Endotoxin-induced hypertriglyceridemia is mediated by suppression of lipoprotein lipase at a post-transcriptional level

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Abstract Previous studies have demonstrated that endotoxin/lipopolysaccharide treatment causes a decrease in adipose tissue and heart lipoprotein lipase (LPL) activities in rats, producing hypertriglyceridemia in these animals. To examine the mechanisms for this effect of endotoxin, we studied the effects of endotoxin administration on LPL mRNA, and LPL synthetic rates and activity in rat adipose tissue and heart. Endotoxin treatment (i.p., 3 mg/100 g body weight or higher doses) produced a pronounced increase in serum triglycerides associated with a 65% decrease in adipose tissue and heart LPL activities within 7 h. Fast protein liquid chromatography (FPLC), used to separate lipoproteins in rat serum, showed that the increase in triglyceride was all in the very low density lipoprotein fraction which was accompanied by a concomitant decrease in high density lipoprotein. In contrast, there was no change in adipose tissue or heart LPL mRNA up to 24 h after treatment and no change in adipose tissue LPL synthetic rate, as measured by L-[^{35}S]methionine incorporation and immunoprecipitation. Plasma insulin levels remained unchanged. The results indicate that endotoxin-induced hypertriglyceridemia in rats can be attributed to an impaired triglyceride clearance associated with a decrease of LPL activity mediated at a post-transcriptional level.—**Gouni, I., K. Oka, J. Etienne, and L. Chan.** Endotoxin-induced hypertriglyceridemia is mediated by suppression of lipoprotein lipase at a post-transcriptional level. *J. Lipid Res.* 1993. **34:** 139–146.

Supplementary key words rat • mRNA

Hypertriglyceridemia is frequently observed in patients during the course of gram-negative, protozoan, and viral infections, and in animals given endotoxin, i.e., the lipopolysaccharide component of the cell wall of gram-negative organisms. Existing evidence suggests that impaired triglyceride (TG) clearance, secondary to suppression of lipoprotein lipase (LPL), the enzyme responsible for the TG clearance, is mainly responsible for the hypertriglyceridemia in infection. It has been shown that there is decreased clearance of intravenously administered fat emulsion and reduced postheparin plasma lipase activity in endotoxin-treated monkeys (1) along with a decrease in postheparin plasma and adipose tissue lipase activity with no decrease in the heart LPL activity in endotoxin-injected mice (2).

On the other hand, Bagby and Spitzer (3, 4) reported that endotoxin-treated rats have decreased heart and postheparin plasma LPL activity but no decrease in adipose tissue LPL activity, but Kawakami and Cerami (5) found a decrease in adipose, heart, and postheparin plasma LPL activity. Although TG kinetic studies in septic dogs demonstrated an increased hepatic production of very low density lipoproteins (VLDL) with no impairment of TG clearance (6), studies in endotoxin-treated rats showed no increase in the TG output by the liver but a substantial decrease in heart, skeletal muscle, and postheparin plasma LPL activities (7).

Therefore, the mechanism for the endotoxin-induced hypertriglyceridemia in gram-negative infection or after endotoxin administration is still unclear. The purpose of the present study was to examine the effects of endotoxin on LPL and at what level (e.g., transcriptional, post-transcriptional, or translational) these effects occur. This was accomplished by studying LPL activity, mRNA, and synthetic rate in adipose tissue and hearts of control and endotoxin-treated rats. The results indicate that the hypertriglyceridemia in rats given endotoxin is due to an impaired clearance associated with a decrease of LPL activity attained at a post-transcriptional level.

Abbreviations: TG, triglycerides; LPL, lipoprotein lipase; VLDL, very low density lipoproteins; SDS, sodium dodecyl sulfate; BSA, bovine serum albumin; TCA, trichloroacetic acid; FPLC, fast protein liquid chromatography; HDL, high density lipoproteins; LPS, lipopolysaccharide; TNF, tumor necrosis factor; IL-1, interleukin-1; γ-INF, γ-interferon; mRNA, messenger RNA; *E. coli, Escherichia coli;* EDTA, ethylenediaminetetraacetic acid; PMSF, phenylmethylsulfonylfluoride; PAGE, polyacrylamide gel electrophoresis; cDNA, complementary DNA.

