Fatty acid and very low density lipoprotein metabolism in obese African American and Caucasian women with type 2 diabetes

Bernard V. Miller III, Bruce W. Patterson, Adewole Okunade, and Samuel Klein

Center for Human Nutrition and Atkins Center of Excellence in Obesity Medicine, Washington University School of Medicine, Saint Louis, MO 63110

Abstract  Type 2 diabetes mellitus (T2DM) is associated with increased plasma triglyceride (TG) concentrations, but African Americans (AA) have lower plasma TG than Caucasians (CC). We evaluated the hypothesis that obese AA women have lower plasma TG than obese CC women do because of differences in lipid kinetics. Eleven AA and 11 CC obese women with T2DM, matched on body mass index (BMI) (AA = 37 ± 1, CC = 37 ± 1 kg/m²), age, duration of diabetes, percentage body fat, and insulin sensitivity (S, determined by an intravenous glucose tolerance test), were studied. Plasma TG concentration (AA = 1.14 ± 0.11, CC = 1.88 ± 0.18 mmol/l), FFA rate of appearance (Ra) into plasma (AA = 419 ± 27, CC = 503 ± 31 µmol·min⁻¹), and total VLDL-TG secretion rate (AA = 18 ± 2, CC = 29 ± 4 µmol·min⁻¹) were lower in AA than CC women (all P < 0.05). In contrast, plasma total apolipoprotein (apo)B-100 concentration (AA = 1,542 ± 179, CC = 1,620 ± 118 nmol/l) and VLDL-apoB-100 secretion rate (AA = 1.3 ± 0.1, CC = 1.3 ± 0.1 nmol·min⁻¹) were similar in both groups, so the molar ratio of VLDL-TG secretion rate to VLDL-apoB-100 secretion rate was lower in AA women than in CC women. VLVDL-TG concentration was lower in AA women due to lower total VLDL-TG secretion rate. However, the VLDL-apoB-100 secretion rate was the same in both groups, demonstrating that AA women secrete smaller VLDL particles containing less TG than do CC women.—Miller III, B. V., B. W. Patterson, A. Okunade, and S. Klein. Fatty acid and very low density lipoprotein metabolism in obese African American and Caucasian women with type 2 diabetes. J. Lipid Res. 2012. 53: 2767–2772.

Supplementary key words  race  •  triglyceride metabolism  •  insulin sensitivity  •  body fat distribution

Obesity is a major cause of multiorgan insulin resistance, which is associated with increased plasma triglyceride (TG) concentration, increased intrahepatic triglyceride (IHTG) content, and type 2 diabetes mellitus (T2DM). The relationships among obesity, plasma TG concentration, IHTG content, and T2DM, however, are influenced by race (1–6). Although obesity and T2DM are associated with an increase in plasma TG concentration, obese African American (AA) women who have T2DM usually have lower plasma TG concentrations than do Caucasian (CC) women (1, 2, 6). The mechanisms responsible for the racial differences in TG concentration are not known but must involve an alteration in very low density lipoprotein-triglyceride (VLDL-TG) metabolism, because most TG in plasma circulates within VLDL particles produced by the liver (7). The availability of fatty acids derived from the lipolysis of subcutaneous adipose tissue, visceral adipose tissue (VAT), and IHTG, as well as from de novo lipogenesis, are important regulators of VLDL-TG production within hepatocytes (8). Obese AA women have a reduced whole-body adipose tissue lipolytic rate (9, 10), less VAT (11, 12), and lower IHTG content (4, 13) than do obese CC women. These differences in FFA kinetics and body fat distribution could reduce substrate availability for VLDL-TG particle assembly and secretion in AA women.

The purpose of the present study was to test the hypothesis that the VLDL-TG secretion rate is lower in obese AA women with T2DM than in obese CC women with T2DM because of a lower contribution of fatty acids derived from both systemic sources (primarily from the lipolysis of subcutaneous adipose tissue) and nonsystemic sources (primarily from the lipolysis of VAT and IHTG). We evaluated VLDL-TG, VLDL-apolipoprotein B-100, and FFA kinetics in vivo in obese AA and CC women with T2DM, who were matched on percentage body fat and measures of insulin sensitivity. 

