Effect of sex and obesity on basal VLDL-triacylglycerol kinetics1–3

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ABSTRACT
Background: Plasma fatty acid availability is a major regulator of VLDL-triacylglycerol production. Basal whole-body lipolysis is higher in women than in men and is higher in persons with abdominal obesity than in lean individuals.

Objective: Our goal was to determine whether sex and abdominal obesity affect VLDL-triacylglycerol kinetics. We hypothesized that basal VLDL-triacylglycerol production would be greater in women than in men and greater in obese than in lean subjects.

Design: VLDL-triacylglycerol kinetics were measured in 20 lean (10 men, 10 women; body mass index, in kg/m2; 23 ± 1) and 20 abdominally obese (10 men, 10 women; body mass index: 35 ± 1) subjects by using a bolus injection of [1H2]glycerol and compartmental modeling analysis.

Results: The rate of VLDL-triacylglycerol secretion was greater in the lean women than in the lean men (5.1 ± 0.7 and 2.6 ± 0.3 μmol·L plasma⁻¹·min⁻¹, respectively; P < 0.002). Obesity was associated with increased VLDL-triacylglycerol secretion in the men (P < 0.001) but not in the women, which resulted in greater rates of VLDL-triacylglycerol secretion in the obese men than in the obese women (6.8 ± 0.5 and 5.0 ± 0.5 μmol·L plasma⁻¹·min⁻¹, respectively; P < 0.05). The clearance of VLDL-triacylglycerol from plasma was greater (P < 0.05) in the lean women than in the lean men (42 ± 7 and 27 ± 4 mL plasma/min, respectively) or in the obese men and obese women (28 ± 3 and 20 ± 4 mL plasma/min, respectively). The plasma VLDL-triacylglycerol concentration was directly related to the rate of VLDL-triacylglycerol secretion in the men (R² = 0.79, P < 0.001) and inversely related to VLDL-triacylglycerol clearance in the women (R² = 0.84, P<0.001).

Conclusion: Sex and obesity have independent effects on basal VLDL-triacylglycerol kinetics. Am J Clin Nutr 2003;77:573–9.

KEY WORDS Stable isotopes, mathematical modeling, fatty acid, lipolysis, VLDL-triacylglycerol, kinetics

INTRODUCTION
VLDLs are complex particles, containing triacylglycerols, cholesterol, phospholipids, and apolipoproteins, that are produced by the liver and are secreted into the systemic circulation. During postabsorptive conditions, most of the triacylglycerols in plasma circulate as a component of VLDL and are progressively hydrolyzed by lipoprotein lipase (LPL) present in muscle and adipose tissue capillary endothelia (1). Fatty acids released by LPL action are taken up by local tissues, where they can be oxidized for fuel or stored as triacylglycerols, depending on the hormonal and physiologic conditions. Therefore, the formation of VLDL provides an important mechanism for converting water-insoluble triacylglycerols into a water-soluble form that can be exported from the liver and delivered to peripheral tissues.

Alterations in VLDL metabolism are involved in the pathogenesis of coronary heart disease. Epidemiologic studies have shown a direct relation between plasma triacylglycerol concentration and the risk of coronary heart disease in both men and women (2, 3). Moreover, an increase in plasma VLDL-triacylglycerol concentration is often associated with a decrease in plasma HDL cholesterol (3, 4), which is also an important risk factor for heart disease (5, 6). The inverse relation between triacylglycerol and HDL-cholesterol concentrations in plasma is presumably mediated by increased transfer of HDL cholesteryl esters to VLDL (7). In addition, the metabolism of VLDL generates LDL particles (8, 9), which can also contribute to the development of coronary heart disease (3, 5).

