THE CHALLENGES OF MANAGING A CHRONIC HIGH BLOOD CHOLESTEROL LEVEL

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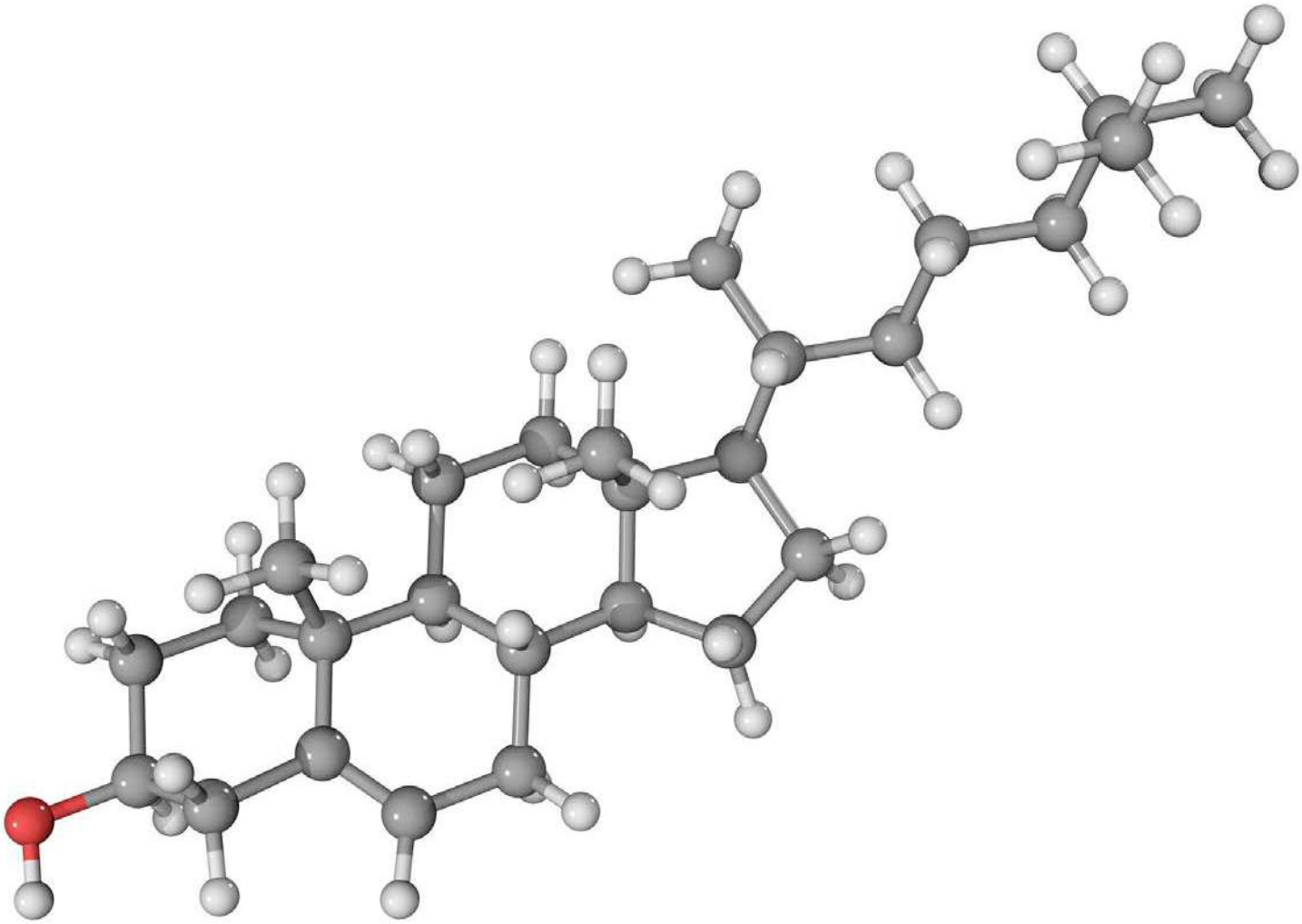

A large amount of my clinical care of patients over the last 30 plus years has been the assessment and management of a chronically high blood cholesterol level. This issue has been the source of many consults, particularly in my advanced preventive cardiology practice in suburban Detroit.