Abbreviations:  AA, African American; BMI, body mass index; CC, Caucasian; FCR, fractional catabolic rate; FFM, fat-free mass; FM, fat mass; IHTG, intrahepatic triglyceride; Ra, rate of appearance; S, insulin sensitivity index; SAT, subcutaneous abdominal adipose tissue; T2DM, type 2 diabetes mellitus; TG, triglyceride; TTR, tracer-to-tracee ratio; VAT, visceral adipose tissue.

1To whom correspondence should be addressed. 
e-mail: sklein@wustl.edu
sensitivity, using stable isotopically labeled tracer infusions in conjunction with mathematical modeling.

**RESEARCH DESIGN AND METHODS**

**Subjects**

Eleven AA and 11 CC obese women with T2DM, matched on age, duration of diabetes, body weight, body mass index (BMI), whole-body fat mass, fat-free mass, and insulin sensitivity participated in this study. Written informed consent was obtained from all subjects before their participation, which was approved by the Human Studies Committee of Washington University School of Medicine in St. Louis, MO.

Potential subjects completed a comprehensive medical evaluation that included a physical history and examination, standard blood and urine tests, and an electrocardiogram. Subjects who had markedly increased fasting plasma TG concentrations (>300 mg/dL), who smoked tobacco, or who took diabetes medications (other than sulfonylureas and biguanides) or medications/dietary supplements that can affect plasma lipids were excluded. All subjects had been weight stable (<2% change in body weight) and sedentary (regular exercise <1 h/week) for >2 months before the beginning of the study.

**Experimental protocols**

**Body composition analyses.** Body fat mass (FM) and fat-free mass (FFM) were determined by using dual-energy X-ray absorptiometry (Delphi W-Densitometer; Hologic, Waltham, MA) (14). Subcutaneous abdominal adipose tissue (SAT) and visceral adipose tissue (VAT) volumes were determined using magnetic resonance imaging (Siemens, Iselin, NJ) (15). Eight 10 mm thick axial images were obtained beginning at the L4–L5 interspace and analyzed for SAT and VAT content using Analyze 6.0 software (Mayo Foundation, Biomedical Imaging Resource, Rochester, MN); the volumes of fat were calculated for each slice, and the sum of these values was determined. The product of the fat volumes and the density of adipose tissue (0.9096 kg·L⁻¹) was used to determine adipose tissue masses. Proton magnetic resonance spectroscopy (1.5 T Siemens Magneton Vision scanner; Siemens, Erlanger, Germany) was used to measure HTG content as previously described (16). Three 2 × 2 × 2 cm³ voxels were examined in each subject, and the values were averaged to determine HTG content.

**Insulin sensitivity.** A frequently sampled insulin intravenous glucose tolerance test (IVGTT) was performed to determine insulin sensitivity (S) using the minimal model approach (17). Subjects were instructed to adhere to their regular diets and to refrain from exercise for 3 days before the study. Diabetes medications were discontinued 48 h before the IVGTT. At 0800 h, after subjects fasted overnight (12 h), one catheter was inserted into a forearm vein to administer glucose and insulin boluses, and a second catheter was inserted into a contralateral hand vein, which was heated to 55°C with a thermostatically controlled box, and arterialized blood samples were obtained. At 0800 h, a bolus of [1,1,2,3,3-²H₅]glycerol (75 µmol·kg⁻¹) dissolved in 0.9% NaCl solution was administered through the catheter in the forearm vein, and constant infusions of [2,2-²H₂]palmitate (0.035 µmol·kg⁻¹·min⁻¹) bound to 25% human albumin and [5,5,5-²H₃]leucine (0.12 µmol·kg⁻¹·min⁻¹; priming dose: 7.2 µmol/kg) dissolved in 0.9% NaCl solution were started and maintained for 12 h. Blood samples were obtained before tracer administration (time = 0), and at 5, 15, 30, 60, 90, and 120 min and then every hour until 12 h after tracer administration to determine glycerol and palmitate tracer-to-tracee ratios (TTR) in plasma and in VLDL-TG and to determine leucine TTR in plasma and in VLDL-apolipoprotein B-100 (VLDL-apoB-100).

