

Official Publication of the National Lipid Association

# LipidSpin

## pot·pour·ri

noun /,pou pu'ri:/

1. a mixture of dried flower petals, leaves, and spices that is used to make a room smell pleasant
2. a collection of different things<sup>1</sup>

■ **Special Freelance Edition Featuring:**  
Current Initiatives for Detecting Patients with  
Familial Hypercholesterolemia in Primary Care

1. [merriam-webster.com/dictionary/potpourri](http://merriam-webster.com/dictionary/potpourri)

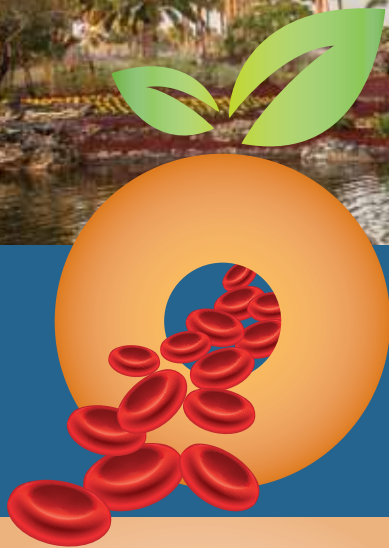
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\*indicates ABCL Diplomate status

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# From the NLA President:

## Update on NLA Initiatives



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I'm happy to give you an update on an important initiative the NLA and its partners are pursuing to kick off 2014.

Just more than a month ago the National Lipid Association submitted a proposal to the National Center for Health Statistics (NCHS), the federal agency responsible for revising the ICD codes, to create new, specific ICD-10 codes for familial hypercholesterolemia (FH). This includes homozygous FH and heterozygous FH. The NLA worked collaboratively with The FH Foundation to draft this proposal that we hope will have a profound impact on the diagnosis, treatment, and research of FH.

Although there are ICD codes in place for many other genetic diseases, there has never been a specific ICD code for FH. The lack of a specific ICD code has greatly hampered clinicians' ability to collect data, identify FH patients and implement cascade screening efforts, and obtain non-preferred and non-formulary lipid-lowering

pharmacotherapy for patients. The recognition that a patient has a specific genetic disorder makes it more likely that aggressive treatment can be justified and provided.

The ICD-10 Coordination and Maintenance Committee will review this proposal and, if approved, it would go into effect on October 1, 2015. The committee will release its decision on the proposal in June, and I hope the NLA has good news to share at that time.

Speaking of FH, the NLA Annual Scientific Sessions "**New Era in Lipidology: Familial Hypercholesterolemia, Guidelines and Risk Assessment in the Clinic,**" hosted by the Southeast Lipid Association are fast approaching. The sessions will be held May 1-4, 2014 at the Hyatt Regency Grand Cypress in Orlando, FL. This will be a very informative and interactive session with international experts from the US and other countries. We hope you take advantage of the early bird rate of \$550 for NLA members, available until March 12. See the "Education and Meeting News and Notes" in the back of this issue of Lipid Spin for more information about this year's meeting.

I hope to inform in the very near future you about other exciting initiatives the NLA has taken on. Take care and I hope to see you in Orlando. ■

### Membership Renewal

You should have received your NLA dues renewal notice in the mail recently (unless of course you are a Lifetime Member!). **In order to continue to receive all the great benefits that NLA has to offer with no interruption, renew by March 31.** To pay your dues online, update your profile and to participate in our member needs survey visit [lipid.org/about/dues](http://lipid.org/about/dues).

Pay your dues by March 31 to avoid this being your last issue of *LipidSpin*!

# Letter from the *Lipid Spin* Editor: Lipidology is not “Other-ology” – Can Social Media Help?

**JAMES A. UNDERBERG, MD, MS, FACPM, FACP, FNLA**  
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*Diplomate, American Board of Clinical Lipidology*

The field of Clinical Lipidology is growing slowly. Each year new members of the National Lipid Association are approved, and every year some of them choose to pursue training and certification pathways via the ACCL and ABCL. Many of our members have an interest in lipidology, but may spend most of their time in other specialties such as Internal Medicine, Cardiology, Family Practice, Endocrinology, Pediatrics, Ob/GYN or Osteopathy just to name a few. Others practice Lipidology as their primary vocation. They may direct lipid clinics, research programs or teaching & education programs in lipidology. The NLA, the ABCL and ACCL along with a growing number of health care practitioners interested in Lipidology have all increased awareness about this specialty. Recognition, for our field both by patients and colleagues, however remains stubbornly low.

How do I know this? Observational (shudder) data! Simply go on line and sign up for a medical website. When faced with a drop down menu asking for area of specialty, lipidology is often absent. Rather than being a lipidologist, I often feel like an “other-ologist.” We are facing an identity crisis; all too often letting others categorize and describe us.

I believe it is only through our own bully pulpit that we can make others aware of who and what we are. Social media is a wonderful

tool to help us — if used properly and appropriately.<sup>1</sup> Where else can someone “self-proclaim” their own expertise and receive immediate validation by others? Why wait for others to recognize and promote our cause? We can do this ourselves. Social media offers a wonderful chance to tell others who we are, what we do, and, most importantly, engage the reader in the process.<sup>2</sup>

Practice patterns have changed, and so have referral patterns. Patients no longer wait for primary providers to refer them to specialists. They read about illness online; they find specialists no longer through work or family networks, but instead they use online communities, chat rooms, web sites and search engines.<sup>3</sup> If we want to provide our expertise for the benefit of patients in need of our services, we need to let those looking for us know that we are here.

But wait, does this mean we should all take to Twitter, Facebook, Instagram, and reduce our message to 140 characters? Of course not! I believe we cannot hide our collective heads in the sand! For those inclined using social media in a responsible way improves overall online visibility via search engines and makes others take notice.

The next time “Lipidology” is absent from a drop down message, send an email to their Webmaster, or even better, post your



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thoughts online! Given the social media mandate to engage and respond, results can and do occur. Just recently, a company that does online scheduling reached out to me. They were hoping to start a dialogue with our group. When I noticed that lipidology was not a choice for specialty for them, I told them not to waste my time. Within 24 hours it was added to the menu.

Collectively we can choose to be ignored, or we can choose to be recognized. Wonderful tools currently exist that enable and engage both the layperson and the expert professional. No tool can function if not utilized properly. By understanding and embracing the roles these social media and online communities play, patient referrals can increase and most importantly, patient care will improve.<sup>4,5</sup>

This, in turn will advance our mission to improve awareness and recognition of our valued and chosen field of Clinical Lipidology. ■

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# Letter From the *Lipid Spin* Editor: Potpourri



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**Potpourri** /,pou pu'ri:/ is a mixture of dried, naturally fragrant plant material, used to provide a gentle natural scent inside buildings, most commonly in residential settings. It is usually placed in a decorative (often wooden) bowl, or tied in a small sachet made from sheer fabric.

Potpourri is used inside the home to give the air a pleasant smell. The word “potpourri” comes into English from the French word “pot-pourri.” The French term has two connotations. It is the French name for a Spanish stew with a wide variety of ingredients called “olla podrida,” specialty of the town of Burgos. The word was taken and copied by the French military during the Napoleonic occupation of Burgos (1808-1813). Literally, however, the word “pot” in French has the same meaning as it does in Spanish and English, while the word “pourri” means rotten. In English, “potpourri” is often used to

refer to any collection of miscellaneous or diverse items.<sup>1</sup>

This edition is so named because we are providing a hodgepodge of important opinions, facts, viewpoints, burning issues and anecdotes to our readers. We have had so many requests for publication that we had to make difficult choices. If your article did not get in bear with us. The NLA plans to continue to publish yearly a Potpourri edition.

Routinely we focus with the expressed desire to target matters of currency and importance to the clinical lipidologist. We rotate by region and this adds representation and fairness and currency for all of our constituency. In this instance we are publishing peer-reviewed articles without respect for region. We are publishing with strong respect to differences of opinion and the desire that the clinician practicing in lipidology gets a flavor of how their colleagues think.

The NLA does not necessarily endorse some of the opinions presented in this edition. What the NLA does however is

sponsor a forum for the written word to be seen.

We invite each of you to think outside the box. If, however, you meet with resistance we suggest that this is good. Growth comes from diversity of opinion and this leads to further insight. So we hope you read this edition with this spirit in mind.

We thank the NLA for sponsoring this extra edition. We thank the board for providing a forum for people to be heard.

In this era of evidenced-based practice we applaud every effort to encourage practice based on best evidence. We also recognize that every patient we see is not average. Unique circumstances are the rule and we all have to think outside the box to best serve the patients we are entrusted to serve. ■

1. <http://en.wikipedia.org/wiki/Potpourri>

# Current Initiatives for Detecting Patients with Familial Hypercholesterolemia in Primary Care

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## Abstract

Databases of primary care practices and pathology providers in Queensland and South Australia were screened using variable cut-off levels for total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) to detect patients with possible familial hypercholesterolemia (FH). Over a 12-month period, 1,728,805 lipid tests were performed in the Queensland population of 4,332,739. Of these, 52.4% included LDL-C measurement. The proportion of the population having lipid testing increased from 12% at age <25 years to 93% at age >74 years. Females aged <35 years were tested almost twice as often as males and with similar frequency in those aged >44 years. For all ages, the proportion of patients with LDL-C >251

mg/dL was 0.13%. This proportion declined with increasing age. Dutch Lipid Clinic Network (DLCN) scores were assigned to LDL-C levels of 691 patients in primary care practices, and 57.8% had TC levels >290 mg/dl (possible FH). Among 1,057 patients retrieved from pathology provider and primary practice databases, 82.6% of those with TC levels >290 mg/dl had type II hyperlipidemia [HLP], 8.5% had types III and IV HLP and 1.8% had types I and V HLP. Database interrogation conveniently detected large numbers of patients with potential FH at minimal cost. In contrast, cascade family screening (CFS) of index patients with FH Morocco detected 12 cases of FH Morocco in near relatives. Screening was time-consuming, costly and relatively inefficient, with almost 50% of relatives either refusing to be tested

or being non-contactable. These data suggest that online prospective flagging of pathology results – with DLCN scoring and clinical confirmation of the diagnosis – may provide a convenient means for identifying patients with possible FH in primary care. Tracing of relatives of FH cases through published family histories also could facilitate screening.

## Introduction

Only an estimated 1% of FH patients are being diagnosed worldwide, although



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this percentage varies considerably in different countries.<sup>1-5</sup> This gap needs to be addressed by developing appropriate management strategies.<sup>4</sup> With a prevalence of 1:500, there are about 666,000 and 44,000 individuals with FH, living in about 222,000 and 15,000 U.S. and Australian families, respectively. Recent studies have suggested an even higher prevalence, and these numbers could be considerably greater.<sup>6</sup> FH patients, therefore, need to be mostly managed by primary care physicians.<sup>4,5</sup> With a focus on primary care, we performed two studies to compare different strategies for detecting patients with possible FH, with the aim of reducing the future burden of coronary heart disease (CHD).

The Severe Hypercholesterolemia In Primary Care (SHIP) study aimed to provide data on the prevalence of severe hypercholesterolemia (SHC) and its lipoprotein subtypes in primary care. It investigated databases of primary care physicians and pathology providers to retrieve patients with sufficiently elevated levels of TC and LDL-C. Such patients have a variety of lipoprotein disorders. Those with predominant elevation of LDL-C levels are at high risk of CVD, while those with predominant hypertriglyceridemia (HTG) are at risk of acute pancreatitis. Others have variable CVD risk, depending on the lipoproteins present to excess. It is important to distinguish these different lipoprotein subtypes, because management strategies differ.

Patients with type II HLP also may be screened for FH using either Make Early Diagnosis to Prevent Early Deaths in Medical Pedigrees with FH (MEDPED-FH), Simon Broome or DLCN diagnostic criteria (Table 1).<sup>4</sup> DNA analysis also can be performed to confirm the diagnosis.<sup>4</sup>

The Barossa Family Heart Study (BFHS) is based in rural South Australia, where

Points	Criteria
8	DNA mutation or LDL-C > 330 mg/dL
6	Tendon xanthomas
5	LDL-C 250 - 329 mg/dL
4	Arcus senilis < 45 years
3	LDL-C 190-249 mg/dL
2	First-degree relative with tendon xanthomas or premature arcus; or child (<18 years) with LDL-C > 95 <sup>th</sup> percentile (males: >160 mg/dL; females: >166 mg/dL)
1	First-degree relative with premature CVD (males: <55 years; females <60 years) or LDL-C > 95 <sup>th</sup> percentile (females: >194 mg/dL; males: >160 mg/dL)
1	Personal history of premature cardiovascular disease (males <55 years, females <60y)
1	LDL-C 155-189 mg/dL

Definite FH: >8 points  
 Probable FH: 6-8 points  
 Possible FH: 3-5 points

Table 1. Dutch Lipid Clinic Network criteria for FH diagnosis in an index patient.<sup>4</sup>

German Lutherans first settled in 1842. They brought not only skills in farming and winemaking, but also the LDL receptor (LDLR) mutation FH “Morocco” (LDLR\_00037, c.682G>T [exon4, pGlu228X] according to FH mutation nomenclature), resulting in the synthesis of a severely truncated (by 75%) LDLR protein. This mutation occurs relatively frequently in Germany.<sup>7</sup> Other Lutherans migrated in the mid-1800s to Texas, Nebraska and South Africa, and also may have imported the FH Morocco gene to these sites.<sup>8,9,10</sup>

Many Lutheran families in Australia and the U.S. published family histories, often through Lutheran Church publishing houses, which allow identification of people with premature deaths who may have inherited FH.

