Influence of human obesity on the metabolic fate of dietary long- and medium-chain triacylglycerols

Christophe Binnert, Christiane Pachiaudi, Michel Beylot, Didier Hans, Jacques Vandermander, Philippe Chantre, Jean-Paul Riou, and Martine Laville

ABSTRACT The metabolic fate of an oral long-chain-triacylglycerol (LCT) load and of a mixed oral LCT and medium-chain-triacylglycerol (MCT) load was followed for 6 h in eight control and eight obese subjects with normal postabsorptive triacylglycerol concentrations. Labeled triacylglycerol and indirect calorimetry were used. Results showed that LCTs were less oxidized in obese than in control subjects (3.2 ± 0.5 compared with 6.0 ± 0.4 g, P < 0.01). Moreover, the amount of LCT oxidized was negatively correlated with fat mass (r = −0.77, P < 0.01). Appearance in plasma of dietary triacylglycerol-derived long-chain fatty acids was blunted in obese subjects and it was negatively related to fat mass (r = −0.84, P < 0.01) and positively to LCT oxidation (r = 0.70, P < 0.01). On the contrary, MCT oxidation was not altered in obese subjects compared with control subjects. Furthermore, the proportion of MCTs oxidized was higher in both groups compared with LCTs (x ± SEM: 57.5 ± 2.6% compared with 15.2 ± 1.6%, P < 0.01, n = 16). Our conclusion is that obesity is associated with a defect in the oxidation of dietary LCTs probably related to an excessive uptake by the adipose tissue of meal-derived long-chain fatty acids. MCTs, the oxidation of which is not altered in obesity, could therefore be of interest in the dietary treatment of obesity.

KEY WORDS Oral lipid load, fatty acid oxidation, medium-chain triacylglycerol, obesity, long-chain triacylglycerol, women

INTRODUCTION Obesity is characterized by an increase in lipid stores. It is generally associated with enhanced lipid consumption, which contributes to its development (1). Thus, the study of the metabolic fate of dietary lipids in obese subjects is crucial in the understanding of this disease. However, few studies have been concerned with dietary fat metabolism during obesity. Moreover, in most of these studies, patients had hypertriglyceridemia, a condition that does not allow for testing the effect of obesity per se (2–4). Many of these studies reported the evolution of postprandial lipid concentrations, but their approach did not allow exogenous lipids to be distinguished from endogenous ones. This information could only be obtained by using labeled triacylglycerol. Moreover, with use of breath carbon dioxide tests and indirect calorimetry measurements, exogenous and total lipid oxidation can be calculated. Using [13C]triolein, we recently reported the different steps involved in the metabolism of orally ingested fat from intravascular release to oxidation.

Medium-chain triacylglycerols (MCTs) are metabolized differently from LCTs. After absorption by enterocytes, medium-chain fatty acids are released in the portal blood and taken up by the liver (7), where they are largely oxidized. Their intramitochondrial transport does not require carnitine palmitoyltransferase (8) and therefore does not represent a limiting step. Consequently, MCTs are oxidized more than are LCTs (9). For these reasons, MCTs could be useful in the dietary treatment of obesity.

Therefore, our aim was to determine the effect of obesity on the different steps of dietary fat metabolism. Subjects were chosen so that they had large differences in fat mass, but no lipid disorders, to test the effect of obesity per se. Triacylglycerol labeled with stable isotopes was used in combination with indirect calorimetry measurements. The metabolism of LCTs was compared with that of a mixture of MCTs and LCTs (1:1) to evaluate the influence of a substitution of LCTs by MCTs. Some data from the control subjects presented in this paper were already reported (5).

SUBJECTS AND METHODS

Materials

[1,1,1-13C3]Triolein [99 atom % (AP) 13C] and [1,1,1-13C3]trioctanoin (99 AP 13C) were purchased from Eurisotop (Saint Aubin, 69008 Lyon, France. E-mail: binnert@cimac-res.univ-lyon1.fr.

1 Address reprint requests to C Binnert, INSERM U449, Rue G Paradin, 69008 Lyon, France. E-mail: binnert@cimac-res.univ-lyon1.fr.

