Effects of Energy-Restricted Diets Containing Increased Protein on Weight Loss, Resting Energy Expenditure, and the Thermic Effect of Feeding in Type 2 Diabetes

N.D. Luscombe, bsc hon[1]
P.M. Clifton, md[2]
M. Noakes, msc, phd[2]
B. Parker, bsc hon[1]
G. Wittert, md[3]

OBJECTIVE — To determine the effect of a high-protein (HP) diet compared with a low-protein (LP) diet on weight loss, resting energy expenditure (REE), and the thermic effect of food (TEF) in subjects with type 2 diabetes during moderate energy restriction.

RESEARCH DESIGN AND METHODS — In this study, 26 obese subjects with type 2 diabetes consumed a HP (28% protein, 42% carbohydrate) or LP diet (16% protein, 55% carbohydrate) during 8 weeks of energy restriction (1,600 kcal/day) and 4 weeks of energy balance. Body weight and composition and REE were measured, and the TEF in response to a HP or LP meal was determined for 2 h, at weeks 0 and 12.

RESULTS — The mean weight loss was 4.6 ± 0.4 kg ($P < 0.001$), of which 4.5 ± 0.4 kg was fat ($P < 0.001$), with no effect of diet ($P = 0.6$). At both weeks 0 and 12, TEF was greater after the HP than after the LP meal (0.064 vs. 0.050 $\text{kcal} \cdot \text{kcal}^{-1}$ energy consumed $\cdot$ 2 h^{-1}, respectively; overall diet effect, $P = 0.003$). REE and TEF were reduced similarly with each of the diets (time effects, $P = 0.02$ and $P < 0.001$, respectively).

CONCLUSIONS — In patients with type 2 diabetes, a low-fat diet with an increased protein-to-carbohydrate ratio does not significantly increase weight loss or blunt the fall in REE.

Diabetes Care 25:652–657, 2002

A low-fat, high-carbohydrate diet has traditionally been advocated for type 2 diabetic patients (1); however, there is some evidence that this diet may increase plasma glucose and triacylglycerol concentrations (2,3). Combined with a low-fat (30%) content, replacement of some dietary carbohydrate with protein was shown to enhance weight loss in 65 healthy overweight and obese subjects during a controlled ad libitum diet (4) as well as in 13 obese hyperinsulinemic-normoglycemic male subjects during a hypocaloric diet (5). Although an increase in the ratio of protein to carbohydrate has been shown to lower blood glucose and plasma insulin concentrations in diabetic patients (6,7), to our knowledge, the effects of fixed-intake, energy-restricted diets, with an increased ratio of protein to carbohydrate, on weight loss and energy expenditure in type 2 diabetes have not been reported.

A number of mechanisms may explain how greater weight loss can be achieved on such a diet. First, diets with an increase in the ratio of protein to carbohydrate may increase the thermic effect of food (TEF). Acute feeding studies in lean and obese nondiabetic subjects have shown that protein can exert up to three times more TEF compared with isocaloric loads of either carbohydrate or fat (8,9). Numerous studies have examined the thermogenic effect of carbohydrate in type 2 diabetes (10,11), but there is minimal information as to the thermic effect of protein in insulin-resistant states. Tappy et al. (12) showed that the thermic effect of exogenous amino acids was similar in diabetic, obese nondiabetic, and lean control subjects.

The blunting of the reduction in resting energy expenditure (REE) after a decrease in weight is a second mechanism through which protein may facilitate long-term weight loss. In nondiabetic obese and lean populations, weight loss is frequently, but not always (13), associated with a decrease in total and resting energy expenditure after an energy-restrictive diet (14,15). Recently, two small studies showed that 24-h energy expenditure (16) and REE (5) were reduced to a lesser extent in response to hypocaloric, high-protein diets (36–45% protein) than in response to low-protein diets (12–15% protein). The effect of high-protein diets on REE after weight loss in subjects with type 2 diabetes is not yet known.

The aims of this study were to compare the effects of two isocaloric diets, one high and one low in dietary protein (30% and 15% of energy, respectively) on weight loss, REE, respiratory quotient

From the [1]University of Adelaide, Department of Physiology, South Australia; [2]CSIRO Health Science and Nutrition, Adelaide, South Australia; and the [3]University of Adelaide, Department of Medicine, South Australia.