The classic method for FH case detection is by cascade family screening (CFS).<sup>4</sup> This

method involves screening of TC and/or LDL-C levels of near relatives of patients with FH to detect the disorder at as early a stage in life as possible.

## Methods

### SHIP Study

Selection of SHC patients involved computer interrogation of patient records of general practitioner (GP) surgeries and lipid profiles of local pathology providers. De-identified data were obtained for ethical reasons. Lipid data from the Queensland population were adjusted to exclude repeat tests, with the latest test being included for analysis.

Primary care patient records were interrogated using either the PEN clinical auditing tool or PARIS, a software interrogation tool provided by Merck Sharp & Dohme (Australia).<sup>11</sup> Pathology providers used their private software

to identify two groups of patients with hypercholesterolemia (HC): moderate HC (TC>274 mg/dL plus LDL-C >174 mg/dL) or severe HC (LDL-C ≥251 mg/dL). The latter represented patients with possible FH.<sup>12</sup>

Patients with severe HC defined as TC>290 mg/dl were retrieved from two metropolitan and four rural primary practices using PEN or PARIS auditing tools. This TC cut-off is used in the UK to detect patients with possible FH, those for whom family screening is recommended.<sup>5</sup> Lipoprotein subtypes were determined by a modification of the Fredrickson

classification, and LDL-C levels given point scores according to DLCN criteria (Table 1).<sup>4,13</sup> The likelihood of a mutation causing FH is related to the DLCN point score, such that positive LDLR mutation rates are ~5% in those with scores <3, ~12% in those with scores 3-5, ~25% in those with scores 6-8, and ~90% in those with scores >8.<sup>14</sup>

#### Barossa Family Heart Study

The FH Morocco mutation was initially detected in two Barossa residents, both sixth-generation descendants of Georg Eckert, who migrated from Silesia (in modern-day western Poland, near the

German border) to South Australia in 1849.<sup>8</sup> CFS was performed on near relatives of these index patients. Questionnaires were sent requesting details of family history of premature CHD or death, personal history of premature CHD, family physician details, highest recorded cholesterol level, current cholesterol-lowering treatment, and number of first-degree relatives. DNA consent forms were sent for completion and return by reply-paid post.

Lipids were measured by standard automated techniques in fasting blood, and standard DNA techniques and primers

Age (years) and gender	Qld population N	N lipid tests performed (% population)	N lipid tests including LDL-C (% total lipid tests)	N lipid tests with TC >274 and LDL-C >174 mg/dL (% lipid tests including LDL-C)	N lipid tests with LDL-C >251 mg/dL (% lipid profiles including LDL-C)	
<25	All	1,463,623	176,436 (12.05)	20,712	377 (1.8)	50 (0.24)
	M	747,739	65,305 (8.73)	8,995		23 (0.26)
	F	715,884	111,131 (15.52)	11,688		27 (0.23)
25-34	All	587,408	171,166 (29.14)	47,145	1,301 (2.8)	93 (0.020)
	M	304,084	59,506 (19.57)	23,172		43 (0.19)
	F	296,828	111,660 (37.62)	23,908		50 (0.21)
35-44	All	620,751	232,510 (36.2)	113,656	4,345 (3.8)	212 (0.19)
	M	304,084	98,515 (32.40)	58,452		114 (0.20)
	F	316,667	133,995 (42.31)	55,041		98 (0.18)
45-54	All	590,883	313,570 (51.3)	201,309	9,218 (4.6)	295 (0.15)
	M	290,311	147,029 (53.07)	102,857		124 (0.12)
	F	300,572	166,541 (55.41)	98,152		171 (0.17)
55-64	All	501,088	354,930 (70.83)	239,884	10,387 (4.3)	329 (0.14)
	M	249,208	174,374 (69.97)	125,235		102 (0.08)
	F	251,880	171,556 (68.11)	114,436		226 (0.20)
65-74	All	322,643	262,688 (81.42)	176,327	4,960 (2.8)	154 (0.09)
	M	160,858	133,291 (82.86)	91,595		31 (0.03)
	F	161,785	129,397 (79.98)	84,624		123 (0.15)
>74	All	246,343	228,430 (92.73)	107,668	2,052 (1.9)	83 (0.08)
	M	105,441	98,842 (93.74)	49,818		13 (0.03)
	F	140,902	129,588 (91.97)	57,782		70 (0.12)
Total	All	4,332,739	1,728,805 (38.3)	906,701	32,640 (3.6)	1,216 (0.13)
	M	2,148,221	776,862 (36.16)	460,124		450 (0.10)
	F	2,184,518	953,868 (43.66)	445,631		765 (0.17)

Moderate hypercholesterolemia: TC > 274 mg/dL and LDL-C > 174 mg/dL

Severe hypercholesterolemia: LDL-C > 251 mg/dL

Table 2. Proportion (%) of lipid profiles with hypercholesterolemia, according to age and gender in two Queensland pathology laboratories (1/10/11 to 1/10/12).

were used to detect FH Morocco using an automated analyzer and DNA isolated from peripheral blood.<sup>14</sup>

The Eckert family history was examined for ages of death in males and females before the statin era, making a diagnosis of presumed FH Morocco in those dying prematurely (age <55 years in men and <65 years in women), excluding those recorded with deaths under age 30 and those with a recorded non-CVD cause such as pneumonia, infection or accident. Other deaths were presumed to be the result of non-FH Morocco-related causes.

Griffith University and Bellberry Human Research Ethics Committees provided ethical approval.

## Results

### SHIP Study

#### *Queensland population: lipid testing and prevalence of SHC*

During a 12-month period, the age- and gender-specific proportions of the Queensland population (total 4.3 million) referred for lipid profiles increased progressively by about 10% per increasing decade of age, from 11.4% (ages <25 years) to 91.8% (ages >74 years), with an average of 38.3% for all ages (Table 2).

The proportion of patients with moderate HC (TC>274 mg/dL plus LDL-C >174 mg/dL) at age <25 years was 1.8% of lipid tests that included LDL-C, and increased with age to peak (4.6%) at ages 45-54 years. The proportion for all ages was 3.6% (N=32,640).

The proportion of patients at all ages with severe HC (LDL-C >251 mg/dL) was 0.13% of lipid tests that included LDL-C, 35% below that expected for FH (0.2%) (Table 2). The proportion of these patients with probable FH was lower than expected for FH in those ages 45-64 years (0.14-0.15%)

but was as expected for FH (about 0.2%) in those ages <45 years. The observed proportions were considerably lower than expected for FH in those ages >65 years (0.03-0.12%), particularly in males.



Legend: Includes 551 patients from primary care practices (1/10/11 to 1/10/12) and 507 patients from pathology providers (1/10/07 to 1/10/12).

\*Type IIA: TG<203 mg/dL (N = 618)

Type IIB: TG 203-390 mg/dL (N = 267)

Types III and IV: TG 524-709 mg/dL (N = 20)

Type IV: TG 391-523 mg/dL and 710-964 mg/dL (N = 70)

Types I and V: TG >= 965 mg/dL (N = 19)

Missing data (N = 63)

Figure 1. Proportions of lipoprotein subtypes\* in patients with TC > 290 mg/dL retrieved from primary practice and pathology provider databases.

#### *Primary care: prevalence of severe hypercholesterolemia*

Including two metropolitan and four rural primary care practices, the SHIP Study identified 726 patients with TC >290 mg/dL using PARIS interrogation software; 49.5% were men and mean age was 61.3 years; 644 (89%) were on lipid therapy with mean (mg/dL) lipids: TC 193, triglycerides (TG) 146, HDL-C 54 and LDL-C 112; 82 (19%) were not on therapy with mean lipids: TC 309, TG 195, HDL-C 62 and LDL-C 193.

One rural practice interrogated its patient database (N= 17,612) for total cholesterol (TC) levels. For all ages, TC was recorded in 30%, of whom the proportions of patients with TC <154 mg/dL, 154–208 mg/dL, 212–290 mg/dL and >290 mg/dL were 38%, 53%, 7%, and 2% (N= 138), respectively. The latter were patients with potential FH.

#### *Lipoprotein subtypes in patients with severe hypercholesterolemia*

The Figure shows the proportions of patients in South Australian and Queensland primary care and pathology practices who had TC>290 mg/dL,

according to type of hyperlipidemia (HLP) and using arbitrary levels of TG based on the original Fredrickson classification.<sup>13</sup> During a period of one year, the proportions of 754 patients in primary care databases with types IIA, IIB, III plus IV, IV and I plus V HLP were 53%, 18%, 2%, 5% and 1%, respectively, with some variation between practices and whether patients were being treated with lipid-modifying drugs. Similar proportions were observed for the five-year pathology provider database and for patients with SHC overall (Figure 1).

*Dutch Lipid Clinic Network (DLCN) scores*  
DLCN scores for LDL-C levels of >330, 250-329, 190-249 and 155-189 mg/dL are 8, 5, 3 and 1 points, respectively (Table 1). Diagnoses of definite FH, probable FH and possible FH require >8, 6-8 and 3-5 points, respectively.<sup>4</sup> The proportions of 691 patients with TC>290 mg/dL

and DLCN scores of 8, 5, 3 and 1 points were 8.2%, 15.7%, 33.9% and 27.8%, respectively, with missing data recorded in 5.1%.

### Barossa Family Heart Study

#### Family history analysis

According to the *Eckerts of Tauer*,<sup>8</sup> premature deaths to 1979, including those resulting from FH Morocco, occurred in 27 direct descendants of Georg Eckert, with a mean age of 45.2 +/- 7.8 (SD) years in 14 men and 57.3 +/- 9.1 years in 13 women. This gender difference was statistically significant ( $p < 0.01$ ). There also were six female spouses with premature deaths (mean age 49.2 +/- 9.6 years); these also may have had FH Morocco, because they had the same ethnic (German/Lutheran) and community backgrounds.

Presumed non-FH-affected direct relatives (those without premature death) had mean ages of death of 69.76 +/- 8.7 years in men (N=17) and 72.9 +/- 5.4 years in women (N=8). There were 26 presumed non-FH-affected spouses with mean ages of death 71.12 +/- 9 years in men (N=17) and 76.18 +/- 7.4 years in women (N=11).

#### Cascade family screening and DNA analysis

Of the 151 people included in CFS, 107 (71%) were near-relatives of the two index cases with FH Morocco and 44 were unrelated (Table 3). DNA testing was performed in 39 people, of whom 23 (59%) were related to the index cases. The majority of the latter (70%) had FH Morocco, and the remaining relatives were negative for FH Morocco. All individuals who were not related to the index cases (N=16) were negative for FH Morocco. One relative of index case No. 2 refused to consent for DNA analysis; 11 relatives of index case No. 1, 27 relatives of index case No. 2 and one unrelated individual did not reply to telephone calls, emails or letters and were classified as not responding. The

	Index case Family 1	Index case Family 2	Other families
Contacted	41	66	44
DNA tested	14	9	16
FH Morocco positive	10	6	0
FH Morocco negative	4	3	16
No DNA test required	7	5	7
Refused to consent	0	1	0
Not Responding	11	27	1
DNA yet to be processed	9	24	20

Table 3. Results of cascade family screening and DNA analysis of families in Barossa Family Heart Study.

proportion of non-responders was 13% of those screened. DNA testing has yet to be performed in 53 people (of whom 33 are near relatives of the index cases).

“These studies provide further information on the prevalence of severe hypercholesterolemia and possible FH in primary care.”

Cases of FH Morocco had a severe FH phenotype with mean untreated total cholesterol 355.1 +/- 34.7 (SD) mg/dL (N=7). Two males had premature CHD, one receiving two angioplasties and stents between the ages of 45 and 55, in addition to coronary artery bypass graft CABG surgery at age 60. The other had a myocardial infarction at age 55.

### Discussion

These studies provide further information on the prevalence of severe

hypercholesterolemia and possible FH in primary care.

In the SHIP study, the high proportion of lipid testing in older patients may reflect current guidelines for lipid-lowering drug therapy, which relate more to co-morbidity and absolute CVD risk than to lipid levels. Lipid testing of younger patients may have been for FH screening since the proportion of patients with LDL-C >251 mg/dL was ~0.2%, approximating the expected prevalence of FH in most populations.<sup>4</sup> The proportion of lipid profiles with moderate HC (TC>274 mg/dL and LDL-C >174 mg/dL) was considerably higher than expected for FH (1-8-4.6% vs. 0.2%), suggesting these cut-off levels may not be high enough for FH diagnosis.

The proportion of patients with HC and severely elevated LDL-C levels consistent with probable FH (>290 mg/dL) was similar to that expected for FH in the age groups <45 years (Table 2). Reasons for the greater proportion of women than men in the age groups >45 years, especially in those >74 years of age, are speculative and may be related to hormonal changes, differences in lipid-lowering therapy, differences in survival, compliance or factors such as secondary causes of HLP.

Controlling LDL-C levels is important in patients with type II HLP; nevertheless, significant numbers of uncontrolled or untreated patients were detected, suggesting significant gaps in management that require addressing in future studies.

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“Cascade family screening was found to detect relatively small numbers of potential FH cases in comparison with screening of primary practice and pathology provider databases.”

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The TC cut-point >290 mg/dL for identifying potential patients with FH also detected 17.4% of cases with lipoprotein subtypes other than type II, which are associated with lower CVD risk. Most of these had mixed HLP (8.5%), and a small percentage had chylomicronemia (1.8%) (Figure 1). Management of these patients requires consideration of specific secondary causes (especially glucose intolerance and alcohol intake) in addition to specific therapy.<sup>15</sup>

In the Barossa Family Heart Study, examination of published family histories was helpful in estimating longevity before the statin era, although exact causes of death usually were not recorded. Most early German immigrants had a normal life expectancy, and those with presumed FH had about a 20-years-shorter lifespan.