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MATERIALS AND METHODS

Chemicals and solutions

[^{3}H]oleoylglycerol (22 mCi/mmol), Amplify, and ^{14}C-labeled protein molecular weight markers were purchased from Amersham (Arlington Heights, IL). Tran ^{35}S-Label (1123 Ci/mmol) was purchased from ICN Radiochemicals (Costa Mesta, CA). Lecithin, triolein, Trasylol, Triton X-100, bovine serum albumin, protein A, ethylendiaminetetraacetic acid (EDTA), goat serum, phenylmethylsulfonylfluoride (PMSF), HEPES, yeast RNA, β-mercaptoethanol, rabbit anti-goat IgG, Krebs-Ringer, leupeptin, and pepstatin were all from Sigma (St. Louis, MO). Sodium dodecyl sulfate (SDS) was from BDH (Poole, U.K.). Lipopolysaccharide from *E. coli* serotype 0127:B8 was purchased from Difco (Detroit, MI). Heparin sodium salt was from Gibco (Gaithersburg, MD). Zeta probe membranes and Tris base were from Bio-Rad (Richmond, CA). Trichloroacetic acid (TCA), sodium azide, and sodium phosphate (dibasic) were from Fisher (Pittsburgh, PA). GF/B filters were obtained from Whatman (Clifton, NJ). En^{3}hance and Solvable were from Dupont (Wilmington, DE). Human β-actin DNA probe was obtained from Clontech (Palo Alto, CA). Rat LPL and polyclonal anti-rat LPL antibody were prepared as previously described (8). Rats were obtained from Harlan (Indianapolis, IN).

Animal procedures

Male Sprague-Dawley rats (approximately 200 g) were maintained under an artificial light–dark cycle of 12 h (lights on at 7:00 AM) and fed rat chow and water ad libitum. They were kept in a fed state throughout the experiments. Rats were injected intraperitoneally (i.p.) with 3 mg per 100 g body weight of *E. coli* endotoxin dissolved in 2 ml of 0.9% saline, or saline alone and killed at various predetermined times after injection. Heart and left epididymal fat pads were excised and frozen immediately in liquid nitrogen. Blood was collected by cardiac puncture for measurement of serum glucose, cholesterol, triglycerides, and insulin.

Serum chemistries

Serum triglyceride and cholesterol levels were measured by using Sigma diagnostic kits. Glucose levels were measured by using a Boehringer Mannheim reagent set. Insulin levels were determined by a two-antibody system radioimmunoassay with a rat insulin standard (9). Protein was measured by the Coomassie Brilliant Blue method as described by Bradford (10).

Lipoprotein lipase assay

LPL activity was assayed on fresh tissues by a modification of a previously described technique by Iverius and Östlund-Lindqvist (11). Assays were carried out in a total volume of 500 μl consisting of 300 μl of triacylglycerol emulsion, 75 μl of 0.223 M Tris-HCl (pH 8.5), 25 μl of heat-inactivated (56°C, 30 min) rat serum, and 100 μl of sample. The reaction was continued at 37°C for 1 h and 3.25 ml of methanol–chloroform–heptane 1.41:1.25:1.0 (v/v) was added to stop the reaction. After vortexing, 1.05 ml of 0.05 M carbonate/borate buffer was added; the reaction mixture was further vortexed and then centrifuged in a benchtop centrifuge at 3,000 *g* for 15 min. Two ml of the upper aqueous phase was removed, mixed with 4 ml of Aquasol, and radioactivity was measured in a liquid scintillation counter. LPL activity is expressed as μmol of free fatty acids released per mg of protein per hour of incubation. The inter-assay coefficient of variation was 4.4% and the intra-assay coefficient of variation was 5.7%.

Measurement of LPL synthetic rate

LPL synthetic rate was measured by immunoprecipitation of lysates prepared from pulse-labeled adipose tissue using a goat polyclonal antibody raised against purified rat adipose tissue LPL (8).

