Contribution of apoB-48 and apoB-100 triglyceride-rich lipoproteins (TRL) to postprandial increases in the plasma concentration of TRL triglycerides and retinyl esters

Jeffrey S. Cohn,† Elizabeth J. Johnson,* John S. Millar,* Susan D. Cohn,* Ross W. Milne,‡ Yves L. Marcel,§ Robert M. Russell,* and Ernst J. Schaefer†*

Lipid Metabolism Laboratory and Gastrointestinal Nutrition Laboratory,* USDA Human Nutrition Research Center on Aging at Tufts University, 711 Washington Street, Boston, MA 02111, and Clinical Research Institute of Montreal, †110 Pine Avenue West, Montreal, Quebec H2W 1R7, Canada

Abstract After the ingestion of a fat-rich meal, there is a postprandial increase in the plasma concentration of both apolipoprotein B-48- and apoB-100-containing triglyceride-rich lipoproteins (apoB-48 and apoB-100 TRL). In order to determine the contribution of these lipoproteins to postprandial lipemia, the concentration of triglycerides (TG) and retinyl esters (RE) was measured in apoB-48 and apoB-100 TRL after an oral fat load. Six normolipidemic male subjects were fed heavy cream (1 g fat per kg body weight) containing vitamin A (3000 retinol equivalents). TRL were isolated by ultracentrifugation from plasma samples obtained at regular intervals after the meal, and apoB-100 TRL were separated from apoB-48 TRL by affinity chromatography using monoclonal antibodies. Postprandial increase in plasma TG concentration was due to an increase in TG in the TRL fraction, which in turn was predominantly (82 ± 4%) due to an increase in TG in apoB-48 TRL. Contribution of apoB-100 TRL to postprandial increase in TRL TG was 3–27% in individual subjects. ApoB-100 TRL remained a significant carrier of total plasma triglyceride in the fed state, as reflected by similar apoB-48 and apoB-100 TRL TG concentrations at 2, 4, and 6 h after the fat meal. Retinyl esters were regularly detected in apoB-100 TRL. Seventy-five (±9) percent of the increase in TRL-RE was due to RE in apoB-48 TRL and 25 ± 9% was due to RE in apoB-100. These data suggest that RE in plasma are not always associated with apoB-48-containing lipoproteins. Furthermore, we conclude that apoB-100 TRL, as well as apoB-48 TRL, make a significant contribution to postprandial triglyceridemia.—Cohn, J. S., E. J. Johnson, J. S. Millar, S. D. Cohn, R. W. Milne, Y. L. Marcel, R. M. Russell, and E. J. Schaefer. Contribution of apoB-48 and apoB-100 triglyceride-rich lipoproteins (TRL) to postprandial increases in the plasma concentration of TRL triglycerides and retinyl esters. J. Lipid Res. 1993. 34: 2033–2040.

Supplementary key words postprandial lipemia • atherogenesis

It has been proposed that the interaction of triglyceride-rich lipoproteins (TRL) of intestinal and liver origin with lipoprotein lipase and cells of the artery wall constitutes an atherogenic process (1, 2). This concept is supported by studies showing that partially delipidated very low density lipoproteins (VLDL) and chylomicrons are able to load cultured smooth muscle cells and macrophages with esterified cholesterol (3–5). The documented in vitro atherogenicity of postprandial lipoproteins has led to numerous in vivo studies documenting the qualitative and quantitative changes of plasma lipoproteins in the fed state (as reviewed in refs. 6 and 7). We have shown in previous studies that after the ingestion of a fat-rich meal there is a postprandial increase in the plasma concentration of both apoB-48- and apoB-100-containing TRL (8). These lipoprotein species contribute to both early (0–6 h postprandially) and late (6–12 h) changes in plasma triglyceride (TG) concentration (9). The rate of TRL apoB-100 production is also increased in the fed compared to the fasted state, as measured by the in vivo rate of incorporation of intravenously administered [D3]-L-leucine into apoB-100 in the d<1.006 g/ml fraction of plasma (10). In order to substantiate the concept that both apoB-48 and apoB-100 TRL contribute to postprandial triglyceridemia, we have assessed the contribution of these lipoproteins to postprandial increases in the plasma concentration of TRL TG.

