exercise, significantly higher than those of either the FFA or control group. Although blood glucose was significantly elevated in the exercise glucose group above

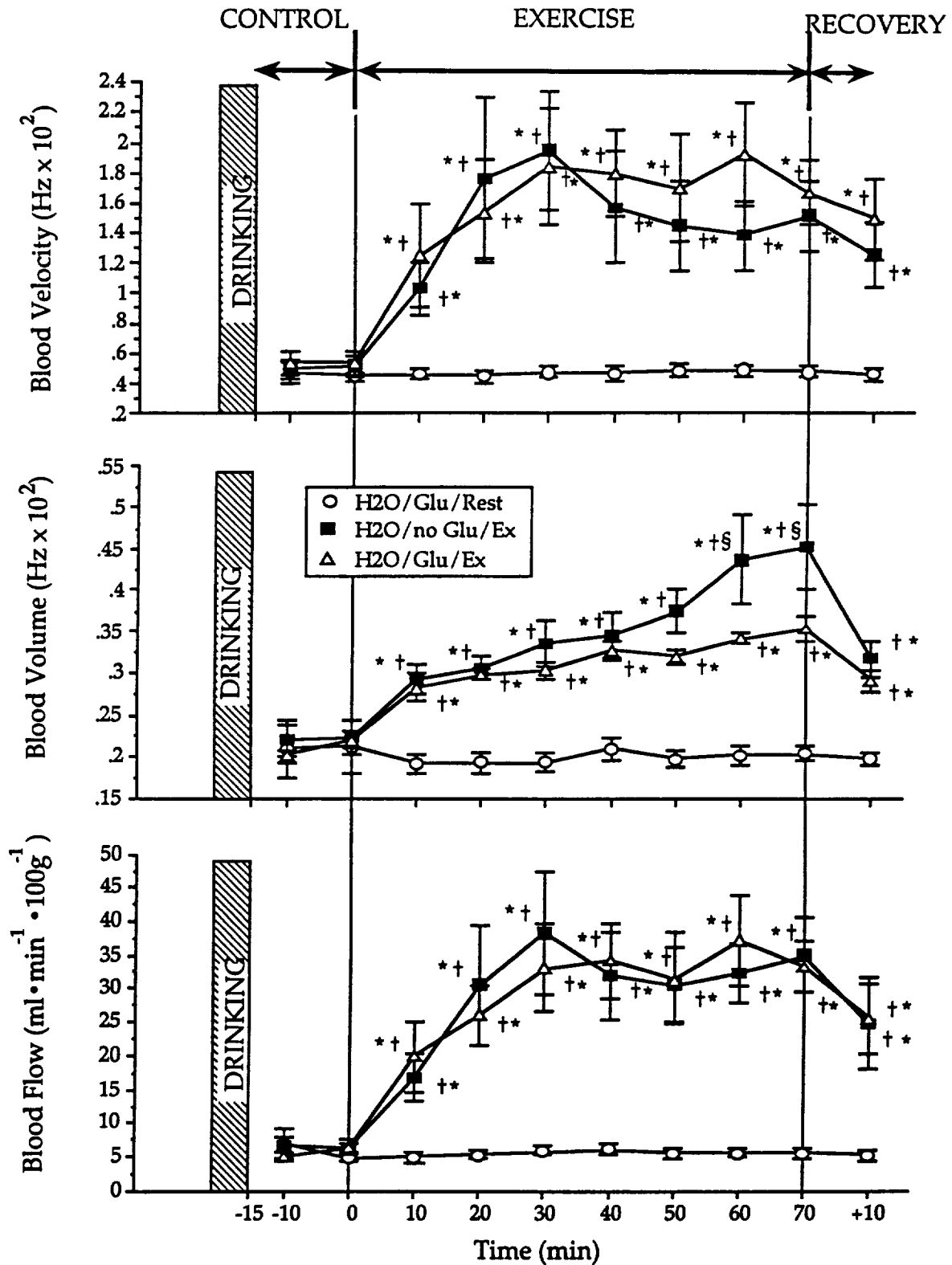


Figure 9. Laser Doppler blood velocity, volume, and flow (mean \pm SE) during control, 70 min of exercise, and after 10 min recovery with subjects ingesting glucose beverage or not, and at rest after glucose ingestion, all following 4 hr water immersion. § No Glucose is significantly different from Glucose at this corresponding time ($P < 0.05$). † Significantly different from Rest at this corresponding time ($P < 0.05$). * Significantly different from initial value (0) for that trial ($P < 0.05$).

