Postprandial Free Fatty Acid Kinetics Are Abnormal in Upper Body Obesity

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Excess free fatty acid release (rate of appearance) is seen in overnight postabsorptive, upper body obese women and, if present postprandially, could contribute to glucose intolerance. These studies examine the antilipolytic effect of a mixed meal in upper body obese, lower body obese, and nonobese women and the contribution of meal triglyceride fatty acids to circulating free fatty acids. Eight upper body obese, 8 lower body obese, and 8 nonobese age-matched, premenopausal women were studied. Systemic oleate R_a ([^{3}H]oleate) was measured before and after an evening meal that contained triolein labeled with [^{14}C]triolein as the only source of fat. Premeal oleate R_a was greater in both upper body obese and lower body obese women than nonobese women. The nadir of total oleate R_a occurred 90–240 min postprandially and was less ($P < 0.01$) in nonobese and lower body obese women (63 ± 10 and 87 ± 17 μmol/min) than in upper body obese women (140 ± 21 μmol/min). Meal oleate R_a contributed substantially to total oleate R_a. The nadir for endogenous oleate R_a in nonobese and lower body obese women was less ($P < 0.01$) than that observed in upper body obese women. We conclude that the antilipolytic effect of a mixed meal is reduced in upper body obese women and that meal triglyceride fatty acids contribute significantly to postprandial free fatty acid flux. *Diabetes* 42:1567–73, 1993

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FFA, free fatty acid; NIDDM, non-insulin-dependent diabetes mellitus; R_a, rate of appearance; TG, triglyceride; SA, specific activity; HPLC, high-performance liquid chromatography; GH, growth hormone; RIA, radioimmunoassay; BCM, body cell mass; BMI, body mass index; WHR, waist-to-hip circumference ratio; ANOVA, analysis of variance; VLDL, very-low-density lipoprotein.

Although the concept of the glucose-fatty acid cycle is now 30 years old (1), only in the last 10 years have studies clearly demonstrated that increased FFA inhibit insulin-stimulated glucose uptake in humans (2–11). This concept has been expanded to include a role for FFA in modulating insulin suppression of endogenous glucose production (2,7,8, 10,11). Because obesity and NIDDM are associated with resistance to the antilipolytic and glucoregulatory effects of insulin (12–15), failure to normally suppress postprandial FFA availability has been sugested to contribute to the metabolic disturbances characteristic of these conditions (16). If excess FFA are to be invoked as a potential factor leading to abnormal postprandial glucose metabolism, however, it would be important to document that meal consumption does not adequately suppress adipose tissue lipolysis in obesity and NIDDM. Early experiments that addressed this issue found that the insulinemic response to food ingestion in obese individuals was sufficient to suppress FFA flux to normal values (17). If this were generally true, it would be difficult to attribute glucose intolerance to excess postprandial FFA availability.

Not all human obesity is the same, however. Greater resistance to the antilipolytic effects of insulin is found in upper body obesity than in lower body obesity (15,18,19). Despite this, the greater postprandial hyperinsulinemia that occurs in upper body obesity (20) could potentially offset adipose tissue resistance to insulin action. Thus, whether an upper body fat distribution is associated with excess postprandial and postabsorptive FFA flux is unknown (15). If abnormal postprandial FFA metabolism does contribute to the pathophysiology of obesity, it would likely be more apparent in the upper body obesity phenotype.

In addition to FFA entering the circulation from adipose tissue, the possibility that meal-derived fatty acids may

TABLE 1
Clinical characteristics of study subjects

	Upper body obese women	Lower body obese women	Nonobese women
n	8	8	8
Age (yr)	36 ± 1	37 ± 3	35 ± 2
BMI (kg/m^2)	33.4 ± 0.7	32.7 ± 0.7	21.5 ± 0.5
WHR	0.90 ± 0.01	0.73 ± 0.01	0.71 ± 0.01
Weight (kg)	91.9 ± 3.6	90.3 ± 3.6	62.9 ± 2.5*
Body fat (kg)	40.3 ± 2.2	43.7 ± 2.0	19.4 ± 1.5*
BCM (kg)	27.2 ± 2.3	23.5 ± 1.4	21.7 ± 1.2

Data are means ± SE.
*$P < 0.001$ compared with obese groups.

enter the plasma FFA pool during the postprandial interval must be considered (21,22). It is therefore necessary to distinguish between FFA that originate from meal TGs and those that do not to assess how meal-related events influence the release of endogenous FFA from adipose tissue. With this in mind, these studies were undertaken to determine whether suppression of postprandial FFA flux is less complete in upper body obesity and, if so, whether differences in endogenous adipose tissue lipolysis are primarily responsible for the excess FFA availability.

