Meal fatty acid uptake in adipose tissue: gender effects in nonobese humans

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Romanski, Susan A., Rita M. Nelson, and Michael D. Jensen. Meal fatty acid uptake in adipose tissue: gender effects in nonobese humans. Am J Physiol Endocrinol Metab 279: E455–E462, 2000.—We tested for gender differences in dietary fatty acid metabolism in 12 nonobese men and 12 nonobese women using the meal fatty acid tracer/adipose tissue biopsy study design. In addition to determining body composition, measurements of regional adipose tissue lipoprotein lipase activity, blood flow, and fat cell size were performed to place the meal fatty acid kinetic studies in perspective. Twenty-four hours after ingesting the test meal, the concentration of meal fatty acids was greater (P < 0.05) in abdominal subcutaneous than in thigh adipose tissue in both men (0.61 ± 0.12 vs. 0.45 ± 0.09 mg/g) and women (0.59 ± 0.10 vs. 0.43 ± 0.05) but was not different between men and women. A greater percentage of dietary fat was stored in subcutaneous adipose tissue in women than in men (38 ± 3 vs. 24 ± 3%, respectively, P < 0.05), and a greater portion of meal fatty acid disposal was unaccounted for in men. Significant gender differences in regional adipose tissue blood flow after meal ingestion were noted; the differences were in the direction that could support greater nutrient storage in lower body fat in women.

[^14C]triolein; body composition; visceral fat; adipose tissue blood flow

NORMAL-WEIGHT ADULT MEN and women have remarkably different body composition. Women have more body fat, a greater proportion of fat in their lower body, and much less visceral fat than men do at the same body mass index. The reasons for these differences in body fat distribution have not been clearly identified but are potentially important. If these same processes determine body fat distribution as obesity develops, understanding the factors regulating body fat distribution in men vs. women could help us understand upper-body vs. lower-body obesity. Regional differences in lipolysis (27) and/or triglyceride (TG) storage capacity (23) have been proposed as determining regional fat accumulation. In vitro studies of adipocytes obtained from different regions have suggested that both mechanisms may be operative (23, 27). We have looked for variations in regional lipolysis in vivo (10, 12, 21) but have been unable to document important gender differences in this regard. Thus studies of adipose tissue fatty acid uptake would seem appropriate.

The approach of Björntorp et al. (1) and Marin and colleagues (16–19) to study fatty acid uptake in human adipose tissue in vivo appears promising. The meal fatty acid tracer/adipose tissue biopsy technique involves administering a radiolabeled fatty acid tracer together with a fat-containing meal, followed some time later by adipose tissue biopsies from different regions to assess the relative efficiency of meal fatty acid uptake. Marin and co-workers (17, 19) reported that meal fatty acids are more concentrated in upper body subcutaneous than in lower body subcutaneous adipose tissue in women (19) and in men (17). Direct comparisons of meal fatty acid uptake in adipose tissue between men and women have not been made, however. Thus it is unknown whether the relative difference in the ability of adipose tissue to concentrate meal fatty acids is different between lower body and upper body adipose tissue in men and in women. Likewise, it is unknown whether women oxidize a different proportion of meal fatty acids than men, which could perhaps lead to greater net fat accumulation. The present studies were designed to address these issues and to examine whether there were physiological correlates of regional meal fat storage in nonobese men and women. We examined whether regional differences in fat cell size, lipoprotein lipase (LPL) activity, or adipose tissue blood flow were related to the regional meal fatty acid uptake.

METHODS AND MATERIALS

Subjects. Written, informed consent was obtained from 24 nonobese, healthy volunteers (12 males and 12 premenopausal females). The subjects were taking no medications, including oral contraceptives. All volunteers were weight stable (<1.0 kg weight variation) for at least 2 mo before the study. The women were studied in the follicular phase of their menstrual cycle. These are the same subjects and the same experiments described in the previous companion report (24).

Materials. L-[^14C]triolein (Du Pont NEN Research Products) and [3H]triolein (American Radiolabel Chemical, St. Louis, MO) were sonicated into a liquid meal. [133Xe (Syncor,
St. Paul, MN) was dissolved in sterile saline and was used to measure regional adipose tissue blood flow.

