

Differential oxidation of individual dietary fatty acids in humans<sup>1-3</sup>

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**ABSTRACT**

**Background:** Dietary fatty acids that are more prone to oxidation than to storage may be less likely to lead to obesity.

**Objective:** The aim of this study was to determine the effect of chain length, degree of unsaturation, and stereoisomeric effects of unsaturation on the oxidation of individual fatty acids in normal-weight men.

**Design:** Fatty acid oxidation was examined in men consuming a weight-maintenance diet containing 40% of energy as fat. After consuming the diet for 1 wk, subjects were fed fatty acids labeled with <sup>13</sup>C in the methyl or carboxyl position (10 mg/kg body wt). The fatty acids fed in random order were laurate, palmitate, stearate, oleate, elaidate (the *trans* isomer of oleate), linoleate, and linolenate blended in a hot liquid meal. Breath samples were collected for the next 9 h and the oxidation of each fatty acid was assessed by examining liberated <sup>13</sup>CO<sub>2</sub> in breath.

**Results:** Cumulative oxidation over the 9-h test ranged from a high of 41% of the dose for laurate to a low of 13% of the dose for stearate. Of the 18-carbon fatty acids, linolenate was the most highly oxidized and linoleate appeared to be somewhat conserved. <sup>13</sup>C recovery in breath from the methyl-labeled fatty acids was ≈30% less than that from the carboxyl-labeled fatty acids.

**Conclusions:** In summary, lauric acid is highly oxidized, whereas the polyunsaturated and monounsaturated fatty acids are fairly well oxidized. Oxidation of the long-chain, saturated fatty acids decreases with increasing carbon number. *Am J Clin Nutr* 2000;72:905-11.

**KEY WORDS** Lauric acid, myristic acid, palmitic acid, oleic acid, *trans* fatty acid, stearic acid, linoleic acid, linolenic acid, oxidation, dietary fatty acids, obesity

**INTRODUCTION**

The diversity in fatty acid structure resulting from differences in chain length, degree of unsaturation, and position and stereoisomeric configuration of the double bonds may affect the rate of fatty acid oxidation. Several early reports showed differences in fatty acid oxidation with use of <sup>14</sup>C-labeled fatty acids in animals (1-3). Rats were shown to oxidize linoleate more than palmitate (1). In rat liver preparations, oxidation of the various fatty acids was as follows: linoleate > butyrate > linolenate > acetate > stearate (2). In mice the order of oxidation was oleate > linoleate > stearate (3). In contrast, in rats fed a fat-free meal or just the labeled fatty acids, the oxidation of linoleate and palmitate was similar (4). The general trend in these studies was that

long-chain fatty acids were oxidized more slowly and unsaturated fatty acids were oxidized more rapidly than were saturated fatty acids. Measurement of fatty acid oxidation in rats with a more complete series of fatty acids showed that oxidation of the saturated fatty acids decreases with increasing carbon length (laurate > myristate > palmitate > stearate) (5). For unsaturated fatty acids, 24-h oxidation was in the following order: linolenate > oleate > linoleate > arachidonate. Through 7 h, the oxidation of oleate was greater than that of linolenate. Thus, the medium-chain fatty acids (8-14 carbons) were oxidized the most rapidly, with linolenate and oleate oxidation occurring nearly as rapidly.

Several studies in humans have been reported in which <sup>13</sup>C-labeled substrates were fed to study fatty acid oxidation (6-8). The first such report was one in which various <sup>13</sup>C-labeled substrates were examined for use in breath tests (7). In this study, octanoate was oxidized much faster than was palmitate. Another study from the same group used <sup>13</sup>C-labeled lipids in children to diagnose fat malabsorption (8). Octanoate was oxidized much more rapidly than was oleate, which was oxidized much faster than was palmitate. A more recent study compared fatty acid oxidation in men consuming a test diet of normal foods to which <sup>13</sup>C-labeled 18-carbon fatty acids differing in degree of unsaturation were added (6). Oxidation of oleate (18:1n-9) was greater than that of linoleate (18:2n-6), which was in turn greater than that of stearate (18:0). Therefore, considerable data in animals, and some data in humans, show that the short- and medium-chain fatty acids oleate and linolenate are oxidized rapidly, whereas the long-chain saturated fatty acids palmitate (16:0) and stearate are oxidized more slowly. Data regarding the effect of label position in humans are lacking. However, there is some evidence in humans and in rats that long-chain saturated fatty acids are only partially chain shortened (9, 10). In rats the location of label did not affect oxidation (11). The current study was undertaken to examine fatty acid oxidation in humans by using fatty acids labeled with <sup>13</sup>C in the carboxyl or methyl position and to examine the role that chain length, degree of unsaturation, and stereoisomeric configuration of the double bonds play in determining the relative rates of oxidation of individual fatty acids.

