Quantitative Studies of Transfer In Vivo of Low Density, Sf 12–60, and Sf 60–400 Lipoproteins Between Plasma and Arterial Intima in Humans

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To assess the potential of various plasma lipoprotein classes to contribute to the lipid content of the arterial intima, influx and efflux of these plasma lipoprotein fractions into and from the intima of human carotid arteries were measured in vivo. While low density lipoprotein (LDL) is known to transfer from plasma into the arterial wall, there is less information on the atherogenic potential of lipoproteins of intermediate density (Sf 12–60) or of very low density (Sf 60–400). Aliquots of the same lipoprotein (LDL, Sf 12–60 lipoprotein particles, or Sf 60–400 lipoprotein particles) iodinated with iodine-125 and iodine-131 were injected intravenously 18–29 hours and 3–6 hours, respectively, before elective surgical removal of atheroma-tous arterial tissue, and the intimal clearance of lipoproteins, lipoprotein influx, and fractional loss of newly entered lipoproteins were calculated. Intimal clearance of Sf 60–400 particles was not detectable (<0.3 μl/hr·cm²), whereas the average value for both LDL and Sf 12–60 lipoprotein particles was 0.9 μl/hr·cm². Since the fractional loss of newly entered LDL and Sf 12–60 lipoprotein particles was also similar, the results suggest similar modes of entry and exit for these two particles. However, due to lower plasma concentrations of Sf 12–60 lipoproteins as compared with LDL, the mass influx of cholesterol in the Sf 12–60 particles was on the order of one 10th of that in LDL, and that of apolipoprotein B was about one 20th. The present results suggest that elevated plasma concentrations of Sf 12–60 or “remnant” lipoproteins share with LDL the potential for causing lipid accumulation in the arterial intima in humans. (Arteriosclerosis and Thrombosis 1991;11:569–577)

That elevated plasma levels of low density lipoprotein (LDL) play a causal role in the development of atherosclerosis is suggested by epidemiological studies,1,2 clinical findings,3 controlled trials,4,5 and studies of the cell biology of the arterial wall.6,7 The role of triglyceride-rich lipoproteins is far less clear. While clinical findings and observations of cholestero-fed animals suggest that lipoproteins of intermediate density (IDL; remnant particles; Sf 12–60 lipoproteins) have atherogenic potential,8,9 the status of plasma triglyceride as a causally important independent risk factor for atherosclerotic heart disease and, hence, the role of very low density lipoprotein (VLDL) are controversial.

If the relative rates of transfer of these lipoproteins between plasma and the arterial wall are a measure of their potential for contributing to lipid deposition and atherogenesis, then their measurement would help to clarify the pathogenic significance of hypertriglyceridemia due to elevated levels of some or all classes of triglyceride-rich lipoproteins. We have used a newly described procedure10 to address these issues by measuring influx in vivo of LDL, Sf 12–60 lipoprotein particles, and Sf 60–400 lipoprotein particles from plasma into the human atherosclerotic intima and the fractional loss in vivo from the arterial intima of newly entered lipoproteins belonging to these lipoprotein classes.
Methods

Patients

The participants were 18 patients undergoing elective carotid endarterectomy for atherosclerotic stenoses who presented with transient ischemic attacks or amaurosis fugax. None had clinical evidence of major primary or acquired disorders of lipoprotein metabolism, although one (patient H.E.) possibly had heterozygous familial hypercholesterolemia. Patients were entered into the various studies on a consecutive basis, without selection according to their lipoprotein distribution. Each patient gave written consent after being fully informed of the purpose and protocol of the study. The protocol was approved by the hospital’s ethical committee.

Radioiodination of Lipoproteins

The entire labeling procedure was performed under sterile conditions. Blood (100 ml) was drawn and transferred into tubes containing 0.01% EDTA after each patient had fasted overnight for 12 hours. Plasma was promptly separated by centrifugation at 800g for 10 minutes at 4°C. Lipoprotein fractions of Sf 60–400 and Sf 12–60 and LDL were isolated by sequential preparative ultracentrifugation.11,12 Particles with an Sf greater than 400 were removed by centrifuging aliquots of 3 ml plasma overlaid with 2 ml of d=1.006 g/ml solution at 20,000g for 10 minutes at 4°C. The top fractions were aspirated and discarded, and 3-ml aliquots of the bottom fractions were overlaid with 2 ml of d=1.006 g/ml solution and centrifuged at 105,000g for 110 minutes at 4°C to isolate the Sf 60–400 lipoproteins in the top fraction. To obtain Sf 12–60 lipoproteins, the bottom fractions, after isolation of lipoproteins with Sf greater than 60, were adjusted to a final density of 1.019 g/ml and centrifuged at 105,000g for 18 hours at 4°C. The top fractions containing Sf 12–60 lipoproteins were aspirated. LDL was isolated after flotation and removal of lipoproteins of d<1.019 g/ml; the bottom fractions were adjusted to d=1.006 g/ml and centrifuged at 105,000g for 20 hours at 4°C. The top fractions containing LDL were aspirated. All lipoprotein fractions were washed and then finely minced with scissors. The minced specimen was extracted overnight in a solution of dodecyl sulfate–polyacrylamide gel electrophoresis (SDS-PAGE).