Adipose tissue was minced, washed three times with methionine-free KRB-HEPES buffer with 1% bovine serum albumin (BSA), and incubated in the same medium which was gassed continuously with a mixture of O_2/CO_2 (95%/5%). A mixture of L-[^{35}S]methionine and L-[^{35}S]cysteine (4.67:1) was added at a concentration of 0.4 mCi per ml and the incubation was continued for 30 min. To stop the labeling process, the tissues were transferred to ice-cold KRB-HEPES buffer supplemented with 1% BSA and excess unlabeled methionine. After a 5-min incubation, the tissues were homogenized with a Polytron homogenizer for 1 min in buffer A [0.025 M ammonia buffer (pH 8.2), containing heparin (5 IU/ml), leupeptin (10 μg/ml), pepstatin (1 μg/ml), Trasylol (25 IU/ml), Triton X-100 (0.8%, w/v), SDS (0.04%, w/v), and EDTA (5 mM)] (12). The radiolabeled homogenates were centrifuged for 30 min at 10,000 *g* at 4°C and the aqueous phase was collected. One-ml aliquots of clear supernatants were transferred and 8 μl of goat anti-LPL antiserum or non-immune goat serum was added. After overnight incubation at 4°C, 20 μl of rabbit anti-goat IgG (2 mg/ml) was added and the incubation was continued for 2 h. The immunoprecipitates were collected on protein A (50 μl of a 10% slurry), washed three times with buffer D [pH 7.4, (per liter: 3.564 g $Na_2HPO_4 \cdot H_2O$, 0.055 g NaN_3, 8.766 NaCl, 10 g Triton X-100, 1 g SDS, 100 mg heparin, 745 mg EDTA, 17.4 mg PMSF)], boiled for 5 min in 35 μl of sample buffer consisting of 62.5 mM Tris-HCl (pH 6.8) (2%, w/v) SDS, and 5% (v/v) β-mercaptoethanol, and centrifuged; the supernatant was subjected to SDS-PAGE using a 6% stacking and a 10% separating polyacrylamide gel at 150 V for 3 h. The gel was fixed with En^{3}hance, dried, and exposed to X-ray film

(Kodak XAR-5) for 3 days at −70°C. The amount of L-[^{35}S]methionine incorporated in LPL was determined by excision of a 4-mm slice in the 56 kDa region of the dried gel. The gel slice was incubated in a gel solubilizer overnight, and the radioactivity was determined in a liquid scintillation counter. L-[^{35}S]methionine incorporation into total protein was determined as follows: 5 μl of the radiolabeled supernatant was added to 1 ml of 10% trichloroacetic acid (TCA), boiled for 10 min, and quickly transferred to ice. Precipitates were then collected on GF-B glass fiber filters, washed with 10% TCA, followed by a wash with absolute ether, and then air-dried. The dried filters were incubated overnight in 2 ml of Solvable at 60°C in scintillation vials to dissolve precipitates, and counted as described for the gel slices.

Extraction of RNA and slot-blot analysis

Isolation of RNA from adipose tissue was performed according to the guanidium-phenol-chloroform method (13), and RNA was quantitated spectrophotometrically. For slot-blot analysis, total RNA was denatured just before blotting. Under our conditions yeast RNA did not show detectable hybridization to the mouse LPL cDNA. Samples containing approximately 5 μg of total RNA were blotted onto Zeta-Probe membrane by using a Minifold II apparatus and fixed by a UV lamp. A 622 base pair Bam H1 fragment of mouse LPL complementary DNA (cDNA) (14), was labeled with [^{32}P]dCTP by random oligonucleotide priming. Prehybridization, hybridization, and posthybridization washes were carried out as per the Zeta-Probe protocol. Blots were exposed to film (Kodak XAR-5) in the presence of two intensifying screens for 20 h at −70°C. Autoradiograms were scanned using a Visage 110 densitometer (BioImage, Kodak, Ann Arbor, MI). Human β-actin cDNA probe was labeled as described above and used for hybridization. Data were normalized to the β-actin signal. Different amounts of RNA loaded gave a linear response.

Fast protein liquid chromatography (FPLC)

Gel permeation fast protein liquid chromatography (FPLC) was performed as described previously (15). Briefly, rat plasma was loaded into a 400-μl Teflon sample loop for application to two Superose-6 columns (~50 ml of vol, Pharmacia, Sweden) connected in series. Elution of proteins was at 0.5 ml/min with 1 mM EDTA, 154 mM NaCl, 0.02% NaN_3, pH 8.2, and was monitored by measurement of absorbance at 280 nm. After the first 12 ml had eluted, forty 500-μl fractions were collected. Cholesterol and triglyceride concentrations in the fractions were measured by Sigma diagnostic kits.

Statistics

All data are expressed as the mean ± SEM. Statistical differences were determined by using a two-tailed Student's *t*-test. *P* values less than 0.05 were considered significant.

RESULTS

We conducted two series of experiments to examine the effect of endotoxin on heart and adipose tissue LPL activity and mRNA. In the first series the effect of various doses of endotoxin on tissue LPL activity and mRNA was studied. Animals were given injections of saline (control) or endotoxin (3–9 mg/dl) i.p. and killed 7 h after injection.