**Sample collection and analyses**

Plasma insulin concentration was measured by radioimmunoassay (Linco Research, St. Louis, MO). Plasma FFA molar composition (%) and concentrations were quantified by gas chromatography (HP 5890 series II GC; Hewlett-Packard, Palo Alto, CA) after adding heptadecanoic acid to plasma as an internal standard (20). Total plasma TG and VLDL-TG concentrations were determined with a colorimetric enzymatic kit (Sigma Chemicals, St. Louis, MO). Total plasma apoB-100 and VLDL-apoB-100 concentrations were measured by using a turbidimetric immunoassay (Wako Pure Chemical Industries, Osaka, Japan).

After blood samples were obtained, plasma was separated by centrifugation within 30 min of collection. Aliquots of plasma were kept in the refrigerator for immediate isolation of VLDL and measurement of total plasma and VLDL-apoB-100 concentrations. The VLDL fraction was prepared as previously described (21). Approximately 1.5 mL of plasma was transferred into OptiSeal polylamellar tubes (Beckman Instruments, Palo Alto, CA), overlaid with a NaCl/EDTA solution (density 1.006 g/cm³), and centrifuged at 100,000 g for 16 h at 10°C in an Optima LE-80K preparative ultracentrifuge equipped with a type 50.4 Ti rotor (Beckman Instruments). The top layer, which contained VLDL, was removed by tube slicing (CentriTube Slicer; Beckman Instruments).

Plasma free glycerol, palmitate, and leucine TTR, the TTR of glycerol and palmitate in VLDL-TG, and the TTR of leucine in VLDL-apoB-100 were determined by using gas chromatography-mass spectrometry (Agilent Technologies/HP 6890 series GC System-5973 mass selective detector; Hewlett-Packard) as previously described (20–23).

Fatty acid and VLDL kinetics. Subjects were instructed to adhere to their regular diets and to refrain from exercise for 3 days before the study. Diabetes medications were discontinued 48 h before the kinetics study. Subjects were admitted to the Clinical Research Unit (CRU) at Washington University School of Medicine in the afternoon. They consumed a standard meal containing 12 kcal/kg FFM (55% of total energy from carbohydrate, 30% from fat, and 15% from protein) at 1930 h, and then fasted (except for water) until completion of the study the next day. At 0630 h the following morning, one catheter was inserted into a forearm vein to administer stable isotopically labeled tracers, and a second catheter was inserted into a vein in the contralateral hand, which was heated to 55°C with a thermostatically controlled box, and arterialized blood samples were obtained. At 0800 h, a bolus of [1,1,2,3,3-²H₅]glycerol (75 µmol·kg⁻¹) dissolved in 0.9% NaCl solution was administered through the catheter in the forearm vein, and constant infusions of [2,2-²H₂]palmitate (0.035 µmol·kg⁻¹·min⁻¹) bound to 25% human albumin and [5,5,5-²H₃]leucine (0.12 µmol·kg⁻¹·min⁻¹; priming dose: 7.2 µmol/kg) dissolved in 0.9% NaCl solution were started and maintained for 12 h. Blood samples were obtained before tracer administration (time = 0), and at 5, 15, 30, 60, 90, and 120 min and then every hour until 12 h after tracer administration to determine glycerol and palmitate tracer-to-tracee ratios (TTR) in plasma and in VLDL-TG and to determine leucine TTR in plasma and in VLDL-apolipoprotein B-100 (VLDL-apoB-100).
Calculations

Palmitate rate of appearance ($R_p$) in plasma was calculated by dividing the palmitate tracer infusion rate by the average plasma palmitate TTR between 60 and 180 min during physiologic and isotopic steady-state conditions; total FFA $R_p$ was calculated by dividing palmitate $R_p$ by the proportional contribution of palmitate to total plasma FFA concentration (22). Plasma FFA clearance rates (ml·min⁻¹) were calculated by dividing total FFA $R_p$ (µmol·min⁻¹) by total FFA concentration (µmol·ml⁻¹).