The lipoprotein under investigation was separated into two 2-ml aliquots; one was labeled with carrier-free [125I]Iodide and the other with [131I]Iodide (Amer sham International, Buckinghamshire, U.K.) by the iodine monochloride method of McFarlane13 as modified by Langer et al.14 Two hundred microcuries of radiolabeled iodine was added to 0.5 ml lipoprotein (protein concentration, 4–6 mg/ml), and a specific activity of about 80 cpm/µg protein was obtained. After passing the two radiolabeled lipoproteins through Sephadex G-10 columns (20x1 cm; Pharmacia, Uppsala, Sweden), 2.5 ml of 10% pyrogen-free sterile human albumin (Blood Products Laboratory, Elstree, Hertfordshire, U.K.) was added to each dose to minimize autoirradiation. The doses were subsequently dialyzed extensively against sterile saline containing 0.01% EDTA. In previous studies employing the same labeling and purification procedures used in this laboratory, it has been shown that apolipoprotein B-100 in labeled LDL is homogeneous as assessed by SDS-PAGE (4–10% gradient gels) and autoradiography.15-17 Immediately before intravenous injection, the doses were passed through a 0.22-µm filter (Milipore U.K. Ltd., Harrow, Middlesex, U.K.).

Protocol

Approximately 25 µCi of the autologous iodine-125 dose was injected intravenously 18–29 hours before the patient underwent surgery, and approximately 25 µCi of the autologous iodine-131 dose was injected intravenously 3–6 hours before surgery. The exact dose injected was determined by weighing the syringe before and after injection. Serial timed blood samples (10 ml in tubes containing 0.1% EDTA) were obtained at 10 minutes, 30 minutes, 1 hour, and thereafter every 2–4 hours after administration of the 125I dose, and at 10 minutes, 30 minutes, and thereafter every hour after the administration of the 131I dose until the time of operation. The amounts of radiolabeled lipoproteins remaining in the plasma 10 minutes after injection were 89.5±0.9%, 76±1.5%, and 73.2±6.7% (mean±SEM) for LDL, Sf 12–60, and Sf 60–400 lipoproteins, respectively.

The carotid endarterectomy specimen was received and processed immediately after resection. If any media was attached, it was removed by gentle cleavage from the intima and discarded. The intima was then washed with 25 ml ice-cold saline 10 times to remove adhering plasma. Most labile tissue radioactivity, presumably due to adhering plasma, was removed by the first four to six washes (Figure 1). Most of the remaining radioactivity was subsequently extracted from the minced tissue as described below. If appropriate, the specimen of intima was separated into regions with macroscopically elevated atherosclerotic regions and the remaining area that comprised fatty streaks or macroscopically normal intimal tissue. Each region was weighed and its area mapped by planimetry, after which the tissue was washed and then finely minced with scissors. The minced specimen was extracted overnight on a tube rotator (Denley Spiramix 10, Denley Tech Ltd., Sussex, U.K.) at 4°C. Arterial tissue of individuals given radiolabeled lipoproteins of Sf greater than 12 was extracted in a solution of d=1.006 g/ml and of those given LDL, in a solution of d=1.019 g/ml.

