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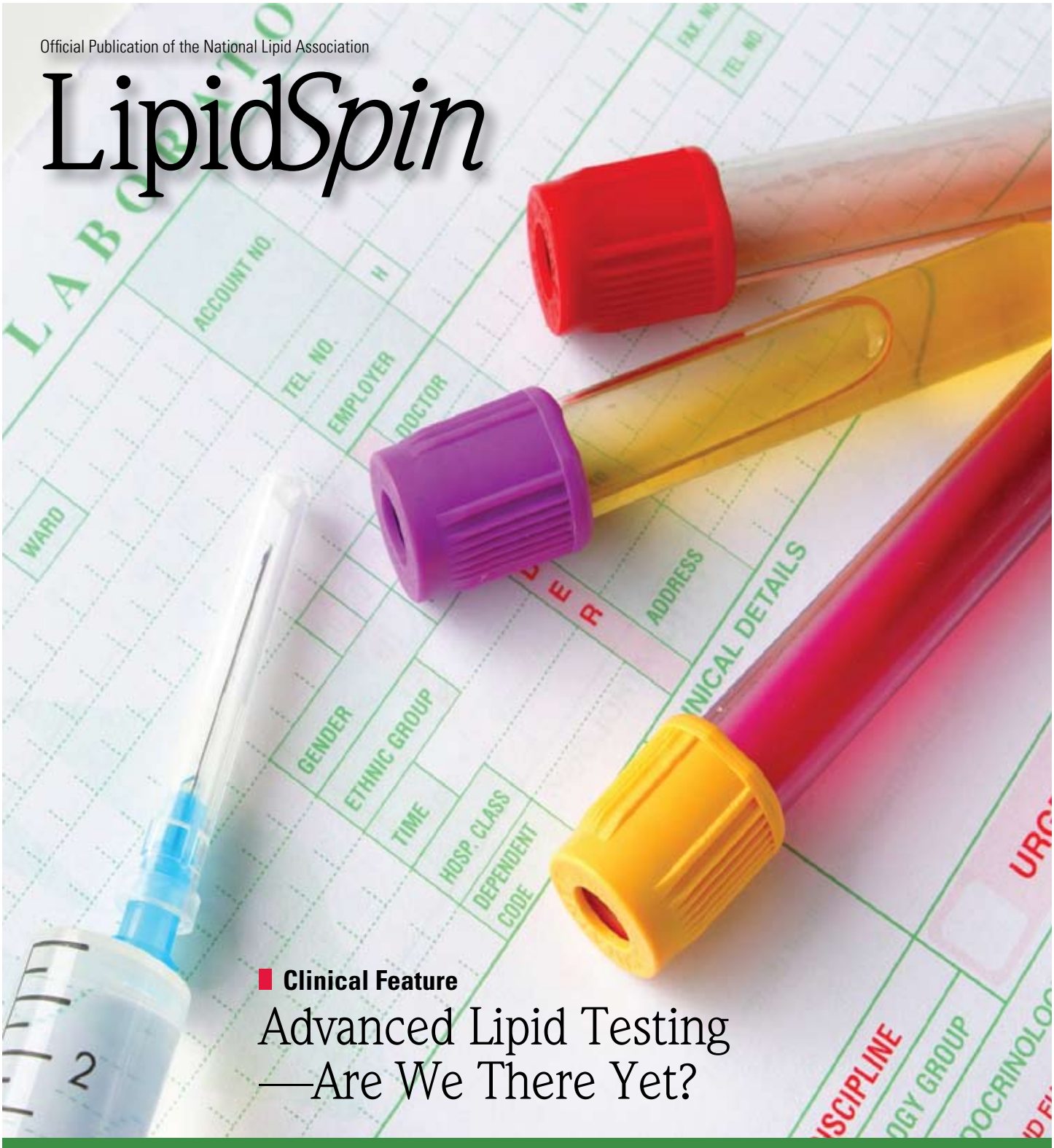
LipidSpin



Clinical Feature

Advanced Lipid Testing —Are We There Yet?

Also in this issue:

Management of Dyslipidemias in Chronic Kidney Disease

Atherosclerosis Imaging Trials Targeting HDL-C

This issue sponsored by the Midwest Lipid Association

Volume 9 Issue 3 | Summer 2011
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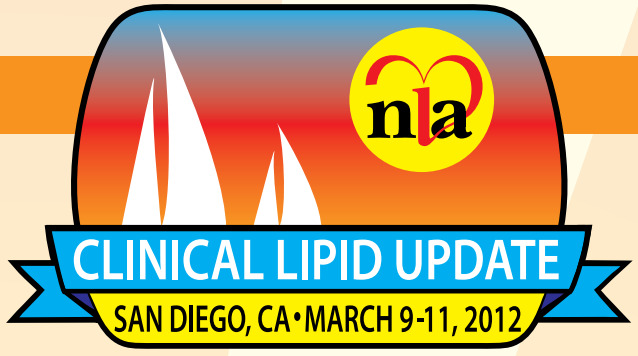
NATIONAL LIPID ASSOCIATION

2012 NLA MEETINGS

SPRING

NLA Clinical Lipid Update

Hosted by the Midwest Lipid Association and the Pacific Lipid Association
March 9-11, 2012
Hilton Bayfront
San Diego, CA



ANNUAL MEETING

NLA 2012 Annual Scientific Sessions

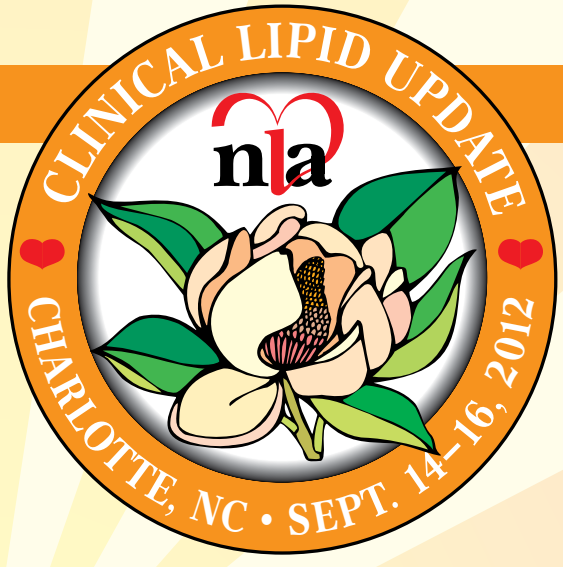
Hosted by the Southwest Lipid Association
May 31-June 3, 2012
JW Marriott
Scottsdale, AZ

10-Year Anniversary of the NLA

FALL

NLA Clinical Lipid Update

Hosted by the Southeast Lipid Association and the and Northeast Lipid Association
September 14-16, 2012
Charlotte Westin
Charlotte, NC



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In This Issue: Summer 2011 (Volume 9, Issue 3)

Lipid Spin is published quarterly by the
National Lipid Association
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Jacksonville, FL 32216
Phone: 904-998-0854 | Fax: 904-998-0855

Visit us on the web at **www.lipid.org**.

The National Lipid Association makes every effort to provide accurate information in the *Lipid Spin* at the time of publication; however, circumstances may alter certain details, such as dates or locations of events. Any changes will be denoted as soon as possible. The NLA invites members and guest authors to provide scientific and medical opinion, which do not necessarily reflect the policy of the Association.

In May 2011, the NLA Board of Directors voted not to include for-profit advertising in future issues of *Lipid Spin* beginning with the Fall 2011 issue.

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From the NLA President:
Building on the Legacy

PENNY KRIS-ETHERTON, PhD, RD, CLS, FNLA
National Lipid Association President

Distinguished Professor of Nutrition
Penn State University
University Park, PA

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The new NLA leadership team is carrying on the legacy of the previous leaders and building new international partnerships. I am pleased to share that we are exploring possible partnerships with societies in Argentina and Puerto Rico. Because there is interest in developing education programs in Puerto Rico, which is aligned with the Southeast Lipid Association, discussions are under way about forming a special interest group to take the lead in evolving programmatic activities there.

We also are tapping the expertise and experience of NLA members to create a new Practice Management Committee. This committee will oversee the formation of groups that develop and issue best practices statements for a variety of clinical topics relevant to Clinical Lipidology. This process is in the early developmental stage and can go in many different directions at this juncture. For example, these statements could describe practice management strategies for optimizing organizational management of lipid clinics where physicians, nurse practitioners, pharmacists, exercise physiologists and nutritionists all work together. Developing treatment strategies for different patient groups is another consideration. It is possible that there will be several committees formed to deal with different best practices topics. We will be working with your chapter presidents to identify people to serve. Members of the Practice Management Committee are **Jennifer Robinson, MD, MPH, FNLA* Ralph La Forge, MSc, CLS, FNLA, Kaye-Eileen Willard, MD*, Gretchen Benson, RD, Jackie Boucher, RD, John Nelson, MD, FNLA*** and me. This is a great opportunity for NLA members to get involved; I encourage you to contact me or your chapter president if you would like to help.

Another major focus of the NLA during the next year will be to position the organization to respond to the draft Adult Treatment Panel IV Guidelines (Detection, Evaluation and Treatment of High Blood Cholesterol in Adults; ATP IV), as well as the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC-8) and new obesity guidelines. To do this effectively, it is imperative that we build the organizational structure that will be needed to accomplish this objective. In addition, educational programs that are focused on ATP IV will be disseminated to NLA members via various venues. Inherent to the release of the new treatment guidelines will be the necessity to update the current Self-Assessment Programs (SAP) and associated activities.

Since the NLA Annual Scientific Sessions in New York City in May, there has been considerable enthusiasm about launching numerous member-initiated programs and activities. We are thrilled about this! In responses, we are developing a process whereby interested NLA members can submit a proposal to the Board for review and approval for these activities/initiatives. Shortly, we will post on the NLA website the form for submitting these proposals.

We are in the process of establishing special interest groups for our members who share a common expertise. For example, we are forming a Nutrition Interest Group for registered dietitians that will be led by **Julie Bolick, MS, RD, CLS**. A major goal of these special interest groups, apart from networking, is to share ideas, expertise and knowledge that advances Clinical Lipidology practice.

In summary, there are many opportunities for members to get involved with the NLA and grow the association with new programs that attract new members. ■

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From the MWLA President:
The *Lipid Spin*—A Case Example of Membership Opportunity

J. CHRIS BRADBERRY, PharmD, CLS, FAHA, FNLA
Midwest Lipid Association President
Dean, School of Pharmacy and Health Professions
Creighton University
Omaha, NE

On behalf of the Midwest Lipid Association (MWLA), I welcome NLA members to this issue of the *Lipid Spin*. This issue is a product of collaboration between the MWLA Chapter and the NLA. The theme of this issue is "Advanced Lipid Testing" and, in the Clinical Feature section, **Suneet Verma, MD***, takes the lead with an article that reviews the evolutionary components involved in advanced lipid testing. This is followed by two sections focusing on evidenced-based tools and an applied case study by **Daniel Stock, MD***, and **Tara Dall, MD, FNLA***, respectively. As our understanding increases as to how and why we can more appropriately utilize biomarkers in clinical care, our patients will most certainly benefit. **Dr. William Feeman, Jr., MD**, provides us with an excellent editorial on the Adult Treatment Panel IV guidelines and **CoraLynn Trewet, PharmD, FNLA**, gives us additional practical insights into the ever-troubling issue of patient adherence to drug therapy. Other sections update us on imaging trials and high-density lipoprotein (HDL), and the NLA Lipid Pulse Membership Survey. Additionally, there is an interesting member spotlight on **Janet Maxson, PhD, NP, FNLA**.

As President of the MWLA, it has been my responsibility to identify the theme for this issue and authors for the *Lipid Spin* sections. Because of a fairly short turnaround time for development of the articles, I put out an e-mail blast to the MWLA membership, asking for volunteers for the sections. I was immensely impressed by our MWLA membership's rapid and generous response with offers to participate. I believe this is only one example of the interest, collegiality and uniqueness of the NLA. For instance, think about the interdisciplinary nature and opportunities provided by our organization. We are in rare air among clinical/scientific organizations in this regard. It is clear to me that our NLA is unique and innovative and our membership and staff support continue to be our keys to success. Many authors of this and other *Lipid Spin* issues are excellent examples of our young members becoming involved as they are growing their own careers. Opportunities and networking abound for our NLA members at both the regional and national levels at every stage in their career development. This is indeed exciting!

I hope you enjoy this issue of *Lipid Spin* and I look forward to seeing you at an upcoming meeting. ■

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Editor's Corner:
Why Not Evidence-based Medicine?

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"Evidenced-based practice" is a phrase that, for many, seems to have drifted into ambiguity, much like the term "meta-analysis" did before the international guidelines for reporting systematic reviews and meta-analyses were developed.[1]

If one remembers that the goal is to practice based on the best available evidence, then there really should be no ambiguity. Science and our understanding of diagnosis, therapy and/or prognosis will always be advancing. That does not give us an excuse, however, not to seek out the best information available and to integrate that best information into our clinical decision making.

There are a number of reasons why we don't always practice based on best evidence. No time, exploding information supply, textbooks are out of date—to name a few. Traditional continuing medical education (CME) doesn't give us the tools we need to critically evaluate information and develop the skills to convert that information into clinical decision making.

At the Annual Scientific Sessions in May in New York City, we held the second "Enhancing Tools for Evidenced-based Practice Workshop." The concept is to learn the terms, learn how to find the best evidence available, and then learn how to integrate the evidence with our own already well-honed clinical judgment. The object is to enjoy the process and feel comfortable practicing the art of EBM.

We welcome your participation as you join us in this lifelong journey. It makes no difference whether you are just starting out or are well along the pathway. Much like the NLA, in general, the fact that all of us who participate are from different backgrounds is a plus. We celebrate diversity of background. The goal is to demystify what is out there. We also want to allow participants a chance to become confident in their abilities to learn how to find the best actionable information and in understanding strengths and limitations of resources. We hope to see many of you at the third workshop. It will be August 26 in Orlando, during the Midwest and Southeast regional chapters-sponsored meeting of the NLA. We have assembled—for your benefit—a distinguished faculty with multiple talents. Come learn the art of practicing based on best evidence. ■

References are listed on page 38.

Guest Editorial:
Critique of the Upcoming NCEP ATP-IV Guidelines

WILLIAM E. FEEMAN JR., MD
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Bowling Green, OH

I read with great interest the Clinical Feature article by Drs. Rohatgi and Khera about the upcoming revision of the NCEP guidelines, which were due out in 2009 and may be coming out in 2011.[1] I assume that the authors may have inside information about ATP-IV, and on that basis I would like to offer a personal commentary.

The NCEP guidelines have been in a constant state of flux since they first began to be promulgated in the press conference of 1987. Some would say that they keep changing as the evidence continues to accumulate, but others might equally say that the guidelines are no more than exploratory since they have never been vetted by a randomized controlled trial (RCT). Some might say that the guidelines continue to be revised because the earlier guidelines were inadequate to meet the goals of the primary and secondary prevention of atherothrombotic disease (ATD). The reason, in part, is that some guidelines are simply post hoc analyses of short-term clinical trials, usually involving patients at high risk to have an ATD event during the trial timeframe, and some are merely an assembly of "expert opinions." Therein lies one of the difficulties with guidelines: applying short-term results to long-term problems does not always give satisfactory solutions, especially since most ATD events occur in lower-risk patients over a longer span of time. For these reasons, I believe that it is time to perform a RCT to determine which lipid predictor best predicts the population at risk of ATD and which lipid predictor best guides therapy to stabilize/regress extant ATD, before the next guidelines revision (ATP V) is released.