Subjects in the present study were also fed vitamin A in order to measure the distribution of retinyl esters (RE)

Abbreviations: TRL, triglyceride-rich lipoproteins; VLDL, very low density lipoproteins; LDL, low density lipoproteins; HDL, high density lipoproteins; TG, triglyceride; RE, retinyl esters.

†Present address: Clinical Research Institute of Montreal, 110 Pine Avenue West, Montreal Quebec H2W 1R7, Canada.
§Present address: University of Ottawa Heart Institute, 4th Floor, Room H453, 1053 Carling Avenue, Ottawa Ontario K1Y 4E9, Canada.
*To whom correspondence should be addressed.
between apoB-48 and apoB-100 TRL. Retinyl esters in the circulation have previously been used to identify the presence in plasma of lipoproteins of intestinal origin (chylomicrons and chylomicron remnants). The rationale for this approach ([11-14] is based on the concept that dietary vitamin A is esterified in the intestine and is incorporated into the core of chylomicron particles. These lipoproteins are secreted into intestinal lymph and their component TG are hydrolyzed by lipoprotein lipase in the circulation. It is believed that the RE remain associated with chylomicrons during lipolysis and are taken up by the liver within chylomicron remnants via a receptor-mediated process. Evidence suggests that the liver does not resecrete these RE, and they are either stored or resecreted as unesterified retinol bound to retinol-binding protein. As plasma exchange of RE between lipoproteins is believed to be minimal and RE are not resecreted into the circulation, it is postulated that RE in plasma are appropriate markers for lipoproteins containing apoB-48 of intestinal origin. Circumstantial evidence has been presented, however, suggesting that plasma RE are not always associated with apoB-48-containing lipoproteins ([15]. Postprandial changes in the plasma concentration of TRL apoB-48 are not always mimicked by changes in TRL RE concentration. Furthermore, in the fasting state and 12 h after a fat-rich meal, a significant proportion of plasma RE in normolipidemic subjects is found in the low density lipoprotein (LDL) and high density lipoprotein (HDL) fractions, apparently unassociated with apoB-100 TRL. Retinyl esters in plasma RE are not resecreted into the circulation, it is postulated that RE in plasma are appropriate markers for lipoproteins containing apoB-48 of intestinal origin. Circumstantial evidence has been presented, however, suggesting that plasma RE are not always associated with apoB-48-containing lipoproteins ([15]. Postprandial changes in the plasma concentration of TRL apoB-48 are not always mimicked by changes in TRL RE concentration. Furthermore, in the fasting state and 12 h after a fat-rich meal, a significant proportion of plasma RE in normolipidemic subjects is found in the low density lipoprotein (LDL) and high density lipoprotein (HDL) fractions, apparently unassociated with apoB-48. The second purpose of the present experiments was, therefore, to directly examine the extent of RE associated with apoB-48 in the TRL fraction.

METHODS

Subjects

Six healthy male subjects (30 ± 1 years, mean ± SEM) who were of average height and weight were recruited. They had normal fasting lipid levels (cholesterol: 4.40 ± 0.32 mmol/l; triglycerides: 0.86 ± 0.09 mmol/l; HDL cholesterol: 1.24 ± 0.12 mmol/l). They were not taking vitamin A or medications known to affect plasma lipids. All studies were conducted in the Metabolic Research Unit at the U.S. Department of Agriculture Human Nutrition Research Center on Aging at Tufts University. Informed consent was obtained from all volunteers under the guidelines established by the Human Investigation Review Committee of the New England Medical Center and Tufts University.

