Changes in regional fat redistribution and the effects of estrogen during spontaneous weight gain in women with anorexia nervosa

Steven Grinspoon, Lisa Thomas, Karen Miller, Sarah Pitts, David Herzog, and Anne Klibanski

ABSTRACT

Background: Anorexia nervosa is a disease of severe acquired undernutrition with a high and increasing prevalence among young women in the United States.

Objective: The objective was to investigate the effects of spontaneous weight recovery and estrogen administration on fat distribution in patients with anorexia nervosa.

Design: Twenty-seven amenorrheic women aged 26.6 ± 1.2 y with anorexia nervosa were identified through an outpatient study of bone loss and were randomly assigned to receive or not receive estrogen without any dietary intervention other than calcium and multivitamin supplements. Body composition was measured at baseline and at 6 and 9 mo and was compared with cross-sectional values obtained in 20 healthy, eumenorrheic, age-matched (25.4 ± 0.5 y) control subjects.

Results: Twenty of the 27 patients with anorexia aged 27.0 ± 1.3 y spontaneously gained weight (4.1 ± 0.9 kg); body mass index (in kg/m²) increased from 16.1 ± 0.3 to 17.5 ± 0.4. Fat mass and lean mass accounted for 68% and 32% of the gain in total body mass, respectively. With spontaneous weight gain, there was a significant increase in the percentage of trunk fat from 32.4 ± 1.3% at baseline to 36.5 ± 1.0% at 9 mo (P = 0.03), which correlated with urinary free cortisol (r = 0.66, P = 0.003). Estrogen treatment was not protective against the gain in trunk fat with spontaneous weight gain.

Conclusions: In women with anorexia nervosa, spontaneous weight gain is associated with a significant increase in trunk adiposity, and estrogen administration may not protect against the accumulation of central fat with weight gain. Am J Clin Nutr 2001;73:865-9.

INTRODUCTION

Anorexia nervosa is a disease of severe undernutrition and is widely prevalent among women in the United States (1, 2). Weight gain is the goal for all patients with anorexia nervosa; however, relatively little is known about how such patients adapt to increasing weight and how the relative distribution of body fat is affected during spontaneous weight recovery in this population. Previous studies showed abnormalities in fat redistribution, resulting from intensive refeeding programs in women with anorexia nervosa (3–5); however, the effects of spontaneous, long-term weight gain on fat redistribution in ambulatory patients with anorexia nervosa are not known. Furthermore, the effects of exogenous estrogen administration on fat distribution during weight recovery in anorexia nervosa have not been investigated.

In the present study we investigated the effects of spontaneous weight gain and estrogen on regional body composition in women with anorexia nervosa, the degree to which trunk and extremity fat changed with weight gain, the effects of estrogen on fat distribution during weight gain, and whether changes in fat distribution with weight gain were correlated with other hormonal indexes, including cortisol.

SUBJECTS AND METHODS

Subjects

Fifty-four women were recruited through advertisements in local community newspapers, posted advertisements on local college campuses, and referrals from local physicians for this prospective, longitudinal treatment study of bone loss due to anorexia nervosa. Anorexia nervosa was diagnosed on the basis of Diagnostic and Statistical Manual of Mental Disorders IV criteria (6). All of the subjects had an anterior-posterior spinal density T score ≤ 1.0 SDs. None of the women with anorexia nervosa had received estrogen within 6 mo of the beginning of the study. Screening bone density data for these subjects were previously published (7). Control subjects had a history of regular menstrual cycles and were studied in the early follicular phase within 7 d of the onset of menses. Subjects maintained a menstrual diary during the study.

Patients with anorexia nervosa and control subjects with abnormal thyroid-stimulating hormone concentrations; elevated follicle-stimulating hormone, prolactin, or testosterone concentrations; or a ratio of luteinizing hormone to follicle-stimulating hormone concentrations > 2.5 were excluded from participation.

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Twenty-seven of the 54 subjects were receiving active treatment for bone loss with a nonestrogen-based hormone and were considered ineligible for the study (Figure 1). All subjects gave written consent and the protocol was approved by the Subcommittee on Human Studies of the Massachusetts General Hospital.

