Comparison of Carbohydrate-containing and Carbohydrate-restricted Hypocaloric Diets in the Treatment of Obesity

ENDURANCE AND METABOLIC FUEL HOMEOSTASIS DURING STRENUOUS EXERCISE

CLIFTON BOGARDUS, BETTY M. LAGRANGE, EDWARD S. HORTON, and ETHAN A. H.
SIMS, *Metabolic Unit, Department of Medicine, University of Vermont,
Burlington, Vermont 05405*

ABSTRACT   Eight untrained, obese females (>30% body fat), ages 25–33 yr, were studied before, at 1 wk, and after 6 wk while taking either of two 830-kcal/d diets: carbohydrate-containing (CC) group ($n = 4$): 35% protein, 29% fat, 36% carbohydrate; carbohydrate-restricted (CR) group ($n = 4$): 35% protein, 64% fat, 1% carbohydrate.

Endurance, at ~75% of VO_2max (maximum oxygen uptake) on a cycle decreased from base line by 50% at 1 and 6 wk in the CR group, but there was no change in the CC group. Preexercise muscle glycogen (vastus lateralis) did not change significantly in the CC group, but was decreased by 49% in the CR group after 1 wk, and by 51% after 6 wk. There was a close correlation between percent decrease in resting muscle glycogen and percent decrease in endurance ($r = 0.79, P < 0.01$).

The mean fasting and exercise plasma glucose concentration was lower in the CR group than in the CC group after 6 wk, but no subject became hypoglycemic during exercise. Serum FFA, lactate, pyruvate, beta-hydroxybutyrate, acetoacetate, insulin, and glucagon changed similarly in the two groups during exercise at base line, 1 and 6 wk. Glycerol concentration was higher in the CR group during exercise only after 6 wk. Increases in serum lactate concentrations, and a mean exercise respiratory quotient of 0.93 suggested that cycle exercise at ~75% VO_2max used predominantly glucose as a fuel.

Conclusions: Resting muscle glycogen and endurance, during cycle exercise at ~75% VO_2max, were maintained during a 36% carbohydrate, 830-kcal/d diet. In contrast, significant decreases occurred in resting muscle glycogen and endurance, during similar exercise, after 6 wk of a 1% carbohydrate, 830-kcal/d diet.

INTRODUCTION

Physical exercise has been recommended as therapy adjunctive to low calorie diets in the treatment of obesity (1–3). There is little data, however, on the capacity for exercise during rapid weight loss. Christensen and Hansen (4) and later Bergstrom et al. (5), showed that the capacity for exercise was reduced after a few days of carbohydrate restriction, but these were acute experiments in which little time was allowed for adaptation. McClellan et al. (6) in 1930 studied two subjects who took a 1–2% carbohydrate, weight-maintaining diet for 1 yr. Although no formal exercise testing was done, neither subject noted any change in his ability to perform a 2.25 mile "run" in ~20 min after 3 mo of the diet.

These early studies of carbohydrate restriction have current relevance to the renewed interest in low carbohydrate diets, but they do not delineate the capacity for exercise after adaptation to these diets.

In an earlier study in this laboratory (7), obese subjects were studied before, and after 1 and 6 wk of eating a hypocaloric, low carbohydrate diet. Endurance, while walking on a treadmill at ~60% maximum oxygen uptake (VO_2max) was decreased after 1 wk, but by 6 wk had increased to 155% of base line. Whether endurance could be maintained at higher work loads that place more stress on specific muscle groups and con-

sequently on muscle glycogen stores, was not determined.

The purpose of our study was to determine the endurance capacity and substrate use during strenous exercise after adaptation to either a carbohydrate-containing or carbohydrate-restricted, hypocaloric diet. Cycle exercise at heavy work loads was used to specifically stress the muscle glycogen stores of the quadriceps.

