Composition of Weight Lost during Short-Term Weight Reduction

METABOLIC RESPONSES OF OBESE SUBJECTS TO STARVATION AND LOW-CALORIE KETOGENIC AND NONKETOGENIC DIETS

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ABSTRACT The effects of starvation, an 800-kcal mixed diet and an 800-kcal ketogenic (low carbohydrate-high fat) diet on the composition of weight lost were determined in each of six obese subjects during three 10-day periods. The energy-nitrogen balance method was used to quantify the three measurable components of weight loss; protein, fat, and water. On the 800-kcal ketogenic diet, subjects lost (mean±SE) 466.6 ±51.3 g/day; on the isocaloric mixed diet, which provided carbohydrate and fat in conventional proportions, they lost 277.9±32.1 g/day. Composition of weight lost (percentage) during the ketogenic diet was water 61.2, fat 35.0, protein 3.8. During the mixed diet, composition of loss was water 37.1, fat 59.5, protein 3.4. The mean quantity (grams per day) of fat lost during the ketogenic diet was 163.4; during the isocaloric mixed diet, it was 166.7. Mean protein loss (grams per day) during the ketogenic diet was 17.9; during the mixed diet, it was 9.5. During starvation, mean rate of weight loss was 750.7±50.9 g/day, the composition (percentage) being water 60.9, fat 32.4, protein 6.7. Mean protein and fat losses (grams per day) during starvation were 50.4±4.6 and 243.1±14.6, respectively. Urinary excretion of energy yielding materials (largely ketones) increased by 16 and 32 kcal/day during ketogenic and starvation periods, respectively. Basal metabolic rates (kcal/24 h) were unaffected by the nature of the reducing regimen, but decreased in direct proportion to weight loss during the 50-day study period. The findings demonstrate that, over a 10-day period, the energy value of body constituents lost during adherence to an 800-kcal diet is minimally affected by wide variations in the proportions of fat and carbohydrate ingested. Discrepancies in rate of weight loss induced by ketogenic vs. nonketogenic isocaloric regimens result almost entirely from differences in water balance. Rate of fat loss is a function of degree of energy deficit.

INTRODUCTION

In recent years, there have been conflicting reports (1–5) concerning the effects on body composition of various regimens for weight reduction. In 1968 Grande (6) reviewed three contemporary publications (2–4) in which the effects of starvation and food restriction on the composition of weight lost were reported. In his analysis, Grande compared the caloric value of the tissue components said to have been lost from the body during caloric deficit with an estimate of the likely energy expenditure of the subjects. Application of this criterion to the data often disclosed marked discrepancies between the caloric value of the constituents that were catabolized and the estimated energy output of the subjects.

In the present study, three regimens, starvation, an 800-kcal "mixed" diet, and an 800-kcal "ketogenic" diet were compared in terms of their effects on the composition of weight lost. The energy-nitrogen balance method (7, 8) was used to estimate changes in body composition. This procedure is believed to be more

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Table I
Data on Experimental Subjects

Male Subjects	Age	Height	Admission weight	Relative weight*
	yr	*cm*	*kg*	*%*
I. G.	24	184	135	169
E. F.	32	169	156	236
I. H.	19	178	177	239
E. B.	58	184	108	135
P. A.	22	168	118	179
O. G.	32	180	148	195
Mean	31	177	140	192

* Percent of desirable weight (9).

Table III
Daily Intakes during Experimental and Adjustment Periods

Diet*	Protein	Fat	Carbo-hydrate	Sodium	Potassium
	g	*g*	*g*	*meq*	*meq*
1,200 kcal Adjustment	50 (17)‡	40 (30)	160 (53)	60	60
800 kcal Mixed	50 (25)	27 (30)	90 (45)	60	60
800 kcal Ketogenic	50 (25)	62 (70)	10 (5)	60	60
Starvation	0	0	0	60	60

* Each subject also received one maintenance multivitamin tablet (Unicap) per day. Water was taken ad lib.
‡ Values in parentheses represent percent of total energy intake.

reliable for short-term studies than the commonly employed methods which are based on the serial measurement of total body water or total body potassium (6, 7).

METHODS

Subjects. Six grossly obese male subjects were studied in a metabolic ward for approximately 50 days each. Table I provides data concerning age, height, admission weight, and relative weight for each subject and for the group as a whole. On the average, the subjects exceeded desirable weight (9) by 92%.