Fat-feeding protocol

After a 12-h overnight fast, subjects were given an oral fat load (1 g fat/kg body weight) in the form of heavy cream, together with 3000 retinol equivalents of vitamin A (three times the recommended daily allowance). The vitamin was given as retinyl palmitate in corn oil (PIMO, a gift from Hoffman LaRoche Inc., Nutley, NJ). Blood samples (10 ml) were obtained via a small forearm indwelling catheter prior to the fat load and at 2, 4, 6, 9, and 12 h thereafter. Blood samples were collected in tubes containing ethylenediaminetetraacetate (EDTA) to give a final concentration of 0.1% EDTA, and were protected from light with the use of aluminium foil. Water, but no food, was allowed during the course of the study.

Lipoprotein separation

Plasma was separated from red blood cells by ultracentrifugation at 1000 g for 15 min at 4°C. TRL fractions (containing chylomicrons, very low density lipoproteins, and intermediate density lipoproteins) were isolated from 5 ml of plasma by a single ultracentrifugal spin (39,000 rpm, 18 h, 4°C) at d 1.019 g/ml in a Beckman 50.3 Ti rotor. Fraction volumes were adjusted to 3.0 ml with normal saline and were assayed for protein by the method of Lowry et al. ([16]), using bovine serum albumin as a standard. Turbidity was cleared with chloroform.

Freshly isolated TRL fractions were subjected to affinity chromatography, using specific apoB-100 monoclonal antibodies 4G3 and 5E11, which do not cross-react with apoB-48 ([17, 18]. These antibodies have previously been used to characterize the very low density lipoprotein fraction of Type III and Type IV hyperlipoproteinemic subjects ([19, 20]. Antibodies (mixed together in a 1:1 protein ratio) were coupled to activated Sepharose 4B (Pharmacia Fine Chemicals, Inc., Uppsala, Sweden) as described previously ([17]. Routinely, 16 mg of 4G3 protein and 16 mg of 5E11 protein were coupled to 8 ml of activated Sepharose. Binding capacity of the gel was 0.75-1.0 mg TRL protein/ml gel.

Separation of apoB-48 and apoB-100 fractions was carried out in 1.5-ml Eppendorf tubes. Sepharose gel (1.2 ml) in phosphate-buffered saline (PBS, pH 7.4, 0.02% NaN,) was aliquoted into tubes and centrifuged for 5 min at 1,000 rpm. The supernate was aspirated and TRL (300 µg protein) was added to 0.6 ml of packed gel. Tubes were vortexed gently, rocked for 1 h at room temperature on an oscillating platform, and centrifuged, and the supernate was collected (approximately 0.5 ml was retrieved). The gel was washed with 1.0 ml PBS, rocked for 15-20 min, and after centrifugation, the supernate was aspirated and added to the first supernate. The washing procedure was repeated with a second volume of PBS (final volume of fraction: 2.5 ml). This sample (the unbound fraction) contained the apoB-48 TRL. Lipoproteins bound to the gel were dissociated by the addition of 3 M Na thiocyanate (1.0 ml). Samples were rocked for 1 h at room temperature, centrifuged, and the supernate was collected. The gel was washed with two further 1.0-ml aliquots of Na thiocyanate, and these washes were added to the first...
thiocyanate supernate to give the bound fraction, containing apoB-100 TRL. Recovery of initial TRL added to the affinity gel was 92 ± 4% as estimated by measuring the recovered protein in the bound and unbound fractions.

The adequacy of lipoprotein separation was assessed by SDS polyacrylamide gel electrophoresis using 4–22.5% acrylamide gradient gels as previously described (8). Nondelipidated lipoprotein samples (30 μg protein), reduced in SDS sample buffer containing 3% mercaptoethanol, were routinely loaded onto the 1.5-mm thick vertical slab gels. The apoB-48 (unbound) fractions were concentrated before electrophoresis to allow for adequate visualization of the apoB-48 protein band. The apoB-100 band of TRL comigrated with the major stainable protein of a narrow-cut LDL fraction (1.040 < d < 1.050 g/ml). The apoB-48 band of TRL comigrated with the major high molecular weight band of lymph chylomicrons. The identity of the apoB bands was confirmed by Western blotting analysis using a polyclonal antibody that was known to react with both apoB-48 and apoB-100.