Hepatic fatty acid availability is a major regulator of VLDL-triacylglycerol production; increasing the availability of plasma fatty acids stimulates the production of VLDL-triacylglycerol (10). Both body composition and sex influence the rate of lipolysis of adipose tissue triacylglycerols and the release of fatty acids into plasma. Obesity, particularly abdominal obesity, and female sex are associated with increased basal whole-body lipolytic rates and fatty acid release into plasma (11–13). These data suggest that basal VLDL-triacylglycerol production rates may be greater in obese than in lean persons and in women than in men. However, it is difficult to interpret the results of previous studies that evaluated the effect of obesity or sex on VLDL-triacylglycerol production (14–17) because the tracer method used in those studies did not account for hepatic tracer recycling, which can have a considerable effect on the calculation of VLDL-triacylglycerol kinetics (18). The results from these studies are also confounded by the study of subjects in the fed state (14, 15) or the inclusion of subjects with glucose intolerance or hypertriacylglycerolemia (15, 16), which can affect VLDL-triacylglycerol production.

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2 Supported by National Institutes of Health grants HD 01459, DK 37948, RR-00036 (General Clinical Research Center), DK 56341 (Clinical Nutrition Research Unit), and RR-00954 (Biomedical Mass Spectrometry Resource), and by a grant from Roche Laboratories.
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Received February 1, 2002.
Accepted for publication June 11, 2002.
Subjects and Methods

Subjects

A total of 20 lean subjects (10 premenopausal women aged 31 ± 3 y and 10 men aged 36 ± 3 y) and 20 subjects with abdominal obesity (10 premenopausal women aged 34 ± 2 y with waist circumference > 90 cm and 10 men aged 35 ± 3 y with waist circumference > 102 cm) were studied (Table 1). Men and women within the lean and obese groups were matched by body mass index to avoid the potential influence of sex differences in body mass index on VLDL-triacylglycerol metabolism. All subjects were considered to be in good health, except for being obese, after completing a comprehensive medical evaluation that included a history and physical examination, an electrocardiogram, and standard blood and urine tests. All subjects had normal oral glucose tolerance. None of the subjects were taking regular medications or smoked tobacco. All subjects had been sedentary (regular exercise < 1 h/wk) for at least 6 mo before the study. Written informed consent was obtained from all subjects before their participation in the study, which was approved by the Human Studies Committee and the General Clinical Research Center (GCRC) Scientific Advisory Committee of Washington University School of Medicine in St Louis.

Experimental protocol

Subjects were admitted to the inpatient unit of the GCRC at Washington University School of Medicine the day before the isotope infusion study. Each subject’s fat mass and fat-free mass (FFM) were measured by dual-energy X-ray absorptiometry (Hologic QDR 1000/w; Hologic Inc, Waltham, MA). At 1900, the subjects consumed a standard meal containing 12 kcal/kg body wt for lean subjects and 12 kcal/kg adjusted body weight for obese subjects to eliminate marked differences in energy balance (energy intake minus energy expenditure) between lean and obese individuals. Adjusted body weight was calculated as ideal body weight [the midpoint of the standard frame of the Metropolitan Life Insurance Company Table (19)] + 0.25 × (actual body weight − ideal body weight). The meal consisted of 55% of total energy as carbohydrates, 30% of energy as fat, and 15% of energy as protein. At 2000, the subjects ingested a liquid formula (Ensure; Ross Laboratories, Columbus, OH) containing 250 kcal (40 g carbohydrates, 6.1 g fat, and 8.8 g protein) and then fasted until completion of the study the next day.

The following morning, an isotope tracer study was performed to measure VLDL-triacylglycerol kinetics. At 0530, one catheter was inserted into a forearm vein to inject the stable-isotope-labeled tracer, and a second catheter was inserted into a contralateral hand vein, which was heated to 55°C by using a thermostatically controlled box to obtain arterialized blood samples. At 0700, 50 μmol [1,1,2,3,3-2H5]glycerol/kg body wt (Cambridge Isotope Laboratories, Andover, MA) dissolved in 0.9% saline was injected as a bolus.

