Introduction
Acute coronary syndromes usually result from an interaction between a vulnerable atherosclerotic plaque and thrombus formation, a process now referred to as “atherothrombosis.” Two major hypotheses to explain the pathogenesis of atherosclerosis were put forward in the 19th century: the incrustation hypothesis proposed by von Rokitanski in 1852, and the lipid hypothesis proposed by Virchow in 1856. These two hypotheses constituted the basis for the response-to-injury hypothesis postulated by Ross more than a century later. Lipoprotein accumulation and chronic inflammation are the main players in the early stages of the disease and inflammation also plays a role in the final stages, being intimately involved in plaque rupture and thrombosis. Therefore, atherothrombosis represents the integration of the major theories to explain atherosclerosis and acute coronary events.

Until the last decade, it was conventionally accepted that acute coronary events were associated with marked vessel lumen narrowing but this concept was abandoned when it became clear that most of the lesions associated with myocardial infarction were only mildly or moderately stenotic and therefore not detectable by angiography. In reality, nearly two thirds of all patients with acute coronary ischemic syndromes show that the culprit lesion had often less than 50% narrowing, as shown by coronary angiograms performed weeks or months before. Thus atheromatous plaques producing non-flow limiting stenoses accounted for more acute events than those producing a more severe stenosis. One of the main reasons for this seemingly incongruent finding is the fact that severely stenotic lesions are more likely to stimulate neovascularization leading to the formation of collateral circulation or, in other words, to a “natural bypass.” Thus, these sites if ruptured are more likely to be clinically silent due to the protective effect of the “natural bypass.” The above findings led to studies that tried to evaluate methods of identifying atherosclerotic lesions prone to trigger acute coronary syndromes, and the concept of plaque vulnerability emerged from these studies.

Definition of Vulnerable Plaques
As mentioned earlier, vulnerable plaques are usually not associated with vessel luminal stenosis. The net effect of a plaque on lumen size is not necessarily due to the size of the plaque but to positive versus negative remodeling. Greater outward or positive remodeling minimizes luminal encroachment regardless of the plaque size. In contrast, negative or inward remodeling leads to narrowing of the arterial lumen. Interestingly, human studies using intravascular imaging have shown that vulnerable plaques are typically smaller than non-vulnerable plaques.

Clinical Insights continued on page 4
Making Ourselves Heard

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Richmond, Virginia

When you think about other medical associations that promote the goals of their members, you realize just how young the NLA is. Yet, in only 4 years, we’ve come a long way toward establishing as the role of the clinical lipidology practice. By any assessment, we’re growing faster than ever and major milestones lie just ahead. This January will see the launch of the Pacific Lipid Association, shortly afterward the NLA will have its own journal, and the second Task Force report, the Report of the National Lipid Association’s Safety Task Force on Lipid Altering Drugs will be published as a supplement to the American Journal of Cardiology. As lipidologists, we are raising our presence and growing into a distinct and authoritative voice in the medical community.

Allow me to share with you several examples of how we are making ourselves known, and the kinds of responses we’ve been receiving in turn. First, every member of the NLA recently received a copy of our Statin Safety newsletter, Recommendations for Primary Care, which summarized the conclusions of the Task Force in brief for our association’s members and for the benefit of primary care physicians. This publication was sent directly to over 40,000 MDs working in primary care. In the days that followed, many of these physicians obtained online CME credit and some have contacted the NLA requesting additional copies. The companion Webcast held October 24, drew hundreds of participants.

We are continuing to work toward the launch of our association’s journal, the Journal of Clinical Lipidology. By the time you read this, ads in the trade press will be appearing along with calls for papers. On that note, remember that once our journal is accredited, every accepted article will be indexed retroactively to Issue 1, Volume 1. Please consider publishing your work with us first. We have every intention of becoming the premier source of information about clinical lipidology and a must-read resource for everyone in our field.

The most important item on our agenda is the need to offer clinical lipidology certification to our entire membership. The development of this certification was the number one priority of the NLA’s Strategic Plan adopted by the Board of Directors and membership in 2006. Our progress toward that objective continues, and it is my pleasure to announce the establishment of the Accreditation Council in Clinical Lipidology, or ACCL. The ACCL will oversee the certification of our non-MD membership, and administer the board examination for pharmacists, nurse practitioners, physician assistants and dietitians. A pilot exam will be administered at the NLA annual meeting in Montreal Canada on April 14. The national examination day at the NLA annual meeting in Scottsdale Arizona on June 2, 2007 is planned to be held pending a successful pilot program.

I will serve as the first chairman of the ACCL, and joining me on the executive board are Carol Mason, ARNP, Barbara Wiggins, PharmD, and Ralph LaForge, MSc. Ultimately, the organization will consist of 19 Board Governors (4 officers, 5 members on the council on nursing and physician assistants, 5 members on the council on pharmacy, and 5 members on the council of nutrition and exercise). The Board will be a separate entity from the NLA and is incorporated as an independent organization. Full criteria for examination eligibility will be available at www.lipid.org this February.

I’m especially pleased with the results of our Beyond Cholesterol survey. This project was guided by the NLA’s Consumer Affairs Committee headed by Dr. Jerome Cohen. In June 2006, Harris Interactive was commissioned to conduct a study for public release by Chamberlain Communications, who wished to assess awareness and knowledge of lipid subfractions such as triglycerides among adults diagnosed with dyslipidemia. The overall objective of the research, on which the National Lipid Association would be a partner, was to provide a platform from which to spark the patient-physician dialogue and raise disease awareness. Funding was provided by an unrestricted grant from Abbott Laboratories that allowed the NLA to control the design, construction, and implementation of the survey, and we were given a completely free hand to assess the data collected and interpret it.

The consumer survey was conducted via the Internet among...
2,089 US adults age 18+ sampled from Harris Interactive’s online consumer panel. The sample includes both diagnosed dyslipidemia patients and adults not diagnosed with dyslipidemia. The sample was stratified and weighted to ensure readable sub-samples as well as appropriate representation of key subgroups such as African-Americans, Hispanics, women and diabetes sufferers.

On the physician side of the survey, a total of 510 physicians were sampled by specialty from the AMA Masterfile, and these included 205 PCPs (family practice, general practice and internal medicine physicians), 155 cardiologists and 150 endocrinologists. Both questionnaires averaged 20 minutes in length and it was determined that statistical significance is tested at the 95% confidence level for all samples >30 respondents. We gathered an enormous amount of data.

Some of the key findings are available at the Press Page at www.lipid.org. We discovered the following:

**Patient Awareness**
A significant majority of patients do not consider themselves to be particularly knowledgeable about cholesterol, and even fewer about lipids. Only 31% of patients consider themselves to be “knowledgeable” or “very knowledgeable” about cholesterol, and only 20% consider themselves so with respect to lipids.

It comes as little surprise, then, that patients are less familiar with triglycerides and the combined lipid profile than with total cholesterol, and their understanding of the constituent elements of total cholesterol—HDL and LDL—falls in between. They also attach less importance to knowing about triglycerides than to knowing about total cholesterol.

Encouragingly, 69% feel that it is “important” or “very important” to know about total cholesterol, along with 65% for HDL, 67% for LDL, 61% for triglycerides and 59% for combined lipid profile. These findings suggest that the public is increasingly aware of the importance of lipid management and ready for more information about it. We discovered that nearly half of patients believe that they know what levels are considered safe for various lipids. Based on their answers to specific questions, however, we find that very few actually do know.

**Physician Awareness**
The responses revealed that physicians are much more familiar with high blood cholesterol guidelines than they are with elevated triglyceride guidelines, as 74% of physicians said they were “familiar” or “very familiar” with the high blood cholesterol guidelines, compared to 56% of physicians for the elevated triglyceride guidelines.

Accordingly, 95% of physicians follow target cholesterol guidelines “a fair amount” or “a great deal,” compared to 84% of physicians who follow secondary goal guidelines (triglycerides). Yet physicians also appear to demonstrate a knowledge gap, because while nearly 3 out of every 4 physicians report familiarity with the high blood cholesterol guidelines, and 56% with the secondary goal guidelines, only 55% of physicians in total correctly identified all four NCEP ATP III Guidelines.