Metabolic steady-state was assumed for VLDL-TG and VLDL-apoB-100 because plasma VLDL-TG and VLDL-apoB-100 concentrations remained constant throughout the 12 h sampling period. The fractional catabolic rate (FCR) of VLDL-TG was determined by fitting the TTR time courses of glycerol in plasma and VLDL-TG to a compartmental model (23). The VLDL-TG secretion rate (in mmol·L⁻¹ of plasma·h⁻¹), which represents the amount of VLDL-TG released by the liver per unit of plasma, was calculated by multiplying the FCR of VLDL-TG (in pools·h⁻¹) by the concentration of VLDL-TG in plasma (in mmol·L⁻¹). VLDL-TG secretion rate (in µmol·min⁻¹), which represents the total amount of VLDL-TG released by the liver, was calculated by multiplying the rate in mmol·L⁻¹ of plasma·h⁻¹ by plasma volume estimated at 55 ml/kg FFM (21). The relative contribution of systemic plasma fatty acids and nonsystemic fatty acids to total VLDL-TG production was calculated by fitting palmitate TTR in plasma and VLDL-TG to a compartmental model that accounts for isotopic dilution between plasma palmitate and VLDL-TG palmitate (21). Systemic sources represent isotopically labeled fatty acids from the systemic circulation that are taken up by the liver and directly incorporated into VLDL-TG or temporarily incorporated into rapidly turned over intraperitoneal TG stores in VAT and the liver before incorporation into VLDL-TG. Nonsystemic sources are derived from pools of fatty acids that are not labeled with tracer during the infusion period; these sources include fatty acids released from preexisting TG stores in the liver or tissues draining directly into the portal vein, such as VAT, and fatty acids derived from hepatic de novo lipogenesis (8). The proportion of systemic fatty acids used in the production of VLDL-TG was calculated as $\left[3 \times \text{VLDL-TG secretion rate derived from systemic fatty acids (in } \mu\text{mol} \cdot \text{min}^{-1} \right] / \text{systemic FFA } R_p$ (in µmol·min⁻¹).

The FCR of VLDL-apoB-100 was calculated by fitting the TTR time courses of free leucine in plasma and leucine in VLDL-apoB-100 to a compartmental model (21). The rate of secretion was calculated based on plasma VLDL-apoB-100 concentration and VLDL-apoB-100 FCR as described above for VLDL-TG. A molecular mass of 512,723 g/mol for apoB-100 was used for unit conversions (24). The molar ratio of VLDL-TG secretion rate to VLDL-apoB-100 secretion rate was calculated to estimate the relative amount of TG in nascent VLDL particles.

Statistical analyses

A one-way ANOVA was used to test for significant differences between AA and CC women in datasets with homogenous variance. A Welch’s ANOVA was used for datasets with nonnormal distribution. ANCOVA was used to test for main-effects of race and for interactions between race and variables of interest. Based on our own reproducibility studies, we estimated that seven subjects in each group would be sufficient to detect a 25% difference in the rate of VLDL-TG secretion or VLDL-apoB-100 secretion between races with a power (1 - β) = 0.80 and an α (Type I error) of ≤ 0.05 (25). Standard least-squares linear regression models were used to evaluate the relationships between variables of interest. Datasets with normal distribution were presented as the mean ± SEM. Datasets with nonnormal distribution were shown as the median [25th percentile, 75th percentile]. A P value ≤ 0.05 was considered statistically significant for all analyses. All statistical tests were performed with JMP version 8.0, SAS Institute, Cary, NC.

RESULTS

Subject characteristics, body composition, and insulin sensitivity

Age (AA = 51 ± 2 and CC = 53 ± 3 years), duration of T2DM (AA = 7 ± 1 and CC = 9 ± 1 year), blood pressure (AA = 141/80 ± 5/4, CC = 129/72 ± 5/2 mmHg), body weight, BMI, percent body fat, total FM, and FFM were similar in AA and CC women (Table 1). In contrast, body fat distribution was different between groups; VAT mass and HFTG content were ~45% lower in AA than CC women. Markers of glucose homeostasis, including plasma hemoglobin A1c, glucose, insulin, QUICKI and S values, and total apoB-100, were similar in both groups, but plasma FFA, total TG, VLDL-TG, and VLDL-apoB concentrations were lower in AA than in CC women (Table 2). The number of subjects treated with metformin was similar in the AA (n = 6) and CC groups (n = 7).

