Effect of short-term fasting on lipid kinetics in lean and obese women

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Effect of short-term fasting on lipid kinetics in lean and obese women. Am. J. Physiol. 276 (Endocrinol. Metab. 39): E278–E284, 1999.—We evaluated whole body and regional adipose tissue lipid kinetics and norepinephrine (NE) spillover during brief fasting in six lean [body mass index (BMI) 21 ± 1 kg/m²] and six upper-body obese (UBO; BMI 36 ± 1 kg/m²) women. At 14 h of fasting, abdominal adipose tissue glycerol and free fatty acid (FFA) release rates were lower (P = 0.07), but whole body glycerol and FFA rates of appearance (Rₐ) were greater (P < 0.05) in obese than in lean subjects. At 22 h of fasting, glycerol and FFA Rₐ increased less in obese (19.8 ± 7.0 and 87.1 ± 30.3 µmol/min, respectively) than in lean (44.2 ± 6.6 and 137.4 ± 30.4 µmol/min, respectively; P < 0.05) women. The percent increase in glycerol Rₐ correlated closely with the percent decline in plasma insulin (r² = 0.85; P < 0.05). Whole body NE spillover declined in lean (P < 0.05) but not obese subjects with continued fasting, whereas regional adipose tissue NE spillover did not change in either group. We conclude that, compared with lean women, in UBO women 1) basal adipose tissue lipolysis is lower, but whole body lipid kinetics is higher because of their greater fat mass; 2) the increase in lipolysis during fasting is blunted because of an attenuated decline in circulating insulin; and 3) downregulation of whole body sympathetic nervous system activity is impaired during fasting.

ADIPOSE TISSUE triglycerides are the body’s major source of fuel during periods of food deprivation. Therefore, increased mobilization of adipose tissue triglycerides is an important adaptive response to fasting. In lean adults, whole body lipolytic rates double during a 3-day fast (19, 40), and most of this increase occurs between 12 and 24 h of fasting (19). However, the increase in whole body lipolysis during 3 days of fasting is blunted in severely obese subjects (40). The mechanism(s) responsible for the differences in the lipolytic response to fasting in lean and obese subjects is not known but must be related to alterations in the factors that regulate lipolysis.

Insulin and catecholamines are the two major hormones that regulate lipolytic activity in humans. During fasting, a decline in plasma insulin concentration (19, 31) and an increase in adipose tissue resistance to the antilipolytic effect of insulin (14) enhance lipolysis. In addition, increased adrenal medullary catecholamine secretion (27) and increased adipose tissue lipolytic sensitivity to catecholamines (40) contribute to an increase in β-adrenergic-mediated lipolysis (17). Although fasting causes a decrease in whole body sympathetic nervous system (SNS) activity in lean adults (43), the effect of fasting on adipose tissue SNS activity is unknown. Heterogeneity in the SNS response of different tissues to fasting could be advantageous by decreasing whole body SNS activity to conserve energy (43) and increasing adipose tissue SNS activity to enhance endogenous fuel mobilization.

In the present study, we evaluated whole body and abdominal subcutaneous adipose tissue lipolytic rates, and the major factors that regulate lipolysis, in vivo during short-term fasting in lean and obese women. Both stable and radioactive isotopes were infused to evaluate lipid and norepinephrine (NE) kinetics. Subjects were studied at 14 and 22 h of fasting because maximal changes in fasting-induced lipolysis occur during this period (19). The obese group contained only women with upper-body obesity (UBO) because of the increase in basal lipolytic rates observed in this phenotype (24). We hypothesized that the increase in lipolysis that occurs during fasting is blunted in obese compared with lean women because of differences in circulating insulin and adipose tissue SNS activity.

