Composition of Weight Lost during Short-Term Weight Reduction

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

MEI-UH YANG and THEODORE R. VAN ITALLIE

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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 30-day periods. The energy-nitrogen balance method was used to quantify the three measurable components of weight loss: protein, fat, and fat. 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 277.0±32.1 g/day. Composition of weight lost (percentage) during the ketogenic diet was water 61.2%, fat 33.0%, protein 3.8%. During the mixed diet, composition of lost was water 37.1%, fat 95.3%, protein 3.4%. The mean quantity (grams per day) of fat lost during the ketogenic diet was 168.4 g; during the isocaloric mixed diet, it was 166.7 g. Mean protein loss (grams per day) during the ketogenic diet was 17.9 g; during the mixed diet, it was 9.5 g. During starvation, mean rate of weight loss was 250.7±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 30.4±4.6, 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 30-day period. The findings demonstrate that, over a 30-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 values. Rate of fat loss is a function of degree of emaciation.

INTRODUCTION

In recent years, there have been conflicting reports concerning the effects on body composition of various regimes for weight reduction. In 1968 Grandjean (1) 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. Grandjean compared the caloric value of body components and to have been lost from the percentage in the ketogenic diet in the young men studied. Application of this criterion to the data often disclosed marked discrepancies between the caloric value of the constituents that were established and the estimated energy output of the subject.

In the present study, three regimens, starvation at 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

<table>
<thead>
<tr>
<th>Male Subjects</th>
<th>Age</th>
<th>Height</th>
<th>Initial weight</th>
<th>Relative weight*</th>
</tr>
</thead>
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<tr>
<td>J. G.</td>
<td>24</td>
<td>154</td>
<td>198</td>
<td>169</td>
</tr>
<tr>
<td>E. E.</td>
<td>32</td>
<td>169</td>
<td>156</td>
<td>236</td>
</tr>
<tr>
<td>J. H.</td>
<td>19</td>
<td>178</td>
<td>177</td>
<td>339</td>
</tr>
<tr>
<td>E. E.</td>
<td>58</td>
<td>184</td>
<td>108</td>
<td>555</td>
</tr>
<tr>
<td>P. A.</td>
<td>22</td>
<td>168</td>
<td>118</td>
<td>179</td>
</tr>
<tr>
<td>D. G.</td>
<td>22</td>
<td>180</td>
<td>148</td>
<td>195</td>
</tr>
<tr>
<td>Mean</td>
<td>31</td>
<td>177</td>
<td>140</td>
<td>192</td>
</tr>
</tbody>
</table>

*Percent of desirable weight (9).”

### METHODS

Subjects. Six growth obese male subjects were studied in a metabolic ward, for approximately 30 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%.

Diet. On admission, each subject was randomly assigned to one of six experimental schedules as shown in Table II. Each schedule entailed three 10-day regimens: a) an 800-calorie per day benzene diet very low in carbohydrates and, on 500-calorie mixed diet that provided carbohydrate and fat in conventional proportions. To eliminate possible untoward effects, the diet regimens were rotated incounterbalanced sequence among subjects. Also, a 1,200-calorie mixed diet was provided for 5 days before and after each experimental diet to obviate possible carryover 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 posthypocaloric period. Accordingly, the data for the posthypocaloric period is based on five subjects.

Diet and supplements. 70% of the fluid in the present study was 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 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.

### Table II

**Sequence of Study Periods for Each Subject**

<table>
<thead>
<tr>
<th>Period</th>
<th>Subject</th>
<th>Initial weight</th>
<th>Relative weight*</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. G.</td>
<td>1,200 kcal</td>
<td>Starvation</td>
<td>1,200 kcal Mixed</td>
</tr>
<tr>
<td>E. E.</td>
<td>1,200 kcal</td>
<td>Starvation</td>
<td>1,200 kcal Mixed</td>
</tr>
<tr>
<td>J. H.</td>
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<td>Starvation</td>
<td>1,200 kcal Mixed</td>
</tr>
<tr>
<td>E. E.</td>
<td>1,200 kcal</td>
<td>Starvation</td>
<td>1,200 kcal Mixed</td>
</tr>
<tr>
<td>P. A.</td>
<td>1,200 kcal</td>
<td>Starvation</td>
<td>1,200 kcal Mixed</td>
</tr>
<tr>
<td>O. G.</td>
<td>1,200 kcal</td>
<td>Starvation</td>
<td>1,200 kcal Mixed</td>
</tr>
</tbody>
</table>

The protein used was sodium caseinate, the fat was corn oil, and the carbohydrate was sucrose.

