Changes in resting energy expenditure and body composition in anorexia nervosa patients during refeeding
DEAN D. KRAHN, MD; CHERYL ROCK PhD, RD; RONALD E. DECHERT, MS; KAREN K NAIRN, RN; SHERYL A HASSE, MS, RD

ABSTRACT: Accurate prediction of the energy level necessary to promote weight restoration in patients with anorexia nervosa would be clinically useful. Resting energy expenditure (REE), respiratory quotient, and body composition were measured in 10 nonmedicated women with anorexia nervosa during a vigorous refeeding protocol. REE was measured three times per week by open-circuit indirect calorimetry after an overnight fast. Subjects ranged in age from 19 to 38 years and weighed 39.9 ± 4.3 kg (mean ± standard deviation) at admission. The refeeding protocol was as follows: phase 1, 1,200 kcal/day for 1 week (baseline); phase 2, an increase of 300 kcal/day for 1 week; phase 3, 3,600 kcal/day until target weight was reached; phase 4, 1,800 to 2,800 kcal/day (stabilization). REE was 30.0 ± 6.4, 33.5 ± 6.7, 37.3 ± 6.6 and 34.5 ± 4.4 kcal/kg body weight during phases 1, 2, 3, and 4, respectively. The Harris-Benedict equation overestimated phase 1 24-hour REE by a mean of 14% and underestimated REE in phases 2, 3, and 4 by a mean of 8%, 24%, and 23%, respectively. Skinfold measurements revealed percent body fat to be 12 ± 4% at admission and 19 ± 5% at discharge, with a mean of 48% of the weight gained during refeeding attributable to increased body fat. These findings indicate that refeeding in anorexia nervosa is associated with increased REE, which cannot be explained by increased body mass, and that caloric requirements for weight restoration in patients with anorexia nervosa are best determined by monitoring individual response. J Am Diet Assoc. 1993; 93:434-438.
have suggested that the caloric requirements of patients with anorexia nervosa are either higher (9) or lower (10) than those of normal subjects. Many of the metabolic alterations and physiologic abnormalities that are characteristic of anorexia nervosa are identical to those of protein-energy malnutrition or severe starvation. However, some nutritional aspects of anorexia nervosa may be uniquely different from protein-energy malnutrition because of behavioral patterns, specific food choices, and neuroendocrine changes.

Few data have been reported on actual measurements of REE in anorexia nervosa patients during weight recovery. Problems with interpreting early reports include adolescents (who may still be growing) grouped with adults in study samples and the failure to use a standardized refeeding regimen.

The purpose of our study was to determine what changes in body composition and basal energy expenditure occur during a refeeding protocol for weight restoration in adult patients with anorexia nervosa. We also evaluated the usefulness of various equations for estimating the energy requirements of these patients.

MATERIALS AND METHODS

Subjects
Ten consecutively admitted women, aged 19 to 38 years, were recruited for this study. The patients had been admitted voluntarily and consented to the overall treatment regimen. Subjects were nonmedicated, had no endocrinopathies, and met established criteria for anorexia nervosa (1). All were at least 15% below expected weight for height upon admission. Seven reported some bulimic behavior before hospitalization, and three appeared to have controlled their weight primarily through restrictive eating. Patients were housed in the Eating Disorders Inpatient Unit, which is a locked facility. Procedures were approved by the University of Michigan Hospitals Institutional Review Board.

Methods
Nutritional rehabilitation consisted of a refeeding protocol that was implemented in four phases. Phase 1, which was prescribed for 1 week after admission, provided intake of 1,200 kcal/day. Phase 2 also lasted 1 week, during which time the energy level was increased at a rate of 300 kcal/day. Caloric intake was 3,600 kcal/day in phase 3, and this level was maintained until patients attained a target weight that was within 10% of ideal body weight (the midpoint of average weight for height derived from the 1983 Metropolitan Life tables). During phase 4, which was designed to promote weight stabilization, patients consumed 1,800 to 2,800 kcal/day, with caloric levels adjusted individually for weight maintenance.

The diet prescribed for patients consisted of foods from the hospital menu. Of the total caloric intake, 50% was from carbohydrate, 30% from fat, and 20% from protein. Patients consumed all food served on the tray. All meals were consumed under observation and all patients were monitored for 1 hour after each meal. Bathrooms were used only with supervision until after target weight was reached. Daily activities were regulated. Physical exercise was limited to walking 30 minutes per day and was allowed only after the patient achieved her target weight.