These results suggest that systematic examination of published family histories may detect premature deaths related to presumed FH, and facilitate CFS in their descendants.

CFS required a large time commitment with a low return because of the numbers of relatives who could not be contacted for a variety of reasons (including change of address, change of name and relatives unknown to index cases). Some hypercholesterolemic relatives of FH Morocco index cases had no detectable LDLR mutation. These data do not support CFS as the primary means for FH case detection, but this may reflect the small sample numbers involved and the limited research resources available, preventing detection of other possible mutations.<sup>4</sup>

Similar results were obtained in the recent MEDPED-FH program in Australia, in which many relatives of FH patients could not be contacted for a variety of reasons, and cascade family screening was difficult to perform effectively.<sup>16</sup>

### Conclusions

Cascade family screening was found to detect relatively small numbers of potential FH cases in comparison with screening of primary practice and pathology provider databases. Dutch Lipid Clinic Network scoring of LDL-C levels showed that 58% of 691 patients with severe HC had possible FH. Published family histories of index FH cases could facilitate FH detection. The results of the SHIP and BFHS studies suggest that online prospective flagging of patients with severe HC (TC>290 mg/dL) by pathology providers may provide an efficient means for identifying patients with possible FH in primary care. Flagging also may alert primary care physicians to perform online Dutch Lipid Clinic Network scoring for confirmation of FH diagnosis, in addition to the need for cascade family screening.

The cost-effectiveness of FH detection in these studies needs to be determined, with the aim of convincing governments to fund national programs for FH detection and treatment, which are required in many countries, including Australia and the U.S.

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*References are listed on page 37.*

# Omega-3 Fatty Acids and Prostate Cancer – A Study “Spun” Out of Control

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The report by Brasky, et al., in the *J Natl Cancer Institute* titled, “Plasma Phospholipid Fatty Acids and Prostate Cancer Risk in the SELECT Trial”<sup>1</sup> attracted widespread media attention. It reported that higher baseline levels of omega-3 fatty acids in the plasma phospholipid fraction were associated with a significantly increased risk for prostate cancer over 9 years.

The authors wrote, “The consistency of these findings suggests that these fatty acids are involved in prostate tumorigenesis and recommendations to increase long-chain omega-3 fatty acid intake, in particular through supplementation, should consider its potential risks.” In a news release, they said, “We’ve shown once again that use of nutritional supplements may be harmful.”

The problem here is that the authors confuse association with causality. The study design was very common: measure a biomarker in a disease-free group at baseline and then correlate it to incident disease. The problems were their unfounded extrapolations and the

irresponsible promotion of their findings. The media failed to call them on this – Why should they? The 24/7 news beast must be fed with controversy! – and the endless echoes of “fish oil causes prostate cancer” screaming across the headlines elicited tremendous confusion among patients and may be reversing years of progress in raising the public’s awareness of the benefits – and safety – of these nutrients.

What did Brasky, et al., actually find? Were omega-3 levels “high” in those who developed cancer? The answer is no. Eicosapentaenoic acid and docosahexaenoic acid (EPA+DHA) levels were 3.52% in the no-cancer control group, 3.67% in the low-grade cancer group and 3.74% in the high-grade group. Translated into the Omega-3 Index (red blood cell [RBC] EPA+DHA), these range from 4.45% to 4.55% – barely above deficient levels (Figure 1).

Were those taking fish oil supplements (FOS) at increased risk? No. Brasky, et al., did not give anyone FOS. They do not even know who was or was not taking them. Nor did they collect data on fish intake. In Framingham study, people who were taking

FOS had an average Omega-3 Index of 7.5%.<sup>2</sup> This suggests fish oil intake was low in the SELECT trial.

It is possible that some component of whatever fish these patients were consuming was carcinogenic. The serum omega-3 levels could be merely a marker of fish (i.e., carcinogen) intake. The authors failed to consider the possibility of reverse causation. A much larger proportion of men who ultimately developed cancer (30%-40%) had prostate-specific antigen (PSA) levels >3 at baseline (compared to 7% of the controls). It is possible that sub-clinical prostate cancer was already developing in the higher-risk men. He, et al.,<sup>3</sup> and Azordegan, et al.,<sup>4</sup> provide evidence that, in pre-cancerous tissues, early changes in fatty acid metabolism might increase at least tissue levels of long-chain n-3 fatty acids. It also is conceivable that there were



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Trial	n	Duration (yrs)	Placebo	N-3
Alpha-Omega <sup>19</sup> (prostate cancer)	4837	3.4	0.8%	1.4%
GISSI-Heart Failure <sup>20</sup> (cancer death)	6975	3.9	3.2%	3.1%
GISSI-Prevenzione <sup>21</sup>	11,320	3.5	2.25%	2.65%
JELIS <sup>22</sup>	18,645	4.6	2.4%	2.6%
SUFOLOM3 <sup>23</sup> (cancer death)	2501	4.2	6.5%	7%
Origin <sup>24</sup>	12,536	6.2	"no difference in the rate of cancer"	
Risk and Prevention <sup>25</sup>	12,513	5	7.2%	7.9%
Omega <sup>26</sup>	3851	1	1.4%	1.7%

Table 1. Reported incident cancer diagnosis (or cancer deaths)

higher estrogen levels in these men.<sup>5</sup> If so this could have up-regulated delta-5, 6-desaturases producing long-chain from short-chain omega-3 fatty acids.<sup>6</sup> Although untested, these biological hypotheses could, in theory, explain the slightly increased omega-3 levels in those at higher risk – without blaming fish intake or FOS use.

It is important to put these findings into perspective. Consider the risk of dying from prostate cancer vs. ischemic heart disease (IHD). Based on the National Vital Statistics Report for deaths in the U.S. in males in 2010, there were about 28,500 deaths from prostate cancer and 207,500 deaths from IHD – this translates into a 7.3x higher rate of death for heart disease. A study similar to the one by Brasky, et al., but receiving far less news coverage, used exactly the same methodology (a biomarker-based prospective cohort) and found that higher plasma phospholipid EPA+DHA levels were associated with – we cannot say *caused* – **lower mortality rates in older Americans.**<sup>7</sup> One might ask: Why did this paper not receive the same attention as Brasky's report?

Brasky, et al., failed to present the complete story. The same team reported in 2010 that the use of FOS was *not* associated with any increased risk for prostate cancer.<sup>8</sup> A 2010 meta-analysis of fish consumption and prostate cancer

reported a reduction in late-stage or fatal cancer among cohort studies, but no overall relationship between prostate cancer and fish intake.<sup>9</sup> Terry, et al., in 2001<sup>10</sup> reported that higher fish intake was associated with a lower risk for prostate cancer incidence and death, and Leitzmann, et al., in 2004<sup>11</sup> reported similar findings. Higher intakes of canned, preserved fish were reported to be associated with reduced risk for prostate cancer.<sup>12</sup> Epstein, et al., found that a higher omega-3 fatty acid intake predicted better survival for men who already had prostate cancer,<sup>13</sup> and increased fish intake was associated with a 63% reduction in risk for aggressive prostate cancer in a case-control study by Fradet, et al.<sup>14</sup> A 2012 review of omega-3 and prostate cancer concluded, "the epidemiological data is inconsistent [but] suggest an *inverse* association of LC n-3 PUFA [and prostate cancer]."<sup>15</sup>

There is little evidence showing harm and substantial evidence for benefit with fish oil.

The Japanese typically eat about 8x more omega-3 fatty acids than Americans do<sup>16</sup> and their blood levels are twice as high,<sup>17</sup> and yet rates of prostate cancer in Japan are about 10% of those in the U.S.<sup>18</sup> Clearly this is not consistent with the conclusions

of Brasky, et al. However one has to be careful about an ecological fallacy meaning population comparison data may not be the same as individual comparison data.

Evidence from randomized clinical trials with fish oils provides the highest quality of evidence of the effects of omega-3 supplementation on the incidence of cancer

(which is tracked among potential adverse events). Table 1 shows the findings for eight major clinical trials, including more than 78,000 patients. In *none* of these studies was cancer incidence significantly increased by omega-3 fatty acid supplementation.

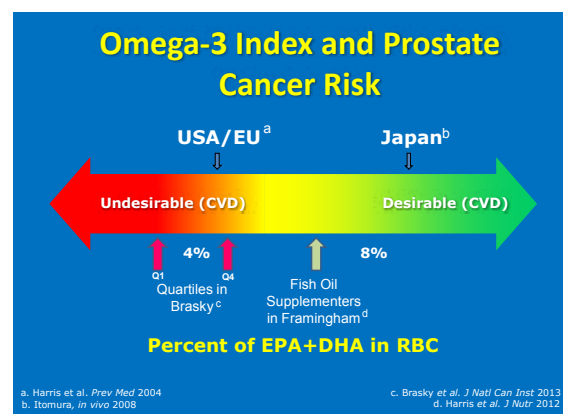


Figure 1. The spectrum of Omega-3 Index (RBC EPA+DHA as a % of total fatty acids) values in the U.S./EU and Japan vs. levels in subjects taking fish oil supplements. The approximate Omega-3 Index in the lowest and highest quartiles from Brasky, et al.<sup>1</sup> are indicated.

In summary, the work of Brasky, et al., is not necessarily bad research. It is a poor interpretation of the findings. The antidote to Brasky, et al., is more good science, rationally interpreted. Without media spin. ■

*Disclosure statement: Dr. Harris is employed by Health Diagnostics Lab, Inc. He is owner of Omegaquant Analytics, LLC and has received consulting fees from Omthera Pharmaceuticals and Aker Biomarine Antarctica.*

*References are listed on page 37.*

# Heterozygous Familial Hypobetalipoproteinemia: Case Study and Literature Review

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A 12-year-old male was referred to our Pediatric Lipid Clinic by his pediatrician for evaluation of a low total cholesterol level. A fasting lipid profile noted the following; total cholesterol (TC): 84 mg/dL, triglyceride: 50 mg/dL, high-density lipoprotein cholesterol (HDL-C): 47 mg/dL, low-density lipoprotein cholesterol (LDL-C): 27 mg/dL and apolipoprotein B (apo B): 24 mg/dL. His medical history is remarkable for Attention Deficit Disorder, seasonal allergies, vitamin D insufficiency and chronic, bilateral, mild leg pain. He was born at full term, without complications. He is currently taking over-the-counter fish oil (1,000 mgs daily), a daily multivitamin and cetirizine (as needed). He has no apparent medication allergies and has had no prior surgeries. He denies tobacco, alcohol or drug use. He is a very active seventh-grader and does well academically.

### Family History

It was noted that several maternal family members have low total cholesterol levels. The total cholesterol levels of his mother (42 years-old), maternal aunt (44 years-old) and maternal grandfather (66 years-old), are 90 mg/dL, 84 mg/dL and 87 mg/dL, respectively. His maternal great-grandmother (94 years-old) has no reported chronic medical conditions. His paternal family indicates that his father (42 years-old) and paternal grandfather (69 years-old) are being treated for hypercholesterolemia. The hypercholesterolemia appears to be secondary to high-fat diets and unhealthy body weights. His paternal grandfather had a myocardial infarction at age 66. The patient has no biologic siblings (Figure 1).

### Physical Examination

Afebrile; heart rate (HR): 86 bpm; blood pressure (BP): 116/59 mm Hg; height:

68 inches; weight: 158 pounds; waist circumference: 37.5 inches; and body mass index (BMI): 24.0 Kg/m<sup>2</sup> (93<sup>rd</sup> percentile for age and gender). The patient was alert, oriented and appeared well-nourished. Physical exam was unremarkable.

### Pertinent Chemistry Results

Vitamin D: 22 nmol/L, retinyl palmitate: <0.02 mg/L, alpha-tocopherol: 5.6 mg/L, TSH: 1.69 uU/mL, Free T4: 1.19 ng/dL, normal liver transaminase levels, and thyroid and glycemic indices.



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## Impression and Recommendations

The laboratory data, maternal family history of low total cholesterol levels in several relatives (Figure 1) and a lack of secondary causes suggest that this patient's low LDL-C and apo B levels are the result of heterozygous Familial Hypobetalipoproteinemia (FHBL). FHBL is a relatively rare genetic disorder of lipoprotein metabolism that is associated with low serum levels of LDL-C and apo B. Since fat-soluble vitamins are largely bound to low-density lipoproteins, very low LDL-C levels can result in their deficiencies. Therefore, we recommended periodic assessment of these vitamin levels, (i.e., vitamins A, D and E) with supplementation, as necessary. We encouraged the patient to follow a healthy diet, take a daily vitamin D supplement (1,000 units), continue the daily multivitamin, and avoid tobacco use and unhealthy weight gain. We recommended a follow-up fasting lipid profile and vitamins A, D and E assessment in six months.