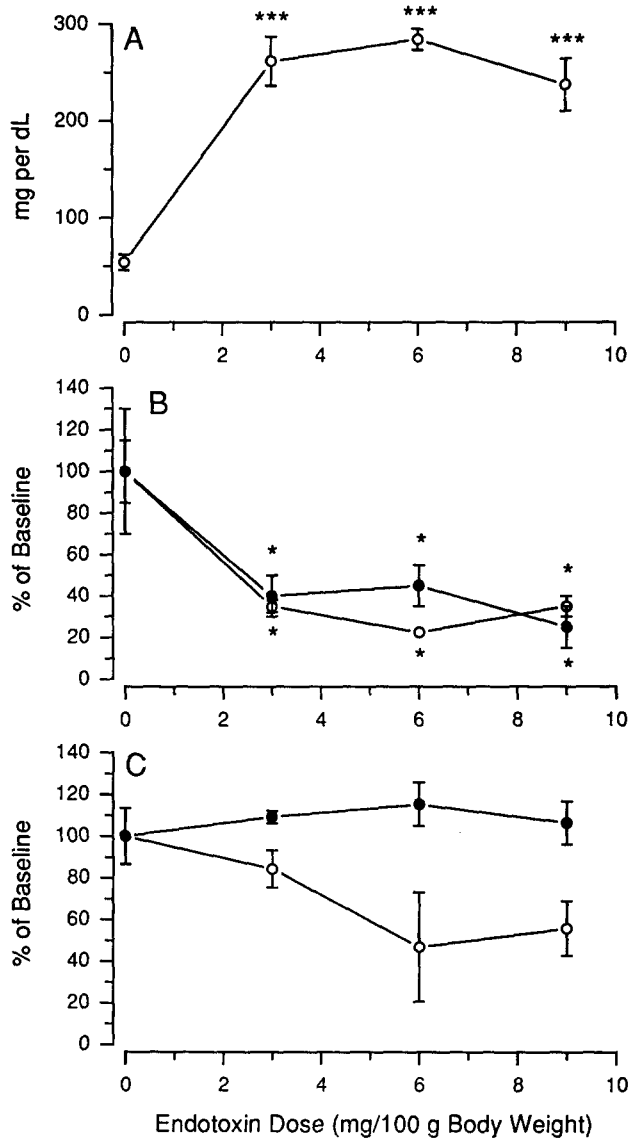

Fig. 1. Effect of three different doses of endotoxin on (A) triglyceride concentrations in plasma; (B) lipoprotein lipase activity in heart (filled circles) and adipose tissue (open circles); and (C) lipoprotein lipase mRNA/β-actin mRNA in heart (filled circles) and adipose tissue (open circles). Measurements were made 7 h after intraperitoneal injection. Values are means ± SEM; n = 4–6, expressed as changes from baseline; $^{*}P < 0.05$; $^{***}P < 0.001$.

Endotoxin doses of 3 mg/100 g body weight were not lethal in any rats observed over a 24-h period; administration of 9 mg/100 g body weight killed 50% of the animals tested. Rats given endotoxin survived at least 4 h with most deaths occurring 7–12 h after injection. TG levels increased by ~300% ($P < 0.001$) and the response was not dose-dependent (**Fig. 1A**). Cholesterol levels did not change (data not shown), which is consistent with previous reports (16, 17).

LPL activity was greatly reduced (~60%; $P < 0.05$) in hearts from endotoxin-treated rats (Fig. 1B). Similarly, adipose tissue LPL activity decreased significantly (~65%; $P < 0.05$) in the endotoxin-treated rats compared to controls (Fig. 1B). Heart and adipose tissue enzyme activities were decreased to the same extent regardless of the dose injected over the range studied. On the other hand, LPL mRNA levels did not change with any of the doses of endotoxin given (Fig. 1C).