RESEARCH DESIGN AND METHODS

Informed written consent was obtained from 16 healthy, moderately obese (BMI, 30–35 kg/m^2), premenopausal women and 8 age-matched, nonobese, premenopausal women. The obese women were selected such that 8 had a WHR of >0.85 and 8 had a WHR of <0.76 (18). Subjects were taking no medications known to affect FFA metabolism and had maintained a stable weight for >2 mo before the study. None of the volunteers exercised regularly. Clinical characteristics of the study subjects are found in Table 1. The study protocol was approved by the Mayo Clinic Institutional Review Board.

[9,10-^{3}H]oleate (NEN-Du Pont, Boston, MA) was prepared for intravenous infusion as a 0.3% albumin in 0.9% NaCl solution as described previously (23). [1-^{14}C]triolein (New England Nuclear) was prepared and stored for oral administration by dissolving each aliquot in 1 ml of ethanol. Unlabeled triolein, donated by Karlshamns (Columbus, OH) was assayed and contained 90.5% oleic acid, 4.9% linoleic acid, 3.0% stearic acid, 0.7% palmitic acid, and 0.6% linolenic acid. Meals were prepared individually with measured amounts of food obtained from a local grocery. Nutritional information was obtained from standard tables.

Plasma oleate and palmitate concentrations and oleate SA were determined by a modification (24) of a published HPLC technique (25) using [$^2H_{31}$]palmitate as an internal standard. Plasma insulin (26), C-peptide (27), glucagon (28), GH (29), and cortisol (Cortisol MAIA kit, Serono, Braintree, MA) concentrations were determined by RIA. Plasma glucose concentrations were determined by a YSI glucose analyzer (Yellow Springs, OH). The unlabeled triolein was weighed to within 0.1 g of the necessary amount for each study meal in a clean, tared milk shake container. [1-^{14}C]triolein (90 μCi) was added to the triolein and mixed with a stir bar for 5 min. A 100 L aliquot of this mixture was stored in a polystyrene tube at −20°C until it was assayed for oleate SA as described previously (30). The remainder of the milk shake ingredients (nonfat strawberry yogurt, skim milk, and frozen strawberries) were blended together and then added to the triolein. The milk shake was kept cold and shaken by hand immediately before serving to ensure a homogeneous mixture.

Total body fat and fat-free mass were determined by dual energy X ray absorptiometry (Lunar Radiation, Madison, WI) (18). Extracellular water was estimated using the bromide space technique (31). Total body water was determined by ^3H_2O dilution (32), and BCM (33) was calculated as

$$\text{BCM} = \frac{(\text{total body water} - \text{extracellular water})}{0.72}$$

The 4-h postprandial insulin secretion rates were calculated with the use of the Eaton model of insulin secretion (34) from plasma C-peptide concentrations and extracellular water measurements.

Protocol. Each subject consumed all meals as prepared in the research kitchen of the General Clinical Research Center for 2 wk before the study. The diet matched their habitual food preferences and therefore provided 40–45% of total calories as fat, 35–40% as carbohydrate, and 20% as protein. Energy intake was adjusted to achieve weight maintenance over the 2-wk period. Each volunteer was admitted to the General Clinical Research Center on the morning of the overnight study and was provided with her usual lunch at noon. A retrograde catheter was placed in a dorsal hand vein, and the hand placed in a hot box set at 55°C to obtain arterialized blood samples (35). A second catheter was placed in a contralateral forearm or ipsilateral antecubital vein and kept patent with a controlled infusion of 0.45% NaCl. An infusion of [9,10-^{3}H]oleate (0.2 μCi/min) was begun through the infusion catheter 60 min before the evening meal (−60 min) and continued throughout the remainder of the study. The study meal was consumed over 20 min beginning at 1800 (time 0 min). This meal contained 33% of each individual's daily, weight maintenance, energy intake (which was comparable in all three groups) and consisted of 30% fat, 50% carbohydrate, and 20% protein with essentially all of the fat as triolein in the milk shake. The mixed meal consisted of corn flakes with sugar and skim milk, Egg-Beaters, and canned peaches. After consumption of the mixed meal, each subject drank the entire shake including that scraped from the lid and container.