**Communication**
The surveys were also designed to capture information about how physicians and patients talk about lipid management and risks. We found some surprises here. For example, less than half of patients (only 43%) have discussed lipids with their physicians. Of those who have, more have discussed total cholesterol than HDL or LDL, and ever fewer have discussed triglycerides (59%) and combined lipid profile (50%). Discussions about total cholesterol tend to lead to the greatest levels of understanding and awareness, followed by discussions about HDL and LDL, while discussions about triglycerides and combined lipid profile lead to the lowest levels of understanding and awareness.

Although few patients report discussing lipids with their physicians or having them tested, physicians report that they discuss lipids with 3 in 4 patients. What’s more, physicians report conducting lipid panels on 8 in 10 patients and supplying patients with healthy targets for most lipid components. Perhaps one reason for this disconnect is a lack of time; physicians indicate that they wish they had more time to discuss lipid with their patients.

**Media Messages**
Once we had determined the major implications of the survey findings, we drafted a press release and circulated it to major news agencies and health information publishers. The response was tremendous, to say the least. We received uniformly favorable coverage in newspapers and magazines, and responded to numerous requests for interviews. Dr. Cohen was the subject of a television news spot that was released in California. These activities are still continuing. The NLA Consumer Affairs Committee is working on several articles targeted for journal publication as well.

If you’d like to learn more about the Beyond Cholesterol survey project and view the data for yourself, visit the NLA homepage at www.lipid.org and select the Press Page. Our Consumer Affairs Committee has done an outstanding job and they and Dr. Cohen are to be congratulated on their effort that has raised the profile of the NLA and helped us make our voices heard.
ultrasound have shown that outward remodeling is more common in unstable angina and that inward or negative remodeling is more common in stable angina,\textsuperscript{5,6} thus suggesting that angiography has little value for identifying lesions that will likely trigger acute coronary events.

Histologically, plaques that are prone to rupture consist of a thin fibrous cap with reduced collagen content, a large lipid core, and a high density of macrophage foam cells\textsuperscript{7} (Table 1 and Fig. 1). The fibrous cap is often thinner at the shoulder regions, where disruption most frequently occurs.\textsuperscript{8} Pathology studies found that disrupted caps contain less collagen and fewer smooth muscle cells (SMC) than undisrupted caps.\textsuperscript{9} Collagen comprises up to 40% of the total protein in fibrous plaques and 60% in advanced lesions.\textsuperscript{7} Most of the collagen (50–75%) in a diseased intima is type I collagen, a substrate of MMP-1 or interstitial collagenase.\textsuperscript{10–12} Collagens are synthesized and assembled by vascular SMCs. Zymography studies have shown that vulnerable plaques have higher MMP expression and activity than stable plaques.\textsuperscript{13,14}

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Major features of vulnerable plaque</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Thin fibrous cap</td>
</tr>
<tr>
<td>2</td>
<td>Low in SMCs and collagen content</td>
</tr>
<tr>
<td>3</td>
<td>High expression of MMPs</td>
</tr>
<tr>
<td>4</td>
<td>Large lipid-rich core (&gt;40% of lesion)</td>
</tr>
<tr>
<td>5</td>
<td>High in macrophages</td>
</tr>
<tr>
<td>6</td>
<td>SMC apoptosis</td>
</tr>
<tr>
<td>7</td>
<td>Usually &lt;70% stenosis</td>
</tr>
<tr>
<td>8</td>
<td>Eccentric shape with irregular borders</td>
</tr>
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The lipid core in vulnerable plaques is rich in cholesteryl esters and appears hypocellular except at the margins where macrophage foam cells are accumulated. The softness of atheromatous core renders the plaques vulnerable.\textsuperscript{15–17}

**Role of Metalloproteinases (MMPs) and Their Inhibitors (TIMPs) in Plaque Vulnerability**

MMPs and TIMPs

MMPs belong to an important family of zinc- and calcium-dependent proteinases that degrade various constituents of the extracellular matrix (Table 2). MMPs participate in many physiological and pathological processes such as tissue reshaping, wound healing, inflammation, organ development, tumor metastasis, and cardiovascular diseases (e.g., atherosclerosis, abdominal aortic aneurysms, and heart failure).\textsuperscript{14}

As shown in Table 2, MMPs are capable of degrading almost all components of the extracellular matrix (ECM). Since MMPs are crucial in many physiological and pathological processes, MMP activity is tightly controlled at several levels.

Metalloproteinases are regulated at the transcriptional level by a wide spectrum of inflammatory cytokines, growth factors, and tumor promoters, such as IFN\textsubscript{γ}, TNF, IL-1β, IL-6, PDGF, EGF, M-CSF.\textsuperscript{18} Additionally, several other factors that are involved in atherosclerosis and inflammation, such as oxidized LDL, CD40 ligand, and reactive oxygen species, may also regulate MMP gene expression in vitro.\textsuperscript{18} Another form of MMP regulation is enzymatic activation. All MMPs are secreted as latent forms and require activation by proteases such as other MMPs, elastase, trypsin or by nonproteolytic agents such as plasmin or urokinase plasminogen activator to exert their function.\textsuperscript{14} Interestingly, four inhibitors of MMPs (TIMPs) have also been isolated and characterized. They bind to active or latent forms of MMPs in a molecular 1:1 ratio. The equilibrium between active MMPs and their inhibitors determines the net proteolytic activity of MMPs.\textsuperscript{14}

**Figure 1.** Vulnerable plaques differ from stable plaques by the following major features: (1) thin fibrous cap; (2) larger lipid core; (3) less smooth muscle cells; (4) more macrophage foam cells; (5) more cholesterol content; (6) higher MMP expression and less collagen content; (7) more neovessels.
The role of MMPs in plaque destabilization

A large number of studies have well documented that MMPs play a crucial role in plaque rupture by degrading extracellular matrix in fibrous caps\textsuperscript{13,19–21} (Fig. 2). Plaque rupture is the major cause of acute coronary syndromes.\textsuperscript{20} Expression of MMP-1, -3, -7, -9, -11, -12, -13, and -16 is increased in human atherosclerotic plaques, especially at the macrophage-rich shoulder regions where plaque rupture frequently occurs.\textsuperscript{13} Genetic studies also demonstrated that MMP-3 and MMP-9 polymorphisms were associated with greater progression of coronary disease in a small cohort of patients.\textsuperscript{21,22} Furthermore, several studies have related MMP levels to clinical or histological features associated with plaque instability. For example, it was found that MMP-11 immunoreactivity is confined to advanced atherosclerotic plaques, not fatty streaks.\textsuperscript{23} It was also reported that positivity for MMP-1 correlates with the percentage of the lipid core occupied with hemorrhage.\textsuperscript{24} More interestingly, 2 laboratories studied the effect of TIMP-1 knockout in apoE knockout mice on atherosclerosis and both found that TIMP-1 knockout significantly increased destruction of medial elastic fibers.\textsuperscript{25,26}

Can vulnerable plaques be identified?

