Body composition, energy utilization, and nitrogen metabolism with a 4.25-MJ/d low-energy diet supplemented with pyruvate[1-3]

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ABSTRACT We measured body composition, energy deficit, and nitrogen metabolism in 14 obese women housed in a metabolic ward, who consumed a 4.25-MJ/d liquid diet (68% carbohydrate, 22% protein) for 21 d with or without pyruvate (PY; $n = 7$) partially, isoenergetically substituted for glucose (placebo; $n = 7$). Body composition and leucine oxidation and turnover were determined before and after weight loss. Energy deficit was calculated from resting metabolic rates. Subjects fed pyruvate showed a greater weight loss (PY = 5.9 ± 0.7 kg, placebo = 4.3 ± 0.3 kg, $P < 0.05$), fat loss (PY = 4.0 ± 0.5 kg, placebo = 2.7 ± 0.2 kg, $P < 0.05$), kg wt loss/4.25-MJ deficit (PY = 0.22 ± 0.01 kg, placebo = 0.17 ± 0.01 kg, $P < 0.05$, and kg fat loss/4.25-MJ deficit (PY = 0.15 ± 0.01 kg, placebo = 0.11 ± 0.01 kg, $P < 0.05$). Nitrogen balance (urine and stool) and leucine oxidation and turnover were similar in both groups. We conclude that the dietary modification whereby the three-carbon compound pyruvate is isoenergetically substituted for the six-carbon compound glucose in a 4.25-MJ/d, low-energy diet will increase fat and weight loss. *Am J Clin Nutr* 1992;56:630–5.

KEY WORDS Pyruvate, energy, body composition

Introduction

In an effort to evaluate whether dietary modification can influence energy utilization (1), we performed studies in which rats and swine were fed diets that induced body mass gain, but in the experimental diet the three-carbon compounds dihydroxyacetone and pyruvate were isoenergetically substituted for a portion of the six-carbon compound (glucose) content of the placebo diet. In both animal models, isoenergetic substitution of the three-carbon compounds for glucose in the diet resulted in inhibition of expected lipid deposition while nitrogen stores were maintained (2, 3). We recently investigated the effects of the above three-carbon compounds on body-composition changes associated with hypoenergetic feeding (4). In human subjects consuming a severely restricted (2.1-MJ/d) low-energy diet, addition of dihydroxyacetone and pyruvate resulted in increased weight and fat loss without increased loss of nitrogen (4). Cortez et al (5) evaluated the effects of the above three-carbon compounds, alone or in combination, on metabolism in growing obese Zucker rats. Pyruvate alone was found to have comparable or greater effects on body composition and metabolic indices than did the combination of dihydroxyacetone and pyruvate (5).

The effects of individual three-carbon compounds on body composition in human subjects consuming low-energy diets have not been evaluated. Because many weight-reduction programs initially use severely restricted low-energy diets followed by therapy with mildly restricted low-energy diets, the effects on body composition of individual three-carbon compound supplementation of mildly restricted low-energy diets is of interest. The present study was designed to determine the effects of pyruvate alone on body composition with a low-energy diet fed in mildly restricted amounts. We evaluated the effect of pyruvate on weight loss, composition of weight loss, kilograms of weight lost per 4.25-MJ deficit, amino acid oxidation, and nitrogen balance in obese women consuming a 4.25-MJ/d diet for 21 d.

Methods

Subjects

Fourteen obese women, after giving informed consent to participate in this study, were admitted to the Clinical Research Center of the University of Pittsburgh School of Medicine. The criteria for selection included absence of pregnancy and of heart, kidney, liver, intestinal, and pulmonary diseases. Two subjects had hypertension controlled with mild diuretics. All medications in all subjects were discontinued 3 d before the study period. Subjects were confined to bed except for walking to lavatory facilities or to the metabolic kitchen, where they could be closely observed to completely consume the diets. Subjects were requested to refrain from exercise and were observed continuously for compliance. This study was approved by the Institutional Review Board for Biomedical Research of the University of Pittsburgh.

