Apolipoproteins C-III and A-V as Predictors of Very-Low-Density Lipoprotein Triglyceride and Apolipoprotein B-100 Kinetics

Dick C. Chan, Gerald F. Watts, Minh N. Nguyen, P. Hugh R. Barrett

Objective—We investigated the associations between plasma very-low-density lipoprotein (VLDL)–apolipoprotein (apo)C-III and apoA-V concentrations and the kinetics of VLDL–apoB-100 and VLDL triglycerides in 15 men. We also explored the relationship between these parameters of VLDL metabolism and VLDL–apoC-III kinetics.

Methods and Results—ApoC-III, apoB, and triglyceride kinetics in VLDL were determined using stable isotopes and multicompartmental modeling to estimate production rate (PR) and fractional catabolic rate (FCR). Plasma VLDL–apoC-III concentration was significantly and inversely associated with the FCRs of VLDL triglycerides ($r = -0.610$) and VLDL–apoB ($r = -0.791$), and positively correlated with the PR of VLDL–apoC-III ($r = 0.842$). However, apoA-V concentration was not significantly associated with any of the kinetic variables. There was a significant association ($P < 0.01$) between the PRs of VLDL triglycerides and VLDL–apoB ($r = 0.641$), and between the FCRs of VLDL triglycerides and VLDL–apoB ($r = 0.737$). In multiple regression analysis, plasma VLDL–apoC-III concentration was a significant predictor of VLDL triglyceride FCR ($\beta$-coefficient $= -0.575$) and VLDL–apoB FCR ($\beta$-coefficient $= -0.839$).

Conclusions—Our findings suggest that increased VLDL–apoC-III concentrations resulting from an overproduction of VLDL–apoC-III are strongly associated with the delayed catabolism of triglycerides and apoB in VLDL. We also demonstrated that the kinetics of VLDL triglycerides and apoB are closely coupled. Our data do not support a role for plasma apoA-V in regulating VLDL kinetics. (Arterioscler Thromb Vasc Biol. 2006;26:590-596.)

Key Words: apoA-V ■ apoC-III ■ cardiovascular disease ■ lipoprotein metabolism

Hypertriglyceridemia is associated with increased risk of coronary artery disease. It is the most consistent lipid disorder in subjects with obesity and type 2 diabetes mellitus. In the postabsorptive state, this abnormality is chiefly a consequence of alterations in kinetics of very-low-density lipoprotein (VLDL), including overproduction and/or delayed clearance of VLDL. The metabolism of VLDL involves regulatory processes governing the turnover of triglycerides and apolipoprotein B-100 (apoB). However, the precise mechanisms involved are incompletely understood.

Apolipoprotein (apo)C-III, a glycoprotein synthesized by the liver and intestine, plays a central role in regulating the metabolism of triglyceride-rich lipoproteins (TRLs) including VLDL and their remnants in plasma. ApoC-III exchanges between TRL, and high-density lipoprotein (HDL). In normolipidemic subjects, the majority of apoC-III is bound to HDL, whereas in hypertriglyceridemic subjects, the majority is bound to TRLs. ApoC-III is an inhibitor of lipoprotein lipase (LPL) and of TRLs remnant uptake by hepatic lipoprotein receptors. Elevated apoC-III, in particular VLDL–apoC-III, may induce hypertriglyceridemia because of accumulation in plasma of TRLs, and this could relate to oversecretion of VLDL–apoC-III. Using stable isotopes and multicompartmental modeling, we have previously found that in overweight and obese men, increased plasma apoC-III concentration was associated with reduced catabolism of TRLs. However, we did not examine the association with VLDL triglyceride kinetics or the role of VLDL–apoC-III kinetics.

ApoA-V is a newly discovered member of the APOA1/C3/A4/A5 gene cluster that is involved in lipoprotein metabolism. Studies in humans have also demonstrated that polymorphisms and/or mutations in the apoA-V gene result in moderate to severe hypertriglyceridemia. The mechanism whereby apoA-V affects plasma triglycerides is undergoing intensive investigation. Compelling experimental and molecular data suggest that apoA-V reduces plasma triglycerides by 3 potential mechanisms: inhibition of VLDL production, stimulation of LPL-mediated VLDL triglyceride hydrolysis, and acceleration of hepatic uptake of VLDL particles. However, the precise role of apoA-V in control of VLDL metabolism remains to be clarified in humans.

