Cholesterol and Heart Disease: What's New?

Left to right: Eric Sontz,MD, Philip Shaver, MD, moderator, and Charlie Shaeffer, MD

It is estimated that 70 percent of patients with coronary artery disease have an abnormality of cholesterol and/or lipid metabolism. Controlled trials of statin drugs (such as Lipitor®, Zocor®, Pravachol®, Crestor®) involving more than 80,000 patients provide irrefutable evidence that lowering the LDL cholesterol reduces the risk for cardiovascular events and prolongs life. Healthy Living magazine assembled three prominent physicians from Eisenhower Medical Center who practice Preventive Cardiology to discuss the latest information on cholesterol and heart disease. The physicians included Board Certified Cardiologists Charlie Shaeffer, MD, Eric M. Sontz, MD and Philip Shaver,MD,who moderated the discussion.

Dr. Shaver: The fact that cholesterol is the genesis of atherosclerosis [build-up of fatty deposits that degenerates arteries] is indisputable. Deaths from coronary artery disease increase with high levels of total cholesterol and LDL cholesterol in patients with known heart disease, but particularly in patients with pre-existing coronary artery disease. Preventive Cardiology includes both primary prevention – treating risk factors in patients before they develop clinical coronary artery disease, and secondary prevention – treating patients who already have coronary artery disease. These patients can present in many ways, including a heart attack, angina or an acute coronary syndrome where the patient presents in an unstable state requiring, often times, an emergency intervention.

First, let us define our terms. Dr. Sontz, why do we need cholesterol in the first place if it can be harmful and contribute to coronary artery disease?

Dr. Sontz: Cholesterol is necessary for the production of several key components of metabolism and digestion. It is important for forming bile acids to allow us to absorb ingested fats. It is also important in the genesis of critical steroid hormones and sex hormones. It is a requirement in the metabolic function of nervous tissues and cell membranes.

Dr. Shaver: Dr. Shaeffer, would you define the terms that we use in assessing the different fats in the blood, specifically lipids? What do we mean by "good" and "bad" cholesterol? "One can lower the cholesterol approximately 10 percent with diet alone."

Dr. Shaeffer: The HDL, or "good" cholesterol, functions as a scavenger of cholesterol from undesirable areas. HDL extracts cholesterol from the arterial wall and returns it to the liver for metabolism and disposal.

The LDL cholesterol, although essential for synthesis of cell membranes and hormones, can accumulate when present in excess in the vessel walls, leading to progressive atherosclerosis, which can eventually cause angina, heart attacks, and sudden death.

Triglycerides function as fat storers, since fat is the most efficient energy source our bodies have. Our body, the heart in particular, prefers fatty acids to glucose for metabolism.

Dr. Shaver: What do we mean by the term "lipoprotein?"

Dr. Sontz: Cholesterol and triglycerides are insoluble in blood. They cannot be conducted through the blood alone, and must be bound to a protein.The protein is called a "lipoprotein," and is quite important in that it allows these lipid particles to circulate.

Dr. Shaver: We often hear the term "ratios."What do we mean by that term?

Dr. Shaeffer: The most common ratio used is a person's total cholesterol divided by their HDL, or good cholesterol. While ratios do suggest overall risk, most guidelines use the LDL cholesterol to assess risk. HDL itself is also important.

Dr. Shaver: What is atherosclerosis and how does cholesterol play a role in its evolution?

Board Certified Cardiologist, Eric M. Sontz,MD. Dr. Sontz: We now understand that atherosclerosis is an inflammatory process. It is inflammatory, just as an infection occurs due to bacteria. It is hallmarked by inflammatory cells, but the genesis of atherosclerosis is the introduction of the LDL cholesterol into the blood vessel wall.

At that point, circulating scavenger cells engulf the LDL cholesterol. Unfortunately, these cells become "foam" cells continuing to engulf the LDL cholesterol until they rupture, and creating even more inflammation. Should the creation of plaque continue, it could actually erode through the vessel wall causing a clot and either an acute coronary syndrome or heart attack.

Dr. Shaver: Understanding the central role of LDL cholesterol and atherosclerosis, what interventions can we do to prevent or control it?

Dr. Shaeffer: The LDL receptor is activated in the liver where it senses a deficit of cholesterol.The most efficient way to limit the production of cholesterol is to inhibit its formation in the liver, which is best accomplished by the use of statin drugs. Once the production of cholesterol drops, the liver triggers the LDL receptor to extract LDL from

the blood, making it less available to the vessel walls. Multiple trials have shown, both in primary prevention and secondary prevention, that statins are clearly beneficial in this regard. “It is important to be aware that a low HDL is often present in patients who have components of the metabolic syndrome – obesity, glucose intolerance, hypertension and pre-diabetes.”

