

Hey there Lipidaholics: I love receiving cases from Gynecologists who are at the forefront of lipid management. The following is from a recent e-mail I received.

Today, a long time patient came in for her annual check up. She is a healthy 62 yr. old w/f, a 20 yr. old survivor of colon cancer, with no family history of CVD, hypertension. She weighs 169 is 5'6" (BMI=27.5), BP 110/80. She was Premarin 0.625 mg./d following her hysterectomy years ago but stopped this medication when WHI came out. She had been on 20 mg. of Zocor when I last saw her in 2001 but is on no medication at this time. Her PCP has gotten her lipids and also her NMR studies as follows:

CBC and liver studies all normal FBS- 93 mg/dl TSH 1.54
TC = 323 HDL-C = 85 Non-HDL-C = 238 LDL-C = 224 TG = 69
CHOL/HDL Ratio 3.0
LDL-P = 2001 nmol/L (very high risk)
LDL-Size large at 22.0 nm
Large HDL 54 mg./dl) above 30 is desirable)
Large VLDL 4 mg/dl (less than 7 is desirable)

She has been advised to start anti-lipid therapy by her PCP, a GP, but another MD "**an Internist**" told her not to start therapy because her CHOL/HDL ratio was only 3.0 and her "high" HDL-C" was protective. She comes to me for the deciding opinion because she has been my patient for years. She is at a low Framingham Risk for cardiac disease since her only risk factors are age and weight and of course, her lipid profile.

I said she should definitely start on therapy with life style changes including weight loss and exercise. Even though she has large LDL particle size, large HDL and low VLDL, I would start her on Pravachol 40 mg and Zetia 10 mg per day with the goal to lower her LDL in less than 130 and LDL-P to 1100 and repeat her studies and NMR tests in 6 weeks.

DAYSRING ANALYSIS

At any age, never mind 62, NCEP would allow as an option a doc to prescribe therapy for anyone with an LDL-C > 160 mg/dL, despite the high HDL-C no matter what her Framingham risk. I certainly agree with the gynecologist's desire to treat. The LDL-C and especially the LDL-P is much too high to ignore. It would put the patient in the top 10% of 'human beings: ie 90% of patients would have less. This is familial Type IIa hyperlipidemia. The patient should be told that 20% of American women who have an MI, have elevated HDL-C between 60 and 80. So high HDL is no guarantee of immortality especially when other CV risk is present. If one did not have the LipoProfile LDL-P, despite her very high HDL-C, the give away with the lipids is that her non HDL-C value is way too high at 238!!! This has to make one realize there are likely way too many apoB (atherogenic) lipoproteins in the plasma. Since her triglyceride level is perfect, the increased apoB particles are almost certainly LDL particles. The NMR LDL-P confirms that.

With regard to her high HDL-C, be very cautious what you make of that. I refer all to an editorial in this weeks Circulation by Wolfe and Rader (Circulation. 2004;110:1338-1340): "Although it is widely accepted that HDL directly protects against atherosclerosis, the mechanisms by which HDL exerts its protective effect remain uncertain, and the biomarkers and methods for measuring these effects have yet to be developed and validated. **For example, the rate of RCT from vessel wall to liver is likely to be more important than the plasma levels of HDL-C**, and therefore validated measures of the rate of RCT in humans are sorely needed. Furthermore, HDL has been shown in vitro to have a variety of other properties, such as anti-inflammatory, antioxidative, antithrombotic, and nitric oxide-promoting effects, but whether these are relevant in humans in vivo and how best to assess these effects after administration of HDL-raising drugs remain unknown." Common single-nucleotide polymorphisms (SNPs) in the human CETP gene also have been investigated for their association with cardiovascular disease.

Subjects carrying the I405V SNP has been associated with increased HDL-C and increased risk of CHD in women in the Copenhagen City Heart Study.

So if she is my patient she is going on therapy. She is postmenopausal and we have data that such women not only have abnormal levels of cholesterol in plaque but also noncholesterol sterols such as sitosterol or campesterol (plant sterols). So Zetia (ezetimibe) is definitely going to be part of my therapy. With and LDL-P > 2000 she is going to need a potent statin with the Zetia. The gynecologist used Pravachol 40 mg plus Zetia. Gynecologists love Pravachol as it is a very, very safe statin with virtually no drug interactions and no need for liver follow up testing. However with LDL-P > 2000 I probably would have advised 80 mg of Prava and Zetia or I would have jumped right to Crestor 10 mg with Zetia. If co-pays are a problem, Vytorin 20 mg (Zocor20/Zetia 10 in the same tablet) would be an option. If the above options did not normalize her LDL-P, I would definitely go to Crestor 20 mg/Zetia.

There is no reason to consider a fibrate or Niaspan in this patient. A bile acid sequestrant like Welchol also remains a tertiary (add-on) option to get to LDL-C, Non HDL-C, apoB or LDL-P goal.

One might want to look at hs-CRP or Coronary Calcium score (EBCT). If she wants to pursue an exercise regimen I would also advise an exercise test. If osteopenia or osteoporosis is present Evista would be a nice add on because of its apoB lowering abilities.

REFERENCES OF THE WEEK

- 1) Plasma Levels of Cholesteryl Ester Transfer Protein and the Risk of Future Coronary Artery Disease in Apparently Healthy Men and Women. Conclusions—Elevated CETP levels are associated with an increasing risk of future CAD in apparently healthy individuals, but only in those with high triglyceride levels. (Circulation. 2004;110:1418-1423.)
- 2) Impact of the Metabolic Syndrome on Mortality From Coronary Heart Disease, Cardiovascular Disease, and All Causes in United States Adults. Conclusions—CHD, CVD, and **total mortality** are significantly higher in US adults with than in those without MetS. (Circulation. 2004;110:1245-1250.)
- 3) Effect of hormone replacement therapy, tibolone and raloxifene on serum lipids, apolipoprotein A1, apolipoprotein B and lipoprotein(a) in Greek postmenopausal women. Gynecol Endocrinol 2004;18:244–257
- 4) Editorial: The Fitness, Obesity, and Health Equation Is Physical Activity the Common Denominator? In summary, the majority of studies show that regular physical activity has health benefits at any weight, and for those who want or need to lose weight, physical activity is a critical component of long-term weight management. JAMA, September 8, 2004—Vol 292:1232-33

DAYSRING TRAVELS

Branchburg, Mendham, NJ
Chicago (October),
Greenville, NC
Manhattan, Brooklyn, Newburgh, NY
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

Patriots Day (9/11) was a great opportunity to reflect and be so grateful that our armed forces are full of special men and women who preserve the freedoms of the American Way.

Happy Lipiding,

Tom

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