In the present study, we tested the hypothesis that apoC-III and apoA-V have opposing regulatory effects on VLDL metabolism. Specifically, we examined the associations be-
tween plasma VLDL–apoC-III and apoA-V concentrations and the kinetics of VLDL triglycerides and VLDL–apoB. We also measured VLDL–apoC-III kinetics and explored their relationship with the other indices of VLDL metabolism and apoA-V concentrations.

Methods

Subjects

We studied 15 nonsmoking men selected from the community with body mass index (BMI) ranging from 22 to 40 kg/m^2. None had diabetes mellitus, apoE2/E2 or E4/E4 genotype, macroproteinuria, creatinemia (>120 µmol/L), hypothyroidism, abnormal liver enzymes; or consumed >30 g alcohol/d. None reported a history of cardiovascular disease or was taking agents affecting lipid metabolism. The study was approved by the Ethics Committee of Royal Perth Hospital. We have previously reported on the kinetics of apoB in some of these subjects and now relate these findings to the kinetics of VLDL–apoC-III and VLDL-triglycerides.

Clinical Protocols

All subjects were admitted to a metabolic ward in the morning after a 14-hour fast. Venous blood was collected for measurements of biochemical analytes. Plasma volume was determined by multiplying body weight by 0.045 and by a correction factor to adjust for the decrease in relative plasma volume associated with an increase in body weight as described by Riches et al. A single bolus of d1-leucine (5 mg/kg body weight) and d3-glycerol (10 mg/kg body weight) was administered intravenously and blood samples were taken at baseline and after isotope injection at 5, 10, 20, 30, and 40 minutes, and 1, 1.5, 2, 2.5, 3, 4, 5, 6, 8, and 10 hours. Additional fasting blood samples were collected in the morning on the next 4 days of the same week. Diets were assessed for energy and major nutrients using at least 2 24-hour dietary diaries.

Measurements of ApoB-100, ApoC-III, and Triglyceride Enrichments

ApoB-100

Laboratory methods for isolation and measurement of isotopic enrichment apoB have been fully described. Briefly, apoB in the VLDL fraction was separated by sequential ultracentrifugation, precipitated by isopropanol, delipidated, hydrolyzed, and derivatized. Isotopic enrichment was determined by ion monitoring of derivatized apoB precipitate. The samples were then re-centrifugated for 10 minutes at 425 g; 50 µL of the isopropanol sample extract (supernatant) was saponified with 500 µL of 2% potassium hydroxide at 80°C for 30 minutes. The free glycerol was first purified by passage through a mixed bed of ion exchange resins and then dried in a centrifugal evaporator at room temperature. Glycerol was reconstituted in 100 µL acetonitrile/pyridine (1:5) and derivatized with 50 µL pentafluorobenzoyl chloride. Plasma glycerol was also isolated from plasma by precipitation with 6% perchloric acid, followed by ion exchange chromatography and derivatized as described. Isotopic enrichment was determined by selected ion monitoring of derivatized samples at a mass to charge ratio (m/z) of 674 and 679.

Biochemical Measurements

Laboratory methods for measurements of lipids, lipoproteins, and other biochemical analytes have been previously detailed. VLDL apoC-III was quantitated using electroimmunodiffusion method (Hydragel, Sebia, France) with appropriate standards and quality controls according to the manufacturer’s instruction. Plasma apoA-V concentration was determined using a dual-antibody sandwich enzyme-linked immunosorbent assay (Linco Diagnostic Services) as described recently by O’Brien et al. Insulin resistance was estimated using the homeostasis model assessment (HOMA) score.

Model of ApoB, ApoC-III, and Triglyceride Metabolism and Calculation of Kinetic Parameters

VLDL–ApoB

The apoB compartment model used for the analysis of the VLDL–apoB tracer data has been described previously. In brief, the compartment model consisted of a plasma leucine subsystem, intrahepatic delay compartment, and 5 compartments (4-compartment delipidation cascade and a single compartment for slowly turning over VLDL). The SAAM II program (SAAM Institute, Seattle, Wash) was used to fit the model to the observed tracer data. VLDL–apoB metabolic parameters, including fractional catabolic rate (FCR) and production rate (PR), were derived following a fit of the compartment model to the apoB tracer/tracee ratio data.