Address correspondence and reprint requests to Assoc. Prof. Gary Wittert, University of Adelaide, Department of Medicine, Royal Adelaide Hospital, Adelaide, SA 5000, Australia. E-mail: gwittert@medicine.adelaide.edu.au.

Received for publication and accepted in revised form.

Abbreviations: CV, coefficient of variation; HP, high protein; LP, low protein; REE, resting energy expenditure; RQ, respiratory quotient; TEF, thermic effect of food.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Table 1—*Subject characteristics at baseline*

	LP diet	HP diet
n (F/M)	11 (5/6)	15 (10/5)
Age (years)	64.2 ± 3.3	62.1 ± 2.2
Body weight (kg)	90.7 ± 5.0	94.5 ± 3.9
BMI (kg/m^2)	32.6 ± 1.4	33.9 ± 1.2
Waist circumference (cm)	107.8 ± 3.8	110.8 ± 3.0
Body fat (%)	37.8 ± 2.0	42.2 ± 2.2
Total body fat mass (kg)	34.4 ± 2.8	40.0 ± 2.8
Total body lean mass (kg)	53.4 ± 3.4	51.5 ± 2.8
Fasting REE (kcal/day)	1873 ± 107	1918 ± 83
Fasting RQ	0.76 ± 0.01	0.77 ± 0.01
Urinary albumin (mg/day)	2.7 ± 0.4	6.2 ± 2.5

Data are means ± SEM. Baseline measurements were assessed using two-way ANOVA, with diet and gender as the fixed factors, to determine whether there were differences between the HP and LP dietary groups before the intervention commenced.

(RQ), and TEF in subjects with type 2 diabetes after energy restriction and subsequent weight maintenance.

RESEARCH DESIGN AND METHODS

Subjects

We recruited 32 Caucasian volunteers with type 2 diabetes by public advertisement. Subjects were excluded if they had proteinuria or a history of liver, unstable cardiovascular, respiratory, or gastrointestinal disease or a malignancy. All subjects gave informed written consent to participate in the study, which was approved by the Human Ethics Committees of the Commonwealth Scientific Industrial Research Organization and the Royal Adelaide Hospital.

Of those 32 subjects, 26 (15 women and 11 men) completed the study. Four subjects withdrew during the course of the study, and two subjects were not included in the analysis (one subject was unable to comply, and data for another subject was incomplete because of a computer crash). Of the remaining 26 subjects, 3 managed their diabetes by diet, 21 required oral hypoglycemics, and 2 required insulin. Subjects on antihypertensive or lipid-lowering medication were asked to maintain their same dosage throughout the study. Most subjects were sedentary at baseline and were requested to maintain their usual physical activity levels and refrain from drinking alcohol throughout the study.

Experimental design

Subjects were matched for fasting plasma glucose, BMI, age, gender, and medication and then randomly assigned to the high-protein (HP) or low-protein (LP) diet. Table 1 shows the physical characteristics of subjects at baseline. The study was conducted on an outpatient basis and consisted of an 8-week energy-restriction component (~1,600 kcal/day or 30% caloric restriction) followed by a 4-week period of the same macronutrient composition, but in an energy-balanced mix.

During weeks 0 and 12, subjects visited the Department of Medicine research clinic after fasting for at least 6 h. On each occasion, the same investigator measured height, weight, REE, and RQ. Thereafter, subjects consumed a test meal and the RQ and TEF were measured for the next 2 h. Before these visits at weeks 0 and 12, subjects were instructed to maintain similar activity and food intake, and a 24-h recall was used to assess compliance. In addition, subjects collected 24-h urine samples for assessment of urea/creatinine ratio at weeks 0, 8, and 12.

Diets

The HP diet consisted of 30% energy from protein (~110 g/day) and 40% from carbohydrate, whereas the LP diet consisted of 15% energy from protein (~60 g/day) and 55% from carbohydrate. Diets were matched for fatty acid profile (8% saturated, 12% monounsaturated, and 5% polyunsaturated fatty acids). The diets were prescriptive, fixed-menu plans, and the subjects were supplied with the key foods, which made up 60% of their energy intake, to assist with dietary compliance. These included preweighed portions of beef and chicken suitable for six meals per week, shortbread biscuits, Canola Lite margarine, and Sunola oil-plus (MeadowLea Foods, Mascot, Australia), Kraft Free cheese (3% fat; Kraft Foods, Melbourne, Australia), skim milk powder, and diet yogurt for the HP diet and sultanas and rice for the LP diet. Further differences between the two diets are described in detail elsewhere (17).

