Rat Plasma Triglycerides and Hepatic Fatty Acid Synthetase mRNA, but Not Apolipoprotein B and A-IV mRNA, Respond to Dietary Fat Content$^{1,2}$

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ABSTRACT The objective was to determine whether apolipoprotein B and A-IV mRNA abundance or plasma lipid concentrations would be altered by chronic or acute consumption of diets that differed in fat content. Forty Wistar male rats were fed either a low fat (5 g/100 g) or high fat (20 g/100 g) diet for 4 wk. Animals were killed unfed or 3 h after consumption of a test meal of the diet to which they had been adapted (n = 8). In addition, a low fat diet—adapted group was fed a high fat test meal and killed 3 h after the meal. Adaptation to the high or low fat diets did not result in differences in triglyceride or cholesterol concentrations in the plasma of unfed rats. In fed animals, plasma, VLDL, and LDL triglyceride concentrations were significantly higher in those fed the high fat test meal than in those fed the low fat test meal. Feeding did not alter plasma cholesterol concentrations; however, LDL cholesterol concentrations in the groups fed the high fat meals were significantly higher than in the group fed the low fat meal. There were no differences in plasma apolipoproteins B, A-IV, E, and A-I nor in the liver or intestinal apolipoprotein B and A-IV mRNA contents. Fatty acid synthetase (FAS) activity was significantly higher in rats adapted to the low fat diet, and no increase in activity due to feeding was observed. Hepatic FAS mRNA was higher in fed than unfed rats, and the low fat test meal resulted in a higher level than the high fat test meal. Plasma lipid concentrations were affected by the fat content of test meals rather than by the adaptation diet fat content. Apolipoprotein B and A-IV mRNA do not seem to respond to dietary fat or meal feeding. J. Nutr. 126: 1627–1634, 1996.

INDEXING KEY WORDS:
- fatty acid synthetase
- apolipoprotein B
- triglycerides
- alimentary lipemia
- rats

Apolipoprotein (apo) B and apo A-IV are associated with secretion of triglyceride-rich lipoproteins from the small intestine. The flux of fat, cholesterol and bile acids in the small intestine has been proposed as a regulator of synthesis and secretion of apo B and apo A-IV. Regulation of apo B seems to occur at the post-translational level, primarily by control of intracellular degradation rates (Dashti et al. 1989, Davidson 1988, Dixon et al. 1991, Magun et al. 1988, Pape et al. 1991). There are a few studies that have shown that dietary factors can affect apo B mRNA abundance. Feeding mice a high fat, high cholesterol diet for 2 wk resulted in higher intestinal levels of apo B mRNA and inconsistent changes in the liver (Srivastava et al. 1991). Fisher et al. (1988) demonstrated a twofold increase in intestinal apo B mRNA 2 h after a gastric tube feeding of a meal in rabbits. In addition, rats adapted for 4 wk to a diet containing oat bran fiber had a higher content of apo B mRNA in the ileum, compared with rats adapted to a diet containing cellulose as a fiber source (Redard et al. 1992). This response to oat bran is related to a shift in the site of lipid absorption to include more of the ileum when a source of viscous polysaccharide is included in the diet (Chun et al. 1989, Sigleo et al. 1984). Apolipoprotein A-IV synthesis is controlled at the pre-translational level, and changes in plasma concentrations have been reported to parallel changes in mRNA levels (Apelbaum et al. 1987, Black et al. 1990). Apolipoprotein A-IV synthesis is stimulated by the events involved in packaging and secretion of chylomicrons from the intestine (Hayashi et al. 1990), and plasma concentrations are reportedly significantly cor-

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4 Abbreviations used: apo, apolipoprotein; FAS, fatty acid synthetase; TRL, triglyceride-rich lipoproteins.
related with plasma triglyceride concentrations (Apfelbaum et al. 1987). Stimulation of apo A-IV output is related to the length of small intestine exposed to lipid (Kalogeris et al. 1994).