### Table III

**Sequence of Study Periods for Each Subject**

<table>
<thead>
<tr>
<th>Period</th>
<th>Subject</th>
<th>Initial weight</th>
<th>Relative weight*</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. G.</td>
<td>1,200 kcal</td>
<td>Starvation</td>
<td>1,200 kcal Mixed</td>
</tr>
<tr>
<td>E. E.</td>
<td>1,200 kcal</td>
<td>Starvation</td>
<td>1,200 kcal Mixed</td>
</tr>
<tr>
<td>J. H.</td>
<td>1,200 kcal</td>
<td>Starvation</td>
<td>1,200 kcal Mixed</td>
</tr>
<tr>
<td>E. E.</td>
<td>1,200 kcal</td>
<td>Starvation</td>
<td>1,200 kcal Mixed</td>
</tr>
<tr>
<td>P. A.</td>
<td>1,200 kcal</td>
<td>Starvation</td>
<td>1,200 kcal Mixed</td>
</tr>
<tr>
<td>O. G.</td>
<td>1,200 kcal</td>
<td>Starvation</td>
<td>1,200 kcal Mixed</td>
</tr>
</tbody>
</table>

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-calorie conservation period; therefore a second 1,200-calorie hypocaloric adjustment period was added to this schedule upon return to the experiment.”

1 This subject left the study before completion of the 1,200 kcal hypocaloric period.

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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.

Outputs 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. Energy intake was determined by measuring the energy expended under basal or resting conditions, that is, in resting calorimetry. The respirometer used for this purpose, a Nicon respirometer (Kips & Zonne, Drift, Holland), automatically measures by thermocoupling 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.

Computation of weight loss (or gain). The composition of weight change was estimated from data obtained by the energy metabolism (E-N) balance method (7, 8). This method utilizes the measurement of nitrogen balance 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 weight are considered to be 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 ultimately 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:

\[
\Delta_{\text{protein}} (g) = AN (g) \times 6.25
\]

\[
\Delta_{\text{fat}} (g) = \text{kcal from body fat} \times 9.3
\]

where kilocalories from body fat

\[
\Delta_{\text{water}} (g) = \text{body weight gain} (g) - (\Delta_{\text{protein}} + \Delta_{\text{fat}}) \times 6.25
\]

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

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No correction was made for the approximately 0.5 g/day nitrogen said to be lost via shedding of estrus 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 a given daily 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 sequentially in Fig. 1A. During the preexperimental 1,200-kcal period, the rate of weight loss (mean±SE) was 3.1 ± 0.6 kg/day. Among the experimental periods, the subjects lost weight most rapidly while fasting (70.3 ± 5.9 g/day) and least rapidly during consumption of the mixed diet (27.9 ± 3.2 g/day). Weight loss during the ketogenic diet was intermediate between these two extremes (44.6 ± 5.1 g/day). During the 1,200-kcal period that followed the mixed diet, all of the subjects continued to lose weight slowly, the mean change

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**Figure 1.** Effect of various weight reduction regimes on (A) mean (±SE) daily nitrogen balances of six obese subjects. Values are plotted cumulatively.

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**Table 1.** Gross energy costs of 2,000-kcal diets.

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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±1.5 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 71-80% of the total output. The mean energy value of urine and feces averaged 5.2% (range 4-8%). 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±92 kcal/day, respectively. It should be recalled that, in one 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**

<table>
<thead>
<tr>
<th>Subject</th>
<th>Adj. 1</th>
<th>Exp. 1</th>
<th>Adj. 2</th>
<th>Exp. 2</th>
<th>Adj. 3</th>
<th>Exp. 3</th>
<th>Adj. 4</th>
</tr>
</thead>
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<tr>
<td>E. G.</td>
<td>2,272</td>
<td>2.2N</td>
<td>2,203</td>
<td>1,977</td>
<td>2,020</td>
<td>2,116</td>
<td>1,957</td>
</tr>
<tr>
<td>E. F.</td>
<td>2,176</td>
<td>2,009</td>
<td>1,976</td>
<td>1,727</td>
<td>1,821</td>
<td>1,782</td>
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<tr>
<td>E. H.</td>
<td>2,080</td>
<td>2,205</td>
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<td>2,244</td>
<td>2,277</td>
<td>2,048</td>
<td>2,151</td>
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<tr>
<td>E. B.</td>
<td>1,891</td>
<td>1,737</td>
<td>1,699</td>
<td>1,552</td>
<td>1,697</td>
<td>1,657</td>
<td>1,555</td>
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<tr>
<td>P. A.</td>
<td>1,729</td>
<td>1,888</td>
<td>1,573</td>
<td>1,144</td>
<td>1,581</td>
<td>1,553</td>
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<tr>
<td>O. G.</td>
<td>2,368</td>
<td>2,062</td>
<td>1,948</td>
<td>2,013</td>
<td>1,830</td>
<td>1,840</td>
<td>1,988</td>
</tr>
</tbody>
</table>