Nutritional treatment

During the initial 3 d, subjects were fed a balanced diet that provided 8.8–10 MJ/d. For the subsequent 21 d, all subjects

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consumed a 4.25-MJ/d liquid, low-energy diet (Appendix A) that consisted of 68% carbohydrate, 22% protein (50 g, high quality, highly digestible), and 10% fat. The subjects were randomly assigned to receive either pyruvate (Chemical Dynamics Company, South Plainfield, NJ) or a polyglucose placebo (Polycose; Ross Laboratories, Columbus, OH) as 13% of energy intake (as a portion of carbohydrate energy). To closely match energy and elemental content, we chose glucose as the placebo for pyruvate. The polyglucose was chosen as placebo because it had been extensively studied and shown to be similar to glucose, is approved for human consumption because of many years of clinical usage without major metabolic complication, and was prepackaged and readily available. For accuracy, pyruvate or polyglucose were added to the prepackaged powdered form of the liquid low-energy diet rather than glucose being extracted from the diet and adding pyruvate. Thirty grams pyruvate [20 g sodium pyruvate (0.010 MJ/kg) plus 16 g calcium pyruvate (0.010 MJ/kg)] or 22 g polyglucose (0.016 MJ/kg) were added to the liquid diet. At the time of this study, sodium pyruvate and calcium pyruvate were the only compounds of pyruvate approved for human consumption. The dosage of pyruvate is approximately one-half of the dose of the combination of three-carbon compounds (dihydroxyacetone and pyruvate) shown to induce body-composition changes in human subjects fed a low-energy diet in severely restricted (2.1 MJ/d) amounts (4), but is the maximum dose usable to maintain sodium (5.6 g) and calcium (2.2 g) intakes at amounts (determined by preliminary trials) that were without major complication with 21 d of consumption. The sodium and calcium contents of the diets were made similar by adding sodium citrate and calcium hydroxide to the placebo diet. The placebo and pyruvate supplement to the diets were determined to be isoenergetic by bomb-calorimetric analysis.

Body composition

To estimate body composition, bioelectrical impedance was determined with a plethysmograph (RJL Systems, Detroit). Plethysmograph leads were placed on the right hand and foot of the subjects when they were in a supine position and wearing light clothing and no shoes and socks. Bioelectrical impedance was determined at 0900 1 d before and the day of initiation of the low-energy diet. The results were averaged and used to determine initial body composition. Impedance was also determined on the final 2 d of the low-energy diet, averaged, and final body composition calculated. Fat-free mass (FFM; lean body mass in kg) and body fat content (BFC) were calculated with the following equations (6):

$$\text{FFM (in kg)} = 0.00091186(\text{H})^2 - 0.01466\text{R} + 0.299\text{W} - 0.07012\text{A} + 9.37938$$

$$\text{BFC} = \text{W} - \text{FFM}$$

where H is height (in cm), R is resistance (in Ω), A is age (in y), BFC is body-fat content (in kg), and W = weight (kg).

Body-fat distribution was characterized by estimating fat depots at the waist and hips. Three measurements of waist circumference (midway between the lower rib margin and the iliac crest) and hip circumference (at the widest point between the hip and buttock) were performed and results averaged and expressed as waist circumference/hip circumference.

Energy metabolism

Resting metabolic rate (RMR) was determined postabsorptively at 0700 on the day the diets began and after 21 d of diet consumption by indirect calorimetry with a metabolic cart with a canopy collection system (MMC Horizon, Sensormedics, Anaheim, CA). Because preliminary studies showed that gas-exchange measurements were similar at durations of 15, 30, or 60 min, gas exchange was collected for two 15-min periods separated by 1 h of bed rest. Energy expenditure (EE) of daily activity in the metabolic ward was estimated as 30% of RMR and daily total EE calculated as 1.3 RMR (7). Daily energy deficit for individual subjects throughout the study was determined by subtracting 4.25 MJ from daily EE. Garrow and Webster (8, 9) recently measured changes in RMR in 108 obese women consuming a 3.3-MJ/d hypoenergetic diet for 21 d. RMR decreased by 8.8% during the 21 d, with 6% (68% of total change) occurring during the final 7 d of weight loss and 2.8% (32% of change) occurring during the final 14 d of weight loss. Therefore, to account for this variability in energy changes with weight reduction, the daily energy deficit throughout our study was determined from daily RMR calculated with the following equations:

Week 1: RMR (day x)

$$= \text{RMR}_{\text{baseline}} - 0.68 \times (\text{RMR}_{\text{baseline}} - \text{RMR}_{\text{day 21}})/7$$

where x = 1–7.

