Recent epidemiologic studies have revealed that hypertriglyceridemia is associated with atherosclerosis independent of other coronary risk factors. However, it is difficult to select patients at high risk for coronary artery disease using only serum triglyceride levels compared with low-density lipoprotein cholesterol levels since multiple factors are associated with elevating triglycerides. Atherosclerotic diseases with high triglyceride levels can be found in patients with familial combined hyperlipidemia, diabetes mellitus, and metabolic syndrome, in which remnant lipoproteins accumulate in the circulating blood. Recent researches have paid attention to remnant lipoproteins as atherogenic particles with the development of methods for measuring remnant cholesterol levels and apolipoprotein B-48 levels directly from human serum. Measurement of these parameters in addition to serum triglycerides may help to distinguish high-risk patients and enable us to prevent or suppress the progression of atherosclerotic diseases in those patients. However, questions remain to be answered to evaluate the significance of remnant lipoproteins. Here, we focus on three issues: the underlying problems in measuring remnant lipoprotein cholesterol, the assessment of postprandial hyperlipidemia as an atherogenic condition, and finally a review of our experimental and clinical findings about the mechanisms by which remnant lipoproteins induce atherosclerosis.

**Key words:** postprandial hyperlipidemia, chylomicron remnants, remnant-like particles (RLP), apolipoprotein B-48 (apoB-48)

**Introduction**

Hypercholesterolemia, especially a high concentration of serum cholesterol in low-density lipoproteins (LDL), is strongly related to the development of atherosclerotic diseases, including coronary artery diseases (CAD)\(^1\). Recent epidemiologic studies reveal that hypertriglyceridemia is also associated with atherosclerosis independent of other coronary risk factors\(^2, 3\); however, people with slightly elevated triglyceride levels without other metabolic disorders or severe hypertriglyceridemia such as primary chylomicronemia, rarely have CAD. This is a challenge to distinguish high-risk patients from all subjects with hypertriglyceridemia. Atherosclerotic diseases with high triglyceride levels can be found in patients with familial combined hyperlipidemia, diabetes mellitus, and metabolic syndrome, in which triglyceride-rich lipoproteins (TRL), especially chylomicron remnants and very-low-density lipoproteins (VLDL) remnants, accumulate in the circulating blood. Recent researches have focused on these remnant lipoproteins as atherogenic particles; however, questions remain to be answered to evaluate the significance of remnant lipoproteins. To resolve these problems, it is important to understand remnant lipoprotein metabolism and the mechanisms by which remnant lipoproteins induce atherosclerosis. Here, we used the term “TRL” for whole triglyceride-rich lipoproteins, including chylomicron, VLDL, and their remnants.

**Remnant Lipoprotein Metabolism**

**Chylomicrons and Chylomicron Remnants**

The metabolic pathway for the delivery of dietary
triglycerides and cholesterol from the intestine to the peripheral tissues and liver is described as the exogenous pathway. Nascent chylomicrons synthesized by enterocytes have a higher triglyceride-to-cholesterol mass ratio and consist primarily of apolipoprotein (apo) B-48 and A-I. These range in size from 75 to 3,000 nm in diameter, depending on the dietary lipid mass. They are secreted into the intestinal lymphatic capillaries and are subsequently passed through the network of mesenteric lymphatic vessels into the thoracic lymph duct before they enter the general blood circulation. Chylomicrons acquire apoC-II and apoE in the thoracic lymph duct. In tissue capillaries, chylomicrons bind to lipoprotein lipase (LPL), which is activated by apoC-II: this induces the lipolysis of triglycerides in the chylomicrons. The depletion of triglycerides, apoA, and C proteins results in a reduction of chylomicron size, referred to as chylomicron remnants, or “remnants.” Finally, chylomicron remnants are cholesteryl ester-rich and retain apoB-48 and apoE. The liver is the major organ that removes remnants from the blood. Of note, the cholesterol content of chylomicrons and chylomicron remnants increases with cholesterol content in the diet. In addition, chylomicron remnants contain lysophosphatidylcholine as a result of hydrolysis. Lysophosphatidylcholine has potent biological effects involving the regulation of adhesion molecules and cytokines. Oxidized LDL also include lysophosphatidylcholine.