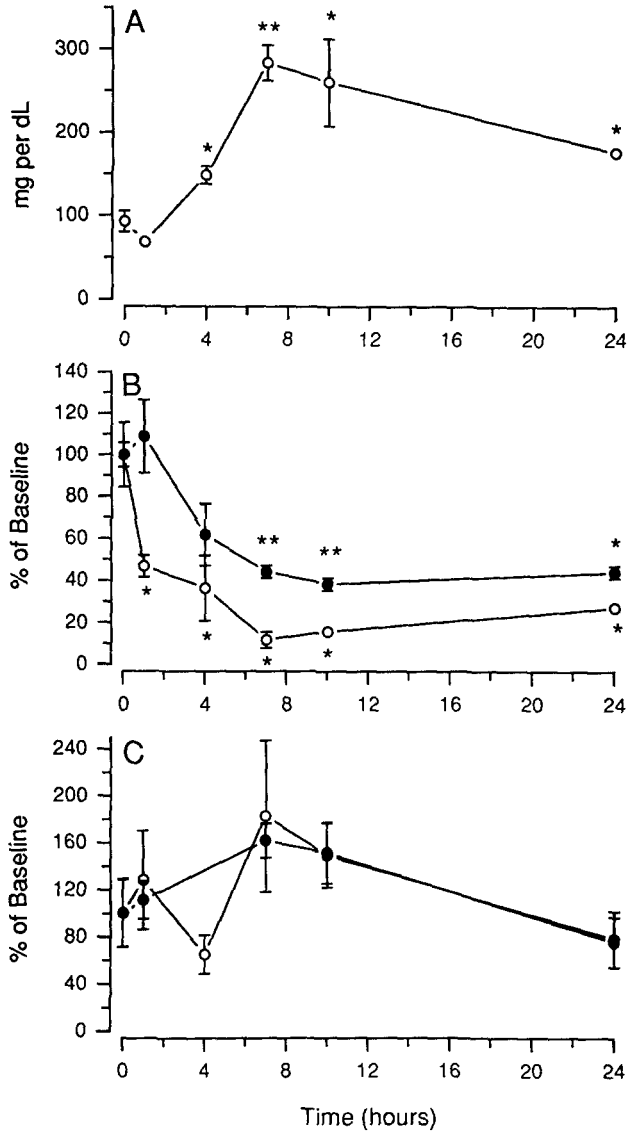

Fig. 2. Time course after intraperitoneal injection of 3 mg per 100 g body weight endotoxin. (A) Triglyceride concentrations in plasma; (B) lipoprotein lipase activity in heart (filled circles) and adipose tissue (open circles); and (C) lipoprotein lipase mRNA/β-actin mRNA in heart (filled circles) and adipose tissue (open circles). Values are means ± SEM (n = 4–6) expressed as changes from baseline (100%); $^{*}P < 0.05$; $^{**}P < 0.01$; $^{***}P < 0.001$.

TABLE 1. Time course of glucose and insulin concentrations in rat plasma after intraperitoneal administration of 3 mg/100 g body weight of endotoxin

Time after Injection	Glucose	Insulin
h	*mg/dl*	*μU/ml*
Control	153.2 ± 13.5	21.2 ± 4.78
1	325.6 ± 20.8[a]	24.2 ± 5.24
4	150.2 ± 8.1	30.1 ± 4.80
7	109.2 ± 9.8[b]	30.4 ± 3.46
10	101.7 ± 10.3[b]	35.9 ± 2.48
24	152.0 ± 32.7	27.7 ± 6.69

Values are means ± SEM. n = 6.
[a], $P < 0.001$; [b], $P < 0.05$, significantly different from baseline.

In the second series of experiments, the time course of the endotoxin effect on heart and adipose tissue LPL activities and mRNA was investigated. Animals were given i.p. injections of 3 mg/100 g body weight and were killed at 1, 4, 7, 10, and 24 h after injection. Control rats were killed at 1 and 24 h. The observed fluctuations in control rat heart and adipose tissue LPL activities and mRNA were not statistically significant. TG levels increased by 60% within 4 h of injection ($P < 0.05$), by 200% within 7 h ($P < 0.001$), and remained elevated 24 h after injection (**Fig. 2A**). Heart LPL activity decreased by 45% ($P < 0.001$) at 7 h and by 60% ($P < 0.001$) at 10 h. At 24 h enzyme activity was still suppressed by 45% (Fig. 2B). Adipose LPL activity also decreased significantly compared to controls and remained suppressed after 24 h of injection (Fig. 2B). Heart and adipose tissue LPL mRNA did not change significantly at any time during the treatment period (Fig. 2C).

Plasma glucose levels increased during the first hour of injection, and subsequently decreased below baseline at 7–10 h, finally returning toward baseline levels after 24 h (**Table 1**), a pattern previously seen after TNF administration (18). Plasma insulin levels did not change during that period (Table 1) in agreement with previous reports (17).

In order to separate and quantitate the different lipoprotein fractions, plasma from control and treated rats was subjected to gel permeation fast protein liquid chromatography (FPLC). The results are shown in **Fig. 3.** The increase in TG was all in the very low density lipoprotein (VLDL) fraction which was accompanied by a concomitant decrease in high density lipoproteins (HDL). Since it has been shown that there is a positive correlation between HDL_2 and LPL activity (19), the