Assays and methods. Fat cell size was assessed using the approach of Di Girolamo et al. (3). Oxygen consumption and carbon dioxide expiration were measured by indirect calorimetry using a DeltaTrac Metabolic Cart (Yboria Linda, CA). Volunteers were acclimatized to the hood for the first 10 min of each 30-min measurement. The basal metabolic rate measurements were made at 0700, after a 12-h overnight fast, before the volunteer had arisen from bed. Urinary nitrogen was measured using an Analox GM7 Fast Enzymatic Metabolite Analyzer (Analox Instruments, Lunenburg, MA). Plasma glucose concentrations were measured with a Beckman glucose analyzer (Beckman Instruments, Fullerton, CA). Plasma insulin concentrations were measured using a chemiluminescence method with the Access Ultrasensitive Immunoenzymatic assay system (Beckman, Chaska, MN). A modified Pasteur pipette was used to aspirate the chylomicron layer that had been separated from 2.0 ml of fresh plasma by ultracentrifugation at 780,000 g/min in a 50.8 Ti rotor (Beckman Instruments, Spinco Division, Palo Alto, CA). The TG concentrations were measured on a small portion of the sample (9), and the remainder of the sample was subjected to a Dole extraction (4) to measure chylomicron TG radioactivity. Adipose tissue and meal lipids were extracted using standard (5) procedures, and the TG SA was measured as previously described (19). The meal aliquots were subjected to serial dilution to be able to compare the ratio of 3H to 14C at the same level of radioactivity in adipose tissue and meal.

Adipose tissue heparin-releasable LPL activity was measured using the approach of Nilsson-Ehle and Schott (22). Body fat and fat-free mass (FFM) was measured using dual-energy X-ray absorptiometry (DEXA; DPX-IQ; Lunar Radiation, Madison, WI; see Ref. 14). Thigh adipose tissue and muscle areas were measured using a single-slice computed tomography (CT) at the mid-thigh level; intra-abdominal and abdominal subcutaneous fat areas were measured at the L2–3 level by a single-slice CT scan (13). Total body water was measured with 2H2O (26). The triolein tracers were assayed for radiochemical purity by measuring the radioactivity in the TG and non-TG fractions by HPLC (2). To assess the proportion of radioactivity present in oleate, the TG fraction was subjected to alkaline hydrolysis followed by conversion to a phenacyl derivative and injection on a second HPLC (20). The non-TG fraction (nonesterified fatty acids) was also derivatized and assayed for purity by HPLC (20).

Protocol. The volunteers underwent all body composition measurements before the adipose tissue biopsy study. A complete blood count, chemistry group, and lipid profile were documented to be within normal limits before the study. All female volunteers had a negative pregnancy test before participating in the study. Subjects consumed all of their meals in the General Clinical Research Center (GCRC) for 1 wk before the study to ensure consistent macronutrient intake (50% carbohydrate, 35% fat, and 15% protein). They were instructed not to eat anything except what was provided for them through the study, and food intake was adjusted if necessary to maintain a stable weight. Each volunteer’s energy requirement was estimated using the Harris-Benedict formula (8) and usual daily activity. The macronutrient intake the week before the tracer study for the men and women, respectively, was as follows: energy intake 2,952 ± 64 and 2,114 ± 62 kcal/day; protein intake 115 ± 3 and 84 ± 3 g/day; carbohydrate intake 379 ± 9 and 271 ± 8 g/day (53 ± 3% simple carbohydrate); fat intake 118 ± 3 and 83 ± 3 g/day (37 ± 2% saturated fat).

The volunteers were admitted to the Mayo Clinic GCRC the evening before the study. The morning of the study after an overnight fast, a catheter was placed in a forearm vein and was used to collect blood samples. Before the administration of the experimental meal, baseline breath and urine samples were collected for measurement of 14CO2 (7) and 3H2O (11) specific activity (SA).