VLDL–ApoC-III

A model of apoC-III metabolism was developed using the same 4-compartment leucine subsystem used in the apoB model described previously. In this study, a single compartment (Figure 1A) was used to account for the plasma kinetics of VLDL–apoC-III. As with the apoB model, a single compartment was used to account for the intrahepatic delay associated with the synthesis and secretion of apoC-III. This compartment model was fit to the apoC-III tracer/tracee ratio data to derive metabolic parameters for VLDL–apoC-III, including FCR and PR.

VLDL Triglycerides

The VLDL triglyceride compartment model was developed on the backbone of the VLDL–apoB model, as has been previously described. In this way, the VLDL–apoB tracer data are used to describe the kinetics of VLDL particles and the triglyceride tracer data reflects both the kinetics of the VLDL particles and the rate of VLDL triglyceride hydrolysis. A 3-compartment subsystem (compartments 1 to 3) (Figure 1B) is used to describe the plasma glycerol kinetics. Compartments 4 and 5 describe the slow and fast triglyceride production pathways. Compartments 6 to 9 represent triglycerides associated with VLDL particles in the delipidation cascade. Triglycerides in compartment 10 are associated with a slowly turning over pool of VLDL particles. In addition to the pathways that show the flow of triglycerides along the delipidation cascade, triglycerides are lost as a result of hydrolysis from each compartment. The glycerol subsystem was fit to the plasma glycerol tracer data to derive the model parameters for this section of the model. The apoB tracer/tracee ratio data were used to describe the kinetics of the VLDL–apoB particles and modeled with the VLDL triglyceride tracer/tracee ratio data to estimate VLDL–apoB and triglyceride metabolic parameters.
Statistical Analysis

All analyses were performed SPSS 11.1 (SPSS, Inc, Chicago, Ill). Associations were examined by simple and multivariate linear regression methods. Hypertriglyceridemic waist was defined as plasma triglycerides ≥2.0 mmol/L and waist circumference ≥90 cm.19 Age, waist circumference, and HOMA score were selected in these models because they are known causal factors for dyslipidemia.2 Statistical significance was defined at the 5% level using a 2-tailed test.

Results

Table 1 shows the anthropometric and biochemical characteristics of the 15 men. On average, the subjects were middle-aged, normotensive, and mildly dyslipidemic, with a wide range of BMI (24 to 36 kg/m²). Seven were obese and 8 were nonobese (BMI ≤30 kg/m²). Plasma remnant-like protein (RLP) cholesterol, apo-C-III and insulin concentrations, and HOMA score were, however, significantly elevated in this group compared with the corresponding reference range shown in Table 1.20 Plasma concentrations of apoA-V were comparable to other published data.16 Ten subjects were E3/E3 homozygotes, 2 were E2/E3 heterozygotes, and 3 were E3/E4 heterozygotes. Average daily energy and nutrient intake (mean ± SD) was: 8755 ± 2560 kJ, 31 ± 4% energy from fat, 43 ± 10% energy from carbohydrates, 19 ± 5% energy from protein, and 7 ± 7% energy from alcohol.

Table 2 shows the plasma VLDL–apoC-III, VLDL–apoB, and VLDL triglyceride concentrations and respective kinetic parameters in the subjects studied. The VLDL kinetic data were comparable to other studies of near normolipidemic or mildly dyslipidemic subjects.21,22 When dividing the subjects into low (<1.7 mmol/L) and high plasma triglyceride (≥1.7 mmol/L) groups,23 subjects with high triglycerides (n = 7) had significantly elevated VLDL triglycerides and VLDL–apoB, compared with those in low plasma triglycerides (data not shown). Obese subjects (n = 7) also had elevated VLDL–apoC-III concentration (81 ± 9 mg/L versus 58 ± 26 mg/L; P < 0.05) and production rates (2.8 ± 0.5 mg/kg per day versus 1.9 ± 0.9 mg/kg per day; P < 0.05) compared with nonobese subjects (n = 8). Similar findings were also observed in subjects with a hypertriglyceridemic waist (n = 7) compared with those without a hypertriglyceridemic waist (n = 8) (VLDL–apoC-III concentration 84 ± 2 mg/L versus 54 ± 24 mg/L; VLDL–apoC-III production 14 ± 2 mg/kg per day versus 11 ± 1 mg/kg per day; P < 0.05).
apoC-III PR 2.8±0.6 mg/kg per day versus 1.9±0.9 mg/kg per day; P<0.05 for both).