METHODS

Subjects. Six women with UBO (>40% body wt as fat; waist-to-hip circumference ratio >0.85, and waist circumference >100 cm; 38 ± 3 yr old) and six lean women (<30% body wt as fat; 28 ± 2 yr old) participated in this study (Table 1). Although all women were premenopausal, the differences in age between lean and obese women were statistically significant (P < 0.05). The obese and lean subjects were matched for fat-free mass. Fat mass and fat-free mass were determined by dual energy X-ray absorptiometry (QDR 1000/W; Hologic, Waltham, MA). All subjects were considered to be in good health after a comprehensive medical examination, which included a history and physical examination, blood tests, and an electrocardiogram; obese subjects had normal glucose tolerance based on a 2-h oral glucose tolerance test. No subjects were taking any medications, and all were weight stable for at least 2 mo before the study, which was performed within the first 2 wk of the follicular phase of their menstrual cycle. Written informed consent was obtained before participating in this study, which was approved by the Institutional Review Board and the General Clinical Research Center of Washington University School of Medicine.
Table 1. Subject characteristics

<table>
<thead>
<tr>
<th></th>
<th>Lean</th>
<th>Obese</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight, kg</td>
<td>58.4 ± 2.5</td>
<td>96.2 ± 1.6</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>21.2 ± 0.6</td>
<td>36.4 ± 0.4</td>
</tr>
<tr>
<td>Total fat mass, kg</td>
<td>14.4 ± 1.4</td>
<td>50.3 ± 1.8</td>
</tr>
<tr>
<td>Body fat, %</td>
<td>24.6 ± 1.9</td>
<td>52.3 ± 1.7</td>
</tr>
<tr>
<td>Fat-free mass, kg</td>
<td>41.7 ± 1.9</td>
<td>43.5 ± 1.8</td>
</tr>
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</table>

Values are means ± SE.

Experimental procedure. Subjects were admitted to the General Clinical Research Center at Washington University School of Medicine in the evening before the infusion study. At 1800, subjects ingested a standard meal containing 12 kcal/kg body wt for lean subjects and 12 kcal/kg adjusted body wt for obese subjects (adjusted body wt = ideal body wt + [(actual body wt − ideal body wt) × (0.25)]. Therefore, this meal contained a total of ~700 and 800 kcal for the lean and obese women, respectively. Carbohydrate, fat, and protein represented 55, 30, and 15%, respectively, of total energy intake. At 2000, subjects ingested a defined liquid formula snack containing 250 kcal, 40 g carbohydrate, 6.1 g fat, and 8.8 g protein (Ensure, Ross Laboratories, Columbus, OH). After this snack, all subjects fasted until completion of the study the following day.

The following morning, 20-gauge catheters were inserted in a forearm vein for isotope infusion and in a radial artery for arterial blood sampling. A 22-gauge catheter (Hydrocath; Viggo-Spectramed, Oxnard, CA) was placed in an abdominal vein draining abdominal subcutaneous adipose tissue by using the Seldinger technique (4). The catheter was positioned so that the tip was superior to the inguinal ligament as judged by surface anatomy.

An overview of the infusion study protocol is shown in Fig. 1. At 0800 (12 h of fasting), a primed (1.5 µmol/kg), constant (0.10 µmol·kg⁻¹·min⁻¹) infusion of [1,2,3,3-²H]glycerol [99% atom percent excess (APE); Cambridge Isotopes, Andover, MA] dissolved in 0.9% saline was started and continued for 2 h using a calibrated syringe pump (Harvard Apparatus, Natick, MA). At 0830, a constant infusion (0.04 µmol·kg⁻¹·min⁻¹) of [2,2-²H]palmitate (98% APE; Cambridge Isotopes) bound to human albumin was started and continued for 90 min. At 0930, a constant infusion (10 nCi·kg⁻¹·min⁻¹) of levo-[ring-2,5,6-³H]NE (New England Nuclear, Boston, MA) was started and continued for 30 min. An arterial blood sample was obtained before isotope infusion to determine background tracer-to-tracee ratios and specific activity. Blood samples were obtained from artery and abdominal vein simultaneously every 5 min (four samples) between 0945 and 1000 (13 h 45 min and 14 h of fasting) to determine plasma hormone concentrations, plasma substrate concentrations, tracer-to-tracee ratios of glycerol and FFA, and NE specific activity.

