The development of atherosclerosis is a complex, chronic process, which appears to begin as an inflammatory response to vessel wall injury. Atherosclerotic lesions demonstrate characteristic proliferation of smooth muscle cells, an elaboration of extracellular matrix, and the presence of lipid-laden, macrophage-derived, foam cells. In advanced lesions, the core becomes necrotic and lipid is released into the intima, where cholesterol crystals may form.1,2

While it is now well established that certain lipoproteins, notably LDL, are associated with an increased risk for atherosclerosis, it has also become apparent that LDL modification is necessary before its unregulated uptake by macrophages, and hence foam cell formation, can occur.3 Lipoprotein oxidation is a physiologically relevant form of lipoprotein modification. In vitro studies have demonstrated that oxidized LDL can cause cholesteryl ester accumulation in macrophages;4 this uptake may occur via the scavenger receptor or by receptors specific for oxidized LDL.5 Oxidized LDL is also a chemoattractant for monocytes and is cytotoxic to endothelial cells, both potentially atherogenic functions (reviewed in Reference 3).

The existence of oxidized LDL in vivo is supported by its detection in atherosclerotic plaque both by immunohistochemical techniques6 and by direct measurement.7 Furthermore, serum autoantibodies against oxidized LDL (α-oxLDL) have been detected in humans6 and in animal models.8 The fact that serum α-oxLDL levels are not correlated with levels of serum lipoprotein— or oxidation-related analytes suggests that their relevant antigen is not in the plasma compartment.9 Rather, it appears likely that LDL becomes oxidized in the subendothelial space, where it has the opportunity for a prolonged residence time, together with exposure to the oxygen radicals produced by activated macrophages.

Data from clinical studies also support the oxidation theory of atherosclerosis. Stringer et al10 reported that serum lipid peroxide levels were higher in subjects with coronary artery disease compared with controls. Similar findings have been reported for α-oxLDL in some,11–16 but not all,17–19 studies. Recent reports from the Physicians’ Health Study20,21 and the CHAOS (Cambridge Heart Antioxidant Study) trial22 indicate that a high dietary intake of vitamin E is associated with decreased risk for future coronary artery disease. Because

Received May 28, 1998; revision accepted November 25, 1998.
From the Foundation for Blood Research, Scarborough (W.Y.C., S.E.P., L.M.N.); the Maine Medical Center, Portland (M.W.R., C.A.R., E.R., L.M.K.); and The Jackson Laboratory, Bar Harbor (P.M.N.), Me.
Correspondence to Wendy Y. Craig, PhD, Foundation for Blood Research, PO Box 190, Scarborough, ME 04070-0190. E-mail wcraig@fbr.org
© 1999 American Heart Association, Inc.

Arterioscler Thromb Vasc Biol is available at http://www.atvbaha.org
vitamin E decreases the susceptibility of LDL to oxidation.\textsuperscript{23} These data are also consistent with an in vivo role for oxidation in the development of atherosclerosis.

From a clinical standpoint, assessing the degree of lipoprotein oxidation in an individual might yield important information relevant to atherosclerosis. Before this approach can be used, however, several difficulties must be resolved. For example, it has not yet been established which of the many potential estimates of oxidation status are the most relevant clinically. Because the analytes of importance are most likely to be in the vessel wall rather than in the circulation, it has been suggested that α-oxLDL could act as a surrogate measure of vessel wall oxidation status.\textsuperscript{24} Direct data to support this approach are lacking. Furthermore, data relating potential measurements of oxidation status to the clinical and physiological degrees of atherosclerosis are scarce.

In the present study, we have begun to address these issues among patients presenting for coronary artery bypass graft (CABG) surgery. Atherosclerotic lesion lipid composition was examined in tissue specimens from the aorta obtained at the time of CABG surgery; fasting plasma and serum specimens for the assay of lipoprotein- and oxidation-related analytes were obtained before surgery. Thus, we were able to examine the in vivo relationship between atheroma lipid composition and levels of circulating analytes related to lipoprotein metabolism and oxidation.

Methods

Subjects

The study group included 66 patients (53 males, 13 females) presenting for elective CABG surgery (≥2 vessels). The study was approved by the Institutional Review Boards at the Foundation for Blood Research and the Maine Medical Center and was conducted in accordance with institutional guidelines. Patients were recruited and informed consent was obtained at the time of the preoperative outpatient visit. Current vitamin E supplementation, hormone replacement therapy, antilipemic therapy, or a history of myocardial infarction, angioplasty or other surgical procedures within the previous 3 months were criteria for exclusion from the study.