Weeks 2 and 3: RMR (day x)

$$= \text{RMR}_{\text{day 7}} - 0.32 \times (\text{RMR}_{\text{baseline}} - \text{RMR}_{\text{day 21}})/14$$

where x = 1–14.

Total energy deficit for the period of feeding of the low-energy diets was determined by summing the 21 daily energy deficits.

Nitrogen metabolism

During the entire 21 d of feeding the low-energy diets, all urine and stool was collected and analyzed for nitrogen by a micro-Kjeldahl technique (10). Insensible losses of nitrogen were assumed to be 5 mg · kg body $wt^{-1} \cdot d^{-1}$ (11). At 0900 on the last day of the study, peripheral venous blood was obtained for analysis of serum proteins. As a measure of nitrogen metabolism, leucine oxidation and turnover were determined postabsorptively at 0900 on the d of initiation of the low-energy diet and after 21 d of feeding the diet. Leucine oxidation and turnover were determined according to the technique described by Vazquez et al (12). In brief, a bolus dose of 0.019 MBq [1-^{14}C]leucine (Amersham Corp, Arlington Heights, IL; 2072 MBq/mmol) was administered through an indwelling antecubital catheter. A continuous infusion was begun immediately after the priming dose. [1-^{14}C]Leucine in saline was infused at a rate of 0.21 mL/min (0.0017 MBq/min) over a 3-h period. Breath samples were collected at 0, 60, 90, 120, 150, and 180 min. Samples were collected in a scintillation counting vial containing 4 mL of a 1:1 (vol:vol) hydroxide of hyamine-10×, absolute ethanol, and thymolphthalein indicator. The solution was calibrated to change color from blue to clear when 2 mmol CO_2 had been collected. Samples were then counted in a scintillation counter.

Venous blood samples were collected at 135, 150, 165, and 180 min (after equilibrium of [^{14}C]leucine occurred and specific activities of leucine had reached near constant values). Blood samples were spun and the plasma precipitated with 6% sulfo-

TABLE 1
Patient profile

Diet and subject	Waist/hip circumference	Initial weight	Initial body fat	Initial BMI*	Initial REE†	Weight loss	Fat loss	Energy deficit
		kg	*kg*		*MJ/d*	*kg*	*kg*	*MJ*
Placebo								
1	0.83	140.7	71.4	47.5	9.4	5.2	3.0	146.2
2	0.78	114.7	61.7	47.8	6.4	3.7	1.9	83.0
3	0.98	103.2	48.8	36.1	8.6	5.1	3.1	125.4
4	0.86	98.0	42.2	33.1	8.0	4.3	2.7	122.5
5	0.78	97.4	46.8	35.3	6.4	3.3	2.3	71.4
6	0.83	97.2	44.3	34.0	8.1	5.1	3.4	124.0
7	0.78	78.1	32.9	28.0	6.7	3.2	2.4	86.2
$\bar{x}$	0.83	104.2	49.7	37.4	7.7	4.3	2.7	108.4
SE	0.03	7.3	4.9	2.8	0.4	0.3	0.2	10.5
Pyruvate								
1	0.80	149.0	79.8	51.6	8.6	9.2	6.1	145.5
2	0.83	138.2	72.0	52.7	8.8	6.6	4.7	145.8
3	0.78	114.6	61.6	47.7	6.5	4.0	2.1	83.8
4	0.76	101.7	45.2	35.6	8.5	6.4	4.7	118.5
5	0.96	101.7	48.8	38.2	7.4	5.0	3.5	106.7
6	0.77	97.2	47.6	43.2	7.9	5.9	3.8	117.9
7	0.93	74.9	28.6	27.8	6.2	3.9	3.1	75.4
$\bar{x}$	0.83	111.0	54.8	42.4	7.7	5.9‡	4.0‡	113.4
SE	0.03	9.6	6.6	3.4	0.4	0.7	0.5	10.3

* In kg/m^2.
† Resting energy expenditure.
‡ Significantly different from placebo, $P < 0.05$.

salicyclic acid (3:1, vol:vol). The rate of carbon dioxide production was measured throughout the experiment by a metabolic cart and canopy system.