As mentioned above, the degree of lumen obstruction is not a good indicator of plaque vulnerability. Angiographic progression of a lesion is a weak predictor of MI or sudden death. Even a wide array of clinical and angiographic factors have been quite disappointing in their ability to predict acute clinical events. Since the composition of the plaque is a strong indicator of plaque vulnerability, several invasive and non-invasive imaging techniques have been developed to identify vulnerable plaques. Among the invasive techniques,

\begin{table}
\centering
\caption{Matrix metalloproteinases and their substrates}
\begin{tabular}{|c|c|c|}
\hline
Groups & Enzyme name & Matrix substrates \\
\hline
Collagenases & MMP-1, Collagenase-1 & Collagens (I, II, III, VII, VIII, X), Gelatin, proteoglycans, MMP-2, -9 \\
& MMP-8, Collagenase-2 & \\
& MMP-13, Collagenase-3 & \\
& MMP-18, Collagenase-4 (xenopus collagenase) & \\
\hline
Gelatinases & MMP-2, Gelatinase A & Gelatin, collagens (I, IV, V, VII, X, XI, XIV), Fibronectin, laminin, elastin, MMP-1, -9, -13 \\
& MMP-9, Gelatinase B & \\
\hline
Stromelysins & MMP-3, Stromelysin-1 & Proteoglycan, fibronectin \\
& MMP-10, Stromelysin-2 & laminin, gelatin I, III, IV, V, Collagen III, IV, V, IX \\
& MMP-11, Stromelysin-3 & \\
\hline
Matrilysins & MMP-7, Matrilysin-1 & Collagens (IV, X), gelatin, fibronectin, laminin, MMP-1, -2, -9, MMP-9/TIMP-1 complex \\
& MMP-26, Matrilysin-2 & \\
\hline
Membrane type metalloproteinases (MT-MMP) & MMP-14, MT1-MMP & \\
& MMP-15, MT2-MMP & \\
& MMP-16, MT3-MMP & \\
& MMP-17, MT4-MMP & \\
& MMP-18, MT5-MMP & \\
& MMP-25, MT6-MMP & \\
\hline
Other MMPs & MMP-12, Macrophage metalloelasta se & Collagen IV, gelatin, elastin, fibronectin, casin, fibrinogen, plasminogen, MMP-2, Aggrecan, cartilage oligomeric matrix protein \\
& MMP-19, MMP-20 & \\
\hline
\end{tabular}
\end{table}

\textbf{Figure 2. The role of MMPs in plaque vulnerability}
intravascular ultrasound, angioscopy and optical coherence tomography are available, and among the non-invasive techniques are computed tomography and high-resolution magnetic resonance. The latter is the leading in vivo imaging modality for studying the characteristics of the plaque but, although feasible, its clinical application is still very limited due to technical difficulties related with the size and tortuosity of the coronary arteries as well as to artifacts due to cardiac and respiratory motion.

Due to the difficulty in identifying the histomorphologic characteristics of the vulnerable plaque by direct imaging, several surrogate markers have been proposed. Among these some new risk factors such as C reactive protein, myeloperoxidase, and lipoprotein associated phospholipase A2 have been suggested but the results have been equally disappointing. A recent necropsy study has examined conventional risk factors in 113 men with sudden coronary death and found that smoking was a predictor of acute thrombosis regardless of plaque etiology and that plaque rupture correlated with high total cholesterol levels, low HDL-cholesterol, and high total cholesterol/HDL cholesterol ratio. The increase in levels of total cholesterol was nicely correlated with increased incidence of thin cap atheromas. Other studies have also shown that plaque erosion is highly associated with smoking in women less than 50 years of age and with elevated levels of cholesterol in women over 50 years of age.

Sudden rupture of a vulnerable plaque may occur without obvious triggers. However, some events are known to trigger sudden rupture of vulnerable plaques. Among them are extreme physical activity (mainly in unfit individuals), severe emotional trauma, sexual activity as well as acute infections and exposure to extreme cold or to recreational drugs (mainly cocaine and amphetamines). It is noteworthy that in 40–80% of cases with acute coronary syndromes, multiple plaque ruptures may occur in sites other than the acute culprit site.

The thrombotic response to the ruptured plaque is related to the composition of the plaque itself and the local hemorheology. Lipid-rich plaques are more thrombogenic than fibrous plaques since the lipid core has a high content of tissue factor. Apoptic macrophages in the lesion are the major source of tissue factor in the lesion.

Thrombosis can also be associated with slight erosion of the plaque even when plaque rupture does not occur. These erosions happen in 20–40% of cases and are mainly observed in young subjects with sudden death, smokers, and women. The precise mechanism for thrombus formation in these cases is not clear and may be secondary to increased systemic thrombogenic state or decreased fibrinolytic state.

**Treatment options**

Obviously important therapeutic options include stabilization of the plaque as well as treatment of the thrombotic complications secondary to plaque rupture/erosion. Stabilization of plaques can be attained using a multifaceted approach. In addition to lifestyle modifications, which are essential, several medications have been shown to play an important role in plaque stabilization such as treatment with statins and angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers.

Statins are the best known of the drugs that lead to plaque stabilization, offering a 20–25% reduction in cardiovascular events. Statins reduce the lipid content of atheromas, thus decreasing the vulnerability of the plaques. Furthermore, lipid lowering with statins improves endothelial function, reduces platelet thrombus formation, and normalizes clotting and fibrinolytic activity. Statins are also considered as having anti-inflammatory properties leading to decreased expression of MMPs and preventing tissue factor expression in endothelial cells. The MIRACL (Myocardial Ischemia with Aggressive Cholesterol Lowering) study indicated that early initiation of aggressive cholesterol-lowering therapy after an acute coronary syndrome reduces ischemic events, although no effect was observed in death or non-fatal MI. Although the advantages of early treatment was not definitively proved by the MIRACL trial, some observational studies seem to support the hypothesis. In the Swedish Registry of Cardiac Intensive Care of approximately 20,000 patients, the risk of mortality was reduced by 25% in patients in whom statin therapy was initiated before hospital discharge.

Stabilization of plaque can be also attained by treatment with ACE-inhibitors. The Heart Outcomes Prevention Evaluation trial reported a 22% reduction in major cardiovascular events among high-risk patients treated with ramipril. Although results of large trials are not available for other types of anti-inflammatory or lipid-lowering drugs, several other possibilities of treatment for plaque stabilization hold some promise, such as administration of HDL-cholesterol or Apo A-1 Milano and LDL-apheresis in patients with familial hypercholesterolemia. Also, numerous novel anti-inflammatory agents and local gene therapy targeting—among others—TNF, interferon γ, monocyte chemotactic protein 1, vascular adhesion molecule 1 (VCAM-1) are also in development and may play an important role in plaque stabilization.

Besides plaque stabilization, treatment of the thrombotic complications of plaque rupture is also important. Several pharmacologic strategies have been developed to inhibit thrombogenesis as well as to dissolve formed thrombi. Dissolving formed thrombi has been performed using fibrinolytic therapy. Early fibrinolytic therapy leads to vascular reperfusion and...
myocardial salvage thereby reducing morbidity and mortality among patients with myocardial infarction.\textsuperscript{50} Other mechanisms to normalize coronary flow after an MI include percutaneous coronary intervention. There has been conflicting evidence regarding the advantage of using percutaneous coronary intervention (PCI) in patients with acute coronary syndromes, although evidence supporting the benefit of early percutaneous intervention in acute coronary syndromes is increasing.\textsuperscript{51} A meta-analysis of randomized trials performed recently that included 5,253 patients\textsuperscript{52} showed that rescue PCI for failed fibrinolysis reduces mortality significantly [odds ratio (OR) 0.63, 95% confidence interval (CI), 0.39 to 0.99, \(p=0.055\)] and the rate of death or re-infarction (OR 0.6, 95% CI 0.41–0.89, \(p=0.012\)) compared to a conservative approach. When comparing the outcomes in patients with acute MI treated with thrombolysis versus primary PCI (Danish Trial in Acute MI–2), the overall mortality did not differ between the two groups.\textsuperscript{53} Reinfarction rate was, however, particularly high in patients with grade 3 ischemia (ST elevation with terminal QRS distortion in 2 or more leads) and in this group of patients early PCI significantly reduced the rate of reinfarction. Systematic and early PCI performed in the “stent” era led to a trend towards reduction of mortality in comparison to delayed or ischemic-guided intervention but no statistical significant difference was observed.\textsuperscript{54} The trend in the “balloon” era was for an increase in mortality.\textsuperscript{55} Although the risk of restenosis is less with stents than angioplasty, the usefulness of drug-eluting stents versus bare stents has not been established.\textsuperscript{54} Drug-eluting stents lead to reduced revascularization and SMC proliferation as expected, but they seem to lead to a late cardiac death or non-fatal MI, probably due to late stent thrombosis,\textsuperscript{54,55} which occurs usually after stopping clopidogrel.\textsuperscript{55} Other independent predictors of stent thrombosis besides premature interruption of anti-platelet therapy are primary stenting in acute MI and the length of the stent.\textsuperscript{56} It is necessary to conduct trials with a longer period of follow-up to clearly evaluate the benefits of drug-eluting stents versus bare stents. It is important to note that PCI performed 3 to 28 days after MI does not reduce the occurrence of death, reinfarction or heart failure. In reality, there is a trend to higher rates of reinfarction in a 4 year follow-up period in the patients subjected to delayed PCI intervention than in those subjected to intensive medical therapy alone.\textsuperscript{57} In other words, PCI should be either performed early after an acute event or should not be performed.