Circulating lipoproteins enter the liver via the hepatic artery and the hepatic portal vein, and flow into the liver sinusoids. The endothelial cell layer is separated from underlying hepatocytes by the subendothelial space (space of Disse). The gates (fenestrae) function as a lipoprotein selection filter. Only small remnants digested by lipoprotein lipase may pass through the fenestrae; larger particles cannot enter the space of Disse. Chylomicron remnants are (1) taken up directly by the LDL receptor (LDLR); (2) taken up directly by the LDL receptor-related-protein (LRP) after acquiring additional apoE; (3) sequestered by binding to heparan sulfate proteoglycans (HSPG), mediated by apoE, lipoprotein lipase, and/or hepatic lipase (HL). Sequestered particles are transferred to LDL receptors and LRP. Modified from Ref. 10 and 11.

Fig. 1. Pathways of chylomicron remnant uptake by hepatocytes. This figure demonstrates the hypothesis of chylomicron remnant uptake in the liver. Lipoproteins enter the liver via the hepatic artery and the hepatic portal vein, and flow into the liver sinusoids. The endothelial cell layer is separated from underlying hepatocytes by the subendothelial space (space of Disse). The gates (fenestrae) function as a lipoprotein selection filter. Only small remnants digested by lipoprotein lipase may pass through the fenestrae; larger particles cannot enter the space of Disse. Chylomicron remnants are (1) taken up directly by the LDL receptor (LDLR); (2) taken up directly by the LDL receptor-related-protein (LRP) after acquiring additional apoE; (3) sequestered by binding to heparan sulfate proteoglycans (HSPG), mediated by apoE, lipoprotein lipase, and/or hepatic lipase (HL). Sequestered particles are transferred to LDL receptors and LRP. Modified from Ref. 10 and 11.
the uptake of chylomicron remnants but to a lesser extent. Heparan sulfate proteoglycans (HSPG), which are extracellular matrix proteins and are abundant in the space of Disse, have important roles to attach ApoE, lipoprotein lipase, and hepatic lipase and enhance effective uptake of chylomicron remnants via LDL receptors and the LRP.\(^6,7\)

Regarding lipid composition, Lambert et al. reported that the fatty acid composition of chylomicron remnants influenced their binding and internalization by isolated hepatocytes.\(^{10}\) Potentially important to the progression of atherosclerosis, oxidized products in dietary lipids may be carried to the vascular wall by chylomicron remnants or to the liver where they are utilized for synthesis of VLDL; the significance of direct delivery of oxidized lipids in atherogenesis has not yet been evaluated.\(^{10}\)

**VLDL and VLDL Remnants**

Hepatic production of VLDL and conversion to LDL is called the endogenous pathway. VLDL are TRL with apoB-100, Cs, and E. Endothelial-bound LPL induces lipolysis of the triglycerides in VLDL to form smaller particles as VLDL remnants and finally to intermediate-density lipoproteins (IDL), which are depleted apoCs. Hepatic lipase functions mainly for the lipolysis of IDL to form LDL, although liver and peripheral tissues take up a part of them. In addition, hepatic lipase induces the conversion of high-density lipoproteins 2 (HDL2) to HDL3. Hepatic lipase itself may function as a molecule that mediates hepatic uptake of lipoproteins. It is suggested that hepatic lipase alone is insufficient, but that it may act in tandem with other molecules, such as HSPG and apoE, and may accelerate chylomicron remnant uptake. Plasma LPL may also be combined with remnants during lipolysis and mediate hepatic uptake. Recently, Zheng et al. demonstrated that plasma LPL might enhance the clearance of apoB-containing lipoproteins, particularly apoB-48-containing lipoproteins in humans.\(^{15}\)

Thus, there are intestine- and liver-originated remnant lipoproteins in circulating blood. As described in the next section, this induces heterogeneity of TRL, resulting in the difficulty of separating and measuring atherogenic remnant lipoproteins.