that of the exercise control group in the present study, both groups showed similarly elevated RER levels implying equal dependence on carbohydrate, whether endogenous or exogenous, during exercise (Dill et al., 1932; Christensen and Hansen, 1939). It is possible that the meal consumed by all subjects prior to water immersion, almost exclusively carbohydrate, fully saturated muscle glycogen stores providing ample carbohydrate availability for exercise in the exercise control group. Coyle and associates (1985, 1991) found that a high carbohydrate meal, similar to that used in the present study, ingested 4 hr. prior to moderate exercise (~70% of peak uptake) produced elevated RER levels (0.90-0.95); individuals who had fasted for 16 hr. showed an intermediate (even balance between CHO/protein and FFA) RER (0.85-0.87). Since the subjects in the present study ate a high-carbohydrate meal an average of 5.5 hr. prior to exercise testing, it is probable that the RER for the exercise control group was elevated for this reason. Therefore, any metabolic effects postulated for explaining differences in thermal responses for the studies using dogs as subjects (Turlejska and Nazar, 1977; Kruk et al., 1987) would not be possible here due to the identical oxygen uptake observed for the exercise groups and the confounding fuel utilization patterns induced in these human subjects.

Glucose appears to affect sweat production in exercising subjects. The farther the sweat monitoring sight was from the exercising muscle, the greater the degree that glucose attenuated the rise in sweat rate at that sight. Forearm sweat rate showed the greatest attenuation, and at certain points during exercise this effect was significant. Whole body sweat rate, as suggested by the change in body weight over exercise, however, showed no significant difference between the two exercise groups. Furthermore, none of the other physiological indices typically associated with the reduction or impairment of sweating, including elevated osmolality and declining plasma volume, showed significant differences between the exercise groups (Nadel et al., 1980; Fortney et al., 1981b, 1984). The calculated % change in plasma volume for both exercise groups indicated the typical early drop followed by a more moderate decline over exercise (Rowell, 1974; Smith et al., 1976; Harrison, 1985). The only difference between the two groups was after 15 min of exercise where the decline in plasma volume for the glucose-exercise group was not as rapid. This might reflect that some volume of the beverage had entered the vascular space and, because of the osmotic nature of glucose, produced a larger water retaining capacity of the vasculature not normally associated with this point in exercise. In a like but opposite manner, the disappearance of glucose from the vascular space from 15 min to 45 min

may have contributed to the more rapid decline in plasma volume for the glucose-exercise group over this time.

Osmotic changes of the Glu/Ex group mirrored those of the exercise control group over the course of exercise. Sodium ion concentration showed similar consistency between the exercise groups. Potassium ion concentration, though not affecting overall osmolality, was significantly different between the exercise groups. The predictable rise in $[K^+]$ with exercise was apparently attenuated in the Glu/Ex group, and showed a significant drop in the Glu/Rest group. Since elevations in $[K^+]$ with exercise may be linked to elevated muscle glycogenolytic activity (Harrison, 1985) as well as hemoconcentration, perhaps the attenuation observed as well as the sharp drop in concentration in the resting control group, is related to the use of exogenous CHO by muscle tissue and reduced glycogenolysis.

Cardiovascular indices of vascular volume distribution during exercise namely heart rate, and the blood pressure quantities both measured and derived, indicated similar and predictable physiological adaptations for the two exercise groups. The rising heart rate and declining diastolic pressure and, as a consequence, declining mean arterial pressure are consistent with peripheral shunting of blood flow and "cardiovascular drift" (Krogh, 1912; Ekelund and Holmgren, 1967; Rowell, 1974). Finally, laser Doppler measurements of peripheral blood flow changes provided no suggestion of significant differences in vascular adaptation between the two exercise groups.