Finally, inhibitors of the intrinsic coagulation pathway such as heparin have been used to inhibit thrombogenesis. The effects of unfractionated heparin when used together with aspirin are modest\textsuperscript{48} and require monitoring patients for bleeding. Low molecular weight heparins have been recently used and constitute a major improvement in treatment, mainly due to the fact that monitoring of bleeding is not necessary. Also, some studies suggest that low molecular weight heparins such as enoxaparin are superior to heparin in reducing a composite endpoint of MI and emergency revascularization.\textsuperscript{59} Larger trials, however, are needed to allow for more definitive conclusions about the therapeutic value of enoxaparin. Another approach to prevent thrombosis is the use of anti-platelet agents. Aspirin is the most widely used agent and its efficacy has been well demonstrated in both primary and secondary prevention trials.\textsuperscript{60,61} Death from cardiac causes as well as fatal and non-fatal MI are reduced by 50–70\% in patients with acute coronary syndromes when taking aspirin between dosages of 80 and 325 mg per day.\textsuperscript{62,63} Aspirin blocks the cyclooxygenase pathway and the synthesis of thromboxane A2, a potent platelet activator. However, since aspirin does not block platelet activation triggered by other agonists such as thrombin, collagen and adenosine diphosphate (ADP), other inhibitors of platelet activation such as thienopyridine derivatives, which block ADP, as well as antagonists of platelet glycoprotein IIb/IIIa complex have been developed and are being evaluated.

**Conclusions**

In conclusion, although we now have a much more clear understanding of the risk factors and plaque characteristics that lead to acute cardiovascular events, we are a long way from being able to identify vulnerable plaques in vivo. Whether it is useful to locate vulnerable plaques is not clear from a treatment point of view, as it is not clear that surgical intervention such as angioplasty or stent placement are useful except in symptomatic cases and if performed within hours of a myocardial infarction. However, identification of vulnerable plaques may be valuable to the patient, as it may lead to intensification of medical treatment with both lifestyle modifications and drug therapy (lipid-lowering, anti-hypertensive, anti-diabetic, etc.), which may be life-saving. It may also be a major factor in patient compliance and frequency of monitoring. In addition, it may guide the patient toward resolving personal issues that otherwise might be neglected.

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CERTIFICATION IN CLINICAL LIPIDOLOGY
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The American Board of Clinical Lipidology is an independent certifying organization offering
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This is a very exciting time in the field of clinical lipidology. With the creation of the National Lipid Association (NLA) and the American Board of Clinical Lipidology (ABCL), clinical lipidology is now an established clinical discipline with its own certification of competency examination. Due to the leadership and vision of Michael Davidson, the Masters in Lipidology course has been taken by hundreds of physicians and mid-level providers around the country. The Masters course will be offered in five major cities next year and attendance is expected to exceed that observed in 2006. The NLA is also launching its own journal in the spring of 2007, the Journal of Clinical Lipidology. The journal will be published by Elsevier. Virgil Brown of Emory University has been named Editor-in-Chief and will develop this journal into a world-class forum for research and an invaluable resource for dyslipidemia identification and management.

There is considerable enthusiasm among healthcare professionals to identify and treat dyslipidemias in a comprehensive and efficacious manner. Many members of the NLA have expressed a demand for a textbook in lipidology that is authoritative and practical, yet comprehensive in scope.

I am pleased to inform the NLA membership that Therapeutic Lipidology (edited by Michael Davidson, Peter Toth, and Kevin Maki) has gone to press and is being published by Humana Press. It is expected to debut at the American College of Cardiology meeting in New Orleans in March 2007. Therapeutic Lipidology is intended to serve as a comprehensive resource for the identification and management of a variety of dyslipidemias. This volume will also complement the Masters in Lipidology self-assessment modules and serve as a primary reference. Many members of the NLA (Dan Rader, Tom Dayspring, Neil Stone, Bill Cromwell, Carol Mason, et al.) have prepared meticulously crafted chapters on a broad range of issues in lipidology. Topics such as Lipoprotein Metabolism and Vascular Biology, International Dyslipidemia Guidelines, Genetic Disorders of Lipoprotein Metabolism, Metabolic Syndrome, and Lipoprotein Subfraction Analysis are all aptly represented. Some areas where questions frequently arise and guidance can be hard to come by, such as Dyslipidemia Management in Children, the Allied Health Professional’s Role in the Management of Dyslipidemia, Imaging Modalities for Atherosclerotic Disease, and Development and Management of a Lipid Clinic, also receive comprehensive treatment. The various lipoprotein species (LDL, VLDL, HDL, Lp(a)), antilipidemic therapies (medication, dietary intervention, apheresis), phytosterols, and lipid management in women and the elderly are also addressed. In all the book is composed of 22 chapters written by leading experts in the field. It is anticipated that Therapeutic Lipidology will undergo regular revision (likely every 3 years) as novel lipid species, therapies, and diagnostic modalities are continually developed and refined.

Another textbook that lipidologists may find useful is Comprehensive Management of High Risk Cardiovascular Patients (edited by Antonio Gotto and Peter Toth), which was published this fall by Informa. This textbook also takes a comprehensive approach to lipid management, but emphasizes the need to identify and treat all risk factors for atherosclerotic disease in an intensive, evidence-based manner. Many members of the NLA and ABCL also contributed to this book (Ron Goldberg, Vera Bittner, Peter Wilson, Neil Stone, Jennifer Robinson, and Michael Davidson, et al.). Topics in addition to lipid management include Framingham Risk Assessment, Risk Factor Management in Women and Minority Populations, Management of Type 1 and Type 2 Diabetes, Hypertension, Markers of Inflammation, Peripheral Arterial Disease, Stroke Prevention, Metabolic Syndrome, Identification and Management of Myocardial Infarction, Nephropathy, and others. This volume includes 21 chapters spanning the spectrum of atherosclerotic disease and its established and emerging risk factors. Chapters include flow charts, case studies, and highlighted, boxed recommendations for ease of clinical applicability.

Lipidology is moving into a new era of legitimacy. It is hoped that by combining the educational offerings of the Masters in Lipidology course, The NLA SAPs, the Journal of Clinical Lipidology, and new textbooks exploring the role of lipids in the etiology of disease, significant progress will be made in expanding the clinical insight and ability of the many clinicians who comprise the NLA and have dedicated their professional lives to the prevention and treatment of lipid-related illness.

Reference
High-Dose Atorvastatin after Stroke or Transient Ischemic Attack

RONALD B. GOLDBERG, MD
Professor of Medicine, University of Miami School of Medicine Director, Lipid Disorders Center
Associate Director, Diabetes Research Institute
Miami, Florida

Although statin trials with primary coronary heart disease (CHD) endpoints have shown in secondary analyses that strokes are also reduced by statin therapy, there have been no studies testing primarily whether statin therapy is effective in individuals with stroke but no overt CHD. This is an important unanswered question for several reasons; first, in a secondary analysis of the Heart Protection Study (HPS), those individuals with cerebrovascular disease at baseline showed no reduction in cerebrovascular events on statin therapy. Second the NCEP ATP III designated stroke as a CHD-risk equivalent yet there has been no formal demonstration in these individuals that statin treatment is beneficial for CHD. Third, stroke is more heterogeneous than CHD comprising cardio-embolic, lacunar, hemorrhagic and atherothrombotic subtypes. These may not all respond to statin therapy and there is evidence that antihypertensive treatment may be more beneficial for stroke than it is for CHD. Indeed there is epidemiologic evidence that low cholesterol levels are positively associated with hemorrhagic stroke. Hence, the results of the recently published SPARCL (Stroke Prevention by Aggressive Reduction in Cholesterol Levels) trial were awaited with great interest.