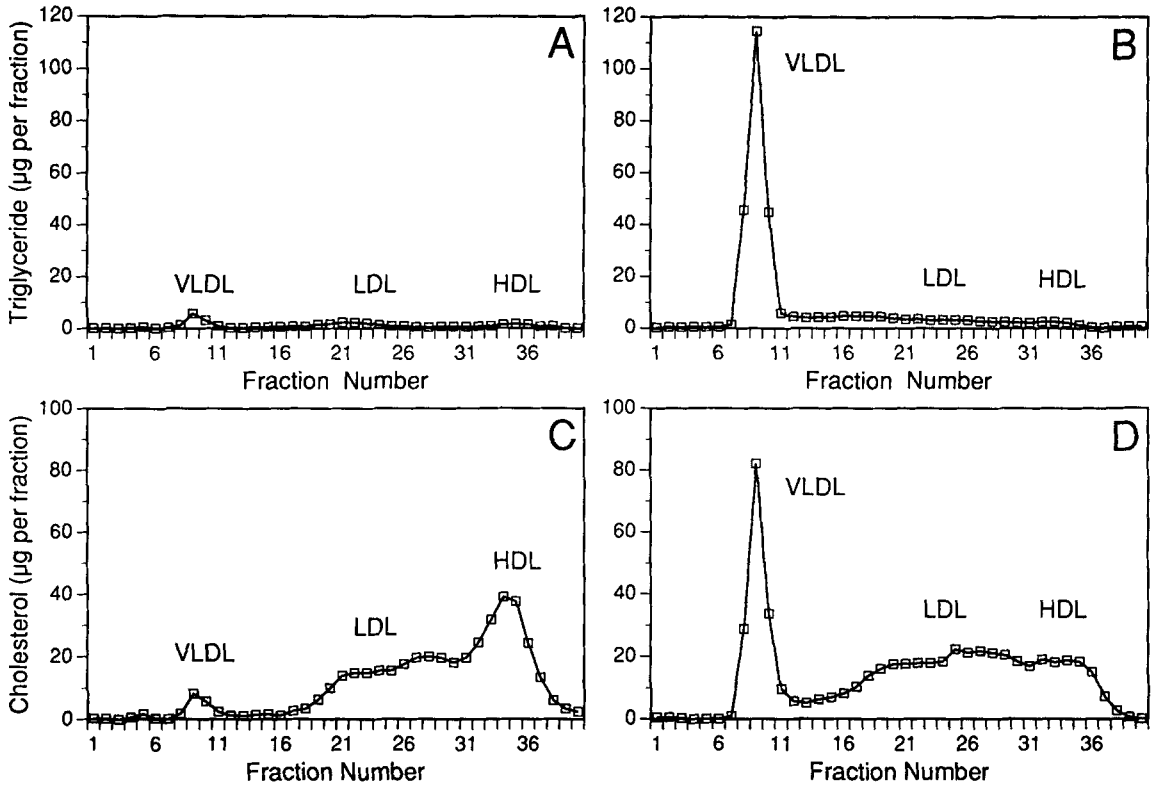

Fig. 3. Fast protein liquid chromatography (FPLC) of rat plasma. Rat plasma was loaded onto two Superose-6 columns connected in series. Elution of proteins was monitored by measurement of absorbance at 280 nm. After the first 12 ml had eluted, forty 500-µl fractions were collected and triglyceride (A, control; B, endotoxin-treated) and cholesterol (C, control; D, endotoxin-treated) were measured in the fractions.

reduction of the latter in both heart and adipose tissue could explain the fall of HDL during infection.

In order to investigate whether the decrease in the LPL activity is due to decreased translation of LPL mRNA in situ, incorporation of L-[^{35}S]methionine and L-[^{35}S]cysteine into immunoprecipitable LPL was examined at 7 h after treatment.

L-[^{35}S]methionine and L-[^{35}S]cysteine were incorporated into the 56 kDa band in agreement with the known molecular weight of rat adipose tissue LPL (20) (**Fig. 4**). The rate of incorporation into total protein and immunoprecipitable LPL was linear up to 30 min (data not shown). Titrations of goat anti-rat LPL and rabbit anti-goat IgG were done to optimize assay conditions. To ensure the specificity of immunoprecipitation, excess unlabeled purified LPL was added in the immunoprecipitation mixture. As shown in Fig. 4 (lanes C and D), the addition of unlabeled LPL diminished the 56 kDa band, indicating the specificity of the antibody reaction. A band persistently present in the 40 kDa area was not competed by the presence of excess unlabeled LPL, indicating that this is a nonspecific band. Furthermore, endotoxin treatment did not alter the LPL synthetic rate (**Fig. 5,** lanes B and C). To quantitate this effect, the radioactive bands corresponding to LPL were cut from the gels and radioactivity was determined as described in Materials and Methods. Endotoxin decreased the overall rates of incorporation into total TCA-precipitable protein by 35% and the incorporation into LPL by 25%. When LPL synthetic rate was expressed as percentage of the total protein synthetic rate, there was no significant difference between controls and endotoxin-treated animals. Experiments were performed in triplicate twice. The relative LPL synthetic rates (mean ± SD) were: control, 0.010 ± 0.003; treated, 0.014 ± 0.011.