Table 3 shows the relationship between VLDL–apoC-III and VLDL triglyceride and VLDL–apoB kinetic parameters. Plasma VLDL–apoC-III concentration was significantly and positively associated with the concentrations of both VLDL triglycerides (r=0.638, P<0.05) and VLDL–apoB (r=0.619), the production rate of VLDL–apoC-III (r=0.842), and inversely with the FCRs of both VLDL triglyceride (r=−0.610) and VLDL–apoB (r=−0.791). Figure 2 shows the associations of plasma VLDL–apoC-III concentrations with the FCRs of VLDL triglyceride and VLDL–apoB. VLDL–apoC-III production rate was significantly (P<0.05) and positively correlated with the concentrations of plasma VLDL triglyceride (r=0.585) and VLDL–apoB concentrations (r=0.599), and inversely with VLDL–apoB FCR (r=−0.548). Plasma VLDL–apoC-III was also significantly associated with the plasma concentrations of total apoC-III (r=0.958, P<0.001), total triglycerides (r=0.596, P=0.032), and RLP cholesterol (r=0.596, P=0.032). Plasma VLDL triglyceride concentration was significantly associated with VLDL–apoB concentration (r=0.885, P<0.01), VLDL–apoB FCR (r=−0.543, P<0.05), and VLDL triglyceride PR (r=−0.674, P<0.01). VLDL–apoB concentration was also significantly associated with the PRs of VLDL triglycerides (r=0.606, P<0.05) and VLDL–apoB (r=0.599, P<0.05), and inversely with VLDL–apoB FCR (r=−0.552, P<0.05). As shown in Figure 3, there was a significant positive association between the production rates of VLDL–apoB and VLDL triglycerides (r=0.641, P=0.010), and between the FCRs of VLDL–apoB and VLDL triglycerides (r=0.737, P=0.002). However, apoA-V concentration was not associated with any of the lipid and lipoprotein levels shown in Table 1 or with the kinetic variables shown in Table 2.

In multiple regression analysis including age, waist circumference, and HOMA score, plasma VLDL–apoC-III was an independent and significant predictor of plasma VLDL triglyceride concentrations (β-coefficient=0.819, P=0.007), VLDL–apoB concentrations (β-coefficient=0.882, P=0.008), and the FCRs of VLDL triglyceride (β-coefficient=−0.575, P=0.013) and VLDL–apoB (β-coefficient=−0.839, P=0.004). These findings were confirmed in stepwise regression analysis showing that plasma VLDL–apoC-III was the best predictor of these dependent variables (data not shown). Including BMI instead of waist circumference in these models, VLDL–apoC-III remained an independent and significant predictor of plasma VLDL triglyceride concentrations (β-coefficient=0.716, P=0.014), VLDL–apoB concentrations (β-coefficient=0.831, P=0.010), and of the FCRs of VLDL triglyceride (β-coefficient=−0.711, P=0.029) and VLDL–apoB (β-coefficient=−0.869, P=0.004). Addition of plasma apoA-V into these models as a predictor variable did not alter these findings (data not shown).

**Figure 2.** Association between plasma VLDL–apoC-III concentration and VLDL triglyceride FCR (A) and VLDL–apoB FCR (B).
Discussion

Our major finding was that increased plasma concentration of VLDL–apoC-III, caused by apoC-III overproduction, was significantly and independently predictive of delayed catabolism of VLDL triglycerides and VLDL–apoB in men with wide range of BMI and mild dyslipidemia. Another new finding was that plasma apoA-V concentrations were not significantly correlated with plasma lipid, lipoprotein, and apolipoprotein concentrations, or with VLDL kinetics parameters. We also demonstrated close coupling between the production rates of VLDL triglyceride and apoB, as well as between their corresponding fractional rates of catabolism.