Received February 28, 1997.

Accepted September 26, 1997.
France). MCTs were composed of trioctanoin and tridecanoin (2:1; Arkopharma, Carros, France). Thin-layer chromatography was performed on 60 G silica gel plates (Merck, Darmstadt, Germany). Triheptadecanoin acid and heptadecanoin acid were from Sigma (St Louis). All solvents were from Merck. Boron trifluoride methanol (Sigma) was used for fatty acid methyl ester preparation.

The labeled oil was prepared by adding 200 mg [1,1,1-13C3]triolein to 30 g olive oil; 150 mg [1,1,1-13C3]trioctanoin was added to a 30-g mixture of 50% (by wt) olive oil and 50% MCTs (2:1, trioctanoate and tridecanoate). Tracers were carefully homogenized. An aliquot of the labeled oil was collected to assess the isotopic enrichment.

Subjects

Eight obese [body mass index (BMI; in kg/m2) > 26] and eight normal-weight control women participated in this study. The characteristics of the subjects are presented in Table 1. None of the control subjects had a familial or personal history of dyslipidemia, obesity, or diabetes, or was taking any medication except for oral contraceptives. Three of the obese subjects had a familial history of obesity, one was taking an antihypertensive drug, and none was diabetic. Obese subjects were chosen to have normal postabsorptive concentrations of triacylglycerol and fatty acids. All subjects gave their written consent to the study after being informed of its nature, purpose, and possible risks. The experimental protocol was approved by the ethics committee of Hospices Civils de Lyon according to the Huriet law.

Total lean body mass and total fat mass were evaluated by using a dual-energy X-ray absorptiometer (Hologic QDR 2000; Hologic Inc, Waltham, MA). The in vivo, short-term reproducibility of these measurements was assessed in control and obese subjects. The CV between two measures was determined for fat mass and for fat-free mass. For fat mass, the CVs were 1.9 ± 2.1% and 1.8 ± 1.6% for obese and control subjects, respectively (NS, Student’s t test). For fat-free mass, CVs were 1.9 ± 2.0% and 1.6 ± 1.7% for obese and control subjects, respectively (NS, Student’s t test). These results are comparable with those reported in the literature (10).

Experimental protocols

Each subject underwent the LCT and MCT-LCT experiments, which were done in random order and separated by an interval ≥ 1 wk. All experiments were performed with subjects in the postabsorptive state after an overnight fast. An indwelling, nonheparinized in 4 °C. Plasma was then stored at −20 °C until the determination of metabolite and insulin concentrations. In the LCT experiment, additional blood samples were collected at each sample time in tubes with EDTA and kept at 4 °C to prepare chylomicrons and VLDL by ultracentrifugation as described previously (5). Respiratory exchange measurements (Deltrac metabolic monitor; Datex, Helsinki) were used to estimate total lipid oxidation rate and energy expenditure rate as described previously (5). Urine was collected in the basal state and from 0 to 360 min after the start of the experiments to determine nitrogen excretion. Two samples of expired gases were obtained in the basal state to determine basal 13CO2 abundance, then expired gas samples were collected each 30 min as described previously (11).

Analytic procedures

Plasma glucose, triacylglycerol, β-hydroxybutyric acid (12), and fatty acid (13) concentrations were measured by enzymatic methods. Plasma insulin was measured by radioimmunoassay (14). Urinary nitrogen was determined by chemiluminescence (Antek 703C; Sopares, Paris). Because MCTs are mostly oxidized in the liver, plasma medium-chain fatty acids were not extracted. In the LCT experiments, lipids were extracted from chylomicrons, VLDL, or plasma according to the method of Bligh and Dyer (15) by using chloroform:methanol (1:2, vol:vol). Triheptadecanoin acid and heptadecanoin acid were added as internal standards. Fatty acids [retardation factor (RF) = 0.22] and triacylglycerol (RF = 0.5) were separated by thin-layer chromatography on 60 G silica gel plates with hexane:diethyl ether:acetic acid (80:20:1, by vol) as the mobile phase (16). Fatty acids and triacylglycerol were scraped off the plate and then treated with heptane/methanol (250 μL) (20:80, vol:vol) and 14% boron trifluoride in methanol (250 μL) at 100 °C for 30 min for fatty acid methyl ester preparation (17).