**Lipid and lipoprotein analyses**

Plasma and lipoprotein fractions were assayed for total cholesterol and TG with an Abbott Diagnostics ABA-200 bichromatic analyzer using enzymatic reagents (21). Assays were standardized through participation in the Centers for Disease Control—National Heart, Lung and Blood Institute Standardization program. All lipid measurements (including separated TRL fractions) were carried out in duplicate. HDL cholesterol was quantitated by analyzing the supernate obtained by the precipitation of a plasma aliquot with dextran-Mg⁺⁺ (22). Retinyl esters were measured under red lights by high-performance liquid chromatography using retinyl acetate as an internal standard (23). Using this method, all the major plasma RE (retinyl palmitate, stearate, and oleate) coeluted together and appeared as a single peak on the chromatograms.

**Statistics**

Paired t-tests were used to determine the statistical significance between lipid measurements obtained from fasting (0 h) and postprandial samples. Postprandial increase in TRL TG and RE was measured by planimetry as the area under the concentration-time curve, where the baseline was the zero-time (fasting) concentration. Area measurements are expressed in the units of mmol • h/l.

**RESULTS**

Mean (± SEM) plasma cholesterol, TG, and RE concentrations before and after the ingestion of the fat load are shown in Fig. 1. Mean plasma cholesterol concentration did not change significantly during the course of the experiment. This is consistent with our previous studies (24) and those of others (6). Plasma TG concentration peaked either 2 or 4 h after the fat load in individual subjects, and the mean plasma TG concentration was significantly (P < 0.05) elevated above fasting concentration 2 and 4 h postprandially. Mean plasma RE concentration peaked at 6 h and was significantly greater than baseline at all postprandial timepoints. As shown previously (9, 15) and as reflected by the different time course of the curves for the mean data (Fig. 1), change in plasma RE concentration occurred after change in plasma TG in all subjects.

TRL fractions (d < 1.019 g/ml) were isolated by ultracentrifugation and were separated into apoB-48 and apoB-100 TRL species by affinity chromatography. The apolipoprotein composition of bound and unbound fractions is shown in Fig. 2. Very adequate separation of apoB-48- and apoB-100-containing fractions was achieved. ApoB-48 was not detectable in the bound (apoB-100-containing) fractions. A faint apoB-100 band was often observed in the unbound fractions (see right hand gel of Fig. 2). Minor contamination of the unbound fraction has been noted previously using these antibodies (19, 20). Additional chromatography was not carried out to remove contaminating apoB-100 material, as this was found to adversely affect recovery. Laser scanning densitometry showed that less than 1% of the apolipoprotein composition of apoB-48 TRL was apoB-100 (assuming equal chromogenicity of apolipoprotein bands). Two percent of apoB-48 TRL protein was apoB-48, 15% was albumin, 8% was β-2-glycoprotein 1, 21% was apoA-IV, 2% was apoE, 19% was apoA-I, and 34% was C-apolipoproteins. In apoB-100 TRL, 35% of total protein by gel scanning was apoB-100, 15% was albumin, 10%...
Fig. 2. Apolipoprotein composition of TRL fractions separated by affinity chromatography using monoclonal antibodies against apoR-100. The bound fraction containing apoR-100 is on the left, and the unbound fraction containing apoR-48 is on the right. Bound TRL contained relatively more apoE and less apoA-IV and apoA-I than unbound TRL. The unbound fraction was concentrated before loading onto the gel. Trace amounts of apoR-100 were routinely detected in the unbound fraction.

was β-2-glycoprotein 1, 1% was apoA-IV, 9% was apoE, and 31% was C-apolipoproteins.