METHODS

Subjects. Eight, untrained obese female volunteers, ages 25–33 yr, weighing between 63 and 108 kg (mean 81 kg), and with body mass indices from 25–39 kg/m² (mean 31 kg/m²) were studied (see Table I). All volunteers gave informed consent before participation in the study. They were admitted to the Clinical Research Center of the University of Vermont College of Medicine for the 8-wk study period. Participants were allowed to continue their jobs at the hospital or clinic, but with rare exceptions they slept and took all meals under supervision in the center. Preadmission evaluation included complete history and physical examination, hepatic and renal function tests, thyroid indices, serum electrolytes, uric acid, total protein, albumin, calcium, phosphorus, fasting glucose, complete blood count, chest x-ray, and electrocardiogram. One volunteer in the carbohydrate-containing diet group took oral contraceptives throughout the study. All others were taking no medication. All volunteers maintained their usual physical activity which in no case included any physical training.

Diets. During an initial 11-d base-line period, the participants were fed a weight-maintaining diet containing 45% carbohydrate, 40% fat, and 15% protein. They were then assigned randomly to one of two 830-kcal/d diets for the next 6 wk: carbohydrate-containing (CC)[1] diet group: (n = 4) 35% protein, 29% fat, 36% carbohydrate; or carbohydrate-restricted (CR) diet group: (n = 4) 35% protein, 64% fat, 1% carbohydrate. The diets consisted of lean meat, fish, or fowl, with margarine to provide extra fat and grape juice for extra carbohydrate. Bouillon was given two to three times per day to provide additional sodium, and potassium intake was supplemented with 25 meq/d of the chloride. Calcium intake was supplemented with 200 mg/d of the carbonate. Multivitamins with iron were given daily. Noncaloric beverages were allowed ad lib.

Measurements and calculations. Weight and vital signs were measured daily, and urine ketones were measured twice daily. The percentage of body fat was estimated during the base-line period and during the final week of the study by hydrostatic weighing (8) after corrections for residual lung volume as measured by the helium dilution technique. The VO₂max was determined for each subject after an overnight fast during the base-line period and in the 6th wk of the experimental diet period. Serial 4-min work bouts of increasing severity on a cycle ergometer were interrupted by sufficient time to allow subjective recovery. The test was stopped when the subject could not complete 4 min of exercise at a higher work load. During this and all other bouts of strenuous exercise, each subject was constantly monitored by electrocardiogram. Expired air was collected in weather balloons during the final 60 s of each work bout, and the

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[1] *Abbreviations used in this paper:* CC, carbohydrate-containing; CR, carbohydrate-restricted; RQ, respiratory quotient, VO₂max, maximal oxygen uptake.

volume was measured in a Tissot apparatus and reduced to standard temperature and pressure. Aliquots of gas were collected over mercury for carbon dioxide and oxygen measurement by the Scholander method (9). VO₂max was defined as the highest calculated oxygen uptake of the serial samples.

Endurance of the subjects was measured after an overnight fast at the end of the base-line period and after consuming the experimental diet for 1 and 6 wk. On the morning of the test, an indwelling cathether was placed in a forearm vein and kept open with an infusion of 0.9% saline. Just before catheter placement, a percutaneous muscle biopsy was obtained from the vastus lateralis muscle. After local anesthesia, a 3.5-mm Diam side cutting needle was passed through a 5-mm skin incision and subcutaneous adipose tissue, and then advanced ~ 3 cm beyond the muscle fascia. A single pass with the inner cutting cylinder yielded muscle samples of 10–25 mg in size. The muscle tissue was rapidly dissected free from visible connective tissue and fat. Samples were suspended from a stainless steel wire attached to the enclosed weighing arm of a Mettler balance and weighed at timed intervals for 2–3 min. Initial weights were calculated by extrapolation to time zero when the sample was extracted from the needle. The sample was then immediately solubilized for glycogen determination.