Design. On admission, each subject was randomly assigned to one of six experimental schedules as shown in Table II. Each schedule embodied three 10-day regimens: starvation, an 800-kcal per day ketogenic diet very low in carbohydrate content, and an 800-kcal mixed diet that provided carbohydrate and fat in conventional proportions. To minimize possible order effects, the dietary regimens were imposed in counterbalanced sequence across subjects. Also, a 1,200-kcal mixed diet was provided for 5 days before and after each experimental diet[1] to reduce possible carry-over effects from the preceding regimen. All of the subjects completed every schedule except for O. G. who left the metabolic ward before the end of the postketogenic period. Accordingly, the data for the postketogenic period are based on five subjects.

[1] The term "preexperimental period," as used in this report, refers only to the first 5-day 1,200-kcal period of the study. Any 1,200 kcal period that follows an experimental period is referred to as a "postexperimental period."

Diets and supplements. All diets used in the present study were liquid homogenates prepared in the metabolic kitchen in sufficient quantity for each period and immediately frozen. Every night an appropriate quantity of formula was thawed at 4°C and served to the subjects in four isocaloric feedings at approximately 8:00 a.m., 11:00 a.m., 1:00 p.m., and 6:00 p.m. on the following day. The composition of each regimen is shown in Table III.

Noncaloric fluids such as distilled water, and coffee and tea, both made from distilled water without cream or sugar, were allowed ad lib. Intake of all liquids was measured.

Every subject was given one maintenance multivitamin-mineral tablet (Unicap; The Upjohn Co., Kalamazoo, Mich.) each day. All subjects received supplemental potassium chloride (Kaon Elixir; Warren-Teed Pharmaceuticals, Inc., Columbus, Ohio) and sodium chloride (table salt) so that their intake of each cation was maintained at 60 meq/day.

Body weight. Each subject, wearing a hospital gown, was weighed at the same time each morning after voiding. Measurements of body weight were made on a Brookline Metabolic Bed Scale (model 100; Brookline Instrument Co., Elmsford, N. Y.), which has an accuracy of ±6 g.

Chemical analysis. Urine was collected in 24-h lots and stored at 4°C. Each fresh sample was measured and divided

Table II
Sequence of Study Periods for Each Subject

Subject	Days: 5	10	5	10	5	10	5
I. G.	1,200 kcal	Starvation	1,200 kcal	Mixed	1,200 kcal	Ketogenic	1,200 kcal
E. F.*	1,200 kcal	Starvation	1,200 kcal	Ketogenic	1,200 kcal	Mixed	1,200 kcal
I. H.	1,200 kcal	Ketogenic	1,200 kcal	Starvation	1,200 kcal	Mixed	1,200 kcal
E. B.	1,200 kcal	Ketogenic	1,200 kcal	Mixed	1,200 kcal	Starvation	1,200 kcal
P. A.	1,200 kcal	Mixed	1,200 kcal	Ketogenic	1,200 kcal	Starvation	1,200 kcal
O. G.‡	1,200 kcal	Mixed	1,200 kcal	Starvation	1,200 kcal	Ketogenic	1,200 kcal

The protein used was sodium caseinate, the fat was corn oil, and the carbohydrate was sucrose.
* Study of this subject was interrupted for 1 mo after completion of the 1,200-kcal poststarvation period; therefore a second 1,200-kcal preexperimental adjustment period was added to his schedule upon return to the experiment.
‡ This subject left the study before completion of the 1,200-kcal postketogenic period.

into two equal portions, one preserved with toluene (10 ml) and the other with concentrated hydrochloric acid (10 ml). At the end of 24 h, total volume was measured, and an aliquot of urine from each portion was stored at −10°C for chemical analysis.

Feces were collected in 5-day lots and stored at 4°C until they were homogenized, and aliquots taken for analysis. The results of all such analyses were divided by five to provide an estimate of daily losses. The derived values for mean daily loss were used in the metabolic balance calculations.

Aliquots of urine, homogenized feces, and liquid formula diet were analyzed for energy value by Parr bomb calorimetry (10) and nitrogen by an adaptation (11) of the Kjeldahl method. Aliquots of urine were also analyzed for ketones (12) and creatinine.