DISCUSSION

The mechanism responsible for the increase in plasma triglycerides during infection is not fully understood and has remained controversial (1–7, 16, 21, 22). The purpose of our study was first to establish that endotoxin, the lipopolysaccharide component of the cell wall of gram-negative organisms, suppresses LPL activity in both adipose tissue and heart, a fact that has been questioned by some authors (2), and then to determine the molecular mechanism by which that suppression is mediated. Our

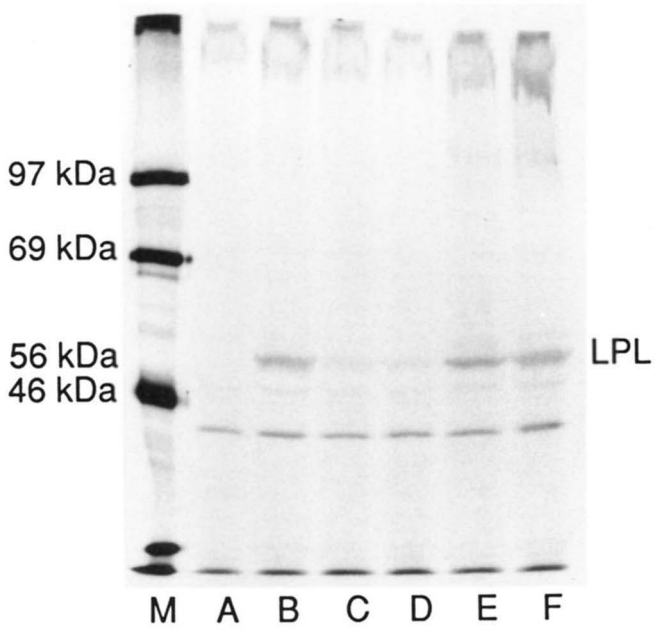

Fig. 4. Fluorogram of ^{35}S-labeled lipoprotein lipase from adipose tissue with and without competition by excess unlabeled lipoprotein lipase. Lane M, ^{14}C-labeled molecular weight markers [phosphorylase b (97.4 kDa), albumin (69 kDa), ovalbumin (46 kDa)]; lane A, non-immune goat serum; lane B, goat anti-rat LPL antibody + bovine serum albumin; lanes C and D, goat anti-rat LPL antibody in the presence of excess unlabeled LPL; lanes E and F, goat anti-rat LPL antibody in the absence of excess unlabeled LPL.

results show that endotoxin causes a marked increase in serum VLDL with a concomitant decrease in HDL associated with a significant decrease in heart and adipose tissue LPL activity. In contrast, we did not find any significant change in the steady state LPL mRNA levels of either the heart or the adipose tissue, suggesting that the endotoxin effect occurs at a post-transcriptional level. Furthermore, the lack of change in the adipose tissue LPL synthetic rate is consistent with a post-translational effect of endotoxin. Other factors have been shown in the past to affect LPL activity at post-transcriptional (insulin), and post-translational (insulin, fasting) levels (23, 24).

Endotoxin might exert its effect by affecting the intracellular transport or the degradation of the enzyme (25–27), interfering with processing of LPL's oligosaccharide chains, or affecting the transport of LPL to its functional site, i.e., the endothelial surface. It has been shown that endotoxin disrupts the surface of the vascular endothelium (20, 28). As LPL is normally anchored to heparin sulfate proteoglycans on the endothelial surface, damage of the latter by endotoxin would release LPL into the circulation, enabling it to be rapidly cleared by the liver.

Does endotoxin exert its effect on LPL directly or indirectly through the production of specific mediators? A substantial body of recent literature suggests that endotoxin acts through the production of cytokines such as tumor necrosis factor (TNF) and interleukin-1 (IL-1). However, TNF is unlikely to be the mediator of endotoxin-induced LPL suppression as TNF has been shown to increase LPL activity in heart (29), whereas we found a significant reduction of heart LPL activity. TNF has also been reported to suppress adipose tissue LPL mRNA in guinea pig (30), but we showed no change in LPL mRNA in rat adipose tissue. Furthermore, the TNF-suppressed LPL activity appears to be limited only to adipose tissue. It actually increases LPL activity in most other tissues, particularly in the liver and in postheparin plasma (29). It has also been reported that endotoxin decreases macrophage LPL mRNA independently of TNF (31) and that TNF decreases LPL synthesis in vitro (32, 33) and in vivo (29). This is in contrast to our observation that there was no change in the LPL synthetic rate. Since several hours are required for the maximal effects of LPL to become evident, and TNF disappears from blood after 6 h of induction in humans (34), it is likely that the effect of endotoxin is mediated via effects on macromolecular synthesis. Another argument to support this hypothesis is that endotoxin-induced decrease in macro-