| Subject | Exp. | Adj. | \( BM_{\text{test}} \) | \( 
\text{Weight} \) | Change |
<table>
<thead>
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<th></th>
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<tr>
<td>E. G.</td>
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<td>2.2N</td>
<td>2,203</td>
<td>1,977</td>
<td>-13.9</td>
</tr>
<tr>
<td>E. F.</td>
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<td>1,976</td>
<td>1,727</td>
<td>-19.0</td>
</tr>
<tr>
<td>E. H.</td>
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<td>2,310</td>
<td>2,244</td>
<td>-9.6</td>
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<td>1,699</td>
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<td>-17.8</td>
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<td>1,888</td>
<td>1,573</td>
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<td>-4.3</td>
</tr>
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<td>2,062</td>
<td>1,948</td>
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<td>-18.9</td>
</tr>
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<td>Mean</td>
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<td>2,027</td>
<td>1,924</td>
<td>1,881</td>
<td>-12.3</td>
</tr>
</tbody>
</table>

*BM, kilocalories per day.

1 Not Table II for specific sequences of study periods (Adj., 1,200 kcal, Exp., starvation, ketogenic, or mixed).

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

**Nutritional 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 increased 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 (12.5%) almost exactly paralleled the mean decrease in body weight (13.5%).

**Urine constituents**

Ketones. The mean of the daily excretion rates of ketone bodies of the six subjects during each of the experimental and 1,200-calorie periods are plotted sequentially in Fig. 3A. During the 800-calorie mixed diet period and the 1,200-calorie period that followed it, ketone excretion was negligible, with individual values ranging from 0.02 to 0.39 g/d. In contrast, ketone excretion during the starvation period was substantial, ranging from 0.07 to 0.4 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 d of the 1,200-calorie poststarvation period. During the 1,200-calorie 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-calorie postketogenic diet period.

**Energy-yielding materials.** The urinary excretion rates of energy-yielding materials for each experimental and adjustment period are shown in kilocalories/day in Fig. 3B. During the 800-calorie mixed diet period, urinary energy excretion remained quite stable, the mean energy 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 105.27 kcal/day.

As in the case of the ketone excretion rate, the rate of urinary excretion of energy during the 800-calorie ketogenic period was intermediate between those during the mixed 800-calorie diet period and starvation, ranging from 90.27 kcal/day.

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

**Figure 4** Mean daily rate and composition of weight change of obese subjects during experimental periods.
was more water was lost during the ketogenic and
fat content in the same group (obese individuals) for the short-term effect on rate and composition of weight loss. In confirmation of earlier reports (19, 22, 25), we
found that subjects lost weight more rapidly during the low-carbohydrate 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 exclusion 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

**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 isoenergetic 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, Scow and Maun (19) subsequently proposed that high-fat diets may also speed weight reduction in these 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 isoenergetic nonketogenic diet in terms of effect on composition of weight lost. Thus, little if any definitive information has been avail-

able 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, 25), we found that subjects lost weight more rapidly during the low-carbohydrate 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 exclusion 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
equiocaloric 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 such circumstances, the direction of weight change may be especially deceptive. By our measurements, the subjects lost all fat at the same rate during the consumption of the 1,200-kcal post-experimental 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 regained 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 pre-experimental period was more rapid than that during the 800-kcal mixed period. This enhanced rate of weight loss appears to be due to an unusually high rate of water excretion; with water accounting for 60% of the lost weight. It is conceivable that a reduced carbohydrate and energy intake during the pre-experimental period resulted in a decrease in liver glycogen and a corresponding increase in water excretion (25-27).

In addition, the sodium in the sodium-depleted group 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 nitrogen in terms of its ability to provide reliable data about composition of weight loss of subjects on weight reduction regimens. We have found 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 require comparison with a more direct measurement of body fat change, such as might be obtained by the use of an X-ray caloric-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 diets, 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. Thus, 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 expenditure of all of the subjects fell between 2,000 and 3,000 kcal/day, in agreement with that described by other workers (29, 30).

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. Dunstone 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 (by percentage) of the aggregate weight lost contained 73% body fat, 4% body water, 20% lean body mass. These results are similar to ours if one also accounts for the lower calorie intake and longer duration of their study.

In view of the widespread interest in the subject (31), it is surprising that Benoit et al. (22) appear to have made a systematic study of the effect of a ketogenic diet on composition of weight loss. They reported that when a 1,500-kcal ketogenic diet (containing 50 g carbohydrate/day) was fed for 10 days, their obese adults lost an average of 600 g of weight. However, there was no increase in energy intake of the obese loss reported by Benoit et al. (22) calculated out to be about 7,000 kcal/day, a highly improbable level of energy expenditure for four subjects confined to a metabolic ward.

Our predictions for the proportion of fat in the weight lost during starvation (24-48% by weight) are similar to the 35-61% reported by Benoit et al. (22) for 36%.
The authors are grateful to Dr. Otto 7 for his advice and Dra. R. S. Barron, W. C. Hashagen, and F. M. Pietsch for valuable clinical assistance. This work was supported in part by grants from the National Institute of Health (Grants 58-33724) and from the Wright-Foundation.

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