Increased plasma VLDL–apoC-III concentration has previously been associated with hypertriglyceridemia and cardiovascular disease. Our data extend our previous study by examining the association of plasma VLDL–apoC-III concentrations with both VLDL triglyceride and apoB kinetics and the potential role of VLDL–apoC-III kinetics in regulating VLDL metabolism. Using a stable isotopic technique, Cohn et al indicated that increased VLDL–apoC-III concentration is a consequence of overproduction of VLDL–apoC-III in patients with marked hypertriglyceridemia (types IIB and III). They studied patients with apparent genetic hyperlipidemia, whereas we studied subjects with a wide range of BMI and mild dyslipidemia; 50% of whom had the metabolic syndrome with plasma triglyceride >1.7 mmol/L. Our results are consistent with their findings showing that VLDL apoC-III production is an important determinant of plasma concentrations of VLDL–apoC-III, VLDL triglyceride, and VLDL–apoB. Using radiolabeling techniques, Huff et al examined the relationship between the kinetics of VLDL–apoC-III and VLDL–apoB in normolipidemic subjects consuming high-carbohydrate diets. They found that increased apoC-III production was associated with increased VLDL triglyceride concentration and production rate and decreased FCR of VLDL–apoB. However, the study did not study VLDL triglyceride kinetics or subjects with metabolic syndrome. Using a stable isotope technique, only one study has examined the plasma kinetics of VLDL–apoC-III in relation to VLDL triglyceride and VLDL–apoB metabolism. Cohn et al found that in 10 healthy men (BMI, 27±0.9 kg/m²; plasma triglycerides, 1.61±0.28 mmol/L) VLDL–apoC-III production rate (or VLDL–apoC-III concentration) was significantly associated with VLDL triglyceride production rate and VLDL triglyceride concentration. They failed to find a significant correlation between VLDL–apoC-III concentration and the FCRs of VLDL triglycerides and VLDL–apoB. Given the functional role of VLDL–apoC-III on the catabolism of TRLs, these findings were unexpected. It is generally believed that increased apoC-III in plasma inhibits the lipolysis of VLDL triglycerides by LPL and interferes with the hepatic uptake of TRL remnant by low-density lipoprotein (LDL) receptors. Consistent with this notion, we found that in a larger sample size plasma VLDL–apoC-III concentration was a determinant of plasma VLDL-triglyceride concentration and the FCRs of VLDL triglycerides and VLDL–apoB. The discrepant findings, particularly regarding VLDL catabolism, might be accounted for by differences in sample size, subject characteristics, experimental protocols, and method of data analysis.

We also found that VLDL–apoC-III production rate was significantly associated with VLDL–apoB FCR and, to a less significant extent, VLDL triglyceride FCR (r = −0.412, P = 0.127). These results reinforce the notion that increased VLDL–apoC-III concentration is a consequence of an overproduction of VLDL–apoC-III, leading to delayed catabolism of VLDL particles. The lack of correlation between the production rates of VLDL–apoC-III and VLDL–apoB also suggests that increased VLDL–apoC-III production rate is not simply caused by more apoC-III being secreted along with the increased number of VLDL particles. Because our study was based on correlational analyses, we cannot directly infer a causal mechanism for the effect of plasma VLDL–apoC-III levels on VLDL catabolism. However, experimental data clearly demonstrate that overexpression of apoC-III delays, whereas apoC-III deficiency enhances, the catabolism of VLDL. Although we report a postabsorptive study, we anticipate a similar relationship between plasma VLDL–apoC-III concentrations and VLDL kinetics in the postprandial state when catabolic pathways are operating under rate-limiting conditions. We did not study the kinetics of apoC-III₆ and apoC-III₃ subspecies. ApoC-III₀ and apoC-III₃₃ are the most abundant C-III apolipoproteins in human plasma compared with apoC-III₆. Given that apoC-III₀ and C-III₃₃ have similar fractional catabolism in both normal and hypertriglyceridemic subjects, we would anticipate similar findings in our population had we studied apoC-III₀ turnover. Given our relatively small sample size, further studies are required to establish whether our findings on apoC-III kinet-
ics could apply to men with or without obesity, as well as to those with or without hypertriglyceridemia.

This is the first kinetic study to examine the role of plasma apoA-V in regulating VLDL metabolism in humans. Although several studies have indicated that alteration in the expression of apoA-V significantly affects plasma triglyceride levels, the concentration of apoA-V used in most was 1000-fold greater than the physiological range. A weak association between plasma levels of apoA-V and triglycerides has, however, been consistently observed in human studies. The reason for the lack of a significant association between plasma apoA-V and triglyceride concentrations and corresponding VLDL kinetic parameters in the present study remains unclear. There are several explanations. Because apoA-V is present in human plasma at much lower concentrations than other lipoproteins, a direct action of circulating apoA-V on LPL-mediated lipolysis seems unlikely, consistent with an observation in type 2 diabetes. The plasma concentrations of apoA-V may not directly reflect the influence of apoA-V expression on hepatic VLDL production intracellularly. Whether this also relates to an intracellular effect of apoC-III requires further investigation. A potential weakness of the study is that we did not examine the distribution of plasma apoA-V in VLDL and HDL fractions in relation to VLDL metabolism. Our study was also performed in the fasting state, so we cannot conclude that plasma apoA-V levels do not influence VLDL kinetics in the postprandial state. However, previous studies have failed to demonstrate an association of apoA-V subpopulations with postprandial plasma triglyceride concentrations.