Specimen Handling

Fasting blood samples, obtained on the morning of surgery, were centrifuged immediately, and serum and EDTA-plasma specimens were kept at −4°C. When necessary, samples were transported, on ice, between institutions by courier. As described in more detail below, assays were performed using either fresh samples or sample aliquots stored at −70°C. Preservatives (final concentrations: 100 μg/mL gentamicin, 30 μg/mL chloramphenicol, 1 mmol/L PMSF, 2.7 mmol/L EDTA, 2 mmol/L benzamidine, and 0.01% aprotinin; all from Sigma Chemical Co) and 1 μmol/L PPACK (Chemica Alta Ltd) were added to plasma samples before storage at −70°C.

Ascending aorta tissue specimens were obtained during the CABG procedure. Tissue specimens ~4 mm in diameter were removed from different locations of the anterior aorta to allow for the insertion of saphenous vein grafts. The specimens were immediately immersed in ice-cold saline containing 0.1% EDTA and were transferred to the laboratory for processing. The aortic specimens were frozen rapidly at −70°C in hexane according to the method of Waugh and Small\textsuperscript{25} and kept at −70°C until sectioning. All specimens were coded, so analyses were blinded as to patient identity and clinical status.

Histological Studies

Frozen blocks of aorta were mounted on chucks in the cryostat chamber (Tissue-Tek II, Miles Laboratories Inc) at −25°C with Cryomatrix (Shandon Southern Instruments, Inc). Sections were cut at −25°C to a thickness of 5 μm and picked up onto subbed microscope slides for physical and histological studies. Slides used for the histological classification of lesion severity\textsuperscript{27} were stained with hematoxylin and eosin (Rapid-Chrome staining kit, Shandon Southern Instruments).

Determination of Tissue Specimen Lipid Composition

Aortic tissue specimen lipid composition was analyzed using a combination of hot-stage polarizing light microscopy and digital image analysis.\textsuperscript{25,28} Sections to be examined for lipid content by hot-stage polarizing light microscopy were unstained and mounted with a drop of glycerol under a No. 1 glass coverslip (Fisher Scientific). Microscopy was performed on an Olympus BH-2 microscope fitted with a polarizer, analyzer, and heating stage control (Rocky Mountain Microscope Corp). Photomicrographs were taken with a Nikon F3 camera system (Nikon, Inc) with 35-mm film (Kodak Ektachrome ASA 400).

In brief, unstained aortic sections for physical microscopy were placed on the microscope stage with a heating stage control and viewed under crossed polars. Samples were heated at the rate of 1°C to 2°C/min to 60°C; the temperature above which all cholesteryl esters (CEs) become isotropic.\textsuperscript{29–30} The remaining birefringence represented cholesterol crystal (Cx) plus phospholipid (PL).\textsuperscript{31} Samples were then cooled on dry ice to 10°C to observe all lesion lipids in crystalline or liquid-crystalline phases. Two sets of photomicrographs were taken at 10°C and 60°C. In the first set, camera exposure time was varied to obtain optimal detail contrast on transparency film; this set was used for visual inspection only. In the second set, the camera exposure time was constant for both temperature settings; this set was used for digital image analysis.

Image processing was performed with custom software written in PVWave Advantage 5.0 from Visual Numerics Inc (Houston, Tex), a fourth-generation language for data visualization and processing, run on a UNIX RISC workstation (DECstation 5000/200, ULTRIX V4.3). Irregular region-of-interest (ROI) areas were selected by the user via a custom-designed graphical-user-interface. First, the contours of the lesion area were outlined by an experienced operator using a computer mouse. A standard binarization technique was then used, based on visual inspection of the image, to delineate the areas of lipid birefringence within the selected ROI. Given a digital image $f(x,y)$, where $x$ and $y$ are the spatial coordinates of the image and $0 ≤ f(x,y) ≤ 255$ is a luminance value, a threshold value $T$ was selected such that $0 ≤ T ≤ 255$. An image pixel was classified as background if $f(x,y) < T$ or as lipid if $f(x,y) > T$. The total lesion area was obtained by enumeration of all pixels in the ROI, and the area of lipid birefringence was obtained by enumeration of all pixels in the ROI with $f(x,y) > T$. Area was calculated from pixel number by scaling with $\delta$, the image plane dimensions of an individual pixel (in micrometers). The area of lipid birefringence was expressed as a percentage of total lesion area.