Rates of leucine turnover and oxidation were calculated with the following formulas:

$$Q = I/SA_{pl}$$

where Q is the turnover rate (mmol/h), I is the infusion rate of tracer (disintegrations $\cdot$ $min^{-1} \cdot h^{-1}$), and SA_{pl} is the plasma specific activity of tracer during steady state (disintegrations $\cdot$ $min^{-1} \cdot mmol^{-1}$).

$$Ox = (SA_{CO_2} \times PR)/(SA_{pl} \times FR)$$

where Ox is the oxidation rate (mmol/h), SA_{CO_2} is the specific activity of carbon dioxide in expired air at steady state, PR is the carbon dioxide production rate (mmol/h), SA_{pl} is plasma specific activity of tracer at steady state (disintegrations $\cdot$ $min^{-1} \cdot mmol^{-1}$), and FR is the fraction of carbon dioxide recovered during infusion of [^{14}C]bicarbonate. All values of leucine oxidation were corrected by the same $^{14}CO_2$ recovery factor of 60%.

Laboratory evaluations

Laboratory evaluations included complete blood count; urinalysis; electrocardiogram; blood concentrations of glucose, cholesterol, triglyceride, creatinine, urea nitrogen, and electrolytes; liver-function tests [serum bilirubin, pyruvic transaminase (SGPT), oxaloacetic transaminase (SGOT), and alkaline phosphatase]; albumin; total protein; transferrin; thyroxine; triiodothyronine uptake; and free thyroxine index. These tests were performed before initiation of and subsequent to feeding the low-energy diets.

Statistical analysis

Because previous studies have shown that three-carbon compounds would induce changes in body composition (2–5), and differences in weight and fat loss between groups should be expected in this study, weight and body-fat changes between the two groups were evaluated with the Mann-Whitney one-tailed *t* test (13). Because no other differences were expected between groups, other changes between groups were evaluated with the Mann-Whitney two-tailed *t* test (13). Statistical analysis of changes within the same group (before and after feeding the low-energy diet) was performed with the paired *t* test (13). Differences were considered significant at $P < 0.05$. All data are presented as mean ± SE of seven subjects.

Results

After randomization, initial body weight, body mass index, body fat, body-fat distribution (waist circumference/hip circumference), and RMR of the groups of obese subjects receiving the placebo and pyruvate diets varied slightly but were not significantly different (**Table 1**).

Weight and fat loss were greater after pyruvate consumption than after placebo consumption ($P < 0.05$, Table 1). Although the total energy deficit during the 21 d of feeding the low-energy diet was similar in both groups (Table 1), weight and fat loss/4.25-MJ deficit were greater in the pyruvate group ($P < 0.05$, **Table 2**). To account for minor variability in initial body weight

TABLE 2
Characteristics of body-composition changes*

	Placebo group	Pyruvate group
FFM loss (kg)	1.6 ± 0.2	1.9 ± 0.2
Change in body mass index†	1.5 ± 0.1	2.2 ± 0.2‡
Weight loss/4.25-MJ deficit (kg)	0.17 ± 0.01	0.22 ± 0.01‡
Fat loss/4.25-MJ deficit (kg)	0.11 ± 0.01	0.15 ± 0.01‡
Weight loss/initial body weight (%)	4.1 ± 0.3	5.3 ± 0.4‡
Fat loss/initial body fat (%)	5.4 ± 0.6	7.3 ± 0.9‡
FFM loss/initial FFM (%)	2.9 ± 0.2	3.4 ± 0.3
Fat loss/weight loss (%)	62.8 ± 3.3	67.8 ± 3.2
FFM loss/weight loss (%)	37.2 ± 2.5	32.2 ± 2.4