Free fatty acid kinetics

FFA $R_p$ was lower in AA than in CC women, whereas plasma FFA clearance rates were similar in both groups (Fig. 1A, B). Therefore, plasma FFA concentrations were lower in AA than in CC women (Table 2). Plasma FFA concentration was directly correlated with FFA $R_p$ in both AA and CC women (data not shown).

VLDL-TG and VLDL-apoB-100 kinetics

Total VLDL-TG secretion rate (µmol·min⁻¹) was ~40% lower in AA than in CC women ($P < 0.01$) (Fig. 2A). The relative proportion of secreted VLDL-TG that was derived from nonsystemic fatty acids was lower in AA [31% (26, 45)] than in CC [54% (41, 59)] women ($P < 0.05$) (Fig. 2B), whereas the relative proportion of secreted VLDL-TG derived from systemic fatty acids was higher in AA [69% (55, 74)] than in CC [46% (41, 59)] women ($P < 0.05$). The total amount of secreted VLDL-TG derived from nonsystemic fatty acids (µmol·min⁻¹), presumably derived from fatty acids released from preexisting TG stores in the liver before incorporation into VLDL-TG, was ~40% lower in AA than in CC women ($P < 0.01$) (Fig. 2A).

Table 1. Body composition in obese Caucasian and African American subjects with T2DM

| Composition | Caucasian Women | African American Women |
|-------------|-----------------|------------------------|
| Body weight, kg | 99 ± 4 | 100 ± 4 |
| BMI, kg/m² | 37 ± 1 | 37 ± 1 |
| Body fat, % | 44 ± 1 | 43 ± 1 |
| Fat mass, kg | 44 ± 2 | 43 ± 2 |
| Fat-free mass, kg | 55 ± 2 | 57 ± 2 |
| SAT, kg | 3.5 ± 0.3 | 3.8 ± 0.3 |
| VAT, kg | 1.8 ± 0.2 | 1.0 ± 0.1* |
| HFTG, % | 20 ± 3 | 11 ± 3* |

Values are means ± SEM.  
*Value significantly different from Caucasian women at $P < 0.05$.  
**Value significantly different from Caucasian women at $P < 0.005$.  
†Value significantly different from Caucasian women at $P < 0.005$.
partly from fatty acids released during lipolysis of IHTG and visceral adipose tissue, was lower in AA than in CC women (P < 0.005) (Fig. 2A). The proportion of VLDL-TG derived from nonsystemic fatty acids was positively correlated with IHTG content (R = 0.61, P < 0.005). There was no significant correlation between VLDL-TG production rate and visceral adipose tissue mass (R = 0.22, NS) The percentage of total FFA released into the circulation from the lipolysis of adipose tissue TG (i.e., systemic FFA R_a) incorporated into secreted VLDL-TG was similar in AA and CC women (AA = 8 ± 1% and CC = 9 ± 2%, P = 0.56). VLDL-TG secretion rate correlated directly with total TG concentration (adjusted R^2 = 0.51, P < 0.05) with a race main-effect (P < 0.05) but without a race-VLDL-TG secretion rate interaction (P = 0.65). Both VLDL-TG FCR (AA = 0.75 ± 0.10, CC = 0.76 ± 0.13 pools/h, P = 0.95) and clearance rate from plasma (AA = 39 ± 5, CC = 39 ± 7 ml/min, P = 0.93) were similar in AA and CC women.

VLDL-apoB-100 secretion rate was not different between groups, but VLDL-apoB-100 FCR was greater in AA (0.39 ± 0.04) than in CC (0.24 ± 0.02 pools/h, P < 0.005) women (Fig. 2C). Therefore, plasma VLDL-apoB-100 concentration was ∼60% lower in AA than in CC women, and the molar ratio of VLDL-TG secretion rate to VLDL-apoB-100 secretion rate was lower in AA than in CC women (Fig. 2D) (P < 0.05).