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**TABLE 1**  
Position of the  $^{13}\text{C}$  label in the fatty acids tested

Fatty acid	Carboxyl label	Methyl label
Laurate (12:0)	C-1	C-12
Palmitate (16:0)	C-1	C-16
Stearate (18:0)	C-1	C-18
Oleate ( <i>cis</i> 18:1n-9)	C-1	C-18
Elaidate ( <i>trans</i> 18:1n-9)	C-1	— <sup>1</sup>
Linoleate (18:2n-6)	C-1	C-18
Linolenate (18:3n-3)	C-1	C-18

<sup>1</sup>Not done.

## SUBJECTS AND METHODS

### Subjects

The participants in this study were 4 normal-weight, healthy men ( $67.2 \pm 2.1$  kg,  $16.8 \pm 9.7\%$  body fat,  $29.5 \pm 7.5$  y). Subjects gave informed consent by signing forms approved by the Louisiana State University Institutional Review Board.

### Protocol

For 7 d before they were administered the test fatty acid, subjects were fed a standard diet of defined composition to meet their energy requirements. After 5 d of this standard diet, breath samples were collected after consumption of the liquid meal without any added fatty acids and after consumption of the lunch meal to determine the background  $^{13}\text{C}$  contribution of the test diet. Then, a fatty acid oxidation test was performed every 2–4 d, while the subjects continued to consume the standard diet. The labeled fatty acids were administered to each subject in random order.

### Diets

The nutrient composition of the diet was similar to that of the typical American diet. The menu was formulated by using Moore's Extended Nutrient database (MENU; Pennington Biomedical Research Center, Baton Rouge, LA) to contain 15% of energy as protein, 45% as carbohydrate, and 40% as fat (42% saturated, 36% monounsaturated, and 22% polyunsaturated fatty acids), with a ratio of polyunsaturated to saturated fatty acids of 0.51. Linoleic acid constituted 91% of the polyunsaturated fatty acids, with linolenic acid (8%) and arachidonic acid (1%) accounting for the remainder. A 4-d rotating menu was used, with one menu always fed the day before the test days and another menu always fed on the test days.

Each labeled fatty acid was blended in a heated ( $85^\circ\text{C}$ ) liquid meal (Ensure; Ross Laboratories, Columbus, OH) that was allowed to cool slightly and given to the subjects as breakfast (0800). When a similar procedure was used in a study of deuterated fatty acids, the absorption of even stearate in triacylglycerol form (both the high melting point tristearin and the lower melting point mixed-acid triacylglycerol) was  $\approx 95\%$  (12). The same lunch meal was consumed on each fatty acid test day. Dinner was served at the completion of the oxidation test.

The labeled fatty acids were synthesized by commercial isotope companies (Cambridge Isotopes, Andover, MA; Isotec Inc, Miamisburg, OH; Medical Isotopes, Inc, Pelham, NH; and MSD Isotopes, Dorval, Canada) with the  $^{13}\text{C}$  label in either the carboxyl or methyl end of each fatty acid (Table 1). The chemical purity and isotopic enrichment of each substrate were checked by gas chromatography–mass spectrometry. All labeled fatty

acids used in these experiments were  $\geq 98\%$  chemically pure and isotopically enriched. The dose of the long-chain saturated  $^{13}\text{C}$ -labeled fatty acids was initially 15 mg/kg, but was subsequently reduced to 10 mg/kg body wt, which was the dose used for each  $^{13}\text{C}$ -labeled fatty acid.