All isotope infusions were stopped after obtaining the last blood sample at 14 h of fasting, and catheters were kept patent by infusing 0.9% saline at 25 ml/h. Subjects remained in bed for an additional 8 h, and the infusion study protocol was repeated between 1600 and 1800 (20 and 22 h of fasting; Fig. 1).

Subcutaneous abdominal adipose tissue blood flow (ATBF) was measured by the¹³³Xe clearance technique (20). Between 0830 and 0845, −100 µCi of ¹³³Xe dissolved in 0.15 ml of normal saline were slowly injected over 60 s in subcutaneous adipose tissue, 3 cm lateral to the umbilicus. A cesium iodide detector (Oakfield Instruments LTD, Eynsham, UK) was placed directly over the site of injection and was secured to the skin by tape. The decline in ¹³³Xe was determined by collecting 10-s counts (30) continuously for 15 min between 0945 and 1000 (13 h 45 min and 14 h of fasting) and again between 1745 and 1800 (21 h 45 min and 22 h of fasting).

Analytical procedures. Plasma insulin (8) and glucagon (9) concentrations were measured by radioimmunoassay. Plasma catecholamine concentrations were determined by a radioenzymatic method (32). Plasma fatty acid concentrations were determined by gas chromatography (25).

Glycerol and palmitate tracer-to-tracer ratios in plasma were determined by gas chromatography-mass spectrometry using an MSD 5971 system (Hewlett-Packard, Palo Alto, CA) with a capillary column. An internal standard ([2-¹³C]glycerol) was added to each plasma sample to determine glycerol concentration. Acetone was used to precipitate plasma proteins, and hexane was used to extract plasma lipids. The aqueous phase was dried by speed vac centrifugation (Savant Instruments, Farmingdale, NY). Heptafluorobutyric anhydride was used to form a heptafluorobutyric derivative of glycerol, and ions were produced by electron-impact ionization. Glycerol tracer-to-tracee ratios were determined by selectively monitoring ions at mass-to-charge ratios 253, 254, and 257. Free fatty acids (FFA) were isolated from plasma and converted to their methyl esters. Ions at mass-to-charge ratios 270.2 and 272.2 produced by electron-impact ionization were selectively monitored.

Calculations. Physiological and isotopic steady states were present during the last 15 min of isotope infusion at 14 and 22 h of fasting, so Steele's equation for steady-state conditions (36) was used to calculate whole body glycerol, FFA, and NE kinetics.

Subcutaneous ATBF was calculated from ¹³³Xe clearance (20)

\[ \text{ATBF (ml·100 g adipose tissue}^{-1} \cdot \text{min}^{-1}) = -k \cdot \lambda \cdot 100 \]

where \( k \) is the rate constant of the ¹³³Xe monoeponential washout curve and \( \lambda \) is the adipose tissue-to-blood partition coefficient for ¹³³Xe. The values for \( k \) were determined experimentally as \( \ln (y_2) - \ln (y_1)/15 \), where \( y_1 \) and \( y_2 \) were the counting rates at times 0 and 15 min, respectively. The value for \( \lambda \) was assumed to be 10 ml/g (41) for both lean and obese subjects (13). Subcutaneous adipose tissue plasma flow (ATPF) was calculated as \( \text{ATBF} \cdot (1\text{-hematocrit}) \).

Net regional release of glycerol and FFA from subcutaneous abdominal adipose tissue into plasma was quantified by calculating arteriovenous concentration balance

\[ \text{Net regional release} = \left( \text{[substrate]}_a - \text{[substrate]}_v \right) \cdot (\text{ATBF or ATPF}) \]
where \([substrate]_a\) and \([substrate]_v\) are either plasma glycerol or FFA arterial and abdominal venous concentrations, respectively. Glycerol release was calculated using ATBF, whereas FFA release was calculated using ATPF because of the absence of FFA in red blood cells.