Patients may arrive with considerable fear regarding the decision to take prescription drugs their primary care or specialist health care professionals have advised them to use chronically. Many have adopted a whole-food plant diet recently or even for years. They fear the consequences of not taking the medications and they fear the possible side effects of taking the drugs too.

Here, the issues considered, and the approach used at my clinic, will be discussed. All individuals, even those on plant-based diets, are advised to pursue advanced testing and not consider themselves to be “bulletproof” to the risk of cardiovascular events.

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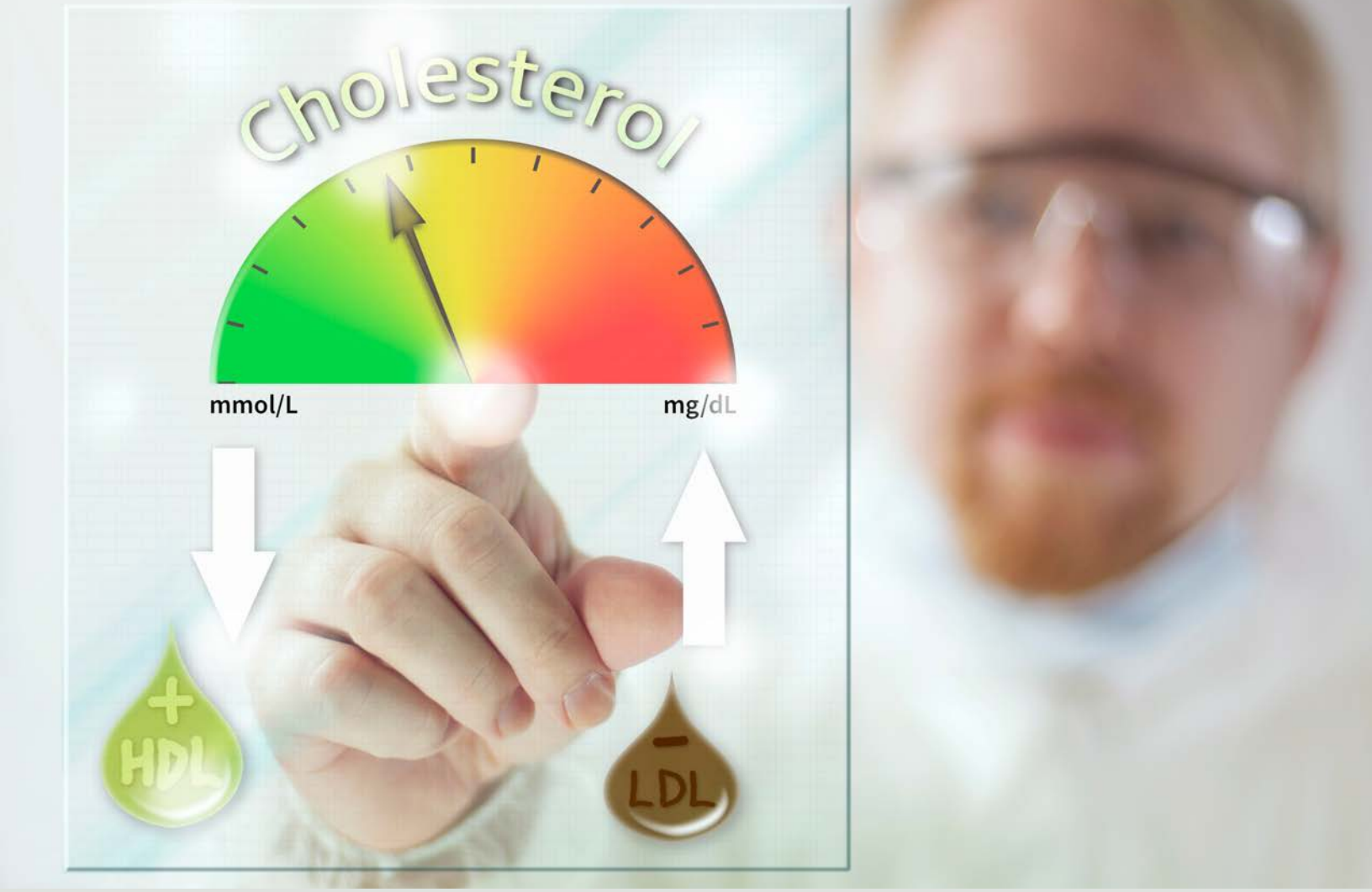
WHAT IS CHOLESTEROL?