In this double blind, placebo-controlled clinical trial, 4,731 subjects with a documented stroke or transient ischemic attack (TIA) within the prior 6-month period, with no known CHD and with an LDL-C between 130 and 190 mg/dL, were randomized either to atorvastatin (atorva) 80 mg or placebo, to test whether high dose statin therapy prevented recurrent stroke or TIA (average follow-up of 4.9 years). A stroke diagnosis was present in 70% of which 95% were considered to be ischemic in type, and the remaining 30% of participants carried the diagnosis of TIA. The LDL-C averaged ~133 mg/dL, HDL-C 50 mg/dL, triglycerides ~144mg/dL, 17% had diabetes, 19% were current smokers and 62% had documented hypertension. Although open label statins were taken by 25% of the placebo group and 11% of the atorva group, the mean on-trial LDL-C values in the atorva and placebo groups were 72.9 ± 0.5 and 128.5 ± 0.5 mg/dL respectively (p<0.0001). The primary endpoint, namely fatal and non-fatal stroke, occurred in 13.1% of the placebo group and, among secondary endpoints, TIA occurred in 8.8%, any coronary event in 8.6%, and any death in 9%. These findings illustrate the serious consequences of recurrent disease or death in subjects presenting with a stroke or TIA and provides support for the concept of stroke as a CHD risk equivalent. Atorva treatment was associated with a 2.2% absolute risk reduction in fatal or non-fatal stroke, which translated into a 16% relative risk reduction (265 vs 311 cases, p=0.03). Among secondary outcomes, there was a 43% reduction in fatal stroke (24 vs 41 cases, p=0.03), a 13% reduction in non-fatal stroke (p=0.11), a 35% reduction in major coronary events (81 vs 120 cases, p=0.002) and a 26% reduction in any cardiovascular event (530 [22.4%] vs 687 [29.0%] cases, p<0.001). The cause-specific hazard ratios were 0.78 (0.66–0.94) for ischemic stroke but 1.66 (1.08–2.55) for hemorrhagic stroke. There were no differences in overall or cause-specific death rates. Finally there were 2 cases of rhabdomyolysis in the atorva and 3 in the placebo group, with >3X elevation in transaminases occurring in 2.2% and 0.5% of cases in the 2 groups respectively.

These results demonstrated that treatment with 80 mg of atorva significantly and safely reduced recurrent cerebrovascular as well as coronary events in subjects without CHD and a recent stroke. The authors speculate that the reason that those with baseline stroke in the HPS did not experience a reduction in recurrence on simvastatin 40 mg daily compared to placebo might relate to the fact that, in that study, participants were enrolled on average 4.3 years after their cerebrovascular event, whereas most recurrences occur within the first years following a stroke. Another possible explanation is that there was a greater degree of LDL-C lowering in this study—56 mg/dL—as compared to the 39 mg/dL experienced in HPS. Since the effect size on the primary outcome in this study is relatively small (16%) compared to results in statin trials with primary coronary outcomes or even compared to the effect on the coronary outcomes within SPARCL (35%), it is possible that statins are less effective in prevention of stroke as compared to preventing CHD recurrence. On the other hand, since 15% of all strokes in this study were hemorrhagic and experienced worse outcomes with statin therapy, inclusion of this group would be expected to diminish overall statin efficacy on the primary outcome.

In the final analysis, an individual presenting with a stroke or TIA who is not known to be hemorrhagic should be started on statin therapy as soon as possible. Preferably this should be initiated within the hospital setting as is recommended for patients with an acute coronary syndrome in order to maximize adherence. As to the degree of LDL-C lowering targeted, since it is highly unlikely that a dose-comparison study along the lines of the TNT trial for CHD will ever be performed in subjects with primary cerebrovascular disease, given the negative results in HPS and the positive results here in

Continued on page 19
Hurry — Register Today!

There’s still time to be a part of the Inaugural Scientific Forum of the NLA’s newest regional chapter—the Pacific Lipid Association.

Established to serve our members in Washington, Oregon, California, Idaho, Montana, Nevada, Utah, Alaska and Hawaii, the PLA is off to a strong start already. Join your colleagues at this exciting and educational event.

Target Audience
This activity is designed to meet the needs of physicians, physician assistants, pharmacists, nurses, and registered dietitians interested in lipid management.

NLA CME Reviewer: Peter H. Jones, MD
2007 PLA Program Co-Chairs: Thomas Bersot, MD, PhD and Eliot Brinton, MD

Accommodations
Nestled at the water’s edge on spectacular San Diego Bay, the Sheraton San Diego Hotel and Marina offers panoramic views of the bay and the downtown city skyline.

Sheraton San Diego Hotel
1380 Harbor Island Drive
San Diego, California

Call 800-325-3535 and make your room reservation today! Ask for the PLA room block to obtain the group rate.

Saturday Night President’s Dinner
Join PLA on the historic tall ship Star of India for a night of dinner, drinks and entertainment. Enjoy one of the most unique icons of San Diego, if not all of southern California. Built in 1863, with its magnificent top decks and tall masts, the Star is surrounded by a 360-degree, breath-taking view of the San Diego skyline and harbor.

Note: This is a ticketed event. Purchase tickets on the Registration form.
### Friday, January 19, 2007

**Thomas Bersot, MD, PhD and Eliot Brinton, MD – Program Chairs**

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
</tr>
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<tbody>
<tr>
<td>6:00 PM</td>
<td>WELCOME RECEPTION</td>
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</tbody>
</table>
| 7:00–9:00 PM | SATELLITE DINNER SYMPOSIUM  
Moving Toward Total Lipid Control for Optimal Cardiovascular Risk Reduction in Patients with Type 2 Diabetes and/or the Metabolic Syndrome  
—Thomas P. Bersot, MD, PhD, Chair |
|            | Triglycerides as a Risk Factor and Therapeutic Target for Cardiovascular Disease  
—Ronald M. Krauss, MD |
|            | Overview of Clinical Trial Evidence: Using Lipid-Modifying Therapies to Reduce Cardiovascular Risk in Patients with Diabetes or the Metabolic Syndrome  
—Thomas P. Bersot, MD, PhD |
|            | Role of Combination Therapy for Total Lipid Control in Patients with Diabetes or the Metabolic Syndrome  
—Peter H. Jones, MD |