Energy balance. Energy balance was calculated as the difference (in kilocalories per day) between energy intake and output. Output included the energy expended under basal or resting conditions, that expended in overt physical activity, and that lost via collectible excreta. The energy expended in physical activity was calculated (13) from a physical activity diary calibrated in minute intervals kept by each subject, and from the measured energy cost (kilocalories per min) of each activity. The activities recorded in the diary were generally divided into four categories: lying awake, sitting, standing, and walking. Metabolic rate under basal conditions and during the performance of each of the four "activities" was determined at least three times during every 5-day interval throughout the entire study by indirect calorimetry. The respirometer used for this purpose, a Noyons diaferometer (Kipp & Zonen, Delft, Holland), automatically measures by thermoconduction the oxygen consumed and carbon dioxide produced per minute (14). In a few cases, when appropriate, the energy cost of additional activities such as playing cards or typing was also measured.

Composition of weight loss (or gain). The composition of weight change was estimated from data obtained by means of the energy nitrogen (E-N) [2] balance method (7, 8). This method utilizes the measurement of nitrogen balances to estimate changes in body protein content. If changes in body protein content are known, changes in body fat can be estimated from measurements of energy balance. Changes in body water are considered to be those changes in body weight not attributable to changes in body fat and protein. It is also assumed that the oxidation of adipose tissue triglycerides within the body uniformly yields 9.3 kcal/g, while oxidation of body protein yields 4.1 kcal/g (7). The E-N balance method does not take into account changes in body glycogen content (see Discussion).

The following formulas were used to quantify the principal measurable components of short-term weight change, namely, protein, fat, and water:

$$\Delta\text{protein (g)} = \Delta\text{N (g)} \times 6.25 \quad (1)$$

$$\Delta\text{fat (g)} = \frac{\text{kcal from body fat}}{9.3}, \quad (2)$$

where kilocalories from body fat

$$= \text{energy deficit (kcal)} - (\Delta\text{N} \times 25.6\ \text{kcal}),$$

$$\Delta\text{water (g)} = \Delta\text{body weight (g)} - (\Delta\text{protein} + \Delta\text{fat})\ g. \quad (3)$$

[2] *Abbreviations used in this paper:* BMR, basal metabolic rate; E-N, energy-nitrogen.

No correction was made for the approximately 0.5 g/day nitrogen said to be lost via shedding of cutaneous epithelium, loss of hair, nail fragments, and various secretions (15).

Presentation of results. When the experimental data are presented on a day-by-day basis, they represent group means (±SE) derived from the daily values obtained for each of the six subjects. When the data are presented on a period-by-period basis, they represent group means (±SE) derived from the means of daily values obtained over a given study period for each of the six subjects. Differences between the group means were tested for statistical significance with the two-tailed *t* test for paired observations.

RESULTS

Changes in body weight. The mean daily weight changes of the six obese subjects during each of the experimental and 1,200-kcal periods are plotted cumulatively in Fig. 1A. During the preexperimental 1,200-kcal period, the rate of weight loss (mean±SE) was 571.6±70.6 g/day. Among the experimental periods, the subjects lost weight most rapidly while fasting (750.7±50.9 g/day) and least rapidly during consumption of the mixed diet (277.9±32.1 g/day). Weight loss during the ketogenic diet was intermediate between these two extremes (466.6±51.3 g/day). During the 1,200-kcal period that followed the mixed diet, all of the subjects continued to lose weight slowly, the mean loss being