DISCUSSION

T2DM is associated with an atherogenic dyslipidemia that is manifested by an increase in serum TG and a decrease in HDL-cholesterol concentration (26). Although the prevalence of T2DM is greater (3), serum TG concentrations are lower in AA than in CC women with T2DM (1, 2, 6). In the present study, we evaluated the potential physiological mechanisms responsible for the racial differences in plasma lipids by assessing FFA and VLDL kinetics in obese AA and CC women with T2DM who were matched on BMI, percentage body fat, and measures of insulin sensitivity. Our data demonstrated that both FFA R_a and VLDL-TG secretion rate were lower in AA than in CC women, which likely contributed to the lower plasma FFA and VLDL-TG concentrations in the AA women. Plasma VLDL-apoB-100 concentrations were also lower in AA women; however, this was due to a faster VLDL-apoB-100 FCR, not a lower VLDL-apoB-100 secretion rate. In fact, VLDL-apoB-100 secretion rates were the same in AA and CC women and resulted in similar total plasma apoB-100 concentrations in both groups. Accordingly, race has profound effects on FFA and lipoprotein metabolism that are independent of insulin sensitivity in women with T2DM.

Although FFA R_a increased linearly with increasing FM in all subjects, FFA R_a was lower at any given FM in the AA than in CC women. The lower rate of lipolysis of adipose tissue triglyceride in the AA than in the CC women was likely responsible for the lower plasma FFA concentrations in the AA subjects, because plasma FFA clearance was similar in both groups. The effect of race on FFA kinetics has been reported before (9, 10); our findings extend those previous observations by demonstrating that FFA R_a is also lower in obese AA women who have T2DM than it is in obese CC women who have T2DM. The mechanism responsible for the decrease in lipolytic activity in AA women is likely related to a decreased adipose tissue hormone-sensitive lipase content (27) and TG lipase expression (28).

The rate of hepatic secretion of VLDL-TG was lower in AA than in CC women, primarily due to a reduced contribution of fatty acids derived from nonsystemic fatty acid sources. Presumably, the lower amount of intraabdominal and intrahepatic TG masses affected the availability of fatty acids from these sources for hepatic VLDL-TG production. There was also a trend toward a lower contribution of systemic fatty acids to VLDL-TG secretion in AA than in CC women, which is consistent with the lower availability of systemic plasma FFA caused by decreased
whole-body lipolytic rate in AA women. These data demonstrate that lower VLDL-TG secretion, not greater VLDL-apoB-100 secretion, was primarily responsible for the lower plasma VLDL-TG concentration observed in the AA women because VLDL-TG FCR and clearance rates were the same in both groups.

The secretion rate of large VLDL (VLDL₁) particles increases with increasing IHTG content (29). AA women have smaller VLDL particles and lower concentrations of large VLDL₁ than do CC women (30–32). Our kinetic data are consistent with these observations because the molar ratio of VLDL-TG secretion rate to VLDL-apoB-100 secretion rate was lower in obese AA women than it was in obese CC women, demonstrating the release of smaller VLDL particles containing less TG in AA women than in CC women. In addition, we found VLDL-apoB-100 FCR was greater in AA women than in CC women, even though VLDL-TG FCR and plasma clearance rates were the same in both groups. These data suggest that the removal of TG from VLDL caused a more rapid conversion of apoB-100 from VLDL to IDL and LDL, presumably because of the lower initial TG content of VLDL particles in AA women than in CC women.

In conclusion, postabsorptive plasma FFA and VLDL-TG concentrations were lower in obese AA women with T2DM than in obese CC women with T2DM who were matched on BMI, percentage body fat, and insulin sensitivity. Our data demonstrate that lower adipose tissue lipolytic activity and hepatic VLDL-TG secretion rate were likely responsible for the racial differences in plasma lipids.

The authors thank the nursing staff of the Clinical Research Unit for their help in performing the studies; Freida Custodio, Jennifer Shew, and Gary Skolnick for their technical assistance; and the study subjects for their participation.