20 min after the biopsy and catheter placement, the first base-line blood samples were drawn for complete blood count, serum electrolytes, blood urea, nitrogen, creatinine, total protein, albumin, and various substrates and hormones. The latter included glucose, lactate, pyruvate, beta-hydroxybutyrate, acetoacetate, FFA, insulin, glucagon, and growth hormone. Upon completion of blood sampling, each subject cycled for 5 min with no load (unloaded pedaling). Immediately after stopping, blood for measurement of substrates and hormones was drawn. When fully rested, subjects pedaled for repeated bouts of 15 min separated by 5 min of rest. Work load was adjusted to 70% of each subject's tested base-line maximum work load and was held constant for each of the three endurance tests. For example, if the base-line VO₂max was achieved at a work load of 200 W, the endurance test was performed at 140 W (0.70 × 200 W) at base line, 1 and 6 wk. The ergometer (Godart, DeBilt, Holland) was electromagnetically controlled to hold the work load constant, independent of revolutions per minute. Expired gases were collected in weather balloons for 60 s during the final minute of unloaded pedaling and during the 12th–13th min of each exercise bout for calculation of minute ventilation, oxygen consumption, carbon dioxide production, and respiratory quotient. At 14 min into each exercise period, blood samples were obtained for the substrate and hormone measurements. When a volunteer reported that she was near exhaustion before the end of a full 15 min work bout, the gas collections and then the blood samples were immediately collected. In all cases this was in the final 5 min of exercise. The test was ended when the volunteer was unable to continue pedaling at the determined work load. Immediately after stopping exercise, the muscle biopsy was repeated for glycogen determination.

Analyses and calculations. Muscle glycogen was determined by first solubilizing muscle tissue in 30% KOH and then precipitating the glycogen with iced ethanol, and hydrolyzing in 6 N H₂SO₄. The glucose released was measured colorimetrically with orthotoluidine (10).

Plasma insulin and growth hormone were measured by a double antibody immunoassay method using I¹²⁵-labeled pork insulin and human growth hormone as tracers and human insulin and growth hormone standards. Plasma glucagon was measured by a double antibody immunoassay method using

I[125]-glucagon purchased from Nuclear Medical Laboratories, Dallas, Tex., antiglucagon serum 30K (R. Unger, University of Texas [S.W.], Dallas, Tex.), and porcine glucagon standards (Eli Lilly and Company, Indianapolis, Ind.). Blood specimens were collected in the presence of 500 U/ml kallekrein inhibitor (Trasylol, FBA Pharmaceuticals, New York) to retard degradation of glucagon.

Lactate, pyruvate, betahydroxybutyrate, acetoacetate, and glycerol were measured in protein-free filtrates obtained by adding blood to an equal volume of iced 30% perchloric acid. The assays were modifications of enzymatic methods described in Bergmeyer (11) using an American Instruments Co. (Silver Spring, Md.) Fluoro-colorimeter to record changes in NADH concentrations. Plasma FFA were determined by the colorimetric method of Novak (12). Plasma glucose was measured by a glucose oxidase method with a YSI model 23A glucose analyzer (Yellow Springs Instrument Co., Yellow Springs, Ohio).

Statistical analysis. Statistical analysis of the data was by repeated measures of analysis of variance (13). The substrate and hormone concentration data during exercise and rest periods are reported as the means of all work bouts of all participants, regardless of the number of exercise periods. This was done to compensate for variations in the number of completed work bouts among volunteers and the same volunteer during different tests. Although this analysis minimizes changes in substrate and hormone concentrations that occur as work progresses, it is the most straightforward way to report the data, and does not distort the relevant results. All data are expressed as mean and the standard error of the mean unless otherwise noted.