On the basis of published studies in which the flux of lipid through the intestine was typically manipulated by bolus infusions, we hypothesized that adaptation to high or low fat diets might result in differences in the amount of mRNA for apo B and A-IV in the small intestine. Thus, one objective of the present study was to determine whether chronic consumption of diets differing in fat content would lead to differences in the mRNA abundance for these apolipoproteins. In humans, flux of lipid through the intestine is associated with consumption of a meal, and a second objective of the present study was to determine whether consumption of a test meal would enhance the mRNA abundance for either apolipoprotein. In addition, we determined the differences in plasma lipid concentration associated with chronic and acute consumption of diets differing in fat content. Fatty acid synthetase (FAS, EC 2.3.1.85) activity and mRNA abundance in the liver have been shown to be sensitive to dietary fat content (Clarke et al. 1990) and were measured in this study as an indicator of adaptation to differences in fat content of the diet. Oat bran was included in all of the experimental diets to prolong the intestinal exposure to dietary lipid.

**MATERIALS AND METHODS**

**Animals.** Male Wistar rats weighing approximately 180–200 g were obtained from Simonson Labs (Gilroy, CA). Animals were individually housed in wire-bottom cages in a temperature-controlled room (23°C) with a 12-h reverse light:dark cycle. Rats were fed a purified low fat (5%, wt/wt) or high fat (20%, wt/wt) diet containing 6% oat bran fiber (Mother’s Oat Bran, Quaker Oats, Chicago, IL) during the first 8 h of the dark cycle for 4 wk. The composition of the purified diet is shown in Table 1. The fat contribution of the oat bran was taken into account, and the corn and coconut oils were added to approximate a 1:1:1 ratio of polyunsaturated, saturated and monounsaturated fatty acids. The energy density of the diets was estimated using the Atwater values of 37.66, 16.74 and 16.74 kJ/g for fat, carbohydrate and protein, respectively. Eight rats from each group were killed either unfed or 3 h after consumption of a 5-g test meal of the diet to which they were adapted. In addition, a low fat group was fed a 5-g high fat test meal and killed 3 h after meal. Thus, there were five experimental groups: unfed, adapted to low fat; fed low fat, adapted to low fat; fed high fat, adapted to low fat; unfed, adapted to high fat; and fed high fat, adapted to high fat. All animals consumed the test meal within 30 min. The protocol for animal use was approved by

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Low fat</th>
<th>High fat</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>g/kg diet</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Casein</td>
<td>136</td>
<td>136</td>
</tr>
<tr>
<td>Cornstarch</td>
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<td>78</td>
</tr>
<tr>
<td>Sucrose</td>
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<tr>
<td>Oat bran3</td>
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<td>323</td>
</tr>
<tr>
<td>Mineral mix4</td>
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<td>35</td>
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<tr>
<td>Vitamin mix4</td>
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<tr>
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<tr>
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<tr>
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</tr>
<tr>
<td>Fat</td>
<td>11.1</td>
<td>38.3</td>
</tr>
</tbody>
</table>

1. Composition of adaptation diets fed to rats for 4 wk.
2. Corn and coconut oils were added to provide a polyunsaturated:monounsaturated:saturated ratio of approximately 1:1:1.
3. Oat bran was added at the level of 333 g/kg to provide dietary fiber at the level of 60 g/kg.
4. Composition of vitamin and mineral mixtures was published previously (Schneeman and Richter 1993).

The University of California, Davis, Animal Health and Welfare Committee.