Consistent with earlier studies, we observed that the production rates of VLDL triglycerides and apoB were closely correlated, as were their corresponding FCRs (Figure 3). This suggests that the regulation of VLDL metabolism in subjects with similar characteristics to our sample population involves coupling of the kinetics of triglycerides and apoB in VLDL. In 10 diabetic subjects, Adiels et al found that the kinetics of triglycerides and apoB in VLDL1 and VLDL2 subpopulations were also closely coupled, consistent with the present findings on total VLDL. They also demonstrated that the overproduction of VLDL1 particles, because of enhanced secretion of VLDL1 triglyceride and apoB, is a dominant feature of diabetic dyslipidemia. However, whether coupling of triglycerides and apoB kinetics in VLDL would hold had we studied subjects with severe hypertriglyceridemia remains to be investigated. We did not study VLDL subpopulations or subjects with type 2 diabetes mellitus. Because our mean ratio of VLDL triglyceride to VLDL–apoB production rates was similar to that reported by Adiels et al (ratios were 22 and 28, respectively), we anticipate that the ratios of triglyceride to apoB production rates in VLDL1 and VLDL2 would also be close to the values reported in that study (ie, VLDL1: 34 and VLDL2: 14). Given that the distribution of apoC-III in VLDL1 and VLDL2 particles is a function of their triglyceride contents, we anticipate that apoC-III concentrations would also be associated with the catabolism of triglycerides and apoB in both VLDL1 and VLDL2 subpopulations, but this requires further investigation.

Several studies have clearly demonstrated a close association of genetic variations in the apoA1/C3/A4/A5 gene cluster with hypertriglyceridemia and progression of coronary heart disease. Our kinetic studies of VLDL metabolism provide useful information on the underlying mechanisms responsible for these related disorders. The lack of correlation between plasma apoC-III and either plasma triglycerides or indices of VLDL metabolism does not preclude an intracellular role in regulating triglyceride metabolism in the liver. Because our study was based on correlational analysis, more research is required to further confirm these relationships in interventional studies. Recent observations suggest that apoC-III and apoA-V gene expression is regulated by peroxisome proliferator-activated receptor-α and/or retinoic acid receptor-related orphan receptor-α agonists. Further studies should determine the effect of peroxisome proliferator-activated receptor-α and related nuclear receptor agonists on plasma VLDL–apoC-III and apoA-V as a basis for their beneficial effects in regulating dyslipidemia in subjects with obesity and the metabolic syndrome.

Acknowledgments

This work was supported by grants from the National Health and Medical Research Council (NHMRC) and the National Heart Foundation (NHF) of Australia. Support was also provided by the Raine Medical Research Foundation, the Royal Perth Hospital Medical Research Foundation and Pfizer. DCC was supported by a postdoctoral fellowship from the Raine/NHF of Australia. PHRB is a fellow of the NHMRC of Australia and is partially supported by National Institute of Health (NIBIB grant P41 EB-001975).

References


26. Cohn JS, Patterson BW, Uffelman KD, Davignon J, Steiner G. Rate of production of plasma and very-low-density lipoprotein (VLDL) apolipoprotein C-III is strongly related to the concentration and level of production of VLDL triglyceride in male subjects with different body weights and levels of insulin sensitivity. *J Clin Endocrinol Metab*. 2004;89:3949–3955.


Apolipoproteins C-III and A-V as Predictors of Very-Low-Density Lipoprotein Triglyceride and Apolipoprotein B-100 Kinetics
Dick C. Chan, Gerald F. Watts, Minh N. Nguyen and P. Hugh R. Barrett

Arterioscler Thromb Vasc Biol. 2006;26:590-596; originally published online January 12, 2006; doi: 10.1161/01.ATV.0000203519.25116.54
Arteriosclerosis, Thrombosis, and Vascular Biology is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2006 American Heart Association, Inc. All rights reserved.
Print ISSN: 1079-5642. Online ISSN: 1524-4636

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://atvb.ahajournals.org/content/26/3/590

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Arteriosclerosis, Thrombosis, and Vascular Biology can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Arteriosclerosis, Thrombosis, and Vascular Biology is online at:
http://atvb.ahajournals.org//subscriptions/