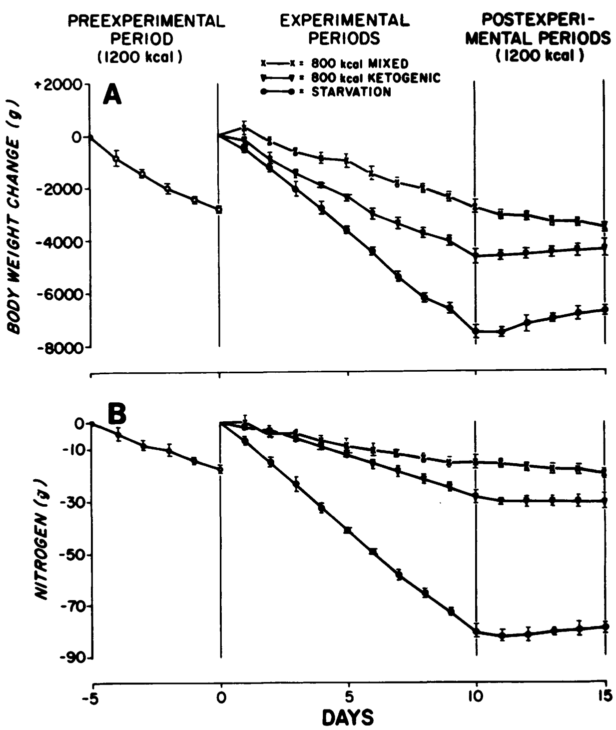

FIGURE 1 Effect of various weight reduction regimens on (A) mean (±SE) daily changes in body weight and (B) mean (±SE) daily nitrogen balances of six obese subjects. Values are plotted cumulatively.

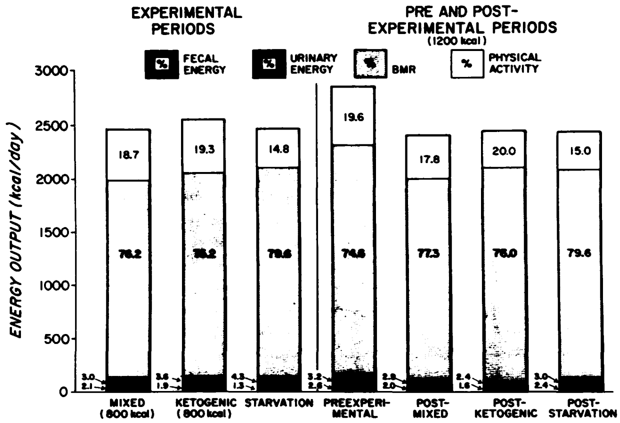

FIGURE 2 Mean daily energy output of obese subjects during experimental and 1,200-kcal pre- and postexperimental periods together with the mean contribution (percentage) of various components to the total.

163.0±20.1 g/day. When the immediately preceding regimen was either the 800-kcal ketogenic diet or starvation, the subjects usually gained weight during the postexperimental period.

Nitrogen balance. The means of the daily nitrogen balances of the six subjects during each of the experimental and 1,200-kcal periods are plotted cumulatively in Fig. 1B. A significantly greater rate of nitrogen loss (8.06±0.74 g/day) occurred during starvation than during either the ketogenic period (2.86±0.92 g/day) or mixed diet period (1.57±0.71 g/day). Although the ketogenic diet induced a nitrogen deficit that was somewhat greater than that associated with the mixed diet, the difference between the two means was not significant.

During the 5-day preexperimental 1,200-kcal period, four of the five subjects in whom nitrogen balances were measured showed nitrogen deficits which averaged 3.56±1.31 g/day. I. H. exhibited a small positive balance of 1.12 g/day. This subject had been on a calorically restricted diet for several weeks before the initial adjustment period. During the 1,200-kcal periods that followed each of the three experimental regimens, mean nitrogen balances remained close to zero and did not differ significantly from one another.

Energy balance. Necessarily, energy balances were negative in each of the subjects during all of the experimental and 1,200-kcal periods. The mean energy output (kilocalories per day) of the six subjects during every period is shown in Fig. 2. The principal component of the energy expenditure was the basal metabolic rate which comprised 75–80% of the total output. The mean energy value of urine and feces averaged 5.2% (range 4–5.8). In terms of kilocalories per day, the range for the energy value of the collectible excreta was 100–170.

The contribution of physical activity to energy expenditure was extremely low, varying between 14.8 and 20% of the total output. The lowest mean voluntary physical activity levels occurred during and after fasting, being 364±46 and 365±42 kcal/day, respectively. It should be recalled that, in our procedure for measuring energy expenditure, the energy output of subjects lying at rest was considered to be an activity. For this reason, the thermic effect of food ("specific dynamic action") and the increment of "resting" over "basal" metabolism are both subsumed under the energy moiety assigned to physical activity.