* $\bar{x}$ ± SE; n = 7. FFM, fat-free mass.
† In kg/m^2.
‡ Significantly different from placebo, $P < 0.05$.

and body fat between groups, we also expressed weight and fat losses as a percent of initial body weight and fat. Weight loss/initial body weight and fat loss/initial body fat were increased in the pyruvate group ($P < 0.05$). FFM loss/initial body FFM, fat loss/weight loss, and FFM loss/weight loss were similar in both groups of subjects (Table 2).

There was no difference in weekly and cumulative nitrogen balance between groups (**Table 3**). Leucine oxidation and turnover decreased with weight reduction but changes were similar between groups of subjects. Similarly, serum concentrations of albumin (long half-life protein) and transferrin (short half-life protein) were not different with feeding of placebo or pyruvate (data not shown).

There were no differences between any blood biochemical variables reflecting heart, liver, or thyroid function of subjects treated with placebo or pyruvate. With weight reduction only minor differences, all within the range of normal values, were seen within groups (data not shown).

With weight reduction, RMR decreased by 9% in the placebo group and 7% in the pyruvate group. After 21 d of feeding the low-energy diet, RMR was 6.9 ± 0.4 MJ/24 h in the placebo group and 7.2 ± 0.4 MJ/24 h in the pyruvate group (NS).

Discussion

In our subjects consuming a 4.25-MJ/d, low-energy diet for 21 d, partial isoenergetic substitution of the three-carbon compound pyruvate for the six-carbon compound carbohydrate increased weight and fat loss and the amount of weight and fat loss per 4.25-MJ deficit. Patients in the pyruvate group increased weight loss by 37% and fat loss by 48%. Weight loss/4.25-MJ deficit was enhanced by 29% and fat loss/4.25-MJ deficit by 36% with pyruvate consumption. Weight loss/initial body weight increased by 29% and fat loss/initial body fat increased by 37% in the pyruvate group. The decrease in body mass index was also greater by 47% with pyruvate. Nitrogen losses (nitrogen balance) and leucine oxidation and turnover were not increased with pyruvate supplementation of the diet. Weight loss, quality of weight loss (weight and fat loss compared with protein loss), and weight loss per energy deficit induced by feeding a low-energy diet in mildly restricted amounts were improved with partial isoenergetic substitution of a three-carbon compound for the six-carbon compound content of the diet.

Three-carbon compounds increase RMR (2) and the respiratory quotient (5) in rats. However, as we found in human subjects consuming a 2.1-MJ/d, low-energy diet supplemented with dihydroxyacetone and pyruvate (4), RMR was not increased in the pyruvate group of subjects in the present study. The pyruvate group showed only a 2% smaller decrease in RMR with weight reduction (NS) and an increase in total energy deficit with hypoenergetic feeding of only 5.0 MJ (NS). This relative increase in EE cannot explain the increased weight loss of 1.6 kg seen with pyruvate supplementation. Our determination of RMR would seem to adequately reflect energy metabolism in our subjects because we found the identical decrease (9%) in RMR with weight reduction in our placebo group that was recently reported in 103 obese women consuming a 3.3-MJ/d diet (8). Nevertheless, the sensitivity of the metabolic-cart measurements of EE used in this study is probably inadequate to detect small energy changes induced by pyruvate.

The energy cost of weight loss in our placebo group was 25.2 MJ/kg. With the increase in weight loss of 1.6 kg in the pyruvate group, hypothetically, 40.3 MJ would need to be expended to account for this enhanced weight loss. Over the 21 d of feeding, energy losses would need to be only 8 J/h greater in the pyruvate group to induce the observed weight loss. This energy loss is probably below the sensitivity and variability of short-term or even daily metabolic-cart measurements. Elucidation of the mechanism by which pyruvate enhances energy loss and subsequent weight loss will require at least weekly evaluation of EE and/or biochemical evaluation of energy metabolism. Comment on this mechanism at the present time would only be speculation. However, one possibility is that pyruvate activates and/or enhances the pyruvate-phosphoenolpyruvate futile cycle (or other futile cycles) with subsequent waste of small amounts of energy (14).