Blood samples were collected every 10 min from −30 to 60 min, every 30 min from 60 to 360 min (2400), and every 60 min from 360 to 840 min (0800). Blood samples were immediately placed in ice, and the plasma separated by spinning in a refrigerated centrifuge within 30 min. Plasma was then immediately transferred to polystyrene tubes and frozen at −20°C. As soon as possible, the samples were transferred to a freezer where they were

kept at −80°C until assayed. In our experience, samples handled in this manner do not undergo in vitro hydrolysis of TGs if heparin is not administered to the subject. Plasma oleate and palmitate concentrations, [^{3}H]oleate and [^{14}C]oleate SA, and glucose concentrations were measured on each sample. Plasma insulin and C-peptide concentrations were determined premeal and postprandially every 30 min for 4 h. Plasma glucagon, cortisol, and GH concentrations were determined before the meal and at 840 min.

Statistical analysis and calculations. Systemic total oleate R_a was calculated with the use of non–steady-state equations (30). Meal oleate R_a was calculated as

$$\text{meal oleate } R_a = \frac{\text{plasma } [^{14}\text{C}]\text{oleate SA} \times \text{total oleate } R_a}{\text{meal } [^{14}\text{C}]\text{oleate SA}}$$

Adipose tissue lipolysis is probably the only source of FFA release in the postabsorptive state; however, in the postprandial state, FFA may appear in the circulation from the hydrolysis of TGs absorbed from the meal (21,22). In our studies, the [^{3}H]oleate tracer measures total oleate R_a. If [^{14}C]oleate appears in the plasma space, it must have originated from meal [^{14}C]triolein. The ratio of plasma [^{14}C]oleate SA to meal [^{14}C]oleate SA is a measure of the fraction of total oleate R_a originating from the meal. For example, if the plasma [^{14}C]oleate SA is equal to the meal [^{14}C]oleate SA (i.e., ratio = 1.0), 100% of oleate flux is of meal origin. Likewise, if plasma [^{14}C]oleate SA is 50% of the meal [^{14}C]oleate SA, 50% of oleate flux is of meal origin, and 50% is endogenous. Endogenous oleate R_a was calculated as the difference between total oleate R_a and meal oleate R_a.

All data are presented as means ± SE. Statistical comparisons between groups were made using a one-way ANOVA and subsequent Newman-Keulstest.

RESULTS

Subject characteristics. The three groups of subjects were well-matched for age, and upper body obese and lower body obese women had comparable amounts of body fat (Table 1). WHRs were selected to be different in the two groups of obese women; the mean WHR in nonobese women was comparable to that observed in lower body obese women. BCM (presumably representing metabolically active tissue) was ~20% less in nonobese women than in upper body obese women; however, the differences did not reach statistical significance (P = 0.09, ANOVA).

Plasma glucose and hormone responses. The premeal and postprandial plasma glucose concentrations were similar in the three groups of women (Fig. 1*A*). The plasma insulin responses to the study meal are shown in Fig. 1*B*. The premeal and peak postprandial plasma insulin concentrations were greater (P = 0.001) in upper body obese women than in lower body obese and nonobese women, whose values were not statistically different. Peak plasma insulin concentrations occurred at 40–50 min and returned to premeal levels within 240–360 min. Postprandial insulin secretion calculated by the Eaton model was greatest in upper body obese women, least in nonobese women, and significantly different between each group (P = 0.001). Fasting plasma insulin concentrations followed the same pattern and were significantly different between each group (P = 0.001) (Table 2).

