Lipoprotein (a)

Before we continue our series discussing more lipid-modulating drugs, I want to talk about another topic that I have been asked about frequently on my message board. I am asked weekly what is Lp(a) and what can one do for it? Lipoprotein (a), which is pronounced “little a”, is simply an LDL particle to which a protein called apolipoprotein (a) is attached. As I have discussed before in a previous posting about advanced lipoprotein testing, LDL particles are the vehicles that transport cholesterol through the body. They “drive” the cholesterol into the arterial wall and then the LDL particle becomes a foam cell which is the hallmark of atherosclerosis. Apolipoprotein (a) can also be attached to triglyceride enriched VLDL particles which can also be atherogenic. Since 90-95% of all the circulating “bad” particles are LDL-P, they become the most important target to modify in order decrease the number of “ cars” that move the cholesterol into the arterial wall. So the question remains that if one has an elevated Lp(a), are they at increased risk of a cardiovascular event?

In most epidemiologic studies, the risk of elevated apolipoprotein (a) depends on the LDL cholesterol level. In the large Physicians Health Study, Lp(a) conveyed no risk unless the LDL-C is > 160mg/dl. In the Women’s Health Study, Lp(a) was of no risk unless it was very high (>90th percentile) and the LDL cholesterol was also elevated. Thus, elevated Lp(a) in the face of normal cholesterol is not a risk factor.

The proper treatment of elevated Lp(a) is to lower one’s bad cholesterol. That means lowering LDL-P or ApoB (or its surrogates—LDL cholesterol and non HDL cholesterol). Although a statin is the primary drug used to treat high cholesterol, they have not been shown to lower Lp(a). The reason why this happens relates to one of the ways a statin works to lower cholesterol. Statins increase the number of receptors made by the liver to bind to the LDL particles. It seems that when apolipoprotein(a) is attached to an LDL particle, it is “camouflaged” from the LDL receptor. Those particles that do not have the apoliporotein (a) attached are cleared in the usual fashion by binding to the LDL receptors. So statins will lower the LDL cholesterol, ApoB, and LDL particle levels but have little to no effect on Lp(a) levels. Despite this, the lowering of the cholesterol carrying particles would greatly lower the clinical risk of a cardiovascular event. The best way to increase the number of receptors to remove the particles is with a statin, statin/zetia combination, or a bile acid sequestrant(I have had a prior posting on both zetia and bile acid sequestrants).

There are drugs they inhibit the synthesis of apolipoprotein (a) by the liver. These include fibrates, estrogen, evista, and niacin. It is most important to remember that there are no clinical outcome studies relating event reduction to what a drug does to Lp(a). As we have talked about previously, there are numerous studies that have conclusively shown that lowering LDL-C or LDL-P saves lives. Some people advocate niacin to lower Lp(a) levels, but there is not one ounce of clinical trial data that outcomes would be affected by using niacin to lower Lp(a). As I have said over and over, the name of the

game is to lower the LDL-P or ApoB and is still the best way to reduce risk if one has dyslipidemia and high Lp(a).