TABLE IV
Successive Values for BMR for Each Subject over Entire Course of Study‡*

Subject	Adj. 1	Exp. 1	Adj. 2	Exp. 2	Adj. 3	Exp. 3	Adj. 4	Change: BMR (initial values)	Change: Weight (admission wt)
								%	%
I. G.	2,272	2,294	2,203	1,977	2,020	2,176	1,957	−13.9	−13.5
E. F.	2,176	2,039	1,976	1,757	1,821	1,782	1,807	−17.0	−19.2
I. H.	2,380	2,205	2,210	2,244	2,277	2,048	2,151	−9.6	−9.3
E. B.	1,891	1,757	1,699	1,552	1,697	1,657	1,555	−17.8	−13.3
P. A.	1,729	1,808	1,573	1,744	1,583	1,535	1,787	+3.4	−13.1
O. G.	2,268	2,062	1,948	2,013	1,830	1,840	Discharged	−18.9	−11.2
Mean	2,119.3	2,027.5	1,934.8	1,881.2	1,871.3	1,839.7	1,851.4	−12.3	−13.3
±SE	±103.5	±86.7	±105.9	±100.2	±100.8	±97.7	±98.7	±3.4	±1.4

* BMR, kilocalories per day.
‡ See Table II for specific sequences of study periods (Adj., 1,200 kcal; Exp., starvation, ketogenic, or mixed).

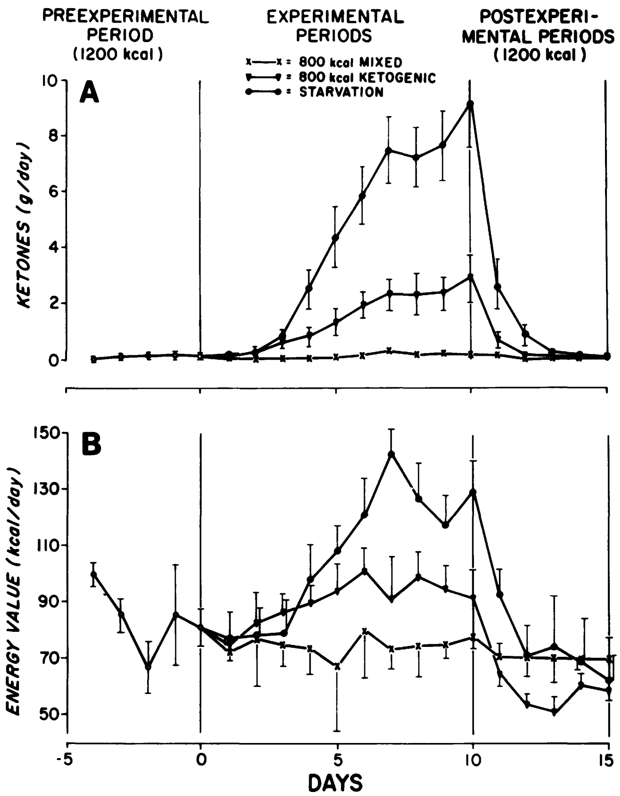

FIGURE 3 Mean (±SE) daily urinary excretion rates of (A) ketones and (B) energy exhibited by obese subjects during different regimens.

Basal metabolic rate (BMR). At the start of the study, two of the subjects (I. H. and P. A.) had BMR values significantly below normal. I. H. had been on a weight-reducing regimen immediately before the study; P. A. apparently had not restricted food intake before entering the study.

Table IV gives the BMR values for each subject at the beginning of the experiment and throughout the course of the entire study. Except for P. A., all the subjects exhibited a gradual decline in BMR, which, at the end of the study, ranged from 9.6 to 18.9% of the initial values. The mean decrease in BMR (12.3%) almost exactly paralleled the mean decrease in body weight (13.3%).

Urinary constituents

Ketones. The means of the daily excretion rates of ketone bodies of the six subjects during each of the experimental and 1,200-kcal periods are plotted sequentially in Fig. 3A. During the 800-kcal mixed diet period and the 1,200-kcal period that followed it, ketone excretion was negligible, with individual values ranging from 0.02 to 0.39 g/day. In contrast, ketone excretion during the starvation period was substantial, ranging from 0.07 g/day on the 1st day of starvation to a maximum of 15.4 g/day later in the same period. Ketone excretion subsided to the base-line level over the first 3 days of the 1,200-kcal poststarvation period. During the 800-kcal ketogenic period, ketone excretion rates were intermediate between those exhibited during the mixed and starvation periods, ranging from 0.04 to 6.22 g/day. Ketone excretion decreased to base-line values during the first 24–48 h of the 1,200-kcal postketogenic diet period.