Study design

The remaining 27 eligible subjects were randomly assigned to receive no treatment (n = 13) or to receive estrogen (n = 14) in the form of a daily oral contraceptive pill (Ovcon 35, 35 μg ethinyl estradiol and 0.4 mg norethindrone; Bristol Meyers Squibb, Princeton, NJ) and were followed longitudinally over 9 mo. All subjects, regardless of estrogen assignment, received 1500 mg Ca/d and a multivitamin supplement for 9 mo. Food intake was ad libitum. All participants were required to maintain regular visits with their primary care physicians and therapists and were encouraged to gain weight. Specific nutritional counseling was not given as part of the study, but patients received individualized counseling from their primary care physicians.

Changes in regional body composition were reported for the subset of subjects who gained weight over the 9 mo of follow up (n = 20). Of this group, 10 subjects were from the estrogen group and 10 were from the no-estrogen group. Body composition before and after weight gain was compared with cross-sectional data obtained from an age-matched group of healthy control subjects (n = 20) who were receiving no medications.

Body-composition analysis

Whole-body fat and lean mass were determined by dual energy X-ray absorptiometry (DXA) with a Hologic-4500 densitometer (Whole Body V8.15a:3; Hologic, Inc, Waltham, MA) at baseline and at 6 and 9 mo. The precision of this technique for whole-body fat and lean mass was 3% and 1.5%, respectively (8). In addition, body composition was determined in the trunk and extremity regions. The regions of interest were standardized according to previously published methods (9). Trunk fat, extremity fat, and the ratios of trunk to total fat (% trunk fat), of extremity fat to total fat (% extremity fat), and of trunk fat to extremity fat were determined.

Biochemical and nutritional assessments

Follicle-stimulating hormone, testosterone, luteinizing hormone, thyroid-stimulating hormone, and prolactin were measured at baseline by using published methods (10). Twenty-four-hour urinary free cortisol excretion was determined by radioimmunoassay at each visit (10). Body mass index (BMI; in kg/m²) and percentage ideal body weight were calculated (11).

Statistical analysis

Clinical variables were compared between patients and control subjects at baseline, before weight gain, and again after weight gain by using a t test with Bonferroni adjustment for multiple comparisons. Body composition and other clinical variables were compared by analysis of variance (ANOVA) for the time trend over all visits (baseline and the 6- and 9-mo visits). Clinical variables were compared between estrogen-treated and nontreated subjects at baseline by t test. The changes between the estrogen-treated and nontreated patients over 9 mo were compared by ANOVA. Simple and multivariate regression models for change in trunk fat were constructed. Change in weight, initial weight, the percentage of trunk fat at baseline, and estrogen treatment status were tested in a multivariate regression model to predict change in the percentage of trunk fat. The analysis was performed by using JMP STATISTICAL DISCOVERY SOFTWARE (SAS Institute Inc, Cary, NC). Results are reported as means ± SEMs.

RESULTS

The baseline clinical characteristics of the study subjects are shown in Table 1. Of the 27 subjects with anorexia nervosa who were identified as eligible for the study, 20 gained weight over the 9-mo study period (BMI: 16.1 ± 0.3 at baseline and 17.5 ± 0.4 at 9 mo; P = 0.03) and were investigated further. Only one patient regained sufficient weight to normalize her BMI (>20.0).

The characteristics of the anorexia nervosa patients were compared at baseline and at 9 mo (after weight gain). Body composition and other clinical endpoints were also compared at each time point with cross-sectional data from a control group of healthy, age-matched subjects (Table 2). At baseline, the anorexia nervosa patients weighed considerably less than did the control subjects (BMI: 16.1 ± 0.3 compared with 21.0 ± 0.4) and had significantly less body fat, as an absolute amount and as a percentage of total fat mass (18.1 ± 1.6% compared with 26.4 ± 0.8%). The percentage of trunk fat (trunk fat/total fat) was not significantly different between the anorexia nervosa patients (32.4 ± 1.3%) and the control subjects (33.7 ± 0.9%) at baseline, but the percentage of extremity fat (extremity fat/total fat) was significantly lower at baseline in the anorexia nervosa patients (56.1 ± 1.6%) than in the control subjects (60.9 ± 0.9%).