Analyses

Plasma and arterial Sf 60–400 and Sf 12–60 lipoproteins and LDL were isolated by ultracentrifugation as described above using a tube slicer. Apolipo-
protein B in lipoprotein fractions from plasma and arterial tissue and in the doses (to which cold LDL of 0.6 mg protein content was added) was precipitated with redistilled 1,1,3,3-tetramethyl urea (Sigma Chemical Co., Poole, Dorset, U.K.) by the method of Kane et al.18 More than 90% of the radioactivity was tetramethyl-urea precipitable. To remove lipids, the precipitates were washed overnight at −20°C in ethanol/ether (3:2, vol/vol) followed by three washes with ether at 4°C. Since low counts were anticipated, radioactivity in the washed precipitates was determined by counting each sample for 3×20 minutes in a double-channel gamma counter (LKB Wallac model 1280 Ultrogamma, Bromma, Sweden) to a precision of 2.5% or better. Protein was determined by the method of Lowry et al19 using bovine serum albumin as a calibrator. Cholesterol and triglyceride concentrations in plasma and lipoprotein fractions were estimated by automated enzymatic methods using Boehringer Mannheim Kit No. 237574 and Wako Chemical Kit number 991-00405, respectively (Boehringer Mannheim, Mannheim, F.R.G., and Wako Chemicals GmbH, Neuss, F.R.G.).

**Equivalency of 125I- and 131I-Labeled Lipoproteins**

The calculation of influx and efflux requires that lipoproteins of a given class (LDL, Sf 12–60, or Sf 60–400 lipoprotein particles) are transported into and out of the arterial intima at the same rate when iodinated with 125I or 131I. To test whether a lipoprotein labeled with the two isotopes behaved identically, plasma curves for the two labeled lipoprotein preparations in each study were superimposed and were found to be satisfactorily congruent (Figure 2). The volume of distribution of 131I-labeled lipoprotein was 97±2% (mean±SEM, N=18) of that obtained with the 125I-labeled lipoprotein. Equivalency regarding arterial uptake of 125I-LDL and 131I-LDL has previously been tested in cholesterol-fed rabbits.20 In these studies, when albumin was added to the labeled lipoproteins as in the present study, the arterial influx of 131I-LDL was 98% of that of 125I-LDL.

**Calculations**

All calculations are based on radioactivity in apolipoprotein B of plasma and of arterial lipoproteins. For studies in which iodinated LDL was injected intravenously, radioactivity in plasma and arterial LDL fractions was taken into consideration. For studies on iodinated Sf 12–60 lipoprotein particles, calculations were performed for Sf 12–60 apolipoprotein B radioactivity in plasma and arterial fractions. For studies on iodinated Sf 60–400 lipoprotein particles, radioactivity in arterial Sf 60–400 apolipoprotein B was indistinguishable from background counts. However, estimates of maximal possible intimal clearances were made using the minimum counts that could have been detected by our method.

The arterial intima is assumed to be a single well-mixed pool for newly entered lipoproteins, that is, lipoproteins that have entered the intima within the experimental period. The intima is assumed to receive plasma lipoproteins in proportion to their concentration in plasma and to be depleted of newly entered lipoproteins in proportion to their concentration in intima. No assumptions concerning the route (into plasma, into media, or degraded or irreversibly attached in intima) or the mechanism by which newly entered lipoproteins leave intima (as intact or degraded lipoproteins, or irreversibly attached lipoproteins to arterial components) are necessary. Furthermore, as usual in isotope experiments, it is assumed that the labeled lipoproteins behave like unlabeled lipoproteins and that the system under investigation is in a steady state. The above assumptions have previously been validated and/or discussed.10
The fractional uptake, $k_{i}$ (hour$^{-1}$ x centimeter$^{-2}$), of plasma lipoproteins into the carotid intima and the fractional loss, $k_{e}$ (hour$^{-1}$), of newly entered lipoproteins from the same intimal sample were calculated as described by Wootton et al.$^{10}$ On the principle of conservation of matter, the rate at which the intimal content of labeled lipoproteins changes, $dq_{a}/dt$, is the difference between the influx, $R$, (counts per minute x hour$^{-1}$ x centimeter$^{-2}$), and efflux, $R_{e}$ (counts per minute x hour$^{-1}$ x centimeter$^{-2}$), of labeled lipoproteins

$$dq_{a}/dt=R_{i}-R_{e}=k_{b}q_{a}-k_{e}q_{a}$$

where $q_{a}$ (counts per minute x centimeter$^{-2}$) and $q_{p}$ (counts per minute) are the contents of labeled lipoproteins in the excised arterial intima and the plasma volume, respectively.