### Saturday, January 20, 2007

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
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</thead>
<tbody>
<tr>
<td>7:00–8:00 AM</td>
<td>BREAKFAST</td>
</tr>
</tbody>
</table>
| 8:00 AM    | Does Raising HDL-C Prevent Cardiovascular Disease?  
—B. Greg Brown, MD, PhD |
| 8:30 AM    | Getting More of a Good Thing: A Real-World Approach to HDL-Raising  
—Eliot Brinton, MD |
| 9:00 AM    | HDL-Raising Therapies in Development: A Promising Future  
—Alan Fogelman, MD |
| 9:30 AM    | Panel Discussion/Q&A                                                   |
| 9:50 AM    | REFRESHMENT BREAK                                                      |
| 10:20 AM   | Insulin Resistance and the Metabolic Syndrome  
—Kenneth Feingold, MD, Moderator |
| 10:20 AM   | Diagnosis of the Metabolic Syndrome: A Controversial and Moving Target  
—Willa Hsveh, MD |
<p>| 10:50 AM   | Current “Non-Lipid” Treatments and Prevention for the Metabolic Syndrome |
| 11:20 AM   | New Agents in the Pipeline for Metabolic Syndrome Prevention and Treatment |
| 11:50 AM   | Panel Discussion/Q&amp;A                                                   |
| 12:10 PM   | LUNCH                                                                 |</p>
<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>1:10 PM</td>
<td>Annual PLA Business Meeting</td>
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<tr>
<td>1:30 PM</td>
<td>Emerging Biochemical CVD Risk Factors — Jeffrey Anderson, MD</td>
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<tr>
<td>2:00 PM</td>
<td>Non-Invasive Imaging in CVD Risk Assessment (CIMT, CT, MRI) — Howard Hodis, MD</td>
</tr>
<tr>
<td>2:30 PM</td>
<td>Long-Range Risk Assessment and “Lifetime CVD Prevention” — Don Lloyd-Jones, MD</td>
</tr>
<tr>
<td>3:00 PM</td>
<td>Panel Discussion/Q&amp;A</td>
</tr>
<tr>
<td>3:20 PM</td>
<td>REFRESHMENT BREAK</td>
</tr>
<tr>
<td>3:50 PM</td>
<td>Statin Safety: Reassuring Findings from the NLA Task Force — James McKenney, PharmD</td>
</tr>
<tr>
<td>4:20 PM</td>
<td>Is there a limit to the benefits of lipid lowering therapy or how much better is LDL-C &lt;70 mg/dL compared to LDL-C &lt; 100 mg/dL? — Thomas P. Bersot, MD, PhD</td>
</tr>
<tr>
<td>4:50 PM</td>
<td>Atheroprevention in Women and Minorities — Karol Watson, MD, PhD</td>
</tr>
<tr>
<td>5:20 PM</td>
<td>Adjourn</td>
</tr>
<tr>
<td>7:00–10:00 PM</td>
<td>President’s Reception and Dinner</td>
</tr>
</tbody>
</table>

**Sunday, January 21, 2007**

**8:00–11:00 AM** Lipid Clinical Crossfire Case Presentations

**Clinical Case Presentations: Multidisciplinary Approaches**
This 3-hour session will explore and illustrate cutting-edge issues for the practicing clinician by utilizing case study presentations on four topics: Imaging, lipid particles, biomarkers, and combination therapy (including lifestyle). A panel of expert dietitians, nurses, pharmacists and physicians will take questions and discuss the implications of these central themes.

**Case 1. A Clinical Approach to Atherosclerosis Imaging**
—Edward Gill, MD and Bryan Pogue, MD

**Case 2. Lipoprotein Particle Size and Practical Issues in Lipid Clinic Management**
—Matthew Ito, PharmD and John Nelson, MD

**Case 3. Use of Emerging Biomarkers in Clinical Practice**
—Bradley Bale, MD and Mike Cobble, MD

**Case 4. Aggressive Lipid Therapy—Medical Combinations and LDL Apheresis**
—Donna Polk, MD and David Hartman, MD

**11:00 AM** Adjourn
Inaugural Scientific Forum of the
Pacific Lipid Association
January 19–21, 2007
Sheraton San Diego Hotel & Marina
San Diego, CA

Full Name ____________________________________________
Organization/Company ____________________________________________
Address __________________________________________________________
City __________________________ State __________ Zip ______________
Phone __________________ Fax ________________ Email __________________

First name to appear on badge __________________

Scientific Forum Registration Fees
Includes course syllabus and one admission badge for food functions in the exhibit hall.
(Saturday Night Dinner NOT included)

<table>
<thead>
<tr>
<th>Option</th>
<th>Fee</th>
<th>Total</th>
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<tbody>
<tr>
<td>Current NLA Member</td>
<td>$225</td>
<td>$225</td>
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<tr>
<td>To join the NLA and register for the PLA Inaugural Meeting</td>
<td>$275</td>
<td>$275</td>
</tr>
<tr>
<td>Non NLA Member</td>
<td>$375</td>
<td>$375</td>
</tr>
<tr>
<td>Residents and Fellows (must submit proof of residency or fellowship with registration)</td>
<td>$0</td>
<td>$0</td>
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</table>

Social Events

☐ I will attend the Saturday Night Dinner $75 = $75
   *Join PLA on the historic tall ship Star of India for a night of dinner, drinks and entertainment.

Registration Total = $____

Guest Name(s) to appear on badge:
NOTE: Your badge is your pass to all exhibit hall events. Only registered individuals will receive a badge.

Payment Information - Checks and money orders must be made payable to NLA. If your institution is paying your registration fee, please ensure that the check is appropriately identified with your name.

☐ Check ☐ MasterCard ☐ VISA ☐ AmEx

Credit card issued in name of:

Card Number: ________________________________ Exp. Date: __________

Signature: ________________________________

Registration Deadline - Registration and payment must be received no later than January 5, 2007 in order to have a name badge and syllabus materials available. On-site registration will only be accepted on a space-available basis.

Cancellation Policy - Telephone cancellations cannot be accepted. A written notice of cancellation must be received no later than two weeks prior to the meeting for a refund. A $25 administration fee will be deducted. No refunds will be made after January 5, 2007.

Hotel Reservations: Sheraton San Diego Hotel and Marina
1380 Harbor Island Drive • San Diego, California
Pacific Lipid Association will hold its meeting in the West Tower.
Only $209/night for a bay view room.*
*Offer ends December 18, 2006
Call 800-325-3535 and make your room reservation today!

Ticketed Guest Fees

Adult Tickets

☐ Saturday Night Dinner $75 x ____ = $____

☐ Friday Night Reception and Saturday a.m. Breakfast $40 x ____ = $____

Child Tickets

☐ Saturday Night Dinner (ages 5–15) $50 x ____ = $____

☐ Friday Night Reception and Saturday a.m. Breakfast $40 x ____ = $____

TOTAL FEES $____

Special Assistance:
I have special needs or diet. Please explain: ____________________________________________

Three Convenient Ways To Register:

Fax: 904-998-0855

Mail: National Lipid Association
8833 Perimeter Park Blvd., #301
Jacksonville, Florida 32216

Website: www.lipid.org

Direct any questions regarding this meeting to Shannon Sheridan at 904-998-0854
LEVEL I–II

Lipid Management Training Course
This interactive 2-day program offers a comprehensive indoctrination to lipid science and is open to all interested healthcare professionals.

2007 Course Dates

<table>
<thead>
<tr>
<th>January 18–19</th>
<th>May 30–31</th>
<th>August 2–3</th>
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<tbody>
<tr>
<td>San Diego, CA, prior to the Inaugural Meeting of the Pacific Lipid Association</td>
<td>Scottsdale, AZ, prior to the 2nd Annual Scientific Forum of the Southwest Lipid Association</td>
<td>Savannah, GA, prior to the 10th Annual Scientific Forum of the Southeast Lipid Association</td>
</tr>
</tbody>
</table>

Call 904.998.0854 or visit www.lipid.org/education/lmtc to register online.

LEVEL II–III

NATIONAL LIPID ASSOCIATION SELF-ASSESSMENT PROGRAM
The NLA-SAP series is a comprehensive, interactive clinical problem-solving program that objectively validates, strengthens and reinforces your knowledge of clinical lipidology.

Volume I: Diagnosis & Management of Dyslipidemia
Volume II: The Metabolic Syndrome
Volume III: Vascular Biology & Advanced Lipid Metabolism

Each module provides up to 60 hours of AMA PRA Category 1 Credit™. Hours obtained in the NLA-SAP can be applied toward meeting the CME requirements for the ABCL certifying examination.

LEVEL IV

Masters in Lipidology — Advanced Training and Board Review Course
This intensive 2-day board review course is offered by the NLA to members seeking an in-depth, advanced review of the specialty and/or certification by the American Board of Clinical Lipidology (ABCL). The 3-volume NLA Self-Assessment Program (NLA-SAP) is included in the course fee.