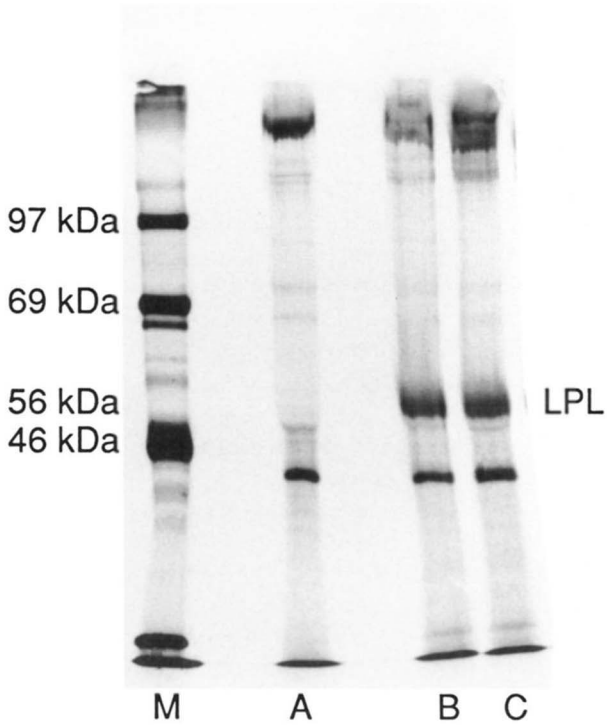

Fig. 5. Fluorogram of ^{35}S-labeled lipoprotein lipase from adipose tissue in control and endotoxin-treated rats. Lane M, ^{14}C-labeled molecular weight markers [phosphorylase b (97.4 kDa), albumin (69 kDa), ovalbumin (46 kDa)]; lane A, non-immune goat serum; lane B, goat anti-rat LPL antibody, control; lane C, goat anti-rat LPL antibody, endotoxin-treated.

phage LPL activity can be blocked by polymixin B (31). Most of the biological effects of endotoxin can be attributed to the lipid A molecule (35), and lipid A's effects can be mediated through protein kinase C activation (36). Thus one can postulate that endotoxin can act, at least in part, through activation of protein kinase C, in view of the fact that stimulatory effects of growth hormone on the LPL gene transcription in preadipocyte Ob1771 cells are partially mediated through such activation (37). Furthermore, LPL mRNA levels in THP-1 cells have been shown to be under the control of signals that activate phospholipase C, resulting in activation of protein kinase C (38). This mechanism, though, is not supported by our results since we found no change in LPL mRNA level. IL-1 also does not seem to be a mediator for the actions of endotoxin as it does not decrease adipose LPL activity in rats (19), IL-1 levels are not increased significantly after endotoxin challenge (34, 39), and IL-1 has been shown to decrease LPL synthesis in 3T3-L1 adipocytes (40). Endotoxin might exert its effect through other inflammatory mediators such as IL-2, IL-6, or γ-Interferon (γ-INF) (41). γ-INF, though, seems unlikely in its role as an endotoxin action mediator since its levels do not increase after endotoxin administration (34), and it has been shown to decrease LPL synthesis in human macrophages (42).

Hypoglycemia is one factor that should be considered in the endotoxin-induced suppression of LPL activity because glucose is required for LPL glycosylation, a modification required for LPL action (43); glucose was also reported to stimulate LPL synthesis and post-translational processing (44). Although the hypoglycemia that we observed might contribute to the endotoxin effects, it is unlikely that hypoglycemia plays any major role in the LPL suppression because the decreased LPL activity preceded the onset of hypoglycemia. Because plasma insulin did not change, it probably had no role in the process.

Catecholamines, glucagon, and corticosteroids also appear to be nonessential in the pathogenesis of the hypertriglyceridemia of infection (17, 41, 45).

In conclusion, we have demonstrated that endotoxin potently suppresses rat heart and adipose tissue LPL activity, but has no effect on the LPL mRNA and adipose tissue LPL synthesis. Hypertriglyceridemia in infection can therefore be attributed to a decrease in LPL activity which is mediated at a post-transcriptional level.

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