Every 2 weeks, subjects visited the same research dietitian, who provided detailed dietary instruction and assessment. Energy and macronutrient intakes were analyzed from 3 consecutive days (2 weekdays and 1 weekend day) of checklists from each 2-week period using Diet One Nutritional software, which is based on Australian food composition tables and food manufacturers' data (Xyris Software, Highgate Hill, Australia) (18).

Body weight and body composition measurements

Body weight was recorded in light clothing using an electronic scale. Body composition was measured by whole-body dual X-ray absorptiometry (Norland densitometer XR36; Norland Medical Systems, Fort Atkinson, WI; coefficient of variation [CV]3–4%).

Resting energy expenditure and respiratory quotient

Fasting REE and RQ were measured by indirect calorimetry using a ventilated hood and Deltatrac metabolic monitor (Datex Division Instrumentarium, Helsinki, Finland). Calibration was performed before each measurement.

Subjects lay supine on a bed in a thermoneutral environment with a clear perspex hood over their head and shoulders, and the REE and RQ were recorded for 30 min. The first 10 min of data were discarded to ensure all subjects had reached equilibrium, and the remaining 20 min of data were averaged and represented the values for fasting REE and RQ. In preliminary studies, the intraindividual CV of the Deltatrac system was established to be 2.3% for fasting REE and 5.9% for TEF.

Postprandial respiratory quotient and the thermic effect of food

A 573-kcal HP (41% protein, 46% carbohydrate), or 656-kcal LP (12% protein, 69% carbohydrate) test meal, representa-

Table 2—*Dietary composition of study diets derived from subjects' daily weighed food checklists*

	LP diet		HP diet	
	Energy restrictive	Energy balanced	Energy restrictive	Energy balanced
n	11		15	
Energy (kcal/day)	1583 ± 62*	1777 ± 130*	1585 ± 42*	1844 ± 78†
Protein (% energy)	16.1 ± 0.4*	15.8 ± 0.3*	28.2 ± 0.2†	27.7 ± 0.3†
Carbohydrate (% energy)	55.3 ± 0.6*	55.6 ± 0.9*	42.1 ± 0.3†	42.6 ± 0.4†
Total fat (% energy)	26.0 ± 0.6*	26.0 ± 0.7*	27.6 ± 0.2†	27.7 ± 0.3†
Saturated fat (% energy)	7.3 ± 0.2*	7.2 ± 0.3*	8.1 ± 0.1†	8.3 ± 0.2†
Monounsaturated fat (% energy)	11.1 ± 0.3*	11.4 ± 0.3*	12.0 ± 0.1†	12.1 ± 0.2†
Polyunsaturated fat (% energy)	4.8 ± 0.1*	4.7 ± 0.2*	4.9 ± 0.1*	4.8 ± 0.1*
Fiber (g/day)	28.3 ± 1.2*	32.9 ± 2.0*	24.0 ± 0.9†	28.5 ± 1.9*
Cholesterol (mg/MJ)	10.6 ± 1.2*	10.3 ± 1.2*	17.1 ± 0.7†	18.7 ± 0.7†

Data are means ± SEM. Three days (2 week days and 1 weekend day) of dietary data were analyzed at weeks 2, 4, 6, and 8 during the energy-restrictive phase of the study, and at weeks 10 and 12 during the energy-balance phase. No significant differences were found between the four diet records in the energy-restrictive phase or between the two records for the energy-balanced phase, so data for recordings in each phase were averaged. *Composition of diets not different ($P > 0.05$); †composition of diets not different ($P > 0.05$).

tive of the diets, was consumed within 20 min. Thereafter, subjects returned to the hood for 120 min, during which RQ and REE values were recorded every 20 min. Fasting RQ was subtracted from every 20-min postprandial RQ value, and the 20-min values over the 120-min period were averaged to determine the mean change in RQ for the subsequent 2 h. Similarly, TEF was calculated from fasting and postprandial REE values.