The amount of lipid birefringence quantitated at 10°C represented the lesion total lipids (CE+PL), whereas that observed at 60°C represented Cx+PL. The birefringence difference between 10°C and 60°C represented CE. All data were expressed as percent of lesion area; data for a given patient represented the average of results from 1 to 4 tissue specimens. The CV for the image processing procedure was 2.6%.

Lipoprotein-Related Assays

Serum cholesterol, triglyceride, and HDL cholesterol testing (CV<4.4%) was carried out on fresh samples on a Johnson and Johnson Vitros 700XR analyser with reagents supplied by the manufacturer. For HDL measurement, dextran sulfate/MgCl\textsubscript{2}–selective lipoprotein precipitation was performed using reagents from Johnson and Johnson. When serum triglyceride levels were >300 mg/dL, LDL cholesterol was determined by beta quantification.\textsuperscript{32} Apolipoprotein AI and B levels were determined in fresh sera by immunoturbidimetry on a Roche Cobus FARA with antisera and a protocol from INCSTAR and apolipoprotein standard sera from Behring Diagnostics.\textsuperscript{33} The apolipoprotein assays were calibrated to the International Federation of Clinical Chemistry reference material.\textsuperscript{34} Within- and between-run CVs for the apolipoprotein assays were <4%. Lipoprotein(a) [Lp(a)] was assayed in fresh sera by ELISA with kits from Strategic Diagnostics; within-run and between-run CVs were <7.5%.
Lesion Lipids: Relation to Lipoproteins and Oxidation

Lipoprotein Isolation

LDL for oxidation studies (LDL conjugated dienes and LDL mobility) was isolated from plasma by sequential floatation ultracentrifugation between densities 1.019 and 1.063 g/mL using the method of Havel et al.18 To minimize oxidative modification of the sample, all isolation steps were performed in the presence of 0.01% EDTA and 0.02% BHT.

Oxidation-Related Studies

Several oxidation-related analytes were assayed to encompass a range of oxidative changes potentially associated with atherosclerosis. Conjugated dienes were assayed as a measure of early lipid oxidation and thiobarbituric acid–reactive substances (TBARS) as an indicator of later aldehyde formation. LDL mobility was measured because, unlike conjugated dienes and TBARS, the changes are reversible and persist through late oxidation.24 Last, autoantibodies against oxidized LDL were determined, because these measurements are not confounded by sample autooxidation and may evaluate the impact of lipoprotein oxidation.24

To measure LDL mobility, electrophoretic separation of lipoproteins was performed in 1% agarose gels (Chiron) and detected with fat red 7B and Chiron Multitrac lipoprotein kit No. 470695. Duplicate control samples were run in the first and central lanes of each gel. The control material comprised LDL pooled from 3 normolipidemic volunteers, contained 100 μmol/L BHT to prevent autooxidation, and was stored in aliquots at −90°C. A storage stability study found that control LDL mobility relative to albumin did not differ between fresh samples and those stored for 1, 3, 6, and 9 months at −90°C (data not shown). The mobility of LDL isolated from study subjects was expressed as the relative mobility of the patient sample compared with that of the control, where control migration = 1 (assay CV <5%).

For the determination of conjugated dienes, lipids were extracted both from LDL and from the aortic tissue specimens according to the method of Folch et al.21 For tissue analysis, separate samples were taken from the aortic specimens used for histological/lipid composition studies (see above). The level of conjugated dienes was determined by spectrophotometric absorbance at 234 nm; data were interpolated from a standard curve, using cholesta-3,5-diene in hexanes (both from Sigma) as the standard. The results were expressed as μmol conjugated dienes/mg cholesterol, with the assumption that cholesterol content reflects the total lipid content of the sample. Plasma cholesterol testing for the lipid oxidation studies was performed using reagents and standards from Sigma. TBARS were assayed, as described previously25 (assay CV <9%), in plasma stored for 2 to 12 months at −70°C in the presence of preservatives (listed above).