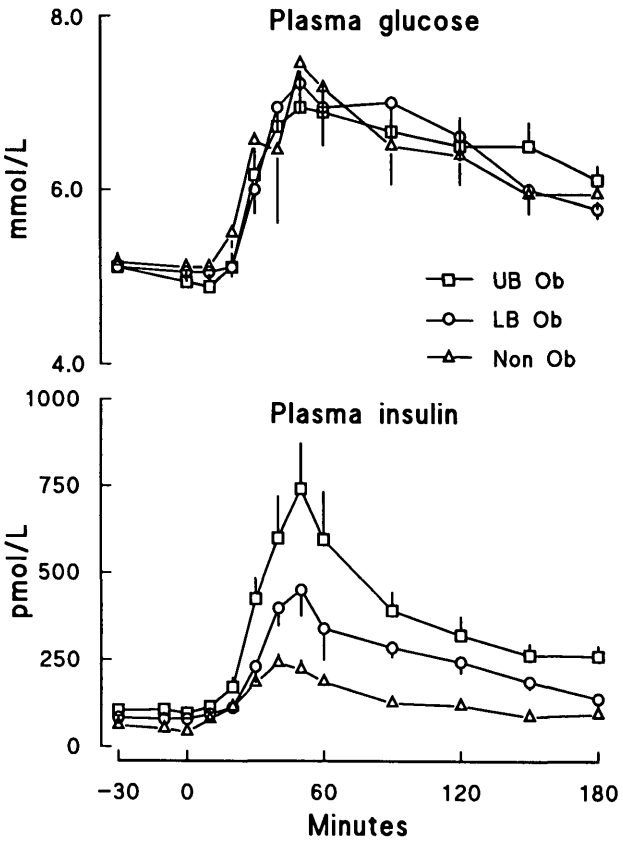

FIG. 1. Plasma glucose and insulin concentrations in response to the consumption of a mixed meal at time 0 in upper body obese (*UB Ob*), lower body obese (*LB Ob*), and nonobese (*Non Ob*) women.

Premeal plasma GH concentrations were not significantly different between groups; however, fasting concentrations were significantly greater in nonobese than in upper body obese women. No significant differences in premeal or fasting plasma cortisol or glucagon concentrations were detected.

FFA kinetics. The plasma oleate and palmitate concentrations are shown in Fig. 2. In all three groups, the premeal and early postprandial oleate and palmitate concentrations paralleled each other. Plasma oleate concentrations began to rise in all three groups before the nadir palmitate concentrations occurred. This discrepancy probably represented the entrance of meal fatty acids (which were 90% oleic acid) into the circulation, whereas endogenous palmitate release remained suppressed. Plasma palmitate concentrations rose slowly until a plateau was reached at 540–600 min.

Total oleate R_a throughout the experiment for each of the three groups is shown in Fig. 3. The premeal total oleate R_a was less (P < 0.01) in nonobese women than in upper body obese and lower body obese women whose premeal oleate flux was similar (122 ± 18 vs. 223 ± 28

TABLE 2
Hormone responses

	Upper body obese women	Lower body obese women	Nonobese women
Insulin			
Premeal (pM)	102 ± 13*	80 ± 15	47 ± 6
Peak postprandial (pM)	742 ± 134†	450 ± 81	225 ± 27
Fasting (pM)	91 ± 8†	56 ± 6†	30 ± 2†
Postprandial secretion (nmol/4 h)	268 ± 34†	208 ± 20†	121 ± 13†
GH (μg/L)			
Premeal	1.2 ± 0.3	1.6 ± 0.4	2.4 ± 0.7
Fasting	1.0 ± 0.3*	3.3 ± 1.0	4.6 ± 1.7
Cortisol (nM)			
Premeal	56 ± 7	86 ± 20	73 ± 8
Fasting	352 ± 31	231 ± 19	232 ± 28
Glucagon (ng/L)			
Premeal	172 ± 16	157 ± 8	176 ± 16
Fasting	154 ± 12	152 ± 10	152 ± 11