Statistical analyses

All data are presented as means ± SEM. Statistical analysis was performed using SPSS, Version 10.0 for Microsoft Windows (SPSS, Chicago, IL). The effects of 8 weeks of energy restriction and 4 weeks of weight maintenance were assessed using repeated-measures ANOVA, with time as the within-subject factor and diet and gender as the between-subject factors. Pearson correlation analysis was used to determine the relationship between change in REE and TEF with the other variables. Significance was set at $P < 0.05$.

RESULTS

Composition of the study diets and subject compliance

The energy and macronutrient contents derived from the subjects' daily weighed food checklists are shown in Table 2 and were similar to the energy content and macronutrient composition of the prescribed diets. The energy content of the HP and LP diets was statistically the same during energy restriction, whereas the percent of energy derived from protein, carbohydrate, and fat was different ($P < 0.01$).

The urea/creatinine ratio was significantly different between diets ($P = 0.003$). An increase from baseline of 13.2 ± 5% and 24.5 ± 7% at weeks 8 and 12, respectively, was observed on the HP diet and a decrease from baseline of 7.7 ± 5% and 2.9 ± 5% at weeks 8 and 12, respectively, was observed on the LP diet. The 24-h activity recalls revealed no significant differences for the previous day's activity level at week 0 as compared with week 12.

Body weight and body composition

After 8 weeks of energy restriction and 4 weeks of energy balance, the mean weight loss was 4.6 kg ($P < 0.001$), but the magnitude of change was not dependent on diet composition (–4.9 ± 0.4 vs. −4.3 ± 0.7 kg on the HP and LP diets, respectively; $P = 0.6$) (Fig. 1). Percent body fat and total fat mass were reduced 3 ± 0.04% and 4.5 ± 0.04 kg (11.9%), respectively, at week 12 ($P < 0.05$). There was a small nonsignificant decrease in lean mass (0.3 ± 0.4 kg) ($P = 0.4$).

Diet composition had no effect on the change in any of the body composition variables. There was no effect of gender or

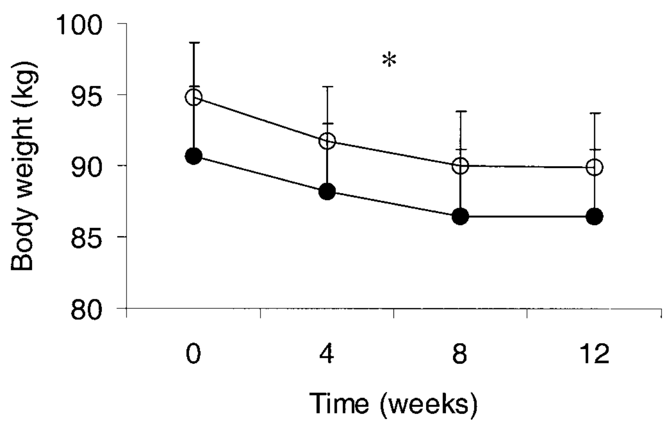

Figure 1—*Body weight (kilograms) during 8 weeks of energy restriction and 4 weeks of energy balance on a LP (●; n = 11) or HP (○; n = 15) diet. Data are means ± SEM. Body weights were measured at weeks 0, 4, 8 (end of energy restriction), and 12 (end of energy balance) of the dietary intervention. *Significant decrease in weight from week 0 to week 8 (P < 0.001), but no significant effect of diet (P = 0.5). There was no significant decrease in weight from week 8 to week 12 (P = 1.0).*