2007 Course Dates

<table>
<thead>
<tr>
<th>January 18–19</th>
<th>April 12–13</th>
<th>May 30–31</th>
</tr>
</thead>
<tbody>
<tr>
<td>San Diego, CA, prior to the Inaugural Meeting of the Pacific Lipid Association</td>
<td>Montreal, Canada, prior to the 3rd Annual Scientific Forum of the Northeast Lipid Association</td>
<td>Scottsdale, AZ, prior to the NLA annual meeting and the Southwest Lipid Association Scientific Forum</td>
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<tr>
<th>August 2–3</th>
<th>September 27–28</th>
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<tbody>
<tr>
<td>Savannah, GA, prior to the 10th Annual Scientific Forum of the Southeast Lipid Association</td>
<td>Minneapolis, MN, prior to the 4th Annual Scientific Forum of the Midwest Lipid Association</td>
<td></td>
</tr>
</tbody>
</table>

Call 904.998.0854 or visit www.lipid.org/education/masters to register online.

UPCOMING MEETINGS

Registration now open at www.lipid.org
The article by Florez and Goldberg on the Metabolic Syndrome as a marker of increased risk of type 2 diabetes mellitus and atherothrombotic disease (ATD) is of interest for two reasons. First, the metabolic syndrome is nothing more than a repackaging of the insulin resistance syndrome to explain ATD events at the lower end of the LDL-cholesterol spectrum. The NCEP needed a means of explaining ATD events that could not reasonably be explained by its focus on LDL-cholesterol. Second, the metabolic syndrome is in essence the insulin resistance syndrome and since insulin resistance is the basis of type 2 diabetes, naturally, the metabolic syndrome is associated with a high risk of diabetes.

I believe that it is time to discard the diagnosis of the metabolic syndrome and return to considering lipid disorders as a spectrum of imbalance between LDL- and HDL-cholesterol. This spectrum is best envisioned by a ratio between LDL- and HDL-cholesterol and the ratio I choose is the Cholesterol Retention Fraction (CRF, or [LDL-HDL]/LDL). I have compared the ATD predictive abilities of the CRF, LDL, total cholesterol (CT), and the Framingham Fraction (FF or CT/HDL). I divided each lipid predictor into sextiles, varying from lowest to highest, and each lipid predictor predicted a greater incidence of ATD events as the sextiles ranged from lowest to highest. However, the number of people (in the general population) in each sextile fell progressively as the sextile value went from lowest to highest for CT, LDL, and FF—but not for CRF. Only for CRF did the number of people actually increase in the higher sextiles. In other words, only the CRF predicted ATD events in more people as the sextile value went from lowest to highest.

I further compared the incidence of each sextile for each lipid predictor in the general population and in the ATD population. Comparing the median sextile in the general population and the ATD population, one would have to treat any CT ≥ 200 mg/dL, LDL ≥ 125 mg/dL, or FF ≥ 4.0. These 3 values are at the lower or middle end of each predictor spectrum. Only for the CRF would one treat the sextile at the high end of the spectrum (≥ 0.70). Finally, I examined the average age of ATD onset for each lipid predictor sextile, stratified by CRF. At any lipid predictor (CT, LDL, and FF), knowledge of the CRF imparted additional information as to the age of ATD onset. Specifically, at any level of the other three lipid predictors, the lower the CRF, the older was the average age of ATD onset.

If one accepts that the CRF is the best lipid predictor, then useful things follow. First one can combine the CRF with the systolic blood pressure (SBP) into a global risk factor graph, with the CRF on the ordinate and SBP on the abscissa. An ATD threshold line can be drawn (CRF-SBP loci [0.74,100] and [0.49,140]) that separates the mainstream of ATD patients from a few outliers. In my practice, 85% of all ATD patients have CRF-SBP plots above the threshold line. Of the 15% of people with CRF-SBP plots below the threshold line, most are cigarette smokers currently or past. That leaves only 6% of all ATD patients who cannot be predicted by CRF-SBP plot position above the threshold line and/or cigarette smoking status—and they are quite old at age of ATD onset: 78 years of age for men and 75 years of age for women, on average. Further, they do not die until an average age of 94 years for men and 84 years for women. Indeed, a CRF-SBP plot position below the threshold line, in the absence of any history of cigarette smoking, implies virtual immunity to ATD. If a patient’s CRF-SBP plot lies above the threshold line, any therapy that brings that plot below the threshold line results in angiographic stabilization/regression of coronary ATD plaque at a minimum average of 75% of cases. Had POSCH (one of the trials cited in the reference) been structures to control blood pressure, the rate would have exceeded 95%. For those concerned about triglycerides (TG), I showed that in absence of elevated LDL (≥170 mg/dL) and or depressed HDL (≤ 39 mg/dL) and in the absence of any history of cigarette smoking, elevated TG were not associated with early onset (or even middle-aged onset) ATD.* I have vetted the graph against eight published angiographic regression trials.

I write this letter to urge physicians not to get caught up in arguments about definitions, but rather to form treatment based on the atherogenic-antiatherogenic balance of the CRF. Since ATD is a multifactorial disease, a global risk approach would appear to be a better means of accomplishing ATD risk reduction, as is evidenced in my practice statistics quoted above.

Sincerely,  
William E. Feeman, Jr., MD

References:

How to get involved

Did you know that, except for the Southeast Chapter (SELA), which will be celebrating its 10-year anniversary in 2007, the NLA is only 3 years old? Getting to this point has taken a tremendous effort on the part of each of you—our membership—because you have taken the time to not only become members but to also spend your time in volunteer service to the community of professionals we serve.

Because there is a progression from service at a regional or committee level to the level of service on the NLA Board, you can safely assume that the NLA Board will look to the Chapters for that leadership. The Chapters themselves have committees, but because of the very young nature of the Chapters, these programs will naturally take time to develop. Recognize these opportunities to get involved and guide the direction of our organization.

From time to time in the Lipid Spin, letters to members, and through association e-mails, the office staff solicits volunteers to serve on committees and education programs. However, from a member’s perspective, finding the information on how and where to volunteer for activities and program has not always been readily available. To address this matter, we have put together a member service webpage at www.lipid.org under the “Service” tab on the left hand navigation bar. We will list the opportunities (committee, board nomination, program, award, etc.) and note whether the opportunity to volunteer is open or closed. Details about the activity will be provided and those interested can fill out a volunteer form and attach any documents necessary. A copy will go to the office database for recordkeeping and the activity chairman will receive a copy for evaluation. Please keep this in mind when thinking about participation.

We hope that in this way we can make it easier for members to get involved and keep our organization moving forward with new ideas and energy.

The NLA Challenge

Very soon you will receive in the mail a game-themed announcement about the NLA Annual Meeting in Scottsdale, to be held in May 2007. The opening session will be an interactive test of member knowledge and skill as we hold our first-ever “NLA Challenge.” Dr. Alan Brown will host this quiz program on Thursday, May 31 as part of the meeting opening session. Everyone who attends can participate and prizes will be awarded. More details will follow in the meeting brochure to be mailed this March.

Safety Task Force on Non-Statin Therapeutics

The Safety Task Force has completed its work on Non-Statin Therapies. This report will be published as a supplement to the American Journal of Cardiology and will appear in January or February 2007. All NLA members will receive a courtesy copy of the AJC supplement from the NLA. This is a major release that raises the profile of our organization.

NLA Invited to participate on ACCF Task Force on Clinical Competence and Training

Dr. Michael Davidson was appointed by the NLA to serve as our representative to the American College of Cardiology Foundation (ACCF) Task Force on Clinical Competence and Training. This initiative is being organized by the American College of Cardiology and the American Heart Association to focus on the establishment of standards for the minimum education, training, experience, and cognitive and clinical skills necessary for physicians to be considered competent and expert as “preventive physicians.” The designation indicates those who evaluate and treat persons deemed to be at high risk for cardiovascular disease—especially atherosclerosis—and evaluate and treat those patients with established cardiovascular diseases to prevent recurrent cardiovascular events. Other members taking part in the Task Force statement include Dr. Roger Blumenthal, Dr. Jaine Underberg and Dr. Christie Ballantyne.