## Hypobetalipoproteinemia

LDL-C and apo B levels below the fifth percentile for age and gender define hypobetalipoproteinemia (HBL). Low LDL-C concentrations are usually heritable and associated with a reduced risk of atherosclerotic cardiovascular disease (ASCVD) and increased longevity when not caused by hyperthyroidism, celiac disease (sprue), intestinal malabsorption or alcoholism.<sup>1</sup> Heritable hypobetalipoproteinemia or FHBL is an autosomal co-dominant disorder. The estimated prevalence of heterozygous FHBL is 1 in 3,000 individuals.<sup>2</sup> The overwhelming majority of simple heterozygotes are asymptomatic, although they may have mild fat-soluble vitamin deficiencies and/or mild hepatic transaminase elevations. The long-term effects of the transaminitis are unknown but appear to be benign.<sup>3</sup>

This lipoprotein disorder was first described by Mars, et al., in 1969.<sup>4</sup> Since the discovery of the first kindred with FHBL, many kindreds subsequently have been

described. This has led to the discovery of numerous single-nucleotide substitutions, gene deletions and linkage abnormalities in the apo B gene causing defects in VLDL and chylomicron synthesis and secretion. More than 40 mutations have been identified in the apo B gene.<sup>3</sup> There are two forms of apo B; apo B-100 and apo B-48. These isoforms are derived from differential splicing of ribonucleic acid (RNA) from a single apo B gene. Apo B-100 is synthesized by the liver and is the major protein component of VLDLs and LDLs. Apo B-48 is synthesized by intestinal enterocytes and is the major protein component of chylomicrons. The apo B gene is on chromosome 2 and is unlinked to other apolipoprotein gene clusters.<sup>5</sup>

The best characterized cases of FHBL are the result of mutations in the apo B gene leading to the production of truncated proteins. Lipoproteins bearing truncated forms of apo B are cleared more rapidly than normal apo B-containing lipoproteins, thereby leading to very low plasma concentrations. This rapid clearance appears to be independent of the hepatic LDL and remnant receptors and may involve megalin of the renal proximal tubular cells.<sup>6</sup>

Individuals with FHBL can be heterozygote or homozygote, with severity of the clinical phenotype related to the number of defective apo B alleles. Heterozygote individuals often have no clinical manifestations other than very low serum apo B-containing lipoprotein levels that may cause minor fat-soluble vitamin deficiencies. The low serum apo B-containing lipoprotein levels likely confer ASCVD protection.<sup>1</sup>

FHBL homozygotes have extremely low LDL-C levels (< 5 mg/dL) and can have a range of clinical symptoms, including neurologic sequelae, fat malabsorption with steatorrhea, non-alcoholic fatty liver disease,

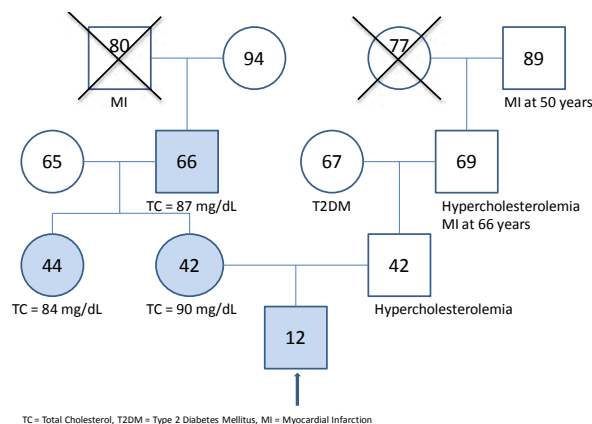


Figure 1. Pedigree of Index Case

and/or red cell acanthocytosis.

The clinical presentation of homozygous FHBL can be indistinguishable from that of abetalipoproteinemia (ABL), which is due to a mutation in the MTTP gene that encodes for microsomal triglyceride transfer protein (MTTP). MTTP is responsible for the assembly and secretion of hepatic (i.e., VLDL) and intestinal (i.e., chylomicron) apo B-containing lipoproteins. Patients with ABL generally have undetectable levels of apo B-containing lipoproteins and the condition segregates as an autosomal recessive trait.

Establishing the diagnosis of heterozygous FHBL requires substantiating the generational presence of low total cholesterol and LDL-C levels in first- and second-degree relatives of the index case and excluding secondary causes.<sup>7</sup> Management of heterozygous FHBL generally does not require intervention. Laboratory assessment of fat-soluble vitamins (A, D and E) and hepatic transaminases is warranted, with vitamin supplementation as necessary. ■

*Disclosure statement: Dr. Anne has no disclosures to report. Dr. Maciejko has received honorarium from Merck.*

*References are listed on page 37.*

# Effects of Post-Transplant Drugs on Lipids and Treatment Options

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## Epidemiology

The ever-increasing population of patients living after organ transplantation has added an important dimension to the specific management needs of these patients. One major area in this regard pertains to the effects of post-transplant immunosuppressive drugs on lipids and lipoproteins. In addition, a number of

agents in this expanding arena cause several metabolic perturbations that lead to development of new-onset diabetes after transplantation (NODAT), with or without high blood pressure (Table 1). It has been estimated that rates of NODAT are approximately 20%-50% after renal transplant, 10%-30% after liver transplant, and up to 30% after heart transplant at one



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year or later post-transplant, depending on age, BMI, ethnic and genetic background and the nature of the immunosuppressive regimen.<sup>1,2</sup> The consequences of NODAT include additional features of dyslipidemia linked to the pathophysiology of diabetes itself, compounded by the specific effects of post-transplant drugs. Moreover, patients with chronic kidney disease (CKD), the most numerous transplantation category, often present with years of suboptimal treatment of background dyslipidemia and atherosclerosis prior to transplantation. In a large cohort of 1.2 million people, followed for a period of four years, the incidence of myocardial infarction (MI) without prior history of MI was greater in those with CKD Stage 3 or worse (GFR < 60ml/min) than in those with diabetes without CKD, and two-fold higher in those with GFR < 45 ml/min, compared to those with diabetes without CKD.<sup>3</sup> However, the incidence

## Effects of Post-transplant drugs on Metabolic Parameters

	Glucose	Blood Pressure	Lipids
Glucocorticoids	++	++	++
Calcineurin Inhibitors			
Cyclosporine	+	++	0
Tacrolimus (FK-506)	++	+	+
mTOR Inhibitors			
Sirolimus	+	0	++
Mycophenolic Acid (MMF)	0	0	0

Table 1.

of coronary heart disease (CHD)-related events and mortality is highest when diabetes and CKD coexist, as documented in the NHNES III survey.<sup>4</sup> The prevalence of CKD in patients with prior diabetes has been increasing because of the increasing prevalence of the latter.<sup>5</sup>

### Mechanism of dyslipidemia related to post-transplant drugs

Immunosuppressive agents used to preserve a transplanted organ's function have variable lipid effects. This is particularly relevant in post-renal transplant patients, given their increased underlying atherosclerosis related to CKD for years prior to transplantation and compounded by numerous alterations in lipoprotein pathophysiology related to progressive proteinuria, azotemia, malnutrition and catabolic state.<sup>6,7</sup> These include changes in virtually all apolipoprotein B (apo B) lipoproteins, remnant particles, lipoprotein lipase, apoprotein CII/CIII ratio, cholesteryl

**“In statin-intolerant patients, bile acid sequestrants or niacin are alternatives, although there are no studies in patients with CKD or post-transplant patients.”**

ester transfer protein (CETP) and high-density lipoprotein (HDL) metabolism. While total cholesterol levels are often increased in the presence of nephrotic-range proteinuria and hypoalbuminemia, the progression to ESRD is typically

Statin	Dose ( mg)§	Comment
Lovastatin #	?	Not studied
Fluvastatin	80	Based on ALERT trial (ref 20, 21)
Atorvastatin #	20	Based on 4D trial (ref 17)
Rosuvastatin	10	Based on AURORA trial (ref 18)
Simvastatin/Ezetimibe	20/10	Based on SHARP trial (ref 19)
Pravastatin	40	
Simvastatin #	40	
Pitavastatin	2	

\* Statin recommendations for CKD stage 1 or 2: same as for general population.  
 \*\* Initiation of statin not recommended but continue if started pre-dialysis, or if evidence of CHD, with dose adjustments.  
 § May need dose reduction if Asian patient.  
 # May need dose reduction, if on Cyclosporine.  
 Adapted from ref 22

Table 2.

characterized by increased triglyceride levels due to impaired apo CII/CIII ratio, impaired LPL activity leading to atherogenic IDL and remnant particle accumulation, as well as low HDL. The latter is propagated by reduced hepatic lipase, and increased CETP activity, and inadequate maturation of HDL 3 to HDL-2.<sup>6</sup>

Glucocorticoids, the mainstay of an immunosuppressive regimen, have pronounced effects on metabolic pathways, including induction of insulin resistance, inhibiting pancreatic b-cell function and augmenting α-cell function.<sup>8,9</sup> By enhancing lipolysis and promoting relocation of adipose tissue, these agents promote visceral adiposity and dyslipidemia of insulin resistance.

Mycophenolic acid (MMF) and calcineurin-inhibitors (CNIs) (such as cyclosporine and tacrolimus) were introduced as a major advancement in the pursuit of a glucocorticoid-sparing regimen in post-transplant patients, and are often used as the preferred combination therapy after short-term use of glucocorticoids in the

induction phase. MMF is largely devoid of metabolic effects. CNIs, however, have significant dose-related metabolic effects, primarily related to their effects on b-cell function and apoptosis.<sup>2</sup> Tacrolimus has a more pronounced effect on glycemia than cyclosporine, but the latter has a more pronounced effect on blood pressure.<sup>2,10</sup>

Mammalian targets of rapamycin (mTOR) inhibitors, such as sirolimus and everolimus, represent an alternative immunosuppressant option when CNIs may be ineffective.<sup>11,12,13</sup> mTOR is a PI\_3-kinase like serine/threonine protein kinase that has emerged as a significant regulator of lipogenesis, lipolysis and adipogenesis.<sup>12</sup> It exists as two complexes, mTORC-1 and mTORC-2, both of which are likely inhibited by rapamycin (sirolimus). The precise mechanism of effects of sirolimus on lipid biology is unclear, but it inhibits catabolism of apo-B-100, raises free fatty acid (FFA) levels and decreases lipoprotein lipase activity.<sup>11</sup> Everolimus, another mTOR inhibitor currently approved for certain cancer treatments, has been reported to cause severe hypertriglyceridemia and

cases of acute pancreatitis.<sup>11,13</sup>

In a 12-month comparative trial of 1,645 patients receiving renal transplants (The Symphony trial), comparing a low-dose regimen of cyclosporine, low-dose tacrolimus and low-dose sirolimus with standard-dose cyclosporine, the cyclosporine-based regimen was associated with a greater increase in blood pressure and sirolimus was associated with the worst lipid profile.<sup>10</sup> The mean LDL-C and Triglycerides levels in the sirolimus group were 11% and 25% greater respectively, at 1 year, compared to the patients on

of evidence of cardiovascular benefits in such patients, despite the high risk of CVD and mortality.<sup>17,18</sup> In another large trial reporting CHD risk reduction with simvastatin plus ezetimibe, a substantial number of patients with advanced CKD initiated dialysis during the trial.<sup>19</sup> In the only clinical trial conducted in > 2000 renal-transplant patients,<sup>20</sup> a 1 mmol reduction in low-density lipoprotein cholesterol (LDL-C) after treatment with fluvastatin 40 mg-80 mg compared to placebo resulted in a significant reduction in cardiac death and definite

possibility of drug interactions because of pharmacokinetic differences in patients with residual renal insufficiency<sup>23</sup> (Table 2). This also is highlighted by the updated National Kidney Foundation guidelines for the selection and dosage for fibrate therapy.<sup>15</sup> There is no definitive evidence that supports the use of fibrates in pre- or post-transplant patients.

The most recent American Heart Association/American College of Cardiology<sup>24</sup> and the KDIGO cholesterol guidelines<sup>22</sup> do not advocate routine measurements of LDL-C if the optimal dosage of statin therapy is utilized as recommended; however, it may be prudent to monitor lipid levels and renal status periodically in post-transplant patients, because the dosage may need to be adjusted if renal function deteriorates over time or the choice of immunosuppressant drug therapy needs to be revised according to clinical circumstances. The AHA/ACC recommendations do support lipid monitoring to assure that appropriate percentage reductions in LDL-C have been achieved.

In statin-intolerant patients, bile acid sequestrants or niacin are alternatives, although there are no studies in patients with CKD or post-transplant patients. ■

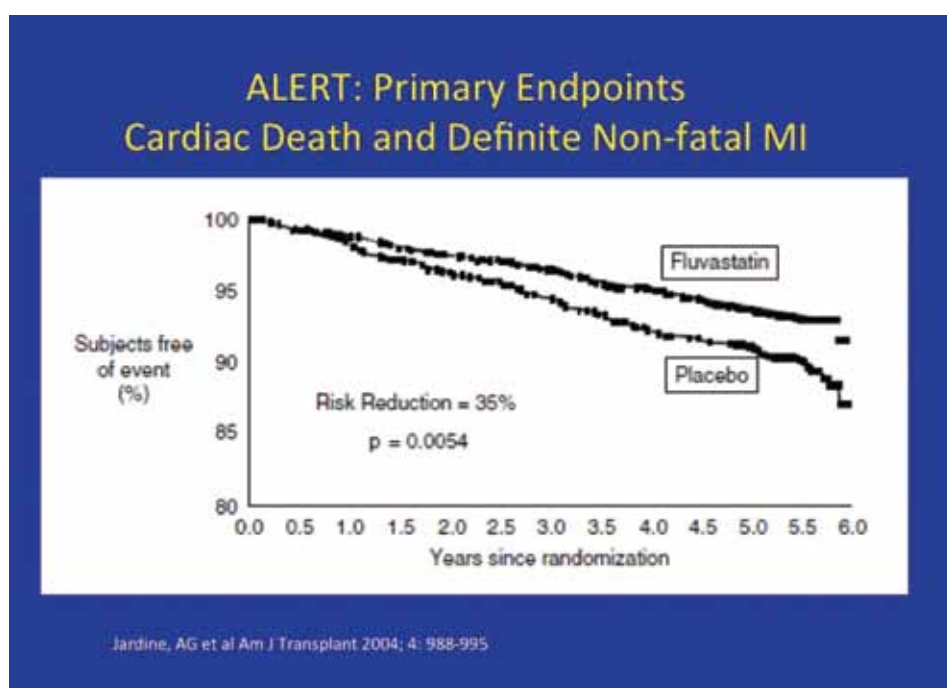


Figure 1.