Rats were anesthetized by an intramuscular injection of ketamine-rompun-acetromazine (50:5:0.75 mg/kg). Cardiac puncture was used to collect whole blood into a 12-mL syringe containing 200 μL of 5% EDTA. Whole blood was centrifuged at 1200 × g for 20 min at 4°C to separate plasma. Plasma samples (2 mL) containing 1.5% DTNB [5,5'-dithio-bis[2-nitrobenzoic acid]] (Sigma Chemical, St. Louis, MO) as a lecithin cholesterol acyl transferase inhibitor were used to isolate lipoprotein fractions. Sequential preparative ultracentrifugation was used to fractionate lipoproteins utilizing a Sorvall fixed angle rotor (TFF 45.6) in a Sorvall ultracentrifuge (ODT65B, DuPont, Santa Clara, CA) using densities (d) as follows: chylomicron/VLDL, d < 1.006 kg/L; LDL, d = 1.006–1.050 kg/L; and HDL, d = 1.050–1.1963 kg/L. The samples were dialyzed as previously described (Ney et al. 1986). Lipo-protein fractions and plasma samples were stored at −20°C for further analyses.

Following blood collection, the liver was removed, rinsed in physiological saline, blotted and weighed. Approximately 1.0 g of hepatic median lobe was removed and placed in 6 mL of sterile-filtered homogenization buffer (4 mol/L guanidine isothiocyanate, 0.05 mol/L sodium acetate, 0.84% β-mercaptoethanol). Samples were homogenized for 15 s and stored at −70°C. The remaining liver was immediately freeze-clamped and stored at −70°C for analysis of FAS activity.
The small intestine was removed and divided into the upper two thirds and lower one third. The segments were rinsed twice with ice-cold 9 g/L NaCl, and the mucosa was removed by scraping with a glass slide. The mucosal samples were weighed and immediately placed in homogenization buffer and homogenized for 15 s and stored at -70°C.

**Analytical methods.** The methods for separating and analyzing plasma lipoproteins were recently published (Middleton and Schneeman 1995) and are briefly outlined here. Plasma and lipoprotein total (with esterase) and free (without esterase) cholesterol concentrations were determined by the cholesterol oxidase method. Liver lipids were extracted using a modification of the Folch extraction, and total and free cholesterol concentrations were enzymatically determined. Esterified cholesterol concentrations were estimated as the difference between total and free cholesterol and are reported as the percentage of total cholesterol for plasma, lipoprotein fractions and liver samples. Triglyceride concentrations of the plasma and lipoprotein fractions were determined enzymatically. Triglyceride concentration was determined colorimetrically in the liver extracts. Recovery of triglyceride and cholesterol from the VLDL, LDL and HDL fractions was estimated, and arithmetic adjustments were proportionally made so that the adjusted cholesterol and triglyceride concentrations from the lipoprotein fractions equaled the plasma concentrations (Tinker 1994). Protein concentration was determined in the lipoprotein fractions using a modified Lowry method and bovine serum albumin (Sigma Chemical) as the standard.

Plasma apo B, A-IV, E and A-I concentrations were measured using Laurell rocket gel immunoelectrophoresis. Antiserum were obtained from Paul Roheim (Louisiana State University Medical Center, Program Project Grant HL 25596, National Heart, Lung, and Blood Institute). A standard curve was simultaneously generated using a dilution series of standardized pooled plasma with known apolipoprotein concentrations. Results are reported in grams per liter.

Fatty acid synthetase activity was measured by incorporation of [1 – 14C]acetyl CoA into fatty acids (Grunfeld et al. 1988, Hsu et al. 1969). Approximately 2.5 g of freeze-clamped liver was homogenized in ice-cold buffer (7 mmol/L KHCO3, 85 mmol/L K2HPO4, 9 mmol/L KH2PO4, 1 mmol/L DL-dithiothreitol, 1 g/L bovine serum albumin). Samples were centrifuged at 105,000 × g using a TFT 45.6 fixed angle rotor in a Sorvall OTD-65B ultracentrifuge at 0°C for 1 h. The supernatant was collected and analyzed for FAS activity. One unit of enzyme activity is defined as that required to incorporate 1 μmol of [1 – 14C]acetyl CoA into fatty acid per minute at 37°C. Values are expressed as milliunits per gram of protein.