Anorexia nervosa patients gained an average of 4.1 ± 0.9 kg over the 9 mo of the study. Fat mass and lean mass accounted for 68% and 32% of the overall weight gain in the patients with anorexia nervosa, respectively. With spontaneous weight gain, there was a significant increase in the percentage of trunk fat from 32.4 ± 1.3% at baseline to 36.5 ± 1.0% at 9 mo, without a concomitant increase in the percentage of extremity fat (Table 2).
After 9 mo of spontaneous weight gain, the ratio of trunk fat to extremity fat was significantly higher in the anorexia nervosa patients (0.67 ± 0.03) than in the control subjects (0.56 ± 0.02), although weight (BMI: 17.5 ± 0.4 compared with 21.0 ± 0.4) and percentage of total fat mass (22.5 ± 1.2% compared with 26.4 ± 0.8%) remained significantly lower in the anorexia nervosa patients. A strong inverse relation was observed between the percentage of trunk fat at baseline and the change in the percentage of trunk fat with weight gain (Figure 2). Similar results were seen in a subanalysis limited to subjects with a final BMI <20.0 (n = 19; data not shown).

Among the subjects who gained weight, there were no significant differences in baseline body composition between the estrogen-treated and nontreated patients (Table 3). Four of the 10 patients who did not receive estrogen resumed regular menstrual function, compared with 6 of 10 patients who received estrogen. The change over 9 mo in the percentage of trunk fat between the nontreated and estrogen-treated groups was not significant (2.7 ± 1.8% compared with 5.6 ± 2.2%, respectively), and the difference was not positive in a regression model in which menstrual function, independent of estrogen treatment status, was controlled for. Furthermore, the percentage of trunk fat at baseline was significant in a multivariate model that predicted change in the percentage of trunk fat (overall $r^2 = 0.71$, $P = 0.0009$ for the whole model), but baseline weight, estrogen treatment status, and the change in weight were not significant.

Urinary free cortisol concentrations were increased above the expected normal range in 20% of the anorexia nervosa patients at baseline and did not change with weight gain (55 ± 8 compared with 54 ± 9 μg/24 h, respectively). The increase in trunk fat was highly correlated with urinary free cortisol concentrations at the end of the study ($r = 0.66$, $P = 0.003$) and, similarly, the change in the percentage of trunk fat also correlated with baseline urinary free cortisol concentrations ($r = 0.44$, $P = 0.05$). The increase in the percentage of trunk fat was 6.8 ± 3.8% in the patients with increased urinary free cortisol concentrations and 3.5 ± 1.5% in patients with reference urinary free cortisol concentrations. Estrogen treatment did not affect urinary free cortisol concentrations significantly.

### DISCUSSION

Relatively little is known about fat distribution and the effects of weight gain on regional body composition during recovery in women with anorexia nervosa. Before spontaneous weight gain, the anorexia nervosa patients had significantly less extremity fat but a similar percentage of trunk fat relative to the healthy control subjects. Furthermore, we showed that spontaneous weight gain in the women with anorexia nervosa was associated with significant central fat accumulation relative to the extremities. The accumulation of central fat did not appear to be prevented by the concurrent administration of estrogen.

Many studies investigated body composition in anorexia nervosa patients. Using DXA and dual-photon absorptiometry, respectively, Mazess et al (12) and Iketani et al (4) showed that fat mass, but not lean mass, was significantly lower in the anorexia nervosa patients than in the control subjects. In contrast, in the present study, lean body mass and fat mass were significantly lower in the anorexia nervosa patients than in the age-matched control subjects. Furthermore, our data showed that the percentage of trunk fat was not significantly different between anorexia nervosa patients and control subjects but that the percentage of extremity fat was significantly lower in the

### TABLE 1

Baseline clinical characteristics of patients with anorexia nervosa who were eligible for study