Tacrolimus ( $p < 0.05$ ), and 39%, compared to 26% respectively needed lipid-lowering medications.<sup>10</sup> It has been postulated that the development of specific mTORC-1 inhibitors might limit the side effects of mTOR inhibitors.<sup>13</sup>

### Management Considerations

Based on extensive meta-analyses, statins are the mainstay for the risk-reduction strategy in all patients at high risk of CHD, including those with CKD.<sup>14,15,16</sup> Two large randomized controlled trials in patients on hemodialysis however, provided a lack

MI (RR 0.65, CI 0.48-0.88;  $p < 0.005$ ) after five years<sup>20,21</sup> (Figure 1). The 10-year risk of coronary death or MI in this trial was > 20% and these results were in line with the effects of statins in the general population.<sup>14</sup> In view of the overall evidence of the benefits of statins, the recent update of the Kidney Disease: Improving Global Outcomes (KDIGO) working group recommended treating **all** post-renal transplant patients with a statin,<sup>22</sup> while adjusting the statin dosage according to the higher risk of adverse effects in such patients or the

*Disclosure statement: Dr. Ganda has received research funding from Amarin Corp. and has received honorarium from Janssen Pharmaceuticals, Inc. and Boehringer-Ingelheim.*

*References are listed on page 38.*

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## Need Help Filling out the FH Patient Registry?

Your health care provider may have suggested you join the FH Patient Registry. If you have been diagnosed with FH (familial hypercholesterolemia) or suspect you may have it, it is important for you to register at [www.thefhfoundation.org](http://www.thefhfoundation.org). Click on "Cascade FH Registry." The purpose of this registry is to collect information that can help researchers and then lead to improved care and a longer and better life for people with FH. *The FH Foundation and the FH Patient Registry are not affiliated with the Foundation of the National Lipid Association.*

To assist you in filling out the online patient registry form, you will need the following information from your health care provider. Take this card to your next appointment and ask your provider to help fill in this information.

**Date of exam:** \_\_\_\_\_ mm/dd/yyyy

**Blood pressure:** Systolic: \_\_\_\_\_ Diastolic: \_\_\_\_\_

**Exams and Labs:** Height: \_\_\_\_\_ Weight: \_\_\_\_\_

Total cholesterol: \_\_\_\_\_ LDL: \_\_\_\_\_

### Your Health Care Provider:

First Name: \_\_\_\_\_

Last Name: \_\_\_\_\_

Office Name: \_\_\_\_\_

Street Address: \_\_\_\_\_

City: \_\_\_\_\_ State: \_\_\_\_\_ Zip code: \_\_\_\_\_

Telephone: \_\_\_\_\_ Fax: \_\_\_\_\_

*The Foundation of the National Lipid Association is pleased to provide this simple worksheet to assist you in signing up for the FH Patient Registry. For more information on FH or cholesterol issues, go to [www.learnyourlipids.com](http://www.learnyourlipids.com).*

To register go to  
[www.thefhfoundation.org](http://www.thefhfoundation.org)



# 2013

## ANNUAL REPORT



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of the National Lipid Association

[www.lipidfoundation.org](http://www.lipidfoundation.org)

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### OUR MISSION

*The Foundation supports  
patient and clinician  
educational, research and  
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that enhance and support the  
initiatives of the National  
Lipid Association in its efforts  
to reduce cardiovascular  
events and deaths related to  
abnormalities of cholesterol  
metabolism.*

## PRESIDENT'S MESSAGE

The Foundation of the NLA achieves its mission through raising funds to support the initiatives of the National Lipid Association. The Foundation continually seeks funding to support programs that raise awareness about dyslipidemia in health care providers and patients through research, education and community outreach grants. Foundation donors in 2013 can say that they have helped us achieve this goal as shown by the impact that several of our initiatives had last year on a national level. I am pleased to give you an update on several successful initiatives by the Foundation of the National Lipid Association in the past calendar year.

- In keeping with the Foundation's mission to educate clinicians (as well as the lay public), the Foundation of the NLA supported and sponsored a public awareness campaign about familial hypercholesterolemia (FH) that was launched August 30, 2013, to coincide with National Cholesterol Education Month for September. The Foundation continues to lay important groundwork for the future regarding FH awareness and ultimately helping to decrease early deaths related to cardiovascular disease. The cornerstone of our campaign was a poster that was sent to 40,000 family practice physicians (as well as all NLA members) and that continues to be downloaded from our web site and posted in physicians' offices across the country. You can still download the "Are You the One?" poster/supplement at [www.learnyourlipids.com](http://www.learnyourlipids.com). This campaign also won an award from the North Florida Chapter of the Public Relations Society of America in the category of best printed collateral.

- Several members of the Foundation of the NLA, as well as other NLA members, participated in a number of important meetings related to FH awareness. In February, the Foundation of the NLA hosted an FH Summit in New Orleans at which individuals representing several different organizations with an interest in FH, gathered as a "coalition" for an all-day meeting to discuss ways in which we could work together to increase awareness of FH and also assist the FH Foundation with the launch of its FH patient registry. In addition, NLA members also participated in the FH Foundation's FH Summit in Annapolis, just before the NLA's Fall CLU in Baltimore. I am gratified to see so many prominent individuals and organizations working together to address the needs of FH patients nationwide. As a result of the FH Summit meeting, the Foundation of the NLA created a tear sheet that can be used by patients when they are filling out the FH Foundation's new patient registry online. You may access this tear sheet directly here: [www.lipid.org/sites/default/files/fh\\_patient\\_tear\\_sheet.pdf](http://www.lipid.org/sites/default/files/fh_patient_tear_sheet.pdf).

- The Foundation hosted three successful events to coincide with the NLA's Annual and Clinical Lipid Update meetings: A cooking demonstration by a renowned Cajun-style chef in New Orleans; a night of dinner and dancing in the desert in Las Vegas; and a food tour of several famous restaurants in Baltimore's historic Fell's Point.



*New Orleans  
Cooking  
Demonstration*

*Las Vegas  
Dinner &  
Dancing in  
the Desert*



*Baltimore  
Restaurant  
Food Tour*

- Lifetime Membership was an extremely successful membership campaign, which ran through December 2013 and netted \$175,000 for the Foundation. Thank you to all 175 Lifetime members for their generous support of both the Foundation and the NLA.
- Foundation members assisted with a patient survey to launch a new registry for patients with high triglycerides. Go to <http://connect.patientcrossroads.org/?org=fnla> for more information on the registry.
- An update to the FH Pocket Guide was released at the Annual Scientific Sessions in May. To access the pocket guide visit: [guidelinecentral.com/medical-society/national-lipid-association](http://guidelinecentral.com/medical-society/national-lipid-association).

As always, thanks for your support of our Foundation, and I look forward to building on this success in the coming year!



Anne C. Goldberg, MD, FNLA  
President  
Foundation of the National Lipid Association

## OUTREACH

### Are You The One? Campaign

In September 2013, the Foundation of the NLA launched a new FH awareness campaign titled "Are You the One?" All NLA members received a poster in the mail that can be hung in patient areas explaining what FH is and how to get tested for it. This same poster supplement was sent to 40,000 family physicians across the United States. It is also available for download on [learnyourlipids.com](http://learnyourlipids.com). The poster was subsequently downloaded more than 600 times, and an article featuring FH patient and NLA President Matthew Ito, PharmD was featured in more than 2,000 newspapers across the country.



The Foundation also partnered with the Northeast Chapter of the National Lipid Association by helping to sponsor a booth at the Yankees Fan Fest in New York City. NELA members volunteered their time to provide advice and guidance on cholesterol testing and lifestyle management to attendees of the Fan Fest. More than 5,000 people took part in the event that offered a special section of health care-related organizations offering screenings and health tips.

During the campaign, we also refreshed [LearnYourLipids.com](http://LearnYourLipids.com), and posted information on [lipid.org](http://lipid.org) as well as the Foundation's web site. This awareness campaign presented an ideal opportunity for you to discuss FH with your staff and identify patient education opportunities not only during September but throughout the year.

### 100 Questions & Answers About Managing Your Cholesterol

This valuable patient resource, produced in partnership with the National Lipid Association, features frequently asked questions with answers that are provided in layperson language. More than 1,898 have been sold since publication in 2011. To order a copy for your office, visit [www.amazon.com](http://www.amazon.com). The book is also available on Kindle and Nook e-readers!



### LearnYourLipids.com

As a patient resource, the Foundation maintains [www.learnyourlipids.com](http://www.learnyourlipids.com). During the 2013 FH Campaign in September during National Cholesterol month, the site was updated with new materials focusing on Familial Hypercholesterolemia (FH). The site receives an average of 245 unique visits each day, **an increase of more than 200% since last year**. In September 2013, we also had the highest number of visits to the website overall, with more than 24,385 views.



## FUNDRAISING

### NLA Lifetime Membership

In November 2012, the NLA launched a new membership program benefiting the Foundation. Each Lifetime Member donated \$1,000 to the Foundation for the purpose of establishing training programs in Lipidology; an additional \$500 went towards the members' lifetime NLA dues. Eligible NLA members were able to become Lifetime members until December 31, 2013. Overall, the Foundation raised \$175,000 through the NLA Lifetime Membership program.

## Thank you to our Lifetime Members: \$1,000 Contribution

Nicola Abate, MD, FNLA	Thomas Dayspring, MD, FNLA	Dana Houser, MD, MHSA	Pamela Morris, MD, FNLA	Charlie Shaeffer, MD
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## Scan for Lipids

2013 was the third year the Foundation benefited from the NLA's "Scan for Lipids" program at its scientific meetings. Participating exhibitors agreed to donate \$1 for every attendee name badge scanned.

## Thank you to the Scan for Lipids participants!

Aegerion Pharmaceuticals, Inc.	Carlson Laboratories	Genzyme Corporation	LipoScience, Inc.	Syanegeva BioPharma
Amarin Corp.	Cleveland HeartLab, Inc.	GuardaHeart	Medscape, LLC	
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# Use of a Disease Registry and Primary Care Office Teams to Improve Lipid Goal Achievement in Patients with Diabetes

**EDWARD SHAHADY, MD, FAAFP**

Medical Director  
Diabetes Master Clinician Program  
Florida Academy of Family Physicians Foundation  
Fernandina Beach, FL  
*Diplomate, American Board of Clinical Lipidology*



## Introduction

Most diabetes care occurs in a primary care setting. Standards of diabetes care from several professional organizations include setting specific lipid goals for diabetic patients. Recommendations include medication and lifestyle changes to achieve lipid and glucose goals. Several studies indicate that about 50% of patients with diabetes achieve their goals and far fewer achieve all of their goals at the same time.<sup>7,8,9</sup> Addressing these gaps in quality requires system changes. A disease registry and a primary care office

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“Standards of care change and different professional organizations have different standards.”

---

team that implements population-based care strategies for diabetes can help. This article describes how the Diabetes Master

Clinician Program (DMCP) has addressed this issue.

The DMCP started in 2003 and currently has 115 offices, greater than 700 clinicians, including family physicians, general internists, nurse practitioners and physician assistants. Demographic and quality-of-care information metrics for each patient are entered into an Internet-based registry. The registry currently contains information on 22,262 patients and 130,263 visits; and from it patient report cards are produced reflecting clinic performance, individual clinician performance, and population reports for segments such as those with low-density lipoprotein (LDL). The primary care office team – composed of a clinician, nurse, medical assistant and front office staff – reviews all of these reports and, with the help of the DMCP program, is part of team-based solutions to decrease gaps in care.<sup>1</sup>

Functioning as a team is a major challenge. Traditional training and experience for clinicians is oriented toward one-on-one care. Training is not usually oriented

toward care of at-risk populations within a practice. Population management requires registries to manage chronic disease, experience with using registry reports to create population approaches to chronic disease and skills to empower office team members to assume significant responsibility for resolving gaps in quality of care.<sup>2</sup> Healthcare reform and the patient-centered medical home will be no more than rhetoric if robust registries and effective primary care teams are not part of the solution. Current patient-centered medical home guidelines stress the importance of registries and teams but do not require documentation of their effective utilization.<sup>3</sup> Decreasing the cost of care for chronic disease will benefit from registries and team care.<sup>4</sup>



Discuss this article at  
[www.lipid.org/lipidspin](http://www.lipid.org/lipidspin)

**Fictional Patient Report Card Mr. J Smith, age 59**

	Goal	12/2013	9/2013	3/2013	9/2012
Weight		199	201	211	215
Blood Pressure	Less than 140/80	140/80	135/68	145/85	148/88
<b>Lab Tests</b>					
HbA1c ( <i>sugar for 3 months</i> )	Less than 7%	7.1	7.4	8.5	8.9
LDL ( <i>lousy cholesterol</i> )	Less than 100	100	130	170	190
HDL ( <i>happy cholesterol</i> )	More than 40	42	42	38	37
Triglycerides ( <i>another fatty substance</i> )	Less than 150	150	170	255	270
<b>Medications</b>					
Aspirin ( <i>prevents heart attacks</i> )	Take daily	Yes	Yes	Yes	No
Important yearly activities	Goal	Status	Next Test Due	Most Recent Test	
Eye Check ( <i>prevents blindness</i> )	1 time a year	Complete	3/2014	3/2013	
Foot Check ( <i>prevents amputations</i> )	1 time a year	Overdue	9/2013	9/2012	
Urine Microalbumin ( <i>prevents kidney failure</i> )	1 time a year	Complete	3/2014	3/2013	
Flu Shot ( <i>prevents flu and pneumonia</i> )	1 time a year	Overdue	9/2013	9/2012	
Special Vaccine	Goal	Status			
Pneumovax ( <i>prevents pneumonia</i> )	Give once in a lifetime unless first before age 65, then give second shot	First shot given			

## Report 2 Clinic Report (represents actual data)

**Patients Meeting Goal on Most Recent Tests**

Clinic ID		HbA1c	LDL	B/P	All 3 same time	
Clinic X	% patients met goals	59%	69%	55%	27%	
All Clinics	% patients met goals	56%	62%	57%	23%	
Goals		<7	<100	130/80		
	Goals	All clinics averages			Clinic X averages	
Number of Patients		22,262			311	
Number of Visits		130,263			1285	
Blood Pressure	130/80	131/76			128/75	
Eye Check	One time a year	25%			47%	
Foot Check	One time a year	34%			64%	
A1C	<7	7.2			7.1	
Total Cholesterol	<200	171			165	
LDL	<100	93			86	
HDL		46			43	
Non-HDL	<130	125			122	
Triglycerides	<150	167			176	
Urine Microalbumin	One time a year	35%			59%	
Flu Shot	One time a year	21%			58%	

## The Patient Report Card

Patients receive their report (report 1) from the medical assistant/nurse before they see the clinician. The MA/nurse will provide a brief explanation of the results in patient terms to prepare the patient for the clinical encounter. The explanation for each of the quality metrics enables the MA/nurse and patient to understand why these items are important. Feedback about this report card indicates that patients are more likely to accept a test, immunization or medication because of the report card. MAs/nurses contribute a lot.