To be effective, ATD guidelines must be simple, accurate, relevant and relatively unchanging (or at least not changing every five years or so). In this light, the new guidelines should involve only the cardinal ATD risk factors, so that the guidelines may be kept simple so patients and physicians will understand and use them. What is the use of guidelines that are so complex that no one uses them? Those cardinal ATD risk factors are well known: cigarette smoking, dyslipidemia, and hypertension.

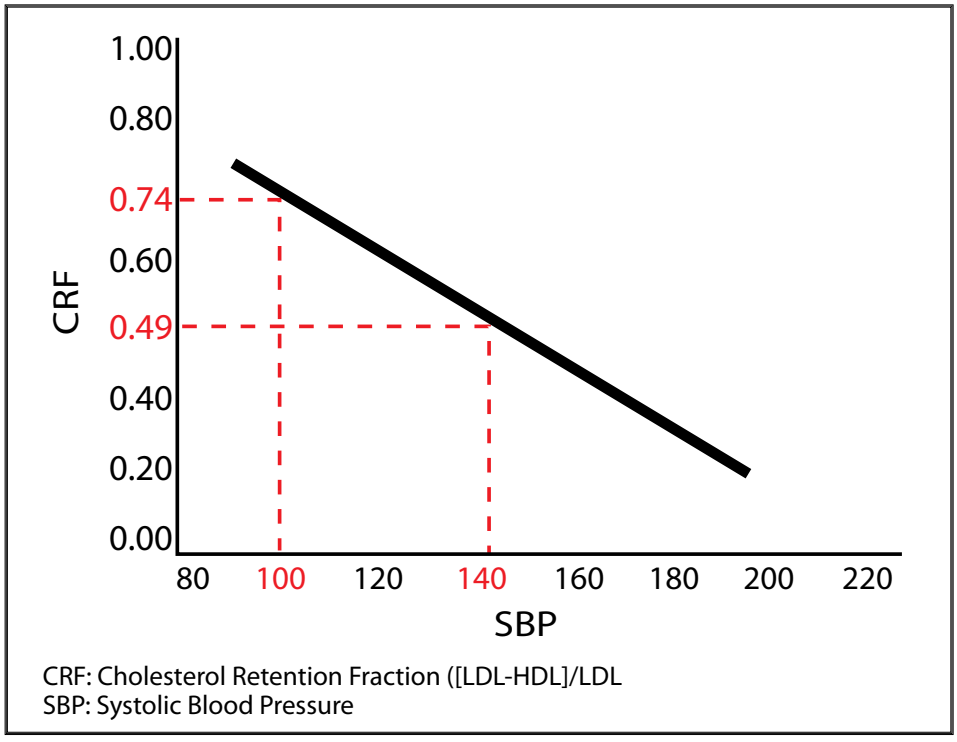
The NCEP has given short shrift to cigarette smoking, but it is the single most important risk factor for ATD events. Cigarette smoking is associated with early onset ATD, early onset multi-system ATD, and early death in ATD. Cigarette smoking produces ATD events even at levels of dyslipidemia and hypertension not usually associated with early-onset ATD. In fact, virtually the entire epidemic of early-onset ATD is a cigarette epidemic, and it is my opinion that the war against ATD will never be won until the war against cigarette smoking is won, because stopping cigarette smoking gives a better result in terms of ATD outcomes than does correction of dyslipidemia or hypertension.[2]

The NCEP never gives a satisfactory definition of dyslipidemia, probably because it is focused on secondary prevention and because it gives second-class citizenship status to HDL. I would define dyslipidemia as a state in which the balance of the pro-atherogenic lipids (mainly LDL) and the anti-atherogenic lipids (mainly HDL) is such that the accumulation of LDL within the intima is favored. This balance is best seen by using a ratio between LDL and HDL. This ratio could be LDL:HDL, but since it predicts the population at risk of

ATD 5% better—at least in my patient population—than LDL:HDL, I would favor the Cholesterol Retention Fraction (CRF, or [LDL-HDL]/LDL).[3] *Author's note: The n-value equals 710 and the comparison comes from the general population (those who have entered my practice), but involves only those people known to have developed ATD.*

If one accepts this definition of dyslipidemia, then it is easy to see why the NCEP guidelines have required continual revision: LDL per se is quite adequate to explain ATD when LDL levels are very high, but most ATD events occur at much lower levels of LDL, where HDL—or lack of it—plays a much bigger role. In my patient population with ATD, the average levels of LDL in male ATD patients are 145 mg/dL and 154 mg/dL in female ATD patients. These levels would not be considered worth treating using current guidelines—and probably not by ATP IV either if Rohatgi and Khera have reported them correctly. The LDL distributions in my ATD population form a bell-shaped curve with the zenith in the 125-149 mg/dL sextile, for both men and women.[3] This is why NCEP guidelines fail in the primary prevention of ATD—they do not call for the treatment of the majority of the dyslipidemias leading to ATD. At any level of LDL, knowledge of the CRF provides additional information as to the average age of ATD onset. The higher the CRF, the earlier is the age of ATD onset and the lower, the later. Incidentally, the distribution curve for CRF in ATD patients is shifted to the right, so that its peak is in the higher ranges of CRF. Whereas with the CRF, there are more and more patients in the higher and higher CRF sextiles, there are fewer and fewer patients in the higher and higher LDL sextiles.[3]

The bell-shaped curve for LDL distribution in ATD has not been tested for normality. The eight angiographic regression trials were all I could get. My request for



CRF: Cholesterol Retention Fraction ([LDL-HDL]/LDL
SBP: Systolic Blood Pressure

Figure 1.

data was refused by many investigators. I presented all the data that I received. Please see No. 6 in my citation list.

Hypertension (defined as systolic blood pressure [SBP] of 140 mmHg or greater) is mainly seen in older patients with ATD. This is not to negate treating in younger patients. Since CRF values in older ATD patients tend to be lower than in younger ATD patients, it would seem plausible mechanistically that SBP could be a force "driving" LDL into the artery wall, and hence it would seem wise to utilize anti-hypertensive medications that do not worsen dyslipidemia.

These three cardinal ATD risk factors can be put together into a global risk-factor graph, with the CRF on the ordinate and SBP on the abscissa (Figure 1).[4] When the CRF-SBP plots of ATD patients are plotted on this graph, and when those plots are segregated by cigarette smoking status (current vs. all others), then the vast majority fall in a mainstream sequence, with only a relative few outliers. The mainstream can be separated from these outliers by a boundary line based on the largest area under the line with the fewest false negatives. This boundary line is termed the threshold line and has the CRF-SBP coordinates (0.74, 100) and (0.49, 140). These line co-ordinates are valid when the indirect method of measuring HDL is utilized. If the direct method of measuring HDL is used, then the line co-ordinates need to be accordingly revised to (0.62, 100) and (0.40, 140). This is because the direct and indirect methods of measuring HDL yield differing values and hence the calculated LDL values will differ accordingly.[5]

HDL is unable to compensate for excess LDL. The protective effect of HDL appears to begin to wane at LDL levels of 170 mg/dL and appears to be absent when LDL levels are 250 mg/dL or higher. Hence, all LDL levels of 170 mg/dL or higher require treatment regardless of CRF values.

If all ATD patients are considered, then 85% of their CRF-SBP plots lie above the threshold line. Of the 15% of ATD patients with CRF-SBP plots below the threshold

line, most are cigarette smokers, current or past. That leaves only 6% of all ATD patients in my practice who could not have been predicted by CRF-SBP plot above the threshold line and/or cigarette smoking—and these patients are quite old at age of their initial ATD event (on average, 78 years for men and 75 years for women) and they do not die, on average, for an additional 10-15 years.

This graph has been validated against eight published angiographic regression trials. In the eight published trials, 95% of the ATD patients' CRF-SBP plots lie above the threshold line. In an additional outcomes trial (PROSPER), the graph and cigarette smoking status predicted 95% of their ATD patients.[6] Moreover, any therapy that brings the ATD patient's CRF-SBP plot below the threshold line results in angiographic stabilization/regression of coronary plaque in a minimum average of 75% of cases.[7]

In my opinion, use of this global risk approach is the reason why acute myocardial infarction is uncommon in my patient population: only two of my treated patients have suffered a fatal acute myocardial infarction since January 1, 2000: One was a cigarette smoker with severe hypertension and wonderful lipids (LDL of 89 mg/dL and HDL of 95 mg/dL); her blood pressure was well controlled, there was no reason to treat her lipids, and she continued to smoke cigarettes. She sustained a sudden cardiac arrest and was found dead. The other was an insulin-dependent (x40 years) diabetic who sustained his first myocardial infarction at age 40 years, allowed me to control his lipids and blood pressure, but who controlled his own insulin therapy. He died of a second myocardial infarction at age 72 years. As my patient population ages, acute cerebral infarctions are becoming somewhat more frequent, but still only averaging one per year, mainly in patients over 75 years of age. The last paralytic cerebral infarction occurred in 2004.

I believe that use of a global risk approach permits the accurate prediction of the population at risk of ATD, and permits treatment to prevent (or if extant, then stabilize/regress) ATD. In this sense, the graph is somewhat like the Framingham Risk Score (FRS), but predicts better than the FRS since it predicts younger men and most women that are missed by the FRS.[8] Since the graph also predicts patients who will develop ATD, but be missed by the NCEP guidelines, it offers the possibility of the prevention of clinical ATD in the years before the ATD event would otherwise have occurred and the need to use less drastic therapies than would be necessary using NCEP guidelines after the ATD event has occurred. ■

Disclosure statement: Dr. Feeman has no relevant disclosures.

References are listed on page 38.

Clinical Feature:
Advanced Lipid Testing—Are We There Yet?

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Editor's Note: Please see an NLA expert panel paper, "Clinical Utility of Advanced Lipid Testing and Inflammatory Markers," in the September/October issue of the *Journal of Clinical Lipidology*.

Introduction

The search for advanced lipid testing started more than 50 years ago. The Framingham Heart Study and the Lawrence Livermore Study first suggested the clinical utility of such advanced testing and provided the groundwork for future research. During this span of five decades with research and advancement in understanding the pathophysiology of atherosclerosis and similar improvement in assay technology we now have capability to do much more sophisticated tests which once were confined to research labs. Traditionally we have used LDL-C, TG and HDL-C to assess risk but as we know currently there are approximately nine apolipoproteins, some cell and plasma proteins, and several transfer proteins involved in cholesterol transport. The ability to measure (test) these constituents offers the potential to increase understanding of our patient's vasculopathic risks above and beyond information offered by traditional tests. Following are some of the tests that are readily available and are increasingly becominging mainstream in assessment of patients with dyslipidemias.

LDL Subfractionation

Low-density lipoproteins have been subclassified based on their size and densities and they all have different molecular properties. We have learned that size of the particle does matter and so does their relative atherogenicity. Determination of the small, dense LDL subclass pattern B identifies a group of individuals that carry a 3-fold increased CHD risk.[1,2]

The Quebec Cardiovascular Study[3] found, after adjustment for systolic blood pressure, medication use, and family history, the odds for ischemic events are increased with a small, dense LDL-C pattern [odds ratio of 2.5 (95% CI: 1.2-5.2)]. In this cohort of patients with ischemic events there was significantly lower mean LDL particle size *(P<.001)* and an increased proportion of very small LDL sizes. This study also reported that the rate of arteriographic progression was nearly two-fold greater as reported in LDL pattern B compared with LDL pattern A CHD patients.

The Multi-Ethnic Study of Atherosclerosis (MESA)[4] compared the associations of small and large LDL with carotid intimal-media thickness. We learned that higher concentrations of large LDL were significantly associated with intima-media thickness within any particular category of small LDL. After particle correlations were accounted for, both small and large LDL were "atherogenic" to a similar extent.

What we learned from different trials is that when number of particles is adjusted for, the LDL size loses its predictive value. Total particle number seems to be a better predictor for risk assessment. and this is in line with recent recommendations from NLA.

HDL Subfractionation

The observation that different "types" of HDL exist was first made by John Gofman, MD, in 1951.[5] We have learned that a difference in HDL subclass distribution helps to predict CHD risk and arteriographic progression. A number of studies have reported significantly lower HDL2 in CHD patients compared with control patients, and in men with Type 2 diabetes mellitus

this inverse relationship between HDL-C, HDL2, and CHD is particularly strong.[6-9] Hyperalphalipoproteinemia is an elevated HDL-C condition often associated with low CHD risk. Presence of HDL2 or LpAI is cardioprotective.[10] There is evidence suggesting that therapeutically induced change in HDL subclass distribution can lead to reduction in cardiovascular events.[11] Not all studies have revealed an association of HDL subclass with CHD. The Caerphilly and Speedwell Collaborative Heart Disease Studies concluded that determination of HDL2 or HDL3 may not improve assessment of risk for CHD based on HDL-C alone.[12] The Atherosclerosis Risk in Communities (ARIC) study has also reported that levels of HDL2-C were not substantially different in subjects with or without known CHD.[13]

TESTS	TARGET VALUES	LIFESTYLE CHANGES
LDL-P	<1000 nmol/L	Add sterols and stanols, high fiber food.
LDL4+3+2+1	<100 mg/dL	As above
Lp(a)	<10 mg/dL	
HDL2	>10 mg/dL	Choose healthy fats, limit refined carbs, alcohol, and stop smoking.
HDL3	>30 mg/dL	As above
Remnant Lipoproteins	<30 mg/dL	Choose omega-3 fatty acids, high fiber food. Limit refined carbs, alcohol and stop smoking.
Apo B100	<109mg/dL	As above and add plant stanols and sterols.
Apo A1	>118mg/dL	Choose healthy fats, limit refined carbs, and stop smoking.
ApoB100/A1 ratio	<0.92	Choose healthy fats, high fiber food, sterols and stanols. Limit refined carbs, alcohol, and stop smoking.

Table 1. Generated with information from VAP test from Atherotech and Liposcience Inc. original reports.

Apolipoprotein B

Many authors are proposing that apoB levels may replace LDL-C as the primary measure of atherogenic lipoproteins.[14] In the setting of patients with normal lipids, plasma apoB levels are lower than the LDL-C value. A remarkably high incidence of elevated apoB levels has been reported in the post-MI population. Two large studies (Apolipoprotein-related Mortality Risk [AMORIS] and INTERHEART) have contributed valuable insight to risk factors and concluded that apoB is superior to standard lipid testings. The Quebec Cardiovascular Study[3] investigated the relationship of small LDL, elevated fasting insulin values, and elevated apoB in relation to CHD risk. Each abnormality individually contributed to CHD risk.

The apoB/apoA-I ratio reflects the relative number of atherogenic apoB containing particles compared with the relatively cardioprotective apoA-I. This ratio is superior to the standard LDL-C/HDL-C ratio in predicting MI risk.[15] The Apolipoprotein-related Mortality Risk Study (AMORIS) investigated these relationships and concluded that standard total cholesterol/HDL-C ratio underestimated risk in 69% of men and 85% of women while overestimating the risk in 26% or men and 12% of women.

