Increased lymphatic lipid transport in genetically diabetic obese rats

HIROSHI HAYASHI,1,2 YUKO SATO,2 SETSUKO KANAI,2 MINEO ICHIKAWA,3 AKIHIRO FUNAKOSHI,4 AND KYOKO MIYASAKA2

1Department of Internal Medicine, Yokohama Red Cross Hospital, Yokohama 231-0836; Departments of 2Clinical Physiology and 3Nutrition, Tokyo Metropolitan Institute of Gerontology, Tokyo 173-0015; and 4Division of Gastroenterology, National Kyushu Cancer Center, Fukuoka 813-1394, Japan

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Hayashi, Hiroshi, Yuko Sato, Setsuko Kanai, Mineko Ichikawa, Akihiro Funakoshi, and Kyoko Miyasaka. Increased lymphatic lipid transport in genetically diabetic obese rats. Am J Physiol Gastrointest Liver Physiol 282: G69–G76, 2002.—Otsuka Long-Evans Tokushima fatty (OLETF) rats are a model for noninsulin-dependent diabetes mellitus (NIDDM), which is first manifested at 18 wk of age. We assessed age-related changes in lymphatic lipid transport in the intestine of OLETF rats and compared them with those of control Long-Evans Tokushima Otsuka (LETO) rats. Olive oil was infused into the rats with a mesenteric lymph fistula, which was created under ethrane anesthesia. A significant increase in lymphatic triglyceride (TG) transport in OLETF rats was observed at 18–19 wk compared with under 17 wk, but no age-related change was observed in LETO rats. Food restriction, exercise training, or troglitazone treatment in OLETF rats prevented the age-related increase in lipid transport. Biliary phosphatidylcholine concentration was higher in OLETF rats than in LETO rats, but no difference was seen in bile acid concentrations or the activity of microsomal TG transfer protein between the two strains. This study shows that increased lipid transport in the intestine may occur in NIDDM.

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striction on lymphatic TG transport were determined (11). The effect of treatment with troglitazone, an antidiabetic drug (26), on lymphatic TG transport in OLETF rats was also assessed.

**MATERIALS AND METHODS**

**Animals**

Male OLETF and LETO rats, 4 wk of age, were obtained from the Otsuka Research Institute (Tokushima, Japan). The animals were maintained at the Tokyo Metropolitan Institute of Gerontology in a specific pathogen-free room at a controlled temperature of 24–25°C with a 12:12-h light/dark cycle (dark cycle, 1700–0500) and were given standard chow (CRF-1, Oriental Yeast, Tokyo, Japan). The body weights of the OLETF and LETO rats were measured weekly.

**Lymphatic Lipid Transport**

**Experimental protocols.** On the day after surgery, the saline-glucose infusion was replaced by a lipid infusion containing 35.4 mg/h of olive oil, which corresponds to 20 mg/h of bile salt. The lipid infusion was introduced 2 cm down the duodenum through the fundus of the stomach, and the fundal incision was closed with a purse-string suture. Postoperatively, the rats were intraduodenally infused with a glucose-saline solution (145 mM NaCl, 0.28 mM glucose) at 3 ml/h and allowed to recover in restraint cages for at least 24 h before lipid infusion.

**Trophic effects of exercise.** In previous studies, exercise resulted in lower body weights compared to sedentary controls (20). Thus, in the current study, the effects of exercise were assessed in OLETF rats. Rats 8 wk of age (before the onset of NIDDM, sedentary, exercised, diet, and troglitazone-treated (n = 4) rats (P = 18.42, P < 0.001). Although the body weight of the troglitazone-treated rats was comparable to that of the sedentary rats, the body weight of the exercised rats was significantly lower (P = 0.05) and significantly higher vs. the diet group (P < 0.01). NM, not measured.