Energy-yielding materials. The urinary excretion rates of energy-yielding materials for each experimental and adjustment period are shown as kilocalories per day in Fig. 3B. During the 800-kcal mixed diet period, urinary energy excretion remained quite stable, the group mean output (±SE) being 75±8 kcal/day. In contrast, the rate at which energy was excreted in the urine during starvation was significantly greater ($P < 0.02$) than that during the mixed diet period, averaging 107±7 kcal/day.

As in the case of the ketone excretion rate, the rate of urinary excretion of energy during the 800-kcal ketogenic period was intermediate between those during the mixed 800-kcal diet period and starvation, averaging 90±7 kcal/day.

When the excretion rate during the 800-kcal mixed diet period was used as a base line, the extra energy

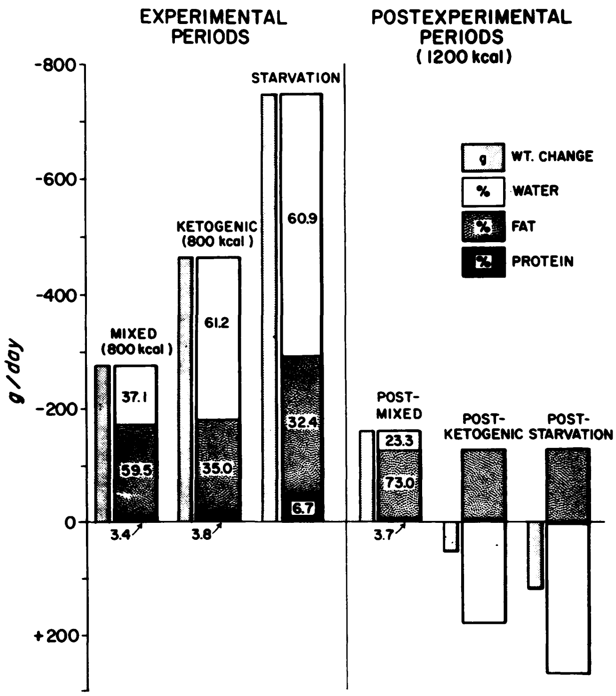

FIGURE 4 Mean daily rate and composition of weight change of obese subjects during experimental and postexperimental periods.

losses that were measured in the urine during the ketogenic diet and starvation periods were largely accounted for (70–100%) by the increments in urinary ketones that occurred at the same time.

Creatinine. Creatinine excretion rates during the mixed, ketogenic, and starvation periods were quite similar, averaging 1.84±0.20, 1.69±0.10, and 1.74±0.14 g/day, respectively. These means did not differ significantly from one another and did not change significantly during the 1,200-kcal postexperimental periods.

Composition of weight lost or gained. As mentioned earlier, rates of weight loss (grams per day) for all subjects averaged 277.9 during the 800-kcal mixed diet period, 466.6 during the 800-kcal ketogenic diet period, and 750.7 during fasting. When the compositions of these losses were determined by the E-N balance procedure, certain striking differences became evident (Fig. 4). Much more water was lost during the ketogenic diet and starvation periods than during the mixed diet period. Indeed, increased water excretion accounted almost entirely for the difference in rate of weight loss between the ketogenic and mixed diet periods.

When responses to the 800-kcal mixed and ketogenic diet periods are compared in terms of mean protein loss, the difference between them is not statistically significant although the mean (±SE) protein deficit during the ketogenic diet period (17.9±5.7 g/day) was somewhat higher than that measured during the mixed diet period (9.5±4.2 g/day). During fasting, the mean protein deficit (50.4±4.6 g/day) was significantly greater ($P < 0.01$) than those occurring during either the mixed or ketogenic diet periods. Mean rates of fat loss calculated by the E-N balance method were almost identical during the 800-kcal mixed and ketogenic diet periods, being 166.7±12.7 and 163.4±17.3 g/day, respectively. During the 10-day fast, the mean rate of fat loss (243.1±14.6 g/day) was substantially greater ($P < 0.001$) than during either of the 800-kcal periods.

The average contribution of body fat (percent of total kilocalories) to the fuel mixture oxidized during the three experimental regimens was calculated to be 97.2 during the 800-kcal mixed period, 94.4 during the ketogenic period, and 92.3 during starvation.