Adipose tissue NE spillover rate was calculated as

\[
\frac{\left(\left[NE\right]_a - \left[NE\right]_v \right) + \left(\left[NE\right]_a \cdot F_{exNE}\right)}{\left[NE\right]_a \cdot SA_a - \left[NE\right]_a \cdot SA_v}
\]

where \(SA_a\) and \(SA_v\) are NE specific activities in arterial and venous samples, respectively.

Statistical analysis. Student’s t-test for paired samples was used to test the significance of differences between 14 and 22 h fasting data within lean and obese groups. Student’s t-test for independent samples was used to test for significant differences between lean and obese subjects. One-tailed Student’s t-test was used for a priori comparisons. Pearson product-moment correlation coefficient was computed to determine the relationship between specific variables. A value of \(P \leq 0.05\) was considered to be statistically significant. All data are expressed as means ± SE.

RESULTS

Plasma hormone concentrations. At 14 h of fasting, plasma insulin concentration was greater (\(P < 0.05\)) in obese than in lean subjects (Table 2). By 22 h of fasting, plasma insulin concentration declined significantly (\(P < 0.05\)) in both groups, but the percent decline was less in obese than in lean women (20 ± 3 and 32 ± 5%, respectively; \(P < 0.05\)), and mean plasma insulin concentration remained more than twofold greater in the obese than in the lean group. Plasma glucagon concentrations were similar in both groups and increased slightly with continued fasting. At 14 h of fasting, mean plasma epinephrine concentration in obese women was about one-half as great as that observed in lean women (\(P < 0.05\)), whereas plasma NE concentrations were similar in both groups (Table 2). Continued fasting did not cause a significant change in plasma epinephrine or NE concentrations in either the lean or obese subjects.

Plasma substrate concentrations. Abdominal vein plasma glycerol and FFA concentrations were always greater than arterial concentrations in lean and obese subjects, indicating net glycerol and FFA release from subcutaneous abdominal adipose tissue at both 14 and

Table 2. Arterial plasma hormone concentrations

<table>
<thead>
<tr>
<th></th>
<th>Lean 14-h Fast</th>
<th>Lean 22-h Fast</th>
<th>Obese 14-h Fast</th>
<th>Obese 22-h Fast</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin, µU/ml</td>
<td>6 ± 1</td>
<td>4 ± 1†</td>
<td>14 ± 1*</td>
<td>11 ± 0.4*</td>
</tr>
<tr>
<td>Glucagon, ng/ml</td>
<td>59 ± 5</td>
<td>73 ± 9</td>
<td>62 ± 4</td>
<td>76 ± 7†</td>
</tr>
<tr>
<td>Epinephrine, pg/ml</td>
<td>49 ± 7</td>
<td>56 ± 5</td>
<td>27 ± 4*</td>
<td>34 ± 5*</td>
</tr>
<tr>
<td>Norepinephrine, pg/ml</td>
<td>157 ± 13</td>
<td>142 ± 12</td>
<td>186 ± 30</td>
<td>196 ± 26</td>
</tr>
</tbody>
</table>

Values are means ± SE. *Significantly different from lean values, \(P < 0.05\). †Significantly different from 14-h fast values, \(P < 0.05\).

Fig. 2. Whole body glycerol rate of appearance (Ra; A) and free fatty acid (FFA) Ra (B) at 14 h (open bars) and 22 h (hatched bars) of fasting in lean and obese women. *Significantly different from lean subjects, \(P < 0.05\). †Significantly different from 14-h values, \(P < 0.05\). Values are means ± SE.

Table 3. Artery and abdominal vein plasma glycerol and FFA concentrations

<table>
<thead>
<tr>
<th></th>
<th>Lean 14-h Fast</th>
<th>Lean 22-h Fast</th>
<th>Obese 14-h Fast</th>
<th>Obese 22-h Fast</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycerol</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Artery</td>
<td>73 ± 5</td>
<td>99 ± 7†</td>
<td>113 ± 13</td>
<td>127 ± 10†</td>
</tr>
<tr>
<td>Abdominal vein</td>
<td>271 ± 32†</td>
<td>347 ± 37†</td>
<td>339 ± 41†</td>
<td>319 ± 35‡</td>
</tr>
<tr>
<td>FFA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Artery</td>
<td>628 ± 43</td>
<td>875 ± 49†</td>
<td>605 ± 71</td>
<td>789 ± 47†</td>
</tr>
<tr>
<td>Abdominal vein</td>
<td>1,198 ± 97‡</td>
<td>1,661 ± 90†</td>
<td>1,247 ± 145‡</td>
<td>1,410 ± 97†</td>
</tr>
</tbody>
</table>