**Table 1. Changes in body weight with age**

| Age, wk | OLETF Sedentary | OLETF Exercised | LETO Sedentary | LETO Exercised | Troglitazone
<table>
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<tr>
<td>12</td>
<td>364 ± 7</td>
<td>362 ± 5</td>
<td>283 ± 8</td>
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<td>14</td>
<td>470 ± 12</td>
<td>419 ± 3</td>
<td>362 ± 12</td>
<td>396 ± 9</td>
<td>456 ± 5</td>
</tr>
<tr>
<td>16</td>
<td>518 ± 15</td>
<td>461 ± 2</td>
<td>393 ± 14</td>
<td>384 ± 7</td>
<td>NM</td>
</tr>
<tr>
<td>18</td>
<td>538 ± 20</td>
<td>475 ± 4</td>
<td>417 ± 16</td>
<td>390 ± 5</td>
<td>545 ± 31</td>
</tr>
<tr>
<td>20</td>
<td>573 ± 16</td>
<td>488 ± 6</td>
<td>436 ± 17</td>
<td>414 ± 8</td>
<td>NM</td>
</tr>
<tr>
<td>22</td>
<td>598 ± 23</td>
<td>502 ± 1</td>
<td>457 ± 18</td>
<td>411 ± 8</td>
<td>NM</td>
</tr>
<tr>
<td>24</td>
<td>594 ± 20</td>
<td>526 ± 4</td>
<td>472 ± 19</td>
<td>424 ± 10</td>
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**Values are means ± SE given in grams (unless otherwise specified).** Body weight was significantly higher in the Otsuka Long-Evans Tokushima fatty (OLETF) sedentary rats (n = 6) than in the Long-Evans Tokushima Otsuka (LETO) sedentary rats (n = 7) at all ages (P = 30.50, P < 0.001). There were significant differences between the OLETF sedentary, exercised (n = 7), and food-restricted (diet; n = 5) rats (P = 36.12, P < 0.001). The body weight of the sedentary group was higher than that in the other 2 groups starting at age 14 wk, and the weight of the exercised group was higher than that of the diet group starting at age 16 wk. At age 18 wk, there were significant differences in OLETF rat body weight between the sedentary, exercised, diet, and troglitazone-treated (n = 4) groups (P = 18.42, P < 0.001). Although the body weight of the troglitazone-treated rats was comparable to that of the sedentary rats, the body weight of the exercised rats was significantly lower vs. the diet group (P < 0.01), and significantly higher vs. the diet group (P < 0.01).

**Effect of Treatment With Troglitazone**

To observe the effect of treatment with troglitazone (kindly donated by Sankyo, Tokyo, Japan), four OLETF rats were fed standard chow containing 0.1% (vol/vol) troglitazone from 6 to 18 and 19 wk of age. At that time, the lipid transport experiment was performed.

**Bile Acid and PC Concentrations in Bile**

Six OLETF and five LETO rats at 8 wk of age (before NIDDM) and six OLETF and five LETO rats at 24 wk of age (after NIDDM) were used for measurement of bile acid concentrations. A Silastic cannula was inserted into the common bile duct below the liver, and bile was collected for 30 min, as described previously (15). The total bile acid concentration was measured enzymatically with 3α-hydroxysteroid dehydrogenase (15). Bile was collected in another set of four OLETF and four LETO rats at 24 wk of age, and PC concentrations in the bile were determined enzymatically as described in Experimental protocols.

**MTP Activity in Mucosa of Small Intestine and Liver**

Four OLETF and four LETO rats each were killed at 12 and 24 wk of age after decapitation by a guillotine, and the small intestinal mucosa and liver were removed and weighed. In a Polytron homogenizer, 1 g of each tissue was homogenized with three times its volume of 0.25 M sucrose and then centrifuged at 10,000 g at 4°C for 15 min. The supernatant was ultracentrifuged at 100,000 g at 4°C for 60 min to obtain the microsome fraction (the pellet). After suspending the pellet in 1 (intestine) or 2 ml (liver) of the buffer (50 mM Tris·HCl, pH 7.4, 50 mM KCl, 5 mM EDTA, 5 µg/ml leupeptin, and 2 mM phenylmethylsulfonyl fluoride), a tenth volume of deoxycholate solution (0.56%) was added (the final concentration of deoxycholate was 0.05%) and mixed with it.