The preparation of cDNA fragments of apo B and A-IV was described previously (Middleton and Schneeman 1995). In addition, rat FAS cDNA, obtained from S. Smith (Children’s Hospital, Oakland, CA) and subcloned into pUC19, was digested overnight at 37°C with Eco RI to yield a 1.2-kb fragment. Human β-actin cDNA in pUC18 was digested overnight at 37°C with Bam H1 to yield a 2-kb fragment. The restriction-digested fragments were recovered after electrophoresis of the digests on a low-melting-temperature agarose gel. Random priming was used to label the isolated apo B, apo A-IV, β-actin, and FAS cDNA fragments (Random Primed DNA Labeling Kit, cat. no. 1004 760, Boehringer Mannheim Biochemica, Indianapolis, IN). Unincorporated nucleotides were removed with a Sephadex G-50 spin column (Bio-Rad Laboratories, Richmond, CA). The labeled probes were stored at -70°C and used within 24 h.

Preparation of RNA samples from intestine and liver for slot blot analysis was described previously (Middleton and Schneeman 1995). A series of dilutions of liver and intestinal total RNA were made and applied to Zeta-Probe GT nylon blotting filters using a dot blot apparatus (Schleicher & Schuel, Keene, NH). These filters were hybridized with the labeled apo B, A-IV and β-actin probes to ensure that dilutions used for the slot blot analysis did not exceed the capacity of the X-ray film. The rinsed filters were subsequently used for autoradiography; a GS-370 densitometer (Hoefer Scientific Instruments, San Francisco, CA) was used to determine the relative intensities, as peak heights, of the resulting bands. To allow comparisons of peak heights between filters, two of the same RNA samples were applied to each filter. Peak heights were determined and a correction adjustment derived to normalize the peak heights across films. Values for mRNA abundance are arbitrary units based on total RNA isolated from hepatic or intestinal tissue and are expressed as band intensity of the apolipoprotein per microgram of total RNA divided by band intensity of actin per microgram of total RNA. Actin was used to normalize any differences due to recovery. In addition to slot blots, several samples of liver and intestinal total RNA were electrophoresed on Northern gels and hybridized with apo B, apo A-IV, FAS and β-actin cDNA to ensure that the probes bound specifically to the correct size mRNA.

**Statistical analysis.** One-way ANOVA was used to determine the effect of the dietary treatments and, if the effect was significant (P < 0.05), the least significant difference test was used to determine differences between groups (Statview 512+, Brain Power, Inc., Calabasas, CA). Values are presented as means with SEM.

**RESULTS**

Initial and final body weights did not differ among groups. Initial body weight was 190 ± 3 g and final body weight was 317 ± 5 g. Average body weight gain was 5.3 ± 0.2 g/d and did not differ among groups. The
three low fat diet groups consumed an average of 15.7 g/d of diet, whereas the high fat diet groups consumed an average of 12.9 g/d of diet [pooled SEM, ±0.6]. The calculated total energy intake did not differ among any of the groups and was 2.57 ± 0.11 MJ/d. The weights of the stomach and the upper two thirds and lower one third of the small intestine expressed per 100 g body wt were significantly greater in the fed rats than in the unfed rats. There were no differences due to adaptation to low or high fat diets [Table 2]. Relative pancreas weights were not affected by adaptation or feeding of test meals [Table 2]. Relative liver weights were significantly lower in the high-fat-adapted groups than in the low fat–adapted groups but were not affected by feeding [Table 2].

Adaptation to low or high fat diets did not affect triglyceride concentrations in the plasma chylomicron/VLDL, LDL, or HDL fractions of unfed rats [Fig. 1]. After the high fat test meal was fed, the concentrations of triglycerides in the plasma, chylomicron/VLDL, and LDL fractions were significantly higher than in unfed rats, but not after feeding a low fat test meal. This effect of a high fat test meal was observed regardless of the adaptation diet. The HDL triglyceride concentration did not differ due to feeding either of the test meals [Fig. 1].