RESULTS

Weight loss and routine laboratory studies. All subjects maintained stable weight during the base-line period after an initial 2–3 d of adjustment. The mean percentage of weight loss of the CR group, taking 1% carbohydrate, was greater than that of the CC group after 1 wk, 4.6±0.5 vs. 3.4±0.2% ($P < 0.05$), but thereafter, weight loss did not differ between groups. The mean fat loss was equivalent between groups after 6 wk (Table I). Fasting serum total protein, albumin, hemoglobin, blood urea, nitrogen, creatinine, calcium, and phosphorus concentrations remained in the normal range throughout the study period, and no difference
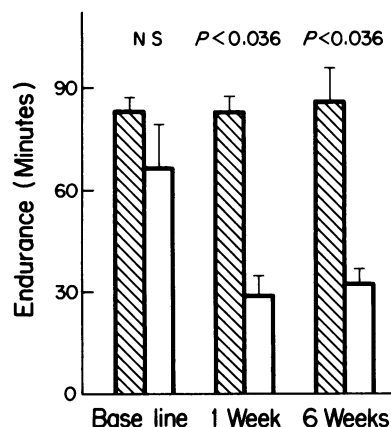

FIGURE 1   Endurance at ~75% VO_{2max}. Endurance time was calculated by adding the time pedaling the cycle ergometer of each successive work bout until subjective enhaustion. The values are expressed as the mean±SEM, $n = 4$ per group. The hatched bars represent the carbohydrate-containing diet group; the open bars represent the carbohydrate-restricted group.

occurred between groups. Serum bicarbonate declined to significantly lower concentrations in the CR group than in the CC group, 17.3±0.43 vs. 21.5±0.65 meq/liter ($P < 0.033$) after 1 wk, but after 6 wk there was no difference between groups (19.8±0.75 vs. 20.8±0.63). The changes in retinol-binding protein, thyroxine-binding prealbumin and transferrin, as well as the assessments of appetite and mood will be reported elsewhere.

Exercise capacity and muscle glycogen. After 6 wk of dieting, the VO_2max did not change significantly from base line in the CC group (2,200±210 ml/min vs. 2,200±90 ml/min) or in the CR group (2,200±110 vs. 1,900±55 ml/min). Whether expressed as milligrams per kilogram per minute, or milliliters per kilogram of lean body mass per minute (as estimated from hydrostatic weighing), no group differences in VO_2max were observed.

The actual workloads for the endurance tests, cal-

TABLE I
Subject Characteristics, Total Weight and Fat Loss

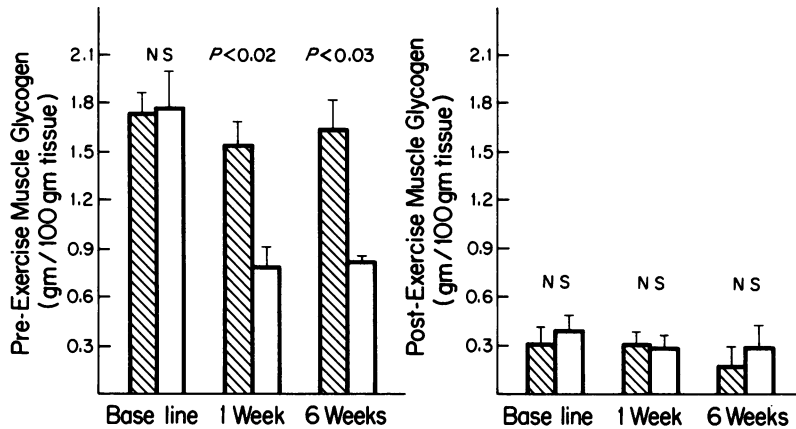| Age		Initial wt		Initial fat*		Total Wt loss		Total fat loss*	
Group A	Group B	Group A	Group B	Group A	Group B	Group A	Group B	Group A	Group B
yr		kg		%		kg		kg	
22	26	63.3	78.6	35	41	5.2	8.4	3.4	5.1
27	30	65.1	67.6	39	31	5.5	7.0	4.8	4.5
24	34	95.6	106.4	41	47	10.0	9.4	5.7	9.5
28	26	85.4	81.1	41	37	8.7	8.8	5.4	3.9
Mean±SEM									
25±1.4	29±1.9	77.4±7.9	83.4±8.2	39±1.4	39±3.4	7.4±1.2	8.4±0.5	4.8±0.5	5.7±1.3

* As estimated by body density measurements (see Methods).