**Remnant Lipoproteins and Postprandial Lipoproteinemia**

**Measurement of Remnant Lipoprotein Cholesterol**

Remnant-like particles (RLP) are isolated from serum samples by the immune adsorption method with the monoclonal antibodies to apoA-I and apoB-100. Cholesterol or triglyceride levels in RLP are denoted RLP-C or RLP-TG, respectively. This method could simplify clinical research and lead to more investigations of the importance of remnant lipoproteins in atherogenic diseases. Because the monoclonal antibodies to apoB-100 in this method fail to recognize an apoE-rich population of VLDL containing apoB-100 as well as all triglyceride-rich lipoproteins containing apoB48, an unbound fraction named RLP contains more molecules of apoE and cholesteryl esters than those that were bound to this antibody; however, RLP are widely heterogeneous in size and composition. Marcoux et al. reported that RLP of type III hyperlipoproteinemic patients were enriched in cholesterol and apoE compared to those of type IV hyperlipoproteinemic patients, RLP of type IV patients were enriched in triglyceride and apoC-III relative to those of normolipidemic subjects, and the majority of RLP in normolipidemic subjects had a size similar to LDL or HDL.\(^{18}\) The elevation of serum RLP-C levels can sometimes be observed even in type IV patients who are thought to be non-atherogenic. Moreover, Campos et al. demonstrated that RLP contained a cholesterol-rich lipoprotein component that was comprised mainly of β-migrating LDL. They suggest that RLP-C levels in subjects with normal plasma triglyceride may not have the same clinical significance as they do in those with hypertriglyceridemia; therefore, in the clinical work, it is further necessary to select high-risk patients for atherogenic diseases among those with elevated RLP-C levels.

Recently, a new homologous assay for serum remnant lipoprotein cholesterol (RemL-C) levels by direct measurement using commercially available kits was developed. This assay utilizes surfactant and phospholipase-D to directly solubilize and degrade remnants. As such, it can be performed with an automated clinical analyzer in a short time (10 min). Lipoproteins targeted by both methods include chylomicron remnants and VLDL remnants. Although a strong correlation between RemL-C levels and RLP-C levels in patients with CAD was found, differences in sensitivity to endogenous and exogenous lipoproteins between both methods may exist. We have found that the response of RemL-C levels was different from that of RLP-C levels after test meal loading in young normolipidemic subjects. Consequently, further study is needed to determine which method can measure atherogenic remnant lipoproteins in hyperlipidemic patients more specifically and accurately.
Postprandial Hyperlipidemia as the Atherogenic Condition

Zilversmit proposed that chylomicrons or chylo-
micron remnants per se might induce atherosclerosis 4),
and a number of investigators have demonstrated a
relationship between postprandial hyperlipidemia and
atherosclerotic diseases, especially CAD 20); however,
questions remain about the evaluation of fasting lipid
levels in postprandial hyperlipidemic patients and the
contribution of intestine- and liver-originated TRL in the
postprandial state.

For the first question, there are many reports
about the evaluation of fasting and postprandial lipid
levels in postprandial hyperlipidemic patients. Tanaka
et al. demonstrated that RLP-C levels increased to sig-
nificantly higher levels in the postprandial state in
patients with CAD or in patients of diabetes mellitus
with insulin resistance 24); however, at present, there
are no standard criteria for lipid levels in the fasting
and postprandial state to define postprandial hyperlip-
idemia. Although measurements of serum lipid levels
are important in not only the fasting period but also
the postprandial period, it is not convenient to per-
form test meal loading as a routine examination;
therefore, it may be necessary to determine useful
parameter(s) in the fasting state to choose high-risk
patients for atherosclerotic diseases among those with
postprandial hyperlipidemia.

High concentrations of RLP-C in the fasting state
were associated with the presence of CAD in dyslipid-
emia 25). Kugiyama et al. reported that higher levels of
remnant lipoproteins in fasting serum predicted future
corony events in patients with CAD independently
of other risk factors 26). Karpe et al. reported that plasma RLP-C levels were related to intima-media
thickness of the common carotid artery in a healthy
middle-aged male population. This was independent
of LDL-C and plasma triglycerides, suggesting that
RLP-C measurement might be useful for assessing car-
diovascular risk 27). The Honolulu Heart Study reported
that RLP-C levels predicted CAD incidence independ-
ent of non-lipid risk factors and of total cholesterol
or HDL-C and LDL-C levels 28). Interestingly, we also
demonstrated that RLP-C and RLP-TG levels were
elevated in subjects with not only type 2 diabetes mel-
litus but also in those with impaired glucose tolerance
(IGT), suggesting that patients with IGT have a
higher risk for atherosclerosis 29). Thus, examination
of the fasting RLP-C levels is significant to select high-
risk patients.