Plasma total cholesterol concentrations were not altered due to adaptation to a high fat vs. a low fat diet [Fig. 2]. Similarly, consumption of a low fat or a high fat test meal did not alter plasma total cholesterol concentrations. Chylomicron/VLDL total cholesterol concentrations were significantly higher than in the unfed group after feeding the high fat test meal to the high fat–adapted animals, but values did not increase significantly from unfed values after feeding either test meal to the low fat–adapted animals. In addition, adaptation to a high fat diet did not increase chylomicron/VLDL total cholesterol concentrations in the unfed groups compared with the low fat–adapted animals [Fig. 2]. Likewise, in the unfed groups, adaptation to a high fat diet did not elevate LDL total cholesterol concentrations compared with the low fat group. However, feeding a high fat test meal to both low fat– and high fat–adapted animals resulted in significantly greater LDL total cholesterol concentrations than in the unfed groups. There was no elevation in LDL total cholesterol concentration relative to unfed controls when a low fat test meal was fed to low fat–adapted rats [Fig. 2]. Adaptation to a high fat diet and feeding of either test meal did not alter HDL total cholesterol concentrations. The concentration of cholesterol esters in the plasma and the lipoprotein fractions followed a pattern similar to that of total cholesterol [data not shown]. Dietary adaptation or feeding of the two test meals did not significantly affect the percentage of cholesterol esters in the plasma or the lipoprotein fractions [data not shown].

Protein concentrations in the chylomicron/VLDL and LDL fractions followed the same pattern as total cholesterol concentrations. The groups fed the high fat test meals had higher concentrations than unfed controls regardless of the adaptation diets [Table 3]. The HDL protein concentration was not affected by either adaptation to a high fat diet or feeding of either test meal [Table 3].

The average plasma apo B concentration was 148 mg/L in the unfed groups and 176 mg/L in the fed groups [pooled SEM, 33], and differences among groups were not significant due to dietary adaptation or meal feeding. Plasma apo A-IV concentrations were 198 and 199 mg/L [pooled SEM, 23] in the unfed and fed groups, respectively. No significant differences due to the treatments were observed. The mRNA abundance was expressed as the ratio of apo B or apo A-IV mRNA to mRNA for β-actin. In the liver, this ratio was 0.61 [pooled SEM, 0.08] for apo B and 1.70 [pooled SEM, 0.27] for apo A-IV, and no differences occurred due to the fat content of the adaptation diet or the fed/unfed state of

### Table 2

<table>
<thead>
<tr>
<th>Group</th>
<th>Stomach</th>
<th>Liver</th>
<th>Pancreas</th>
<th>Upper 2/3 small intestine</th>
<th>Lower 1/3 small intestine</th>
</tr>
</thead>
<tbody>
<tr>
<td>LF, unfed</td>
<td>0.63&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3.58&lt;sup&gt;bc&lt;/sup&gt;</td>
<td>0.30</td>
<td>1.38&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.61&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>LF, HF</td>
<td>1.81&lt;sup&gt;b&lt;/sup&gt;</td>
<td>3.72&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0.36</td>
<td>1.54&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.85&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>HF, unfed</td>
<td>0.62&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3.29&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.33</td>
<td>1.39&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.64&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>HF, LF</td>
<td>1.94&lt;sup&gt;b&lt;/sup&gt;</td>
<td>3.42&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>0.33</td>
<td>1.57&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.79&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

1 Values are means, n = 8, within a column, values with different superscripts are significantly different (P < 0.05).

2 Group abbreviations: LF, unfed = low fat diet adapted, killed unfed. LF, LF = low fat diet adapted, killed after a low fat test meal. LF, HF = low fat diet adapted, killed after a high fat test meal. HF, unfed = high fat diet adapted, killed unfed. HF, HF = high fat diet adapted, killed after a high fat test meal.
**FIGURE 1** Plasma and lipoprotein triglyceride concentrations in rats adapted to and then fed test meals of high and low fat diets. Values are means, n = 8. Different superscripts indicate significant difference at P < 0.05 between dietary treatments within fractions. LF, unfed = low fat diet adapted, killed unfed. LF, LF = low fat diet adapted, killed after a low fat test meal. LF, HF = low fat diet adapted, killed after a high fat test meal. HF, unfed = high fat diet adapted, killed unfed. HF, HF = high fat diet adapted, killed after a high fat test meal. Pooled SEM: plasma = 30.0, Chylo/VLDL = 34.0, LDL = 11.2, HDL = 5.2.