Blood samples were obtained before the injection of labeled glycerol to determine plasma substrate (glucose, fatty acid, total triacylglycerol, and VLDL-triacylglycerol) and insulin concentrations, and background glycerol tracer-to-tracer ratio (TTR) in plasma and VLDL-triacylglycerol. Blood samples were taken at 5, 15, 30, 45, and 60 min, and then every hour for 12 h after the labeled glycerol injection to determine the glycerol TTR in plasma and VLDL-triacylglycerol and total plasma triacylglycerol and VLDL-triacylglycerol concentrations. Subjects remained in bed for the duration of the study.

Sample collection

Blood samples were collected in chilled tubes containing EDTA to determine substrate concentrations and the glycerol TTR and in chilled tubes containing EDTA and trasylool to measure insulin concentrations. Samples were placed in an ice bath, and plasma was separated by centrifugation (2000 × g at 4°C for 30 min) within 30 min of collection. Aliquots of plasma (2 mL) were refrigerated at 4°C for subsequent isolation of VLDL. The remaining plasma samples were stored at −70°C until the final analyses were performed.

Lipoprotein isolation

Immediately after the completion of the study, VLDL was isolated from plasma by ultracentrifugation (20). Two milliliters of each plasma sample was transferred into Optiseal tubes (Beckman Instruments Inc, Palo Alto, CA), covered with a saline solution (d = 1.006 g/mL), and centrifuged (50.4 Ti rotor; Beckman Instruments Inc) for 16 h at 100 000 × g and 8°C. The top layer, containing VLDL, was removed by tube slicing (Beckman Instruments Inc). The exact volume that was recovered (≈1.3 mL) was recorded, and the samples were stored at −70°C until analyzed for triacylglycerol concentration and the glycerol TTR.

Sample analyses

Plasma glucose concentrations were measured in an automated glucose analyzer (Yellow Spring Instruments Co, Yellow Springs, OH).
TABLE 2
Basal plasma insulin and substrate concentrations

<table>
<thead>
<tr>
<th></th>
<th>Lean (n = 10)</th>
<th>Women (n = 10)</th>
<th>Men (n = 10)</th>
<th>Women (n = 10)</th>
<th>Effect of sex</th>
<th>Effect of obesity</th>
<th>Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin (mU/mL)</td>
<td>8 ± 2</td>
<td>7 ± 1</td>
<td>15 ± 3</td>
<td>12 ± 2</td>
<td>NS</td>
<td>P = 0.003</td>
<td>NS</td>
</tr>
<tr>
<td>Glucose (mmol/L)</td>
<td>5.1 ± 0.2</td>
<td>4.8 ± 0.1</td>
<td>5.2 ± 0.1</td>
<td>5.1 ± 0.1</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Fatty acids (μmol/L)</td>
<td>451 ± 65</td>
<td>627 ± 132</td>
<td>396 ± 48</td>
<td>451 ± 48</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Total plasma TG (mmol/L)</td>
<td>0.61 ± 0.06</td>
<td>0.68 ± 0.06</td>
<td>1.55 ± 0.2</td>
<td>1.30 ± 0.2</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>VLDL-TG (mmol/L)</td>
<td>0.43 ± 0.04</td>
<td>0.44 ± 0.05</td>
<td>1.01 ± 0.12</td>
<td>0.83 ± 0.12</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

*≤SEM. TG, triacylglycerol.

Plasma insulin concentrations were measured by radioimmunoassay (21). Total plasma triacylglycerol and VLDL-triacylglycerol concentrations were measured by using a spectrophotometric enzymatic kit (Sigma-Aldrich Co, St Louis). Plasma fatty acid concentrations were quantified by gas chromatography (Hewlett-Packard 5890-II, Palo Alto, CA) after adding heptadecanoic acid (C17:0) as an internal standard (22).

The plasma free glycerol TTR was determined by gas chromatography–mass spectrometry (GC-MS) with an MSD 5973 system (Hewlett-Packard) with capillary column, as previously described (12). Plasma proteins were precipitated with ice-cold acetone, and hexane was used to extract plasma lipids. The aqueous phase was dried by speed-vac centrifugation (Savant Instruments, Inc, Farmingdale, NY) and heptafluorobutyric (HFB) anhydride was used to form an HFB derivative of glycerol. Ions were produced by electron impact, and the glycerol TTR was determined by selectively monitoring ions at mass-to-charge ratios (m/z) of 253 and 257.