During the 5-day 1,200-kcal postexperimental periods, weight gains occurred after the 800-kcal ketogenic and fasting periods, and weight losses were measured after the 800-kcal mixed diet (Fig. 4). In the postexperimental period that followed the 10-day fast, the rate of weight gain averaged 145 g/day. During this time, water was being retained at an average of 271 g/day, fat was being lost at an average rate of 127.9 g/day, and protein was being retained at an average of 1.9 g/day. These data show that the weight gain during the postfasting period was due principally to water retention, a process that occurred even while net fat loss was continuing. A somewhat similar situation obtained during the 1,200-kcal period that followed the ketogenic regimen. After the ketogenic diet period, there was some weight gain (52.0 g/day), also attributed to excessive water retention (180.6 g/day), in the face of continuing fat and protein losses (125.9 and 2.7 g/day, respectively).

After the 800-kcal mixed diet, an entirely different metabolic situation was observed. Weight was lost at a rate of 163 g/day, the composition of the loss being 3.7% protein, 73% fat, and 23.3% water. It is noteworthy that during all three 1,200-kcal postexperimental periods (whether after fasting, ketogenic diet, or mixed diet), the mean rates of fat loss were almost identical (127.9, 125.9, and 119.0 g/day, respectively), despite major differences in loss of body water and small differences in nitrogen balance.

DISCUSSION

It is well known that, over the short-term, high fat-low carbohydrate (ketogenic) diets restricted in calories usually induce a more rapid weight loss than do isocaloric diets providing conventional proportions of carbohydrate and fat (16). Although earlier studies (17, 18) implied that ketogenic diets accelerate weight loss by inducing sodium and water deficits, Kekwick and Pawan (19) subsequently proposed that high-fat diets may also speed weight reduction in obese subjects by somehow altering metabolism so as to increase "expenditure of calories." More recently, other authors (20, 21) have argued that, by reducing plasma insulin levels, a low-carbohydrate, ketogenic diet would spare body protein by minimizing wasteful gluconeogenesis. To our knowledge, there have been no previous reports of studies in man in which a low-calorie ketogenic diet was directly compared with an isocaloric nonketogenic diet in terms of effect on composition of weight lost. Thus, little if any definitive information has been available to indicate whether a ketogenic diet can somehow accelerate rate of fat loss or exert a unique protein-sparing effect.

We used the E-N balance method to compare two 800-kcal diets differing only in carbohydrate and fat content in the same group of obese individuals for the short-term effect on rate and composition of weight loss. In confirmation of earlier reports (19, 22, 23), we found that subjects lost weight more rapidly during the low-calorie ketogenic diet period than during the mixed diet period (Fig. 1). However, the increment in weight loss exhibited during the ketogenic diet period was due solely to excretion of excess water. Rates of fat loss were not significantly affected by the composition of the diet (Fig. 4).

The nitrogen (protein) deficit during the 800-kcal ketogenic diet was slightly greater than that during the equicaloric mixed diet. Thus, in contrast to some published reports (*24*), it would appear that the ketosis induced by carbohydrate restriction conferred no advantage as regards nitrogen sparing during the 10-day ketogenic period.

As anticipated, rate of weight loss during the starvation period was considerably higher than that associated with either of the 800-kcal diets. As in the ketogenic diet, about 60% of the weight loss during starvation was water; however, the rate of dry weight loss during starvation (equivalent to about 2,800 kcal/day) was significantly greater than that occurring during either of the 800-kcal periods (equivalent to about 2,000 kcal/day). Triglyceride loss during starvation was approximately 50% greater than that during the 800-kcal regimens; protein loss was 2.8–5 times that of the ketogenic and mixed diets, respectively. The extra protein loss during starvation presumably resulted from both the greater energy deficit and the lack of any protein intake during the 10-day starvation period.

It is interesting to note that under certain nutritional conditions the body may be losing some constituents while gaining others. Under these circumstances, the direction of weight change may be especially deceptive. By our measurements, the subjects all lost fat at the same rate during the consumption of the 1,200-kcal postexperimental diet; however, they usually gained weight when the 1,200-kcal diet followed starvation or the 800-kcal ketogenic diet (Figs. 1A and 4). They continued to lose weight when the 1,200-kcal diet followed the 800-kcal mixed diet. When weight was gained in the face of a net fat loss, the gain always occurred because of water retention.