Dr. Shaver: What are the major problems in compliance with statin drugs?

Dr. Sontz: The medications can be expensive, but often, by cutting the larger doses into fractions, the cost is reduced, since the price of the drugs doesn’t increase in proportion to the dosage.

Another obstacle of taking these medications is the fear generated by the lay media or anti-pharmaceutical groups with their own agendas. In actuality, liver and severe muscle complications are quite rare with these medications, and properly monitored, there should be no permanent liver damage. Muscle pain, known as myalgia, which is not lifethreatening, is the major reasons people stop these drugs. Sometimes, switching from one statin to a different statin can limit this side effect.

Dr. Shaver: What other medications can we use to supplement the statins or even take their place if the patient experiences statin intolerance?

Dr. Shaeffer: A newer drug on the market is known as ezitimibe (Zetia®), which blocks cholesterol absorption. Ezitimibe can be used with the statins separately or in a combination pill, known as VytorinTM,which enhances the statins. Ezitimibe can also be used alone.

Niacin, which is very effective in raising the HDL cholesterol and lowering triglycerides, should only be used in one or two forms. It can be used as a crystalline, or immediate release, form available at health food stores, but is often associated with intolerable side effects, particularly flushing or itching. The only other form that I would recommend is a prescription drug called Niaspan®, which is better tolerated, but may also produce significant flushing. The flushing can be minimized by taking aspirin before the Niaspan, or by taking food with the Niaspan. I strongly discourage patients from using slow-release niacin, available over-thecounter, since this form of niacin can have increased liver toxicity.

A class of drugs called fibrates, which induces the cell to better regulate lipids, is also useful by itself and in conjunction with other medications. Fibrates are useful in lowering trigycerides and raising HDL.

Dr. Shaver: What about diet as the sole therapy for high cholesterol?

Dr. Sontz: One can lower the cholesterol approximately 10 percent with diet alone. The diet should be low in saturated fats and high in fiber. In patients requiring aggressive lowering of cholesterol, diet alone is rarely enough, but it is an important part of lifestyle modifications.

Dr. Shaver: Several large trials showed that the most well tolerated drugs are the statins, and least tolerated is niacin. What makes the good cholesterol, the HDL cholesterol, “good?”

Dr. Shaeffer: We’ve learned that this, indeed, does act as a scavenger.An HDL greater than 75 mg is associated with the longevity syndrome, an increase in lifespan of five years in men and seven years in women.

Dr. Shaver: What have we learned by the Milano gene?

Dr. Shaeffer: It is known that in a small area outside of Milan, Italy, there is a familial gene, known as the A-I Milano, which markedly decreases atherosclerosis despite very low levels of HDL. The importance of this is that all HDL is not the same. Although exciting, at the present time it remains experimental.

Dr. Shaver: What other measures can we use to raise HDL?

Dr. Sontz: Exercise is one method that is helpful, and some of the drugs we previously discussed, such as the fibrates and niacin, can raise HDL as well. Eating a diet rich in monounsaturates, including almonds and walnuts, is also helpful.

Currently, patient trials are going on with a medication known as Torcetrapib®, which raises HDL levels. When combined with a statin, Torcetrapib appears to be beneficial, but final patient studies are pending regarding its commercial use. It is important to be aware that a low HDL is often present in patients who have components of the metabolic syndrome – obesity, glucose intolerance, hypertension and pre-diabetes.

Dr. Shaver:What about eggs?

Dr. Shaeffer: Having one to three eggs a week is probably acceptable. The egg yolk, as a rule, has 200 mg of cholesterol. The average American eats at least 300 mg of cholesterol a day. In very austere diets used in the Lifestyle Heart Trial, where the ingestion of cholesterol is only 5 mg daily, patients continued to manufacture cholesterol due to the fact that the body needs some cholesterol. Saturated fats probably play a more critical role in raising cholesterol than the ingested cholesterol, but I encourage my patients to eat egg whites and omit the egg yolk if they can.

Dr. Shaver: In summary, we have discussed the fact that LDL cholesterol remains a critical factor in atherosclerosis. Treating patients, particularly with statins, is very useful, and has been shown to prolong life and prevent complications.We’ve discussed other drugs that can be added to and sometimes used instead of statins, if the patient cannot tolerate the statins.

High cholesterol levels, as a rule, will occur in association with hypertension, diabetes, and additional risk factors, such as smoking, family history, obesity, inactivity and metabolic syndrome, greatly magnifying the risk of high cholesterol alone.Although the greatest benefit is observed in the patients who already have coronary artery disease, the ultimate goal is to detect patients at high risk and treat them with primary prevention before they have irreversible heart damage.