Values are means ± SE. Units are µmol/l. FFA, free fatty acid. †Significantly different from 14-h fast values, \(P < 0.05\); ‡Significantly different from arterial plasma concentration, \(P < 0.05\).

22 h of fasting (Table 3). Arterial plasma glycerol and FFA concentrations increased significantly (\(P < 0.05\)) with continued fasting in both lean and obese subjects. ATBF. ATBF was >50% lower in obese compared with lean subjects (1.84 ± 0.18 and 4.29 ± 0.48 ml·100 g adipose tissue·1·min−1, respectively; \(P < 0.05\)) and did not change between 14 and 22 h of fasting in either lean or obese subjects.

Substrate kinetics. At 14 h of fasting, whole body glycerol rate of appearance (Ra), an index of whole body lipolysis, was greater in obese than lean women (201.4 ± 17.1 and 123.5 ± 12.3 µmol/min, respectively; \(P < 0.05\); Fig. 2). Whole body FFA Ra, an index of fatty acid availability in plasma, was also greater in obese
than lean women (526.8 ± 60.6 and 362.2 ± 41.2 µmol/min, respectively; P < 0.05; Fig. 2). However, glycerol and FFA kinetics normalized for body fat mass were ~60% lower in obese than in lean subjects (3.97 ± 0.33 vs. 9.29 ± 1.19 µmol glycerol·kg fat mass⁻¹·min⁻¹ and 10.4 ± 1.2 vs. 26.9 ± 4.5 µmol FFA·kg fat mass⁻¹·min⁻¹; P < 0.05). Continued fasting increased glycerol Ra and FFA Ra in both lean and obese groups (Fig. 2). However, the absolute increase in glycerol Ra and FFA Ra in obese subjects (19.8 ± 7.0 and 87.1 ± 30.3 µmol/min, respectively) was less than the increase observed in lean subjects (44.2 ± 6.6 and 137.4 ± 30.4 µmol/min, respectively; P < 0.05 for both glycerol and nonesterified fatty acid Ra). The percent increase in glycerol Ra correlated closely with the percent decline in plasma insulin concentration in both lean and obese subjects (r² = 0.85; P < 0.05; Fig. 3).

At 14 h of fasting, net regional glycerol and FFA release from abdominal subcutaneous adipose tissue in obese subjects were one-half the value observed in the lean group (Fig. 4), but the difference did not quite reach statistical significance (P = 0.07) because of the small number of subjects studied. Between 14 and 22 h, net regional glycerol and FFA release increased in lean (P < 0.05) but not obese subjects. Glycerol and FFA release was greater in lean than obese subjects at 22 h of fasting (P < 0.05; Fig. 4).

NE kinetics. Whole body NE spillover in the systemic circulation, a marker of SNS activity, was similar in both lean and obese groups at 14 h of fasting (Fig. 5). Fasting caused a significant decrease in NE spillover in lean but not obese subjects. Regional abdominal subcutaneous adipose tissue NE spillover, an index of regional adipose tissue SNS activity, was more than threefold greater in lean than obese subjects (0.91 ± 0.08 and 0.26 ± 0.06 nmol·100 g adipose tissue⁻¹·min⁻¹, respectively; P < 0.05). Regional adipose tissue NE spillover did not change with continued fasting in either lean or obese subjects (Fig. 5).