The rats. No differences due to treatments were observed in these ratios for apo B in the upper two thirds of the small intestine (0.52; SEM 0.05) or the lower one third of the small intestine (0.50; SEM 0.07) or for apo A-IV in the small intestine (the ratio was 11.26, SEM 1.93, in the upper two thirds and 6.43, SEM 1.31, in the lower one third).

Hepatic FAS activity (expressed as mU/g protein) was significantly lower in the groups adapted to a high fat diet than in the groups adapted to a low fat diet.

**FIGURE 2** Plasma and lipoprotein cholesterol concentrations in rats adapted to and then fed test meals of high and low fat diets. Values are means, n = 8. Different superscripts indicate significant difference at P < 0.05 between dietary treatments within fractions. LF, unfed = low fat diet adapted, killed unfed. LF, LF = low fat diet adapted, killed after a low fat test meal. LF, HF = low fat diet adapted, killed after a high fat test meal. HF, unfed = high fat diet adapted, killed unfed. HF, HF = high fat diet adapted, killed after a high fat test meal. Pooled SEM: Plasma = 70.0, Chylo/VLDL = 3.0, LDL = 16.0, HDL = 61.0.
TABLE 3
Protein concentrations of plasma lipoprotein fractions in rats adapted to and then fed test meals of high (HF) or low fat (LF) diets

<table>
<thead>
<tr>
<th>Group</th>
<th>Triglyceride-rich lipoproteins</th>
<th>LDL</th>
<th>HDL</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>mg/L</td>
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<td></td>
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<tr>
<td>LF, unfed</td>
<td>32.8a</td>
<td>53.7a</td>
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<td>LF, LF</td>
<td>41.5ab</td>
<td>61.5a</td>
<td>1000.9</td>
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<td>LF, HF</td>
<td>44.7b</td>
<td>71.3b</td>
<td>961.4</td>
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<tr>
<td>HF, unfed</td>
<td>27.1a</td>
<td>52.1a</td>
<td>1006.3</td>
</tr>
<tr>
<td>HF, HF</td>
<td>44.5b</td>
<td>82.5b</td>
<td>987.9</td>
</tr>
<tr>
<td>Pooled SEM</td>
<td>3.3</td>
<td>3.4</td>
<td>35.4</td>
</tr>
</tbody>
</table>

1 Values are means, n = 8, within a column, values with different superscripts are significantly different (P < 0.05).
2 Group abbreviations: LF, unfed = low fat diet adapted, killed unfed. LF, LF = low fat diet adapted, killed after a low fat test meal. LF, HF = low fat diet adapted, killed after a high fat test meal. HF, unfed = high fat diet adapted, killed unfed. HF, HF = high fat diet adapted, killed after a high fat test meal.

There was no increase in activity with feeding either test meal (Table 4). In the unfed groups, hepatic FAS mRNA did not differ among the high fat- and low fat-adapted groups; however, when either test meal was fed a significantly higher FAS mRNA content was noted in the fed groups than in the unfed groups. Furthermore, in the low fat-adapted animals feeding the low fat test meal resulted in a significantly higher FAS mRNA content than feeding the high fat test meal (Table 4).

Hepatic triglyceride concentration was significantly higher in rats adapted to the high fat diet, and no differences were noted after feeding either test meal (Table 5). Hepatic cholesterol concentrations were not affected by adaptation to the high fat diet or by feeding either of the test meals (Table 5).