IgG and IgM autoantibodies against malondialdehyde-modified LDL (α-oxLDL) were assayed by ELISA in sera stored at −70°C for 2 to 12 months, as described previously,26 with the modification that NaN3 was omitted from the wash buffer. In both assays, the antigen (native or malondialdehyde-modified LDL) was coated at 25 μg/mL and the serum dilution was 1:250. The dilutions of horseradish peroxidase–conjugated rabbit anti-human IgG and horseradish peroxidase–conjugated rabbit anti-human IgM (Jackson ImmunoResearch, Westgrove, Pa) were 1:300 and 1:2000 in the IgG and IgM assays, respectively. To minimize between-run variability, a serum pool (n = 3 sera) was assayed on each plate. Data were calculated as the difference in antibody binding between native and malondialdehyde-modified LDL and then expressed as a percentage of the value for the serum pool, as described previously.26 Within-run and between-run CVs for the IgG and IgM α-oxLDL assays were 10.5% and 5.6% and for the IgM α-oxLDL assay, 5.2% and 10.0%, respectively.

Statistical Methods

Before analysis, analyte data were transformed logarithmically as necessary, to fit a gaussian distribution. Linear regression was used to adjust for age and sex. Bivariate relations between variables were examined by linear regression and multivariate relations by stepwise linear regression. Significance was accepted at P < 0.05. All analyses were performed using a statistical package from BMDP Statistical Software, Inc.

Results

Descriptive Data

Demographic, lipoprotein, and fasting blood sugar data are presented for all subjects, according to sex, in Table 1. The study group included 64 subjects for whom vessel wall data were available. There were no subjects with insulin-dependent diabetes mellitus in the study group and 14 subjects (6 females, 8 males) with non–insulin-dependent diabetes mellitus. The frequency of self-reported smoking was similar in men (22.6%, 12/53) and women (23.0%, 3/13).

Lesion lipid data for a given subject were available from 1 (n = 15 subjects), 2 (n = 31 subjects), 3 (n = 17 subjects), or 4 (n = 1 subject) tissue specimens. Atheromatous lesion was observed in 97% of the 132 histological tissue specimens examined; among lesions, 1.6% were Stary classification type I, 9.6% were type II, 40% were type III, 47.2% were type IV, and 1.6% were type V.17 Variations in lipid lesion composition between aortic samples within an individual, calculated as the within-person CV, were 38% for Cx+PL, 47% for CE, and 27% for total lipid. Lesion lipid data are shown in Table 2. Within lesions, there was no relationship between the content of CE and Cx+PL (r = 0.105, P = 0.414). Table 3 shows oxidation-related data for plasma or serum and for aortic tissue; of the measured variables.

<table>
<thead>
<tr>
<th>Table 1. Demographic and Biochemical Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
</tr>
<tr>
<td>Age, y</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
</tr>
<tr>
<td>Fasting blood glucose, mmol/L</td>
</tr>
<tr>
<td>Total cholesterol, mmol/L</td>
</tr>
<tr>
<td>Triglycerides, mmol/L</td>
</tr>
<tr>
<td>LDL cholesterol, mmol/L</td>
</tr>
<tr>
<td>HDL cholesterol, mmol/L</td>
</tr>
<tr>
<td>Apolipoprotein B, μmol/L</td>
</tr>
<tr>
<td>Apolipoprotein Al, μmol/L</td>
</tr>
<tr>
<td>Lipoprotein(a), mg/L</td>
</tr>
</tbody>
</table>

*Study group N = 66 (53 males, 13 females); data were not always available for all analytes in all subjects, as indicated.

TABLE 2. Lesion Lipid Composition

<table>
<thead>
<tr>
<th>Lesion Lipid*</th>
<th>n</th>
<th>Mean ± SD</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>CE</td>
<td>64</td>
<td>7.7 ± 6.0</td>
<td>6.2</td>
</tr>
<tr>
<td>Cx+PL</td>
<td>64</td>
<td>11.3 ± 9.4</td>
<td>9.6</td>
</tr>
<tr>
<td>Total lipid</td>
<td>64</td>
<td>19.0 ± 10.8</td>
<td>16.8</td>
</tr>
</tbody>
</table>

*All data are expressed as percent of total lesion area.
Independent Predictors of Variability in Atheroma Lipid Composition

Lesion Cx+PL content was used as a surrogate measure of lesion severity. All variables that predicted at least 4% of variability in Cx+PL levels in bivariate analysis (r ≥0.200) were included in a multivariate model to identify independent predictors of variability in Cx+PL: these included HDL cholesterol, apo AI, fasting blood glucose, LDL mobility, IgM a-oxLDL, and IgG a-oxLDL. As shown in Table 5, IgM a-oxLDL, fasting blood glucose, and LDL mobility, in descending order of significance, were independent predictors of Cx+PL levels, together accounting for 35% of the variability in lesion Cx+PL.