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The sample was then ultracentrifuged at 100,000 g at 4°C for 30 min, and the supernatant was dialyzed to the assay buffer (15 mM Tris-HCl, pH 7.4, 40 mM NaCl, 1 mM EDTA, and 0.02% NaN₃). MTP activity was measured according to the method of Wetterau et al. (34). Donor vesicles containing 40 nmol of egg lecithin labeled with $^{3}$H, 0.08 nmol of triolein labeled with $^{14}$C, and 2.92 nmol of cardiolipin were mixed with acceptor vesicles containing 240 nmol of egg lecithin, 0.48 nmol of unlabeled triolein, 5 mg of fatty acid-free BSA, and 10 μl of the microsome sample. The mixture (400 μl) was incubated at 37°C for 1 h. The transfer reaction was terminated by the addition of 0.5 ml of a DEAE-cellulose suspension and low-speed centrifugation to selectively sediment the donor vesicles containing the negatively charged cardiolipin. The measured amounts of $[^{14}$C]TG (transferred from donor to acceptor vesicles) and $[^{3}$H]lecithin (marker of donor vesicles) were used to calculate the percent TG transfer from donor to acceptor vesicles.

**Statistics**

All values are expressed as means ± SE. Repeated-measures ANOVA was used to determine whether differences existed in and between groups for each dependent variable. When ANOVA resulted in a significant $F$-test, the Tukey honestly significant difference test was used for post hoc comparisons. Student’s $t$-test for independent means was used when appropriate. Differences were considered significant at $P < 0.05$.

**RESULTS**

**Changes in Body Weight of Sedentary Rats**

Changes in body weight from 12 to 24 wk of age in sedentary OLETF and LETO rats are shown in Table 1. Body weight was significantly higher in sedentary OLETF rats than in sedentary LETO rats at all ages ($F = 30.50$, $P < 0.001$).

**Changes in Lymph Flow of Sedentary Rats**

Lymph flow in sedentary OLETF and LETO rats is shown in Table 2. The fasting lymph flow of OLETF rats at ages 12–14 ($n = 5$), 15–17 ($n = 5$), and 18–19 wk ($n = 4$) was 1.61 ± 0.3, 2.06 ± 0.23, and 1.66 ± 0.35 ml/h, respectively, with no significant differences between the three groups. In all lymph flows, lymph flow gradually increased after 1 h of lipid infusion, but there were no significant differences in lymph flow between the groups over the 7-h period. The initial decrease in lymph flow in the 12- to 14- and 15- to 17-wk-old rats after the infusion was changed from saline to lipid emulsion had already been observed in previous studies (9, 10). In LETO rats, fasting lymph flow at ages 12–14 ($n = 6$), 15–17 ($n = 5$), and 18–19 wk ($n = 4$) was 1.56 ± 0.41, 1.95 ± 0.21, and 3.06 ± 0.49 ml/h, respectively. Fasting lymph flow at 18–19 wk was higher than in the other two groups, but the differences were not statistically significant. In all of the groups, lymph flow gradually increased after 1 or 2 h of lipid infusion, the same as in the OLETFT rats. There were no significant differences in lymph flow between the groups over the 7-h period.