Cholesterol is a waxy substance, one of the “sterol” family of chemicals that are modified steroids. Our bodies make cholesterol if needed to build cells and make bile acids, vitamins and hormones like cortisol. Cholesterol is not necessarily “bad” but too much cholesterol can pose a problem as will be discussed. Cholesterol comes from two sources. The liver makes all the cholesterol you need. In reality, all cells make cholesterol. The other big sites are the intestines, the brain, the adrenal glands, and the reproductive organs. There is approximately 1000 mg of cholesterol made a day in the body. There is about 35,000 mg stored in the body, mainly in cell membranes. If the diet is completely plant based, there will be no cholesterol ingested. The average omnivore might ingest 300-400 mg a day so there is still more cholesterol produced than consumed.

The foods that are high in cholesterol like egg yolks, meats, dairy, and poultry are also rich in saturated and trans fats. These fats cause the liver to make more cholesterol than it otherwise would so the blood cholesterol levels tends to rise. Although they contain no cholesterol at all, tropical oils – like palm oil, palm kernel oil and coconut oil – contain high amounts of saturated fat that can increase cholesterol. These oils are often found in baked goods.



WHAT ARE LIPOPROTEINS?

Since cholesterol is a fat, it can't dissolve in the blood and travel to organs to provide substrate for metabolism. The body packages cholesterol in protein-covered particles that mix easily into blood. These are called lipoproteins and they move cholesterol and other fats through the blood like a dump truck. There are several different forms of lipoproteins based on density such as low-density lipoprotein or LDL. When it carries cholesterol is called LDL-C or LDL-cholesterol. LDL-C is what is usually reported on a routine lab examination at the doctor. In reality, it is a calculated number, not a directly measured amount, unless special labs are ordered (direct LDL-C). The other lipoproteins you hear of are high-density lipoprotein or HDL, intermediate or IDL, and very-low density or VLDL. All can carry cholesterol and other fats through the blood like dump trucks.

WHY MIGHT CHOLESTEROL MATTER? The Lipid Hypothesis

Cholesterol does serve an important role in healthy metabolism. Why is an important matter to measure and consider lowering if this is so?

The lipid hypothesis, also known as the cholesterol hypothesis, links blood cholesterol to the development of the most frequent cause of death, cardiovascular disease, like heart attacks, strokes, and peripheral vascular disease.

The hypothesis argues that measures to control and lower blood cholesterol will reduced these events and, perhaps, prolong life.

RISK FACTORS FOR HEART DISEASE

One of the most important considerations to master is the concept of risk factors for heart disease. After World War II there was a rise in heart attacks, many fatal and tragic. In 1948 the US government started to fund the famous Framingham Study outside of Boston. Other studies in Minneapolis led by Ancel Keys, PhD, in Chicago by Jeremiah Stamler, MD and in Boston by Paul Dudley White, MD and others sought ought the public health and epidemiology of heart attacks and strokes.

At least as early as 1961, the Framingham Studies reported on “factors of risk” for coronary heart disease (heart attacks). This term was flipped to “risk factors” and is commonly used today too. The Framingham Study identified, high cholesterol as a risk factor for heart disease along with diabetes mellitus, high blood pressure, close family members with heart events at a young age, and, later, cigarette smoking.