In summary, elevated blood glucose may have some effect on human exercise thermoregulation, but this effect is not clear from these experiments. Basal levels of some components (skin temperature and sweat rate) may be altered by elevated blood glucose. Another possible effect may be an alteration in the threshold for response of parameters affecting temperature and sweat rate rather than variations in the gain of the responses themselves. Sweat production may be affected by elevated blood glucose; the slope of the response to thermal inputs was the same, but the threshold for the response had been shifted. Cardiovascular responses indicated that the same level of peripheral vasodilatation occurred for both exercise groups producing cardiac chronotropic adaptation and systemic pressure changes. Because of the structure of the experiment it was not possible to observe the effect of altered metabolism on exercise thermoregulation. Therefore, any comments relating to comparing or contrasting human results and that of other mammalian species would not be appropriate. Future research in this area would be more profitable by reducing the number of variables present between the control and test experiments through improving and/or broadening the scope of the control

experiments themselves. To better delineate a metabolic thermal effect, it might have been useful in this study to fast the subjects prior to water immersion. A second control experiment could have utilized a second beverage with the same water content as the 33% glucose beverage to better separate the rehydrating effects from the metabolic effects. The inclusion of an insulin assay would have provided further information as to the nature of the blood glucose concentration decline seen during the Glu/Ex group exercise phase, and the significant rise in blood glucose concentration during the post-exercise rest phase.

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Appendix

Human Research Consent Form Part I

TITLE: The Effects of Oral Glucose Administration With Exercise On Men After Water Immersion; HR 96

A. Investigators

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B. Purpose

The purpose of this investigation will be to examine the effect of elevated blood glucose, due to the intake of a glucose-containing beverage, on thermal responses to exercise before and after water immersion.

C. Nature of Tests and Experiment

By going into space we expose our bodies to an environment that is unlike our own. We can compensate for the major life support factors, but we haven't been able as yet to compensate for the effects produced by the loss of gravity. The general effect we will be dealing with in this experiment is a decrease in plasma volume, the fluid portion of blood consisting mostly of water, resulting from a general fluid shift towards the chest and head. This can lead to a failure of the body's ability to regulate temperature during activity and the inability to work at peak performance. It has been suggested by results from human and animal research that consumption of electrolyte/carbohydrate containing beverages prior to activity might alleviate symptoms of dehydration, maintain normal fluid balance in the body tissues, supply more energy to the muscles, and thereby maximize work efficiency and the health of the astronaut.

It has been determined that water immersion is an effective means of simulating zero-gravity and thus stimulates a number of the physiological adaptive processes related to space travel, most notably a reduction in plasma volume. It has been shown that the first 2-4 hours of immersion produce the most marked changes in plasma volume. With this condition being met, any fluid intake should be responded to in a representative way of how astronauts will respond after three days in space. Since glucose (a simple sugar) is the body's circulating carbohydrate molecule which supplies energy to the brain and tissues, it would be of value to see how immersion affects your plasma glucose levels, how plasma glucose levels are altered by drinking a glucose containing beverage, and how glucose levels are affected by exercise. Furthermore, by monitoring your body temperature responses to exercise, with and without drinking the glucose beverage, we

may determine if the drink helps to keep your body cooler during exercise. With all this in mind, we will examine the following:

- (a) Plasma volume changes as a result of water immersion.
- (b) Your body's response to an orally administered glucose solution before and after immersion as measured by plasma glucose levels.
- (c) Your body's response to exercise in terms of fuel choice, temperature changes, and blood constituents in the presence of the orally administered glucose solution before and after immersion.

D. Manner in Which Tests or Experiment Will Be Conducted

You will be asked to come to Ames Research Center, Bldg. 239, Room 214, three or four times approximately two weeks prior to the water immersion experiments. This will allow you to familiarize yourself with exercising horizontally on a bicycle ergometer, and to carry out pre-immersion experiments which will provide information for comparison with post-immersion data (refer to fig. A-1). On one occasion your oxygen consumption while exercising at your maximum capacity on the ergometer will be tested. During this procedure your heart rate, blood pressure, and expired air will be monitored. On another occasion you will take an Oral Glucose Tolerance Test (OGTT) consisting of consuming a glucose beverage while resting. Blood samples will be taken at intervals via a catheter to observe changes in blood glucose and other constituents. Rectal temperature and skin temperature will also be monitored. You will also be asked to do two six-hour chair-resting experiments followed by exercise at 60–65% of your previously determined maximum oxygen consumption ($\dot{V}O_2$ max). The exercise will be preceded by consumption of a glucose beverage or nothing. These tests will be done to determine your ambulatory (before water immersion) thermal responses to exercise with and without glucose consumption. For these two tests you need to arrive at Ames at 0730 hours in a fasted condition. The exercise test protocol (duration, blood draws, physiological measurements) will be the same as that of the post-immersion exercise tests which are described later. Your pre-exercise plasma volume will be determined by the Evans blue dye method (refer to Method Explanation (b) and Forseeable Inconvenience (6)).