<table>
<thead>
<tr>
<th>Value</th>
<th>AN patients, n = 20</th>
<th>AN patients, n = 20</th>
<th>AN patients, n = 20</th>
<th>AN patients, n = 20</th>
<th>AN patients, n = 20</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>26.6 ± 1.2</td>
<td>26.6 ± 1.2</td>
<td>26.6 ± 1.2</td>
<td>26.6 ± 1.2</td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>16.1 ± 0.3</td>
<td>16.1 ± 0.3</td>
<td>16.1 ± 0.3</td>
<td>16.1 ± 0.3</td>
<td></td>
</tr>
<tr>
<td>IBW (%)</td>
<td>74.4 ± 1.4</td>
<td>74.4 ± 1.4</td>
<td>74.4 ± 1.4</td>
<td>74.4 ± 1.4</td>
<td></td>
</tr>
<tr>
<td>Fat mass (kg)</td>
<td>8.0 ± 0.8</td>
<td>8.0 ± 0.8</td>
<td>8.0 ± 0.8</td>
<td>8.0 ± 0.8</td>
<td></td>
</tr>
<tr>
<td>Total fat mass (%)</td>
<td>18.2 ± 1.4</td>
<td>18.2 ± 1.4</td>
<td>18.2 ± 1.4</td>
<td>18.2 ± 1.4</td>
<td></td>
</tr>
<tr>
<td>Extremity fat (%)</td>
<td>55.6 ± 1.3</td>
<td>55.6 ± 1.3</td>
<td>55.6 ± 1.3</td>
<td>55.6 ± 1.3</td>
<td></td>
</tr>
<tr>
<td>Trunk fat (%)</td>
<td>32.9 ± 1.1</td>
<td>32.9 ± 1.1</td>
<td>32.9 ± 1.1</td>
<td>32.9 ± 1.1</td>
<td></td>
</tr>
<tr>
<td>%Trunk fat:% extremity fat</td>
<td>0.56 ± 0.02</td>
<td>0.56 ± 0.02</td>
<td>0.56 ± 0.02</td>
<td>0.56 ± 0.02</td>
<td></td>
</tr>
</tbody>
</table>

$\bar{x} \pm$ SEM; n = 27. IBW, ideal body weight.

### TABLE 2

Baseline characteristics of subjects who gained weight, changes with weight gain, and comparison with data from control subjects

<table>
<thead>
<tr>
<th></th>
<th>Control subjects, n = 20</th>
<th>AN patients, baseline, n = 20</th>
<th>AN patients, 9 mo, n = 20</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>25.4 ± 0.5*</td>
<td>27.0 ± 1.3</td>
<td>17.5 ± 0.4</td>
<td>0.267</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>21.0 ± 0.4</td>
<td>16.1 ± 0.3</td>
<td>80.9 ± 1.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IBW (%)</td>
<td>96.8 ± 1.5</td>
<td>74.2 ± 1.5</td>
<td>34.5 ± 0.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total body mass (kg)</td>
<td>56.6 ± 1.4</td>
<td>42.6 ± 1.1</td>
<td>40.3 ± 0.5</td>
<td>0.166</td>
</tr>
<tr>
<td>LBM (kg)</td>
<td>39.3 ± 1.0</td>
<td>33.2 ± 0.9</td>
<td>34.5 ± 0.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Extremity LBM (%)</td>
<td>42.2 ± 0.4</td>
<td>41.2 ± 0.4</td>
<td>51.6 ± 0.4</td>
<td>0.999</td>
</tr>
<tr>
<td>Trunk LBM (%)</td>
<td>50.7 ± 0.4</td>
<td>50.9 ± 0.4</td>
<td>10.7 ± 0.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fat mass (kg)</td>
<td>15.0 ± 0.6</td>
<td>7.8 ± 0.7</td>
<td>11.3 ± 0.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total fat mass (%)</td>
<td>26.4 ± 0.8</td>
<td>18.1 ± 1.6</td>
<td>22.5 ± 1.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Extremity fat (%)</td>
<td>60.9 ± 0.9</td>
<td>56.1 ± 1.6</td>
<td>55.4 ± 1.3</td>
<td>0.020</td>
</tr>
<tr>
<td>Trunk fat (%)</td>
<td>33.7 ± 0.9</td>
<td>32.4 ± 1.3</td>
<td>36.5 ± 1.0</td>
<td>0.808</td>
</tr>
<tr>
<td>%Trunk fat:% extremity fat</td>
<td>0.56 ± 0.02</td>
<td>0.59 ± 0.03</td>
<td>0.67 ± 0.03</td>
<td>0.886</td>
</tr>
</tbody>
</table>

1IBW, ideal body weight; LBM, lean body mass.