For the second question, an increase in postpran-
dial triglyceride levels may not only occur because of
intestine-originated TRL (apoB-48-containing TRL),
but also may be caused by liver-originated TRL (apoB-
100-containing TRL) 30, 31). Cohn et al. reported that
the postprandial increase in TRL triglyceride level
was predominantly (approximately 80%) due to an
increase in apoB-48-containing TRL in normolipid-
emic male subjects with fat load-containing retinyl
esters 30). On the other hand, Karpe et al. reported that
VLDL (apoB-100-containing TRL) were continuously
excreted from the liver during the fasting state, and
that the delipidation process was halted in the post-
prandial state, causing prolonged residence of VLDL
remnants, which resulted from competition by chylo-
microns for removal of triglycerides by lipoprotein
lipase 31). They demonstrated that apoB-100-contain-
ing TRL constituted 96–97% of all TRL in the fasting
state and 91–96% in the postprandial state 32). Thus,
there is a debate about the contribution of apoB-
48-containing and apoB-100-containing TRL to the
increase of the postprandial triglyceride level.

Recently, two groups developed methods for mea-
suring apoB-48 directly from human serum or plasma,
with monoclonal anti-apoB-48 antibodies 33-35). Mea-
suring apoB-48 in the fasting and postprandial state
may help analyze the particle numbers of exogenous
lipoproteins. We have reported that TG, RLP-C,
RLP-TG, RemL-C, and apoB-48 levels in the fasting
state may be available to detect and characterize post-
prandial hyperlipidemia in normolipidemic subjects 22).

In the future, measurement of apoB-48 as well as
RLP-C, RemL-C, and other lipid parameters in the
fasting state should be performed in prospective stud-
ies to clarify to what extent apoB-48-containing rem-
nant lipoproteins are related to future CAD events or
the progression of atherosclerosis in humans.

Mechanism of Atherosclerosis by Remnant Lipopro-
teins

Next, we review how remnant lipoproteins con-
tribute to form atherosclerotic lesions through several
mechanisms. Of note, many investigators used varied
lipoproteins, including chylomicron remnants, VLDL
remnants, IDL, RLP, or beta-very-low-density lipopro-
teins (β-VLDL) in their experiments on this theme.
Remnant lipoproteins, called β-VLDL, which are tri-
glyceride-rich and cholesterol-rich particles of intesti-
nal and hepatic origin, are produced experimentally
in animals fed high cholesterol-enriched diets, or
observed clinically in patients with type III hyperlipo-
proteinemia 36).

Influx and Retention of Remnant Lipoproteins in
Vascular Wall

The influx of lipoproteins from the plasma into
the arterial wall appears to be a prerequisite for atherosclerotic development, especially the earliest type (i.e., fatty streak); however, since the size of nascent chylomicrons synthesized by enterocytes range from 75 to 3,000 nm in diameter, chylomicrons may be too large to enter the vascular wall. Indeed, patients with chylomicronemia rarely have atherosclerotic diseases; however, Daugherty et al. demonstrated aortic accumulation of β-VLDL induced by diet-induced hypercholesterolemia in rabbits. Rapp et al. demonstrated that human atherosclerotic plaques contained intact TRL. In addition, Proctor et al. demonstrated that small particles, such as chylomicron remnants, could penetrate the arterial wall and were retained in the subendothelial space. After injury to the wall, it may be possible for remnant lipoprotein particles larger than LDL to enter the vascular wall. Thus, remnant lipoproteins may enter the vascular wall and cause atherosclerosis.

**Inflammation**

Hypertriglyceridemia is associated with systemic inflammation. Leukocyte activation is induced in hypertriglyceridemic patients, and acute hypertriglyceridemia is a leukocyte activator by direct interaction between TRL and leukocytes with fatty acid uptake; however, the direct relationship between TRL and inflammatory markers, such as C-reactive protein (CRP), remains obscure.

The critical steps of inflammation in atherosclerosis involve adhesion of monocytes to endothelial cells, with subsequent transmigration into the vascular wall. Monocyte chemoattractant protein-1 (MCP-1), a member of the C-C chemokines, stimulates the migration of monocytes through the arterial endothelial layers and is postulated to play a critical role in the development of atherosclerosis. Maeno et al. reported that IDL can stimulate MCP-1 mRNA expression in cultured human umbilical vein endothelial cells (HUVEC). In addition, RLP can induce MCP-1 expression in HUVEC. We have demonstrated that rat chylomicron remnants strongly stimulated mRNA expression and protein secretion of MCP-1 in vascular smooth muscle cells (SMC) by activation of p38 mitogen-activated protein kinase (MAPK). We have also demonstrated that chylomicron remnants induced early growth response factor-1 (Egr-1) mRNA and protein expression in vascular SMC. Egr-1, the zinc-finger transcription factor, is induced by various stimuli, including growth factors, cytokines, hypoxia, and shear stress, and induced genes have been implicated in the pathogenesis of atherosclerosis.