The rate of weight loss during the 1,200-kcal preexperimental period was more rapid than that during the 800-kcal mixed period. This enhanced rate of weight loss appears to have been due to an unusually high rate of water excretion; with water accounting for 69% of the lost weight.[3] It is conceivable that a reduced carbohydrate and energy intake during the preexperimental period resulted in a decrease in liver glycogen with a corresponding increment in water excretion (*25–27*). In addition, the sodium intake during the preexperimental period may have been sufficiently reduced in comparison with the preceding ad lib. diet to cause a water diuresis on this basis.

We have compared the E-N balance method with those based on the measurement of total body water and total body potassium in terms of their ability to provide reliable data about composition of weight loss of subjects on weight reduction regimens. We have found[4] that, when used in short-term studies, the E-N balance method yields data with substantially less variability than the data generated by the application of total body water or potassium-based methods. Assessment of the accuracy of any of the methods would necessarily require comparison with a more direct measurement of body fat change, such as might be obtained by the use of a suitable fat-soluble gas (*28*).

Although physical activity during and immediately after starvation was approximately 5% lower than it was during and after the 800-kcal mixed and ketogenic diet periods, the BMR was unaffected by the nature of the weight reduction regimen. The energy cost of physical activity (lying, sitting, standing, and walking) also was unaffected by the nature of the regimen except that, as the subjects progressively lost weight, the energy cost of voluntary activity decreased proportionally, paralleling the change in BMR. The total energy value of the excreta remained quite constant throughout the study, never exceeding 6% of total energy output. The slightly increased output of urinary energy during starvation was offset by the relative lack of feces during that period.

The total energy expenditures of all of our subjects fell between 2,000 and 3,000 kcal/day, a range similar to that described by other workers (*29–32*) for obese individuals in a hospital setting.

Relatively few investigative groups appear to have used the E-N balance method to estimate composition of weight loss in obese subjects in response to caloric restriction. Passmore et al. (*7*) reported that seven obese adults lost 13–16 kg on a mixed diet providing 400 kcal a day for 42 days. On the average, the composition (in percentages) of the aggregate weight loss exhibited by these subjects was fat 73–83; protein 4–7; water 10–23. These results are similar to ours if one takes into account the lower calorie intake and longer duration of their study.

In view of the widespread interest in the subject (*16*), it is surprising that only Benoit et al. (*2*) appear to have made a systematic study of the effect of a ketogenic diet on composition of weight loss. They reported that when a 1,000-kcal ketogenic diet (providing 10 g carbohydrate/day) was fed for 10 days, their seven male subjects lost an average of 600 g/day, of which 97% was fat. These results differ strikingly from ours; we found only 35% of the weight lost during ingestion of a similar diet to be composed of fat. However, as Grande (*6*) has pointed out, the energy value of the tissue loss reported by Benoit et al. (*2*) calculates out to be about 7,000 kcal/day, a highly improbable level of energy expenditure for subjects confined to a metabolic ward.

Our values for the proportion of fat in the weight lost during starvation (32.4% by weight) are quite similar to the 35.4% reported by Benoit et al. (*2*) and the 36%

[3] This value is a mean derived from data on five subjects. The sixth subject (O. G.) was omitted because a 24-h urine collection was preempted for hormone assay.

[4] Unpublished observations.

in male subjects found by Kjellberg and Reizenstein (5). In contrast, Ball et al. (4, 33) report values for fat loss of 15 and 20%, and Bolinger et al. (3) report a value of 20%. When the fat component of weight loss during starvation is as low as 15–20%, the calculated energy value of the total daily loss (about 1,400–1,600 kcal) falls below the range of energy output anticipated for healthy young adults engaged in light activity.

Because of adaptive responses by the human body to prolonged caloric restriction and changes in dietary composition, the results of our relatively brief studies cannot be applied to longer term situations. It has been reported on many occasions (34–37) that human subjects and other mammals tend to retain dietary nitrogen more tenaciously as body protein is progressively depleted. Thus, obese subjects may achieve nitrogen equilibrium at low levels of energy intake if a restricted diet is adhered to for a sufficiently prolonged period (38, 39). Similarly, subjects who follow a low-carbohydrate ketogenic diet must eventually regain water equilibrium (40). Unfortunately, few, if any, studies in obese human subjects have thoroughly documented these long-term adaptive changes.

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