DISCUSSION

The mobilization of endogenous triglycerides stored in adipose tissue is important for survival during starvation. In lean men, most of the increase in whole body lipolytic rates that occur during starvation takes place within the first 24 h of fasting (19). The results of the present study demonstrate, for the first time, that the increase in lipolysis during early starvation (between 14 and 22 h of fasting) is blunted in women with UBO. However, basal (14-h fast) whole body lipolytic rates were greater in UBO than lean women and were similar to values observed in lean women after 22 h of fasting. Therefore, the attenuated increase in lipolysis during fasting in UBO women did not compromise fatty acid availability as a fuel in these subjects. In fact, the blunted lipolytic response in UBO women may be beneficial by preventing excessive and potentially harmful increases in plasma FFA concentrations (35, 38).

Our data suggest that the mechanism responsible for differences in the lipolytic response to fasting in lean and UBO women may be related to differences in their insulin response. Insulin is a potent inhibitor of lipolysis in both lean and obese persons (3). Therefore, an alteration in plasma insulin concentration represents an important adaptive response to fasting. The decline in plasma insulin observed during fasting is not simply
Values are means on adipose tissue and whole body SNS activity in lean and obese subjects. We used tracer methodology to measure NE spillover in the systemic circulation to provide an index of whole body SNS activity (23). Signal transmission within the SNS involves NE release from sympathetic postganglionic neurons. Most of the released NE is cleared locally by neuronal reuptake and effector cell metabolism while a portion spills over in the bloodstream. Therefore, NE spillover in the systemic circulation represents NE released from sympathetic neurons distributed throughout the body and NE secreted from the adrenal medullas. We combined arteriovenous balance and tracer methodology to determine regional adipose tissue NE spillover to provide an index of adipose tissue SNS activity. This approach eliminates any contribution of NE from the adrenal medullas.

Our results demonstrate that the SNS response to early fasting differs between lean and obese women. In lean women, whole body NE spillover declined, but adipose tissue NE spillover did not change between 14 and 22 h of fasting. This heterogeneity may be advantageous by decreasing SNS activity in lean tissue and thereby decreasing energy expenditure, while maintaining SNS activity in adipose tissue and thereby stimulating the mobilization of endogenous triglycerides. These results are consistent with previous studies that found whole body NE spillover decreased in lean subjects after 10 days of hypocaloric feeding (26) and cardiac muscle NE turnover decreased in rats fasted for 48 h (42). In contrast to the lean women, whole body NE spillover rates did not decrease in obese women during short-term fasting. These results extend those of Bazelmans et al. (1), who found that 10 days of hypocaloric feeding did not affect whole body NE spillover in obese subjects. Therefore, the normal decline in whole body SNS activity that occurs in response to energy deprivation in lean subjects is blunted in obese persons. However, adipose tissue SNS activity is maintained during early starvation in both lean and obese subjects.

Postabsorptive (14-h fast) regional adipose tissue lipolytic rates, expressed per 100 g of adipose tissue, was 50% lower in our obese than in our lean subjects. However, the rate of whole body lipolysis was >60% greater in the obese group because of their large amount of fat mass; total body fat was more than threefold greater in our obese than in our lean subjects. Excessive release of FFA in plasma in persons with UBO may be responsible for several metabolic diseases associated with obesity by impairing the ability of insulin to stimulate muscle glucose uptake (6) and suppress hepatic glucose production (6, 15), by increasing pancreatic insulin secretion (2) and by inhibiting hepatic insulin clearance (28). Furthermore, increased delivery of FFA to the liver can increase hepatic very low density lipoprotein production and plasma triglyceride and cholesterol concentrations (21). The downregulation of lipolysis per unit of fat mass in obese persons helps prevent the generation of even greater whole body lipolytic rates.