Approximately 90 min before the morning test meal, injections of 0.15 mCi of 133Xe were administered (15) in the abdominal subcutaneous and thigh subcutaneous adipose tissue beds. A 1-ml U-100 insulin syringe with a 25-gauge needle was used. The abdominal injection was given just lateral and inferior to the umbilicus at the site of the most abundant subcutaneous fat. The thigh injection was given in the anterior thigh at the junction of the upper one-third and the lower two-thirds of the distance between the hip and the knee. Each injection was given in the middle of the subcutaneous fat. The fluid was injected slowly (over 1 min), and the needle was not removed for an additional 30 s to prevent reflux of 133Xe along the needle track. A 16-gauge 2-mm collimated solid-state cadmium-magnesium endwindow (BMI, Watertown, MA) that has a 96% counting efficiency for 133Xe was positioned over each injection site and held in place with adhesive tape. A pulse height analyzer (Tennelec T246) was set to count only those pulses that corresponded to the energy level of 133Xe (81 keV) and to discriminate against background noise and scattered radiation outside the selected energy range (75–200 keV). A count rate meter (Tennelec T593) was used to average the number of counts over 1-s time intervals, and the results were recorded on a two-channel strip chart recorder (HP 7132A). Each channel recorded the counts from its respective injection site. Measurements were made from the time of the injection until 1 h after the midday meal to allow calculation of subcutaneous adipose tissue blood flow during fasting and after the morning and the midday meals.

At 0800, the volunteers consumed a meal providing 40% of their resting energy needs as determined by indirect calorimetry, providing 692 ± 22 and 509 ± 15 kcal for men and women, respectively. The meal consisted of a liquid formula (Ensure Plus, Ross Laboratories) containing 57% carbohydrate, 27% fat (16% saturated fat, 27% monounsaturated fat, 57% polyunsaturated fat), and 15% protein to which 20 µCi of L-[1-14C]triolein and 40 µCi of [3H]triolein had been added. The volunteers were also provided with solid food meals at 1300 and 1800 that provided the remainder of their usual daily energy intake and contained the same portion of nutrients as the diets provided during the week before the study. The volunteers remained seated or lying in bed during the first 8 h after consuming the test meal except as needed to void. After 8 h, the volunteers were allowed to walk around the room or the GCRC. Because the intravenous saline infusion was continued to maintain venous access, the physical activity of the volunteers was necessarily limited.

To determine the exact amount of L-[1-14C]triolein and [3H]triolein consumed, quadruplicate 50-µl samples of the meal were counted using dual-channel liquid scintillation counting. The meal was weighed to the nearest milligram. Aliquots of the meal were also saved for measurement of meal lipid 14C and 3H SA (see above).

After consuming the test meal, blood and breath samples were obtained hourly for 8 h, every 2 h for an additional 4 h, and then every 4 h until the next morning. The blood samples were analyzed for plasma chylomicron TG and nonchylomicron TG 2H and 14C SA, as well as for plasma glucose and insulin concentrations. Breath samples were collected as described above to measure expired 14CO2 SA. Indirect calo-
rimetry was performed hourly beginning at 0800 for 8 h and at the 10th hour with the volunteers lying quietly in bed. Urine was collected for 24 h after the test meal to assess $^3$H$_2$O losses and concentration as well as nitrogen excretion.

Twenty-four hours after the test meal consumption, adipose tissue biopsies were obtained using the sterile technique under local anesthesia. Biopsies were taken from the left and right abdominal subcutaneous, gluteal, and thigh regions. The lipid was extracted from the tissues, accurately weighed, and counted on the scintillation counter to <2% counting error. The adipose tissue TG ($^3$H and $^{14}$C; dpm/mg lipid) was calculated for each site. Adipose tissue LPL activity and fat cell size were measured on one side (either right or left) at each site. After the adipose tissue biopsies, the intravenous catheter was removed, and the volunteers ate breakfast and were dismissed.