Incubation with RLP in endothelial cells induced the expression of intracellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1), and tissue factors in HUVEC through a redox-sensitive mechanism. Human monocyte U937 cells, cultured in the presence of RLP, increased their adhesion to HUVEC under physiological laminar flow conditions.

**Endothelial Cells**

Hypertriglyceridemia is thought to be associated with hypercoagulability and activation of platelets. Plasminogen activator inhibitor-1 (PAI-1) is an important molecule for regulating thrombus formation. VLDL have been found to induce transcription of the human PAI-1 promoter in endothelial cells, whereas native LDL do not. We have demonstrated that chylomicron remnants increased the production of PAI-1 in endothelial cells via the MAPK pathway and redox system. Interestingly, inhibition of the renin-angiotensin system with angiotensin converting enzyme (ACE) inhibitors and angiotensin type 1 receptor blockers (ARB) could reduce the production of PAI-1 by remnants in endothelial cells. These drugs may decrease PAI-1 levels clinically in hypertensives, and our data suggest that these drugs may act favorably in metabolic syndrome patients.

Remnants are also associated with endothelial cell apoptosis. We have demonstrated that high concentrations of chylomicron remnants could induce endothelial cell apoptosis. RLP induced apoptosis in endothelial cells by NAD(P)H oxidase-mediated superoxide and by cytokine production via the lectin-like oxidized low-density lipoprotein receptor-1 (LOX-1). This evidence supports accelerated endothelial dysfunction through cell death caused by remnant lipoproteins.

**Endothelium Dysfunction**

Hypertriglyceridemia is less clearly related to endothelial dysfunction and controversy persists. The lack of agreement may reflect the fact that hypertriglyceridemia has a heterogeneous clinical phenotype, including variation in plasma concentration, sizes, content of apoproteins, lipids, fatty acids, and antioxidants in TRL particles. Kugiyama et al. demonstrated that RLP levels were independently associated with abnormal endothelium-dependent vasomotor function in large and resistance coronary arteries in humans and suggested that the decrease in coronary nitric oxide bioactivity may be responsible, in part, for the inhibitory effects of remnant lipoproteins. We have demonstrated that forearm blood flow, deter-
mined by strain-gauge plethysmography, was decreased in subjects with high triglyceride and high RLP-C levels, indicating that high remnant levels contribute significantly to endothelial dysfunction. This dysfunction may lead to atherosclerosis.

**Macrophages**

Monocytes migrate from the circulation into the subendothelial space and are activated to differentiate into macrophages. Macrophages can bind and internalize lipoprotein particles by receptor-mediated endocytosis. The uptake of excess lipid converts macrophages into foam cells. One of the requirements for lipoproteins to be atherogenic is if they can cause foam cell formation. The uptake of native LDL does not cause foam cell formation; instead, oxidation of LDL can have atherogenic effects. β-VLDL also causes foam cell formation. We demonstrated that chylomicron remnant uptake caused lipid accumulation in mouse peritoneal macrophages and human monocyte-macrophages in vitro by both LDL-receptor-dependent and -independent mechanisms. In mouse peritoneal macrophages from normal mice, at least 40% of chylomicron remnant uptake was due to the LDL receptor and at least 20% was due to another member of the LDL receptor family, most likely the LRP. The remaining 20–30% was due to unidentified mechanisms. In this experiment, neither acetyl LDL nor fucoidan affected the uptake of chylomicron remnants, indicating that scavenger receptors were not involved. Recently, the macrophage apoB-48 receptor was shown to be involved in the uptake of remnants and may contribute to foam cell formation; it remains unclear if it contributes to atherosclerotic lesion formation in vivo. Kawakami et al. reported that short interfering RNA against the apoB-48 receptor significantly suppressed the expression of apoB-48 receptor in THP-1 cells, and inhibited RLP-induced foam cell formation. Recently, it was reported that the LOX-1 acts as a receptor for RLP in vascular SMC and mediates RLP-induced migration, but its function as a remnant receptor in macrophages remains unknown.