REFERENCES

1. Cook, C. B., D. M. Erdman, G. J. Ryan, K. J. Greenlund, W. H. Giles, D. L. Gallina, I. M. El-Kebbi, D. C. Ziemer, K. L. Ernst, V. G. Dunbar, et al. 2000. The pattern of dyslipidemia among urban African-Americans with type 2 diabetes. Diabetes Care. 23: 319–324.
2. Cowie, C. C., B. V. Howard, and M. I. Harris. 1994. Serum lipoproteins in African Americans and whites with non-insulin-dependent diabetes in the US population. Circulation. 90: 1185–1193.
3. Cowie, C. C., R. F. Rust, E. S. Ford, M. S. Eberhardt, D. B. Byrd-Holt, C. Li, D. E. Williams, E. W. Gregg, K. E. Bainbridge, S. H. Saydah, et al. 2005. Full accounting of diabetes and pre-diabetes in the US population in 1988–1994 and 2005–2006. Diabetes Care. 32: 287–294.
4. Guerrero, R., G. L. Vega, S. M. Grundy, and J. D. Browning. 2009. Ethnic differences in hepatic steatosis: an insulin resistance paradox? Hepatology. 49: 791–801.
5. Ogden, C. L., M. D. Carroll, L. R. Curtin, M. A. McDowell, C. J. Tabak, and K. M. Flegal. 2006. Prevalence of overweight and obesity in the United States, 1999–2004. JAMA. 295: 149–155.
6. Sharma, M. D., and V. N. Pavlik. 2001. Dyslipidaemia in African Americans, Hispanics and whites with type 2 diabetes mellitus and hypertension. Diabetes Obes. Metab. 3: 41–45.
7. Barter, P. J., and P. J. Nestel. 1973. Precursors of plasma triglyceride fatty acids in obesity. Metabolism. 22: 779–783.
8. Lewis, G. F. 1997. Fatty acid regulation of very low density lipoprotein production. Curr. Opin. Lipidol. 8: 146–153.
9. Racette, S. B., J. F. Horowitz, B. Mittendorfer, and S. Klein. 2000. Racial differences in lipid metabolism in women with abdominal obesity. Am. J. Physiol. Regul. Integr. Comp. Physiol. 279: R944–R950.
10. Abba, J. B., M. Curi, M. Shur, L. Murphy, D. E. Matthews, and F. X. Pi-Sunyer. 1999. Systemic resistance to the antilipolytic effect of insulin in black and white women with visceral obesity. Am. J. Physiol. 277: E551–E560.
11. Després, J. P., C. Couillard, J. Gagnon, J. Bergeron, A. S. Leon, D. C. Rao, J. S. Skinner, J. H. Wilmore, and C. Bouchard. 2000. Race, visceral adipose tissue, plasma lipids, and lipoprotein lipase activity in men and women: the Health, Risk Factors, Exercise Training.
and Genetics (HERITAGE) family study. *Atheroscler. Thromb. Vasc. Biol.* **20**: 1932–1938.

12. Albu, J. B., L. Murphy, D. H. Frager, J. A. Johnson, and F. X. Pi-Sunyer. 1997. Visceral fat and race-dependent health risks in obese nondiabetic premenopausal women. *Diabetes.* **46**: 456–462.

13. Solga, S. F., J. M. Clark, A. R. Alkhuraishi, M. Torbenson, A. Tabesh, M. Schweitzer, A. M. Diehl, and T. H. Magnuson. 2005. Race and comorbid factors predict nonalcoholic fatty liver disease histopathology in severely obese patients. *Surg. Obes. Relat. Dis.* **1**: 6–11.

14. Genton, L., D. Hans, U. G. Kyle, and C. Pichard. 2002. Dual-energy X-ray absorptiometry and body composition: differences between devices and comparison with reference methods. *Nutrition.* **18**: 66–70.

15. Abate, N., D. Burns, R. M. Peshock, A. Garg, and S. M. Grundy. 1994. Estimation of adipose tissue mass by magnetic resonance imaging: validation against dissection in human cadavers. *J. Lipid Res.* **35**: 1490–1496.

16. Frimel, T. N., S. Deivanayagam, A. Bashir, R. O’Connor, and S. Klein. 2007. Assessment of intrahepatic triglyceride content using magnetic resonance spectroscopy. *J. Cardiometab. Syndr.* **2**: 136–138.

17. Saad, M. F., G. M. Steil, M. Riad-Gabriel, A. Khan, A. Sharma, R. Boyadjian, S. D. Jinagouda, and R. N. Bergman. 1997. Method of insulin administration has no effect on insulin sensitivity estimates from the insulin-modified minimal model protocol. *Diabetes.* **46**: 2044–2048.