Discussion

Considerable evidence to support a role for oxidative processes in the development of atherosclerosis exists, although much remains to be learned about the specific mechanisms involved. Furthermore, the clinical utility of measuring oxidation status has yet to be fully explored, both in terms of potential analytes and their relevance to clinical populations. The present study addresses these questions by examining the associations between measurable serum parameters of oxidation status and the lipid composition and oxidation status of atherosclerotic plaque. The fact that multiple comparisons can give rise to statistical significance simply due to chance should be kept in mind when interpreting the results of this study.

The use of an in vivo human model presents certain experimental difficulties. Lesion data were obtained using tissue specimens obtained during CABG surgery, rather than the complete arterial specimens available in animal studies. Our approach assumes that the tissue samples obtained were representative of aortic atherosclerosis status in a given patient. Because multiple samples from the aortic arch were available for most subjects, it was possible to assess the extent of within-subject heterogeneity. Given that within-subject variation in lesion lipid composition was evident, our data most likely underestimate the association of these parameters with other measured variables.

The uptake of CE into the lysosomes of macrophages, followed by its conversion to free cholesterol by acid cholesteryl ester hydrolase, leads to the accumulation of free cholesterol in the lysosome and crystallization of cholesterol monohydrate. Interactions between foam cell intracellular Cx and CE pools are not, however, well understood. We found no association between the respective levels of Cx and CE in the aortic lesions. This may indicate either that these 2 pools are regulated separately or that interactions between the 2 pools are not in equilibrium.

Lipid composition contributes to the mechanical properties of plaque and thus may influence plaque stability; plaque rupture and consequent thrombosis is an important determinant of the acute occlusive event in cardiovascular disease. Soft plaque with a high CE content is believed to be less stable than a mechanically stiffer plaque characterized by the presence of Cx. In the present study, the associations

### TABLE 3. Circulating and Aortic Tissue Oxidation-Related Data

<table>
<thead>
<tr>
<th>Variable</th>
<th>n*</th>
<th>Mean ± SD</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic tissue conjugated dienes, nmol/mg cholesterol</td>
<td>63</td>
<td>666 ± 832</td>
<td>429</td>
</tr>
<tr>
<td>LDL conjugated dienes, nmol/mg cholesterol</td>
<td>63</td>
<td>186 ± 74</td>
<td>163</td>
</tr>
<tr>
<td>LDL relative mobility</td>
<td>58</td>
<td>1.10 ± 0.10</td>
<td>1.10</td>
</tr>
<tr>
<td>Plasma TBARS, µmol/L</td>
<td>64</td>
<td>0.67 ± 0.19</td>
<td>0.61</td>
</tr>
<tr>
<td>Serum IgG anti–oxidized LDL, % of pool value</td>
<td>64</td>
<td>0.60 ± 0.23</td>
<td>0.61</td>
</tr>
<tr>
<td>Serum IgM anti–oxidized LDL, % of pool value</td>
<td>64</td>
<td>0.69 ± 0.23</td>
<td>0.70</td>
</tr>
</tbody>
</table>

*Total number of subjects = 66 (53 males, 13 females); complete data were not always available, as indicated.

### TABLE 4. Relationship Between Atheroma Lipid Composition and Circulating Oxidation-Related Variables

<table>
<thead>
<tr>
<th></th>
<th>Total Lipid</th>
<th>CE</th>
<th>Cx+PL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>r</td>
<td>P</td>
</tr>
<tr>
<td>Plasma TBARS</td>
<td>59</td>
<td>-0.041</td>
<td>0.759</td>
</tr>
<tr>
<td>LDL conjugated dienes</td>
<td>57</td>
<td>0.298</td>
<td>0.025</td>
</tr>
<tr>
<td>LDL relative mobility</td>
<td>53</td>
<td>0.128</td>
<td>0.363</td>
</tr>
<tr>
<td>IgG anti–oxidized LDL</td>
<td>59</td>
<td>0.22</td>
<td>0.094</td>
</tr>
<tr>
<td>IgM anti–oxidized LDL</td>
<td>59</td>
<td>0.281</td>
<td>0.031</td>
</tr>
</tbody>
</table>

All data were adjusted for age and sex, and data for TBARS, LDL conjugated dienes, lesion total lipid, lesion cholesteryl ester, and lesion cholesterol crystal plus phospholipid were logarithmically transformed before statistical analysis.
between serum or plasma markers and lesion lipid composition were all with lesion Cx content rather than with CE. Thus, the analytes measured may be more important as markers for plaque development than for plaque instability.