The marked differences that we observed in regional lipolytic rates between lean and obese women is incon-
consistent with the results of a previous study by Jansson et al. (11), who found the rate of glycerol release from abdominal subcutaneous adipose tissue was the same in both lean and obese subjects. It is unlikely that subcutaneous adipose tissue lipolytic rates were the same in our lean and obese subjects for several reasons. First, the greater amount of body fat in our obese subjects would have caused more than a threefold difference in whole body lipolytic rates between the two groups. Instead, whole body lipolytic rates were only 60% greater in our obese than in our lean group. Second, we also found that regional glycerol production measured by tracer balance methodology (39) gave the same results as the arteriovenous concentration balance approach (data not shown). Third, the differences we found in regional glycerol kinetics between lean and obese subjects were concordant with the differences we found in FFA kinetics. The reason for the discrepancy between the Jansson et al. (11) study and ours may be related to differences in gender or methodology. Jansson et al. studied lean and UBO men and measured regional lipolytic activity by using microdialysis probes to sample interstitial adipose tissue glyceral. This latter approach requires an extrapolation of interstitial glyceral concentration to venous values, which may generate errors in the estimation of regional glyceral kinetics. In fact, direct comparisons of the two techniques in the same subjects have found that regional glyceral output measured by arteriovenous balance using abdominal vein samples was double the values obtained by arteriovenous balance using microdialysis samples (34, 37).

Although we found regional adipose tissue lipolysis in our obese subjects was one-half the value observed in our lean subjects, in vivo lipolytic rates per fat cell were probably similar in both groups. Fat cells from obese persons are larger and contain more lipid than fat cells from lean persons (11, 29). Subcutaneous abdominal adipocytes obtained from UBO women with similar body mass index and waist-to-hip ratio as our subjects have two times the cell volume as adipocytes obtained from lean women (29). Therefore, our regional measurement of glycerol and FFA kinetics, which was expressed per 100 g of adipose tissue, represented glyceral and FFA release from approximately one-half as many fat cells in the obese than in the lean group. Thus the rates of glyceral and FFA release per fat cell were similar in both groups. In contrast, studies performed in vitro have demonstrated that basal lipolytic rates in isolated adipocytes obtained from UBO women were threefold greater than lipolytic rates in cells obtained from lean women (29). However, this discrepancy is probably related to differences between in vivo and in vitro studies. Other investigators have also found that lipolysis measured in isolated adipocytes do not agree with in vivo data from the same subjects (22). The differences in lipolytic activity observed between in vitro and in vivo studies may be related to alterations in local adipocyte environment caused by removal of tissue and plasma factors, such as insulin, epinephrine, and adipose tissue SNS activity.

ATBF, expressed per 100 g of adipose tissue, in our obese subjects was less than one-half the rate measured in the lean group. The calculations we used in estimating blood flow assumed that the partition coefficient for $^{133}$Xe is similar in both lean and obese women (13). Although the lower rate of blood flow in subcutaneous adipose tissue in obese compared with lean subjects has been observed previously (11), the mechanism for this phenomenon is not clear but may be a simple function of the anatomical relationship between capillaries and adipocytes. Each fat cell is located in proximity to a capillary (5). Blood flow per fat cell remains constant, independent of fat cell size, so that blood flow per 100 g of adipose tissue decreases with increasing cell volume (12). It is unlikely that decreased local SNS was responsible for the lower rate of adipose tissue blood flow even though subcutaneous fat houses a rich network of blood vessels that contain vascular β-adrenergic receptors (10). Simonsen et al. (33) found that the β-adrenergic blockade prevented the normal meal-induced increase in ATBF but did not affect basal blood flow values. Therefore, adipose tissue SNS innervation may be responsible for the increase in ATBF after carbohydrate ingestion but does not appear to be an important regulator of basal, postabsorptive ATBF.

In summary, basal lipolytic rates per unit of fat mass are lower in UBO women than in lean women, but whole body lipolytic rates are greater in obese women because of their increased adiposity. During short-term fasting, whole body lipolytic rates increase in both lean and obese women, but the increase is blunted in the obese group. This downregulation of adipose tissue lipolysis in UBO women during fasting may be advantageous by preventing excessive and potentially harmful increases in plasma FFA. Our data suggest that the attenuated lipolytic response to fasting in obese women is related to a blunted decline in circulating insulin. Altered adipose tissue SNS activity during fasting does not contribute to the increase in lipolysis in either lean or obese women. Whole body SNS activity decreased in lean but did not change in obese women, whereas adipose tissue SNS activity remained the same during fasting in both groups.

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