DISCUSSION

The main objective of the present study was to determine whether adaptation to diets differing in fat content or feeding would alter mRNA abundance or plasma lipid concentrations. Oat bran fiber was used to provide in a physiological manner a greater exposure of nutrients to the intestine for absorption. Four weeks of adaptation to a high fat (20 g/100 g) diet containing 6 g/100 g oat bran fiber did not alter plasma, chylomicron/VLDL, LDL or HDL triglyceride and cholesterol concentrations compared with results for rats adapted to a low fat diet when rats were unfed before analysis. Chronic feeding of diets with different fat contents did not cause differences in plasma lipid concentrations, and the postprandial response in triglyceride and cholesterol concentrations was based on the fat content of the test meal rather than the fat content of the adaptation diets. Regardless of which diet the rats consumed chronically, plasma, chylomicron/VLDL, and LDL triglyceride as well as LDL cholesterol concentrations were higher after consumption of a high fat test meal than in unfed animals. Feeding a low fat test meal to rats adapted to a low fat diet did not significantly affect either triglyceride or cholesterol concentrations. In humans and rats, the peak in postprandial triglycer-
ide response is about 3 to 4 h after a meal (Cohn et al. 1989 and 1991, Olson and Schneeman 1991, Redard et al. 1990, Schneeman et al. 1993). In addition, when humans (Redard et al. 1990) and rats (Olson and Schneeman 1991) were challenged with a test meal containing a source of soluble fiber, the triglyceride peak was higher than in controls consuming meals either with no fiber or with cellulose. In the present study, all rats consumed the same amount of fiber from oat bran, and the larger triglyceride and cholesterol response was due to the higher fat content of the test meal. The elevation in postprandial triglycerides after the high fat meal is likely due to accumulation of chylomicron remnants or VLDL (Schneeman et al. 1993). Accumulation of remnants of triglyceride rich lipoproteins (TRL) has been implicated as a risk factor for the development of atherosclerosis in humans (Zilversmit 1979).

Both plasma cholesterol and apo B concentrations were not altered significantly by adaptation to diet or in response to feeding the test meals. The lack of change in plasma apo B and cholesterol concentration is consistent with observations in humans. However, studies of humans indicate that both apo B-48 and B-100 increase in the TRL fraction after a meal and cholesterol shifts between the lipoprotein fractions during the alimentary period (Castro and Fielding 1985). In humans, an increase in TRL cholesterol is accompanied by a decrease in LDL cholesterol concentration. This shift is due to the transfer of cholesterol from LDL to TRL during the alimentary period; most of the increase occurs in the VLDL because of the preferential clearance of chylomicrons (Schneeman et al. 1993). In rats, the activity of cholesterol ester transfer protein is low; thus most of the alimentary increase in cholesterol remains in the LDL fraction. The evidence from both humans and rats suggests that this pattern of alimentary lipemia will contribute to the increase in cardiovascular disease risk in response to consuming a diet high in fat.

Plasma apo A-IV concentration was not affected by adaptation to a high fat diet or by feeding a test meal. The lack of increase in plasma apo A-IV concentrations despite the increases in postprandial triglycerides in the groups fed the high fat test meals is consistent with results from a study in which rats were adapted to oat bran and fed a high fat test meal (Redard et al. 1992). These two studies suggest that plasma apo A-IV and plasma triglyceride concentrations may not always be correlated, and they raise questions about the regulation of plasma concentrations of apo A-IV simply by dietary means.

Hepatic and intestinal apo B and A-IV mRNA abundance was not affected by adaptation to diets with different fat content or by feeding the test meals. In contrast, hepatic FAS mRNA was higher due to feeding a meal, and differences were observed between feeding the high and low fat test meal. The differences in FAS mRNA indicate that, in this experiment, it was possible to detect responsiveness to a meal and fat content of the diet and that mRNA content was a more sensitive indicator of response to diet than enzyme activity. The half-life of the FAS enzyme is 3 to 4 d (Flick et al. 1977), whereas the half-life of mRNA is 3 to 4 h (Clarke et al. 1990, Goodridge 1986); consequently the mRNA was sensitive to the change in fat content within one meal. Neither apo B nor A-IV mRNA seems to be regulated in a similar manner by dietary fat content or by meal feeding.

**LITERATURE CITED**