FIGURE 2 Preexercise (resting muscle) glycogen and immediately after exercise muscle glycogen. Values are expressed as the mean±SEM. The hatched bars represent the CC diet group; the open bars represent the CR group. $n = 4$ per group at each base line, 1, and 6 wk except in the CC diet group, $n = 3$ at the base-line determination.

culated as percentage of the base-line VO₂max, were 83±3.5, 76±4.7, and 72±2.9% for the CC group at base line, 1 and 6 wk, respectively. These were not significantly different from the corresponding work loads of the CC group, 76±3.1, 73±2.0 and 71±2.5%. The decline in the percentage of oxygen consumption during the successive endurance tests occurred despite the use of equal work loads for the three tests. This was probably due, in part, to a decrease in the resting metabolic rate while taking the hypocaloric diet. Also, with some loss of weight in the thighs, the actual work load may have been slightly decreased, and the work efficiency may have been slightly increased.
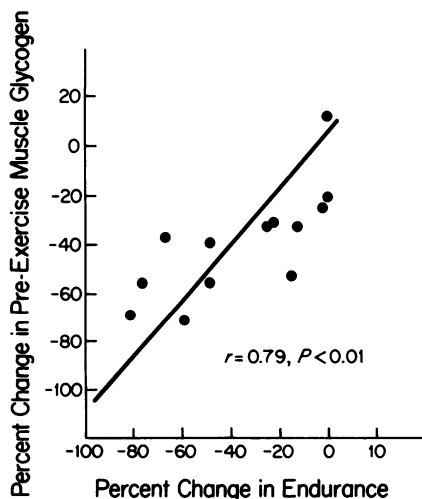

FIGURE 3 Correlation between percent change in endurance and percent change in resting muscle glycogen. The values are calculated as percent changes from the base-line period after 1 and 6 wk on the diet for four subjects in the CR group and three subjects in the CC group.

Endurance capacity in the CR group declined from a base-line mean of 66.5±13.5 to 29.0±4.5 min at 1 wk, and to 31.7±5.0 min after 6 wk. These were large decreases in performance compared with that of the CC group, 83.0±3.1, 82.1±8.7, and 86.0±8.6 min during the three successive periods. The changes in endurance are shown in Fig. 1. All participants appeared to give a maximal effort during each test. They uniformly stopped exercise because of local muscle fatigue, not because of dyspnea, palpitations, or more generalized exhaustion.

Muscle glycogen in the preexercise period in the CC group decreased from 1.74±0.13 g/100 g tissue at base line, to 1.54±0.14 g/100 g tissue after 1 wk, and 1.65±0.22 g/100 g at 6 wk. Significantly larger declines ($P < 0.023$) occurred in the CR group: 1.76±0.22 g/100 g tissue, 0.81±0.14 g/100 g tissue, 0.86±0.04 g/100 g tissue at base line, 1 and 6 wk, respectively (Fig. 2). In the CC group, the base line period preexercise muscle glycogen is the mean±SEM for three volunteers because one volunteer's muscle biopsy sample was inadequate for glycogen determination. All other muscle glycogen results were calculated from four volunteers in each group, at base line, 1 and 6 wk. The mean postexercise muscle glycogen concentration in the CC group, 0.31±0.14 g/100 g tissue, 0.31 ±0.09 g/100 g tissue, and 0.19±0.12 g/100 g tissue were not significantly different from those of the CR group: 0.41±0.08 g/100 g tissue, 0.28±0.09 g/100 g tissue, and 0.28±0.09 g/100 g tissue at base line, 1 and 6 wk, respectively (Fig. 3). The percent changes in muscle glycogen correlated well with the percent changes in endurance ($r = 0.79, P < 0.01$) (Fig. 3).