The finding of inverse relationships between HDL cholesterol or apo AI levels and lesion Cx content (significant for HDL cholesterol) is consistent with the results of epidemiologic studies that have demonstrated a protective role for the HDL particle in atherosclerosis. The relationships were not significant in multivariate analysis, suggesting an interaction between HDL and other variable(s) in the model. With the exception of HDL cholesterol, other traditional lipoprotein measurements demonstrated no significant associations with lesion lipid composition. In contrast, 2 oxidation-related variables, LDL mobility and IgM-oxLDL, were significantly and independently associated with lesion Cx content, providing direct support for the hypothesis that the LDL particle only becomes atherogenic after chemical modification. Furthermore, the association between LDL mobility and aortic tissue oxidation status, as estimated by conjugated dienes, suggests a direct relationship between oxidation processes in these 2 compartments. This relationship may be explained by the uptake of circulating modified lipoprotein by the arterial wall, though other possibilities, such as a common arterial oxidative process followed by migration of modified LDL from the subendothelial space back into the circulation, cannot be ruled out. Further work is needed to define this relationship. For example, both the composition of oxidized lipids and their extent of oxidation are likely to be heterogeneous in plasma and tissue, and additional oxidation assays may be needed for the optimal estimation of oxidation status.

There are at present inconsistencies in the literature regarding the relationship between α-oxLDL and atherosclerosis. Most previous studies have focused on measurements of IgG α-oxLDL rather than IgM α-oxLDL. As demonstrated here, there is a relationship between IgG α-oxLDL and lesion lipid content, but it is weaker than the relationship observed for IgM α-oxLDL and could be easily confounded by the presence of subclinical atherosclerosis in control groups. There are also conflicting data, however, when atherosclerosis is ascertained by imaging techniques. For example, using angiography, Van der Vijver et al found no significant relationship between α-oxLDL and the degree of stenosis, whereas Salonen et al demonstrated a significant association when atherosclerosis was quantified as intima-media thickness of the carotid artery. The type of α-oxLDL measured may explain this discrepancy; however, α-oxLDL may also have different relationships with the physical characteristics of atherosclerosis as detected by imaging techniques, compared with the compositional characteristics as presented here.

Diabetes is an independent risk factor for atherosclerosis and is associated with a 2- to 4-fold increased risk for this disease. Although an adverse lipoprotein profile may account for some of this excess risk, particularly in non-insulin-dependent diabetes mellitus, there has been recent interest in the role of hyperglycemia in the pathophysiology of atherosclerosis. Consistent with a direct effect, we found a significant relationship between fasting blood glucose and lesion Cx content in multivariate analysis, indicating that blood glucose level contributes independently to the development of atherosclerosis. These findings are consistent with the data of Litvak et al, who reported that chronic hyperglycemia was associated with increased atherosclerosis in monkeys, in the absence of hyperlipidemia. Also, McGill and colleagues found in autopsy studies of young males that subjects with glycosylated hemoglobin levels >8% had more extensive coronary and aortic atherosclerosis than did those with lower levels.

In summary, we have examined the in vivo relationships between atherosclerotic lesion lipid composition and serum or plasma measurements of lipoprotein- and oxidation-related variables. LDL mobility, IgM-α-oxLDL, and fasting blood glucose were significant independent predictors of lesion Cx+PL content, accounting for a large portion (35%) of the variability in this analyte. These data support the existence of direct roles for oxidation and hyperglycemia in the pathophysiology of atherosclerosis.

Acknowledgments

This work was supported by National Institutes of Health grant 5 P20 RR10203-02 (to P.M.N.) and Department of Energy grant DE-FGO293ER75945 (to W.Y.C.). The authors would like to thank Mariusz Jankowski, PhD, for assistance with the image processing studies and Agatha Bellevue, RN, for assistance with patient recruitment.

References


Relationship Between Lipoprotein- and Oxidation-Related Variables and Atheroma Lipid Composition in Subjects Undergoing Coronary Artery Bypass Graft Surgery
Wendy Y. Craig, Ming W. Rawstron, Clark A. Rundell, Elizabeth Robinson, Sue E. Poulin, Louis M. Neveux, Patsy M. Nishina and Leonard M. Keilson

doi: 10.1161/01.ATV.19.6.1512

Arteriosclerosis, Thrombosis, and Vascular Biology is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1999 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/19/6/1512

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/