Gas chromatography–isotope ratio mass spectrometry analysis

During the LCT experiment, analysis of the isotopic enrichments of oleic acid from plasma fatty acids and from triacylglycerol in chylomicrons and VLDL was performed by using an isotope ratio mass spectrometer (IRMS, SIRA 12; VG Isogas, Middlewich, United Kingdom) interfaced with a gas chromatograph (5890A; Hewlett Packard, Evry, France) equipped with a Ross injector (230 °C) and a capillary column (SP2380, 0.25 mm internal diameter × 30 m; Supelco, Bellefonte, PA) as described previously (5). Oven temperature was maintained at 170 °C for 3 min, then raised 15 °C/min to 200 °C and then raised 30 °C/min to 250 °C, at which it was maintained for 5 min. Oleate concentrations were measured by gas chromatography with an internal standard. In both experiments, the 13C enrichment of expired carbon dioxide was determined on a dual-inlet IRMS (VG Isogas) as described previously (18).

Calculations

The 13C-13C ratio of the sample and of the reference were used to calculate the δ13C‰ of the sample. The measured δ13C‰ values were transformed to δ13C AP and mole percent excess (MPE) as described previously (18). The quantity of [13C]oleate in chylomicron-triacylglycerol, VLDL-triacylglycerol, and fatty acids was determined at each point as the product of oleate concentration measured by gas chromatography and MPE [13C]oleate.

| TABLE 1 |
| Characteristics of subjects1 |
| Control | Obese |
| Age (y) | 22 (21–25) | 32.5 (23–47)2 |
| Fat mass (kg) | 15.4 (11.2–25) | 46.3 (26–54.9)2 |
| Fat-free mass (kg) | 38.3 (35.9–43.2) | 43.5 (39.8–48.2)2 |
| BMI (kg/m2) | 20.4 (18.7–25.2) | 35.5 (26.5–43.1)2 |

1 Median; range in parentheses.
2 Significantly different from control, P < 0.01 (nonparametric Mann-Whitney U test).
For the LCT experiment, the oxidation of the triacylglycerol load was calculated by using a formula described previously (5). For the MCT-LCT experiment, this formula was adapted to MCT oxidation as follows:

\[
\text{Exogenous lipid oxidized (g/min)} = (1)
\]

\[
\left(\frac{\text{[(AP CO}_2(t) + \text{AP CO}_2(t_{-30})]/2} - \text{AP CO}_2(t_{0})}{\text{[AP TG}_{\text{load}} - \text{AP CO}_2(t_{0})]/100} \times \text{VCO}_2 \times \left(\frac{15.15}{499}\right) \times 29 \times 22.4 \times 0.8\right)
\]

where \( \text{AP CO}_2(t) \) is the AP value of the expired CO\(_2\) at time \( t \) (the end of each 30-min period), \( \text{AP CO}_2(t_{0}) \) is the AP value of the expired \( CO_2\) at time \( t_0 \), \( \text{AP TG}_{\text{load}} \) is the AP value of the labeled oil load analyzed by IRMS, and \( \text{VCO}_2 \) is the production rate of carbon dioxide. Four hundred ninety-nine is the mean molecular weight of ingested MCT composed of two-thirds trioctanoate and one-third tridecanoate. Twenty-nine is the mean number of carbons in MCT. The mass in grams of the labeled MCT moiety could not be differentiated) during the MCT-LCT experiment, this formula was adapted to MCT oxidation were determined by using a stoichiometric equation for the ingested medium-chain fatty acid mixture, which was composed of two-thirds trioctanoate and one-third tridecanoate: \( C_{29}H_{54}O_6 + 79/2O_2 \rightarrow 29CO_2 + 27H_2O \). These \( \text{VCO}_2 \) and \( \text{VCO}_2 \) values were subtracted from total \( \text{VCO}_2 \) to calculate LCT oxidation (endogenous and exogenous LCT oxidation, which could not be differentiated) during the MCT-LCT experiment by using the usual formula. Total lipid oxidation was calculated as the sum of LCT and MCT oxidation.