Height was measured at admission, and body weight was measured daily in the morning immediately after the patient had awakened and had voided. Subjects were weighed without clothes on a digital scale to the nearest 0.1 kg. A trained clinical dietitian obtained weekly skinfold measurements using skinfold calipers. Skinfold thickness was measured at the triceps, biceps, supraclavicular, and subscapular sites. Percent body fat was derived from the sum of these measurements using the values of Durnin and Womersley (11).

Equations to predict energy requirements may have limited usefulness in this population, at least during the initial phase of weight restoration.

Bioelectrical impedance analysis (BIA) was used to estimate total body water. Resistance and reactance determinations were made using a four-terminal impedance plethysmograph (BIA-101, RJL Systems, Detroit, Mich). Measurements were obtained three times per week 2 hours after the subject ate and within 30 minutes after voiding. Estimates of total body water were calculated using previously derived equations (12).

Because previous reports (13) have demonstrated that notable fluid shifts occur during refeeding of anorexia nervosa patients, BIA was not used to assess percent body fat or lean body mass. Respiratory quotient (RQ) and REE were determined three times per week using open-circuit indirect calorimetry with a hood canopy system (MRM-1000, Waters, Milford, Mass). Measurements were obtained between 7AM and 8AM after a 10-hour overnight fast. After patients woke up, they voided, were weighed, and returned to bed. Patients then rested in bed for an additional 30 minutes before the first measurement. Studies were conducted while the patient was at rest until steady instrumentation conditions were maintained.

Measured REE (calculated per kilogram of body weight and per 24-hour period) was compared with values derived from estimates using the Harris-Benedict (14), Owen (15), and Mifflin-St Jeor (16) equations. RQ was calculated from values for inspired \( V_O_2 \) and expired \( V_CO_2 \), which were obtained during REE measurements.

Data Analysis

Because this study was observational, the major type of data analysis performed involved descriptive statistics (17). Results were expressed as mean ± standard deviation (SD). Correlation coefficients were also examined to identify possible relationships between characteristics of the subjects and response to refeeding (17). Statistical significance was considered to be \( P<.05 \).

RESULTS

The refeeding protocol promoted weight gain in all subjects, as predicted. Ten patients completed phases 1, 2, and 3, and six patients remained hospitalized long enough to complete phase 4. The refeeding regimen lasted a mean of 6.3 weeks. None of the patients experienced adverse metabolic or physiologic side effects in response to the regimen.

The Table lists descriptive characteristics of the total group during phases 1, 2, and 3 of the refeeding protocol as well as characteristics of the six patients who completed phase 4 (weight stabilization).
Mean (± standard deviation) measurements obtained from patients with anorexia nervosa during four phases of a refeeding protocol*

<table>
<thead>
<tr>
<th></th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Phase 4</th>
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<tbody>
<tr>
<td>(1,200 kcal/day)</td>
<td>(increase of 300 kcal/day)</td>
<td>(3,600 kcal/day)</td>
<td>(maintenance)</td>
<td></td>
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<tr>
<td>No.</td>
<td>25</td>
<td>25</td>
<td>25</td>
<td>19</td>
</tr>
<tr>
<td>Weight (kg)*</td>
<td>43.9±1.1</td>
<td>42.4±5.3</td>
<td>45.6±3.5</td>
<td>51.4±2.5</td>
</tr>
<tr>
<td>Body water (%)</td>
<td>70±5</td>
<td>72±5</td>
<td>68±4</td>
<td>64±4</td>
</tr>
<tr>
<td>Respiratory quotient* (Vco2/ V02 mL/min)</td>
<td>0.94±0.20</td>
<td>1.12±0.31</td>
<td>1.16±0.23</td>
<td>1.04±0.16</td>
</tr>
<tr>
<td>REE (kcal)* per 24 hr</td>
<td>1,166±210</td>
<td>1,409±351</td>
<td>1,769±363</td>
<td>1,738±149</td>
</tr>
<tr>
<td>REE per kg body weight (kcal)*</td>
<td>30.0±6.4</td>
<td>33.5±6.7</td>
<td>37.3±6.6</td>
<td>34.5±4.4</td>
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*Data for phases 1, 2, and 3 are for all 10 patients; data for phase 4 are for 6 patients who completed the weight stabilization phase.

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Response to refeeding can also be described as the difference between patient data at admission and discharge. Upon admission, mean body weight was 39.9±4.3 kg, height was 161.0±3.2 cm, and percent body fat was 12±4%. According to skinfold measurements, percent body fat at admission ranged from 8% to 21%.