Another major study led by Ancel Keys, PhD and other researchers around the world was called The Seven Countries Study. This prospective analysis of over 12,000 men in 16 communities and 7 countries began in 1958 and was published initially in 1970. A high level of blood cholesterol directly related to the risk of dying of coronary heart disease. The study also found that diets high in saturated fats like meats and cheeses related to high blood cholesterol levels. Soon after, medical organizations like the American Heart Association began recommending the routine measurement of cholesterol levels and avoidance of foods high in saturated fats.

DOES AN ELEVATED SERUM CHOLESTEROL NEED THERAPY?

The comments here are general ones and you are advised to always work with your health care team. A proposal was made over 15 years ago by an organization of experts called the SHAPE society (Society for Heart Attack Prevention and Eradication) that not all asymptomatic patients need prescription therapy for elevated cholesterol levels. This would not apply to those that already know of some form of atherosclerosis (hardening of the arteries) from a cardiac catheterization or heart CT angiogram showing plaque or those with a prior heart attack, stroke, bypass operation or stent procedure.

Most people learn of a high cholesterol from their primary care provider and have no known atherosclerosis. Often a Rx medication is offered based on lab values alone. At my clinic we use a personalized approach as suggested by the SHAPE group, based on precise measures of artery health and multiple lab tests that go beyond the Framingham Study Findings. Some of the practices we use are listed here.

CLINICAL CLUES TO ATHEROSCLEROSIS

There can be clinical clues to clogged arteries needing cholesterol therapies determined by history and physical examination. Men have a built-in warning system for silent CHD. When achieving an erection is difficult or impossible, it can be a sign of clogged arteries in the pelvis that presents before a heart attack hits. There are, on average, three to five years between the onset of ED and the finding of CHD, which is plenty of time to detect and to work on preventing heart issues. If you and your partner are worried about sexual performance, look for and treat root causes of diseased arteries before just popping a blue pill.

Premature baldness could indicate clogged arteries. In a comprehensive study of almost 37,000 men, severe baldness at the crown of the head strongly predicted the presence of silent CHD at any age. In a separate study of more than 7,000 people (including over 4,000 women), moderate to severe baldness doubled the risk of dying from heart disease in both sexes.