Table 3—*Energy expenditure variables at weeks 0 and 12 of dietary intervention*

	LP diet			HP diet		
	Men	Women	Combined	Men	Women	Combined
n	6	5	11	5	10	15
Fasting REE*†						
Week 0	1975 ± 139	1750 ± 164	1873 ± 106	2267 ± 128	1745 ± 48	1919 ± 83
Week 12	1982 ± 110	1685 ± 73	1847 ± 80.1	2156 ± 136	1628 ± 43	1803 ± 83
Difference	7 ± 55	−65 ± 125	−26 ± 62	−111 ± 12	−118 ± 24	−116 ± 17
Fasting RQ						
Week 0	0.76 ± 0.01	0.75 ± 0.01	0.76 ± 0.01	0.76 ± 0.02	0.78 ± 0.01	0.77 ± 0.01
Week 12	0.77 ± 0.02	0.79 ± 0.02	0.78 ± 0.01	0.77 ± 0.02	0.78 ± 0.01	0.78 ± 0.01
Difference	0.01 ± 0.01	0.04 ± 0.01	0.02 ± 0.01	0.01 ± 0.01	0.004 ± 0.02	0.01 ± 0.01
TEF*†‡						
Week 0	0.063 ± 0.004	0.048 ± 0.005	0.056 ± 0.004	0.081 ± 0.010	0.061 ± 0.003	0.068 ± 0.005
Week 12	0.050 ± 0.007	0.034 ± 0.004	0.043 ± 0.005	0.055 ± 0.008	0.061 ± 0.004	0.060 ± 0.004
Difference§	−0.013 ± 0.007	−0.013 ± 0.006	−0.013 ± 0.005	−0.026 ± 0.009	0.0002 ± 0.003	−0.009 ± 0.005
Change RQ‖						
Week 0	0.05 ± 0.01	0.06 ± 0.01	0.06 ± 0.01	0.02 ± 0.01	0.02 ± 0.01	0.02 ± 0.01
Week 12	0.07 ± 0.01	0.07 ± 0.01	0.07 ± 0.01	0.02 ± 0.01	0.02 ± 0.01	0.02 ± 0.01
Difference	0.02 ± 0.01	0.01 ± 0.01	0.02 ± 0.01	−0.01 ± 0.01	0.002 ± 0.01	−0.001 ± 0.01

Data are means ± SEM. Week 0 and 12 data were compared using repeated-measures ANOVA, with diet and gender as between subject factors. *Significant effect of time from week 0 to week 12 ($P < 0.05$); †significant effect of gender at weeks 0 and 12 ($P < 0.04$); ‡significant effect of diet at weeks 0 and 12 ($P = 0.003$); §significant time-by-diet-by-gender interaction ($P = 0.041$); ‖significant effect of diet at weeks 0 and 12 ($P < 0.001$). TEF, thermic response for 2 h after a 656-kcal LP or 573-kcal HP test meal (kcal · $kcal^{-1}$ energy consumed · 2 h^{-1}); change RQ, mean increase in RQ over 2 h after the HP or LP test meal (increase/2 h).

diet-by-gender interaction on the decrease in percent body fat or total fat mass. At week 0, there was no difference between men and women for abdominal fat mass (10.02 ± 1.0 vs. 10.07 ± 0.6 kg, respectively; $P = 0.9$). After 12 weeks, however, abdominal fat had decreased more in men than in women (−1.5 ± 0.2 vs. −0.96 ± 0.2 kg, respectively; $P < 0.001$).

Resting energy expenditure, respiratory quotient, and the thermic effect of feeding

Fasting REE and RQ and postprandial RQ and TEF at weeks 0 and 12 are summarized in Table 3. Overall, there was no effect of diet composition on REE ($P = 0.3$). However, there was an effect of gender on REE. When expressed per kilogram of lean mass, REE was greater in women than in men (38 ± 0.7 vs. 34 ± 0.9 kcal/day, respectively; $P = 0.013$), whereas when expressed as an absolute value, REE was greater in men than women (2084 ± 93 vs. 1,697 ± 44 kcal/day, respectively; $P < 0.001$). At week 12, after stabilization at a reduced weight, REE was reduced 4.1% as compared with baseline (from 1900 ± 65 to 1,822 ± 58 kcal/day; $P = 0.023$). The decrease in REE was not related to diet composition ($P = 0.2$) or gender ($P = 0.5$).

Overall, fasting RQ was not affected by diet composition ($P = 0.6$) or gender ($P = 0.5$). Postprandial RQ increased more after the LP meal than after the HP meal (overall diet effect, $P < 0.001$). There was no significant difference in postprandial RQ from week 0 to week 12 ($P = 0.3$).

The energy intake during the HP test meal was 573 kcal, whereas for the LP meal it was 656 kcal; therefore, TEF was expressed as kilocalorie of energy produced above the resting metabolic rate per kilocalorie of energy consumed. TEF per kilocalorie of energy consumed was greater (28%) after the HP meal than after the LP meal (0.064 vs. 0.050 kcal · $kcal^{-1}$ energy consumed · 2 h^{-1}, respectively; overall diet effect, $P = 0.003$). There was also an overall effect of gender on TEF ($P = 0.03$); TEF was 12.6% greater for men than women (0.062 ± 0.004 vs. 0.055 ± 0.004 kcal · $kcal^{-1}$ energy consumed · 2 h^{-1}, respectively). After 12 weeks, TEF was reduced ($P < 0.001$), but there was no effect of diet composition ($P = 0.8$) or gender ($P = 0.06$) on the decrease. There was, however, a time-by-diet-by-gender effect (regardless of whether TEF was expressed as an absolute value or as kilocalorie of energy consumed), with women on the HP diet experiencing an increase in TEF of 0.0002 ± 0.003 kcal · $kcal^{-1}$ energy consumed · 2 h^{-1} after 12 weeks, compared with women on the LP diet, who experienced a decrease of 0.013 ± 0.006 kcal · $kcal^{-1}$ energy consumed · 2 h^{-1}.