At discharge, mean weight was 50.3±2.0 kg and percent body fat was 19±5%. Final skinfold measurements indicated that body fat ranged from 12% to 29% when the patients were discharged. A mean of 48% of the weight gained during the refeeding regimen was attributable to an increase in body fat. The observed difference in REE (between admission and discharge), which ranged from an increase of 467 to 1,049 kcal/24 hours, did not correlate with patient age or other variables. The degree of increase in body fat during hospitalization also did not correlate with patient age.

The figure illustrates the relationship between measured REE (expressed per 24-hour period) and predicted 24-hour REE, using three different equations. The Harris-Benedict equation (14) underestimated phase 1 24-hour REE by a mean of 14% and underestimated REE in phases 2, 3, and 4 by means of 8%, 24%, and 29%, respectively. Mean figures derived from the Owen equation (15) were within 5% of phase 1 REE but underestimated REE during phases 2, 3, and 4 by 19%, 25%, and 33%, respectively. Similar underestimates were derived from the Mifflin-St Jeor equation (16); figures were a mean of 16%, 30%, and 29% lower than measured values during phases 2, 3, and 4, respectively.

DISCUSSION
Results from our study demonstrate that refeeding to restore weight in anorexia nervosa patients is associated with an increase in REE, even when corrected for increased body mass. At baseline, estimates of REE derived from predictive calculations were found to underestimate basal energy expenditure, but during weight restoration these figures underestimated expenditure substantially.

In a study of 29 patients with anorexia nervosa, Walker et al. (18) observed that a mean excess of 5,026 kcal was required to promote 1 kg weight gain during the first 15 days of treatment with a standardized refeeding protocol, but this figure increased to 7,428 kcal during the subsequent 19 days. Using indirect calorimetry, Dempsey et al. (19) measured REE in four anorexia nervosa patients before they began nutrition support and weekly thereafter. Initially, measured REE was a mean of 70% of the predicted level, but this figure increased to 102% of the predicted value after 63±18 days of nutrition support. Marked interindividual variation in REE among their patients was also observed (19). More recently, Vaisman et al. (20) measured REE with indirect calorimetry in 25 adolescent anorexia nervosa patients. As in our study, predictive equations underestimated REE at the initial evaluation, which ranged from 49% to 92% of predicted value. They also found that REE correlated positively with body weight and lean body mass.

Compared with predicted values, initial REE measurements in our study were relatively higher than the values previously reported for anorexia nervosa patients, possibly because of differences in the age group involved (adults vs adolescents) and in the severity of malnutrition. Also, patients in our study were consuming 1,200 kcal/day during the phase of the protocol when the baseline measurements were obtained.

Casper et al. (21) also observed that REE of six anorexia nervosa outpatients who were maintaining low body weights was lower than that of control subjects, although total daily energy expenditure (measured via doubly labeled water method) was similar in patients and control subjects because of increased physical activity in the patients. Pirke et al. (22), who also used the doubly labeled water method, confirmed that total energy requirements of weight-stable anorexia nervosa patients who are not eating a high-energy diet are high as a consequence of physical activity. Results from early observational studies also documented the influence of physical activity on caloric requirements of anorexia nervosa patients (23). However, weight-stable, low-weight patients are metabolically different from inpatients undergoing weight restoration in an intensive treatment program, as were those in our study.

Caloric requirements for maintaining restored weight have been reported to be higher for patients with anorexia nervosa who do not practice bulimic behaviors than for those who do (24). Weltzin et al. (25) recently reported results of an observational study of the caloric requirements of four subgroups of patients with eating disorders. They found that anorexia nervosa patients of the diet-restricting subtype required a higher caloric intake to maintain weight during the weeks after weight restoration than did bulimic anorexic patients. Caloric requirements for both groups were higher than those for the long-term weight-restored patients, even when corrected for body surface area. They did not observe elevated caloric requirements in the long-term weight-stable patients and suggest that recent weight gain has an influence on caloric requirements in these patients. Results from our study of patients during the short-term weight gain period...
support the hypothesis of abnormal caloric requirements during the early phase of recovery, although no consistent difference in REE was observed in our small diet-restricting and bulimic subgroup samples.

REE, which accounts for the major portion of total energy expenditure, has been shown to be influenced by body composition, prolonged starvation, age, and hormonal factors (26). The phenomenon of decreased basal metabolic rate in response to semistarvation, independent of reduced body cell mass, has been previously observed in underfed normal subjects, patients with anorexia nervosa, and weight-reducing obese individuals (27). Presumably this is mediated by endocrine mechanisms such as alterations in the hypothalamic-pituitary-thyroidal axis and low plasma triiodothyronine levels, which have been observed in patients with anorexia nervosa (28).