## Clinic Report Cards

Clinic report cards (Report 2) provide a clinic/office with an indication of its level of goal achievement for all of its patients with diabetes. Staff members can use these numbers to motivate their team to improve the percentage of patients at goal. The report also compares their clinic's data with the average for all 115 practices that participate in the DMCP. The team can use additional reports to identify which patients are not at goal. Indicators include A1C, LDL, blood pressure, non-high-density lipoprotein HDL and triglycerides (Report 3 is an example for LDL). Additional reports are available that list patients who have not had other important items evaluated like urine microalbumin, flu shots etc. The office team meets periodically to review these reports and to create strategies to communicate with patients. Strategies include phone calls, text messages, emails, group visits and additional office visits. These activities help develop a participatory office.<sup>5</sup>

## Value of Registries and Teams

Health-care reform is changing the reimbursement system for primary care. Volume-based systems will be replaced by value-based systems. Reimbursement will be based on the quality of care provided. Registries and functioning participatory teams are keys to an effective value-based

## Report 3

### Most recent LDL subgroups (fictitious patients) for a clinic

Clinic #	Very high >130	High 130-100	Target <99
# of patients	69	95	145

### Partial List of patients (fictitious patients) with Very High LDL

Medical Record Number	Name	LDL level
43115	Joe Smith	178
34221	Sam Smith	145
33387	Sue Smith	155
77763	Santa Claus	149
65578	Sue Claus	139
23114	Big Bud	156
3345	Red Bud	139

system. There will be challenges, especially when it comes to the benchmarks for quality. Standards of care change and different professional organizations have different standards. Other variables include the type of population within a practice, health insurance coverage, percent of disadvantage patients and level of health literacy. These influence the ability of a practice to increase the percentage of patients at goal.<sup>6</sup> Practice registries may help. Practices in this scenario are able to identify their patient characteristics and metrics at base line (before treatment) and then are able to use improvements over baseline to judge goal achievement and reimbursement. This requires innovation, patience, political/emotional intelligence, and drive. ■

*Disclosure statement: Dr. Shahady has received honorarium from Merck, Janssen and Lilly/Boehringer Ingelheim.*

*References are listed on page 38.*

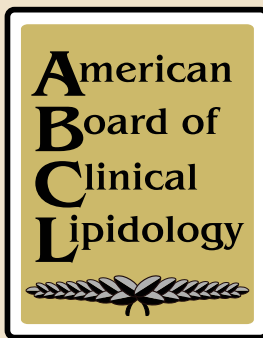
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# Impact of Change in HDL Measurement Technology on the Prediction Atherothrombotic Disease Risk

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Bowling Green, OH



Science occasionally achieves knowledge by a giant leap into the unknown, but it more often does so by the continuous accumulation of knowledge in a layer-on-layer effect, similar to the layering of sediments in a lake bed. As Isaac Newton once remarked, “If I have seen a little farther, it is because I have stood on the shoulders of giants.” So it is with the fields of lipidology and preventive cardiology. The Framingham Heart Study (FHS) led the way in identifying risk factors for atherothrombotic disease (ATD), showing that lipids were a prime cause of ATD and that the spectrum of lipids typical of the ATD population was different from the lipid spectrum of the population without clinical ATD. The FHS eventually developed the concept of the CT (Total Cholesterol):HDL ratio, or Framingham Fraction (FF), as the best lipid predictor. The FF predicts the population at risk of ATD better than LDL by itself.<sup>1-5</sup>

In or around the year 2000, the methodology for measuring HDL changed, and manufacturers of the auto-analyzers switched from the precipitation (indirect) method of measuring HDL to the enzymatic (direct) method. This method change was not much publicized, and disagreements between the two measurements may exist. Since low-density lipoprotein (LDL) is not usually measured but rather calculated by the Friedewald equation, this means that, of necessity, the LDL calculated when the

direct measurement of HDL is utilized may differ from the result that would have been obtained had the indirect method been utilized.

This is important because many clinical trials have been done using the indirect measurement of HDL,<sup>6,7,8,9</sup> which in turn may have impacted results and subsequent interpretations. In other words, the lipids on paper, as determined by the direct method of HDL measurement, may not reflect the atherogenic potential of the lipids, based on the indirect method of HDL measurement, at the level of the arterial wall.

These points are not trivial. I previously reported a case of a 55-year-old patient who sustained an acute myocardial infarction (AMI).<sup>10</sup> There was no obvious reason to measure his lipids – no obesity, cigarette smoking, hypertension, diabetes or even a family history of ATD. He did have recurrent bouts of job-related depression. At the time of his AMI, a lipid panel done at the hospital on admission showed an LDL-C of 143 mg/dl, HDL-C of 43 mg/dl and TG of 66 mg/dl. Many practitioners may have elected not to treat such a lipid panel in a primary-prevention scenario. However, changes in HDL measurement technology might have led to different HDL-C and LDL-C values that would have caused his risk to be interpreted differently and perhaps earlier and more aggressive lipid management.



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With the introduction of new technology, I requested that our hospital laboratory take this into account. Other authors<sup>11,12</sup> have commented on the effects of this change in technology and the interpretation of current lipid values but have not suggested a remedy. I believe my suggestion constitutes such a remedy, and I urge lipidologists start a dialogue with their laboratories regarding these issues.

*NB: Readers of the LipidSpin will know that my preferred lipid predictor is the cholesterol retention fraction ( $(LDL-HDL)/LDL$ ) because it predicts the population at risk of ATD better than the LDL:HDL ratio and avoids the pitfalls of FF.<sup>13</sup>*

*Disclosure statement: Dr. Feeman has no disclosures to report.*

*References are listed on page 38.*

# Pregnancy and Perinatal-Related Determinates of Childhood Cardiovascular Disease Risk



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## Case Presentation

A 10-year-old girl was referred for elevated cholesterol. Her laboratory findings showed a total cholesterol (TC) of 364 mg/dL, triglyceride (Tg) 65 mg/dL, high-density lipoprotein cholesterol (HDL-c) 45 mg/dL, and low-density lipoprotein cholesterol (LDL-c) 300 mg/dL. She had a prior history of obesity with a body mass index (BMI) >95<sup>th</sup> %, but was otherwise healthy.

The child's 42-year-old mother was taking a statin for a TC > 300 mg/dL. The

maternal grandfather had a myocardial infarction at age 44. The paternal family history is unknown.

The girl was diagnosed with heterozygous familial hypercholesterolemia (heFH). Methods to achieve a heart-healthy lifestyle were outlined, including the importance of weight management, and she was treated with atorvastatin 10 mg/daily. Follow-up labs were: TC 146 mg/dL; Tg 70 mg/dL; HDL-C 44 mg/dL; LDL-C 90 mg/dL. Her aspartate aminotransferase (AST), alanine aminotransferase (ALT) and creatine kinase (CK) were normal.

Her weight continued to increase during adolescence. Menarche occurred at 11 years of age, but her menstrual cycles were irregular. By age 17, her BMI was 30.5 kg/m<sup>2</sup> (> 99<sup>th</sup> %) and her blood

## List of Abbreviations:

ACE	- angiotensin-converting enzyme
ALT	- alanine aminotransferase
AST	- aspartate aminotransferase
BG	- blood glucose
BMI	- body mass index
BP	- blood pressure
CK	- creatine kinase
CVD	- cardiovascular disease
DM	- diabetes mellitus
GDM	- gestational diabetes mellitus
HDL-C	- high-density lipoprotein cholesterol
heFH	- heterogeneous familial hypercholesterolemia
LDL-C	- low-density lipoprotein cholesterol
OGTT	- oral glucose tolerance test
TC	- Total cholesterol
Tg	- triglycerides
β-HCG	- beta human chorionic gonadotropin

“Ironically, the impact of excessive gestational weight gain may be most pronounced among mothers who are underweight prior to pregnancy.”

pressure (BP) was 148/88 mmHg, prompting further testing. Her fasting lipid profile showed TC 180 mg/dL; Tg 325 mg/dL; HDL-C 32 mg/dL; LDL-C 114 mg/dL. AST / ALT were mildly elevated. Thyroid function was normal. Oral glucose tolerance test (OGTT): fasting blood glucose (BG) 122 mg/dL; 2 hour 188 mg/dL. She was diagnosed with pre-diabetes and treated with metformin 1000 mg twice daily. An angiotensin-converting enzyme (ACE) inhibitor was prescribed and she was reminded of the importance of therapeutic lifestyle modification, including the need for 5%-10% weight loss.

At the time of her most recent clinic visit, she had gained 12 Kg during the past 6 months and had missed her last two menstrual periods. Despite claims that she was not sexually active, a beta human chorionic gonadotropin (β-HCG) confirmed she was pregnant. Her atorvastatin and lisinopril were discontinued. She remained on metformin and was referred for obstetrical care.

This case represents a growing concern – one that is increasingly seen in clinical practice. Although the problems of teenage pregnancy are long-standing, the

epidemic increase in childhood obesity and obesity-related comorbid conditions makes such pregnancies an even higher risk than before. Since statins are contraindicated during pregnancy, this 17-year-old’s markedly elevated LDL-C poses an additional risk factor. While this teen has several preceding and ongoing health risks, in this article we focus on the consequence of a high-risk in-utero environment on the long-term health of the fetus.

**Does the mother’s pre-pregnancy weight, the amount of weight gained during pregnancy, or both, increase the risk of childhood obesity?**

The mother’s pre-pregnancy weight has consistently been shown to be a strong predictor of childhood obesity.<sup>1</sup> There

In addition to her weight status, the risk of childhood obesity varies by the mother’s race/ethnicity. Compared to non-Hispanic white women, African-American women are at higher risk of being overweight at conception, developing GDM and being less likely to breastfeed their offspring. Hispanic women also are at increased risk.

Ironically, the impact of excessive gestational weight gain may be most pronounced among mothers who are underweight prior to pregnancy (Table 2). Maternal underweight may be associated with childhood obesity if there is excess or inadequate maternal weight gain during pregnancy or rapid catch-up growth of the child during infancy and early childhood.<sup>3,4</sup>

Pre-Pregnancy BMI	BMI (kg/m <sup>2</sup> )	Total Weight Gain (lbs.)	Rate of Weight Gain 2 <sup>nd</sup> -3 <sup>rd</sup> Trimesters (lbs/week)
Underweight	<18.5	28-40	1-1.3
Normal Weight	18.5-24.9	25-35	0.8-1
Overweight	25-29.9	15-25	0.5-0.7
Obese	≥30	11-20	0.4-0.6

From Weight Gain During Pregnancy: Reexamining the Guidelines. Edited by Kathleen M. Rasmussen and Ann L. Yaktine. Institute of Medicine (U.S.) and National Research Council (U.S.) Committee to Reexamine IOM Pregnancy Weight Guidelines. Washington (DC): National Academies Press (U.S.); 2009.

Table 1. Institute of Medicine (2009) goals for weight gain during pregnancy.

was a 3.6 times increased risk among 2- to 14-year-olds whose mothers were obese (BMI ≥ 30) prior to pregnancy versus those who were not obese (BMI ≤ 25). Recommended weight gain during pregnancy is shown in Table 1.

Regardless of a woman’s weight prior to pregnancy, excess weight gain during pregnancy doubles the risk of macrosomia and increases the risk of gestational diabetes (GDM), both predictors of childhood obesity.<sup>2</sup>

**What are the long-term consequences of maternal insulin resistance and diabetes?**

Diabetes mellitus (DM) occurs in approximately 5%-10% of U.S. pregnancies (2% T1DM; 8% T2DM and 90% GDM). Although diabetic women should optimize their health prior to conception, 50% of all pregnancies are unplanned and the majority of those with diabetes have GDM; therefore, the mother’s glycemic control may be inadequate at time of conception and during the early part of her pregnancy.