CONCLUSIONS

— The major finding of this study was that in subjects with type 2 diabetes, the amount of weight loss and the decrease in REE was dependent on energy restriction, but not on the protein-to-carbohydrate ratio of the diet. Of some interest were the observations that the TEF was greatest after HP meals, and that the fall in TEF after weight loss was less for women on the HP than on the LP diet.

Our finding for weight loss is in accordance with results from several short-term studies (7–28 days) in obese nondiabetic subjects, which have shown equivalent weight loss (mean change 3–7%) on HP as compared with LP diets (16,19,20). In contrast, Skov et al. (4) demonstrated that ad libitum choice of an HP (25% of calories) diet from a clinic shop led to a 4.3% greater weight loss compared with a standard protein (12% of calories) diet over 6 months. Subject compliance to the diets was aided by having access to a shop that supplied a large selection of HP, LP, and low-fat foods. A number of studies (21,22) have shown that protein is more satiating than either carbohydrate or fat, which may facilitate weight loss over the longer term. It is possible that a HP diet is easier to comply with over the longer term.

Lean mass was reduced by only 0.3 kg in this study. Other studies have shown sparing of lean mass with very-low-energy diets that have low-carbohydrate (≤30 g/day) and HP content (70–120 g/day) (23) or higher carbohydrate (≥75 g/day) and LP content (30–70 g/day) (19). The significance of the observation that men lost more abdominal fat than women is unclear, as the study was not sufficiently powered to determine a gender-by-diet interaction. We have previously reported benefits of a HP diet on total and abdominal fat loss in women in a larger cohort (17).

The 4.1% decrease in REE after the 5.3% of weight loss observed in the current study was comparable with that reported in studies of short-term energy restriction (800–1,500 kcal/day) in obese nondiabetic subjects (14). Although there is some evidence that protein intake may be a determinant of the change in 24-h (16) and resting (5) energy expenditure in response to short-term energy restriction, we did not observe an effect of diet composition on REE, regardless of whether it was adjusted for weight, lean mass, or fat mass. Baba et al. (5), the only group to our knowledge to have studied the effect of protein on REE, found that after 4 weeks of weight loss in hyperinsulinemic obese subjects, the decrease in REE was 12% (252 kcal/day) less on a HP diet (45% protein) as compared with a LP diet (12% protein). Our study had enough power (80%, α of 0.05) to detect a 7% difference in the mean REE of the HP and LP groups after the intervention; therefore, the lack of agreement between this study and that of Baba et al. may relate to several methodological issues. In their study, the protein-to-carbohydrate exchange between the HP and LP diets was 33% as compared with 15% in our study. We studied the changes in energy expenditure after weight loss had been stabilized rather than immediately after active weight loss. Hyperinsulinemic obese subjects may respond differently than obese subjects with type 2 diabetes.

We measured TEF for 2 h only; Segal et al. (24) have shown that a 2-h measurement of TEF accounts for ~50 to ~60% of the ingested energy. It is likely that our observations are qualitatively correct and permit comparison between groups. The TEF expressed as a percentage of ingested calories is generally 6–15% (10,15). The TEF of the HP and LP meals was ~6.4% and ~4.9% of the ingested calories, respectively. This finding is consistent with results from two recent studies (9,25) showing that the TEF (measured over a 24-h period) was 14 and 10% of ingested calories on a HP as compared with a LP diet (30 vs. 10% protein). As previously shown (15,26,27), we have demonstrated that TEF decreases after weight loss. The decrease in TEF was not affected by diet composition, but after 12 weeks the TEF remained greater on the HP diet as compared with the LP diet. Although the increased TEF of the HP diet had no effect on weight loss in this study, on average the HP diet burned 0.064 $kcal \cdot kcal^{-1}$ energy consumed $\cdot$ 2 h^{-1}, whereas the LP diet burned 0.050 $kcal \cdot kcal^{-1}$ energy consumed $\cdot$ 2 h^{-1}. During energy balance, if we assume that our subjects ate three 640-kcal meals per day (or a total of 1,914 kcal/day), it would mean an extra 26 kcal/day being burned on the HP as compared with the LP diet. Over a 6-month period, providing energy intake and physical activity remained constant, 26 extra kcal/day might potentially equate to a difference of only 1.3 kg body wt between our two isocaloric diets. Physical activity was not continually measured throughout the 12 weeks in this study. Over the long term, both physical activity and energy intake rarely remain constant, and compared with these two factors, the influence of TEF on energy balance would appear trivial.

