

Lipidaholics: Atherosclerosis and atherosclerotic risk factors have many mysteries. The following case proves just how difficult it is to ascertain risk in everyone. A practitioner sent me the following case:

I would like your advice on a patient I recently evaluated on the general physical. She is a healthy 59-year-old woman, with a history of mild diverticulosis, mild osteopenia, chronically dilated pancreatic duct that was incidentally found, but known coronary artery calcification. The scan was done for no other reason than she wanted to have a thorough assessment of cardiovascular risk. The heart scan placed her at the 87th percentile for calcification at her age. EKG was normal. She does not smoke, has a BMI of 23.5, and exercises on a regular basis. She does not have any family history of heart disease.

The lipid panel revealed:

TC = 233, TG = 53, HDL-C = 107, and an LDL-C level of 115.

Because of the heart scan, I performed a Cardiac C-reactive protein which was mildly elevated at 3.8. A homocysteine level was 6.6, and normal.

The NMR LipoProfile panel revealed a particle number of 1118 (bottom 20% of the population). LDL particle size was large or type A, at 22 nm. Her large HDL was phenomenal at 76, and her large VLDL was borderline at 10. This clearly was a low risk panel.

My question is this. I have an asymptomatic patient, with an elevated cardiac C-reactive protein, and known coronary artery calcification. She is postmenopausal. My plan is to perform a stress test, possibly place her on salmon oil, and initiate an 81 mg aspirin. Could I ask you for your opinion.

DAYSRING ANSWER

What a case. One never really knows about those coronary arteries. Just looking at the lipids, one would presume low risk especially with the very high HDL. Interestingly if one would apply the NCEP Framingham risk equation, this lady would have been classified as low risk. However we know she is high risk because she has significant coronary artery disease on EBCT. Stress testing is appropriate to rule out significant obstruction especially in view of her exercise regimen. The CRP is certainly in the worrisome high risk zone so one has to think that some of her plaque may be unstable. Keep in mind that 20% of IR patients have a BMI under 26. However she has no other criteria suspicious for the metabolic syndrome.

Anytime atherosclerosis is present without obvious explanation perform a lipoprotein (a) test. Please check an Lp (a). If you have not done so checking a sitosterol level may be insightful. Postmenopausal women, as well as patients with familial history of CHD are known to hyperabsorb noncholesterol sterols (sitosterol, campesterol, etc.). The very high HDL-C brings into question genetic abnormalities: such as an abnormality of CETP, which raises HDL-C yet may be associated with atherosclerosis. Hepatic lipase deficiency which can be associated with CHD and elevated HDL-C.

In last weeks discussion I reviewed new data that in inflammatory states (typified by elevated CRP) HDL particles become dysfunctional and do not effectively perform their antiatherogenic functions, including RCT. There is a study showing that in such patients, treatment with a statin (simvastatin), correction of the inflammation returned the HDL particles to full functionality. (Circulation. 2003;108:2751-2756.)

Are there any other underlying inflammatory diseases, some of which have been associated with CHD, like Periodontal disease?

In view of the existence of CHD we have to treat very aggressively. LipoScience is now advising LDL-P be under 1000 nmol/L in the very high risk patient. (Anyone with a calcium score like this lady and with elevated CRP must be considered very high risk). I would try to reduce her LDL-P (LDL particle number) well below 1000 (shoot for 800). I would give her a low dose statin and Zetia (ezetimibe). The Zetia will make the statin more efficacious and will keep any noncholesterol sterols from being absorbed. Zetia affords additional CRP lowering to whatever the statin will do (Amer J Card 2003;92:1414-1418).

Thus Vytorin (simvastatin/ezetimibe) 10 or 20 mg, Pravachol 40/Zetia10 or Crestor 5/Zetia 10 mg are all reasonable choices. ASA and omega-3 FA supplementation are sound recommendations. Her first degree relatives should be closely evaluated.

REFERENCES OF THE WEEK

1) Phenotypes, genotypes and response to statin therapy. Muriel J. Caslake and Chris J. Packard. Statins are administered to a wide range of individuals on an empirical basis. Investigation of the phenotype and genotype influences on treatment response will allow a more tailored use of these drugs. This is very interesting stuff, especially on why statins lower TG if they are high but do not if they are not very high.

2) Effectiveness and Tolerability of Ezetimibe Add-on Therapy to a Bile Acid Resin-Based Regimen for Hypercholesterolemia Antonios M. Xydakis, MD, John R. Guyton, MD, Philip Chiou, BS, Judy L. Stein, RN, MSN, ANP, Peter H. Jones, MD, and Christie M. Ballantyne, MD. Conclusion: At an average follow-up of 107 days, ezetimibe coadministered with BAR significantly reduced total cholesterol by 18%, triglycerides by 14%, and low-density lipoprotein cholesterol by 19% (all $p < 0.03$), without significantly changing high-density lipoprotein cholesterol, and the combination was well tolerated.

3) Understanding lipoproteins as transporters of cholesterol and other lipids Kyle D. Biggerstaff and Joshua S. Wooten Exercise Physiology Laboratory, Department of Kinesiology, Texas Woman's University, Denton, Texas 76204 Advances in Physiology Education 28: 105–106, 2004; 10.1152/advan.00048.2003.—A This is one of the best, most concisely presented (2 page) explanation of why we must understand lipoproteins rather than lipid concentrations. It is a great handout and for teaching purposes: It is available free for downloading at the journal website. **I urge you all to download it and read it.**

<http://advan.physiology.org/cgi/content/full/28/3/105>

Here is the abstract:

A clear picture of lipoprotein metabolism is essential for understanding the pathophysiology of atherosclerosis. Many students are taught that low-density lipoprotein-cholesterol is “bad” and high-density lipoprotein-cholesterol is “good.” This misconception leads to students thinking that lipoproteins are types of cholesterol rather than transporters of lipid. Describing lipoproteins as particles that are composed of lipid and protein and illustrating the variation in particle density that is determined by the constantly changing lipid and protein composition clarifies the metabolic pathway and physiological function of lipoproteins as lipid transporters. Such a description will also suggest the critical role played by apolipoproteins in lipid transport. The clarification of lipoproteins as particles that change density will help students understand the nomenclature used to classify lipoproteins as well.

DAYSPRING TRAVELS

Branchburg, Mendham, NJ
Pascack Valley Hospital Grand Rounds Westwood, NJ
Chicago (October),
Manhattan, Brooklyn, Newburgh, NY
Annapolis, MD
Atlanta, GA
New Orleans, Monroe LA
West Palm Beach, Indian Shores (Tampa area) FL
Albuquerque, Santa Fe NM
Phoenix (Paradise Valley), AZ
Milwaukee, WI

National Lipid Association www.lipid.org
North American Menopause Society www.menopause.org

Prayers for the troops and our friends in Florida and Alabama and Mississippi and elsewhere who suffered the hurricane forces.

Happy Lipiding,

Tom

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