Since the intimal content of labeled lipoproteins at time zero is zero, the solution of this first-order differential equation is

$$q_{a}(t)=k_{b}exp(-keT)\int_{0}^{T}exp(keT)q_{p}(T)dT$$

where $T$ is a dummy variable of integration. Since this equation is valid for both a short-term (3–6 hours) exposure and a long-term (18–29 hours) exposure with $^{131}$I- and $^{125}$I-labeled lipoproteins, respectively, two equations with two unknowns $k_{i}$ and $k_{e}$ could be derived and solved as follows. Smooth curves were fitted with cubic spline functions$^{21,22}$ to the observations of both $^{125}$I- and $^{131}$I-apolipoprotein B radioactivity of the plasma lipoproteins under investigation. These curves were the functions $q_{p}(T)$. Based on initial estimates of the fractional uptake and loss, $k_{i}$ and $k_{e}$, respectively, the equations for $^{131}$I and $^{125}$I radioactivity were integrated numerically with an adaptive integration routine.$^{21,22}$ This generated two values for the content of $^{131}$I- and $^{125}$I-labeled lipoproteins in the intima, which were compared with those actually observed. An objective function, the sum of the squared differences between calculated and observed $^{131}$I and $^{125}$I radioactivity in intima, was then minimized by adjusting $k_{i}$ and $k_{e}$ by the modified simplex method of Nelder and Mead.$^{23}$

Intimal clearance of lipoproteins (microliters x hour$^{-1}$ x centimeter$^{-2}$) was calculated as the product of fractional uptake ($k_{i}$) and plasma volume (microliters). Plasma volume was taken as the average volumes of distribution of $^{125}$I- and $^{131}$I-labeled lipoproteins; this was calculated by dividing the injected amounts of labeled material by the concentrations of labeled material in plasma at time zero, obtained by extrapolation of the plasma curves. The influxes of apolipoprotein B (micrograms x hour$^{-1}$ x centimeter$^{-2}$) and of lipoprotein cholesterol (nanomoles x hour$^{-1}$ x centimeter$^{-2}$) was the intimal clearance multiplied by the plasma concentrations of lipoprotein apolipoprotein B (micrograms x milliliters$^{-1}$) and cholesterol (nanomoles x milliliters$^{-1}$), respectively. The calculation of lipoprotein cholesterol influx assumes that the intimal clearances measured for apolipoprotein B are also valid for the cholesterol moiety of the lipoproteins. Stender and Zilversmit$^{24}$ have provided evidence that in cholesterol-fed rabbits, the cholesterol ester and protein of LDL enter the arterial intima in the same proportions in which they are present in plasma LDL.

Intimal clearance (microliters x hour$^{-1}$ x centimeter$^{-2}$) was also calculated by the "sink method," in which the amount of radioactivity in apolipoprotein B (counts per minute x centimeter$^{-2}$) in the intima is divided by the area beneath the plasma apolipopro-
tein B radioactivity-time curve (hour \times \text{counts per minute} \times \text{milliliters}^{-1}).

Statistics

Values are given as mean±SEM. Differences between groups were evaluated by the unpaired Student’s t test.

Results

Table 1 gives the clinical details and lipoprotein levels of the patients studied. Mean plasma LDL apolipoprotein B and cholesterol concentrations were 13 and nine times higher, respectively, than the plasma Sf 12–60 apolipoprotein B and cholesterol concentrations.

The kinetics of transfer in vivo of LDL, Sf 12–60, and Sf 60–400 particles between the plasma and carotid arterial intima are shown in Table 2. Details of lipoprotein transfer in each patient are given in Table 3. In patients studied for the transfer of LDL, the fractional uptake, intimal clearance, and influx (of cholesterol and apolipoprotein B) appeared greater in elevated than in nonelevated regions of the carotid intima of these patients although the difference was not formally statistically significant. Fractional loss of newly entered LDL was similar in the two regions (Table 2).

Influx of LDL apolipoprotein B and cholesterol into specimens with elevated lesions was 19-fold and 16-fold greater, respectively, than those of the Sf 12–60 class (\( p<0.05 \) and \( p=0.05 \), respectively; compare Table 2). However, the intimal clearances of LDL and Sf 12–60 lipoprotein, which normalized for differences in plasma concentrations, were similar. Fractional loss of newly entered lipoproteins from the carotid intima was also similar for these two classes of lipoproteins (Table 2).