### Pilot study

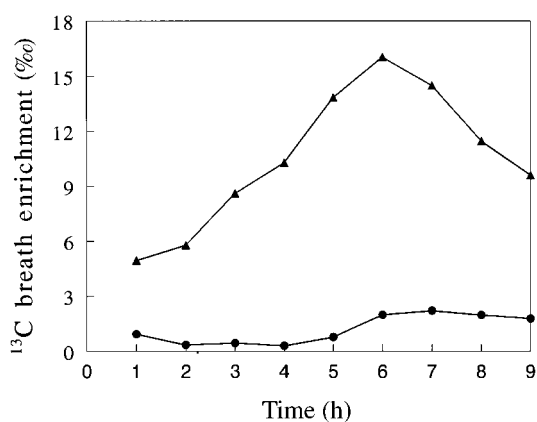
A pilot study was conducted to compare 2 methods of delivering the labeled fatty acids. On 2 separate days, 1 subject received either a capsule containing [ $^{13}\text{C}$ ]palmitate with the breakfast meal or [ $^{13}\text{C}$ ]palmitate blended in a hot ( $85^\circ\text{C}$ ) liquid meal. The capsule protocol was used previously in humans (6), but we were concerned about whether the long-chain saturated fatty acids with high melting points [eg, palmitic acid ( $62^\circ\text{C}$ ) and stearic acid ( $69^\circ\text{C}$ ), both with melting points well above body temperature] would be absorbed effectively even if a correction was made for differential absorption. Thus, to enhance absorption we also administered fatty acids in a hot blended mixture, similar to the method used by Emken et al (12) in their studies of deuterium-labeled fatty acids, in which they observed  $\approx 95\%$  absorption of long-chain saturated fatty acids.

### Breath tests

On the day of a fatty acid oxidation test, the labeled fatty acid was ingested in a hot blended meal. After subjects finished the meal, they lay down under the hood of a metabolic cart (2900Z; SensorMedics, Yorba Linda, CA) for measurements of oxygen consumption and carbon dioxide output. The flow meter was calibrated daily by using a 3.0-L syringe and the analyzers were calibrated daily by using 2 standard span gases and room air. The test was carried out for 9 h. Every 30 min a breath sample was collected for measurement of  $^{13}\text{C}$  enrichment by using a 60-mL syringe with a latex tubing mouthpiece. Background diet  $^{13}\text{C}$  enrichment was subtracted from the fatty acid generated  $^{13}\text{C}$  enrichment. The fraction of the ingested dose of  $^{13}\text{C}$  in breath carbon dioxide was calculated by using 1) the background-diet-adjusted amount of  $^{13}\text{CO}_2$  in breath, 2) carbon dioxide production measured by indirect calorimetry, and 3) the amount and enrichment of the dose administered (13).

### Mass spectroscopy

The abundance of  $^{13}\text{CO}_2$  was measured by using a dual-inlet isotope ratio mass spectrometer (Finnigan Delta S, Bremen, Germany). Breath samples from the 60-mL syringe were placed in a 20-mL evacuated tube (no additive, nonsterile) and placed in an autosampler attached to an automated breath carbon dioxide trapping device (Finnigan). The device cryogenically purifies and transfers the carbon dioxide to the mass spectrometer for isotopic analysis. Several samples of a 5%  $\text{CO}_2$  standard that had been calibrated against known  $^{13}\text{CO}_2$  standards were analyzed with each run to be sure that the trapping device was extracting carbon dioxide from the samples properly and that the mass spectrometer was giving accurate and precise enrichment measures. The measured enrichment of this standard gas was stable, giving a mean enrichment of  $-54.64 \pm 0.14\%$  over a 2-y period. If the internal precision of the mass spectrometer was  $>0.15\%$ , or if the transfer of carbon dioxide from the sample was low, the samples were reanalyzed. The CV of repeat measures of baseline  $^{13}\text{C}$  enrichment in breath samples was 0.7%. The mean ( $\pm$ SD) of 4 duplicate samples with low enrichment was  $3.02 \pm 0.10\%$ , whereas that for 4 duplicate enriched samples was  $34.19 \pm 0.44\%$ .



**FIGURE 1.** Fatty acid oxidation in a single subject after administration of labeled fatty acid in a capsule eaten with a meal (●) or blended in a hot liquid meal (▲).

### Data analysis

Cumulative fatty acid oxidation was analyzed by using a one-way analysis of variance with the general linear models procedure. Waller-Duncan K-ratio *t* tests were used to determine differences between means. A *t* test was used to determine whether there was a carryover effect of the previously ingested labeled fatty acid. Simple regression analysis was carried out to determine the relation between oxidation and chain length and degree of unsaturation. All statistical tests were conducted by using SAS 6.12 for WINDOWS (SAS Institute, Cary, NC) and significance was set at  $P < 0.05$ . Data are presented as means  $\pm$  SEMs.

## RESULTS

### Pilot study

There was a striking difference in oxidation of the labeled palmitate between the 2 methods of administration (Figure 1). When the fatty acid was blended in a hot liquid meal, the recovery of  $^{13}\text{C}$  in breath samples was  $\approx 10$  times higher than when the fatty acid was given in a capsule with a meal. The dose of the long-chain saturated fatty acids we used initially (15 mg/kg) was based on giving the fatty acid in a capsule. Thus, because of the high absorption observed when the fatty acid was given with the hot blended liquid meal, we reduced the dose to 10 mg/kg.