Although there were no overall differences in the change in TEF between the diets, in women, there was a smaller decrease in TEF on the HP diet as compared with the LP diet (13 kcal/day difference). Because the study was not specifically powered to determine gender-by-diet interactions, the significance of this finding remains unknown.

The greater increase in RQ after the LP meal as compared with after the HP meal occurred because of the greater carbohydrate content of the meal (28). This effect was not significantly modified by weight loss, but the magnitude of the effect (at both 0 and 12 weeks) was less than expected, possibly because insulin resistance is associated with lower carbohydrate and higher fat oxidation (29).

In conclusion, we have shown that short-term replacement of some dietary carbohydrate with protein, under energy-restrictive conditions, does not blunt the diet-induced fall in REE or increase the TEF to a level that is large enough to facilitate weight loss in patients with type 2 diabetes. Thus, the reduction in calories appears to be the most important determinant of weight loss in this population, at least in the short term. It has been shown, however, that ad libitum HP diets may lead to greater weight loss in the longer term because subjects are better able to comply with the diet, possibly as a result of increased satiety. Longer-term studies are required to determine whether HP diets may enhance weight loss or the maintenance of a reduced weight, and larger studies will be required to determine gender-specific effects on changes in energy expenditure and body composition.

Acknowledgments— We gratefully acknowledge the support of Meadow Lea Foods for their financial assistance to this study. We thank Kay Pender, Anne McGuffin, and Rosemary McArthur for assistance in performing these studies.

References

1. American Diabetes Association: Nutrition recommendations and principles for people with diabetes mellitus: a position statement of the ADA. *Diabetes Care* 17: 519–522, 1994
2. Garg A, Bantle JP, Henry RR, Coulston AM, Griver KA, Raatz SK, Brinkley L,Chen YD, Grundy SM, Huet BA, et al.: Effects of varying carbohydrate content of diet in patients with non-insulin-dependent diabetes mellitus [see comments]. *JAMA* 271:1421–1428, 1994
3. Riccardi G, Parillo M: Comparison of the metabolic effects of fat-modified vs low fat diets. *Ann N Y Acad Sci* 683:192–198, 1993
4. Skov AR, Toubro S, Ronn B, Holm L, Astrup A: Randomized trial on protein vs carbohydrate in ad libitum fat reduced diet for the treatment of obesity. *Int J Obes Relat Metab Disord* 23:528–536, 1999
5. Baba NH, Sawaya S, Torbay N, Habbal Z, Azar S, Hashim SA: High protein vs high carbohydrate hypoenergetic diet for the treatment of obese hyperinsulinemic subjects. *Int J Obes Relat Metab Disord* 23:1202–1206, 1999
6. Golay A, Felber JP, Dusmet M, Gomez F, Curchod B, Jequier E: Effect of weight loss