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Mary Anne Champagne, RN, MSN
Palo Alto, CA
Luther T. Clark, MD
Brooklyn, NY
Jerome D. Cohen, MD
St. Louis, MO
Carlos A. Dujovne, MD
Overland Park, KS
Barbara J. Fletcher, RN, MN
Jacksonville Beach, FL
Robert H. Knopp, MD
Seattle, WA
Maria F. Lopes-Virella, PhD, RD
Charleston, SC
Mary P. McGowan, MD
Concord, NH

EXECUTIVE DIRECTOR
Christopher R. Seymour, MBA
SPARCL, it is probably prudent to maximize LDL-C lowering in these patients, as is being increasingly recommended for subjects with CHD.

Reference
<table>
<thead>
<tr>
<th>Name and Time of Activity</th>
<th>NLA Sponsored/ Endorsed/Other</th>
<th>Contact and Registration Information</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CME Newsletter: Statin Safety – NLA Recommendations for the Primary Care Community</strong></td>
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<tr>
<td>Online: September 2006 – September 2007</td>
<td>Endorsed – CME Online Activity</td>
<td><a href="http://www.NLACME.com">www.NLACME.com</a></td>
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<td><strong>CME Newsletter: Diabetes &amp; Dyslipidemia: Reports from the ADA Scientific Sessions</strong></td>
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<td><strong>Webcast: New Perspectives on Real World Management of Dyslipidemia in Diabetes : Cases</strong></td>
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<td>and Controversies</td>
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<td>Sponsored by Albert Einstein College of Medicine</td>
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<td><strong>CME Newsletter: Lipid Management Today</strong></td>
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<tr>
<td><strong>Online: January 2007 – January 2008</strong></td>
<td>Sponsored – CME Online Activity</td>
<td><a href="http://www.NLACME.com">www.NLACME.com</a></td>
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<td><strong>Meeting Highlights: Presentations from the 2006 NLA Scientific Meetings</strong></td>
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<td><strong>Online: January 2007 – January 2008</strong></td>
<td>Endorsed – AOA, CME Online Activity</td>
<td><a href="http://www.NLACME.com">www.NLACME.com</a></td>
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<td><strong>Webcast: Why Your Patients Are Not Getting to Goal – Steps You Can Use to Improve</strong></td>
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<td><strong>Dyslipidemia Treatment Outcomes</strong></td>
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<td>Sponsored by American Osteopathic Association</td>
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<tr>
<td><strong>January 18–19, 2007</strong> <strong>NLA Lipid Management Training Course</strong></td>
<td>Sponsored – CME Live Meeting</td>
<td><a href="http://www.lipid.org/education/lmtc">www.lipid.org/education/lmtc</a></td>
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<td>Sheraton San Diego Hotel, San Diego, CA</td>
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<tr>
<td><strong>January 18–19, 2007</strong> <strong>NLA Masters in Lipidology Board Review Course</strong></td>
<td>Sponsored – CME Live Meeting</td>
<td><a href="http://www.lipid.org/education/masters">www.lipid.org/education/masters</a></td>
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<td>Sheraton San Diego Hotel, San Diego, CA</td>
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<tr>
<td><strong>January 19–21, 2007</strong> <strong>Pacific Lipid Association Inaugural Scientific Forum</strong></td>
<td>Sponsored – CME Live Meeting</td>
<td>E-mail: <a href="mailto:ssheridan@lipid.org">ssheridan@lipid.org</a> Ph: 904.998.0854 <a href="http://www.lipid.org">www.lipid.org</a></td>
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<tr>
<td>Sheraton San Diego Hotel &amp; Marina, San Diego, CA</td>
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<tr>
<td><strong>February 8–10, 2007</strong> <strong>Cardiovascular Disease Prevention 2007 5th Annual Symposium</strong></td>
<td>Endorsed – CME Live Meeting</td>
<td>E-mail: <a href="mailto:meded@baptisthealth.net">meded@baptisthealth.net</a> Ph: 786-596-2398</td>
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<tr>
<td>The Biltmore Hotel, Coral Gables, FL</td>
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<tr>
<td>Sponsored by Baptist Health South Florida</td>
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<td><strong>February 24, 2007</strong> <strong>Diabetes and Cardiovascular Disease 4th Preventive Cardiology</strong></td>
<td>Endorsed – CME Live Meeting</td>
<td>E-mail: <a href="mailto:liandis@hrtcare.com">liandis@hrtcare.com</a></td>
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<tr>
<td>Conference</td>
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<td>Wyndham Milwaukee Hotel, Milwaukee, WI</td>
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<tr>
<td>Sponsored by University of Wisconsin School of Medicine and Public Health</td>
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<tr>
<td><strong>March 16, 2007</strong> <strong>Duke Lipid Clinic Preceptorship Program</strong></td>
<td>Sponsored – CME Live Meeting</td>
<td>Ph: 919-490-3794 E-mail: <a href="mailto:raforge@nc.rr.com">raforge@nc.rr.com</a></td>
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<tr>
<td>Duke University, Raleigh, NC</td>
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<td>Sponsored by Duke University Medical School</td>
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<td>New Orleans, LA</td>
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<td><strong>April 12–13, 2007</strong> <strong>NLA Masters in Lipidology Board Review Course</strong></td>
<td>Sponsored – CME Live Meeting</td>
<td><a href="http://www.lipid.org/education/masters">www.lipid.org/education/masters</a></td>
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<td>Queen Elizabeth Fairmont Hotel, Montreal, Canada</td>
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<tr>
<td><strong>April 13–15, 2007</strong> <strong>Northeast Lipid Association 3rd Annual Scientific Forum</strong></td>
<td>Sponsored – CME Live Meeting</td>
<td>E-mail: <a href="mailto:ssheridan@lipid.org">ssheridan@lipid.org</a> Ph: 904.998.0854 <a href="http://www.lipid.org">www.lipid.org</a></td>
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<td>Queen Elizabeth Fairmont Hotel, Montreal, Canada</td>
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<td><strong>April 26–28, 2007</strong> <strong>Preventive Cardiovascular Nurses Association 13th Annual Symposium</strong></td>
<td>Other</td>
<td><a href="http://www.blackwellfuturacourses.com">www.blackwellfuturacourses.com</a></td>
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<td>Hyatt Regency, Minneapolis, MN</td>
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<td><strong>May 4–5, 2007</strong> <strong>Managing the Metabolic Syndrome &amp; Reducing the Risk of Coronary</strong></td>
<td>Other Live Meeting</td>
<td><a href="http://www.blackwellfuturacourses.com">www.blackwellfuturacourses.com</a></td>
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<td>Disease</td>
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<td>The Westin Chicago River North, Chicago, IL</td>
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<td>Sponsored by Blackwell Futura Media Service</td>
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<td><strong>May 30–31, 2007</strong> <strong>NLA Lipid Management Training Course</strong></td>
<td>Sponsored – CME Live Meeting</td>
<td><a href="http://www.lipid.org/education/lmtc">www.lipid.org/education/lmtc</a></td>
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<td>Hyatt Scottsdale Resort at Gainey Ranch, Scottsdale, AZ</td>
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<td><strong>May 30–31, 2007</strong> <strong>NLA Masters in Lipidology Board Review Course</strong></td>
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<tr>
<td><strong>May 31 – June 3, 2007</strong> <strong>National Lipid Association &amp; Southwest Lipid Association</strong></td>
<td>Sponsored – CME Live Meeting</td>
<td>E-mail: <a href="mailto:ssheridan@lipid.org">ssheridan@lipid.org</a> Ph: 904.998.0854 <a href="http://www.lipid.org">www.lipid.org</a></td>
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<td><strong>2007 Annual Scientific Sessions</strong></td>
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<td>Hyatt Scottsdale Resort at Gainey Ranch, Scottsdale, AZ</td>
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<tr>
<td><strong>June 1 or June 2, 2007</strong> <strong>ABCL Physician Certification Exam</strong></td>
<td>Examination</td>
<td><a href="http://www.lipidboard.org">www.lipidboard.org</a></td>
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<tr>
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