Our measurement of RMR does not include the energy cost of physical activity and the thermic effect of diet. Physical activity was restricted to keep energy cost to a minimum. Because both groups of subjects performed the same restricted activity, the energy cost of physical activity should not differentially affect

TABLE 3
Nitrogen balance and nitrogen metabolism as leucine turnover and oxidation*

	Placebo group	Pyruvate group
Nitrogen balance (g)		
Day 0–7	−14.7 ± 6.9	−15.5 ± 4.9
Day 7–14	−10.2 ± 5.4	−5.2 ± 6.5
Day 14–21	−5.9 ± 4.2	−4.0 ± 4.6
Day 0–21	−30.8 ± 16.4	−24.7 ± 15.7
Leucine turnover (mmol/h)		
Day 0	6.6 ± 1.0	7.0 ± 0.6
Day 21	5.4 ± 0.8†	5.2 ± 0.6†
Leucine oxidation (mmol/h)		
Day 0	1.1 ± 0.2	1.4 ± 0.2
Day 21	0.7 ± 0.1†	0.9 ± 0.1†

* $\bar{x}$ ± SE; n = 7.
† Significantly different from day 0, $P < 0.05$.

our results. Also, in preliminary studies, we determined that the thermic effect of diet is not affected by pyruvate. Therefore, the thermic effect of diet should not differentially affect our results.

The energy value of weight loss in our placebo group was 25.2 MJ/kg wt loss. In a 28-d study of two different 2.52-MJ/d diets (15), estimation of the energy value of weight loss with reported data reveals similar values (21–27 MJ/kg). However, after 8 wk of therapy with a 4.25-MJ/d diet, the energy value of weight loss has been reported to be 35.9 MJ/kg (16). In another 8-wk study, the energy value of weight loss was 34–38 MJ/kg for three of five hypoenergetic diets (17). However, in both of these studies, calculation of the energy value of weight loss for the short term (1–4 wk), in direct comparison with our study, reveals values very similar to what we found. Webster and Garrow (9) report an energy value of weight loss of 29.4 MJ/kg for the final 14 d of a 21-d, 3.36-MJ/d diet. However, for the total 21 d of dietary therapy, calculations with their reported data reveal the energy value of weight loss to be $\approx$17 MJ/kg. It would seem that the energy value of weight loss will vary considerably depending on the time period of weight reduction for which this index is calculated. This variability is probably secondary to differences in body-composition changes occurring during given time periods of weight reduction.

We chose to determine the body composition of our subjects with the bioelectrical impedance technique because changes in electrical conductivity have been shown to reflect body composition in obese subjects (18). Also, two recent studies of obese women who had undergone weight reduction suggest that impedance can reliably measure changes in body composition over time for individual subjects during weight loss (19, 20). Because we evaluated changes in body composition within the same subject, the inherent error of the impedance technique should be less. Despite the indirect nature of body-fat measurements used in this study, the effects of pyruvate on fat loss and fat loss/4.25-MJ deficit were similar to the effects of pyruvate on weight loss and weight loss/4.25-MJ deficit determined by standard techniques of weight measurement. Also, when nitrogen losses were used to calculate lean body mass loss in our subjects, fat loss was $\approx$50% greater in the pyruvate subjects, which is nearly identical to that calculated by using the impedance technique. The results of the present study agree with those from our previous investigation of the effects of three-carbon compounds on body-composition changes when feeding a low-energy diet (4). However, with the small differences in body-composition changes that were observed, the sensitivity of any available technique for measurement of body composition is in question, and our results must be considered preliminary and await corroboration of long-term, large-scale clinical evaluation.