For the two patients who received labeled Sf 60–400 lipoprotein, the intimal radioactivity was not significantly different from zero (Table 2). By our method, in these two patients it would have been possible to detect intimal clearances of 0.3 and 0.1 \( \mu \text{g} \times \text{hr}^{-1} \times \text{cm}^{-2} \), respectively (Table 3). Thus, it appears that in human carotid intima, the intimal clearance of Sf 60–400 lipoprotein particles is less than 0.3 \( \mu \text{g} \times \text{hr}^{-1} \times \text{cm}^{-2} \). LDL apolipoprotein B influx into elevated regions of the arterial intima showed a positive correlation with plasma LDL apolipoprotein B concentration (\( r=0.89, p<0.01 \); the positive correlation between influx and plasma level of LDL cholesterol was also significant: \( r=0.93, p<0.001 \)). No significant correlation was observed between apolipoprotein B and cholesterol influxes of LDL in nonelevated regions or of the Sf 12–60 lipoprotein particles and their respective plasma concentrations.

When the sink method was used to calculate intimal clearance using values for the short-term (3–6 hours) exposure to \( ^{131} \text{I} \)-labeled lipoproteins, intimal clearance of LDL was underestimated by 19±3% (mean±SEM; elevated plus nonelevated intima); that of Sf 12–60 lipoproteins was underestimated by 27±5%.

Discussion

Using a recently developed procedure, the validity of which has been tested previously,\(^{10}\) we have compared the influx into and fractional loss from human atherosclerotic intima of LDL, Sf 12–60, and Sf 60–400 lipoproteins. To date, few quantitative studies of lipoprotein transfer have been made in humans; such studies have involved the measurement of influx by the integral or sink method.\(^{25–29}\) To our knowledge, efflux or fractional loss of lipoproteins from human arterial intima has not been measured previously.

The sink method does not take into account efflux of labeled lipoproteins from the arterial wall during the uptake period and may thus underestimate the true influx of lipoproteins from plasma into the arterial wall. The present investigations show that the sink method underestimates lipoprotein intimal clearance (and thus, lipoprotein influx) by 19–27% after 3–6 hours’ exposure of labeled lipoproteins to the arterial wall when measured by use of iodinated lipoproteins. Our results may be compared with those of Bremmelgaard et al,\(^ {29}\) in which the sink method was employed and in which average total plasma cholesterol influx into the intima of lesioned human abdominal aortas was 3.6 nmol/hr \times cm\(^{-2}\). Since high density lipoprotein appears to contribute about 40% to plasma cholesterol influx into the human intima,\(^ {28}\) the total cholesterol influx from VLDL plus LDL in the article by Bremmelgaard et al\(^ {29}\) would be 2.2 nmol/hr \times cm\(^{-2}\). Considering the large interindividual variation in arterial influx measurements, this compares well with our average LDL and Sf 12–60 lipoprotein cholesterol influxes of 6.2 and 0.5 nmol/hr \times cm\(^{-2}\), respectively. An earlier study from this laboratory employing the sink method has shown lower mean values for minimum influx compared with our present estimates of absolute influx.\(^ {20}\) The disparity may reflect the fact that “minimum influx” (the difference between influx and efflux) underestimates true influx even with a mean 3-hour experimental period for VLDL and 25 hours for LDL. Nevertheless, the results were concordant in that LDL minimum influx greatly exceeded that of IDL. Our data suggest that Sf 60–400 lipoproteins do not contribute importantly to cholesterol influx, since the intimal clearance was less than 0.3 \( \mu \text{g} \times \text{hr}^{-1} \times \text{cm}^{-2} \).

The lipoprotein content of the arterial wall reflects the balance between the rates at which lipoproteins enter and leave the arterial wall and are degraded within it. Ghosh et al\(^ {30}\) found an average fractional loss of LDL from aortic fatty streaks of cynomolgus monkeys of 0.09 hr\(^{-1}\). This compares with our average fractional loss for LDL of 0.12 hr\(^{-1}\). Interestingly, Schwke and Zilversmit\(^ {31}\) did not find any loss of labeled cholesteryl ester from uninjured rabbit aortas but did find an average fractional loss from injured...
### Clinical and Lipoprotein Findings in Study Participants