An apoB/apoA-I ratio of 0.90 or higher independently predicts MI risk in men and carotid artery intima-media thickness progression over three years.[16,17]

ApoE Genotype

ApoE has three major isoforms, designated E2, E3, and E4. The most common allele is E3. ApoE genotypes have been linked to elevated CHD risk. The Etude Cas-Temoins sur l'Infarctus du Myocarde (ECTIM)[18] study reported the relative risk of myocardial infarction associated with apoE phenotypes compared with E3/3 was found to increase in the following order: E2/2<E3/2<E3/3 (relative risk=1) <E4/3=E4/2<E4/4 (P<.05). In conclusion, men carrying the E4 allele present atherogenic lipid and lipoprotein profiles compared with E3/3 and are at higher risk of coronary heart disease in the populations under study. Men carrying the E2 allele have lower apoB levels and appear to be at lower risk despite higher triglyceride and Lp E:B levels, at least in some regions. Other studies like European Atherosclerosis Research Study (EARS),[19] also established that apoE polymorphism is responsible for the familial predisposition to CHD.

Remnant Lipoprotein Particles

Remnant lipoproteins are an emerging risk factor. It's common to see elevated triglyceride-rich lipoproteins like VLDL and IDL cholesterol in patients with Type 2 diabetes or the metabolic syndrome hence also referred to as insulin resistance pattern. This pattern renders them high risk for cardiovascular events. Therapeutically reducing levels of remnant lipoproteins is clinically important because of their atherogenic potential. Nakamura, et al., reported that elevated remnant lipoprotein particle cholesterol levels are independent risk factors for impaired flow-mediated, endothelium-dependent dilatation and angiographically proven coronary artery disease in patients with the metabolic syndrome.[20]

In clinical studies,[21] both small VLDL and IDL cholesterol have been shown to be associated with atherosclerotic progression and increased CV risk, independent of total levels of fasting triglycerides. In one study both high-dose atorvastatin (80 mg/d) and a

combination of statin and niacin reduced the levels of VLDL3 and IDL substantially.[22,23] So measuring remnant particle cholesterol may help in directing specific therapy which will modify patient's risk.

Particle Number (P)

The concentration of whole plasma apoB provides a direct measure of the number of circulating atherogenic lipoproteins and provides clinical insight beyond the LDL-C measurement. Some guidelines recommend a target of apoB of < 80 mg/dL in high-risk patients.[24] Higher LDL-P measures have been associated with a higher risk of CAD. This might simply be because there are more particles susceptible to oxidation in circulation. Another hypothesis is that reducing LDL-P increases intra-LDL antioxidant capacity. The European Prospective Investigation of Cancer (EPIC)-Norfolk cohort, a study that has followed 25,663 participants (men and women aged 45-79 years) over 6 years, evaluated associations between LDL-P and risk of CAD. Compared to controls, cases of CAD had a higher number of LDL particles (LDL-P, *P<.0001),* smaller average LDL-particle size (P=.002), and higher concentrations of small LDL particles (P<.0001).[25]

Kuller and colleagues investigated LDL-P levels in females and found females (but not males) had a significantly increased odds ratio for incidence of MI and angina for higher LDL-P, but not for LDL size after adjustments for LDL, age, and race. Males had increased (but not significantly) point estimates showing the same relationship.[26] This is in line with the lesson we learned from the MESA study where relationship of LDL-P to LDL-C in a discordant patient clearly demonstrated superiority of LDL-P in predicting negative outcomes.

Lipoprotein (a)

Lp(a) is a lipoprotein that is similar to LDL, but unlike LDL, Lp(a) has a unique plasminogen-like glycoprotein, apoA, which is linked to the LDL core by a disulfide bond. Assessment of this unique lipoprotein is another emerging test and, in my opinion, is important as Lp(a) responds to therapy differently than does LDL and confers a different CHD risk. Studies have shown that in healthy men and women with no prior history of CHD, an elevated Lp(a) level was associated with an increased risk of developing CHD. The higher the Lp(a) level, the greater the risk of CHD.[27]

In the Prospective Cardiovascular Munster (PROCAM) [28] study, when both LDL cholesterol and Lp(a) levels were elevated, the risk of a CV event increased almost three-fold. If the Lp(a) level was elevated and that of HDL cholesterol was low, the risk of a CV event was increased: over eight times higher than in individuals with normal lipid levels.

The finding of an elevated Lp(a) level in these patients should lead to more aggressive treatment of their underlying lipid abnormalities. Statins have little effect in lowering levels of Lp(a). Niacin is the only agent that effectively lowers Lp(a) by up to 30%.[29]

The European Atherosclerosis Society recently gave huge support to routine checking of Lp(a) in intermediate-to-high risk populations (class 2a recommendation) and advised to start the treatment with niacin 1-3 gm/d to lower the level of Lp(a) to less than 50mg/dL.[30]

Conclusion

Cardiovascular diseases are multifactorial with influences from genetics, hypertension, diabetes, obesity, smoking, etc. Lowering cholesterol with statins and other drugs helps but can't ameliorate the entire risk profile. So we need to ask, is advanced lipoprotein testing useful for detecting or managing residual risk?

We have some data from AMORIS and INTERHEART studies that showed supremacy of apoB as superior to LDL-C as mentioned earlier. The predictive performances of apoB or NMR LDL particle concentration for risk reclassification of asymptomatic individuals compared with standard lipids testing have been in scrutiny too. In the Framingham Study, little additional risk information was obtained from apoB or apoB/apoA-1 ratio compared with the total cholesterol/HDL cholesterol ratio.[31] The difference in the net reclassification index for apoB/apoA-1 compared with total-C/HDL cholesterol was insignificant. In the Women's Health Study,[32] similar results were obtained with not much gain in terms of reclassification index by using apoB or NMR LDL particle concentrations.

Results from MESA[4] helped clarify some confusion and we found that contrary to current opinion, both small and large LDL were significantly associated with subclinical atherosclerosis independent of each other, traditional lipids, and established risk factors, with no association between LDL size and atherosclerosis after accounting for the concentrations of the two subclasses.

Further studies are needed to prove that traditional tests can be routinely replaced by advanced lipid testing. Until then, these tests are best used as tools to better understand risks in intermediate and high risk populations where traditional risk factors are not helping to make the choice to start or intensify treatment, as the case may be different in each clinical situation.

Finally, although these tests have clinical utility, the evidence is based on research laboratory quality tests, and caution is advised relative to the accuracy, reproducibility, and precision of commercially available tests. This variability in the accuracy and reproducibility of standard measurements may also complicate patient management.[33] ■

Disclosure statement: Dr. Verma has received honoraria related to speaking from AstraZeneca and Abbott Laboratories. Dr. Verma has received research grants from GlaxoSmithKline.

References are listed on page 38.

Practical Pearls:
Adherence—Taking Your Patients' "SIDE"

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Medication adherence, by definition, is the extent to which a patient's behavior with respect to taking medication corresponds with recommendations from a healthcare provider.[1] Approximately half of all patients suffering from chronic diseases eventually do not take their medications as prescribed.[2] The problem starts as soon as a prescription is given to a patient. Approximately 83% of patients will never tell their healthcare provider that they don't plan to fill the prescription they just received, and up to 31% of prescriptions are not filled by patients.[1,2] Adherence is the key driver in enabling patients to achieve their treatment goals.[3]

Many perspectives have been introduced regarding patient adherence, and while there are many hypothesized factors, few have been shown to have a consistent impact. There is no specific "type" of person who doesn't take his medications.[3] Demographic characteristics, personality factors, a healthy lifestyle and other factors do not determine medication adherence.[1,3] Less research has focused on solutions and opportunities for improving patient adherence with little consensus on the "magic potion" necessary to get patients to take their medications.

It is important for providers to remember that patients manage their disease, not us. Taking the **SIDE** of the patient can help improve medication adherence (Table 1).

SIMPLIFY

Simplify the patient's medication regimen. Research supports simplifying a patient's number of prescriptions and number of doses each day to improve patient adherence.[4,5] While this seems simple, it is difficult to implement, especially when patients need to be on multiple medications for cardiovascular disease. Utilize combination therapy whenever possible. Optimize therapy by using once-daily dosing. When multiple daily dosings are necessary, develop a plan with the patient regarding the time of day to best take medications.[4] Remember to consider side effects when developing such a plan. For example, patients on beta blocker therapy may feel tired after taking the medication and may benefit from taking it at bedtime. Give the patient ideas for simplification, such as using pill boxes and pill reminders.[6]

INVESTIGATE

Investigate with patients the possible reasons for their non-adherence. There are many possible causes to consider. The Adherence Estimator® developed by Merck can help start a conversation about the concern of adverse events, whether the patient believes the drug is needed, and cost of the medication (Figure 1).[7] Another useful exercise is to determine whether the root cause of missing doses is forgetfulness, confusion or simply not wanting to take the medication.

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Taking Your Patients' "SIDE"

Simplify	• Simplify number of medications and utilize combination agents • Simplify dosing schedule with as many once daily medications as possible • Help patients simplify by using reminders and pill boxes
Investigate	• Utilize adherence tools to assess reasons for non-adherence • Monitor lab values to give adherence clues • Call patient's pharmacy to get refill report • Evaluate patient's medication bottles to assess adherence • Involve interdisciplinary team members
Discuss	• Build relationship of trust and open communication • Help patient understand benefits of medication • Discuss possible side effects in the context of medication benefits • Educate in multiple formats, verbally and written, clearly and concisely • Optimize communication at all points of care with all patient care team members • Notify pharmacy when medications are stopped or changed
Engage	• Engage patients in their lifestyle and health care decisions • Motivate patients utilizing techniques of motivational interviewing (express empathy, develop discrepancy, roll with resistance and support self-efficacy) • Collaborative care-planning and problem solving • Patients develop their own specific and attainable goals • Involve family members for support

Table 1.

Adherence Navigator® Score (points in parenthesis)

1. **I worry that my prescription medication will do me more harm than good.**
   - ☐ Agree completely (14)
   - ☐ Agree mostly (14)
   - ☐ Agree somewhat (4)
   - ☐ Disagree somewhat (4)
   - ☐ Disagree mostly (0)
   - ☐ Disagree completely (0)

2. **I am convinced of the importance of my prescription medication.**
   - ☐ Agree completely (0)
   - ☐ Agree mostly (0)
   - ☐ Agree somewhat (7)
   - ☐ Disagree somewhat (7)
   - ☐ Disagree mostly (20)
   - ☐ Disagree completely (20)

3. **I feel financially burdened by my out-of-pocket expenses for my prescription medication.**
   - ☐ Agree completely (2)
   - ☐ Agree mostly (2)
   - ☐ Agree somewhat (0)
   - ☐ Disagree somewhat (0)
   - ☐ Disagree mostly (0)
   - ☐ Disagree completely (0)

- ☐ **0: Low risk (>75% probability of adherence)**
- ☐ **2-7: Medium risk (32% -- 75% probability of adherence)**
- ☐ **8-36: High risk (<32% probability of adherence)**

Figure 1.

Investigate, on your own, whether a patient is taking their medications. Monitoring can be used to motivate and educate patients with some therapy; however, recent data showed monitoring low-density lipoprotein cholesterol (LDL-C) had only a limited ability to detect non-adherence with statin therapy.[8] Collaborate with pharmacists and pharmacies to optimize adherence. Pharmacists in pharmacies have the luxury of looking at refill histories. The current, disconnected healthcare system does not allow everyone access to this information, but one can call the pharmacy and ask. There is a great opportunity to engage nurses, care coordinators and even students to impact patient adherence. Patients should be instructed to carry a list of their current medications, including the reason for taking them. An extension of this is to have patients bring in their medication bottles at each visit. Each bottle lists the fill date and, by looking at the number of pills left in the bottle, adherence can be assessed and a discussion with the patient can begin.

DISCUSS

Discuss and educate regarding the importance of taking each medication. Communication is an essential component of improved adherence, as seen throughout much of current research.[6] Significant data has shown improved adherence to drug therapy when patients believe they have a relationship of trust and open communication with their provider.[5,9] When a patient is given a new prescription, it is essential for physicians, pharmacists and other healthcare providers to help the patient understand why the medication is needed. Explain the benefits of adherence to the regimen and discuss side effects in the context of risks and frequency of adverse effects compared to medication benefits.[6,10] Instructions should be provided in multiple formats, verbally and written in a clear and concise manner.[11]

At each follow-up visit, healthcare providers should discuss side effects and other possible problems with medication therapy. Keep in mind that, with many asymptomatic cardiovascular risk factors, patients will feel worse once they start taking a medication than prior to starting therapy. There is a great opportunity to involve different members of the patient care team in this process, with all trained on methods of effective communication, such as asking open-ended questions.

> "It is important for providers to remember that patients manage their disease, not us."

Communication also is very important between care providers and different levels of the healthcare delivery system. Research has shown that the more providers a patient sees, the less adherent they are; thus, medication reconciliation is essential at each step of the care process. Communication between all members of the interdisciplinary team caring for a patient and the patient at various transitions of care is needed to optimize drug therapy. For example, medications are often started but are rarely discontinued at a pharmacy. The addition of over-the-counter medications, dose changes and the discontinuation of therapy should be documented at all points of care by the patient, the providers—primary care and specialists—and the pharmacist.

ENGAGE

Engage patients in making decisions about their care. In line with healthcare reform and the patient-centered medical home, motivational interviewing and health coaching have been introduced to involve patients in their lifestyle and healthcare decisions. Motivational interviewing is a client-centered, directive counseling style for enhancing intrinsic motivation to change by exploring and resolving ambivalence.[12] It is a focused and goal-directed approach with the patient at the center of all decisions. The four principles of motivational interviewing are express empathy, develop discrepancy, roll with resistance and support self-efficacy. Emphasize the patient's key role in caring for himself.[5] Empower informed and activated patients by encouraging effective behavior change interventions and assuring collaborative care-planning and problem solving.[5] Patients should actively participate in developing a medication care plan. It is important to empathize throughout this process to better understand the patient perspective and engage and motivate them with their own care. Patients should write down specific and attainable goals for their own therapy. Family members and significant others should be enlisted to offer support for the patient in reaching these goals.

Targeted interventions to improve adherence can impact patient outcomes as well as patient satisfaction. Taking your patients' SIDE to simplify, investigate, discuss and engage can build a practice of adherent patients. ■

Disclosure statement: Dr. Trewet has no relevant disclosures.

References are listed on page 38.

EBM Tools for Practice:
Burying Caesar

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During the NLA Annual Scientific Sessions, a select committee presented what I found to be a very well-thought-out position statement on the major contenders for addition to our prognostic algorithms. Yet, every time "what to add" comes up, I remember my junior-year gynecology rotation, when GYN was in the middle of a controversy. A new pregnancy test, serum β-HCG, was taking attention away from the standard "rabbit test." I recall the teaching staff debating both tests, but no one advocating for doing both. When I asked why not, I was (appropriately) sneered at for wanting to waste the time, trouble and money to measure and react to the same risk in two ways. After all, studies had already shown that, in all commonly encountered situations, serum β-HCG was the better predictor when the assays disagreed. All that was left to debate was the incremental cost/benefit, and then the decision to replace the standard could be made. Needless to say, serum β-HCG won.