Data are means ± SE.
*$P < 0.05$ compared with nonobese women.
†$P \leq 0.001$ compared with other groups.

vs. 204 ± 19 μmol/min, respectively). Total oleate R_a decreased as the meal was being consumed (between 0 and 10 min), reached nadir values between 50 and 90 min, and then increased until midnight (360 min). The nadir total oleate R_a was greater ($P = 0.01$) in upper body obese women than in nonobese and lower body obese women (140 ± 21 vs. 63 ± 10 vs. 87 ± 17 μmol/min, respectively), whose values were not significantly different. Because BCM was somewhat different between groups, we analyzed the nadir oleate flux values taking BCM into consideration. Nadir oleate flux was greater ($P < 0.001$) in upper body obese women than in either lower body obese or nonobese women (5.2 ± 0.4 vs. 3.5 ± 0.4 vs. 3.2 ± 0.4 μmol · kg BCM^{-1} · min^{-1}, respec-

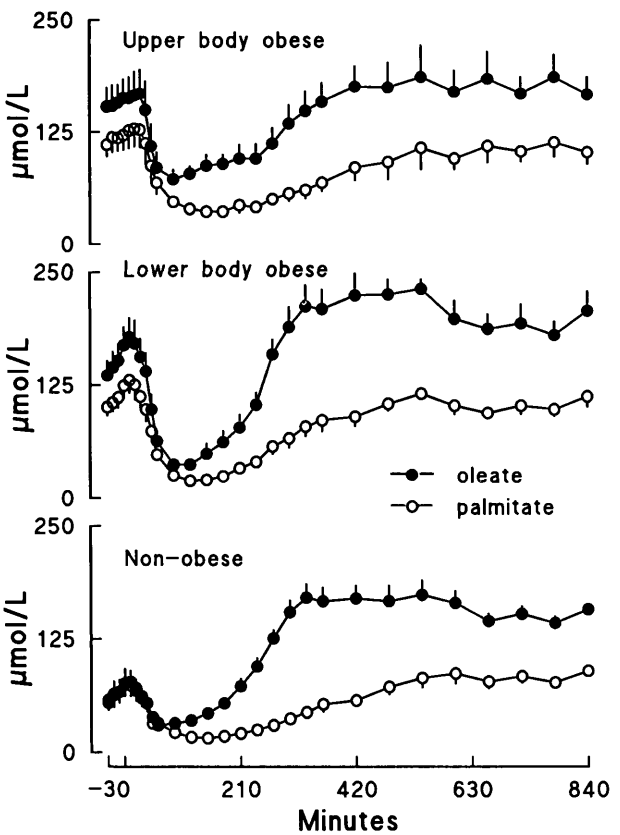

FIG. 2. Plasma oleate and palmitate concentrations in upper body obese, lower body obese, and nonobese women before and after consumption of mixed meal.