### Reproducibility and carryover

Reproducibility of the oxidation of fatty acids was examined for 2 fatty acids. Data on the oxidation of laurate (12:0), which is highly oxidized, and of palmitate, which is less highly oxidized, are shown in Figure 2. The repeat studies showed cumulative recoveries of 42.5% and 46.3% of the label for laurate. For palmitate the oxidation was 12.4% and 15.3% in the 2 trials, implying that oxidation was similar with repeat measurement.

To determine whether there was any carryover effect on baseline  $^{13}\text{C}$  enrichment from the previous administration of a labeled fatty acid, we examined the initial baseline enrichment on the background test diet day and on the morning of the first day a labeled fatty acid was administered (before any  $^{13}\text{C}$ -labeled fatty acids were given). The initial baseline  $^{13}\text{C}$  for the 4 subjects was  $-21.90 \pm 0.41\%$ , whereas the average for the

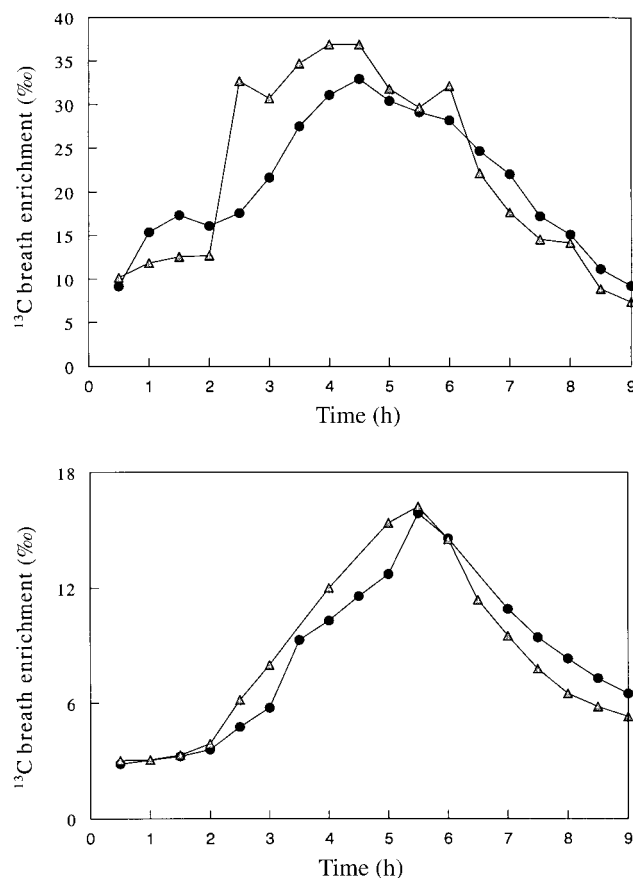
morning of all test days was  $-21.30 \pm 0.83\%$  ( $P < 0.04$ ). This difference of 0.60% in baseline breath  $^{13}\text{C}$  would have had little, if any, effect on the oxidation measures because the baseline enrichment was subtracted from each subsequent time point. In addition, an enrichment of this magnitude is low compared with the enrichment observed at each time point, except for the first few time points (Figure 3).

### Carboxyl- and methyl-labeled fatty acids

The recovery of  $^{13}\text{C}$  from the methyl or carboxyl position of each fatty acid is shown in Figure 3. The pattern of  $^{13}\text{C}$  recovery and the timing of peak enrichment of each fatty acid were similar whether the fatty acid was labeled in the carboxyl or methyl position. However, the recovery of  $^{13}\text{C}$  in breath after feeding the methyl-labeled fatty acid was  $74 \pm 16\%$  of that seen when feeding the carboxyl-labeled fatty acid. The major exception to this was oleate, for which recovery of the methyl label was  $92 \pm 18\%$  of that for the carboxyl label, significantly higher than for all other fatty acids except linolenate (methyl label recovery:  $82 \pm 0.2\%$ ). Excluding oleate, the recovery of the methyl label was  $69 \pm 11\%$  of that for the carboxyl label.

### Oxidation of individual fatty acids

The oxidation of laurate was the highest of all fatty acids tested (Figure 4). The next most highly oxidized fatty acid was linolenate (18:3n-3), followed by elaidate, linoleate, and



**FIGURE 2.** Repeat measures of laurate (top panel,  $n = 1$ ) and palmitate (bottom panel,  $n = 1$ ) fatty acid oxidation tests. ●, first test; ▲, second test.