<table>
<thead>
<tr>
<th>M/F</th>
<th>Age (yr)</th>
<th>Body weight (kg)</th>
<th>Plasma Total cholesterol (mmol/l)</th>
<th>Triglycerides (mmol/l)</th>
<th>Apolipoprotein B (µg/ml)</th>
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<tr>
<td></td>
<td></td>
<td></td>
<td>HDL</td>
<td>LDL</td>
<td>VLDL+IDL</td>
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<tr>
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<td>60</td>
<td>6.6</td>
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**Note:** HDL, high density lipoprotein; LDL, low density lipoprotein; VLDL, very low density lipoprotein; IDL, intermediate density lipoprotein.
The fractional loss measured by our method is assumed to be a combination of 1) efflux of lipoprotein from the intima into plasma, the lumen, or the vasa vorum, 2) the metabolism of apolipoprotein B by the cells of the arterial wall, and 3) lipoprotein that becomes nonexchangeable, that is, by forming complexes with glycosaminoglycans of the arterial wall. The above processes may have different implications for atherogenesis, with the second and possibly the third processes contributing to cholesterol delivery to the intima and the first process decreasing it. These processes are therefore likely to contribute, to different degrees, to the calculated fractional loss in the artery. Further studies are needed to identify the fate of lipoproteins entering the arterial wall.

The early clearance of about one fourth of Sf 12–60 and Sf 60–400 apolipoprotein B from plasma may not be attributable to partial denaturation of labeled apolipoprotein B. Other explanations for early clearance of these particles could be the catabolism of these particles by lipolysis, transfer into extravascular space, or segregation within the circulation, that is, in the liver. The present influx and efflux calculations were based on the specific activity of particles isolated in the same flotation range from arterial tissue and from plasma; rapid lipolytic conversion of injected lipoproteins to denser particles is therefore unlikely to influence our estimates.

The cholesteryl ester content of the artery has been considered as a mixture of an inert pool of cholesterol along with a labile pool of cholesteryl ester entering the wall after injury to the artery. Similarly, the apolipoprotein B content of the intima may be representative of two such pools, the labile one comprising "newly entered" lipoproteins. In the present study, it was not possible to measure the efflux of lipoprotein B content derived from newly entered lipoproteins, and therefore efflux in terms of micrograms x hour"1 x centimeter"2 could not be calculated. Hence, as seen from Tables 2 and 3, the product of fractional loss (k) and the total apolipoprotein B content of the intima exceeds the corresponding influx. However, assuming influx equals efflux, the pool of newly entered lipoproteins (micrograms x centimeter"2) can be calculated as influx (micrograms x hour"1 x centimeter"2) divided by k (hour"1).
### Transfer In Vivo of Plasma Lipoproteins Between Plasma and Intima of Carotid Arteries in Each Patient

<table>
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<th>Type of plaque</th>
<th>Wet weight (mg)</th>
<th>Area (cm²)</th>
<th>Apolipoprotein B concentration (μg/g)</th>
<th>Fractional uptake, $k_x \times 10^{-9}$ (hr⁻¹×cm⁻²)</th>
<th>Intimal clearance</th>
<th>Apolipoprotein B influx (μg/hr×cm²)</th>
<th>Cholesterol influx (nmol/hr×cm²)</th>
<th>Fraction $k_s$ (%)</th>
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**Notes:**
- LDL: low density lipoprotein; apo: apolipoprotein; NE: nonelevated lesions; E: elevated lesions.
- The fractional uptake and loss were not calculated since arterial Sf 60–400 apolipoprotein B radioactivity was not detectable (ND).
- Intimal clearance that could have been measured by our method.
- Intimal fractional uptake of lipoprotein from the plasma pool; $k_f$ represents fractional loss of newly entered lipoprotein from intima. Short-term (3–6 hours) exposure was used to determine clearance by the sink method.
LDL influx into the intima is greater due to its greater concentration in plasma compared with that of Sf 12–60 lipoprotein. Nevertheless, the present findings suggest that at elevated plasma concentrations, Sf 12–60 lipoprotein may share with LDL the potential for mediating cholesterol transfer into the arterial intima. Thus, in conditions where the latter class of lipoproteins accumulate in plasma, such as familial dysbetalipoproteinemia (type III hyperlipidemia), or secondary hyperlipidemic conditions, such as diabetes mellitus and chronic renal failure, the Sf 12–60 lipoprotein class may contribute substantially to lipid accumulation in the intima. Levels of Sf 12–60 lipoprotein are influenced by dietary cholesterol; hence, persons who are hyperresponsive to cholesterol may be particularly at risk.

References


KEY WORDS • low density lipoproteins • intermediate density lipoproteins • very low density lipoproteins • arterial wall-lipoprotein interaction • arterial influx/efflux of lipoproteins
Quantitative studies of transfer in vivo of low density, Sf 12-60, and Sf 60-400 lipoproteins between plasma and arterial intima in humans.
M Shaikh, R Wootton, B G Nordestgaard, P Baskerville, J S Lumley, A E La Ville, J Quiney and B Lewis

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