**Changes in Lymphatic Lipid Transport of Sedentary Rats**

Lymphatic TG output in sedentary OLETF and LETO rats is shown in Fig. 1, $A$ and $B$, respectively. The fasting TG output of OLETF rats at ages 12–14, 15–17, and 18–19 wk was 4 ± 0.8, 5 ± 0.4, and 4.6 ± 1 mg/h, respectively, and there were no significant differences between the three groups (Fig. 1A). In all of the groups, lymphatic TG output began to increase sharply after the infusion was changed to lipid emulsion, and by 3 to 4 h TG transport had reached an almost stable phase. Lymphatic TG output at 7 h in the OLETF rats at ages 12–14, 15–17, and 18–19 wk was 17.6 ± 1.9, 22.1 ± 0.8, and 32.6 ± 2.3 mg/h, respectively. Lymphatic TG output over the 7-h period was significantly higher in the 18- to 19-wk-old rats than in the other two groups ($F = 19.25$, $P < 0.001$). When compared according to the time of the lipid infusion, the TG output of the 18- to 19-wk-old rats was found to be significantly higher vs. the other two groups at 2, 3, 5, 6, and 7 h and the 12- to 14-wk-old rats at 4 h. There was no significant difference in lymphatic TG output between the 12- to 14- and 15- to 17-wk-old rats. Fasting TG output in the LETO rats at ages 12–14, 15–17, and 18–19 wk was 3.3 ± 0.4, 4.4 ± 0.6, and 4.5 ± 0.5 mg/h, respectively, with no significant differences between the three groups (Fig. 1B). A trend in

<table>
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<th>Table 2. Lymph flow of lipid-infused rats</th>
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<table>
<thead>
<tr>
<th>Hour</th>
<th>OLETF 12–14 wk</th>
<th>OLETF 15–17 wk</th>
<th>OLETF 18–19 wk</th>
<th>LETO 12–14 wk</th>
<th>LETO 15–17 wk</th>
<th>LETO 18–19 wk</th>
<th>OLETF Exercised</th>
<th>OLETF Diet</th>
<th>OLETF Troglitazone</th>
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<tr>
<td>0</td>
<td>1.61 ± 0.30</td>
<td>2.06 ± 0.23</td>
<td>1.66 ± 0.35</td>
<td>1.56 ± 0.41</td>
<td>1.95 ± 0.21</td>
<td>3.06 ± 0.49</td>
<td>2.35 ± 0.38</td>
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<td>3.94 ± 0.89</td>
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<td>1.16 ± 0.28</td>
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<td>1.87 ± 0.05</td>
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<td>2.13 ± 0.34</td>
<td>2.25 ± 0.12</td>
<td>2.16 ± 0.31</td>
<td>1.92 ± 0.19</td>
<td>2.82 ± 0.35</td>
<td>2.58 ± 0.33</td>
<td>2.53 ± 0.18</td>
<td>2.47 ± 0.26</td>
</tr>
<tr>
<td>6</td>
<td>1.84 ± 0.16</td>
<td>1.95 ± 0.24</td>
<td>2.41 ± 0.21</td>
<td>2.21 ± 0.24</td>
<td>2.02 ± 0.22</td>
<td>2.89 ± 0.26</td>
<td>2.65 ± 0.28</td>
<td>2.23 ± 0.07</td>
<td>2.09 ± 0.27</td>
</tr>
<tr>
<td>7</td>
<td>1.99 ± 0.13</td>
<td>2.01 ± 0.23</td>
<td>2.04 ± 0.15</td>
<td>2.23 ± 0.24</td>
<td>2.04 ± 0.20</td>
<td>3.03 ± 0.28</td>
<td>2.45 ± 0.33</td>
<td>2.15 ± 0.09</td>
<td>1.93 ± 0.15</td>
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Values are means ± SE given in ml/h. In the sedentary rats, there were no significant differences in lymph flow over the 7-h period among the 3 age groups of OLETF ($n = 5$ each for 12- to 14-wk and 15- to 17-wk groups; $n = 4$ for 18- to 19-wk group; $F = 0.51, P > 0.5$) or LETO ($n = 6$ for 12- to 14-wk group, 5 for 15- to 17-wk group, and 4 for 18- to 19-wk group; $F = 3.28, P = 0.07$) rats. In the 18- to 19-wk-old OLETF rats, there were no significant differences in lymph flow over the 7-h period among the control (sedentary) rats and the diet, exercised, and troglitazone-treated groups ($n = 4$ for each group; $F = 1.47, P > 0.2$).
respectively. There were no significant differences in lymphatic TG output between the three groups over the 7-h period. Comparison of TG output over the 7-h period in 18- to 19-wk-old rats was significantly higher vs. the food-restricted rats at 5, 6, and 7 h, and the food-restricted rats at 2, 3, 5, 6, and 7 h.