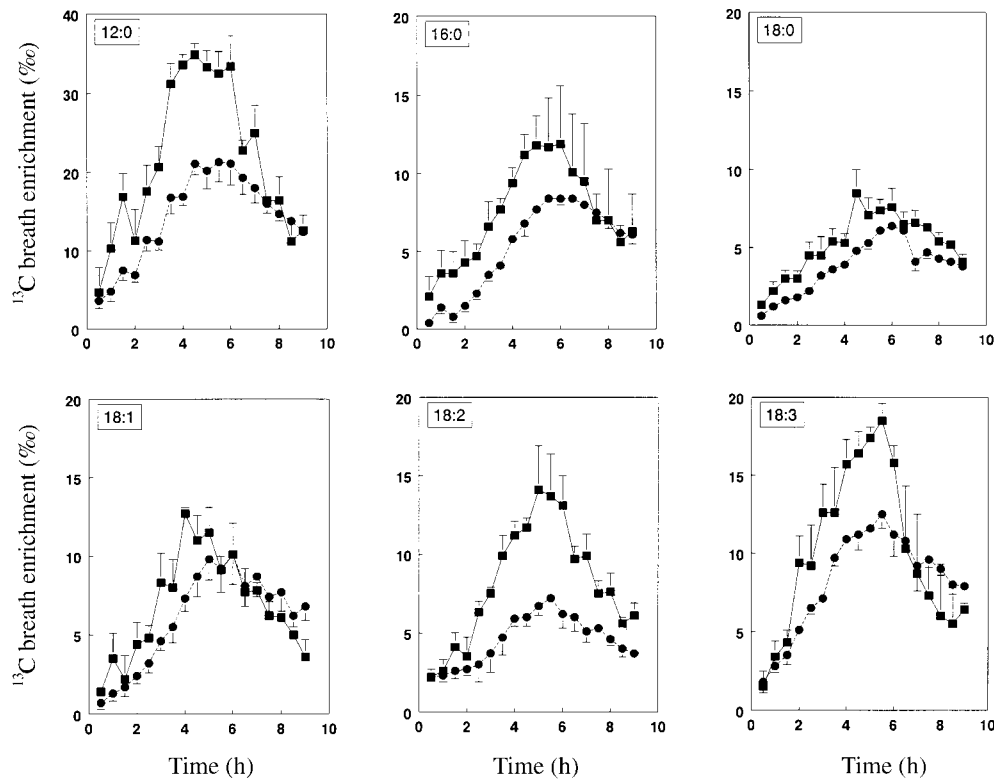


FIGURE 3. Mean ( $\pm$ SD) label recovery from carboxyl-labeled (■) and methyl-labeled (●) fatty acids (see Table 2 for sample sizes).

oleate, which showed similar rates of oxidation. The oxidation of elaidate (*trans* 18:1n-9) appeared to be slightly higher than that of oleate (*cis* 18:1n-9) and the peak oxidation appeared to be delayed by  $\approx$ 30 min (Figure 5). The 2 long-chain saturated fatty acids were the least oxidized, with only 13% of stearate oxidized over the 9-h test.

The ranking, from highest to lowest, of the oxidation of the fatty acids over 9 h was fairly consistent whether we considered the carboxyl- or methyl-labeled fatty acids or according to the overall average regardless of the label position (Table 2). For the carboxyl-labeled fatty acids, the order of oxidation from lowest to highest was as follows: laurate > linolenate > elaidate > linoleate > oleate > palmitate > stearate. When the average of the carboxyl and methyl data were used, the order was laurate > linolenate > elaidate > oleate > linoleate > palmitate > stearate.

## DISCUSSION

The results of our study of fatty acid oxidation in humans are similar to those observed in radioisotopic tracer studies of rats (5). In our studies, as well as in those of rats, oxidation of saturated fatty acids decreased with increasing carbon length (laurate > palmitate > stearate). The relation between oxidation and fatty acid carbon length was highly significant ( $r^2 = 0.94$ ; Figure 6). In the study in rats, the 24-h oxidation of unsaturated fatty acids was in the following order: linolenate > oleate > linoleate (5). These results are similar to ours, in which the oxidation of the 18-carbon fatty acids was significantly correlated with the number of double bonds (Figure 6). There was a nearly perfect linear relation ( $r^2 = 0.9997$ ) between oxidation and the number of double bonds for stearate, oleate, and linolenate. The *trans* fatty acid

elaidate was more highly oxidized and in Figure 6 appears above this regression line. The essential fatty acid linoleate appeared to be less oxidized and appears below the observed regression line. These findings are also similar to those of a 6-h study in which uniformly  $^{14}\text{C}$ -labeled fatty acids were infused into the external iliac vein in pigs (14). Although the absolute numbers in this study were different, the pattern was similar to that observed in our human feeding study, with palmitate being more highly oxidized than stearate (19.1% compared with 6.6%) and oleate more highly oxidized than linoleate (30.1% compared with 13.1%).