The TTR of glycerol present in VLDL-triacylglycerol was determined by GC-MS as previously detailed (18). After the VLDL fraction was isolated from plasma, proteins were precipitated with ice-cold acetone, and lipids were extracted with hexane. The lipid extract was dried by speed-vac centrifugation (Savant Instruments, Inc), and VLDL-triacylglycerol was isolated by thin-layer chromatography and recovered by scraping. Triacylglycerols were extracted with chloroform:methanol (3:1, by vol) and reacted with acetyl chloride in methanol to form methyl esters of the fatty acids. The liberated glycerol was derivatized with HFB anhydride and analyzed by GC-MS by using electron impact ionization and by monitoring ions at m/z 467 and 472.

Calculations

The fractional catabolic rate (FCR) of VLDL-triacylglycerol, expressed in pools/h, was determined by fitting the glycerol TTR time course in plasma and in VLDL-triacylglycerol to a nonlinear multicompartmental model as previously described (18). It was assumed that the rate of VLDL-triacylglycerol production was equal to the rate of VLDL-triacylglycerol catabolism because plasma VLDL-triacylglycerol concentrations remained constant and in a steady state throughout the study. The rate of VLDL-triacylglycerol production (equal to the rate of VLDL-triacylglycerol catabolism) was calculated as \( I \), the total production rate, which represents the total amount of VLDL-triacylglycerol produced by the liver, and 2) the secretion rate per unit of plasma, which represents the rate of release of VLDL-triacylglycerol from the liver into the bloodstream as follows:

\[
\text{Total VLDL-triacylglycerol production rate (μmol/min)} = (\text{VLDL-TG FCR/60}) \times C\text{VLDL-TG} \times PV \quad (I)
\]

where \( C\text{VLDL-TG} \) is the concentration of VLDL-triacylglycerol in plasma and PV is plasma volume, estimated on the basis of each subject’s FFM (PV = 0.055 L × kg FFM) (23). It was assumed that PV was equal to the VLDL-triacylglycerol volume of distribution, because VLDL is restricted to the plasma compartment and does not enter the interstitial space or the lymphatic system (24). The total rate of VLDL-triacylglycerol production was also expressed as the production rate relative to total body weight (in μmol·kg body wt\(^{-1}\)·min\(^{-1}\)) and relative to FFM (in μmol·kg FFM\(^{-1}\)·min\(^{-1}\)).

VLDL-triacylglycerol clearance from plasma (mL/min) was calculated by dividing the rate of VLDL-triacylglycerol disappearance from plasma (VLDL-triacylglycerol catabolic rate in μmol/min) by the plasma VLDL-triacylglycerol concentration (in μmol/mL).

Statistical analyses

A two-way (sex × adiposity) analysis of variance (ANOVA) was performed to test the significance of differences in subject characteristics, basal plasma insulin and substrate concentrations, and VLDL-triacylglycerol kinetics between lean and obese subjects and between men and women. Significant differences (\( F \) ratios) between groups were analyzed by Tukey’s procedure. A three-way ANOVA was performed to test the effects of sex, adiposity, and time on plasma VLDL-triacylglycerol concentrations. Plasma VLDL-triacylglycerol concentration data were not normally distributed, so the data were logarithmically transformed to analyze the significance of differences between groups. The relation between VLDL-triacylglycerol concentration and VLDL-triacylglycerol kinetics in men and women was analyzed by determining Spearman rank order correlation coefficients. Values of \( P \leq 0.05 \) were considered to be statistically significant. Data were analyzed with SIGMASTAT (version 2.0, SPSS Inc, Chicago). All data are expressed as means ± SEMs.