Diet-induced thermogenesis (DIT) was calculated as follows:

\[
\text{DIT} \, \% = \frac{[(\text{postprandial EE} - \text{BMR})/\text{energy (kJ) of the load}] \times 100}{30 \times 360 \times 100}
\]

where EE is energy expenditure and BMR is basal metabolic rate.

**Statistical analysis**

Correlations and incremental areas under the curve (AUC\(_i\), area under the curve above basal values) were calculated with Microsoft Excel 5.0 (by using the trapezoidal method for the AUC calculation; Microsoft, les Ullis, France). Results are expressed as means \( \pm \) SEMs. Comparison of values was done by nonparametric tests. When necessary, the respective effects of diet and subject were analyzed by a two-factor analysis of variance (ANOVA).

**RESULTS**

**Basal state**

**Hormonal and metabolic measures**

In the basal state, only insulinemia was greater in obese subjects than in control subjects: 95 \( \pm \) 17 compared with 47 \( \pm \) 3 pmol/L, \( P < 0.01 \). Glycemia (4.66 \( \pm \) 0.25 compared with 4.56 \( \pm \) 0.10 mmol/L), fatty acids (450 \( \pm \) 56 compared with 405 \( \pm \) 47 mmol/L), triacylglycerol (920 \( \pm \) 110 compared with 752 \( \pm \) 71 mmol/L), and \( \beta \)-hydroxybutyrate (61 \( \pm \) 10 compared with 68 \( \pm \) 8 mmol/L) between obese and control subjects, respectively, were not significantly different. Energy expenditure was greater in the obese subjects (276 \( \pm \) 17 compared with 226 \( \pm \) 8 kJ/h, \( P < 0.05 \)).

**LCT experiment**

**Hormonal and metabolic measures**

After the LCT load, triacylglycerol increased in both groups (Figure 1) and no significant difference in triacylglycerol AUC\(_i\) was observed between groups. After an early peak, fatty acids increased progressively during the test to reach concentrations of 651 \( \pm \) 99 and 731 \( \pm \) 79 mmol/L at 360 min in the control and obese groups, respectively. Glycemia was not increased by the lipid load. A slight but significant insulin peak (69 \( \pm \) 6 pmol/L at 60 min compared with 47 \( \pm \) 3 pmol/L in the basal state, \( P < 0.05 \)) was observed in the control group but not in the obese group. Then, insulin decreased in both obese and control groups (66 \( \pm \) 10 and 46 \( \pm \) 6 pmol/L at 360 min, respectively).

**Appearance of label in chylomicron-triacylglycerol, fatty acids, and VLDL-triacylglycerol**

The evolution of the \(^{13}\text{C}\) enrichment of oleate in chylomicron-triacylglycerol, fatty acids, and VLDL-triacylglycerol in the control and the obese groups is shown in Figure 2. The appearance of the label in chylomicron-triacylglycerol was similar in both groups, as shown by the lack of difference of AUC\(_i\) of \([^{13}\text{C}]\)oleate in chylomicron-triacylglycerol between groups (1192 \( \pm \) 177 and 927 \( \pm \) 121 \( \mu \)mol·h/L for control and obese groups, respectively; NS). The appearance of \([^{13}\text{C}]\)oleate in VLDL-triacylglycerol was not different in control and obese subjects as measured by the AUC\(_i\) of \([^{13}\text{C}]\)oleate in VLDL-triacylglycerol (328 \( \pm \) 59 and 282 \( \pm \) 78 \( \mu \)mol·h/L for the control and obese groups, respectively). On the contrary, the appearance of \([^{13}\text{C}]\)oleate in fatty acids was dramatically reduced in the obese group compared with the control group: AUC\(_i\) of \([^{13}\text{C}]\)oleate in fatty acids, 1.8 \( \pm \) 0.4 compared with 4.4 \( \pm \) 0.4 \( \mu \)mol·h/L (\( P < 0.01 \)). At the plateau, the ratio of enrichment between fatty acids and chylomicron-triacylglycerol was largely decreased in the obese...
A correlation was found between the AUC\textsubscript{i} of [\textsuperscript{13}C]oleate in fatty acids and total lipid oxidation expressed according to fat-free mass (\textit{r} = 0.5 compared with 6.0 \% in the basal state, \( P < 0.05 \) but not in the obese subjects (105 \pm 5 compared with 95 \pm 17 pmol/L, NS).