The lymphatic TG output of the food-restricted, exercised, and troglitazone-treated rats was 4 ± 0.7, 5.2 ± 0.5, and 5.1 ± 0.7 mg/h, respectively. The lymphatic TG output of the food-restricted, exercised, and troglitazone-treated rats increased after the infusate was changed to lipid emulsion, in the same manner as in the control (nontreated, sedentary) OLETF rats, but there were significant differences among the four groups of LETO rats over the 7-h period (Fig. 2).

**Effects of Exercise, Food Restriction, and Treatment by Troglitazone**

The changes in body weight with exercise, food restriction, and troglitazone treatment are shown in Table 1. Both exercise and 60% food restriction induced significant decreases in body weight, and the effect of food restriction was more potent than that of voluntary exercise. At the time of the lipid transport experiments, the body weight of the food-restricted, exercised, and troglitazone-treated rats (n = 4 for each group) at 18–19 wk of age was 395 ± 9, 441 ± 13, and 545 ± 31 g, respectively. The body weight of the nontreated (sedentary) OLETF rats at 18–19 wk of age was 538 ± 20 g (Table 1). The plasma glucose concentration of the food-restricted, exercised, and troglitazone-treated rats at 18–19 wk was 101 ± 3, 102 ± 6, and 115 ± 12 mg/dl, respectively, and significantly lower than in the nontreated OLETF rats (184 ± 1 mg/dl).

The lymph flow of the food-restricted, exercised, and troglitazone-treated rats is shown in Table 2. Although the fasting lymph flow of the food-restricted, exercised, and troglitazone-treated rats was high (i.e., 3.15 ± 0.68, 2.35 ± 0.38, and 3.94 ± 0.89 ml/h, respectively), lymph flow over the 7-h period of lipid infusion was not significantly different among these three groups and 18- to 19-wk-old (control, sedentary) OLETF rats.

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TG output was observed in the LETO rats similar to that seen in the OLETF rats. Lymphatic TG output at 7 h in the LETO rats at ages 12–14, 15–17, and 18–19 wk was 19 ± 2, 18.5 ± 1.5, and 23.5 ± 1.9 mg/h, respectively. There were no significant differences in lymphatic TG output between the three groups over the 7-h period. Comparison of TG output over the 7-h period in the age-matched OLETF and LETO rats showed that it was significantly higher in the OLETF rats than in the LETO rats only at 18–19 wk of age (F = 7.12, P < 0.05).

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groups of rats in lymphatic TG transport over the 7-h period \( (P = 4.70, P < 0.05) \). When compared according to the time of the lipid infusion, TG transport of control (nontreated) rats was significantly higher vs. the food-restricted rats at 5, 6, and 7 h, the exercised rats only at 5 h, and the troglitazone-treated rats at 2, 3, 5, 6, and 7 h.

**Bile Acid and PC Excretion in Bile**

The total bile acid concentrations are shown in Table 3. Although at 8 wk of age the bile acid concentration of the OLETF rats was significantly higher than in the LETO rats, at 24 wk of age the concentrations were comparable.

PC concentrations in the bile of 24-wk-old rats are shown in Table 4. PC concentration in OLETF rats was significantly higher than in LETO rats \( (P < 0.01) \).

**Changes in MTP Activity**

MTP activity in both the small intestine (Fig. 3A) and liver (Fig. 3B) of the OLETF and LETO rats was significantly lower at 18 vs. 12 wk of age, but there were no differences between the strains in regard to organ or age.