Calculations. Meal fatty acid oxidation for the 24 h after the test meal was calculated using both the $^3$H and $^{14}$C tracers. The production of $^3$H$_2$O was calculated by multiplying the concentration of $^3$H$_2$O in body water (using a urine sample obtained 24 h after the test meal) by total body water as measured by the $^3$H$_2$O space and adding the $^3$H$_2$O lost in the urine over the 24 h. This value (total $^3$H$_2$O dpm produced) was divided by the total $[^3$H]triolein consumed to calculate the fraction of meal fatty acids oxidized in the first 24 h after the meal.

As noted in the companion report (24), two volunteers had previously participated in studies involving the infusion of $[^3$H]palmitate, which rendered their $^3$H adipose tissue data unusable. Because there was no $^3$H$_2$O in the baseline urine samples of these two volunteers, the $^3$H$_2$O generation values were used to calculate meal fatty acid oxidation.

The production of $^{14}$CO$_2$ was determined by multiplying the $^{14}$CO$_2$ SA by the CO$_2$ production rate, as measured by indirect calorimetry, at each time point. The nocturnal CO$_2$ production rate time points were not measured in this study, although the $^{14}$CO$_2$ SA was. To estimate the nocturnal CO$_2$ production rates at the nocturnal time points, we used data from a previous study (25) to develop a nonlinear model that predicts CO$_2$ production throughout the night using the 1800 and 0800 O$_2$ consumption and CO$_2$ production rates. This model predicted ~75% of the variance in CO$_2$ production rates of an independent sample. To calculate meal fatty acid oxidation using $[^{14}$C]triolein, the area under the $^{14}$CO$_2$ curve was divided by the amount of $[^{14}$C]triolein consumed.

To calculate adipose tissue blood flow (ATBF), the 10-min slope index was used according to the following equation

$$\text{ATBF (ml/100 g adipose tissue}^{-1} \text{min}^{-1}) = 2.3 \times l \times d \times 100$$

where 2.3 is the factor for converting common to natural logarithms, $l$ is the partition coefficient for adipose tissue, and $d$ is the numerical value of the slope in the semilog (base 10) system. The value used for the partition coefficient is 10 (15).

Oxygen consumption and CO$_2$ production (l/min) and urinary nitrogen excretion (g nitrogen/min) were used to calculate carbohydrate and fat oxidation rates (6). An area under the curve (trapezoidal rule) calculation was used to assess carbohydrate and fatty acid oxidation over the first 5 h after the experimental meal.

Meal fatty acid uptake in adipose tissue was calculated as follows. The adipose tissue TG SA (dpm/mg) was divided by the meal TG SA (dpm/mg) to predict the meal TG fatty acid uptake (mg meal TG/g adipose tissue TG). The average of values obtained using both the $^3$H and $^{14}$C tracers was used for these calculations except for the two volunteers who had previously received a $^3$H fatty tracer (see Ref. 24), in whom only the $^{14}$C values were considered. Visceral fat mass was predicted using the CT measures of intra-abdominal and subcutaneous adipose tissue combined with DEXA-measured abdominal fat as previously described (13). Upper body subcutaneous fat was taken as upper body fat (DEXA) minus visceral fat, and leg fat was measured using DEXA. The average of both sides of the site-specific concentration of meal TG per gram in adipose tissue TG was multiplied by the TG mass to estimate total meal TG uptake in the different adipose tissue depots, similar to the approach of Marin et al. (19).

Statistics. All values are presented as means ± SE. Comparisons of baseline characteristics between men and women were performed using a nonpaired $t$-test. Testing for differences between adipose tissue sites and between men and

### Table 1. Subject characteristics

<table>
<thead>
<tr>
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<th>Men (n = 12)</th>
<th>Women (n = 12)</th>
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</thead>
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<tr>
<td>Age, yr</td>
<td>30 ± 2</td>
<td>28 ± 2</td>
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<td>BMI, kg/m$^2$</td>
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<td>Weight, kg</td>
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<td>56.5 ± 2.0*</td>
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<td>Body fat, %</td>
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<td>28 ± 2*</td>
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<tr>
<td>Leg fat, kg</td>
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<td>6.37 ± 0.41</td>
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<td>138 ± 13*</td>
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<td>CT thigh muscle area, cm$^2$</td>
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<td>210 ± 8*</td>
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<td>CT visceral fat area, cm$^2$</td>
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<td>84 ± 4</td>
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<td>95 ± 3*</td>
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<tr>
<td>Thigh adipocyte diameter, $\mu$m</td>
<td>79 ± 4</td>
<td>96 ± 4*</td>
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</table>