In our debates about risk assessment, we have forgotten gynecology's logic. Immediately after demonstrating that a biomarker has shown additive value, we should ask, "Has a biomarker rendered a standard assay meaningless?" In our economically imploding healthcare system, we can only slightly improve our clinical efficiency by adding tests but, if new tests could replace others, we could increase that efficiency still further. The chemical lipid panel has ruled lipoprotein risk assessment like Caesar for years. Is there a biomarker that can take it from the throne?

Let's first define the necessary credentials. Contenders need to show they retain statistically significant prognostic association in a multivariate analysis adjusted for all traditional risk factors, chemical lipids and their derivations/ratios. The new test also would have to show that chemical lipids/ratios lose their statistical association after adjustment for the new test parameters. Contenders must meet these conditions in multiple commonly encountered clinical populations. There is already one assay that meets those credentials: nuclear magnetic resonance (NMR) lipoprotein quantification.

To date, NMR has been studied with this rigorous standard in several differing risk populations. These settings include a very-low-risk primary prevention population, a very-high-risk secondary prevention population, a multi-ethnic primary prevention population, and even the reference population used in National Cholesterol Education Program (NCEP) guidelines. That NMR has shown those chops in diverse risk populations is an essential shovel of dirt on the lipid panel's grave, as the "rabbit test" could always equal serum β-HCG in the maternity ward and the men's locker room. Another shovelful: NMR not only rendered low-density lipoprotein cholesterol (LDL-C) insignificant, but did the same with all lipid panel ratios/derivations, apolipoproteins and their ratios. NMR has predicted not only events but also anatomic atherosclerosis progression while rendering lipid panel data superfluous. Yet

the ultimate arena for assays isn't before therapy; it's predicting therapy response. Predicting on-therapy risk has always been LDL-C's Achilles' heel, making us turn to derivations/ratios or apolipoproteins. NMR quantification predicted events on fibrate therapy in the Veterans Administration

> "Is there a biomarker that can take Caesar from the throne?"

HDL Intervention Trial (VA-HIT) while leaving all of those other assays without a statistical association. While NMR data on statin therapy has been sparser and, to date only with quantitative coronary angiography, data to be published shortly will show the same statistical associations between NMR and these other assays in a very large event-based, statin-treated population (personal communication). If confirmed, Caesar's grave is covered.

There are caveats to remember about NMR. It has not been shown to diagnose dysbetalipoproteinemia, although there is reason to believe it would. Intermediate-density lipoproteins (IDL) are included in the NMR quantification of LDL particles. Anecdotally, both of the lipid-diagnosed dysbetalipoproteinemia cases I have seen had elevated NMR LDL quantifications and inordinately large LDL size. It took the NMR quantification of both LDL and HDL particles to replace the lipid panel, although there is no added cost to get both. We will still need triglycerides in cases of acute pancreatitis, although a calculation derived from NMR analysis is sufficiently accurate to alert us to pancreatitis risk.

Like β-HCG, NMR has several non-statistical advantages over lipids and apolipoproteins. Data support NMR parameters as facilitators of treatment selection. NMR has much lower reagent and labor costs, a faster turnaround time, greater reproducibility, and can be done non-fasting, all of which should contribute to increased clinical efficiency. While a recent analysis questions the financial feasibility of NMR over lipids, this analysis was performed on a low-risk, therapy-naïve population and assessed cost by the tests' list prices, a price differential we all know very few patients pay. Most of the fixed cost of NMR is shipping to a centralized laboratory and, as lower-cost analyzers are shortly to be available nationwide, wholesaled through many labs, the cost of the assay will likely drop below that of the lipid panel. Given the misery of missed events and unnecessary treatment, let's remember Caesar as a great king. But if you haven't left the cemetery yet, stand close to your shovel. ■

Disclosure statement: Dr. Stock has received honoraria related to speaking from Eli Lilly and Co., LipoScience Inc., and Warner Chilcott, Inc.

References are listed on page 39.

Lipid Luminations:
Atherosclerosis Imaging Trials Targeting High-Density Lipoprotein Cholesterol

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Epidemiologic data have shown a consistent and independent inverse relationship between high-density lipoprotein cholesterol (HDL-C) levels and the risk of cardiovascular disease.[1] Perhaps the most well studied beneficial effect of HDL-C is its involvement in the movement of cholesterol from peripheral tissues to the liver.[2] A number of imaging modalities—including quantitative coronary angiography (QCA)[3-5] intravascular ultrasound (IVUS),[6-8] B-mode ultrasound[9] and magnetic resonance imaging (MRI)[10,11]—have been used in attempts to study the in-vivo atherosclerotic changes in response to HDL-C-raising therapy.

While QCA has high spatial resolution and provides accurate and reproducible measurements of vessel lumen size, it is limited by being invasive and using X-ray radiation.[4] The Armed Forces Regression Study (AFREGS) used coronary angiography to assess the effects of combination therapy with gemfibrozil (600 mg twice daily), niacin (3 g/d) and cholestyramine (16 g/d) aimed at increasing HDL-C in patients with relatively small low-density lipoprotein cholesterol (LDL-C) levels (<160 mg/dL) and low HDL-C (<40 mg/dL).[3] During the study, 143 patients with baseline mean LDL-C (128 ± 27 mg/dL) and HDL-C (34 ± 6 mg/dL) were randomized to the intensive therapy versus conventional treatment. After 30 months of treatment, the intensive therapy group had an increase in HDL-C of 38% and a decrease in LDL-C of 22% with statistically significant reduction in the percentage of coronary stenosis (-0.81%) compared to the control group (1.35% increase) (p=0.04). The HDL-Atherosclerosis Treatment Study (HATS) enrolled 160 patients with coronary artery disease and low HDL (<35 mg/dL for men, <40 mg/dL for women), and randomized them to treatment with simvastatin plus niacin or placebo for three years.[4] There was a 26% increase in HDL-C and a 42% reduction in LDL-C in the simvastatin-plus-niacin group, which resulted in a regression of coronary artery stenosis by 0.4% as compared to a progression of 3.9% in the placebo group.

Unlike QCA, IVUS provides cross-sectional images through the vessel wall and allows detection of vascular remodeling and a more accurate assessment of atherosclerotic burden.[12] Like QCA, though, IVUS requires an invasive procedure and, therefore, may be limited in trials aimed at detecting sub-clinical atherosclerosis. Nissen, et al., in a randomized, placebo-controlled trial, studied the effects of infusions of recombinant Apolipoprotein A-1 (apoA-1) Milano, a variant of apoA-1, in patients recently presenting with an acute coronary syndrome (ACS).[6] In this study, 57 patients were randomized within two weeks of their ACS to five weekly infusions of placebo, apoA-1 Milano (15mg/kg), or apoA-1 Milano (45 mg/kg). After the five weekly infusions, the median percentage

Clinical Imaging Trials of HDL-C Therapy

Imaging	Trial	Patients	N	Treatment	Time	Primary endpoint
Angiography	AFREGS	CAD and low HDL	143	gemfibrozil (600 mg twice daily), niacin (3 g/d), cholestyramine (16 g/d)	30 mos	% stenosis change
	HATS	CAD and low HDL	160	simvastatin (20-40mg/d) plus niacin (2-3gm/day)	3 yrs	% stenosis change
Carotid US	ARBITER 2	CAD and HDL <45 mg/dL	167	extended-release niacin (1gm/d)	1 yr	CIMT change
	RADIANCE 1	FH	850	torcetrapib plus atorvastatin	2 yrs	max CIMT change
IVUS	ApoA-1 Milano	CAD with ACS	57	recombinant apoA-1 Milano	5 wks	% atheroma volume change
	ILLUSTRATE	CAD	1188	torcetrapib plus atorvastatin	2 yrs	% atheroma volume change
	ERASE	CAD with ACS	183	recombinant HDL	4 wks	% atheroma volume change

FH=Familial Hypercholesterolemia

Table 1.

Treatment and Atherosclerosis Effects of HDL-C Therapy

Trial	Treatment	% HDL-C increase			Atherosclerosis change		
		Treatment	Comparator	P	Treatment	Placebo	P
AFREGS	gemfibrozil, niacin, cholestyramine vs. placebo	38	2	<0.01	-0.81%	1.35%	0.04
HATS	simvastatin plus niacin vs. placebo	26	6	<0.01	-0.04%	3.9%	<0.01
ApoA-1 Milano	apoA-1 Milano vs. placebo				-1.06%	0.14%	0.02*
ARBITER 2	statin plus niacin vs. statin alone	21	0	<0.01	0.907	0.912	<0.01**
ILLUSTRATE	torceptrapib plus atorvastatin vs. atorvastatin	58	- 2	<0.01	0.12%	0.19%	0.72
ERASE	recombinant HDL vs. placebo				-3.4%	-1.6%	0.48
RADIANCE 1	torceptrapib plus atorvastatin vs. atorvastatin	35	1	<0.01	0.0053 mm/yr	0.0047 mm/yr	0.87

**compared to baseline within treatment group*
***compared to baseline within placebo group*

Table 2.

atheroma volume decreased by 0.81% (95% confidence interval [CI] -1.53%-0.34%, p=0.02) in the combined treatment arm. In the placebo group, there was no reduction in median percentage atheroma with a median change of 0.03% (95% CI –1.11%-1.43%, p=0.97). Regression was noted in both doses of recombinant apoA-1 Milano and confirmed the possibility of regression with HDL therapy as noted in the earlier HATS study. In a similar study, the Effect of rHDL on Atherosclerosis—Safety and Efficacy (ERASE) trial, Tardif, et al., investigated the effects of recombinant HDL on coronary atheroma volume by IVUS.[7] They randomized 183 patients with a history of ACS within the past two weeks to receive four weekly infusions of rHDL or placebo. After four weeks, IVUS measuring the primary endpoint of percentage change in atheroma volume showed no significant difference between the treatment and placebo groups (-3.4% vs. -1.6%, p=0.48). The Investigation of Lipid Level Management Using Coronary Ultrasound to Assess Reduction of Atherosclerosis by CETP Inhibition and HDL Elevation (ILLUSTRATE) trial used IVUS to evaluate the effects of treatment with torcetrapib, a cholesteryl ester transfer protein (CETP)-inhibitor, plus atorvastatin on coronary atheroma as compared to treatment with atorvastatin alone in 1,188 patients with coronary artery disease (CAD).[8] Treatment with the combination of torcetrapib plus atorvastatin increased HDL-C by 58% from baseline after 24 months of treatment as compared to a decrease of 2% in the atorvastatin-alone group. Despite the dramatic increase in HDL-C, there was no significant difference in the progression of coronary atherosclerosis as noted by the change in percentage atheroma volume (0.19% vs. 0.12%, p=0.72).

Unlike, QCA and IVUS, B-mode ultrasound measurement of the carotid arterial wall is a non-invasive imaging modality that can help to identify sub-clinical disease and follow plaque progression.[9] The Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol (ARBITER) 2 Trial was a randomized, double-blind, placebo-controlled B-mode ultrasound trial evaluating the effects of the addition of extended-release niacin to statin therapy on carotid intima-media thickness (CIMT) progression.[13] ARBITER 2 randomized 167 patients to therapy with extended-release niacin (1gm/d) or placebo. After one year of therapy, HDL-C levels significantly increased, by 21%, from 39±7 mg/dL to 47±16mg/dL (p=0.002) in the niacin group and remained unchanged in the placebo group. At the end of treatment, LDL-C did not differ between the niacin and placebo groups (p=0.61). In the niacin group, mean CIMT did not statistically change compared to baseline (p=0.23) but, in the placebo group, CIMT increased by 0.912 mm ± 0.202, (p=<0.001).

Kastelein, et al., applied B-mode ultrasound to studying the effects of torcetrapib in patients with heterozygous hypercholesterolemia on carotid atherosclerosis in the Rating Atherosclerosis Disease Change by Imaging with a New CETP Inhibitor (RADIANCE 1) study.[14] The study randomized 850 patients to treatment with torcetrapib 60 mg plus atorvastatin or atorvastatin alone. After two years of treatment, HDL-C increased by 54.4 mg/dL in the torcetrapib group and by 2.5 mg/dL in the atorvastatin alone group. The primary endpoint, increase in maximum carotid IMT, was not significantly different between the two groups, 0.0053 ± 0.0028 mm per year vs. 0.0047± 0.0028, p=0.87. Similar to ILLUSTRATE, the lack of vascular efficacy observed with torcetrapib may be explained by the toxic activation of the renin angiotensin system with an increase in blood pressure and resultant higher total mortality.

Unlike QCA, B-mode ultrasound (US) and IVUS, recent studies have documented the ability of magnetic resonance imaging (MRI) to provide detailed information on individual plaque components.[15] MRI studies have been able to correlate HDL-C levels and measurement of carotid plaque lipid content. Frias, et al., recently developed a novel paramagnetic MR contrast agent using recombinant HDL.[16] In apolipoprotein E (apoE) knockout mice, they were able to show that the HDL contrast agent localized to atherosclerotic plaques in vivo. In a small clinical study of 34 CAD patients being treated with simvastatin and niacin, Phan, et al., described an inverse association between HDL-C and carotid plaque lipid content and atherosclerosis burden as assessed by MRI.[10] Soon-to-be-published data from the Carotid Plaque Composition (CPC) Study will further document the effects of HDL-C-raising therapy in combination with statin and colesevelam on atherosclerotic plaque characteristics as assessed by MRI.[11]

Imaging trials using a number of modalities have documented the benefits of HDL-C-raising therapies in retarding the progression and also possibly inducing the regression of atherosclerotic disease. Beyond quantifying plaque burden, future imaging trials will need to use techniques such as positron emission tomography (PET), nuclear magnetic resonance (NMR) and molecular ultrasound to elucidate the additional vascular benefits of HDL-C therapy on plaque inflammation and vulnerability.[17] ■

Disclosure statement: Dr. Phan has received honoraria related to speaking from Abbott Laboratories.

References are listed on page 39.

Case Study:
Advanced Lipid Testing—Beyond LDL-P and Apo B

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JM, a healthy 45-year-old woman who is on a low-glycemic diet and exercises 150 minutes a week, comes in for an evaluation of abnormal lipids despite her excellent lifestyle efforts. She is resistant to "cholesterol-lowering" medication and is interested in understanding her risk for cardiovascular disease (CVD). There is no family history of premature CVD, but her mother and maternal grandmother both had adult onset Type 2 diabetes.