\section*{Exogenous lipid oxidation, total lipid oxidation, and DIT}

Cumulative values of exogenous lipid oxidized for 6 h are shown in Figure 3. Exogenous lipid oxidation was dramatically reduced in the obese compared with the control subjects (3.2 \pm 0.5 compared with 6.0 \pm 0.1 g, \( P < 0.01 \)). Despite this effect, total lipid oxidation measured for 6 h was greater in the obese subjects (18.4 \pm 1.1 compared with 14.0 \pm 1.4 g, \( P < 0.05 \)). However, total lipid oxidation expressed according to fat-free mass was not significantly different between groups (0.36 \pm 0.04 and 0.42 \pm 0.03 g/kg fat-free mass for the control and obese groups, respectively). DIT (expressed as a percentage of energy ingested) was lower in obese subjects than in control subjects: 5.6 \pm 1.2\% compared with 9.8 \pm 0.9\% (\( P < 0.05 \)).

\section*{Relation to fat mass}

To test the influence of fat mass on the metabolism of the lipid load, we analyzed the results obtained in the whole population (\( n = 16 \)) according to fat mass. A negative correlation was found between fat mass and exogenous lipid oxidation (\( r = -0.74, P < 0.01 \); Figure 4) and the AUC\textsubscript{i} of [\textsuperscript{13}C]oleate in fatty acids (\( r = -0.84, P < 0.01 \); Figure 5). Moreover, this last correlation persisted even when the AUC\textsubscript{i} of [\textsuperscript{13}C]oleate was expressed per kilogram fat mass (\( r = -0.94, P < 0.01 \)), suggesting that this relation was not due only to the quantity of fat mass. A correlation was also found between the AUC\textsubscript{i} of [\textsuperscript{13}C]oleate in fatty acids and exogenous lipid oxidation (\( r = 0.70, P < 0.01 \)), thus arguing for a relation between lipid oxidation and the appearance in the blood of dietary fatty acids.

\section*{MCT-LCT experiment}

\subsection*{Hormonal and metabolic measures}

No change in triacylglycerol concentrations was observed after the MCT-LCT load in either group (Figure 6). Fatty acids increased progressively during the test and reached values of 573 \pm 43 \mu mol/L in control subjects and 843 \pm 33 \mu mol/L in obese subjects at 360 min (\( P < 0.02 \) and \( P < 0.05 \) compared with basal values for control and obese subjects, respectively). \( \beta \)-Hydroxybutyrate concentrations increased as soon as 60 min to 252 \pm 61 and 190 \pm 47 \mu mol/L in the control and the obese groups, respectively, and then plateaued. A small but significant insulin peak was observed at 60 min in the control subjects (70 \pm 6 compared with 47 \pm 3 pmol/L in the basal state, \( P < 0.05 \)) but not in the obese subjects (105 \pm 5 compared with 95 \pm 17 pmol/L, NS).

\subsection*{Exogenous lipid oxidation, total lipid oxidation, and DIT}

Cumulative values of MCT oxidation for 6 h were not significantly different between groups: 9.2 \pm 0.4 and 8.1 \pm 0.6 g for control and obese subjects, respectively (Figure 3). Total lipid oxidation for 6 h was also not significantly different between groups: 17.8 \pm 1.6 and 21.6 \pm 2.2 g for the control and obese subjects, respectively. DIT was slightly lower in the obese group: 7.0 \pm 2.1\% compared with 8.3 \pm 1.6\% (\( P < 0.05 \)).

\subsection*{Comparison between LCT and MCT-LCT experiments}

\subsubsection*{Metabolites}

AUC\textsubscript{i} values of fatty acids and triacylglycerol were not different between groups nor between the LCT and the MCT-LCT experiments. On the other hand, the AUC\textsubscript{i} of \( \beta \)-hydroxybutyrate was greater during the MCT-LCT experiment in both groups (\( P < 0.005 \)).