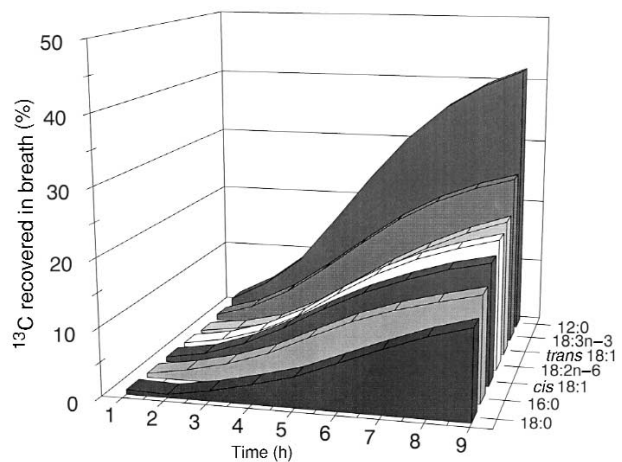
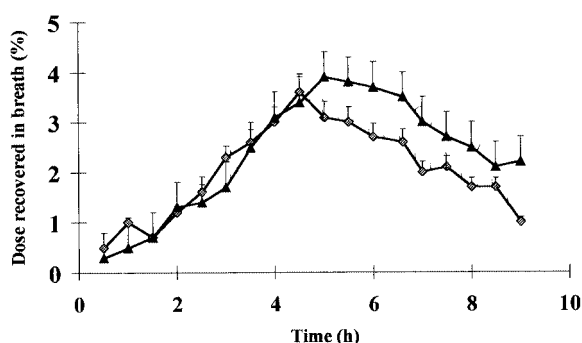


FIGURE 4. Cumulative recovery of  $^{13}\text{C}$  label in breath from each carboxyl-labeled fatty acid over 9 h.



**FIGURE 5.** Mean ( $\pm$ SD) oxidation of *cis* (◆) and *trans* (▲) 18:1n-9 (see Table 2 for sample size).

Our results are similar to those of a few studies that compared the oxidation of various dietary fatty acids in humans. In a study in which  $^{13}\text{C}$ -labeled lipids were used in children to diagnose fat malabsorption, octanoate was oxidized much more rapidly than was oleate, which was oxidized more rapidly than was palmitate (8). In an examination of parenteral administration of medium- and long-chain fatty acids, the oxidation of trioctanoin over 7.5 h was 34.7%, whereas that of triolein was 25.3% (15). We found that a medium-chain fatty acid, laurate, was oxidized more rapidly than was oleate, which was oxidized faster than was palmitate. That medium-chain fatty acids are oxidized more than are long-chain fatty acids was also found in a study of  $^{13}\text{C}$ -labeled medium- and long-chain fatty acids in parenteral feeding of patients in an intensive care unit (16). Another study in humans compared the oxidation of 3  $^{13}\text{C}$ -labeled 18-carbon fatty acids that differed in degree of unsaturation (6). Oxidation of oleate was shown to be greater than that of linoleate, which was in turn greater than that of stearate. We found that oleate and linoleate were oxidized similarly, whereas stearate was the least oxidized. Thus, the data in animals and humans are consistent with the idea that the medium-chain fatty acids (8–14 carbons), oleate, and linolenate are rapidly oxidized, whereas the long-chain saturated fatty acids palmitate and stearate are oxidized more slowly.

Although our results are similar to those of a previous study in humans in which the fatty acid was administered in a capsule with a breakfast meal (6), there are some differences. Both studies showed that stearate is the least oxidized, but the absolute rate of oxidation over 9 h was considerably lower when the fatty acid was given as a capsule than when given in a blended hot meal (3% compared with 13%). For oleate the results were similar (15% compared with 17.9%), whereas for linoleate we found a higher rate of oxidation than did Jones et al (10% compared with 19.8%). In another study examining fatty acid oxidation after administration of [ $^{13}\text{C}$ ]palmitate in capsule form, the oxidation over 9 h was only 3% (17) compared with the 16% that we observed when blending the fatty acid in a hot liquid meal. Therefore, even when differences in absorption are corrected for by measuring fatty acids in stool, considerably higher rates of fatty acid oxidation are observed when the fatty acid is blended in a hot liquid meal.