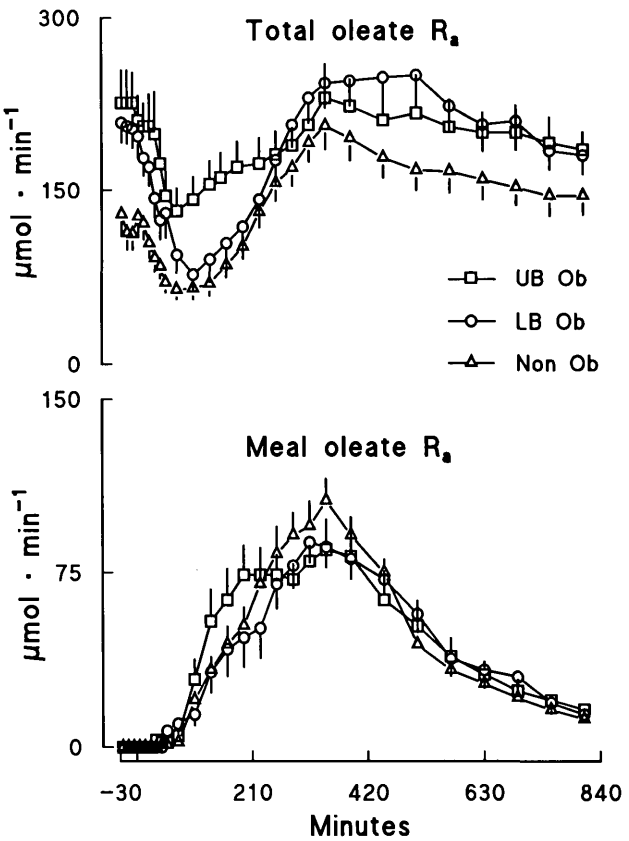

FIG. 3. Total oleate R_a and meal oleate R_a in upper body obese (*UB Ob*), lower body obese (*LB Ob*), and nonobese (*Non Ob*) women before and after consumption of mixed meal.

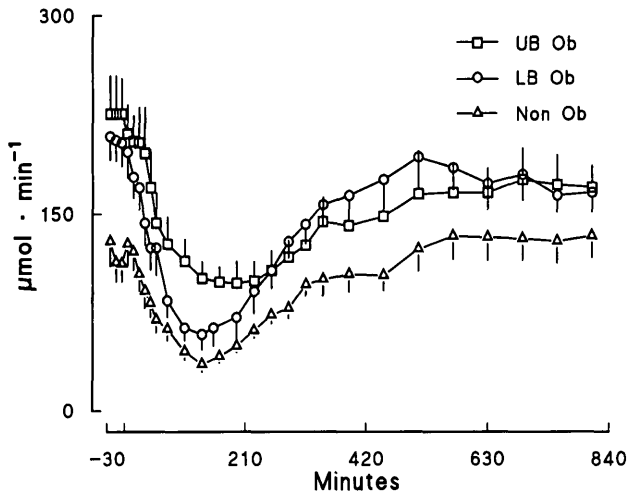

FIG. 4. Endogenous oleate R_a in upper body obese (*UB Ob*), lower body obese (*LB Ob*), and nonobese (*Non Ob*) women before and after consumption of mixed meal.

tively), whose values were not significantly different. If expressed relative to fat mass, nadir total oleate flux in upper body obese, lower body obese, and nonobese women was 3.5 ± 0.4, 2.0 ± 0.4, and 3.1 ± 0.6 μmol · kg fat^{-1} · min^{-1} (P = 0.07).

Total circulating oleate availability (area under the oleate R_a curve) during the first 5 h after meal consumption was significantly greater (P = 0.02) in upper body obese women (51.2 ± 4.9 mmol) than in nonobese women (32.7 ± 2.8 mmol). Postprandial oleate availability in lower body obese women over the same time was 41.2 ± 5.0 mmol and not significantly different from either upper body obese or nonobese values.

Meal oleate (as measured by plasma [^{14}C]oleate) began to appear in the circulation as early as 40 min after beginning meal consumption (Fig. 3), which we found remarkable considering the [^{14}C]triolein-containing milk shake was usually consumed between time 15 and 20 min. The peak meal oleate R_a was similar in upper body obese, lower body obese, and nonobese women (83 ± 12 vs. 84 ± 8 vs. 101 ± 10 μmol/min, respectively) and occurred between 300 and 360 min (Fig. 3). The quantity of meal oleate appearing in the plasma space was estimated by calculating the area under the curve of meal oleate R_a. During the 14 h after the meal, 34.4 ± 3.1, 36.0 ± 2.4, and 35.8 ± 2.5 mmol of meal oleate appeared as circulating FFA in upper body obese, lower body obese, and nonobese women, respectively (P = NS between groups). These values represent 33% of the oleate content of the meal. At 840 min, <10% of total oleate R_a was meal derived.

Endogenous oleate R_a in the nonobese and lower body obese women (Fig. 4) reached nadir values at 120 min, somewhat earlier than the nadir observed in upper body obese women. Nadir endogenous oleate R_a in nonobese and lower body obese women was less (P = 0.005) than that observed in upper body obese women (36 ± 5 vs. 61 ± 13 vs. 98 ± 15 μmol/min, respectively). Endogenous oleate R_a increased in each group until a plateau was reached at 480 min (0200).