**TG to PC Ratio in Lymph**

TG-to-PC ratios, calculated by the division of TG concentration by PC concentration, in lymph during lipid infusion are shown in Table 5. In sedentary OLETF rats, the TG-to-PC ratio in the 18- to 19-wk group tended to be higher than those of the 12- to 14- and 15- to 17-wk groups after the lipid infusion had started \( (F = 4.00, P = 0.050) \). In sedentary LETO rats, there was no significant difference in TG-to-PC ratio in lymph over the 7-h period among the three age groups \( (12–14, 15–17, and 18–19 wk; F = 0.18, P > 0.8) \). In comparing rats aged 18–19 wk, there were no significant differences in TG-to-PC ratio in lymph over the 7-h period among the sedentary OLETF and LETO rats and the three treated OLETF rat groups (diet, exercise, and troglitazone; \( F = 0.89, P > 0.4 \)).

**DISCUSSION**

To our knowledge, this is the first reported study on lymphatic lipid transport in the intestine of an animal model of NIDDM. NIDDM is characterized by insulin resistance with deficiency of insulin action, which seems to interfere with lipid metabolism in several ways, resulting in hyperlipidemia. First, more free fatty acids liberated from adipose tissue are incorporated into the liver and reesterified to TG, resulting in the enhanced production and secretion of very low-density lipoprotein (VLDL) in the liver. Second, hydrolysis of TG by lipoprotein lipase is decreased by insulin deficiency, and catabolism of TG-rich lipoproteins, such as chylomicrons and VLDL, is inhibited. It has been proposed that metabolic syndromes, such as syndrome X (25), deadly quartet (13), and visceral fat syndrome (7), predispose patients to atherosclerosis. These syndromes are based on insulin resistance and consist of several metabolic abnormalities, including glucose in-

**Table 3. Bile acid concentrations in bile**

<table>
<thead>
<tr>
<th>Age, wk</th>
<th>OLETF</th>
<th>LETO</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>37.8 ± 2.9*</td>
<td>21.1 ± 2.2</td>
</tr>
<tr>
<td>24</td>
<td>45.6 ± 3.7</td>
<td>36.3 ± 1.9†</td>
</tr>
</tbody>
</table>

Values are means ± SE in mM. *\( P < 0.001 \) \( (F = 17.3) \), significantly different vs. 8-wk-old LETO rats. †\( P < 0.01 \) \( (F = 12.8) \), significantly different vs. 8-wk-old LETO rats.

**Table 4. PC concentrations in bile of 24-wk-old rats**

<table>
<thead>
<tr>
<th></th>
<th>OLETF</th>
<th>LETO</th>
</tr>
</thead>
<tbody>
<tr>
<td>PC</td>
<td>2.02 ± 0.04*</td>
<td>1.47 ± 0.07</td>
</tr>
</tbody>
</table>

Values are means ± SE in mg/ml. PC, phosphatidylycerol. *\( P < 0.01 \), significantly different from LETO.
tolerance and hyperlipidemia. The results of this experiment show that the increase in lipid transport in the intestine may also occur in NIDDM and in the syndromes based on insulin resistance.

Exercise, food restriction, and troglitazone treatment were effective in inhibiting the increase in intestinal lipid transport in OLETF rats. Troglitazone is an antidiabetic drug that increases insulin sensitivity (26). It is interesting that troglitazone treatment improved hyperglycemia but did not prevent body weight gain, whereas exercise and food restriction not only improved hyperglycemia but also prevented body weight gain. Although there is a possibility that troglitazone directly inhibited the increased lymphatic lipid transport in OLETF rats by its pharmacological action, another interpretation of this result may be that the increased lymphatic lipid transport in OLETF rats is related to their hyperglycemia but not to their obesity.

The mechanism of the increased intestinal lipid transport in OLETF rats was not elucidated in this experiment. Bile acids and lipase are important to the digestion and absorption of TG, and total bile acid concentrations were not significantly different between OLETF and LETO rats at 24 wk of age (Table 3). Most of the lipase in the small intestine is secreted by pancreatic acinar cells, and we (8) previously reported that OLETF rats lack the CCK-A receptor. In the rat, the CCK-A receptor gene is ~10 kb in length and consists of five exons interrupted by four introns (28). Because two exons, including the promoter area, are deleted in OLETF rats, no CCK-A receptor gene is expressed (29).