Pertinent initial labs:

Total cholesterol	250 mg/dL
LDL–C	150 mg/dL
Triglycerides	220 mg/dL
HDL-C	56 mg/dL
Non-HDL-C	194 mg/dL
HsCRP	3
Fasting glucose	98 mg/dL
HbA1C	5.7%
ALT/AST	within normal limits
TSH	1.24 mIU/L
Blood pressure	120/82
Body Mass Index	25

According to the recently published American Heart Association (AHA) guidelines for CVD prevention in women, JM would be characterized as "at risk" based on having a high total cholesterol of >200mg/dL and diastolic blood pressure of >80mmHg.[1] Her Framingham Risk Score is <5%; it is therefore debatable whether lipid-lowering therapy is indicated. Recent data from the Multi-Ethnic Study of Atherosclerosis (MESA) study[2] supporting previous research shows CV risk is more directly related to the low-density lipoprotein particle (LDL-P) concentration than to low-density lipoprotein cholesterol (LDL-C), and one could argue that LDL-P or apolipoproteinB (Apo B) would be a better measure to determine her risk for cardiovascular disease. A nuclear magnetic resonance (NMR) analysis was performed, and results are as follows:

LDL-P	2,552 nmol/L (optimal <1000)
Small LDL-P	1,732 nmol/L (optimal <850)
HDL-P	48 umol/L
LP-IR score	65 (optimal <45/100)

Her LDL-P of 2,552 is considered very high risk and places her in the >95th percentile of the population based on both Framingham and MESA data (Table 1). If there were any hesitation to treat her dyslipidemia, one would be more inclined to treat with this additional information and elevated highly sensitive C reactive protein (hsCRP). She is currently preventing future childbearing, so a statin would be the first choice of therapy. If she is open to pregnancy, then alternatives to statin could include niacin, fibrate or bile acid sequestrant. A bile acid sequestrant would help lower LDL-P but should not be the first choice, because it has the

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> "Insulin resistance is a common secondary cause of dyslipidemia characterized by high triglycerides and low HDL-C. "

potential to raise triglycerides further. Now, let's take a step back before getting out the prescription pad.

It is important to rule out secondary causes of dyslipidemia before initiating lipid-lowering therapy, especially in a patient with no family history of CVD. She is on no medications or supplements, so this is not a secondary cause. She has had a normal thyroid-stimulating hormone (TSH) test, ruling out hypothyroidism as a contributor to dyslipidemia. Her glucose was 98 with optimal being <100 mg/dL. Her glycated hemoglobin (HbA1C) was 5.7. American Diabetes Association (ADA) guidelines published in 2010 now consider HbA1C to be a valid diagnostic tool for diabetes.[3] They define an HbA1C of 6.5 and above to be diagnostic of diabetes and an HbA1Cof 5.7-6.4 to be in the category of "prediabetes."[3] This patient also has predominantly small dense LDL, which encompasses more than 50% of her total LDL-P, suggesting insulin resistance is contributing to high LDL-P.

Insulin resistance is a common secondary cause of dyslipidemia characterized by high triglycerides and low HDL-C. The metabolic changes induced by or accompanying insulin resistance produce even greater and more extensive abnormalities in lipoprotein subclass levels and particle size distributions, which are detected by advanced lipoprotein testing.[4,5] Specifically, large very-low-density lipoprotein (VLDL) and small LDL subclass particle concentrations are higher and large HDL subclass levels are lower in insulin-resistant individuals. NMR-measured VLDL LDL, and HDL particle sizes also reflect insulin-resistance status. VLDL size tends to be greater and LDL and HDL sizes smaller when a patient is insulin resistant. This unique lipoprotein "window" into insulin resistance gives us an opportunity to identify, by nature of the lipoprotein status, a patient who may be a candidate for more aggressive lifestyle efforts or pharmacologic therapy. Liposcience's Lipoprotein Insulin Resistance Index (LP-IR) score, ranging from 0 (most insulin sensitive) to 100 (most insulin resistant), helps summarize a patient's insulin resistance status based on the strength of associations with each of the lipoprotein parameters listed here. Other labs also include various measures of insulin resistance in their profiles.

Insulin resistance precedes the beta cell dysfunction that ultimately leads to the development of diabetes. Early identification of insulin resistance may help prevent, not just delay, the onset of diabetes. The world is undergoing a diabetes pandemic and it is estimated that the total number of cases will increase by more than 50% during the next two decades, from 285 million cases worldwide in 2010 to 438 million cases worldwide in 2030.[6] While these statistics may be depressing, it is empowering to know that diabetes is largely a preventable disease if early intervention and prevention efforts are made. Early intervention may include more aggressive efforts at making lifestyle changes, and, in those at high risk for cardiovascular disease, metformin may be an appropriate initial therapy. It is important to note that no medications are currently FDA-approved to prevent progression to diabetes. However, ADA guidelines recommend metformin therapy for prevention of Type 2 diabetes in those at the highest risk for developing diabetes, such as those with multiple risk factors, especially if they demonstrate progression of hyperglycemia (e.g., A1C ≥6%) despite lifestyle interventions.[7] Because metformin does not produce hypoglycemia it is safe to use as monotherapy in patients with insulin resistance and normal glycemic status.

There also are cardiovascular mortality data with metformin. In the United Kingdom Prospective Diabetes Study (UKPDS), 34 overweight patients with newly diagnosed Type 2 diabetes were randomly allocated to control their glucose levels by dietary modification alone (n=411) or by undergoing intensive blood-glucose control with metformin (n=342). At the

Population Equivalent Cutpoints for Alternate LDL Measures

(LDL-C, MEasured Apo B and NMR LDL-P)

Biomarker	Population	Percentile Equivalent Concentration			
LDL-C (mg/dL)	Framingham[1]	< 70	100	130	160
Measured Apo B (mg/dL)	Framingham[1]	< 60	80	100	120
NMR LDL-P (nmol/L)	Framingham[1]	< 850	1100	1400	1800
	MESA[2]	< 700	1000	1300	1600

[1]Controls, et al. Clinical Chemistry 2009;407-419
[2]Cromwell WC. Clinical Challenges in Lipid Disorders. Oxford: Clinical Publishing, 2008:249-259

Table 1.

end of the sub-study (median treatment duration 10.7 years), the median HbA1C level was 7.4% in the metformin group compared with 8.0% in the conventional-therapy group. Treatment with metformin resulted in risk reductions of 32% for any diabetes-related end point (95% confidence intervals (CI) 13%-47%, p=0.002), 42% for diabetes-related death (95% CI 9%-63%, p=0.017), and 36% for all-cause mortality (95% CI 9%-55%, p=0.011), compared with conventional therapy. The risk of myocardial infarction in the metformin group was reduced by 39% (p=0.011), and the risk of all combined macrovascular disease end points (myocardial infarction, sudden death, angina, stroke and peripheral vascular disease) was reduced by 30% (p=0.02), compared with the conventional-treatment group.[8]

Ten years of post-trial monitoring to determine whether the improved glucose control of intensively treated patients persisted and whether early intensive treatment had a long-term effect on macrovascular outcomes revealed that the difference in HbA1c levels between intensive therapy and conventional therapy was lost after one year. However, the reduction in diabetes-related endpoints was still evident 10 years after completion of the intervention trial. Among patients in the intensive treatment arms, significant reductions in the risk of myocardial infarction (by 15%, p=0.01 and by 33%, p=0.005 for the sulfonylurea-insulin and metformin groups, respectively) were observed.

At least two retrospective cohort analyses of sulfonylurea and metformin therapies support the UKPDS findings. In the eight-year Diabetes Audit and Research in Tayside, Scotland (DARTS) study of 5,730 patients, there was a 30% lower risk for all-cause mortality in the metformin group, after adjustment for baseline confounders, and a 41% lower risk for cardiovascular mortality.[9] In the five-year Saskatchewan Health database study of 2,272 new users of oral antidiabetic agents, the adjusted odds ratio (OR) for all-cause mortality for metformin monotherapy was 0.60 (95% CI 0.49-0.74) compared with sulfonylurea monotherapy and 0.64 (0.49-0.84) for cardiovascular deaths.[10]

47 yr old female maximized TLC

	FIRST VISIT Doing 150 minutes exercise/week on low glycemic diet	FOLLOW UP at 2 months Metformin ER 1500	GOALS OF THERAPY
Total cholesterol	250	229	<200 mg/dL
Triglyceride	220	99	<150 mg/dL
HDL-C	56	62	>50 mg/dL
LDL-C	150	147	<100 mg/dL
LDL-P Small LDL-P	2552 1732	*1440* *592*	*<1000nmol/L* *<850 nmol/L*
Non HDL-C	194	167	<130 mg/dL
IR Score	64	42	<45/100
hsCRP	3	1	

Table 2.

Today, we diagnose diabetes based on impaired glucose tolerance. At the time of diabetes diagnosis, most patients will have lost 60%–70% of beta cell function, which is largely irreversible (Table 2). We need better ways to diagnosis this disease before it causes loss of beta cell function and microvascular and macrovascular complications. In our patient case, metformin ER 1500 mg was initiated at the first visit because of the abnormal HbA1C, family history of diabetes and lipoprotein parameters suggestive of insulin resistance. After two months of metformin use, her lipoprotein and lipid values improved. LDL-P dropped from 2,552 to 1,440 without a significant change in LDL-C. Metformin, as expected, caused triglycerides to improve, and she had a five-pound weight loss without any further change in her diet and exercise regimen.

Advanced lipid testing provides information beyond just LDL-P and Apo B. This information may allow us to better diagnose a secondary cause of dyslipidemia, namely insulin resistance. Metformin ER, an effective therapy for insulin resistance, is available as an inexpensive generic medication. Metformin also causes weight loss, improves lipids and is pregnancy category B, a safe option in women of childbearing age. The main contraindications for metformin are renal disease and/or elevated creatinine>1.4. As monotherapy, there should be minimal risk for hypoglycemia. ■

Disclosure Statement: Dr. Dall has received honoraria related to speaking from Abbott Laboratories, GlaxoSmithKline, HDL Labs, LipoScience Inc., and Santarus Inc.

References are listed on page 39.

Honors and Recognition

The NLA congratulates the following individuals, who were honored during the 2011 Annual Scientific Sessions for their commitment to medicine, research, and the highest standards of patient care:

Distinguished Achievement Award
Antonio Gotto, Jr., MD, DPhil, FNLA

Honorary Lifetime Membership Award
Rodolfo Paoletti, MD

Honorary Lifetime Membership Award
B. Greg Brown, MD, FNLA

President's Service Award
Thomas Dayspring, MD, FNLA

The NLA congratulates the following individuals who were recognized as Fellows of the NLA during the 2011 Annual Scientific Sessions:

They have been recognized by their peers as standards-setters in our field due to their contributions to society and the practice of lipid management.

Harold Bays, MD
John Corbelli, MD
Stephen Daniels, MD
Stephen Devries, MD
Kathleen Dively, MSN
Daniel Duprez, MD, PhD
Edwin Ferguson, MD
Mary Honkanen, MD
Edgar Lerma, MD
Janice McAlister, NP
Catherine McNeal, MD, PhD
John Merenich, MD
Guy Mintz, MD
Shailendra Patel, MD, PhD
Morton Saunders, Jr., DO
John Sink, II, PA
Kari Uusinarkaus, MD
Wayne Warren, MD
Don Wilson, MD
Michael Zema, MD

Specialty Corner:
Management of Dyslipidemias in Chronic Kidney Disease—A Review of Major Clinical Trials Involving Statins

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EDGAR V. LERMA, MD, FNLA
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Chicago, IL

Approximately 26 million people in the United States suffer from chronic kidney disease (CKD), with disproportionally higher numbers among patients with pre-existing cardiovascular disease. It is well known that the risk of cardiovascular events is much higher in dialysis patients compared to the general population; Foly, et al., documented that 25 to 35 year-old patients on dialysis are at the same risk of mortality from cardiovascular disease as someone age 85 in the general population (Figure 1). Blood cholesterol reduction by using 3-hydroxy-3-methyl-glutaryl-CoA (HMG-CoA) reductase inhibitors (statins) in people at risk of cardiovascular disease has been recommended. In regard to hyperlipidemia and the incidence of cardiovascular disease, most retrospective observations of patients with end-stage renal disease and on dialysis have shown no positive correlation between high cholesterol levels and increased rates of cardiovascular events. In fact, the opposite tendencies have been reported in dialysis patients. A large study with 1,167 hemodialysis patients showed mortality actually increased with cholesterol levels <140 mg/dL, when compared with higher levels, up to 220 mg/dL.[2] However, this study was not adjusted for disease severity or inflammatory stage associated with late-stage chronic kidney disease. In dialysis patients, there has been a disconnect between most risk factors related to cardiovascular disease in observational studies and interventional studies designed to modify these risk factors. Although the effects of lowering low-density lipoprotein cholesterol (LDL-C) on the progression of renal disease or cardiovascular events are not fully understood, it is important to note that only one-quarter of dialysis patients die from acute myocardial infarction (MI). At present, there are three randomized placebo controlled studies of three different statin therapies, all with negative results in the dialysis population (Table 1).

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Please view the CME/CE web activity "Lipid Lowering in the Chronic Kidney Disease Patient" at lipid.org/education/online and see the CKD Roundtable in the July/August issue of the *Journal of Clinical Lipidology.*

Risk of Cardiovascular Disease Among Dialysis Recipients Compared to Healthy Males and Females from the General Population

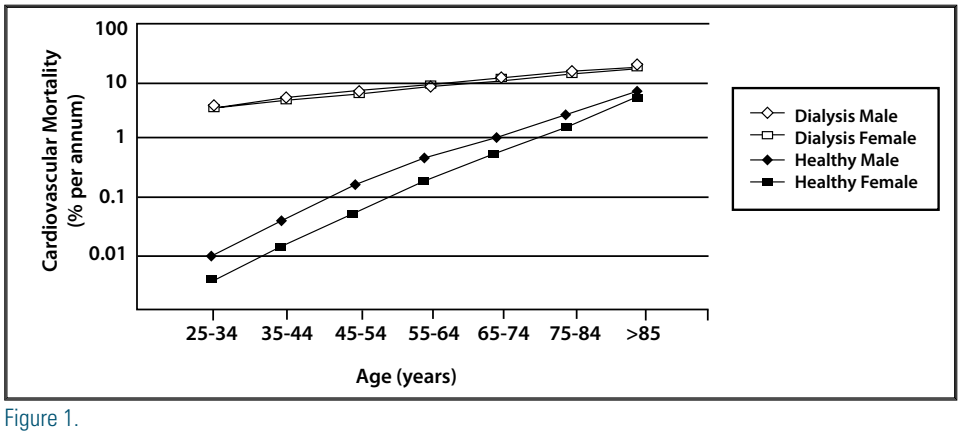

Figure 1.

Studies Specific to the Dialysis Population

Study	Author	Duration	Type of Study	Treatment (n)	Patient Population	Primary Outcome	Study Results
Die Deutsche Diabetes Dialyze Study (**4D**)[3]	Wanner, Christoph	Mar 1998-Mar 2004	Prospective, randomized, double-blind, placebo control	Placebo Atorvastatin 20 mg n=1,255	Age 18-80 years old Type II diabetes and receiving hemodialysis for no more than 24 months	Cardiac death, fatal or nonfatal stroke, or nonfatal MI	No significant trend in occurrence of the primary end points was noted with atorvastatin (relative risk [RR] 0.92, 95% confidence interval [CI] 0.77-1.10, p=0.37)
Evaluation of the Use of Rosuvastatin in Subjects on Regular Hemodialysis (**AURORA**)[4]	Fellstrom C, Bengt	Jan 2003-Oct 2008	Randomized, double-blind, placebo control	Placebo Rosuvastatin 10 mg n=2776	Age 50-80 years old on long-term hemodialysis	Cardiac death, nonfatal stroke, or nonfatal MI	No significant difference was noted in the primary end point with rosuvastatin compared with placebo (hazard ratio [HR] 0.96, 95% CI 0.84-1.11, p=0.59)
The Study of Heart and Renal Protection (**SHARP**)[5]	Baigent, Colin	June 2003-Sept 2010	Randomized, double-blind, placebo control	Placebo Simvastatin 20mg Simvastatin 20 mg/ Ezetimibe 10 mg n=9,270	Age ≥40 years old Chronic kidney disease: Scr ≥ 1.7 mg/dL (men) Scr ≥ 1.5 mg/dL (women), peritoneal or hemodialysis, no history of CVD	Major vascular events: nonfatal MI, cardiac death, revascularization, nonfatal or fatal stroke Major atherosclerotic events: coronary death, MI, non-hemorrhagic stroke, or revascularization	For the primary end point of major vascular events, patients in the active-treatment group experienced a 15.3% reduction (p=0.0012), as compared with placebo. After a median follow-up of 4.9 years, patients randomized to the ezetimibe/simvastatin combination experienced a 17% reduction in major atherosclerotic events compared with the placebo group (p=0.0022).