Values are means ± SE; $n$, no. of subjects; BMI, body mass index. Body fat and leg fat were measured by dual-energy X-ray absorptiometry; CT thigh areas (both thighs) were measured using a single-slice CT at the midthigh; CT abdominal subcutaneous and visceral fat areas were measured using a single-slice CT at the L$_{2-3}$ interspace. *$P$ < 0.05 vs. men.
women (e.g., LPL activity or fat cell size) was done using a 2 (gender) \times 3 (site) repeated-measures ANOVA. Testing for differences in adipose tissue blood flow over time, between thigh and abdominal sites in men and women, was assessed using a 2 (gender) \times 2 (site) \times 5 (time) repeated-measures ANOVA with the factors of site and time as repeated measures. Post hoc testing was performed using paired or non-paired t-tests as appropriate. Comparison of plasma TG concentration data was done using log-transformed values because of the skewed distribution. Univariate linear regression analysis was used to test for associations between fat cell size, adipose tissue LPL activity, and adipose tissue blood flow (independent variables) and relative meal fatty acid uptake in adipose tissue. The relative meal fatty acid uptake was examined as absolute uptake (mg meal fat/g adipose tissue fat) and as the proportion of meal fatty acids stored in lower body and upper body subcutaneous adipose tissue.

RESULTS

Subject characteristics. The men and women participating in this study were well matched for age and body mass index. As expected, men were heavier, with a lesser percentage of body fat and more visceral fat than women. Thigh skeletal muscle area by CT was significantly greater in men than in women, whereas thigh adipose area was less in men. The total amount of leg fat was not statistically significantly less ($P = 0.20$). No statistically significant between-group differences were found. * $P < 0.05$ vs. abdomen.

Fig. 2. Plasma chylomicron triglyceride (TG) concentrations (B) and nonchylomicron TG concentrations (A) in the 12 men and 12 women participating in this study.

Fig. 3. Adipose tissue blood flow in the thigh (A) and abdominal (B) area in the 12 men and 12 women participating in this study. * $P < 0.01$ vs. men.

Fig. 4. Uptake of meal fatty acids in abdominal, gluteal, and thigh adipose tissue in men and women 24 h after the ingestion of an experimental meal. No statistically significant between-group differences were found. * $P < 0.05$ vs. abdomen.

Fig. 5. A: concentration of meal fatty acids in adipose tissue was multiplied by regional adipose tissue mass to determine total meal fatty acid uptake in upper body and lower body adipose tissue in men and women. Data are expressed as a percentage of the total meal fatty acids ingested. B: proportion of meal fatty acids stored in total subcutaneous adipose tissue, oxidized, or unaccounted for (missing) 24 h after the ingestion of the meal. * $P < 0.05$ vs. women; ‡ $P = 0.06$ vs. women (see text for further analysis).
in men than in women; however, the percent of body fat present as leg fat was greater in women than men (42 ± 1 vs. 37 ± 1%, respectively, \( P < 0.05 \)). The estimated amount of visceral fat in men and women was 1.41 ± 0.17 and 0.77 ± 0.12 kg, respectively (\( P < 0.005 \)). Upper body subcutaneous fat was calculated to be 7.7 ± 0.8 and 8.4 ± 0.9 kg in men and women (\( P = \) not significant [NS]), respectively (Table 1).

There was a significant (\( P = 0.002 \)) site difference in adipocyte diameter and a significant gender effect (\( P = 0.02 \)). Gluteal and thigh adipocytes were significantly larger in women than in men; however, abdominal adipocyte diameter was not significantly different between groups. In addition, gluteal and thigh adipocytes were significantly larger than abdominal adipocytes in women, whereas no site differences were found in men.