Fasting total oleate flux was greater (although not statistically significant) in upper body obese and lower body obese women than in nonobese women (188 ± 20 vs. 182 ± 17 vs. 145 ± 18 μmol/min, respectively). Fasting endogenous oleate flux patterns were similar to the total oleate flux pattern.

DISCUSSION

Obesity is associated with resistance to the antilipolytic effects of insulin (12–15) and upper body obese appears to result in the greatest insulin resistance (15,18,19). Food consumption is the primary stimulus for insulin secretion, however, and the greater postprandial hyperinsulinemia in upper body obese women (20) might be sufficient to result in normal suppression of FFA availability. To address this issue, we measured plasma oleate flux before, during, and after an evening meal in age-matched groups of upper body obese, lower body obese, and nonobese women. As expected, the insulinemic response to the meal was greater in upper body obese women than in nonobese or lower body obese women. Despite this, nadir oleate flux in upper body obese women was approximately twice that observed in nonobese and lower body obese women. We conclude that postprandial FFA availability is greater in upper body obese than in lower body obese and nonobese women despite the exaggerated insulin secretory response to similar meals.

The failure to normally suppress postprandial FFA availability in upper body obese women may impair the ability of insulin to suppress hepatic glucose output and stimulate glucose uptake in this obesity phenotype. Although several studies have demonstrated that excess FFA availability decreases glucose disposal during hyperinsulinemia (2–11), whether less than complete suppression of FFA would impair insulin-mediated glucose uptake is unknown. Evidence indicates that it requires 2–4 h of increased FFA availability to inhibit insulin-stimulated glucose uptake (6), suggesting that preprandial FFA flux may be more important than postprandial FFA availability in influencing postprandial glucose uptake. Possibly, the inadequate suppression of postprandial FFA availability could effect hepatic glucose output. Saloranta et al. (8) found that insulin suppression of hepatic glucose output and plasma FFA was impaired in NIDDM; however, when plasma FFA concentrations were suppressed to control values with acipimox, hepatic glucose production suppressed normally. Although it could be argued that this was a direct hepatic effect of acipimox, these data are consistent with other studies demonstrating a stimulatory effect of FFA on endogenous glucose production (2,7,10,11). In this study, postprandial plasma glucose concentrations in upper body obese women were normal but at the expense of marked hyperinsulinemia. This increased insulin secretion in upper body obesity may be necessary to adequately suppress postprandial hepatic glucose production and stimulate glucose uptake in the presence of higher premeal and postprandial FFA flux.

Plasma FFA flux (17) and adipose tissue FFA release

(22) decrease in lean and obese individuals postprandially. Nestel et al. (17) reported that in obese adults the compensatory hyperinsulinemic response to glucose ingestion reduced FFA flux to normal values. Subsequently, however, Coppack et al. (22) found greater postprandial plasma FFA concentrations and greater adipose tissue FFA release in obese than in lean volunteers. Our results may provide some insights into the reasons for these discrepant conclusions. Of subjects studied by Coppack et al., 6 of 8 had NIDDM or polycystic ovarian disease (conditions accompanied by insulin resistance) and most had high WHRs. Conversely, only 1 of 6 obese subjects studied by Nestel et al. had NIDDM (no WHRs were reported). Possibly, the majority of obese volunteers in the later study were lower body obese. If this were true, the relatively normal postprandial suppression of FFA flux observed by Nestel et al. (17) would be consistent with our findings. Thus, in addition to the metabolic differences between upper body obese and lower body obese women reported previously (15,20,37, 38), greater postprandial FFA availability can be included as a potentially important pathophysiological abnormality in upper body obesity.