Modern studies (15,16) of normal populations have produced regression equations that are reported to be better predictors of REE than the classic Harris-Benedict equation (14). For the patient population in our study (hospitalized patients with anorexia nervosa), such predictive equations may have limited usefulness.

Methodologic problems may have affected the measurements obtained in our study. For example, obtaining REE measurements after an overnight fast may not have excluded postprandial thermogenic effects in phases 2 and 3, when caloric intake was high. High RQ values may have been due to inadequate fasting.

Results from previous studies of changes in body composition during weight restoration in patients with anorexia nervosa indicate that fat may compose 32% to 77% of the total weight gained (29). Results from our study, in which all patients were adults fed a standardized diet, fell within this range. The observed increase in RQ also reflects the shift from lipolysis to lipogenesis that occurred in these patients. Subject variables (eg, age), the refeeding protocol, methods of measurement, and stage of recovery all contributed to the variable body fat increases. Considerable interindividual variation in change in body fat was observed in our study, and useful predictive variables were not readily apparent. However, significant correlations among these variables are unlikely because of the small sample size.

Normal levels of body water are reported to compose 50% of body weight in young women (30). In our study, increased levels of body water during the initial phases of refeeding anorexia nervosa patients were evident in the BIA measurements.

Previously, Vaisman et al (13) documented an accumulation of extracellular water during 8 weeks of refeeding in 13 female adolescents with anorexia nervosa. Their calculations were based on total body potassium, extracellular water (measured as the bromide space after oral bromide administration), and skinfold measurements. These marked shifts in fluid balance limit the usefulness of methods for measuring body composition that rely primarily on estimates of body water as predictors of lean body mass (31). Also, these observations do not support the practice of estimating caloric requirements and providing positive feedback for patients on the basis of weight gain alone (5,7,32).

Vigorous refeeding of anorexia nervosa patients with parenteral nutrition has resulted in acute cardiopulmonary decompensation associated with severe hypophosphatemia and other metabolic abnormalities (33). However, reports from other inpatient treatment programs that use a refeeding protocol similar to the one based on everyday foods described here, indicate no deaths and no instances of congestive heart failure (5,6). Patients in our study were hospitalized throughout the refeeding protocol and were carefully monitored for any adverse effects; no adverse effects were observed. Patients with anorexia nervosa are likely to have decreased myocardial muscle mass and other physiologic alterations because of semistarvation, which necessitates medical monitoring during vigorous refeeding as described in our study (34).

APPLICATIONS

Adult patients with anorexia nervosa are a heterogeneous group, although low initial REE has been consistently reported, most likely in response to semistarvation. However, results from this study confirm that REE is likely to be higher than predicted during refeeding, presumably mediated by altered hormonal or metabolic status. High-energy diets may be clinically necessary to promote continued weight gain in these patients.

More importantly, monitoring REE levels and response to refeeding should enable clinicians to prescribe energy intake more accurately. Individualized diet prescriptions are clearly a desirable approach to managing dietary requirements of patients with anorexia nervosa. Predictive equations may have limited usefulness in this patient population, at least during the initial phase of weight restoration.

Changes in fluid balance that occur during refeeding of anorexia nervosa patients affect body composition and how accurately it can be measured (34). Among adults with
anorexia nervosa who do not exercise during weight restoration, nearly half of weight gained may be fat. However, we observed a wide range of increases in body fat among these patients, and neither age nor eating disorder history appeared to predict response. Also, mean percent body fat at discharge is still likely to be lower than levels observed in normal-weight populations, although most patients believe they are too fat.

Levels of body fat at discharge may also affect clinical outcome. Return of menses is more likely to occur in association with higher levels of body fat. However, high body fat may cause increased psychological stress in these patients and, thus, may be more likely to promote relapse. Balancing these positive and negative aspects of body fat regain can be addressed in therapy.

Strategies for nutritional rehabilitation in patients with anorexia nervosa should be based on studies that document short- and long-term responses to such interventions, rather than on the desire to promote weight restoration as rapidly as possible or on fiscal concerns about insurance reimbursement for hospitalization. The optimal approach to refeeding and a possible role for exercise in a weight restoration protocol are yet to be determined.

This study was supported by CRC grant SM01RR00042.

The authors thank the staff of the Clinical Research Center, especially Constance Adair, MS, RD, for support and for obtaining the body composition measures. The authors also thank Robert Bartlett, MD, of the Department of Surgery and Adam Drewnowski, PhD, of the Program in Human Nutrition, University of Michigan, Ann Arbor, for their guidance and support.

References