The LPL activity (\( \mu \text{mol free fatty acid released} \cdot \text{h}^{-1} \cdot \text{mg tissue}^{-1} \)) in abdominal, gluteal, and thigh adipose tissue in women was 0.24 ± 0.03, 0.32 ± 0.06, and 0.44 ± 0.06, respectively, and in men it was 0.19 ± 0.04, 0.23 ± 0.04, and 0.31 ± 0.08. A significant (\( P = 0.03 \)) site difference (greater LPL activity in thigh than abdominal adipose tissue) was noted, but no site by gender effect was present (\( P = 0.75 \)).

Glucose, insulin, and TG responses. The plasma glucose and insulin concentration responses during the experimental day were virtually the same in men and women (Fig. 1). Plasma chylomicron TG concentrations and nonchylomicron TG concentrations are depicted in Fig. 2. No gender differences in plasma chylomicron TG concentrations were found. There was a trend (\( P = 0.06 \)) for average nonchylomicron TG concentrations to be greater in men than in women.

**Energy metabolism.** Resting \( O_2 \) consumption was 188 ± 5 and 251 ± 10 ml/min in men and women, respectively, and the overnight postabsorptive respiratory quotient was 0.77 ± 0.01 and 0.80 ± 0.02 (\( P = \) NS) in men and women.

The total amount of carbohydrate oxidized during the 5 h after the experimental meal was 2.7 ± 0.3 and 3.3 ± 0.3 kcal/kg FFM in men and women, respectively (\( P = \) NS). Total fatty acid oxidation over the same time interval was 3.4 ± 0.4 and 3.4 ± 0.2 kcal/kg FFM in men and women, respectively (\( P = \) NS). As assessed by 24-h \(^{14}\text{CO}_2\) excretion, men and women oxidized 21 ± 2 and 22 ± 1% of meal fatty acids (\( P = \) NS), whereas by \(^3\text{H}_2\text{O}\) generation, 28 ± 1 and 32 ± 2% of meal fatty acids were oxidized the day after consumption of the experimental meal (\( P = \) NS, men vs. women).

**Regional adipose tissue blood flow.** Adipose tissue blood flow in the abdomen and thigh for men and women is depicted in Fig. 3. Baseline (prebreakfast) blood flow in the abdominal (1.9 ± 0.4 and 2.2 ± 0.4 ml·100 ml tissue\(^{-1}\)·min\(^{-1}\)) in men and women, respectively) and thigh (2.3 ± 0.5 and 1.5 ± 0.2 ml·100 ml tissue\(^{-1}\)·min\(^{-1}\)) in men and women, respectively) depots was not different in men vs. women or between sites. A significant (\( P < 0.0001 \)) time effect was noted in abdominal adipose tissue blood flow (midmorning greater than baseline), and a trend was noted for a time-by-gender interaction (\( P = 0.03 \) by multilinear ANOVA [MANOVA], \( P = 0.06 \) for univariate ANOVA).
Post hoc analyses did not uncover significant differences in abdominal adipose tissue blood flow between men and women; however, the increase in abdominal blood flow after lunch was significant ($P < 0.005$) in men but not in women. Likewise, a significant ($P < 0.02$) time effect was noted in thigh adipose tissue blood flow, and a trend for a gender interaction ($P = 0.08$ by MANOVA, $P = 0.002$ for univariate ANOVA) was present. The time of the differences is noted in Fig. 3. Thigh adipose tissue blood flow in women in the midmorning was $7.2 \pm 1.4$ ml $100$ ml tissue$^{-1}$ min$^{-1}$ and after lunch was $5.4 \pm 1.1$ ml $100$ ml tissue$^{-1}$ min$^{-1}$.

Regional meal fatty acid uptake. The experimental meal contained $24.6 \pm 0.8$ and $18.1 \pm 0.5$ g of TG for men and women, respectively. The relative uptake of meal fatty acids in abdominal, gluteal, and thigh adipose tissue for men and women is depicted in Fig. 4. The meal fatty acid uptake in abdominal ($0.61 \pm 0.12$ and $0.59 \pm 0.10$ mg meal fat/g adipose tissue lipid), gluteal ($0.59 \pm 0.11$ and $0.53 \pm 0.11$), and thigh ($0.45 \pm 0.09$ and $0.43 \pm 0.05$) adipose tissue was not different between men and women, respectively, as indicated by the lack of a significant site by gender effect. A significant ($P = 0.005$) site effect was present, however. The concentration of meal fatty acids was significantly greater in abdominal fat than in thigh fat ($P < 0.05$), whereas the uptake in gluteal fat was not significantly different from abdominal or thigh sites.