18. Pacini, G., and R. N. Bergman. 1986. MINMOD: a computer program to calculate insulin sensitivity and pancreatic responsivity from the frequently sampled intravenous glucose tolerance test. *Comput. Methods Programs Biomed.* **23**: 113–122.

19. Katz, A., S. S. Nambi, K. Mather, A. D. Baron, D. A. sollmann, G. Sullivan, and M. J. Quon. 2000. Quantitative insulin sensitivity check index: a simple, accurate method for assessing insulin sensitivity in humans. *J. Clin. Endocrinol. Metab.* **85**: 2402–2410.

20. Patterson, B. W., G. Zhao, N. Elias, D. L. Hackey, and S. Klein. 1999. Validation of a new procedure to determine plasma fatty acid concentration and isotopic enrichment. *J. Lipid Res.* **40**: 2118–2124.

21. Mittendorfer, B., B. W. Patterson, and S. Klein. 2003. Effect of weight loss on VLDL-triglyceride and apoB-100 kinetics in women with abdominal obesity. *Am. J. Physiol. Endocrinol. Metab.* **284**: E549–E556.

22. Mittendorfer, B., O. Liem, B. W. Patterson, J. M. Miles, and S. Klein. 2003. What does the measurement of whole-body fatty acid rate of appearance in plasma by using a fatty acid tracer really mean? *Diabetes.* **52**: 1641–1648.

23. Patterson, B. W., B. Mittendorfer, N. Elias, R. Satyanarayana, and S. Klein. 2002. Use of stable isotopically labeled tracers to measure very low density lipoprotein-triglyceride turnover. *J. Lipid Res.* **43**: 223–233.

24. Law, S. W., S. M. Grant, K. Higuchi, A. Hospattankar, K. Lackner, N. Lee, and H. B. Brewer, Jr. 1986. Human liver apolipoprotein B-100 DNA: complete nucleic acid and derived amino acid sequence. *Proc. Natl. Acad. Sci. USA.* **83**: 8142–8146.

25. Magkos, F., B. W. Patterson, and B. Mittendorfer. 2007. Reproducibility of stable isotope-labeled tracer measures of VLDL-triglyceride and VLDL-apolipoprotein B-100 kinetics. *J. Lipid Res.* **48**: 1204–1211.

26. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). 2002. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation.* **106**: 3143–3421.

27. Barakat, H., R. C. Hickner, J. Privette, J. Bower, E. Hao, V. Udupi, A. Green, W. Porics, and K. MacDonald. 2002. Differences in the lipolytic function of adipose tissue preparations from Black American and Caucasian women. *Metabolism.* **51**: 1514–1518.

28. Smith, L. M., A. Yao-Borengasser, T. Starks, M. Tripputi, P. A. Kern, and N. Rasouli. 2010. Insulin resistance in African-American and Caucasian women: differences in lipotoxicity, adipokines, and gene expression in adipose tissue and muscle. *J. Clin. Endocrinol. Metab.* **95**: 4441–4448.

29. Adiels, M., M. R. Taskinen, C. Packard, M. J. Caslake, A. Sorop-Paavonen, J. Westerbacka, S. Vehkavaara, A. Hakkinen, S. O. Olodsson, H. Yki-Jarvinen, et al. 2006. Overproduction of large VLDL particles is driven by increased liver fat content in man. *Diabetologia.* **49**: 755–765.

30. Freedman, D. S., B. A. Bowman, J. D. Otos, S. R. Srinivasan, and G. S. Berenson. 2000. Levels and correlates of LDL and VLDL particle sizes among children: the Bogalusa heart study. *Atherosclerosis.* **152**: 441–449.

31. Freedman, D. S., B. A. Bowman, J. D. Otos, S. R. Srinivasan, and G. S. Berenson. 2002. Differences in the relation of obesity to serum triacylglycerol and VLDL subclass concentrations between black and white children: the Bogalusa Heart Study. *Am. J. Clin. Nutr.* **75**: 827–833.

32. Johnson, J. L., C. A. Sletz, B. D. Duscha, G. P. Samsa, J. S. McCartney, J. A. Houmard, and W. E. Kraus. 2004. Gender and racial differences in lipoprotein subclass distributions: the STRRIDE study. *Atherosclerosis.* **176**: 371–377.