CCK is an important gastrointestinal hormone that stimulates pancreatic secretion, and chronic administration of CCK induces pancreatic hypertrophy and hyperplasia (19). Indeed, from weaning until 24 wk of age the pancreatic wet weight of OLETF rats is significantly lower than that of LETO rats (21). Therefore, it is possible that pancreatic lipase activity is decreased in OLETF vs. LETO rats, although we did not measure lipase activity in this study. However, it is difficult to interpret the results of this experiment as being due to the decreased lipase activity in OLETF rats, because the increased, but not decreased, lipid transport in the intestinal lymph was shown in OLETF rats.

It has been shown (33) that the concentration of biliary PC correlates with lymphatic lipid transport. Although measurements were taken only in the 24-wk-old rats in our study, PC concentration in the bile was significantly higher in OLETF rats than in LETO rats (Table 4). This increase in biliary PC concentration may be related to the mechanism by which lymphatic lipid transport increases in OLETF rats, but clearly this area requires further investigation to be understood.

The assembly of lipid with phospholipid vesicles containing apolipoprotein B (apo B) in enterocytes is one of the key steps in facilitating lipid transport in the intestine. Pluronic L-81, a hydrophobic surfactant, can inhibit chylomicron formation by preventing TG incorporation into chylomicron particles, resulting in the blockade of intestinal lipid transport (31). MTP is a protein that transfers TG into apo B-containing vesicles, leading to the formation of chylomicrons and VLDL in the intestine and VLDL in the liver. Patients with abetalipoproteinemia lack MTP activity, which causes malabsorption of fat-soluble vitamins as well as lipids (34). Because MTP mRNA has been reported (16) to be increased in the liver of OLETF rats, we measured MTP activity in the intestine and liver. The results showed significantly lower MTP activity in the small intestine and liver at 24 wk of age than at 12 wk of age in both OLETF and LETO rats, with no differences between the two strains with respect to organ or age. No increase in MTP activity seems to occur in the intestine of OLETF rats.

Previous results (9) showed that fat feeding increases the size, but not the number, of lymphatic chylomicrons in Sprague-Dawley rats. Therefore, it is of interest whether the size or number of chylomicrons increased in 18- to 19-wk-old OLETF rats in our experiments. Although we did not measure the size or number of lymphatic chylomicrons directly in this experiment, the TG-to-phospholipid ratio in chylomicrons was reported (6) to correlate with the core-to-surface

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Table 5. TG-to-PC ratio in lymph