The water immersion test days will require that you arrive at Ames Research Center at 0730 hours in a fasted condition. You will be given a light meal of toast, jelly, and a beverage. You will urinate and be weighed. At 0900 hr you will enter the immersion tank where you will remain for 6 hours. Water temperature is maintained at 34°C (isothermic). At 1500 hr you will exit the tank with assistance and be weighed again. You will be carried by stretcher to Rm. 214 for the exercise phase. At 1520 hr a catheter will be inserted into a vein in your arm. At this time a preliminary blood sample will be taken, Evans blue dye will be injected into you, and after 10 min another blood sample will be taken. This procedure allows the measurement of your plasma volume (the fluid phase of your blood) which allows us to be sure that you are

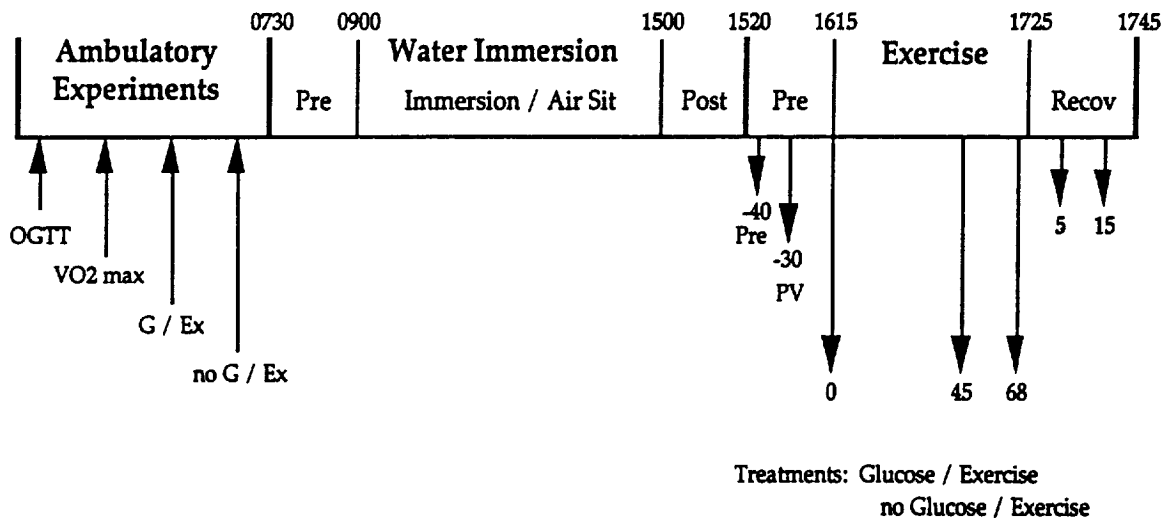


Figure A-1. General scheme of study. (↓) Signify blood draws or Evans blue injection.

dehydrated adequately. You will then consume the glucose beverage and rest for 30 min. At approximately 1615 hr you will begin exercising at 60–65% of your previously determined $\dot{V}O_2$ max, with a duration of 70 min. This will be followed by a monitored 20 min recovery period. Blood will be drawn via the previously inserted catheter at intervals during exercise and recovery for analysis. You will be allowed to leave Ames at roughly 1745 hr.

A second water immersion test will be conducted in another week. This will be followed by an exercise test following the above protocol; however, it will not be preceded by consumption of glucose. This will provide an internal control for comparison to the glucose treatment.

A third and final immersion procedure will be conducted for each subject on another week. This will be followed by an OGTT in a resting, monitored state. This will provide information as to the deconditioning effects of water immersion. The results of this test will be compared to those of the ambulatory test of the same type.