2By $t$ test with Bonferroni adjustment.

3Time trend analysis of baseline and 6- and 9-mo values.

4$x \pm$ SEM.
anorexia nervosa patients than in the control subjects. Taken together, these data suggest a relatively greater loss of fat in the extremities and therefore a more central fat distribution in low-weight women with anorexia nervosa.

Subjects were prospectively studied during outpatient weight gain and showed a significant increase in trunk fat relative to extremity fat. Subjects gained 4.9 kg weight to attain an average BMI of 17.5 ± 0.4. Only one subject achieved a BMI > 20.0. In contrast with previously published studies, weight gain in the present study was spontaneous and not the result of an intensive inpatient or partial inpatient refeeding program. Orphanidou et al (3) previously showed that weight gain was 78% fat mass and 21% lean mass in patients with anorexia nervosa. In the present study, we also showed a relatively greater increase in fat mass than in lean mass (68% of the weight gained was fat mass and 32% was lean mass). However, in contrast with the study of Orphanidou et al, we showed a significant increase in the ratio of trunk fat to extremity fat with spontaneous weight gain. Similarly, Iketani et al (4) showed that trunk fat increased in response to an intensive inpatient feeding program. We did not perform abdominal computed tomography scans in our subjects and, therefore, did not know the composition or location (ie, subcutaneous or visceral) of the excess trunk fat. In a previous study, Zamboni et al (5) showed a highly significant increase in total abdominal fat in response to weight gain, consistent with the results of the present study. Further studies are necessary to characterize the composition of intraabdominal fat with weight recovery in anorexia nervosa.

How do the changes in fat redistribution in low-weight women with anorexia nervosa shown in this study compare with the changes seen in healthy subjects undergoing weight gain? Hainer et al (13) studied 42 obese women and showed that fat redistribution shifted toward a gynoid pattern (decreased abdominal fat) with weight regain after significant weight loss. In contrast, Wadden et al (14) showed no significant difference in follow-up waist-to-hip ratios in women who lost and gained > 18 kg weight. Bonithon-Kopp et al (15) showed a positive association between change in BMI and change in waist-to-hip ratio in a longitudinal study of > 200 French women. However, the association was significant only for women with an android habitus at baseline. Women with a more gynoid body habitus at baseline showed no increase in waist-to-hip ratios with weight gain. Taken together, these data suggest that weight gain after weight loss is not consistently associated with fat redistribution in obese patients, whereas generalized weight gain in normal-weight patients is associated with increased trunk fat, particularly in predisposed subjects with increased baseline trunk fat. In contrast, we found a highly significant inverse association between the percentage of trunk fat at baseline and the change in the percentage of trunk fat, such that subjects with the lowest percentage of trunk fat gained the most trunk fat with weight gain. These data contrast with the more typical pattern seen in healthy female subjects, in whom an increase in trunk adiposity with weight gain was positively associated with baseline trunk fat.

The mechanism by which patients with anorexia nervosa accumulate abdominal fat relative to extremity fat during weight gain is unknown. One potential mechanism suggested by Iketani et al (4) is that weight gain in the initial phase of weight recovery in anorexia nervosa patients occurs in the context of relative estrogen deficiency, which may contribute to changes in fat distribution. Many studies suggest that estrogen administration affects regional and whole-body composition in estrogen-deficient women. For example, Haarbo et al (16) showed that a combination of estrogen and progestin prevented the accumulation of abdominal fat in early menopause. Similarly, Espeland et al (17) showed that conjugated equine estrogen and progestin led to significantly smaller increases in hip girth and less overall weight gain in postmenopausal women. Similarly, we hypothesized that administration of estrogen to premenopausal estrogen-deficient women with anorexia nervosa would protect against the accumulation of central fat during weight gain; however, we

![FIGURE 2.](https://example.com/figure2.png)

**FIGURE 2.** Correlation between the change in the percentage of trunk fat and the percentage of trunk fat at baseline in anorexia subjects (n = 20) during weight gain.