<table>
<thead>
<tr>
<th>Hour</th>
<th>OLETF 12–14 wk</th>
<th>OLETF 15–17 wk</th>
<th>OLETF 18–19 wk</th>
<th>LETO 12–14 wk</th>
<th>LETO 15–17 wk</th>
<th>LETO 18–19 wk</th>
<th>Exercised</th>
<th>Diet</th>
<th>Troglitazone</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>3.30 ± 0.14</td>
<td>3.11 ± 0.10</td>
<td>3.29 ± 0.19</td>
<td>3.25 ± 0.16</td>
<td>3.40 ± 0.10</td>
<td>2.58 ± 0.25</td>
<td>3.18 ± 0.12</td>
<td>3.26 ± 0.20</td>
<td>2.72 ± 0.06</td>
</tr>
<tr>
<td>1</td>
<td>4.82 ± 0.35</td>
<td>4.55 ± 0.12</td>
<td>4.82 ± 0.19</td>
<td>4.71 ± 0.22</td>
<td>4.82 ± 0.21</td>
<td>5.01 ± 0.18</td>
<td>4.59 ± 0.28</td>
<td>5.77 ± 0.25</td>
<td>2.90 ± 0.49</td>
</tr>
<tr>
<td>2</td>
<td>4.74 ± 0.54*</td>
<td>4.75 ± 0.36*</td>
<td>7.01 ± 0.51</td>
<td>5.85 ± 0.44</td>
<td>6.06 ± 0.28</td>
<td>6.29 ± 0.27</td>
<td>6.75 ± 0.21</td>
<td>6.88 ± 0.70</td>
<td>5.71 ± 0.83</td>
</tr>
<tr>
<td>3</td>
<td>5.16 ± 0.57*</td>
<td>4.86 ± 0.56*</td>
<td>7.51 ± 0.38</td>
<td>6.10 ± 0.51</td>
<td>6.39 ± 0.34</td>
<td>6.14 ± 0.36</td>
<td>6.88 ± 0.26</td>
<td>7.78 ± 1.01</td>
<td>6.04 ± 0.91</td>
</tr>
<tr>
<td>4</td>
<td>5.35 ± 0.86</td>
<td>4.49 ± 0.68</td>
<td>7.09 ± 0.38</td>
<td>6.16 ± 0.52</td>
<td>6.30 ± 0.33</td>
<td>6.19 ± 0.15</td>
<td>6.79 ± 0.42</td>
<td>7.46 ± 0.96</td>
<td>6.25 ± 0.99</td>
</tr>
<tr>
<td>5</td>
<td>5.20 ± 0.74</td>
<td>4.73 ± 0.40*</td>
<td>7.09 ± 0.38</td>
<td>6.07 ± 0.47</td>
<td>6.27 ± 0.44</td>
<td>6.15 ± 0.20</td>
<td>6.55 ± 0.40</td>
<td>7.04 ± 0.87</td>
<td>6.30 ± 1.01</td>
</tr>
<tr>
<td>6</td>
<td>5.35 ± 0.82</td>
<td>5.01 ± 0.34</td>
<td>6.81 ± 0.59</td>
<td>5.91 ± 0.40</td>
<td>6.43 ± 0.31</td>
<td>6.13 ± 0.25</td>
<td>6.99 ± 0.61</td>
<td>6.82 ± 0.62</td>
<td>6.11 ± 1.00</td>
</tr>
<tr>
<td>7</td>
<td>5.19 ± 0.79</td>
<td>5.19 ± 0.34</td>
<td>7.22 ± 0.46</td>
<td>6.02 ± 0.42</td>
<td>6.29 ± 0.23</td>
<td>6.00 ± 0.29</td>
<td>6.72 ± 0.46</td>
<td>6.68 ± 0.74</td>
<td>6.08 ± 0.97</td>
</tr>
</tbody>
</table>

Values are means ± SE; n values are as given in Table 2. In the sedentary OLETF rats, there were almost significant differences in triglyceride (TG)-to-PC ratio in lymph over the 7-h period among the three age groups ($F = 4.00, P = 0.050$). In comparing each hour of lipid infusion, TG-to-PC ratios at 2 and 3 h for the 12- to 14- and 15- to 17-wk groups were significantly lower vs. the 18- to 19-wk group; the TG-to-PC ratio at 5 h for the 15- to 17-wk group was significantly lower vs. the 18- to 19-wk group. In the sedentary LETO rats, there were no significant differences in TG-to-PC ratio in lymph over the 7-h period among the three age groups ($F = 1.87, P > 0.8$). In comparing 18- to 19-wk-old rats, there were no significant differences in TG-to-PC ratio in lymph over the 7-h period among the sedentary OLETF rats, LETO rats, and the 3 OLETF treatment groups ($F = 0.89, P > 0.4$). * $P < 0.05$ vs. OLETF 18- to 19-wk group.
area ratio of chylomicrons and to predict the size of particles. The TG-to-PC ratio of lymph in 18- to 19-wk-old OLETF rats after lipid infusion had started was shown to be higher than those in 12- to 14- and 15- to 17-wk-old OLETF rats (Table 5). Therefore, it may be said that 18- to 19-wk-old OLETF rats transported more lipid by increasing the size of chylomicrons in lymph. However, because these data were obtained in measurements of whole lymph and not of separated chylomicrons, we cannot draw any definite conclusion from these calculations.

The results of our study suggest that the increased intestinal lipid transport may occur in NIDDM, but the mechanism of the increase remains unclear.

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