Women who are overweight/obese, even if not diabetic, have more obstetrical complications in pregnancy including a higher-than-usual rate of GDM. While both obesity and GDM were found to be independently associated with adverse pregnancy outcomes, the presence of both had a greater impact than either one alone. Catalano, et al.<sup>5</sup> observed that even small elevations in blood glucose (BG) levels in pregnancy are associated with

potentially toxic uterine environment attributable to maternal risk factors, including DM and hypercholesterolemia. Maternal cholesterol crosses the placental barrier and is a major substrate for the growing fetus. Compared with levels before pregnancy, total cholesterol and LDL-C are typically increased by 30%-50%. Maternal lipid levels may be altered by a variety of factors, including the mother's health before and during pregnancy, use

## Conclusion

The mother's genetic background and the presence of known CVD risk factors – such as obesity, insulin resistance/diabetes and dyslipidemia – during pregnancy function as important determinates of future cardiovascular risk for the fetus. Maternal factors may be particularly strong within population subgroups at increased risk (i.e. African American and Hispanic women). The exceedingly high number of overweight/obese women of child-bearing age, the frequency of genetic hypercholesterolemia and the increasing prevalence of insulin resistance/diabetes call for renewed awareness and aggressive management to improve the health and maintain the welfare of both the mother and her fetus. Optimizing the mother's health prior to conception, as well as appropriate maternal weight gain, lipid levels and glycemic control during pregnancy, may help to prevent long-term adverse consequences in the offspring. ■

*Disclosure statement: Dr. Wilson has served on the speakers bureau for Osler Institute, Advisory Board member of Aegerion Pharmaceuticals and has participated in research funding for Merck Sharp & Dohme and Novo Nordisk Inc. Dr. McNeal has no disclosures to report.*

*References are listed on page 39.*

Mother's pre-pregnancy weight	Odd Ratio of Childhood Obesity at 7 years of age
Normal weight	1.00
Overweight	1.38
Obese	2.56
Underweight	3.36

Table 2. Estimated risk of childhood obesity at 7 years of age based on the mother's pre-pregnancy BMI and excessive gestational weight gain.<sup>3</sup>

increased maternal and fetal complications in pregnancy. Maternal glucose levels were associated with excess fetal growth and later risk of diabetes, even among women with normal glucose-tolerance tests. With each standard deviation increase in maternal BG, birth weight increased significantly and the risk of T2DM in the offspring was increased by 30%.

Does the type of maternal diabetes matter? Several studies have found that the effects of exposure to diabetes in utero on future obesity in the child are similar for pregnancies complicated by T1DM, T2DM and GDM<sup>6</sup>.

### What is the association between maternal hypercholesterolemia and childhood cardiovascular disease (CVD) risk?

In addition to the genetic risk of heFH, research also has focused on the

of medications, BMI and weight gain during pregnancy, smoking and genetics.

Early studies found that fatty streaks were more prevalent in fetuses from hypercholesterolemic mothers and more likely to progress to atherosclerotic lesions after birth, even in offspring with normal cholesterol levels.<sup>7</sup> Other diseases such as maternal DM and obesity alter the flux of cholesterol across the placental membrane and also increase the risk of congenital defects.<sup>8</sup> It has been suggested that the adverse effects of maternal risk factors in the fetus may be explained by epigenetic changes attributable to DNA methylation, chromatin modifications and/or oxidative stress.<sup>9</sup> Although statins are contraindicated in pregnant women (Class X), the bile-acid sequestrants (colesevelam, colestipol) are presumed safe (Class B), while the safety of ezetimibe, fibrates and fish oil are uncertain (Class C).

# Type III Apo E2/2 Dysbetalipoproteinemia Presenting with Rectal Hemorrhaging from Ischemic Colitis

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A 64-year-old woman was hospitalized with abdominal pain and gastrointestinal (GI) hemorrhaging. She was severely anemic with marked elevation of both cholesterol and triglycerides. The patient was transfused. Colonoscopy revealed severe right-sided ischemic colitis. A two-dimensional (2-D) echocardiogram was normal and telemetry showed no arrhythmia. An aortogram did not show the cause of interruption of mesenteric blood flow to the colon, although irregularity and 50% stenosis of the abdominal aorta was noted. The colon did not infarct and she survived without requiring surgical resection.

Fasting lipids were normal prior to menopause. She developed hypothyroidism and cholesterol rose to 517 and triglycerides rose to 403. Her endocrinologist prescribed replacement Synthroid, Questran 4 gms and niacin 1500 mg. Within the next 10 years, she developed peripheral vascular disease (PVD), 50% stenosis of the abdominal aorta and life-threatening ischemic colitis.

The clinical presentation suggests Type

III Dysbetalipoproteinemia as expressed in patients with the Apo E 2//2 genotype, which in her case resulted in spontaneous recurring cholesterol emboli from aortic plaque to the colon. This lipid disorder is highly atherogenic, involves defective apolipoprotein E (apo E) rather than apolipoprotein B (apo B) and its receptor abnormalities, with fascinating paradoxes<sup>1</sup> and intriguing effects that go far beyond lipoprotein metabolism such as Alzheimer's disease, HIV and Hepatitis C virus (HCV).<sup>2</sup>

Hypercholesterolemia is listed as a risk factor for ischemic colitis. Clinically, in a patient with hypercholesterolemia and ischemic colitis, one would expect blockage of mesenteric flow by plaque or emboli. However, if an aortogram were to be performed, flow in the mesenteric vessels will most often appear normal. Unexpectedly, massive caking of atherosclerotic plaque of the aorta may be seen. Although ischemic colitis in hypercholesterolemic and non-hypercholesterolemic individuals is thought to be caused primarily by low-flow states – as during dialysis or hypotensive shock<sup>3,4</sup> – emboli from aortic plaque have

been found in submucosal arterioles of the stomach and colon in resected specimens and at autopsy. The arterioles are usually too deep to be seen on superficial biopsies and too small to be seen on angiography.<sup>5</sup> GI complaints are usually vague and endoscopy may not recognize embolic ischemic gastric ulcers or gastric livido reticularis. A colonoscopy may misdiagnose ischemic changes as chronic ulcerative colitis. Only about 10% are recognized pre-mortem.<sup>6</sup>

Severely elevated lipid values and responses to metabolic changes with diet in a recently menopausal woman with a frighteningly rapid atherogenic hyperlipoproteinemia (HLP) having elevated HDL cholesterol (HDL-C) with markedly elevated very-low-density lipoprotein cholesterol (VLDL-C) but normal glucose suggest Type III



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dysbetalipoproteinemia. Findings of xanthoma stratum palmare (XSP) which appear as orange creases of the palms of the hands and electrophoretic broad bands occur in less than 20% of cases. Isoelectric Focusing done at Rockefeller Research Institute confirmed the diagnosis of Phenotype E 2/2 Type III Beta Dyslipoproteinemia. Genotyping also is now available.<sup>8</sup>

The patient was treated with estrogen, thyroid, vitamin B12, folic acid, dietary modifications and fibrates, with evidence of plaque regression on subsequent aortograms.<sup>9</sup> Currently, estrogen therapy would be considered controversial.<sup>12,13,14</sup>

The most common cause of Type III HLP is fully expressed in only 1 in 50 of the 1% of carriers of Genotype E 2/2. The problems do not reside in abnormalities in apo B or its liver uptake receptors, but rather that the highest-affinity receptors are normal in number and function but cannot recognize lipoproteins that express the E 2/2 allele. These include both the meal-derived chylomicron and hepatic-secreted VLDL remnants. They are removed by other less efficient cellular receptors and fasting lipids may appear normal for decades. Hyperlipidemia is expressed only if new metabolic changes or mutations overwhelm the compensatory modalities when superimposed on the underlying defective E 2/2 genotype. Declining estrogen levels after menopause (increased synthesis, decreased receptors), hypothyroidism (decreased receptors), obesity and insulin resistance (increased synthesis) enhance apo E influence on synthesis, impairment of lipolysis and clearance.<sup>3,8</sup>

In these patient cholesterol accumulates in the increasingly vast numbers of lingering and trapped metabolically deranged VLDL. Prolonged exposure to impaired lipolysis of abundant triglyceride drive downsizing and exchange for cholesterol to ever

smaller and denser remnant particles with the cholesterol content shifting from 20 to 60% and approaching the size of large buoyant LDL. However, although similar in size, there are physical and functional changes that take place.<sup>10</sup> The increased concentration of such particles may cause a gradient-driven diffusion of these particles into the sub-endothelial space, which in turn leads to increased atherosclerosis.

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**“A colonoscopy  
may misdiagnose  
ischemic changes as  
chronic ulcerative  
colitis. Only about  
10% are recognized  
premortem.”**

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Apo E, has multiple forms and functions. Three isoforms are seen on isoelectric-focusing lipoprotein electrophoresis. E3 is the most common form and considered the most normal in structure and function. E4 and E2 have opposing actions when secreted locally in the brain, in the liver, in plasma on lipoprotein metabolism.

The Apo E4/E4 genotype is associated with a 14-fold increase in risk for Alzheimer's disease and other neurodegenerative diseases. Small amounts are secreted locally in brain tissue but become fragmented and leak into the cytosol, interfering with mitochondria and neuronal repair. In the liver, E4 promotes progression of HIV and HCV. The effect of E4 on lipoprotein metabolism is one of only minor lipid variations. Remarkably, in the laboratory, minor changes convert E4 to the normally structured and functioning

E3 genotype.<sup>2</sup>

As opposed to E4, the E2 secreted in brain tissue delays Alzheimer's disease by up to 30 years.<sup>11</sup> Other effects on the brain are not benign. E2 promotes generalized atherosclerosis, including vascular dementia via abnormal lipoprotein metabolism and atherogenic HLP. In the liver, E2 interferes with the lipid envelope of HCV and HIV, preventing their replication.<sup>2</sup>

Over time, the patient became lax, fired her cook, began eating out at restaurants very frequently, resumed drinking two glasses of wine a day and gained 40 pounds. Niacin and then statins were prescribed, but her PVD progressed. At age 77, she required a left circumflex stent and, at age 92, replacement of a xanthomatous – not calcific – aortic valve. She did not develop either atherosclerotic dementia or Alzheimer's Disease. ■

*Disclosure statement: Dr. DuShey has no disclosures to report.*

*References are listed on page 39.*

# Firefighters and CVD: Heroes with Hearts at Risk

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## Background

There are more than one million firefighters in the United States. Excluding the tragic loss of 342 firefighters in New York City on Sept. 11, 2001, approximately 100 firefighters die in the line of duty (LOD) each year in the United States.<sup>1</sup> However, direct fire injury is not – as might be expected – the leading cause of such deaths. In fact, cardiovascular disease (CVD) is the most common cause of LOD deaths among firefighters, accounting for approximately one-half of all firefighter deaths annually.<sup>1</sup> Firefighters experience the highest proportionate LOD mortality because of CVD as compared with other occupational groups, including police and other public safety officers.<sup>2</sup>



## Characteristics of Firefighter CVD Deaths

Approximately 25% of firefighters are employed as full-time career professionals and 75% are volunteers.

LOD deaths among firefighters occur in a similar distribution.<sup>3</sup> Approximately one-

third of all fatal cardiovascular-related events occur during direct fire suppression activity, another one-third en route to or from a fire event, and one-third during other training activities.<sup>3,4</sup> Of particular note, only 1% to 2% of a firefighter's actual time on duty is devoted to fire events. Accordingly, it has been estimated that the relative risk of a cardiovascular event occurring with fire suppression is from 10- to 100-fold greater than the risk during non-fire suppression activities.<sup>4</sup> The majority of these deaths occur between noon and midnight, corresponding to the most likely time of fire occurrence, unlike the typical early morning circadian pattern of most cardiovascular events.<sup>3</sup> Additionally, for every death, it is estimated that 17 nonfatal cardiac events occur.<sup>5</sup> Autopsies have tended to show underlying coronary artery disease and/or left ventricular hypertrophy.<sup>6</sup>

## Contributing Factors

Multiple factors have been identified that may contribute to the cardiovascular disease risk of firefighters. Traditional risk factors do correlate with firefighter CVD deaths: age > 45 years, current smoking, hypertension, diabetes and prior diagnosis of CHD or other arterial-occlusive disease.<sup>3</sup> There is

evidence that traditional risk factors – such as obesity, hypertension, dyslipidemia and diabetes – are more common among firefighters than among the general population.<sup>4</sup> However, smoking appears to be an exception. Firefighters tend to smoke cigarettes less than their comparable male counterparts, although their use of smokeless tobacco may be high.<sup>7</sup> Superko, et al., observed the presence of coronary artery calcium (CAC) in 35.6% (101/286) of asymptomatic firefighters over the age of 40 in a study of male firefighters without a known history of CVD.<sup>8</sup> No age-matched controls were reported. In this study, the presence of positive coronary artery calcium was associated with markers of metabolic syndrome – elevated fasting glucose, blood pressure and weight, as well as dyslipidemia. There are additional factors unique to firefighters that may increase the likelihood of an acute cardiovascular event,



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Potential Cardiovascular Risk Contributors Unique To Firefighters	
• Long sedentary periods	• Smoke inhalation
• “Firehouse” diets	• CO, other toxins
• Sudden interruptions	• High heat exposure
• Irregular sleep patterns	• Dehydration risk
• Extreme workloads	• Loud noise levels

Adapted from Soteriades et al 2007

Table 1.

as listed in Table 1.<sup>4</sup> Potential mechanisms of action are summarized in Table 2.<sup>6</sup>

### Are Firefighters at Greater Risk Than the General Population?

Based on a study of CVD deaths among firefighters in Toronto, Bates estimated that firefighters have an increased risk of fatal CVD from 1.7 to 2.4 times that of the general population.<sup>9</sup> However, there are no prospective studies comparing firefighters with matched controls. Little data are available on the lifetime risk of firefighters. In their review, Soteriades, et al., suggest that the lifetime risk of CVD for firefighters is about 35%, comparable to the general population.<sup>2</sup> One potential confounding factor may be the “healthy worker effect.” Firefighters are likely to be healthier than the general population at the time of hiring, because those with known CVD are likely to be excluded. Therefore, it is possible that firefighters’ overall risk of cardiovascular disease and death is no greater than the general population, except during very stressful but infrequent work conditions (ie, actual fire events), and only for certain predisposed firefighters. Further study is needed.