Interestingly, there are differences in intracellular processing of LDL receptor-mediated transportation between LDL and β-VLDL, in endocytic patterns between LDL and β-VLDL, and between intestinally derived β-VLDL and hepatic-derived β-VLDL. Ellsworth et al. showed that rat chylomicron remnants were hydrolyzed by lysosomal enzymes more slowly than rat β-VLDL. Tabas et al. demonstrated that in mouse peritoneal macrophages, human LDL was rapidly delivered to and degraded in lysosomes, but rabbit β-VLDL was delivered to a set of widely distributed vesicles, degraded much more slowly, and markedly stimulated acyl-coenzyme A:cholesterol acyl transferase (ACAT) to induce cholesteryl ester accumulation. These findings suggest that in spite of the same pathway as LDL, lipid accumulation may be induced by dietary-derived lipoprotein remnants.

The cytokines, including interleukin-1 β (IL-1β), produced by macrophages in atherosclerotic lesions are thought to be important in the initiation and amplification of inflammation. We have demonstrated that chylomicron remnants stimulated IL-1β mRNA expression and IL-1β release by THP-1 cells in a dose- and time-dependent manner and that chylomicron remnants activated caspase-1 and the transcription factor NF-κB. CD40, a cell membrane-spanning protein that belongs to the family of tumor necrosis factor receptors and mediates the activation and differentiation of B-lymphocytes, is expressed in cells found in atherosclerotic lesions and is associated with the expression of matrix metalloproteinases, procoagulant tissue factors, chemokines, cytokines, and adhesion molecules in vascular cells. We reported that physiological concentrations of chylomicron remnants upregulated the expression of CD40 without affecting the viability of THP-1 cells and peripheral blood mononuclear cells by the extracellular signal-regulated kinase 1/2 mediated pathway, which was followed by the redox-sensitive mechanism-dependent and -independent pathway. Chylomicron remnants may contribute to lesion formation not only by lipid supplementation but also by activation of inflammation.

**Smooth Muscle Cells (SMC)**

SMC normally exist in the medial layer and migrate to the intimal layer, proliferating during atherosclerosis development, and increasing cellular cholesterol content by uptake of chylomicron remnants (Sf greater than 100) as well as LDL. β-VLDL induced SMC proliferation by activation of MAPK via G protein-coupled receptor-mediated transactivation of the epidermal growth factor (EGF) receptor. Kawakami et al. reported that RLP from hypertriglyceridemic patients induced SMC proliferation.

**Effects on Other Lipoproteins**

High concentrations of remnant lipoproteins usually accompany elevations in another atherogenic lipoproteins, such as small dense LDL. It is believed that the cholesteryl ester transport protein regulates TG and cholesteryl esters between remnant lipoproteins and LDL. Actually, high small dense LDL levels
are observed with elevations in remnant lipoprotein levels, such as in metabolic syndrome or in patients with abnormal glucose metabolism. In these conditions, HDL cholesterol levels are lowered, suggesting that reverse cholesterol transport does not function well. We should recognize that the accumulation of “bad” profiles of lipids, including “high remnant lipoproteins, high small dense LDL, and low HDL,” may induce atherosclerotic lesion formation.

Finally, we summarize the mechanisms by which remnant lipoproteins induce atherosclerosis, described in this review in Fig. 2. To prevent atherosclerotic diseases, we should know that multiple processes are involved in the mechanisms and it may be important to be aware of each aspect.

**Conclusion**

High concentrations of remnant lipoproteins are atherogenic; however, it is now difficult to select patients at high risk for CAD using only serum triglyceride levels compared with LDL-C since multiple factors are associated with elevated triglycerides. Examination of not only serum triglycerides, but also remnants and other parameters (RLP-C, LmL-C, apoB-48, small dense LDL, and HDL-C levels) may help to distinguish high-risk patients and enable us to prevent or suppress the progression of atherosclerotic diseases in those patients; however, questions remain to be answered to evaluate the significance of remnant lipoproteins, including underlying problems in the measurement of remnant lipoprotein cholesterol and the assessment of postprandial hyperlipidemia as an atherogenic condition. Although both apoB-48- and apoB-100-containing remnant lipoproteins are atherogenic experimentally, it is necessary to clarify to what extent apoB-48-containing remnant lipoproteins are related to future CAD events or to the progression of atherosclerosis in humans.

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