In earlier studies in which  $^{13}\text{C}$ -labeled fatty acids were used, the label was at the carboxyl end, the first carbon to be cleaved in oxidation. However, there is some evidence in humans and in rats that long-chain saturated fatty acids are only partially chain short-

ened (9, 10). Another report in rats indicated that the location of the label in palmitate did not significantly affect oxidation (11). Therefore, we compared the oxidation of carboxyl- and methyl-labeled fatty acids and found that the recovery of  $^{13}\text{C}$  in breath after feeding of the methyl-labeled fatty acid was generally  $\approx$ 30% less than recovery after feeding of the carboxyl-labeled fatty acid (Figure 3). This would be expected if the whole fatty acid chain was oxidized. The carboxyl label would be in the 1-position of the cleaved acetate unit entering the tricarboxylic acid cycle, whereas the methyl label would be in the 2-position, and hence the label would mix with other carbon units in the tricarboxylic acid cycle. The recovery of label in carbon dioxide from [ $2\text{-}^{13}\text{C}$ ]acetate was shown to be 35% lower than recovery from [ $1\text{-}^{13}\text{C}$ ]acetate in 6 human volunteers (18). In a study in rats, the recovery of label in carbon dioxide from infused [ $2\text{-}^{14}\text{C}$ ]acetate was shown to be 27% lower than from [ $1\text{-}^{14}\text{C}$ ]acetate (19).

In our studies, however, the oxidation of oleate was not as expected. The recovery of  $^{13}\text{C}$  from the methyl position of oleate was only 8% lower than the recovery from the carboxyl position. This was particularly low compared with the average difference of 31% observed for the other fatty acids. Of the 4 subjects, oxidation of the methyl-labeled oleate was equal in 1 subject, higher in 1 subject, and lower in 2 subjects compared with oxidation of the carboxyl-labeled oleate. In the 2 subjects having lower oxidation of the methyl-labeled oleate, enrichment was observed in palmitoleate (16:1), indicating chain shortening of oleate (data not shown). This also confirmed that we did feed the methyl-labeled oleate because we would not observe label in 16:1 if the label was in the carboxyl position. Additionally, we found no label in 16:1 when we fed the carboxyl-labeled oleate. There was also an indication that the oxidation of linolenate was not as expected because the difference between recovery from the carboxyl position and that from the methyl position was only 18%.

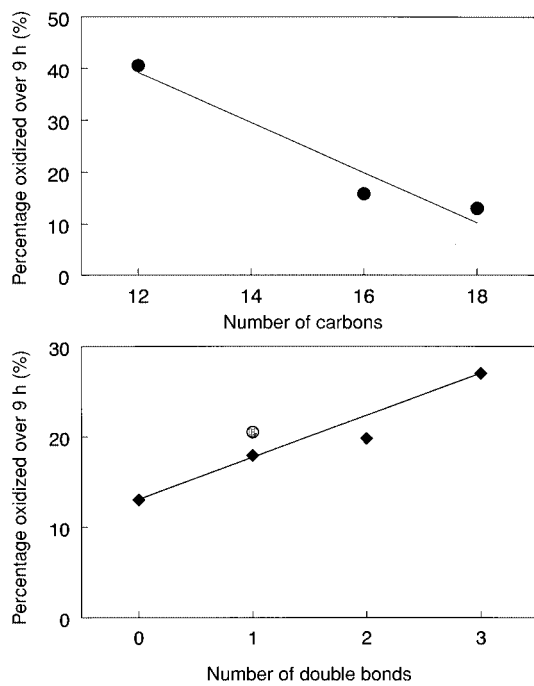
Our finding of similar rates of oxidation of  $^{13}\text{C}$ -methyl- and  $^{13}\text{C}$ -carboxyl-labeled oleate are in contrast with those obtained when [ $1\text{-}^{13}\text{C}$ ] and [ $8\text{-}^{13}\text{C}$ ]triolein were compared in rats and humans (19, 20). In humans the recovery of label in breath was 31% lower from the [ $8\text{-}^{13}\text{C}$ ]triolein than from the [ $1\text{-}^{13}\text{C}$ ]triolein, similar to what one would expect because of the position in the acetate unit (20). In rats, however, even after correction for loss from the second carbon atom in acetyl-CoA, the recovery from [ $8\text{-}^{13}\text{C}$ ]triolein was 13% lower than that from [ $1\text{-}^{13}\text{C}$ ]triolein (19). There could be a difference in metabolism of the carbons before (ie, the 8th carbon of oleate in the study reported above) and after (the 18th carbon used in the present study) the double bond of oleate that leads to differences in recovery of each label. Our data