### Consequences of a Firefighter Cardiovascular Event

There are serious consequences to a firefighter illness or death. Anecdotally, it often is observed that whenever a firefighter “goes down,” for whatever reason, the attention of his/her fellow firefighters is

diverted to their fallen comrade, rather than the fire they are trying to extinguish. This further contributes to the increased risk of life and property. In the event of death or prolonged disability, the department suffers a significant loss of personnel until that firefighter returns or can be replaced. There are additional economic consequences. The diagnosis of CVD in a firefighter

generally is considered work-related, regardless of the circumstances. The 2003 Hometown Heroes Act provides compensation to survivors of firefighters and other emergency personnel who die from CVD.<sup>10</sup>

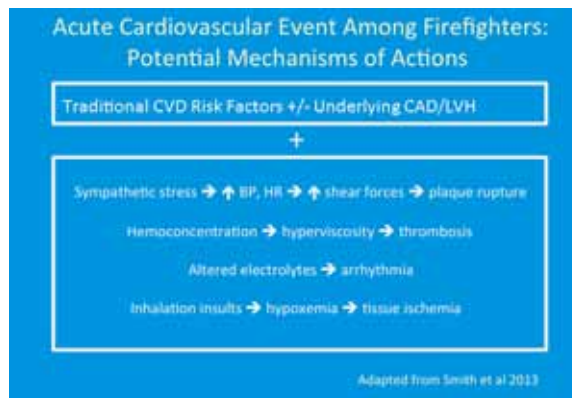


Table 2.

### What Is Being Done?

The National Volunteer Fire Council (NVFC) has made awareness of firefighters and CVD a major priority, offering online education, publications and on-site screenings.<sup>11</sup> The National Fire Protection Association (NFPA) and Occupational Health and Safety Administration (OSHA) currently recommend, but do not require, thorough annual medical evaluations of firefighters, as well as departmental programs to promote health and fitness.<sup>12,13</sup> Primarily due to financial limitations, many departments offer limited, if any, medical evaluations and fitness programs to their firefighters. Kales, et al., observed that only 25 % of the time had firefighters who died from an acute cardiovascular event undergone a medical evaluation in the preceding 24 months.<sup>3</sup> To

date, there are no known studies reporting a proven strategy to reduce cardiovascular disease and events among firefighters.

### Study in Progress

To provide further understanding of firefighters and their risk for CVD, we have initiated a study of firefighters in North Carolina, with attention to lifestyle; traditional risk factors, including standard lipid profiles; “advanced lipid testing” assessing for “discordance” and risk not recognized by traditional low-density lipoprotein cholesterol (LDL-C) levels, and markers of inflammation. We hope to report our findings soon.

### Final notes and Recommendations

Considering the number of firefighters across the country, all clinicians are likely to encounter firefighters in their practices. Lipid specialists should be aware of the cardiovascular risk that exists among firefighters and be familiar not only with the traditional risk factors among firefighters but also those occupational risks that are unique to these public servants.

Additional research is critically needed to determine what, if any, cost-effective strategies might be implemented to more accurately identify those firefighters at risk and, if possible, reduce that risk.

### Acknowledgements

The author wishes to thank Michelle Beidelschies, PhD, of Cleveland HeartLab, Inc., and Debbie Winegar, PhD, of LipoScience Inc. for their editorial assistance and support of on-going research, and all firefighters and their families for their dedication and sacrifices on our behalf. ■

*Disclosure statement: Dr. White has served on the speakers bureau for AbbVie, Amarin, Liposcience and Vivus and is a stockholder in Isis.*

*References are listed on page 39.*

# Education and Meeting News and Notes

## National Lipid Association 2014 Annual Scientific Sessions

The NLA Annual Scientific Sessions will be held May 1–4 at the Hyatt Regency Grand Cypress Hotel in Orlando, Florida. Highlights include a keynote from Jonathan C. Cohen, PhD: *History of PCSK9 from Discovery to Drug Development*; *Using Genetic Tests Critically in Clinical Practice* by Christie Ballantyne, MD, FNLA; *LP(a) as a Target* by Patrick M. Moriarty, MD, FNLA; *Guidelines in Clinical Lipidology: The Essential Components* hosted by W. Brown, MD, FNLA; and *Screening for Heart Disease* by Matthew J. Budoff, MD. Visit [www.lipid.org/sessions](http://www.lipid.org/sessions) to register today!

## Order the NLA Self-Assessment Program Today!

The NLA-SAP, updated and revised as of September 2013, is now available in both print and online. To order your copy visit [www.lipid.org/nlasap](http://www.lipid.org/nlasap).

## NLA Applies for ICD-10 Code for Familial Hypercholesterolemia (FH)

The National Lipid Association (NLA) is excited to announce it has submitted a proposal to the National Center for Health Statistics (NCHS) to create new, specific ICD-10 codes for FH, which would include homozygous FH and heterozygous FH. The NCHS is the federal agency responsible for revising the ICD codes and will review this proposal. The NLA worked collaboratively with The FH Foundation to draft this proposal that will have a profound impact on the diagnosis and treatment of FH. The ICD-10 Coordination and Maintenance

Committee will review this proposal at their meeting in March and, if approved, would go into effect on October 1, 2015. The committee will release its decision on the proposal in June. The NLA thanks the FH Foundation for its contributions to this effort and both organizations will be providing testimony at the March committee hearing. Please stay tuned for additional updates.

## NLA Receives NAMEC Award

The NLA was recently awarded Best Practice in Educational Design & Evaluation by the National Association of Medical Education Companies (NAMEC). The award recognizes the work of the NLA, along with its educational partner, MCM Education, for a series of activities in 2012-2013 titled *Managing Residual CVD Risk: The Role of HDL Cholesterol*.

The award was presented during the Alliance for Continuing Education in the Health Professions conference in Orlando, FL this past weekend. On hand to receive the award were Dr. Robert Wild, Chair of the NLA CME Committee and Chris DeVille, NLA Director of Education along with Dr. Joseph Kim, President of MCM Education and Kristen Petro, MCM Director of Medical Education.

## Congratulate your fellow NLA members at the annual Honors and Awards Ceremony

When you are in Orlando for the Annual Scientific Sessions, please make time to attend the annual Honors and Awards Convocation Ceremony, Saturday, May

3 from 6:30-7:30 p.m. At the ceremony, we will recognize new Fellows of the NLA, new ABCL diplomates, new ACCL diplomates and the NLA special awards: Distinguished Achievement Award, Honorary Lifetime Membership Award and the President's Service Award.

## Attend the Foundation of the NLA Event in Orlando

When: Saturday evening, May 3rd  
Cost: \$150 per person

Join us for a fun evening of dinner, dancing and games with the Foundation of the NLA. The Hyatt Regency Grand Cypress Hotel's luxurious ballroom provides the perfect setting to enjoy a scrumptious buffet. Let your hair down while you eat, drink, enjoy the music and have a little fun playing against friends and colleagues with giant games like Jenga or Connect Four that will be set up during the event. Separate registration is required for this event. Go to [lipid.org/sessions](http://lipid.org/sessions) to register.

## In Memoriam

Dr. Roger Illingworth passed away in early November after a long illness. He was a founding member of the NLA Board. Dr. Illingworth's career was dedicated to understanding, preventing and treating patients with cholesterol and lipid disorders and heart disease, and his research was instrumental in the development of the statin drugs from the earliest days. Our thoughts and prayers go out to Dr. Illingworth's family.



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- 4 Contemporary Management of Dyslipidemia: Pharmacologic Therapy**
- 5 Consultative Issues in Clinical Lipidology**



CME credit provided by the National Lipid Association

These activities have been approved for *AMA PRA Category 1 Credit™*.

These activities are eligible for CPEUs by the Commission on Dietetic Registration

This activity is approved for Maintenance of Certification Points by:



CE credit provided by Advancing Knowledge in Healthcare, Inc.

This activity is eligible for ACPE, ANCC and AANP credit; See final CE activity announcement for details.

Co-provided/Co-sponsored by Advancing Knowledge in Healthcare (AKH Inc.)

Full accreditation information and details regarding order fulfillment available at [www.lipid.org/nlasap](http://www.lipid.org/nlasap)

For questions about this educational activity contact the NLA at 904-998-0854.

## Current Initiatives for Detecting Patients with Familial Hypercholesterolemia in Primary Care

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# NLA Events Calendar



## 2014 Scientific Meetings

### 2014 National Lipid Association

#### Clinical Lipid Update—Spring

*Hosted by the Pacific Lipid Association and the Southwest Lipid Association*

March 13–16, 2014

Grand Wailea Hotel, Maui, Hawaii



### 2014 National Lipid Association Scientific Sessions

*Hosted by the Southeast Lipid Association*

May 1–4, 2014

Hyatt Regency Grand Cypress Hotel, Orlando, Florida



### 2014 National Lipid Association

#### Clinical Lipid Update—Fall

*Hosted by the Midwest Lipid Association and the Northeast Lipid Association*

August 22–24, 2014

JW Marriott Hotel, Indianapolis, Indiana

*For a list of additional scientific meetings visit [lipid.org](http://lipid.org)*

# Lower Your Triglycerides with Lifestyle

Triglycerides (TGs) are a type of fat in the bloodstream. They are used for energy. When TGs become too high, this biomarker suggests risk for cardiovascular disease, especially when accompanied by low HDL-cholesterol and high LDL-cholesterol. High triglycerides are a common problem in the United States. One third of adults have levels above the normal range (< 150 mg/dl).

The good news about TGs is that they are highly responsive to lifestyle modifications. Optimal lifestyle interventions can lower TGs by 20-50%. We suggest that you look at the following chart and select a change or changes you feel ready to make!

Note: When evaluating TG levels over time, be aware that there is considerable variability in the measurement of TG. Look at the trend in TG over time (not just one reading) to evaluate the success of your lifestyle changes. Remember, the same positive lifestyle changes that lower TG, also improve your overall health!

## Effect of Lifestyle Changes on TG Lowering

LIFESTYLE FOCUS	DECREASES TG BY	TIPS FOR GETTING IT DONE
Lose 5%-10% body weight (if needed)  Loss of excess weight is critical to reduce TG levels.	20%  **for each kg loss, TG decrease by 1.9%	Calculate your personal 5-10% weight loss goal. Make a plan to lose a pound a week by decreasing daily caloric intake by 400 calories and increasing activity by 100 calories with a daily 30 minute walk of moderate intensity. Track your food intake with online apps, join a group support/food delivery/meal replacement program and/or visit a Registered Dietitian/Primary Care Physician/Healthcare Team to assist you with a personalized heart healthy weight loss plan.
Enjoy a Mediterranean style of eating; avoid very low fat eating styles.	10-15%	Focus on fresh less processed, whole foods. Eat more vegetables, beans, fruits (no juice), nuts, fish, and whole grains. Use liquid oil in place of butter and solid fats. Avoid refined grains like white bread and white rice as well as added sugars. **Avoid very low fat/high carbohydrate diets
Add marine derived omega-3 fatty acids (for each gram or 1000 mg DHA plus EPA) in the form of oily fish or supplements.	5-10%	Enjoy oily fish such as salmon, trout, sardines and herring often. Eating 12 oz of cooked salmon per week is equivalent to 1 gram of fish oil daily. Discuss an omega-3 fish oil supplement (2-4 grams daily) with your physician if you need substantial TG lowering.
Moderate intensity exercise of at least 150 minutes per week.	20-30%	Get out that pedometer and start walking, an excellent moderate intensity activity. Other activities can include ballroom dancing, gardening, biking and tennis. You can even do small bouts of activity that add up! Go to <a href="http://www.health.gov/paguidelines">www.health.gov/paguidelines</a> for more information. Find something you love to do and "just do it"!
Avoid trans fat /lower saturated fat.	For each gram less trans fat, TG decrease by 1%	Read the ingredient list on food products and avoid all that contain "partially hydrogenated oil." This includes any kind of oil that has been partially hydrogenated. Also limit saturated fat to <5-6% of calories (find your personal limit at <a href="http://www.heart.org/facethefats">www.heart.org/facethefats</a> and go to "My Fats Translator."
Focus on whole grains; limit refined carbohydrates, added sugars (which excludes milk and fruit sugar) as well as a diet high in fructose (>100 grams per day).		Make most of your grains whole. Look for 100% whole wheat bread, cereal and pasta. Limit added sugars to less than 25 grams daily for women and 37 grams daily for men or less than 10% of total calories. Recent studies have shown that fructose may raise TG more than other sugars. High fructose foods include regular soda, agave, honey and raisins.. Low fructose fruits include strawberries, bananas, peaches and cantaloupe.
Limit alcohol; complete abstinence recommended if TG are >500 mg /dl.		If you drink, limit alcohol to one serving daily for women and two for men (one serving is 12 oz beer, 5 oz wine or 1.5 oz hard liquor.)
Note: If TG are greater than 500 mg/ dl, a low fat (15% of calories) eating plan is recommended to reduce the incidence of pancreatitis.		Speak to a Registered Dietitian or Health Care Provider to personalize a low "total fat" lifestyle plan for you.

\*\* TG >1000 mg/dl are associated with increased risk of pancreatitis. Consult your physician for treatment.

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