Respiratory Quotient (RQ). The RQ during unloaded pedaling, at base line, 1 and 6 wk (0.78±0.06, 0.80±0.06, and 0.76±0.04) in the CC group were not

significantly different from the CR group (0.83±0.05, 0.84±0.05, and 0.86±0.7). The RQ during the first endurance work bout was greater in both groups compared with that during unloaded pedaling (P < 0.002), and did not differ between groups; CC group, 0.87 ±0.05, 0.90±0.07, and 0.91±0.04, and the CR group, 1.00±0.02, 0.96±0.06, and 0.93±0.07, at base line, 1, and 6 wk, respectively.

Substrates and hormones (Fig. 4). The mean fasting insulin, growth hormone, lactate, pyruvate, FFA, and glycerol concentrations were equivalent between groups at base line, 1 and 6 wk. The mean fasting serum glucose concentration was lower (P < 0.036) and the mean total ketone concentration higher (P < 0.001) in the CR group than in the CC group at 1 and 6 wk during the experimental diet. The mean fasting glucagon concentration was equal between groups during the base-line diet and after 6 wk, but at 1 wk it was higher (P < 0.03) in the CR group than in the CC group.

The changes in the mean glucose, FFA, betahydroxybutyrate, insulin, and glucagon concentrations during the three endurance tests were similar between groups at base line, 1, and 6 wk. The mean acetoacetate concentration declined during exercise in the CR group, whereas it increased in the CC group (P < 0.007). The mean growth hormone concentration was higher during the exercise and rest period in the CR group (P < 0.008) than in the CC group after 1 and 6 wk. This is possibly due, in part, to the decreased endurance in the CR group, since as the exercise continued the growth hormone concentration gradually declined, and these later values would lower the mean value in the CR group. The mean glycerol concentration was higher in the CR group (P < 0.02) only during the last endurance test.

DISCUSSION

This study was designed to determine whether there are differences in metabolic fuel use and/or the capacity for strenuous exercise after adaptation to a carbohydrate-containing or a carbohydrate-restricted, hypocaloric diet. During 6 wk of a low carbohydrate diet (1% carbohydrate, 830-kcal/d), muscle glycogen stores were depleted to ~50% of base-line levels and there was a similar reduction in the capacity for strenuous exercise (~75% VO₂max on a cycle). The fact that this was an effect of carbohydrate restriction and not due to caloric restriction alone, was evident by the maintenance of resting muscle glycogen and exercise capacity during the period of the isocaloric, carbohydrate-containing diet. Furthermore, since there were no significant differences between groups in body composition changes, or in the fuels used during exercise (as estimated by changes in RQ and substrate concentrations), differences in endurance could not be attributed to these parameters.
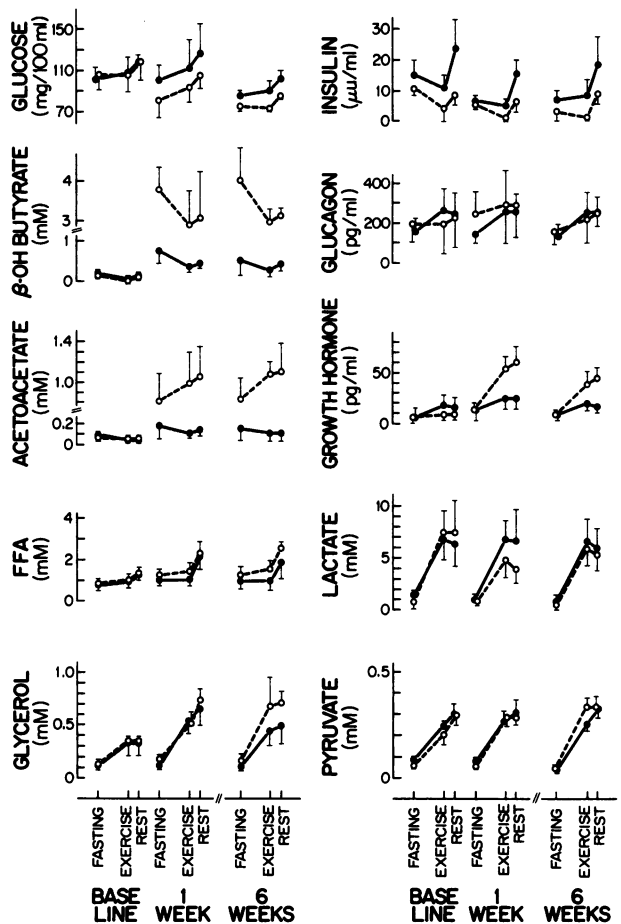