RESULTS

Plasma insulin and substrate concentrations

Basal plasma insulin concentrations were higher in the obese than in the lean subjects, but there was no significant difference in plasma insulin concentrations between the men and women (Table 2). Basal plasma glucose and fatty acid concentrations were not significantly different between groups (Table 2). Basal...
Mean (±SEM) plasma VLDL-triacylglycerol (VLDL-TG) concentrations in lean men (●), lean women (■), obese men (○), and obese women (□) during the 12-h study protocol (n = 10 per group). ANOVA showed no significant effect of sex and time but a significant effect of obesity (P < 0.001).

VLDL-triacylglycerol kinetics

The mathematical model provided an excellent fit with the glycerol TTR in VLDL-triacylglycerol (Figure 2). Analysis of variance showed a significant interaction between sex and adiposity on VLDL-triacylglycerol FCR (P = 0.03), total VLDL-triacylglycerol production (P < 0.001), VLDL-triacylglycerol production relative to body weight (P < 0.001), VLDL-triacylglycerol production relative to FFM (P < 0.001), and the rate of VLDL-triacylglycerol secretion into plasma (P < 0.001).

The mean FCR of VLDL-triacylglycerol in the lean women (1.1 ± 0.2 pools/h) was approximately double the FCR in the lean men (0.47 ± 0.05 pools/h; P < 0.005). The obese women had a lower FCR of VLDL-triacylglycerol (0.43 ± 0.07 pools/h) than did the lean women (P < 0.001), whereas the VLDL-triacylglycerol FCR in the obese men (0.41 ± 0.04 pools/h) was not significantly different from that in the lean men. The rates of total VLDL-triacylglycerol production and the rate of VLDL-triacylglycerol secretion into plasma (Figure 3) were also higher in the lean women than in the lean men (P < 0.002). The rates of total VLDL-triacylglycerol production and VLDL-triacylglycerol secretion into plasma were not significantly different in the obese and lean women, but were greater (P < 0.001) in the obese than in the lean men (Figure 3). Similar results were obtained when VLDL-triacylglycerol production was expressed in relation to body weight (0.12 ± 0.01 and 0.20 ± 0.02 μmol·kg body wt⁻¹·min⁻¹ for the lean and obese men, respectively).

Figure 3. Mean (±SEM) VLDL-triacylglycerol (VLDL-TG) production and secretion into plasma in lean and obese men (●) and women (○); n = 10 per group. ANOVA showed a significant interaction between sex and obesity (P < 0.001). *Significantly different from corresponding value in men, P < 0.002. †Significantly different from corresponding value in lean subjects, P < 0.05.

The total plasma triacylglycerol and VLDL-triacylglycerol concentrations were greater in the obese than in the lean subjects, but there was no significant difference in total plasma triacylglycerol and VLDL-triacylglycerol concentrations between the men and women (Table 2). Plasma VLDL-triacylglycerol concentrations remained constant during the 12-h study (Figure 1).
lean men and lean women, $P < 0.005$, and $0.23 \pm 0.02$ and $0.14 \pm 0.02 \mu$mol·kg body wt$^{-1} \cdot$m in$^{-1}$ for the obese men and obese women, $P < 0.001$) and FFM (0.14 ± 0.02 and 0.28 ± 0.04 μmol·kg FFM$^{-1} \cdot$m in$^{-1}$ for the lean men and lean women, $P < 0.002$, and 0.35 ± 0.03 and 0.27 ± 0.03 μmol·kg FFM$^{-1} \cdot$m in$^{-1}$ for the obese men and obese women, $P < 0.024$).