on glucose disposal in obese and obese diabetic patients. *Int J Obes Relat Metab Disord* 9:181–191, 1985
7. Gulliford MC, Bicknell EJ, Scarpello JH: Differential effect of protein and fat ingestion on blood glucose responses to high- and low-glycemic-index carbohydrates in noninsulin-dependent diabetic subjects. *Am J Clin Nutr* 50:773–777, 1989
8. Karst H, Steiniger J, Noack R, Steglich HD: Diet-induced thermogenesis in man: thermic effects of single proteins, carbohydrates and fats depending on their energy amount. *Ann Nutr Metab* 28:245–252, 1984
9. Westerterp KR, Wilson SA, Rolland V: Diet induced thermogenesis measured over 24h in a respiration chamber: effect of diet composition. *Int J Obes Relat Metab Disord* 23:287–292, 1999
10. D'Alessio DA, Kavle EC, Mozzoli MA, Smalley KJ, Polansky M, Kendrick ZV, Owen LR, Bushman MC, Boden G, Owen OE: Thermic effect of food in lean and obese men. *J Clin Invest* 81:1781–1789, 1988
11. Vansant G, Van GL, De LI: Impact of obesity on resting metabolic rate and glucose-induced thermogenesis in non-insulin dependent diabetes mellitus. *Int J Obes Relat Metab Disord* 16:817–823, 1992
12. Tappy L, Jequier E, Acheson K: Thermic effect of infused amino acids in healthy humans and in subjects with insulin resistance. *Am J Clin Nutr* 57:912–916, 1993
13. Rumpler WV, Seale JL, Miles CW, Bodwell CE: Energy-intake restriction and diet-composition effects on energy expenditure in men. *Am J Clin Nutr* 53:430–436, 1991
14. Leibel RL, Rosenbaum M, Hirsch J: Changes in energy expenditure resulting from altered body weight. *N Engl J Med* 332:621–628, 1995
15. Bessard T, Schutz Y, Jequier E: Energy expenditure and postprandial thermogenesis in obese women before and after weight loss. *Am J Clin Nutr* 38:680–693, 1983
16. Whitehead JM, McNeill G, Smith JS: The effect of protein intake on 24-h energy expenditure during energy restriction. *Int J Obes Relat Metab Disord* 20:727–732, 1996
17. Parker B, Noakes M, Luscombe N, Wittert G, Clifton P: *Diabetes Care*. In press, 2002
18. Cashell K, English R, Lewis J: *Composition of Foods*. Canberra, Australia, Australian Government Printing Service, 1989
19. Vazquez JA, Kazi U, Madani N: Protein metabolism during weight reduction with very-low-energy diets: evaluation of the independent effects of protein and carbohydrate on protein sparing. *Am J Clin Nutr* 62:93–103, 1995
20. Piatti PM, Monti F, Fermo I, Baruffaldi L, Nasser R, Santambrogio G, Librenti MC, Galli-Kienle M, Pontiroli AE, Pozza G: Hypocaloric high-protein diet improves glucose oxidation and spare lean body mass: comparison to hypocaloric high-carbohydrate diet. *Metabolism* 43:1481–1487, 1994
21. Latner JD, Schwartz M: The effects of a high-carbohydrate, high-protein or balanced lunch upon later food intake and hunger ratings. *Appetite* 33:119–128, 1999
22. Poppitt SD, McCormack D, Buffenstein R: Short-term effects of macronutrient preloads on appetite and energy intake in lean women. *Physiol Behav* 64:279–285, 1998
23. Hoffer LJ, Bistrian BR, Young VR, Blackburn GL, Matthews DE: Metabolic effects of very low calorie weight reduction diets. *J Clin Invest* 73:750–758, 1984
24. Segal KR, Edano A, Tomas MB: Thermic effect of a meal over 3 and 6 hours in lean and obese men. *Metabolism* 39:985–992, 1990
25. Westerterp PM, Rolland V, Wilson SA, Westerterp KR: Satiety related to 24 h diet-induced thermogenesis during high protein/carbohydrate vs high fat diets measured in a respiration chamber. *Eur J Clin Nutr* 53:495–502, 1999
26. Schutz Y, Bessard T, Jequier E: Exercise and postprandial thermogenesis in obese women before and after weight loss. *Am J Clin Nutr* 45:1424–1432, 1987
27. Clements F, Hope P, Daniels C, Chapman I, Wittert GA: Thermogenesis in the marsupial *Sminthopsis crassicaudata*: effect of catecholamines and diet. *Australian Journal of Zoology* 46:381–390, 1998
28. Flatt JP: Body composition, respiratory quotient and weight maintenance. *Am J Clin Nutr* 62 (Suppl):11107S−1117S, 1995
29. Zurlo F, Lillioja S, Esposito-Del Puente A, Nyomba BL, Raz I, Saad MF, Swinburn BA, Knowler WC, Bogardus C, Ravussin E: Low ratio of fat to carbohydrate oxidation as predictor of weight gain: study of 24-h RQ. *Am J Physiol* 259: E650–E657, 1990