In the fasting state (at zero time), mean plasma TG concentration was 0.86 ± 0.09 mmol/l and mean TRL TG concentration was 0.54 ± 0.11 mmol/l (representing 61 ± 6% of total plasma triglyceride). In the fed state at the timepoint of maximal TG increase (2 h postprandially), mean plasma TG concentration was 1.26 ± 0.19 mmol/l and mean TRL TG concentration was 1.00 ± 0.19 mmol/l. A mean 77 ± 3% of plasma TG was thus contained in the TRL fraction 2 h after the fat load. Mean TRL TG was significantly increased above fasting concentration 2 and 4 h after the fat load (Fig. 3) in accord with the total plasma TG data. These results are comparable to those obtained in male subjects of different ages, reported previously (8).

The plasma TG concentration of the apoB-48 and apoB-100 fractions before and after the fat load is shown in Fig. 3. Postprandial increase in plasma TG concentration was predominantly due to increase in apoB-48 TRL, which was significantly increased 2, 4, and 6 h after the meal. A smaller but significant increase was observed in apoB-100 TRL TG. The contribution of apoB-48 and apoB-100 TRL fractions to postprandial increase in TRL TG (Table 1) was quantitated by measuring the area under individual TG response curves (fasting [0 h] concentration taken as baseline). Increase in apoB-48 TRL TG was five times greater than increase in apoB-100 TRL TG (2.44 ± 0.45 vs. 0.47 ± 0.15 mmol • h/l). Eighty-two (± 4) percent of the postprandial increase in TRL TG was thus due to apoB-48 TRL (range: 73–97%). The contribution of apoB-100 TRL was not insignificant, accounting for 3–27% of total increase in TRL TG in individual subjects (mean ± SEM: 18 ± 4%). Total area (as opposed to incremental area) was also measured under the TRL TG response curves (zero concentration used as baseline). The apoB-48 TRL TG total area was 3.96 ± 0.48 mmol • h/l and the apoB-100 TRL TG area was 4.64 ± 0.75 mmol • h/l. This means that although apoB-48 TRL were most responsible for the increase in TRL TG concentration after the fat load, in absolute terms apoB-100 TRL were the predominant carriers of plasma TG during the total 12 h postprandial period.

RE were measured in TRL fractions isolated at different postprandial timepoints. It is significant that we detected RE in nearly all apoB-100 TRL, as well as apoB-48 TRL samples. The mean plasma RE concentrations of
the total, apoB-48, and apoB-100 TRL fractions before and after the fat load are shown in Fig. 4. Total TRL RE concentration was significantly elevated 2, 4, 6, and 9 h after the fat load, which mimicked the postprandial changes in total plasma RE concentration (Fig. 1). Increases in both apoB-48 TRL and apoB-100 TRL RE were responsible for the change in total TRL RE. RE concentration peaked on average at 6 h in the apoB-48 TRL fraction, whereas the maximum RE concentration in apoB-100 TRL tended to occur at later timepoints (at 9 h for the mean data). The contribution of apoB-100 TRL and apoB-48 TRL to postprandial increases in plasma TRL RE concentration was quantitated by planimetry and mean area measurements are shown in Table 1. Increase in RE concentration postprandially tended to be 2- to 3-times greater in apoB-48 TRL than in apoB-100 TRL. Thus 75 ± 9% of TRL RE increase was due to apoB-48 TRL and 25 ± 9% was due to apoB-100 TRL. It is worth noting that the contribution of apoB-100 TRL varied from one subject to another, and was quite significant in some individuals (range: 6-56%).

Cholesterol concentrations were also measured in the different TRL fractions and these results are shown in Fig. 5. A postprandial increase in total TRL cholesterol was not observed in every subject (as we have observed in previous studies (8)). In this group of subjects, who had relatively low plasma cholesterol concentrations, a decrease in the mean total TRL cholesterol below fasting concentration was, in fact, observed at later timepoints. This decrease was predominantly due to a fall in the postprandial concentration of apoB-100 TRL cholesterol. In contrast, mean apoB-48 TRL cholesterol was significantly increased 2 and 4 h after the fat load.