Method Explanation

(a) Blood Sampling, Analysis, and Requirements

Blood sampling will be done via an in-dwelling catheter in an antecubital vein inserted by an experienced nurse. Sampling will be done at $T_{\text{exercise}} = -45$ (Plasma blank), -35 (Evans blue, constituents), 0, $+45$, and $+68$ min. Blood will also be drawn at $T_{\text{recovery}} = +5$ and $+15$ min. The $T_e -35$ draw will require 12 ml, with the $T_e -45$ and remaining draws taking 6 ml of blood each. Total blood required for each phase (ambulatory and treatments) will be 48 ml. The OGTT will require about 10 ml. Total blood required for the study: $(48 \text{ ml} \times 4) + (10 \text{ ml} \times 2) = 212 \text{ ml}$.

(b) Plasma Volume Determination

A plasma volume measurement will be made pre- and post-immersion, and prior to each exercise test phase. This will be done utilizing the Evans blue dye (T-1824) dilution technique. An initial 6 ml of blood will be drawn for use as a plasma blank. Then a 3.5 ml volume of a 0.1% Evans blue dye solution (T-1824 in isotonic saline) is injected. After a 10-min equilibration period, a 6 ml blood sample is drawn.

(c) Mean Body Temperature

Skin temperature during the experimental procedures will be recorded every two minutes at six sites (upper arm, forearm, chest, back, thigh, and calf) with Yellow Springs Instruments thermistors using prototype optimum air-flow holders (Greenleaf 1974). Core temperature will be measured using a flexible Yellow Springs Instruments rectal probe inserted to a depth of 12 cm.

E. Foreseeable Inconvenience, Discomfort, and Risks

1. Skin preparation for electrodes.
2. Venipunctures for catheter insertion. There is a small risk of bleeding, bruising, or infection at the site of the needle.
3. Possible nausea, dizziness, and fainting during the blood draws.
4. During the maximal oxygen uptake test: discomfort such as breathlessness, fatigue, muscle soreness, dizziness, and a remote chance of fainting. Skipped heart beats (arrhythmias) occur in 5–10% of healthy subjects; no harm but may be felt by the subject. Chest pain, occurring as a tight feeling under the breast bone or radiating down the arm, may also cause or be only evident as an ECG change (ST depression); observed in less than 1% of normal persons. Abnormal ECG response to exercise; a fall in systolic pressure with an increase in exercise load; a rise in diastolic blood pressure 20 mmHg from resting state; systolic blood pressure above 220 mmHg. Abnormal ECG response to exercise; frequent multiform premature ventricular beats; indications of a bundle branch block or A-V block (2° and 3°). If such abnormal ECG recordings or blood pressure responses occur and warrant concern for the subjects safety, the exercise test will be terminated immediately.
5. During exercise bout: discomfort such as general fatigue.
6. The Evans blue dye has been used in human research for more than sixty years and there are no data to suggest that using it for measuring plasma volume represents a risk to humans. However, like many other dyes and drugs, Evans blue has been found to cause changes in cells (mutagenic effects) in certain animal species when the dye was given to them in

doses several hundred times that used in humans. The dye technique may, on rare occasions, impart a bluish tint to the skin that disappears within a few days.

- 7. Initial discomfort of rectal temperature probe.
- 8. Possible gastric upset from beverage ingestion.
- 9. Smoking, drinking alcoholic beverages or caffeine-containing beverages or the taking of any drugs will not be allowed during the study.
- 10. Subjects will be expected to eat all the food they are given.
- 11. Unforeseeable laboratory mishaps that may require another blood sample being drawn.

F. Rights to Withdraw from the Study; Hazards Associated With Withdrawal

You have the right to withdraw from the study at any time for any reason, although we hope you will not volunteer for the study unless you intend to complete it. Walking out of the bedrest facility after experiencing a period of water immersion may be hazardous to your health, such as weakness, unsteadiness, or light headedness. You may leave after being given medical advice.

G. Answers to Questions

You may receive answers to any questions related to this study that occur before, during, or after the study, by contacting the Principal Investigator, Alan Dearborn at (415) 604-3341 or Dr. John Greenleaf at (415) 604-6604.