The concentration of meal fatty acids per gram adipose tissue lipid in abdominal fat was multiplied by the amount of subcutaneous upper body adipose tissue to estimate the storage of meal fat in this depot. A similar approach was used to estimate the uptake of meal fat in thigh adipose tissue using the concentration of meal fatty acid in thigh adipose tissue. The percentage of meal fatty acids stored in the corresponding adipose tissue depot was greater ($P < 0.05$) in women than in men (Fig. 5A). The sum of meal fatty acid uptake in leg and upper body subcutaneous adipose tissue and in leg adipose tissue was greater ($P < 0.05$) in women than in men (Fig. 5B). The sum of meal fatty acid uptake in leg and upper body subcutaneous adipose tissue (total subcutaneous) plus meal fatty acids oxidized over $24$ h (using the $\text{^{3}H}_{2}\text{O}$ method) is shown in Fig. 5B. A greater portion of dietary fat was stored in subcutaneous adipose tissue in women than in men ($38 \pm 3$ vs. $24 \pm 3\%$, respectively, $P < 0.05$). Because the percentage of meal fatty acids oxidized was not different in women and men (see above), this indicated that the percent of fatty acids that we could not account for was greater ($P < 0.005$) in men than women ($45 \pm 4$ vs. $30 \pm 3\%$, respectively).

Relationships between fat cell size, LPL activity, adipose blood flow, and lipid uptake. No statistically significant correlations were found between fat cell size or adipose tissue LPL activity and the absolute or relative quantities of meal fatty acids stored in the different adipose tissue depots in men or women. Within individuals, the greatest relative uptake of meal fatty acid was in the abdomen ($70\%$ of volunteers) and gluteal ($30\%$ of volunteers) sites, whereas thigh LPL activity was greater than other sites in $67\%$ of volunteers.

We examined the relationship between the average adipose tissue blood flow from the midmorning measurement through the postlunch interval and the percentage of meal fatty acids stored in the corresponding depots in men and women (Figs. 6 and 7). The only statistically significant relationship was that between meal fatty acid uptake in leg fat and average thigh adipose tissue blood flow in women.

**DISCUSSION**

These studies were designed to test for differences in meal-related fatty acid metabolism between nonobese men and women. We also wished to determine whether any differences that might be present would be consistent with the differences in body fat distribution. To assure comparable conditions in men and women, we controlled the diet at isoenergetic levels for $1$ wk before the study and designed the experimental meal test day such that it would be a comparable physiological challenge for both groups. The test meal provided $40\%$ of resting energy needs as measured by indirect calorimetry, and its fat content was comparable to a usual meal. The plasma glucose, insulin, and chylomicon responses during the test day were quite similar in men and women. In addition, substrate oxidation and meal fatty acid oxidation were not different. We found that the concentration of meal fatty acids was greater in abdominal subcutaneous fat than in thigh adipose tissue in both men and women, implying preferential uptake in upper body fat. The main gender difference was that women stored a greater percentage of dietary fat in subcutaneous adipose tissue than did men. In addition, we noted significant gender differences in regional adipose tissue blood flow after meal ingestion, which was in the direction that might indicate a relationship to regional fat storage.