\subsubsection*{Lipid oxidation}

As shown in Figure 7, MCTs were oxidized more rapidly than LCTs. Indeed, the maximum of MCT oxidation occurred 195
observed the same trend although it was not significant: 21.2 MCT-LCT experiment than after the LCT experiment: 17.8 glycerol-derived fatty acids (represented by AUC i of [13 C]oleate) studied independently from lipid metabolism disorders. Thus, the effect of obesity per se could be increase in basal insulinemia and basal lipid oxidation rate, as is lipemia was observed in obese subjects, who had only an During both experiments, no abnormality of postprandial metabolism of dietary lipids. We showed the occur-

DISCUSSION

Our study was designed to determine the influence of obesity on the metabolic fate of dietary lipids. We showed the occurrence, in obese women, of a defect in the oxidation of exogenous LCT, a defect that was proportional to fat mass. On the contrary, we showed that the oxidation of medium-chain fatty acids was not altered in obese subjects and that total lipid oxidation tended to be higher after an MCT-LCT load than after LCT given alone. During both experiments, no abnormality of postprandial lipemia was observed in obese subjects, who had only an increase in basal insulinemia and basal lipid oxidation rate, as is usually found (21). Thus, the effect of obesity per se could be studied independently from lipid metabolism disorders.

In this study, we found that the appearance of dietary triacyl-
glycerol-derived fatty acids (represented by AUC i of [13C]oleate) was reduced in the obese group, and that this defect was related to fat mass. It could not have been due to a dilution phenomenon by endogenous fatty acids because the calculation of [13C]oleate takes this into account. The appearance of label in fatty acid is due to the hydrolysis of chylomicron-triacylglycerol by lipoprotein lipase. Thus, the lack of appearance of [13C]oleate observed in the obese subjects could have been related to a defect in chy-
lomicron-triacylglycerol clearance. This was unlikely in our study, given the absence of a difference between groups for both triacylglycerol AUC i and [13C]oleate in chylomicron AUC i.

These results are different from those of Potts et al (4), who showed a decreased removal of chylomicron-triacylglycerol in obese subjects. This could be explained by differences between the subjects in metabolic profile. Indeed, in our study, obese subjects were chosen to have normal postabsorptive triacylglycerol concentrations, whereas in the Potts et al study postabsorptive triacylglycerol concentrations were almost twofold higher in obese than in control subjects, suggesting that obese subjects already had abnormal lipid metabolism.

Our results are also different from those of Roust and Jensen (6), who found similar meal-derived fatty acid concentrations in control and obese subjects 14 h after ingestion of a mixed meal. This discrepancy may be explained by differences in protocol. In Roust and Jensen’s study, the mixed meal induced an insulin release that could have interfered with lipid metabolism. Moreover, in Roust and Jensen’s study postabsorptive oleate turnover rates were twice as high in obese as in control subjects, as were postabsorptive fatty acid concentrations. In our study, obese and control subjects had similar postabsorptive and postprandial fatty acid concentrations. Because a dissociation between fatty acid concentration and fatty acid turnover rate has never been shown, we supposed that fatty acid fluxes were also similar between obese and control subjects in our study.

Therefore, our data strongly suggest that the release of exoge-
nous fatty acids in plasma is altered in obese subjects. Because no difference in chylomicron-triacylglycerol clearance was observed, the major hypothesis to explain this phenomenon is that it is related to an increase in tissue fatty acid uptake. However, it is not known whether this uptake occurs mostly in white adipose tissue or in muscles or liver.

Because the appearance of labeled fatty acids was negatively correlated with fat mass, it could be speculated that this defect was due to an enhanced uptake of fatty acids by hypertrophic adipose tissue. However, a relation with fat mass persisted even when data are expressed per fat mass, suggesting that an increased uptake per unit of fat occurred. Because it has been shown that lipoprotein lipase activity is greater in adipose tissue of obese people than in nonobese people (22), enhanced lipoprotein lipase activity could play a role in triacylglycerol-derived fatty acid uptake, explaining the differences
between obese and control subjects. However, lipoprotein lipase may not be the only mechanism responsible for fatty acid uptake, as suggested by Marín et al (23). The acylation-stimulating protein appears to also be involved in fatty acid uptake and in adipocyte esterification of fatty acid into triacylglycerol, as suggested by Cianflone et al (24). Moreover, this protein’s plasma concentration was greater in control subjects during a high-fat meal than during a glucose load. Nevertheless, its role in this increase in fatty acid uptake during obesity remains to be determined.