In our previous study of subjects consuming a 2.1-MJ/d, low-energy diet supplemented with dihydroxyacetone and pyruvate, weight and fat-loss increases induced by these three-carbon compounds were 0.9 and 0.8 kg (16% and 23% greater than placebo), respectively (4). Increases in weight and fat losses induced by pyruvate in the present study were 1.6 and 1.3 kg (37% and 48% greater than placebo), respectively. The amount of three-carbon compounds consumed by subjects in both studies was similar (28 vs 30 g/d), but the amount of pyruvate consumed by subjects in our previous study was 16 g/d whereas the amount of pyruvate consumed by subjects in the present study was nearly twofold greater (30 g/d), as were the effects on body composition. Although our two studies of the effects of three-carbon compounds with feeding low-energy diets are not directly comparable because of different energy contents of the diets evaluated, the results of these studies suggest that pyruvate is the more active three-carbon compound with respect to body-composition changes. Cortez et al (5), likewise, found pyruvate to be the more active three-carbon compound with respect to effects on body composition, but in growing obese rats.

As evaluated by standard laboratory testing and clinical evaluation, no major metabolic side effects were seen in the patients fed 30 g pyruvate (13% of energy). The only adverse effects observed in our patients fed pyruvate were diarrhea and borborygmus in three patients. Heart rate, blood pressure, body temperature, electrocardiogram, urine output, and stool output were unaffected by pyruvate consumption (data not shown).

A reasonable goal of weight reduction appears to be to maximize body-fat loss and minimize body-protein loss. In this process, a low-energy diet that would increase weight or fat loss per energy deficit would also provide an improved treatment for weight reduction. The pyruvate diet accomplished the above goals, but, as seen in our previous study of three-carbon compound supplementation of a 2.1-MJ/d, low-energy diet (4), the effects (1.6 kg body wt, 1.3 kg body fat) were not large. Because of metabolic adaptation to weight reduction (21, 22), supplementation of low-energy diets with any weight-reduction agent probably will result in small changes in body composition. Large changes in body composition probably would be accompanied by major detrimental physiologic changes. As we previously hypothesized, there probably is a limit to the amount of weight loss, without side effects, for a given low-energy diet (4). Nevertheless, the physiologic, clinical, and psychological significance of the selective catabolic effects of pyruvate supplementation of a low-energy diet fed in mildly restricted amounts remains to be established.

Many weight-reduction programs use severely restricted hypoenergetic dietary therapy followed by mildly restricted dietary therapy. Our studies suggest that three-carbon compounds will enhance weight and fat loss with low-energy diets fed in both severely restricted and mildly restricted amounts (4). A major problem associated with unsuccessful weight-reduction programs is failure to maintain lost weight, especially with refeeding after low-energy dietary therapy. Because three-carbon compounds are known to inhibit weight and fat gain in growing animals (2, 3, 5), they may decrease weight and fat gain with refeeding and/or maintenance diets used after weight reduction. With few nontoxic weight-reduction agents presently available, our results encourage future studies to evaluate the effect of pyruvate on long-term weight reduction and weight maintenance.

Finally, the results of the present study, in conjunction with our previous investigation of a 2.1-MJ/d, low-energy diet (4), and studies of anabolic diets in rats and swine (2, 3, 5), provide rather convincing evidence that dietary modification can influence the manner and efficiency with which consumed energy is utilized. We conclude that pyruvate supplementation of a low-energy diet fed in mildly restricted amounts will increase weight and fat loss.

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APPENDIX A

Content of liquid, low-energy diet (per 0.85-MJ serving)

Component	Amount
Sodium (mg)	660
Potassium (mg)	660
Chloride (mg)	500
Vitamin A (μg)	300
Vitamin C (mg)	21
Thiamin (mg)	0.53
Riboflavin (mg)	0.6
Niacin (mg)	7
Vitamin D (μg)	3.5
Vitamin E (mg)	10.5
Pyridoxine (mg)	0.7
Folic acid (μg)	140
Vitamin B_{12} (μg)	2.1
Vitamin K (μg)	25
Biotin (μg)	105
Pantothenic acid (mg)	3.5
Phosphorus (mg)	350
Calcium (mg)	350
Magnesium (mg)	140
Iron (mg)	6.3
Iodine (μg)	52.5
Zinc (mg)	5.25
Copper (mg)	0.7
Manganese (mg)	1.3
Choline (mg)	135