DISCUSSION

Specific monoclonal antibodies for apoB-100 have been used before (19, 20) to isolate and characterize the very low density lipoprotein (VLDL) fraction of dyslipidemic subjects in the fasted state. The same antibodies were used in the present study to isolate the apoB-48- and apoB-100-containing TRL of plasma obtained from subjects in the fed state. In order to obtain reliable quantitative data with these antibodies, we have separated single sample aliquots in individual Eppendorf tubes (see Methods), containing antibodies bound to Sepharose, rather than eluting fractions from affinity chromatography columns, as described previously (19). In addition, sodium thiocyanate rather than citric acid was used to separate the bound TRL fraction from the affinity chromatography gels. These modifications resulted in acceptable recovery (85-95%) of TRL samples and allowed for the plasma concentration of different fractions to be estimated. Adequacy of separation was also controlled as closely as possible by monitoring the apolipoprotein composition of isolated fractions by polyacrylamide gel electrophoresis (Fig. 2). Some contamination of apoB-48 fractions was noted (see Methods), leading to a small underestimation of apoB-100 TRL lipid concentrations. This underestimation, if taken into account, would only
increase the contribution of apoB-100 TRL and enhance
the significance of the present results.

We have shown that increase in plasma triglyceride
concentration after an oral fat load is predominantly due
to triglyceride contained within apoB-48-containing
lipoproteins in the TRL fraction of plasma. In normalipi-
demic male subjects, we have found that 82 ± 4% of the
postprandial increase in TRL TG was attributable to
triglyceride in apoB-48 TRL. This is consistent with the
established concept that dietary fat is incorporated into
large triglyceride-rich chylomicrons in the intestine that
have apoB-48 as their major structural apolipoprotein
(25). These lipoproteins are secreted into intestinal lymph
and then into the circulation where their triglycerides are
hydrolyzed by lipoprotein lipase. ApoB-48-containing
lipoproteins in the circulation, therefore, represent a spec-
trum of partially catabolized lipoproteins of intestinal ori-
gin, which make a significant contribution to postprandial
triglyceridemia.

Although the increase in plasma TRL TG concentra-
tion in the fed state was predominantly due to an increase
in apoB-48 TRL, the contribution of apoB-100 TRL was
not insignificant; 18 ± 4% of the total TRL TG increase
following the oral fat load was attributable to apoB-100
TRL, and this varied among individual subjects (range:
3–27%). In absolute terms, apoB-100 TRL were respon-
ible for transporting a significant proportion of plasma
apoB-100 in TRL, and this varied among individual subjects (range:
3–27%). In absolute terms, apoB-100 TRL were respon-

The plasma clearance of apoB-100 TRL is inhibited by the influx into plasma of
postprandial chylomicrons; 2) the ingestion of a fat-rich
meal stimulates the synthesis and secretion of apoB-100
TRL from the intestine; and 3) hepatic apoB-100 TRL are secreted postprandially in response to lipid of dietary
origin reaching the liver via the portal vein or via
chylomicron transport. The first possibility is supported
by the studies of Brunzell et al. (27) showing that
chylomicrons and VLDL are catabolized by a common
pathway. Triglycerides in both chylomicrons and VLDL
are hydrolyzed by lipoprotein lipase at the capillary en-
dothelial surface and these lipoproteins can compete for
enzyme-mediated lipolysis. Reduced availability of lipo-
lytic activity due to the postprandial presence of apoB-48-
containing chylomicrons could explain the observed in-
crease in apoB-100 TRL triglyceride. An increase in the
production of apoB-100 TRL is, however, an equally pos-
sible explanation. We have previously found that in the
fed state there is an increase (50% on average) in the
plasma concentration of apoB-100 in the TRL fraction
(8), as well as an increase in the rate of production of
TRL apoB-100 (10). We have suggested that this
represents a postprandial increase in postprandial synthe-
sis and secretion of TRL by the liver, as it is normally as-
sumed that apoB-100 in plasma is of hepatic origin. Data
from a recent study in which apoB-100 epitopes were de-
termined in human subjects before and after liver trans-
plantation (28) support the hepatic origin of circulating
apoB-100. Other lines of evidence, however, have sug-
gested that the human intestine has the capacity to synthe-
size apoB-100 (29, 30), and it cannot be ruled out that in
the fed state apoB-100 in TRL is partly of intestinal origin.