Table 1.

The Deutsche Diabetes & Dialysis study (4D) was the first randomized study aimed at investigating the benefits of using an HMG-CoA reductase inhibitor (atorvastatin) in patients on hemodialysis with Type 2 diabetes mellitus.[3] The 4D study was a multicenter, randomized, double-blind, prospective study of 1,255 (18- to 80-year-old) Type 2 diabetes mellitus patients receiving maintenance hemodialysis for less than two years. It was supported by the pharmaceutical industry and patients were enrolled in 178 centers in Germany. Patients were excluded if they had: LDL-C <80 or >190 mg/dL, serum triglycerides >1,000 mg/dL, abnormal liver function tests, or a cardiovascular event during the past three months.

A total of 619 patients were enrolled into the atorvastatin 20mg/day arm of the study, and 636 were given a matching placebo. Lipid-lowering agents were discontinued upon enrollment, and all eligible subjects were given a placebo during a four-week run-in phase. If LDL-C levels fell below 50 mg/dL, the dose of atorvastatin was reduced to 10 mg/day, and a randomly selected subject from the placebo group would receive an identical dose reduction. Data was then recorded every six months. This study was started in March 1998 and ran through October 2002. All eligible patients were followed until their final visit in March 2004. Overall, the two groups were similar in baseline characteristics, which included a median LDL-C level of 121 mg/dL in the atorvastatin group and 125 mg/dL in the placebo group.

The primary endpoints were cardiovascular death, fatal and nonfatal myocardial infarction, and stroke. Secondary endpoints were all-cause mortality, cardiac and cerebrovascular events. At four weeks, patients treated with atorvastatin 20 mg daily experienced decreases in LDL-C,

total cholesterol and triglycerides (TG). The mean from baseline to four weeks was significantly different in the atorvastatin group (42%). At the median follow-up of four years, there were no statistically significant changes in primary end points; 12.6% vs. 11.2% at one year and 31.9% vs. 30.5% at three years in the atorvastatin group vs. the placebo group, respectively. The most serious adverse drug reactions in this study were consistent with age and underlying medical conditions. However, the incidence of fatal stroke was significantly higher in the atorvastatin-treated group (relative risk of 2.03 95% confidence interval, 1.05-3.93; p=0.04) compared to placebo.

A number of editorials questioned the results of the 4D study, suggesting the study population selection and the use of atorvastatin was too little and too late in continuum of their underlying disease, or that the study was not powered to detect the mortality or cardiovascular event differences. In fact, 4D was powered to detect cardiovascular event benefits from the use of statins. Others suggested that the results of the 4D study were not valid because these patients were at higher risk of cardiovascular disease than the general dialysis population, since all patients had a Type 2 diabetes diagnosis with normal or low lipid levels.

The AURORA study—A study to evaluate the use of rosuvastatin in subjects on regular HD: an assessment of survival and cardiovascular events—was aimed at comparing the effects of rosuvastatin 10 mg/day vs. a placebo on cardiovascular morbidity and mortality in chronic hemodialysis patients without regard to their baseline lipid status.[4] AURORA was a double-blind, randomized placebo-controlled, multicenter trial. A total of 2,776 patients were enrolled from 25 countries. Unfortunately, AURORA included only dialysis patients between 50 and 80 years old and on dialysis for more than three months. Patients with statin use within six months, elevated liver function tests or creatinine kinase >3x upper limit of normal (ULN), or uncontrolled hypothyroidism verified by a thyroid-stimulating hormone (TSH) level >1.5x ULN were excluded. Patients initially entered a two-week screening period, and then were randomized in blocks of four in a 1:1 ratio to rosuvastatin 10mg or placebo. A total of 1,389 patients were assigned rosuvastatin 10mg/day, and 1,384 received a matching placebo. The median follow-up was 3.8 years with visits every three months during the study period. The primary end point was timed to major cardiovascular events, which included fatal and nonfatal myocardial infarction and stroke. Secondary end points included all-cause mortality, cardiovascular event-free survival, revascularization and death from cardiovascular and non-cardiovascular causes. Change in baseline lipids and high sensitivity to C-reactive protein were tertiary end points.

Baseline LDL-C levels in the rosuvastatin group was 100 mg/dL and 99 mg/dL in placebo. Overall baseline characteristics were evenly distributed among the two groups. The mean duration of study medication was 2.4 years, with a mean length of follow-up of 3.2 years. A total of 1,296 patients died during the study and another 810 patients discontinued the treatment because of adverse drug reactions or renal transplantation (a total of 2,106 patients). Within the first year, LDL-C was reduced by a mean of about 43% in the rosuvastatin group and high sensitivity C-reactive protein (Hs-CRP) decreased by 11.5% in patients taking the statin. No statistically significant changes in mortality, primary or secondary end points were observed for any treatment arms. This finding was consistent in all predefined subgroup analyses, including patients with diabetes at baseline. Combined outcome of major cardiovascular events occurred in 396 rosuvastatin groups (9.2%) vs. 405 (9.5%) in the placebo group HR 0.96 (0.84-1.11 p=0.59). The all-cause mortality rate of rosuvastatin vs. the placebo group (13.5 rosuvastatin vs. 14.0 placebo events per 100 patient-years, hazard ratio 0.96, 95% confidence interval (CI) 0.86-1.07; p=0.51) also was insignificant. No clinically important differences between the groups were observed for safety parameters; however, similar to the 4D study, an increased rate of fatal stroke (hemorrhagic stroke) was noted in the rosuvastatin arm of the study in patients with diabetes (12 in the rosuvastatin group vs. 2 in placebo group; p=0.03).

The last study is the Study of Heart and Renal Protection (SHARP). The SHARP study was a randomized controlled trial to determine the benefits of cholesterol-lowering treatment in patients with CKD and on dialysis.[5] SHARP was sponsored, designed, run and analyzed by the University of Oxford. Funding was provided by Merck/Schering-Plough, the UK Medical Research Council (MRC), British Heart Foundation and Australian National Health MRC. The trial was guided by an independent steering committee of nephrologists.

A total of 9,270 patients with chronic kidney disease (3,023 of whom were receiving dialysis) were randomized to simvastatin 20 mg/day plus ezetimibe 10 mg or a placebo. Patients with previous cardiovascular disease were excluded from this study. The median follow-up was 4.9 years. Baseline LDL-C level was 108 mg/dL for all non-dialysis CKD patients and 100 mg/dL for dialysis patients. LDL-C was reduced at one year—30 mg/dL with simvastatin 20 mg alone and 43 mg/dL with simvastatin 20 mg/day plus ezetimibe 10 mg. As in the two previous studies, baseline characteristics were

Major Atherosclerotic Events in SHARP

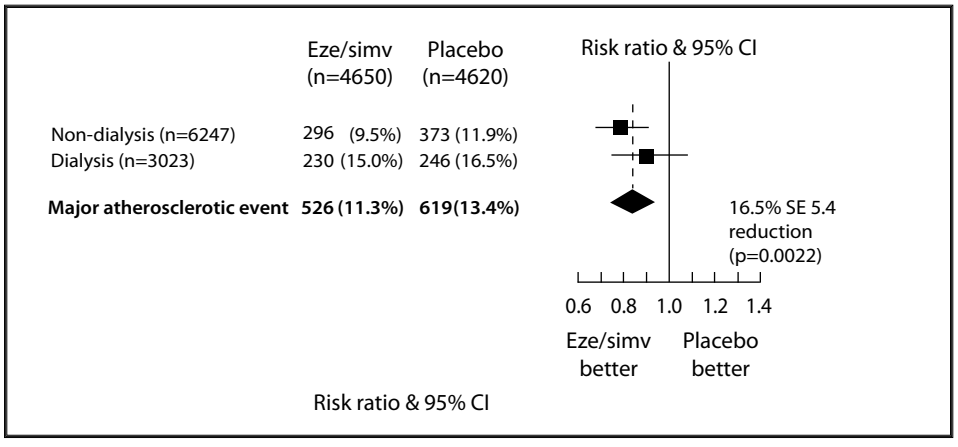

Figure 2.

evenly distributed among the two groups. The objective of the SHARP study was to investigate whether lowering LDL-C may prevent "major vascular events" (i.e. fatal or non-fatal strokes, non-fatal myocardial infarction or cardiac death, and operations to unblock arteries) or slow down the progression of CKD in non-dialysis patients with CKD. The estimated glomerular filtration rate (eGFR) for both groups was approximately 27 ml/min/1.73.

The revised primary end point was the occurrence of a major atherosclerotic event that included coronary death, myocardial infarction, nonhemorrhagic stroke or the need for revascularization procedures. Initially, patients underwent a six-week placebo trial run-in to help determine those likely to be compliant. In the first year, patients were randomized to placebo, simvastatin 20 mg plus ezetimibe 10 mg, or simvastatin tablet 20 daily. After one year, patients initially on simvastatin alone were rerandomized to placebo-combination or ezetimibe/simvastatin combination. Post-randomization follow-up was conducted at two and six months, and then biannually for at least four years. The overall result was significant for the reduction of major atherosclerotic events by 17% in the simvastatin and ezetimibe treatment arm compared to placebo [relative risk (RR) 0.83; 95% CI 0.74, 0.94, log rank P <0.002]. However, neither a clinical nor statistically significant reduction in mortality rates or cardiovascular events was observed in the dialysis population (15% vs. 16.5%). The result of the SHARP study on dialysis was similar to the AURORA and 4D studies. The number needed to treat for dialysis patients is 67 for five years to avoid one cardiovascular event. At the cost of $145 for a month of ezetimibe/simvastatin combination for five years, it costs more than $500,000 to avoid one cardiovascular event. This risk reduction can be accomplished by other methods with much less expense.

The results of the SHARP study have received a fair amount of attention in the general media. Despite the misleading recommendation in news releases, this study should not be extrapolated to the general population. In addition, the SHARP study did not compare simvastatin vs. the combination of simvastatin plus ezetimibe. This study did not shed any light on controversies related to the use of an expensive drug such as ezetimibe without any proven long-term cardiovascular benefit. Two separate studies of ezetimibe use in the past have not shown any reduction on major clinical end points compared to placebo or niacin.[6,7] Similarly, as in the two previous renal studies, SHARP was designed and powered to detect any mortality and cardiovascular events benefits from the use of lipid-lowering therapy.

Prevention of cardiovascular disease in dialysis patients requires identification of major risk factors and a reduction of global cardiovascular risk factors. Although hyperlipidemia-related cardiovascular events are important risk factors—accentuated by other risk factors and patient characteristics—most hyperlipidemia studies are sponsored by pharmaceutical companies and results have, in part, been misleading. The use of statins in dialysis patients continues to rise and the results of these studies have had very limited impact on prescribing patterns. Finally, a new meta-analysis has cast new doubt on the value of statins in primary prevention.[8,9] Taylor and colleagues reviewed 16 studies with more than 34,000 patients and reported very limited long-term benefits. This review from available randomized clinical trials did not demonstrate that aggressive lipid lowering in a low-risk patient population provided any clinical benefit compared to other patients without statin exposure.

The results of three large well-designed clinical studies indicate that statins may have a very limited role in primary prevention in dialysis patients. Therefore, three strikes and statins are out for the primary prevention of cardiovascular disease in dialysis patients. ■

Disclosure statement: Dr. Olyaei has no relevant disclosures. Dr. Lerma has no relevant disclosures.

References are listed on page 39.

Lipid Pulse Membership Survey: Who Are We?

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Any medically based organization that hopes to move forward and make a positive impact on its members needs periodically to perform a careful self-examination. Who are the members? What are its demographics? What are the practice patterns of the members? What are the perceived educational needs? What can the organization do to be more responsive to the members?

In early 2010, a team consisting of representatives from the NLA Board leadership, the NLA staff, Genzyme and Reckner/Blueberry were convened to develop a survey targeted to the membership of the NLA. Participants were recruited via an initial emailing to 2,492 active members, and the survey was timed to coincide with the NLA Annual Scientific Sessions in Chicago in May 2010.

This article summarizes key findings from that survey. A more detailed analysis is presented in a recent article in the *Journal of Clinical Lipidology*.[1]

Among the 628 respondents to the survey, there was a greater concentration of practitioners in the eastern United States compared to the western half. The observed distribution mirrored the pattern of regional chapter development, which began in the Southeast and then moved progressively to the Midwest, Northeast, Southwest and Pacific areas. About 67% of respondents were physicians, 16% were nurse practitioners and physician assistants, and 8% were pharmacists. Among physicians, 50% were internal medicine or family physicians, 32% were cardiologists, and 11% were endocrinologists. About 42% were members of a single specialty group, 36% belonged to a multispecialty group, and 22% were in solo practice. Clinical lipidology was shown to attract more established physicians, with more than 41% having spent more than 26 years and 83% at least 10 years in practice.

Questions about the lipid practice profile demonstrated than 24% worked in a lipid clinic, 33% received referrals for lipid management, and 43% identified themselves as not being lipid specialists. Among those working in lipid clinics, 39% were internal medicine or family physicians, 36% were cardiologists, and 11% were endocrinologists. Among those self-designated as lipid specialists, 34% were internal medicine or family medicine specialists, 44% were cardiologists and 15% were endocrinologists.

Among the respondents, 41% reported they were board certified, 27% were preparing for certification, and 29% were aware of but not pursuing certification. However, because only 28% of the NLA membership at that time was certified by the American Board of Clinical Lipidology, it is likely that the respondents represented a more engaged group than the general membership.

Respondents in lipid clinics spent fewer hours per week seeing patients but spent

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more time per patient than those who designated themselves as lipid consultants not working in a lipid clinic or those who were not lipid specialists. The lipid clinic clinicians and those receiving consultation for lipid disorders reported they worked with more full-time equivalent staff members than those not designated as lipid specialists.

As expected, respondents provided a variety of clinical services, including diabetes management, nutrition and exercise counseling, weight management, clinical trial participation, cardiac rehabilitation and low-density lipoprotein (LDL) apheresis. Lipid clinic practitioners generally reported that their patient volume had increased over the past year and expected that their patient volume would increase over the next three years. Two-thirds of these clinicians reported that their clinic was operating at a "break even or better" level financially. When questioned about referral sources, physicians, nurse practitioners and physician assistants working either in lipid clinics or as lipid specialists received 67% of their referrals from internal medicine specialists or family physicians, 20% from cardiologists and the rest from other physicians.