H. Remedy in the Event Of Injury

You will be covered by Worker's Compensation insurance during the course of your participation in this study. If you sustain an injury caused by this study, the benefits you will receive are those currently provided under the Worker's Compensation law in California. You can not sue your employer for benefits other than those provided by this Compensation because the law makes Worker's Compensation your only remedy against him. You may have other remedies against persons or organizations other than your employer depending on the circumstances of your injury.

I certify that the series of tests for which _____ is to serve as a subject has been explained to him in detail and that he understands what is involved.

Signature of Principal Investigator

Date

Signature of Responsible Ames Researcher

Date

Signature of Medical Monitor

Date

Human Research Consent Form Part II

TO THE TEST SUBJECT: Read Part I carefully. Make sure all your questions have been answered to your satisfaction. Do not sign this form until Part I has been read by you and signed by the Principal Investigator and Government Medical Monitor. You will receive a copy of this consent form.

A. I, _____, agree to participate as a subject in the tests and experiments described in Part I of this form.

B. I am aware of the possible foreseeable harmful consequences that may result from such participation, and that such participation may otherwise cause me inconvenience and discomfort as described in Part I.

C. My consent has been freely given. I may withdraw my consent, and thereby withdraw from the study, at any time. I understand (1) that the Principal Investigator may request my employer to dismiss me from the study if I am not conforming to the requirements of the study as outlined in Part I; (2) that the NASA Medical Monitor may request my employer to dismiss me from the study if, in his opinion, my health and well-being are threatened; and (3) that the Facility Safety Manager may terminate the study in the event that unsafe conditions develop that cannot be immediately corrected. I understand that if I withdraw from the study, or am dismissed, I will be paid for the time served up to the point of my departure, but not thereafter.

D. I am not releasing NASA from liability for any injury arising as a result of these tests. I understand that if I am injured in connection with this experiment, I am covered under California law by Worker's Compensation. If I receive worker's Compensation benefits, I cannot sue my employer because the law makes Worker's Compensation my only remedy against him.

E. I hereby agree that all records collected by NASA in the course of this experiment are available to the Medical Monitor and the Principal Investigator and Co-investigators.

F. I have had an opportunity to ask questions and I have received satisfactory answers to each question I have asked.

Signature of the Test Subject

Date

Address

(Area Code) Telephone No.

City, State, Zip Code

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503.

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13. ABSTRACT (Maximum 200 words) To test the hypothesis that elevated blood glucose would attenuate the rise in exercise rectal temperature, six men age 35 ± S. D. 7 years participated in each of three trials preceded by 4-hr water immersion to the neck: (1) 2.0 g/kg body wt of oral glucose (33.8% wt./vol.) was consumed followed by 80 min controlled rest (Glu/Rest), and 70 min horizontal supine cycle exercise at 62.8% ± S.E. 0.5% (1.97 ± 0.02 L/min) of peak O ₂ uptake followed by 10 min recovery (2) with (Glu/Ex) and (3) without prior glucose (No Glu/Ex). Blood samples were taken at -25, 0, 15, 45, and 68 min of exercise and after +10 min of recovery for measurement of hemoglobin, hematocrit, and blood glucose. Both mean skin (\bar{T}_{sk}) (from six sites) and rectal temperatures (T_{re}) were monitored continuously. Sweat rate was measured by resistance hygrometry. The mean % ΔPV for the exercise trials was -12.2 ± 2.1%. Mean blood glucose for the Glu/Ex trial was higher than that of the No Glu/Ex trial (108.4 ± 3.9 and 85.6 ± 1.6 mg/dl, respectively, P < 0.05). At the end of exercise, T_{sk} for the Glu/Ex trial was lower than for No Glu/Ex (32.0 ± 0.3 and 32.4 ± 0.2°C, respectively, P < 0.05); T_{re} for the Glu/Ex trial was lower than for No Glu/Ex (38.22 ± 0.17 and 38.60 ± 0.11°C, respectively, P < 0.05); and forearm sweat rate for the Glu/Ex trial was lower than for No Glu/Ex (0.34 ± 0.04 and 0.43 ± 0.04 g/cm ² , respectively, P < 0.05). These data suggest that elevation of blood glucose prior to horizontal exercise following hypohydration attenuates the increase in body temperature without altering heat production or exercise hypovolemia.			
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