Muscle may have been a site of increased uptake of fatty acids. However, muscle fatty acid uptake has been shown to be reduced with obesity in the postabsorptive state (25). Moreover, an important finding of our study was the defect of dietary triacylglycerol oxidation. Thus, if muscle was the site of the increase in fatty acid uptake, taking into account the decrease in fatty acid oxidation, a significant increase in the reesterification process should have occurred. Although this cannot be totally excluded, it is more likely that the decrease in exogenous lipid oxidation during obesity is due to a lack of supply of long-chain fatty acids for muscle. This hypothesis is supported by the strong correlation between exogenous lipid oxidation and the appearance of exogenous fatty acid ($r = 0.70, P < 0.01$).

Finally, enhanced reesterification by liver must be discussed because this phenomenon has been shown in obese subjects (26). However, in our study the appearance of labeled VLDL was similar in obese and control subjects both kinetically and by the AUC of $[^{13}C]$ oleate in VLDL.

Oxidation of the LCT load was dramatically reduced in the obese subjects (by 47%) and this defect was related to the appearance of the fat load-derived fatty acids. These results agree with those of Raben et al (27), which showed that the decrease in fat oxidation after a high-fat load was associated with low fatty acid concentrations. They also agree with our previous results in normal subjects, suggesting that dietary lipid oxidation was related to the intravascular release of dietary fatty acids (5). The defect in lipid oxidation could also have been due to an alteration of muscle oxidation. However, no relation was found between fat mass and total lipid oxidation expressed according to fat-free mass after the fat load, thus arguing for normal lipid oxidation by muscle in obesity.

We also showed that MCT oxidation, in contrast with LCT oxidation, was not altered in obese subjects. Because MCT metabolism shows large differences from that of LCT, such as portal release of fatty acids and oxidation in the liver, abnormalities observed in LCT metabolism were not seen. As already shown by Metges and Wolfram (9), MCT oxidation values over 6 h were dramatically higher than LCT values: 57% of the 15 g MCT ingested was oxidized compared with only 15% in the LCT experiment (means of the control and obese subjects). Like these authors, we also found large differences in oxidation kinetics between MCTs and LCTs. Although the AUC values of $\beta$-hydroxybutyrate concentrations during the MCT-LCT experiment were higher than during the LCT experiment, $\beta$-hydroxybutyrate concentrations did not reach supraphysiologic values.

Total lipid oxidation during the MCT-LCT experiment was higher than during the LCT experiment in both groups (although in the obese group it was not significantly so). Thus, fat balance was therefore less positive after the MCT-LCT experiment than after the LCT experiment. DIT during the MCT-LCT experiment was lower than in Seaton et al’s study (28), probably because of the smaller amount of MCT ingested (15 compared with 45 g). On the contrary, DIT after the LCT experiment was lower in obese than in control subjects. Blunted DIT in obese subjects has been shown after a glucose load (29), a mixed diet (30), and a high-protein diet (31), but to our knowledge only one study has reported blunted DIT after a pure fat load (32).

In conclusion, we report here the occurrence of a defect in dietary LCT oxidation during obesity. This defect appears to be related to an enhanced uptake of diet-derived fatty acids, probably in adipose tissue. On the other hand, MCT oxidation was unaltered in obese subjects. Thus, MCTs may be of interest in the dietary treatment of obesity. However, our study was brief and used a pure fat load. Long-term studies including mixed diets will precisely determine the role of MCTs in nutritional recommendations for obese people.

We thank M Odéon and V Chapelon for technical assistance, and the nurses at Hôpital E Herriot for assistance during the experiments. We are indebted to L Tappy for his comments about the manuscript.

REFERENCES