Our studies are the first to document that meal fatty acids rapidly appear in plasma FFA and that 33% of meal TG fatty acids enter the FFA pool but do not address the mechanism of the entry of meal TG oleate into the plasma FFA pool. It seems unlikely that free oleate directly enters the plasma space during meal absorption. Early studies of chylomicron kinetics found that as intravenously administered chylomicron TGs were cleared, some of the TG fatty acids entered the plasma FFA pool (21). These investigators suggested that, during TG hydrolysis at the capillary endothelium, some of the fatty acids are not immediately transported into cells and therefore enter the circulation. The results of in vivo studies of abdominal subcutaneous adipose tissue (22) are consistent with this hypothesis. Alternatively, meal-derived FFA are possibly incorporated into newly synthesized TGs in adipocytes and then rapidly rereleased by ongoing lipolysis. If intravascular TG hydrolysis is the source of the meal-derived FFA, we suspect that chylomicron hydrolysis, which proceeds much more rapidly than VLDL hydrolysis (38), is the source. In addition, VLDL TG clearance does not appear to involve FFA release (39).

The inclusion of a meal fatty acid tracer in these studies permitted us to trace the appearance of meal fatty acids in the plasma FFA pool and allowed a more reliable estimate of nonmeal (endogenous) FFA R_a (Fig. 4). These data suggest that differences in endogenous FFA release, rather than differences in meal oleate R_a, are responsible for the greater postprandial FFA availability in upper body obese women. The plasma oleate and palmitate concentration data are consistent with this conclusion (Fig. 1). Thus, we conclude that a reduced ability of insulin to suppress adipose tissue FFA release is primarily responsible for the differences we have observed between upper body obese, lower body obese, and nonobese women. Note that measurement of total FFA R_a alone after ingestion of a mixed meal may not provide an adequate index of the regulation of adipose tissue lipolysis because plasma FFA may originate both from the meal and from adipose tissue lipolysis.

The mixed meal ingested by our research volunteers contained triolein (>90% of fatty acids as oleate) as virtually the only source of fat. This approach allowed us to more reliably distinguish the contribution of meal fatty acids to plasma fatty acids; however, some limitations may exist in extrapolating this data to mixed meals containing a variety of TG fatty acids. Significant differences between meal fatty acid absorption and oxidation (40) have been reported, and slight differences in tissue uptake of different FFA may exist (41). Although the overnight nature of this study allowed us to observe the transition from the preprandial to postprandial and postabsorptive phases of FFA metabolism, the stress of frequent arousals caused by repeated blood sampling may have influenced the study results. For example, in previous studies we (15,18) and others (19) have observed that fasting plasma FFA flux is greater in upper body obese women than in lower body obese or nonobese women. In contrast, fasting oleate flux was not significantly different between groups in this study. Substantial intra-individual variability occurs in fasting FFA flux (42), and the need to draw blood samples overnight might have aggravated this variability. Although our overnight FFA flux values may not be quantitatively what would be seen in the unaroused state, the patterns we observed are probably representative of those that occur under more usual circumstances.

When expressed as total oleate flux or flux relative to metabolically active tissue, meal suppression of FFA availability was reduced only in upper body obese women. In contrast, when nadir total oleate flux was expressed relative to total fat mass, upper body obese and nonobese women were more alike, and lower body obese women had the greatest (although not statistically different) suppression. The dramatic differences in postprandial plasma insulin concentrations preclude direct, between-group comparisons of insulin regulation of effective adipose tissue lipolysis, however. Unfortunately, these experiments were not designed to determine whether between-group differences in postprandial suppression of FFA release were the result of generalized or regional variations in lipolysis. The data of Coppack et al. (22) suggest that abdominal subcutaneous adipose tissue FFA release may be much less suppressible in upper body obese than in nonobese humans. This would be consistent with our finding that upper body subcutaneous adipose tissue in upper body obese women is metabolically abnormal (43). Definitive conclusions regarding the importance of excess total fat versus regional fat (e.g., abdominal subcutaneous or visceral) in postprandial FFA metabolism will probably require regional catheterization experiments combined with meal studies.

In summary, we have found that upper body obese women have a significantly greater postprandial insulinemic response than lower body obese and nonobese women. Despite this, FFA flux is not suppressed to levels seen in lower body obese and nonobese women. Meal fatty acids contributed a substantial amount to circulating FFA in the postprandial state; however, the proportion

was comparable in all three groups. We conclude that impaired suppression of adipose tissue lipolysis is a potentially important abnormality present in upper body obesity and that this may be relevant to the ability of insulin to regulate postprandial glucose metabolism.

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