The clearance rate of VLDL-triacylglycerol from plasma was greater in the lean women than in the lean men or in the obese men and women ($P < 0.005$; Figure 4). There was a direct relation between VLDL-triacylglycerol secretion into plasma and plasma VLDL-triacylglycerol concentration in the men ($R^2 = 0.79$, $P < 0.001$) but not the women ($R^2 = 0.02$, $P = 0.9$). In contrast, there was an inverse relation between plasma VLDL-triacylglycerol clearance and VLDL-triacylglycerol concentration in the women ($R^2 = 0.84$, $P < 0.001$) but not in the men ($R^2 = 0.21$, $P = 0.4$; Figure 5). Therefore, basal VLDL-triacylglycerol secretion rate was a determinant of plasma VLDL-triacylglycerol concentration in the men, whereas VLDL-triacylglycerol clearance was a determinant of plasma VLDL-triacylglycerol concentration in the women.

DISCUSSION

In this study, VLDL-triacylglycerol production rates were evaluated in normotriacylglycerolemic lean and obese men and women during basal postabsorptive conditions with the use of a recently validated method that involves a bolus injection of [${}^3$H$_5$]glycerol in conjunction with compartmental modeling analysis (18). This approach eliminates the confounding effect of intrahepatic tracer recycling on the calculation of VLDL-triacylglycerol kinetics. We found that, in lean subjects, VLDL-triacylglycerol production rates were greater in women than in men, whereas in obese subjects, VLDL-triacylglycerol production rates were greater in men than in women. Furthermore, the VLDL-triacylglycerol production rate was greater in obese than in lean men but was not significantly different in obese and lean women. The plasma VLDL-triacylglycerol concentration was directly related to the VLDL-triacylglycerol production rate in men, but not in women, suggesting that sex may affect the factors that determine plasma triacylglycerol concentration. These results show that sex and obesity have independent effects on basal VLDL-triacylglycerol kinetics and the relation between VLDL-triacylglycerol kinetics and plasma triacylglycerol concentration.

The mechanism or mechanisms responsible for the differences in VLDL-triacylglycerol production between lean men and women are not known but may be related to sex differences in the delivery of plasma fatty acids to the liver. Fatty acid availability from plasma is an important regulator of VLDL-triacylglycerol production. In lean subjects, most (> 80%) fatty acids in VLDL-triacylglycerol are derived from plasma (25–27). Manipulating plasma fatty acid concentrations affects the VLDL-triacylglycerol production rate; increasing plasma fatty acids by infusing a lipid emulsion and heparin increases VLDL-triacylglycerol production, whereas decreasing plasma fatty acids by inhibiting lipolysis of adipose tissue triacylglycerol decreases VLDL-triacylglycerol production.
production (28). We recently showed that the basal lipolytic rate and fatty acid release into the bloodstream are greater in lean women than in lean men (13). Therefore, it is possible that greater fatty acid availability was responsible for the greater rate of VLDL-triacylglycerol production in our lean women than in our lean men.

In contrast with the finding in lean subjects, obesity was associated with a greater VLDL-triacylglycerol production rate in men than in women. In obese subjects, one-half of the fatty acids in VLDL-triacylglycerol are derived from plasma (27); the remaining fatty acids are presumably derived from lipolysis of intrapitoneal and intrahepatic triacylglycerols. Even though our obese men and women were matched on the basis of body mass index, it is likely that our obese men had more intraperitoneal fat than did our obese women (29, 30). Adipocytes from intraperitoneal fat stores are more lipolytically active than are adipocytes from subcutaneous adipose tissue (31). Therefore, the availability of fatty acids for VLDL-triacylglycerol production was probably greater in our obese men than in our obese women and might be responsible for the differences in VLDL-triacylglycerol production rates.

Although several investigators have measured VLDL-triacylglycerol kinetics in lean and obese men and women (14–17, 27, 32–34), it is difficult to determine the true effect of sex or obesity on basal VLDL-triacylglycerol production from these studies because of confounding factors that influenced the measurement or the rate of VLDL-triacylglycerol production. These factors include the following: 1) the tracer method used in most studies did not account for intrapathic tracer recycling (15–17, 27, 32, 34), 2) subjects were studied in the fed state (14, 15, 33), 3) subjects with glucose intolerance or hypertriacylglycerolemia were included (15, 16), or 4) results from lean and overweight subjects were combined and total plasma triacylglycerol rather than VLDL-triacylglycerol was analyzed (17). In concert with our findings, a study that was conducted in overnight fasted Pima Indians found that VLDL-triacylglycerol production was greater in obese than in lean men (34).