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**TABLE 3**

Comparison of baseline values and change over 9 mo of follow-up by estrogen treatment status

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Change over 9 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estrogen (n = 10)</td>
<td>No estrogen (n = 10)</td>
</tr>
<tr>
<td>Age (y)</td>
<td>27.6 ± 1.9</td>
<td>26.4 ± 1.9</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>16.4 ± 0.5</td>
<td>15.7 ± 0.4</td>
</tr>
<tr>
<td>Fat mass (kg)</td>
<td>7.8 ± 1.2</td>
<td>7.8 ± 0.9</td>
</tr>
<tr>
<td>Total fat mass (%)</td>
<td>17.1 ± 2.6</td>
<td>19.2 ± 1.9</td>
</tr>
<tr>
<td>Extremity fat (%)</td>
<td>54.0 ± 2.3</td>
<td>58.2 ± 1.9</td>
</tr>
<tr>
<td>Trunk fat (%)</td>
<td>33.0 ± 1.7</td>
<td>31.7 ± 2.1</td>
</tr>
<tr>
<td>%Trunk fat: % extremity fat</td>
<td>0.62 ± 0.04</td>
<td>0.56 ± 0.05</td>
</tr>
</tbody>
</table>

*1 By t test.
2 By one-way ANOVA.
3 ± SEM.
observed no protective effect of estrogen in this regard. The subjects in the present study were premenopausal and received a dose of estrogen equal to 35 μg ethinyl estradiol. In prior studies, the administration of similar doses of estrogen to premenopausal women was not associated with either a weight gain or changes in anthropometric measures (18). Similarly, our data suggest that factors other than estrogen deficiency contribute to central fat accumulation with weight gain in anorexia nervosa. However, only a limited number of patients were investigated and further studies are necessary before definitive conclusions can be drawn regarding the effects of estrogen on body composition during weight recovery in anorexia nervosa.

Hypercortisolemia is another potential mechanism contributing to trunk fat accumulation with weight gain in anorexia nervosa. Activation of the hypothalamic-pituitary-adrenal axis is well known to occur in anorexia nervosa, most likely secondary to increased secretion of hypothalamic corticotropin-releasing factor (19–21). Indeed, 20% of the patients in this study had increased urinary cortisol excretion, consistent with prior studies in this population. Of note, trunk fat accumulation was most severe in those patients with the greatest increases in urinary free cortisol concentrations. To our knowledge, our study is the first to show a relation between central fat accumulation and cortisol concentrations in anorexia nervosa. Although patients with anorexia nervosa do not have the classic stigmata of Cushing syndrome, relatively increased cortisol secretion may contribute to abnormal partitioning of substrate with weight gain, resulting in central fat accumulation. It is possible that with further weight gain and disease recovery, hypothalamic-pituitary-adrenal activity decreases, allowing a redistribution of accumulated central fat over time. Gold et al (19) previously showed persistent abnormalities in hypothalamic-pituitary-adrenal axis function 4 wk after weight recovery, which resolved within 6 mo of achievement of normal weight. Therefore, initial weight gain in the setting of hypercortisolemia may predispose anorexia nervosa patients toward greater central fat accumulation. We do not have longitudinal data in this regard, and our data do not prove causality with respect to cortisol and central fat accumulation. Furthermore, it is most likely that hypercortisolemia is but one of many factors that tend to contribute to central fat accumulation with weight gain in this population. Our data suggest the need for further studies to investigate this hypothesis as a potential mechanism of central fat accumulation with weight gain in anorexia nervosa and other conditions of severe low weight associated with stress activation of the hypothalamic-pituitary-adrenal axis.

In the present study, we showed significant central fat accumulation with spontaneous weight gain in women with anorexia nervosa. The gain in central fat occurred even though weight recovery was incomplete and the subjects were still at a very low weight. The weight gain was associated with increased cortisol excretion in the patients with anorexia nervosa. Of note, the gain in central fat was an inverse function of the degree of central fat at baseline. In contrast with estrogen administration in other settings, estrogen administration to women with anorexia nervosa did not appear to prevent the gain in central fat with weight gain. These data suggest that recovery from anorexia nervosa results in abnormal fat redistribution. The mechanisms and long-term cardiovascular complications associated with central fat accumulation in this population need to be investigated further.

We thank the nursing and dietary staffs of the Massachusetts General Hospital General Clinical Research Center for their dedicated patient care and particularly Jane Hubbard and Ellen Anderson for help in the assessment of the nutritional status of the subjects.

REFERENCES