With regard to test-ordering patterns and beliefs, 90% of respondents routinely ordered a standard lipid profile. About 66% ordered C-reactive protein and half ordered apolipoprotein B, LDL particle concentration or lipoprotein(a) more than once a month. Genetic testing for familial hypercholesterolemia was ordered by 9% of those practicing in lipid clinics and 3% of other respondents. Lipid clinic practitioners rank-ordered lipid parameters most predictive of cardiovascular risk as: high-density lipoprotein (HDL) cholesterol, non-HDL cholesterol and apolipoprotein B (tie), LDL cholesterol, lipoprotein particle concentration and C-reactive protein.

The five topics identified as being of the greatest educational interest included statin intolerance, strategies to improve compliance with therapy, the metabolic syndrome, lipoprotein particle concentration, and non-HDL cholesterol or apolipoprotein B concentration. The educational sources that were most valued included the *Journal of Clinical Lipidology* (45%), the *New England Journal of Medicine* (23%), the *Lipid Spin* (20%), the *Journal of the American College of Cardiology* (20%), *Circulation* (16%) and the *Journal of the American Medical Association* (10%). The most popular conference preferences included the NLA conferences and the American Heart Association and American College of Cardiology annual meetings. The most popular websites were the NLA website (www.lipid.org) and the *New England Journal of Medicine* (www.nejm.org).

Respondents tended to attribute the greatest value in their membership to NLA-related education, certification and the *Journal of Clinical Lipidology*. More than 95% reported a desire to continue their membership and promote it to colleagues. More than half requested enhancement of educational conferences and increased use of web-based activities.

In summary, the 2010 NLA Lipid Pulse Membership Survey provided a robust sampling of an involved and diverse membership whose identity is being more clearly defined and whose professional and educational needs are being actively served by the parent organization. The NLA will use this information to continue to be perceived as a vibrant and responsive organization that works for the benefit of its membership. ■

Disclosure statement: Dr. Orringer has no relevant disclosures.

References are listed on page 39.

Member Spotlight:
Hormones and Lipid Therapy—Taking A Full-bodied Approach

JANET L. MAXSON, PhD, NP, FAHA, FNLA
Minot Health and Wellness
Minot, ND

Unfortunately, few women understand the impact of hormones and hormone therapy on their lipid profiles.

Janet Maxson, PhD, NP, does. She uses hormone replacement therapy questions as an opportunity to diagnose and treat lipid disorders—ranging from those who may be affected by aromatase inhibitors, used for breast cancer prevention, to other primary dyslipidemias like diabetes and the cardiometabolic syndrome at menopause transition.

"Studies have shown that insulin sensitivity improves with estrogen use," Dr. Maxson said, noting that the most enjoyable part of her job is teaching women patients about their health and seeing that this makes a difference in their health risk factors.

Dr. Maxson starts her CVD risk assessment using the Framingham Risk Score or the Reynolds Risk Score tools.

"I review their past lipid profiles, current medications, and then discuss the guidelines for lipid management. The next step is managing their menopausal symptoms and customizing their hormone therapy," she said.

Peri-menopause makes up the largest percentage of her patient base. The majority of patients are in their mid-40's to their 70's.

She became interested in lipids in the 1990's, at a time when there was little concern about women's cardiac risk. A major educational campaign introduced lipid training clinics and drew attention to gender-specific health issues.

While awareness has grown considerably since the 1990's, Dr. Maxson said the biggest misconception she faces is that most women fear their risk of developing breast cancer more than their risk for developing CVD. This is in spite of the "Go Red" Campaign by the American Heart Association in an attempt to increase awareness that heart disease is the No. 1 killer for women.

Dr. Maxson likens women understanding their own risk for CVD to a phenomenon described by Nanette Wenger, MD, of Emory University as a *bikini approach*: "looking essentially at the breast and reproductive system, and almost ignoring the rest of the woman, as part of women's health."

Diagnosing risk for the cardiometabolic syndrome in peri-menopausal women offers an opportunity to improve their health before they have progressed into overt CVD.

"The impact on their awareness levels increases when I take out my tape measure to measure their abdomen at the level of the iliac crest to show them they are above 35 inches. This helps them understand that some of their risk is reflected by

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Go to *"Topics/Lipid Spin Summer 2011"*
and look for *"Member Spotlight."*

increased abdominal circumference," she said.

She receives referrals from cardiologists who send their patients for hormone and lipid evaluations after diagnostic procedures and interventions.

"People come in for hormone therapy because it affects their quality of life," Dr. Maxson said. "It's less of a risk factor than CVD, but it presents an excellent opportunity to teach about risk factors for their heart health." ■

Member Update

Gustav Schonfeld, MD, the Samuel E. Schechter Professor and former head of the Department of Medicine at Washington University School of Medicine passed away in May 2011 at Memorial Sloan Kettering Cancer Center in New York City. He was "the quintessential physician-scientist, taking observations made with genetically engineered mice and translating them in ways most likely to improve the lives of patients with a host of disorders, including heart disease, hyperlipidemia and fatty liver," said Larry Shapiro, MD, dean of the Washington University School of Medicine. "He was a person of consummate integrity and wisdom."

Joshua Liberman, MD*, recently was named the Medical Director for the Women's Heart Program of the Columbia-St. Mary's Hospitals system in Milwaukee.

Biofortis-Provident has promoted **Mary Dicklin, PhD**, to Associate Director of Medical Writing. A lead scientist who specializes in dietary lipid management, Dr. Dicklin has been with the company since 2006 and has more than 15 years of clinical/medical writing experience.

Randy Orsborn, MPAS, PA-C, CLS, recently was selected for advancement to Associate of the American College of Cardiology (AACC) status with the American College of Cardiology.

A website that discusses primary and secondary prevention of atherothrombotic disease (ATD) is maintained by **W.E. Feeman, Jr., MD**, and includes all of his presentations and publications. To access the website, please visit www.bowlinggreenstudy.org.

Joel Kahn, MD, recently accepted a new position as Medical Director of Preventive Cardiology and Medical Director of Cardiac Rehabilitation at the Detroit Medical Center Cardiovascular Institute. He also will be serving as Clinical Professor of Medicine for the Wayne State University School of Medicine.

A comprehensive lipid clinic recently was launched at the Omaha Veterans Affairs Medical Center by **Sudha Ravilla, MD***. The clinic aims to aggressively lower risk for cardiovascular disease in a high-risk population, with a particular focus on patients with the metabolic syndrome.

CoraLynn Trewet, PharmD MS, FNLA, was named Iowa Distinguished Young Pharmacist of the Year and promoted to Associate Professor (Clinical) at the University of Iowa. She also received the New Investigator Award from the American Association of Colleges of Pharmacy.

The American Heart Association chose **Lynne Braun, PhD, CNP, CLS, FNLA**, to receive its Healthcare Volunteer of the Year Award.

Michael Davidson, MD, FNLA*, served on a *U.S. News & World Report* expert panel to help develop its first-ever Best Diets rankings, which were released in June.

Malec Mokraoui, MD*, was named "Physician of the Year" by Provena United Samaritans Medical Center.

Martha Gulati, MD, recently joined The Ohio State University Medical Center as the Sarah Ross Soter Chair in Women's Cardiovascular Health and Section Director for Preventive Cardiology and Women's Cardiovascular Health. She also will be part of the OSU Cardiovascular Risk Reduction and Lipid Clinics (CRRLC) with **Scott Merryman, MD***, and **John Larry, MD**. The CRRLC is directed by **Dr. Merryman** and its pharmacists include **Mel Baughman, PharmD; Margie Hevezi, PharmD, CLS; Andrea Hirsch, PharmD; Ginny Mitchell, PharmD; Maria Pruchnicki, PharmD, CLS**; and **Melissa Snider, PharmD, CLS**.

Patrick Moriarty, MD, of the University of Kansas Medical Center, has been named the President of the International Society for Apheresis (ISFA).

News and Notes

New *Journal of Clinical Lipidology* Impact Factor

The *Journal of Clinical Lipidology* received its new impact factor of 1.467 in June 2011. This is a slight increase from its inaugural impact factor of 1.462 announced in June 2010. The NLA wishes to thank the Editor-in-Chief, **Virgil Brown, MD, FNLA*,** for all of his efforts to develop and grow the *Journal*. The *Journal* currently is only able to accept 50% of submissions. While the quality of papers is improving, the acceptance rate is falling due to an increase in submissions. Dr. Brown would like to thank the Editorial Board for its dedication and work, which has caused a growing interest in the *Journal* by authors from all over the world.

Member Benefits

The NLA offers great member benefits, including:

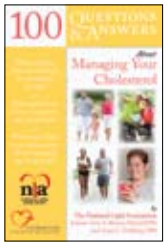
- The NLA PQRIwizard℠, a simple and cost-effective online tool to collect and report quality measure data under the CMS PQRI 2011 incentive payment program;
- Discounts on ADP services, which can reduce administrative burdens with outsourced human resources; and
- Discounts on LifeLock® Identity Theft Protection Services.

To access these member benefits, please visit **lipid.org/members** and click on the options on the left-hand menu bar.

Ask Colleagues to Join the NLA

The NLA is a young and dynamic organization and we thank you for your membership. Together we have accomplished much in our short 10 years, but we need your help to continue growing and expanding the field of Clinical Lipidology. Take a few minutes to talk to your colleagues about NLA and the value of membership. For additional information, please visit **lipid.org/join.**

100 Q&A Book Project



The Foundation of the NLA and the NLA partnered on a book project, *100 Questions & Answers About Managing Your Cholesterol*, which will be available in early September. The book will be available on the Amazon and Barnes & Noble websites, as well as at a discounted rate on the NLA Bookshelf at lipid.org. Thanks to **Vera Bittner, MD, FNLA***, and **Anne Goldberg, MD, FNLA***, and all of the authors for their work on this project.

NLA Web Tutorials

The NLA has produced tutorial videos to help members become familiar with the Community features on lipid.org. To watch a tutorial or suggest new tutorial topics, please visit **lipid.org/help.**

CAC Vets Consumer Survey

The Consumer Affairs Committee (CAC) and officers from the NLA Board of Directors recently reviewed a large-scale consumer survey focusing on statin adherence. The survey is expected to commence in August 2011 through a third-party vendor and survey results will be available to the NLA. Stayed tuned for more details.

Help Publicize Our New FH PSA

Help the Foundation of the NLA distribute its important message about Familial Hypercholesterolemia (FH) by including

the FH PSA on your personal and professional websites, as well as on your social media profiles. For a complimentary code to add the video to your website, or if you have a strong relationship with local media, please contact Amy Waller, Sr. Communications Manager for the NLA, at awaller@lipid.org.

Lipid Spin Support

Thanks to **Wayne Warren, MD, FNLA***, for helping to review articles for this issue.

NLA Staff Corner

Chris DeVille joined the National Lipid Association in May as an Education Program Manager. He brings 14 years of experience in training and development, event coordination, and project management. Prior to joining the NLA, Chris served as a Program Manager for Blue Cross Blue Shield of Florida, where he developed the company's first online training library of non-CME courses to keep healthcare practitioners up-to-date on the latest health care information. Chris earned his bachelor's degree in Education and Development from Southern Illinois University in 2001.

Education and Meeting Update

International Update

Best of the NLA 2011

Back by popular demand is the "Best of the NLA" which will take place in Delhi and Hyderabad, India, this September. Program volunteers include **George Bakris, MD, Kris Vijay, MD, FNLA*,** and **Allan Sniderman, MD***, to represent the NLA along with the co-chair of the International Committee, **Michael Davidson, MD, FNLA***. These speakers will present selections from the 2011 Annual Scientific Sessions.

Australian Atherosclerosis Society

In 2012, the NLA and the Australian Atherosclerosis Society (AAS) will collaborate on a program about Familial Hypercholesterolemia and genetic dyslipidemias at the International Symposium on Atherosclerosis in Sydney, Australia.

Polish Lipid Association

The NLA is pleased to announce our endorsement of a new international liaison, the Polish Lipid Association. The new organization is spearheaded by **Maciej Banach, MD**, from the Medical University of Lodz, Poland. The NLA will be represented at their inaugural meeting this September in Warsaw, Poland, and will present "NLA and PoLA: A Model of Global Cooperation."

2011 Annual Scientific Sessions

The 2011 NLA Annual Scientific Sessions in New York City was our largest meeting to-date, with 700 attendees. View sessions slides and audio highlights at **lipid.org/sessionshighlights.**

Cardiovascular Risk Prevention Symposium Highlights

The American Society for Preventive Cardiology (ASPC), American Society of Hypertension (ASH) and the NLA convened a Cardiovascular Risk Prevention Symposium in conjunction with the ASH and NLA Annual Scientific Sessions. Visit **aspconline.org** to view and listen to presentations from nationally-recognized thought leaders as they provide insight into the evolving healthcare landscape and its potential impact on cardiovascular risk prevention.

Tune in to Lipid Insights Webcasts

The next Lipid Insights webcast will feature moderator and speaker **Kevin Maki, PhD, CLS, FNLA**, along with **Christopher Gardner, PhD**, discussing "Dietary Approaches to Weight Management: Efficacy and Metabolic Effects." This CME-CE certified activity will take place on **Tuesday, September 20 at 7 p.m. EDT**. Please visit **lipid.org** in late August to register. To view our previous webcast featuring moderator **Anne Goldberg, MD, FNLA*,** along with presenters **Samuel Gidding, MD,** and **Paul Hopkins, MD*,** synthesizing the NLA's FH recommendations and providing clinical guidance, please visit **lipid.org/lipidinsights** (no CME\CE credit provided for archived activities).

NLA-SAP Update Available

An updated version of the NLA's 4-volume set of self-assessment exam books became available this month. You may order the 2011 NLA SAP Update online at **lipid.org/sap**. Thanks to our Chair**, Carl Orringer, MD, FNLA***, and faculty reviewers, **Harold Bays, MD*, Vera Bittner, MD, MSPH, FNLA*, Joseph Saseen, PharmD, CLS, FNLA**, and **Peter Toth, MD, PhD, FNLA***. If you have questions, please call the NLA office at (904) 998-0854 or e-mail CME@lipid.org.

CLM-SAP Edition #14: Evaluation and Management of Familial Hypercholesterolemia

The CLM-SAP Edition #14: Evaluation and Management of Familial Hypercholesterolemia provides a comprehensive, interactive self-assessment that will strengthen and reinforce your knowledge of the most clinically relevant, evidence-based medicine related to FH. Edition #14 of the CLM-SAP is sponsored by the NLA for 3.0 *AMA PRA Category I Credits*™ and for CE Credit. You may order NLA CLM-SAP Edition #14 online at **lipid.org/sap**.

2012 Save the Dates

NLA Clinical Lipid Update—Spring
Hosted by the Midwest Lipid Association and the Pacific Lipid Association
March 9–11, 2012
Hilton Bayfront
San Diego, CA

NLA 2012 Annual Scientific Sessions
Hosted by the Southwest Lipid Association
May 31–June 3, 2012
JW Marriott
Scottsdale, AZ

NLA Clinical Lipid Update—Fall
Hosted by the Southeast Lipid Association and the Northeast Lipid Association
September 14–16, 2012
Charlotte Westin
Charlotte, NC

ABCL and ACCL Leadership

The **American Board of Clinical Lipidology (ABCL)** and **Accreditation Council for Clinical Lipidology (ACCL)** are independent certifying organizations that have developed standards and examinations in the field of Clinical Lipidology for the growing number of physicians and allied health professionals who are involved in lipid management. Both groups aim to reduce morbidity and mortality from dyslipidemia and related diseases by assessing qualifications and certifying knowledge in Clinical Lipidology.