The plasma VLDL-triacylglycerol concentration reflects the balance between the rates of VLDL-triacylglycerol production and removal from plasma. Our data suggest that sex influences the interrelation between basal VLDL-triacylglycerol production, plasma VLDL-triacylglycerol clearance, and plasma VLDL-triacylglycerol concentrations. The plasma VLDL-triacylglycerol concentration was directly related to basal VLDL-triacylglycerol production in men but was inversely related to VLDL-triacylglycerol clearance in women. Therefore, despite greater VLDL-triacylglycerol production in lean women than men, plasma VLDL-triacylglycerol concentrations were not significantly different in the 2 groups because of increased VLDL-triacylglycerol clearance in the women. Plasma VLDL-triacylglycerol concentrations were greater in obese than in lean women despite no significant difference in the VLDL-triacylglycerol production rates because of decreased VLDL-triacylglycerol clearance in obese women.

The clearance and uptake of VLDL-triacylglycerol from plasma depends largely on LPL activity in muscle and adipose tissues. Data from previous studies indicate that maximal adipose tissue and skeletal muscle LPL activity is affected by both sex and obesity (35–39). However, the VLDL-triacylglycerol clearance rates observed in our study groups are not entirely consistent with measurements of tissue LPL activity reported previously. We found that plasma VLDL-triacylglycerol clearance was greater in lean women than in lean men or in obese men and women. Moreover, the sex effect observed in the lean subjects was eliminated by obesity. In agreement with our in vivo observations, in vitro maximal basal LPL activity in both skeletal muscle (35) and subcutaneous adipose tissue (36, 37) is much greater in lean women than in lean men. However, in contrast with our findings, maximal basal skeletal muscle LPL activity tended to be greater in obese than in lean men but was not significantly different in obese and lean women (35); adipose tissue LPL activity was greater in obese than in lean men and women (38, 39). These data suggest that maximal basal tissue LPL activity measured in vitro may not be a good predictor of plasma VLDL-triacylglycerol clearance observed in vivo. Although maximal basal tissue LPL activity provides a measure of tissue capacity to clear triacylglycerol from plasma, it does not provide a measure of actual LPL action on VLDL-triacylglycerol. Therefore, factors other than maximal LPL activity are also important in determining the rate of VLDL-triacylglycerol clearance from plasma.

In summary, the data from the present study show that sex and obesity have independent effects on basal VLDL-triacylglycerol production and on the interrelation among VLDL-triacylglycerol production, plasma VLDL-triacylglycerol clearance, and plasma triacylglycerol concentrations. We found that the rate of VLDL-triacylglycerol production was higher in lean women than in lean men, but lower in obese women than in obese men. In addition, the concentration of VLDL-triacylglycerol in plasma was determined primarily by the VLDL-triacylglycerol production rate in men but by the VLDL-triacylglycerol clearance rate in women. These results underscore the importance of controlling for sex and adiposity in future studies evaluating lipid metabolism in human subjects.

We thank Jennifer McCrea for assistance in subject recruitment; the nursing staff of the General Clinical Research Center for their help in performing the studies; Junyoung Kwon, Sarah Rupe, and Freida Custodio for their technical assistance; and the study subjects for their participation.

BM was involved in designing and conducting the infusion studies, processing the study samples, collecting the data, performing the final data analyses, and writing the manuscript. BWP was involved in sample processing, sample analyses, mathematical modeling, and writing the final manuscript. SK was involved in study design, data collection and analysis, and preparation of the final manuscript and provided medical supervision of the infusion studies. BM and BWP have no financial or personal interest in any company or organization sponsoring the research, including advisory board affiliations. SK has received speaker honorarium and grant support from Roche Laboratories, who contributed support for this study.

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