FIGURE 4 Substrate and hormone concentrations during the three successive exercise tests. The fasting concentrations are the mean±SEM of all subjects within each diet group (n = 4 per group). The substrate and hormone concentration data during exercise and at the end of the 5-min rest periods are reported as the means±SEM of all work bouts of all subjects within each group, regardless of the number of exercise periods. The dashed lines (- - -) represent the CR diet group, the solid lines (—) represent the CC diet group. See Results for statistics.

In our previous study (7), six untrained obese subjects were evaluated before and after 1 and 6 wk of a low carbohydrate, hypocaloric diet. The base-line endurance test was performed on a treadmill at a mean intensity of 76% VO₂max, but despite carrying a backpack with weight equivalent to the weight loss, the 6-wk test was performed at only 60% VO₂max. This probably accounted for part of the 55% increase in endurance during treadmill exercise after 6 wk. It is also possible that after adaptation the elevated FFA concentrations during the period of the diet decreased the rate of glycogen depletion, and thus improved endurance. This has also been shown by the study of Costill et al. (14) during similar FFA elevations and work loads (68% VO₂max on a treadmill). The "glyco-

gen sparing" effect, however, probably only applies to slow twitch, high oxidative fibers, which are the predominant fibers recruited during moderate work loads, and not to fast twitch, glycolytic fibers (15), which are recruited at high work loads. In our study, using cycle exercise at 75% VO₂max, a much greater work load was applied to the quadricep muscles, and glycolytic pathways were recruited, as indicated by a mean exercise RQ of 0.93 and the elevations of lactate during exercise. Fiber typing was not done, but it is likely that the fast-twitch fibers were recruited. Thus, at work loads > 70% VO₂max on a cycle (in untrained subjects) compared with 60% VO₂max on a treadmill, as in the previous study, muscle glycogen is not "spared" after adaptation to the diet, and the depletion of muscle glycogen occurring during carbohydrate restriction limits endurance. If the glycogen stores are maintained, as during the hypocaloric carbohydrate-containing diet, endurance at these higher work loads is maintained.

These results are important for the design of combined exercise and diet programs for the treatment of obesity. Subjects taking a carbohydrate-containing, hypocaloric diet (36% carbohydrate, 830-kcal/d) can exercise at a broad range of work loads. In contrast, untrained subjects taking a carbohydrate-restricted, hypocaloric diet (1% carbohydrate, 830-kcal/d) probably should not enter a physical training program requiring exercise at high submaximum work loads. This apparent disadvantage should be weighed with other known advantages and disadvantages of low carbohydrate, hypocaloric diets when devising a weight reduction program for obese, untrained subjects. More studies are needed, however, to delineate more exactly the quantity of calories and/or carbohydrate that is required to maintain resting muscle glycogen and the capacity for strenuous exercise.

Conclusions. During 6 wk of a carbohydrate-containing or carbohydrate-restricted 830-kcal/d diet, similar changes in blood substrate concentrations are achieved during exercise at ~75% VO₂max on a cycle. The relative .contributions of glucose and lipids to energy production, as estimated by the steady-state RQ appear to be the same.

Resting muscle glycogen content and endurance, at ~75% VO₂max on a cycle, are maintained while taking a 36% carbohydrate, 830-kcal/d diet. In contrast, after 6 wk of a 1% carbohydrate, 830-kcal/d diet, significant decreases occur in resting muscle glycogen and in the capacity for cycle exercise at ~75% VO₂max.

ACKNOWLEDGMENTS

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