**TABLE 2**  
Cumulative  $^{13}\text{CO}_2$  recovery in breath over 9 h<sup>1</sup>

Fatty acid	Carboxyl label	Methyl label	Average
12:0	40.6 $\pm$ 7.0 <sup>a</sup> [4]	25.0 $\pm$ 3.2 <sup>a</sup> [3]	33.9 $\pm$ 9.9 <sup>a</sup> [7]
16:0	15.8 $\pm$ 2.8 <sup>c,d</sup> [4]	12.0 $\pm$ 0.9 <sup>c,d</sup> [3]	14.2 $\pm$ 2.9 <sup>c,d</sup> [7]
18:0	13.0 $\pm$ 4.7 <sup>d</sup> [4]	9.1 $\pm$ 2.5 <sup>d</sup> [3]	11.3 $\pm$ 4.2 <sup>d</sup> [7]
<i>cis</i> 18:1n-9	17.9 $\pm$ 3.8 <sup>c,d</sup> [4]	16.2 $\pm$ 3.6 <sup>b,c</sup> [4]	17.0 $\pm$ 3.6 <sup>b,c,d</sup> [8]
<i>trans</i> 18:1n-9	20.5 $\pm$ 3.0 <sup>b,c</sup> [3]	— <sup>2</sup> [0]	20.5 $\pm$ 3.0 <sup>b,c</sup> [3]
18:2n-6	19.8 $\pm$ 5.4 <sup>b,c</sup> [3]	11.5 $\pm$ 3.9 <sup>c,d</sup> [3]	16.1 $\pm$ 6.6 <sup>c,d</sup> [6]
18:3n-3	27.0 $\pm$ 7.0 <sup>b</sup> [3]	20.1 $\pm$ 5.0 <sup>a,b</sup> [3]	23.6 $\pm$ 6.6 <sup>b</sup> [6]

<sup>1</sup> $\bar{x} \pm$  SD; *n* in brackets. Means within columns with different superscript letters are significantly different,  $P < 0.05$ .

<sup>2</sup>Not done.




**FIGURE 6.** Relation between oxidation and carbon length and between oxidation and the number of double bonds in the 18-carbon fatty acids. In the lower panel, the *trans* fatty acid is the filled circle.

suggest that for oleate, in contrast with other fatty acids, the C-18 and C-1 positions can behave the same biochemically.

A human feeding study in which the ratio of polyunsaturated to saturated fatty acids in the diet was altered suggested that polyunsaturated fatty acids are more highly oxidized than are saturated fatty acids (21). These results confirm our findings of relatively high oxidation of the polyunsaturated fatty acids linolenate and linoleate. Unsaturated fatty acids, particularly at the usual low dietary levels, may be transported from the intestine directly to the liver via the portal system (22, 23).

The rates of oxidation of individual dietary fatty acids may relate to differences in weight gain observed when different types of fat are fed to animals. The unsaturated fatty acids are more highly oxidized than are the saturated fatty acids; thus, mice fed corn oil, which is high in polyunsaturated fatty acids, might be expected to gain less weight than mice fed beef tallow, which is high in saturated fatty acids (24). Our finding that linolenate, an *n*-3 fatty acid, is highly oxidized is consistent with this idea (25, 26). A higher oxidation of the *trans* fatty acid elaidate than of oleate could explain the lower epididymal fat pad and body weight in mice fed a diet high in *trans* fatty acids than in mice fed a similar *cis* fatty acid diet (27). The very high oxidation of the medium-chain fatty acid laurate could also explain the finding that rats infused with medium-chain triacylglycerol gained one-third less weight than did rats infused with long-chain triacylglycerol emulsions (28).

In summary, this study is the most complete investigation to date of the oxidation of individual fatty acids in humans. Laurate, a medium-chain fatty acid, was the most highly oxidized fatty acid, followed by the unsaturated fatty acids; the long-chain saturated fatty acids were the least oxidized. For the saturated fatty acids, oxidation was inversely related to carbon length. Of the

unsaturated fatty acids, the *n*-3 fatty acid linolenate was the most highly oxidized and linoleate was the least oxidized. The recovery of label from methyl-labeled fatty acids was  $\approx 30\%$  lower than that from the carboxyl-labeled fatty acids, except for oleate, for which the difference was only 8%. Finally, differences in the rates of oxidation of individual fatty acids may partially explain differences in weight gain observed in animals fed different types of dietary fat and may also play a role in human obesity. 

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