The ABCL wishes to recognize **John Guyton, MD, FNLA***, who recently ended his term as President, and congratulates the new officers, effective May 2011: **Anne Goldberg, MD, FNLA* (President); Eliot Brinton, MD, FNLA*; Ernst Schaefer, MD, FNLA*; and Wm. James Howard, MD, FNLA***.

The ACCL wishes to recognize **Carol Mason, ARNP, CLS, FNLA**, who recently ended her term as President, and congratulates the new officers, effective May 2011: **Ralph La Forge, MSc, CLS, FNLA (President); Barbara Wiggins, PharmD, CLS, FNLA; Joseph Saseen, PharmD, CLS, FNLA;** and **Lynn Cofer-Chase, MSN, RN, CLS, FNLA**.

For the complete listing of the Board of Directors, visit the ABCL website at **lipidboard.org** and the ACCL website at **lipidspecialist.org.**

**indicates ABCL Diplomate status*

ABCL and ACCL-CLS Testing Windows

Fall 2011
October 10–November 25, 2011
(Application Deadline: September 16, 2011)

Spring 2012
April 16–May 25, 2012
(Application Deadline: April 2, 2012)

Summer 2012
July 19–August 31, 2012
(Application Deadline: July 2, 2012)

Fall 2012
October 22–December 7, 2012
(Application Deadline: October 9, 2012)

The ACCL Basic Competency in Clinical Lipidology exam is offered year-round.

Young Investigator Award:

Electronic Medical Record Chart Review of a Multispecialty Internal Medicine Practice Evaluating Appropriate Identification of Patients with Familial Hyperlipidemia

By Lourdes Gonzalez-Santos MD, and James Underberg MD, FNLA

Objectives/Purpose

Early detection of heterozygous familial hyperlipidemia (HeFH) is crucial in prevention of cardiovascular disease. Affected individuals are at increased risk for cardiovascular events compared to age-matched healthy controls. HeFH diagnosis leads to screening of similarly affected relatives. Existing data suggests this condition is under diagnosed. We conducted a chart review of a university based outpatient internal medicine practice to evaluate appropriate identification of patients with HeFH.

Methods

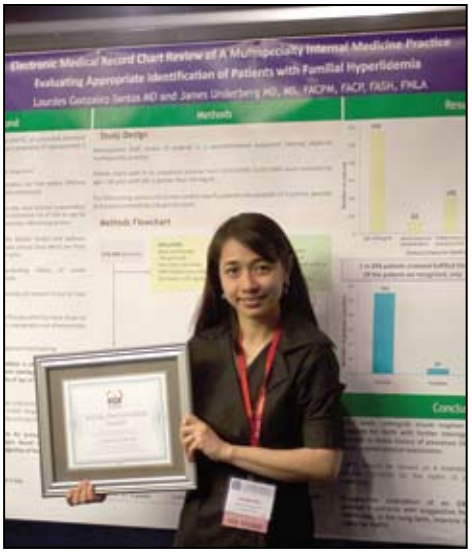
Patient charts seen in an outpatient practice from 12/31/1999-12/31/2009 were screened for age >18 years with LDL-C greater than 195 mg/dL. These were then screened with the search terms "coronary artery disease premature," "family history of ischemic heart disease," "cerebrovascular disease family history," "peripheral vascular disease" and "familial hypercholesterolemia." Clinical notes were reviewed for documentation of family and personal history of premature coronary disease (CAD), elevated LDL-C, personal history of premature CAD or peripheral vascular disease (PVD). Physical exam findings of xanthoma and arcus cornealis were sought. The Dutch Lipid Network (DLN) Clinical Criteria scoring system criteria was used to classify patients into probable (3-5 points), possible (6-8 points) and definite (>8 points) HeFH. Patients with secondary causes of LDL-C elevations (nephrotic syndrome, chronic renal failure, steroid and anti-retroviral therapy) were excluded.

Results

Of 176,363 patients: 552 possible, 42 probable and 2 definite HeFH patients were classified. One in 294 patients screened fulfilled the clinical criteria for possible HeFH. Of the patients we recognized, only 0.5% were correctly identified.

Conclusion

LD-C levels >195mg/dL should heighten physician suspicion for the diagnosis of HeHF and induce further interrogation into personal or family history of premature CAD or PVD and a targeted physical examination for stigmata of hyperlipidemia. This analysis supports data regarding under diagnosis of HeFH and suggest a prospective evaluation of an EMR based prompt could show improved diagnosis rates for HeFH. ■



Dr. Santos, a cardiovascular prevention Fellow at the NYU Langone Medical Center, received the Young Investigator Award during the 2011 Annual Scientific Sessions. She hopes to return to the Philippines in 2012 as the country's first Diplomate certified by the American Board of Clinical Lipidology.

Foundation Update

FOUNDATION
of the National Lipid Association

ANNE C. GOLDBERG, MD, FNLA
President, Foundation of the National Lipid Association

Associate Professor of Medicine
Washington University School of Medicine
St. Louis, MO

Diplomate, American Board of Clinical Lipidology

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Discuss this article at **www.lipid.org**
Go to *"Topics/Lipid Spin Summer 2011"*
and look for *"Foundation Update."*

Dear Colleagues,

Thank you for your support during the launch of the Foundation of the NLA's first campaign, "FH: It's Relative—Know Your Cholesterol History" during Annual Scientific Sessions this past May. Together, we have moved the prevalent but practically unknown genetic disorder of Familial Hypercholesterolemia (FH) towards national attention.

In addition to publishing the *only* major FH recommendations paper in the United States in the *Journal of Clinical Lipidology*, we worked with the NLA's educational division to develop a special FH supplement and self-assessment program (see page 32 of this *Lipid Spin* for more details) to increase awareness and knowledge of the disorder among practitioners. Our recommendations paper was endorsed by the American Society of Preventive Cardiology, the Association of Black Cardiologists, the International Cholesterol Foundation, and the Preventive Cardiovascular Nurses Association, and it also served as the framework for the national, multifaceted FH campaign.

The FH campaign incorporated major educational components, including presenting topics from the FH recommendations paper to the more than 700 attendees at the NLA's 2011 Annual Scientific Sessions, recording five audio features on FH topics for the ReachMD station on XM Satellite Radio, producing special CME/CE webinars on the topic, and creating an online resource library for healthcare practitioners.

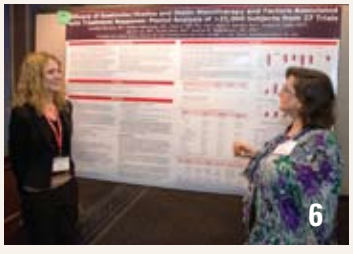
Additionally, the campaign featured a major public awareness initiative that included the creation of an FH tear sheet for patients, the development of a patient-friendly website, a series of ads on the Yahoo! Ads Network that have garnered *more than six million impressions*, a live satellite broadcast media tour, coverage in more than 260 media outlets, and a public service announcement that has aired more than 160 times nationwide since July 2011. We also organized and led a special conference in Boston with more than a dozen FH patients and their families to talk about how FH has affected their lives and how practitioners can improve awareness and management of the disorder.

Without question, the estimated *600,000 Americans* who have FH will see their health and quality of life improved as a result of the Foundation's efforts, which will also benefit future generations.

You can help us spread the message by including the FH PSA on your professional and personal websites, as well as on your social media profiles. To receive your complimentary code to embed the video on your website, or if you have a strong relationship with local media, please contact Amy Waller at awaller@lipid.org.

I encourage you to stay involved by making a donation at **lipidfoundation.org/donors/donate** or by joining a Foundation committee. To learn about volunteer opportunities, please contact Chris Seymour at cseymour@lipid.org. Thanks again for your support. Together, we are accomplishing great things. ■

Snapshot:
2011 Scientific Sessions in New York City



Snapped during the 2011 Annual Scientific Sessions in New York City were 1.) Michael Davidson, MD, presenting the President's Service Award to Thomas Dayspring, MD; 2.) Virgil Brown, MD, presenting the Distinguished Achievement Award to Antonio Gotto, Jr., MD, DPhil; 3.) Attendees at the sessions; 4.) Board members from the Accreditation Council for Clinical Lipidology (ACCL); 5.) Christie Ballantyne, MD, being interviewed by Alan Brown, MD, for the Lipid Luminations show on ReachMD; 6.) Presenters at the poster session; 7.) An attendee scoping out the NLA's booth; and 8.) An attendee commenting during the Q&A session following a talk.

More photos from the 2011 Annual Scientific Sessions are posted at lipid.org/newcommunity/slideshows.php.

International Update:
Message from Diplomate Abroad

Some years ago, a lipidologist came to talk with me about statins. I was quite intrigued as I did not know much about lipidology. That meeting actually introduced me to lipidology, and after many meetings and lectures, my understanding was better about the subject and I pursued it. Today, I still feel it was the one of the best decisions I have made. Lipidology provided great insight into the complicated mechanisms of atherosclerosis and I am very proud of being a Diplomate of the American Board of Clinical Lipidology.

I always had a desire to return to India and provide free care, especially after hearing about how many Indians have cardiac problems.

I repatriated to India in October 2009 and started my free care clinic. After some time I realized there was not much attention given to preventive cardiology. I tried discussing my ideas with cardiologists and it appeared that they were more keen on treatment aspects than working on the preventive side, as they had not had much exposure to lipidology.

So I started conducting free camps where we visit different rural and urban areas to talk about about cardiovascular disease (CVD) and how to prevent future complications.

To date, I have screened more than 5,000 people for diabetes and high blood pressure. Once we identify individuals with risk factors, we contact them and provide free consultations about the prevention and management of CVD. So far, the reception has been very good and people are beginning to understand the value of prevention.

I think India needs serious help to increase awareness of chronic diseases and methods of prevention, especially in the rural village areas. As an organization, the NLA can help to increase awareness about lipidology and prevention of cardiac problems.

Thank you for this opportunity to share my adventures and experiences in India.

Sincerely

Ashok Sonnad, MD
Diplomate, American Board of Clinical Lipidology
ashoksonnad@gmail.com

Events Calendar

2011 Meetings

Conference of Polish Lipid Association
September 9–10, 2011
Warsaw, Poland

The Obesity Society's Annual Scientific Meeting
September 30–October 5, 2011
Orlando, FL

Third Annual Orange County Symposium
October 22, 2011
Anaheim, CA

AOA/OMED Osteopathic Medicine Conference
October 30–November 3, 2011
Orlando, FL

World Congress on Insulin Resistance
November 3–5, 2011
Hollywood, CA

AHA Scientific Sessions 2011
November 13–15, 2011
Orlando, FL

2012 NLA Meetings

NLA Clinical Lipid Update—Spring
Hosted by the Midwest Lipid Association and the Pacific Lipid Association
March 9–11, 2012
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Scottsdale, AZ

NLA Clinical Lipid Update—Fall
Hosted by the Southeast Lipid Association and the Northeast Lipid Association
September 14–16, 2012
Charlotte Westin
Charlotte, NC

2012 Meetings

Cardiovascular Disease Prevention 2012: Tenth Annual Symposium
February 23–26, 2012
Miami Beach, FL

AHA EPI/NPAM Sessions 2012
March 12–16, 2012
San Diego, CA

American College of Cardiology (ACC) i2 Summit 2012
March 24–27, 2012
Chicago, IL

XVI International Symposium on Atherosclerosis (ISA)
March 25–29, 2012
Sydney, Australia

PCNA 18th Annual Symposium: "Cardiovascular Risk Reduction: Leading the Way in Prevention"
April 12–14, 2012
National Harbor, MD

ASH Annual Scientific Meeting & Exposition 2012
May 19–22, 2012
New York, NY

AACE 21st Annual Meeting
May 23–27, 2012
Philadelphia, PA

80th European Atherosclerosis Society (EAS) Congress
May 26–29, 2012
Milan, Italy

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It's your NLA Community...

Participate in the conversation online at www.lipid.org/topics.

Excerpt from the "*Lipid Spin* Article Discussion" thread:

"Understanding the drug interactions and mechanisms of statin induced myopathy are important to contemporary practice."
—Ken Kellick, PharmD

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Editor's Corner References

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FOR YOUR PATIENTS

Advanced Lipid Testing

WHAT YOU NEED TO KNOW

What is Advanced Lipid Testing?

Advanced lipid testing may be recommended by your healthcare provider to optimize your cholesterol treatment. Advanced lipid tests are performed because standard cholesterol tests may not completely represent cholesterol-related risk for heart attacks and strokes. Some people—especially people with diabetes, insulin resistance, or cardiovascular disease—continue to have progression of cardiovascular disease, even when their low-density lipoprotein (LDL) cholesterol is at goal.

Advanced lipid testing is usually performed in addition to a standard cholesterol test or "lipid panel," which measures total cholesterol, LDL cholesterol, high-density lipoprotein (HDL) cholesterol and triglycerides. Two commonly used advanced lipid tests are apolipoprotein B (apoB) and LDL particle number (LDL-P).

How are advanced lipid tests performed and how often should I have testing?

ApoB and LDL-P are both simple blood tests and do not require fasting. Advanced lipid testing is offered at many labs and also may be available at your healthcare provider's office. Insurance coverage can be discussed with your healthcare provider and insurance company. Some providers recommend advanced lipid testing at the initial visit and intermittently throughout treatment. Some providers recommend advanced lipid testing after you have successfully achieved your LDL cholesterol and non-HDL cholesterol goals.

What are good results and how do I achieve them?

As with standard cholesterol testing, your healthcare provider may recommend a specific target number based on your risk factors. As with cholesterol goals, advanced lipid goals are reached through a combination of healthy lifestyle and cholesterol-lowering medication.

How are advanced lipid tests different from regular cholesterol tests?

Cholesterol is carried in lipoprotein particles. Advanced lipid tests can be useful because some people do not have a lot of LDL cholesterol, but they have a lot of LDL particles. This can occur when they have mostly small particles or, alternatively, particles that contain less cholesterol per particle. A higher number of these lipoprotein particles make it easier for them to invade the walls of the arteries and induce a series of events that can lead to plaque formation.

The LDL particle number measures the actual number of LDL particles that carry LDL cholesterol per liter of plasma. In addition to the number of LDL particles, advanced lipid tests report the size of these LDL particles, which may help your provider diagnose the cause of your cholesterol abnormality. For example, increased numbers of small, dense LDL particles can be caused by insulin resistance, a condition that raises your risk for developing diabetes. Understanding this information will help your healthcare provider utilize the right combination of diet and drug therapy to prevent onset or progression of disease.

The apoB test measures the concentration of lipoprotein particles that have an apolipoprotein B on their surface. All of the particles that have the potential to cause disease are labeled with one molecule of apo B. ApoB, like LDL-P, can be a better measure of risk than LDL cholesterol in certain people.

Name:_____ Date:_____ Health Care Provider:_____

LDL Goals:_____ Weight Loss Goals:_____

Activity/Exercise Goals:_____

Medications Recommended:_____

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