Irrespective of the source of apoB-100 TRL in the fed
state, and irrespective of the mechanism for the increased
presence of apoB-100 TRL in postprandial plasma, our
studies suggest an additional reason why the postprandial
state is potentially atherogenic. Zilversmit (1) originally
proposed that atherogenesis was a “postprandial
phenomenon” because it involved the “binding of chylomicrons to the arterial surface, the hydrolysis of
triglyceride by arterial lipoprotein lipase and the subse-
quently internalization of cholesterol-enriched chylomicron remnants by arterial smooth muscle cells.” Postprandial
apoB-100 TRL may, however, be of equal significance, es-
pecially since a certain proportion of TRL containing
apoB-100 are the precursors of potentially atherogenic
LDL (31) and partially degraded apoB-100 TRL rem-
nants have themselves been shown to be atherogenic (2).

An important finding of the present study is that RE
were routinely detected in apoB-100 TRL. The presence
of RE in apoB-100 TRL was of greater significance at
later postprandial timepoints (Fig. 4), and for the 12-h
period as a whole 25 ± 9% of TRL RE was contribu-
ted by RE in apoB-100 TRL. These data lend support to the
circumstantial evidence that we and others have presented
previously, suggesting that plasma RE are not always as-
sociated in plasma with apoB-48-containing lipoproteins
(12, 15, 32). There are three possible explanations for the
presence of RE in apoB-100 TRL. 1) RE are secreted by
the intestine within chylomicrons containing apoB-100 or
possibly within smaller “VLDL-sized” apoB-100 particles;
2) RE are secreted by the liver in VLDL containing
apoB-100; or 3) RE are transferred to apoB-100 TRL in
the circulation from other plasma lipoproteins. As dis-
cussed before, evidence has been presented showing that
the intestine has the capacity to synthesize apoB-100 (29,
30). The quantitative significance of this synthesis and
whether it results in the secretion of a mature protein re-
 mains, however, to be substantiated. As far as hepatic
secretion of RE is concerned, there are data from isolated cell studies (33) and from experimental animals (34) that suggest that RE are not secreted by the liver. Nevertheless, it cannot be totally ruled out that the human liver in vivo is able to secrete RE incorporated into apoB-100-containing lipoproteins. The third possibility is supported by evidence that small amounts of RE are able to transfer between plasma lipoproteins (35, 36), however several investigators consider this transfer to be quantitatively insignificant (12, 14, 37).

Finally, plasma RE have been used as a measure of the duration and extent of postprandial lipemia in order to establish the role of postprandial lipoproteins (specifically intestinal lipoproteins) in the etiology of atherosclerosis (38-40). As suggested before, however (15), studies tracing the presence of RE in plasma for relatively long periods of time after meal-feeding need to be interpreted with caution. Small amounts of RE not associated with the TRL fraction (associated with LDL and HDL at later timepoints) are probably not associated with remnant lipoproteins. In addition, RE within the TRL fraction are not always associated with apoB-48-containing lipoproteins and they are therefore not necessarily indicative of TRL of intestinal origin.

Supported by grant HL 39326 from the National Institutes of Health and contract 53-3K-06 from the U.S. Department of Agriculture Research Service.


REFERENCES