**Fig. 8.** Visceral fat mass plotted vs. the percentage of meal fat that was unaccounted for (not oxidized, nonsterolal subcutaneous fat) $24$ h after meal ingestion. Open and closed symbols represent values from female and male volunteers, respectively. One of the open symbols is obscured by a closed symbol. Circles represent values from individuals who received the first (less pure) lot of $\text{^{3}H}_{3}\text{triolein}$, and squares represent values from individuals who received the second lot of $\text{^{3}H}_{3}\text{triolein}$.
Meal fatty acid oxidation for the 24 h after the ingestion of the experimental meal was not different in men and women. Meal fatty acid disposal in subcutaneous adipose tissue was estimated by multiplying the regional adipose tissue concentration of meal fatty acids by appropriate subcutaneous adipose tissue mass for each individual. After accounting for meal fatty acid oxidation and uptake in subcutaneous adipose tissue, some dietary fatty acids could not be accounted for. This proportion was significantly greater in men than in women. Considering the more avid uptake of meal fatty acids in intra-abdominal adipose tissue than in subcutaneous adipose tissue previously reported by Marin et al. (16), it is possible that the “missing” meal fatty acids were stored in this depot. Indeed, a positive correlation was noted between the percentage of meal fatty acids that were missing and visceral fat mass (Fig. 8). The experimental design that we employed does not allow us to discern whether the differences in meal fat uptake in subcutaneous fat between men and women create the differences in body composition between men and women or are due to the differences in body composition. Additional experiments will be needed to address these possibilities.

As noted in the companion report (24), the first lot of [3H]triolein used in these studies was less pure (~82% oleate) than the second lot (>90% pure). Differences in tracer purity affected the ability to directly compare adipose tissue fatty acid uptake using the two different tracers. These differences did not, however, affect the relationship between the two isotopic measures of meal fatty acid oxidation (24) or the relationship between “missing” meal fat and visceral fat (Fig. 8). We conclude that any skewing of results that occurred due to the ~10% difference in tracer purity between the two [3H]triolein lots did not materially affect the cross-sectional usefulness of the data. This likely reflects the fact that the majority of the purity differences were in long-chain unsaturated fatty acids that would be expected to have a metabolic fate similar to oleate.

We could not find previous reports of regional differences in adipose tissue blood flow in men and women after mixed meal ingestion. The observation that thigh adipose tissue blood flow increased more in the postprandial period in women than in men is of interest; greater blood flow could deliver more chylomicrons to leg adipose tissue in women, potentially increasing the opportunity for additional fat storage. A tendency was noted for the proportion of dietary fatty acids stored in abdominal and thigh adipose tissue to relate to blood flow to that region (Figs. 4 and 5). These trends are of interest and, if confirmed in future studies, may indicate that blood flow to adipose tissue in the postprandial period is one of the regulators of regional meal fatty acid storage.

Consistent with a previous report (19), we could not detect a significant association between adipose tissue LPL activity and meal fatty acid storage. We acknowledged, however, that the LPL activity was measured in the postabsorptive state, whereas the majority of clearance of meal fatty acids occurred in the initial 2–12 h after meal ingestion (24). Sampling adipose tissue at the time of maximum clearance of dietary fatty acids may allow one to better detect a relationship between LPL activity and the relative uptake of meal fatty acids in adipose tissue.

Of interest, the concentration of meal fatty acids in glutel adipose tissue was intermediate between that of abdominal adipose tissue and thigh adipose tissue in both men and women. Thus glutel adipose tissue may not be entirely representative of lower body/leg adipose tissue. Some investigators use glutel adipose tissue as a representative site for lower body, whereas others use thigh adipose tissue. If meal fatty acid uptake can be used as a distinguishing marker for regional differences in adipose tissue fatty acid metabolism, our results suggest that thigh adipose tissue is the preferred site for comparisons with upper body subcutaneous adipose tissue.

In summary, these studies have examined the fate of dietary fatty acids in nonobese men and women. We found that men and women oxidized comparable proportions of dietary fat but that a greater fraction of dietary fat was stored in subcutaneous adipose tissue in women than in men. The relationship between the missing dietary fat and visceral fat mass (Fig. 8) leads us to suspect that those fatty acids we could not account for by subcutaneous adipose tissue storage or oxidation are taken up by visceral fat. Men and women had regional differences in adipose tissue blood flow during the day. The observed differences were in the direction that would support greater nutrient deposition in lower body fat in women. Regulation of postprandial adipose tissue blood flow could be another mechanism by which dietary fat is directed toward one adipose tissue depot compared with another. Future studies will be needed to address this possibility.

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