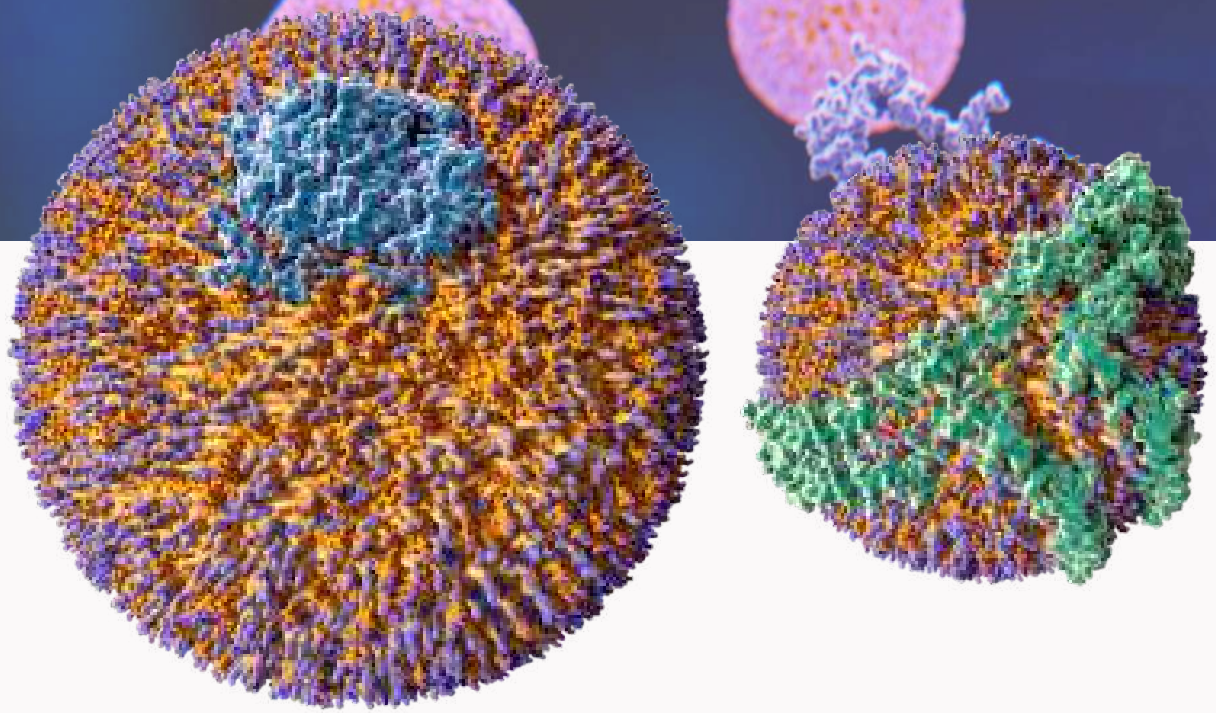
Gray hair may be a clue to blocked arteries. A study presented in Europe at EuroPrevent 2017 found that a high amount of gray hair is a risk factor for silent heart atherosclerosis. A total of 545 adult men without known heart disease had a CT angiogram of their heart arteries, a very accurate way to identify silent problems. Having equal amounts of gray and dark hair, or mainly gray and white hair, correlated with finding silent heart blockages. The researchers commented that “atherosclerosis and hair graying occur through similar biological pathways”.

A diagonal ear lobe crease might indicate clogged arteries. The diagonal ear crease may result from poor circulation, including in arteries in the heart. Although some medical professionals have argued that a crease is just a general sign of aging, researchers used the most sophisticated CT scan method to measure silent CHD and found that ear crease predicted heart disease even after the other risk factors, such as age and smoking were factored in.

Calf pain on walking is known as claudication (from the Latin for “to limp”). Atherosclerosis can block leg arteries, particularly in smokers, before CHD is diagnosed. This symptom requires an evaluation without delay. Your doctor will examine the pulses in your legs and perform simple measurements of leg blood pressure and blood flow to confirm a diagnosis of poor circulation.

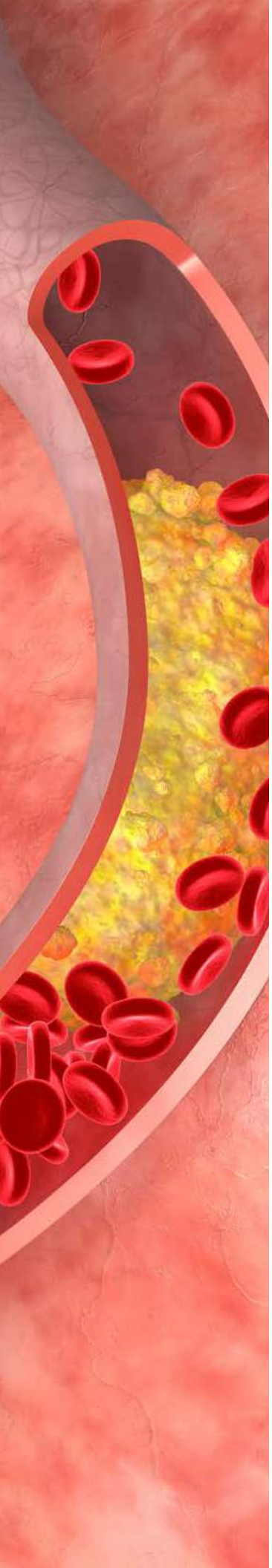
After a detailed history and physical exam searching for clinical clues to atherosclerosis, a review of any prior imaging studies like CT scans, mammograms, ultrasounds, and heart testing will be performed. Often prior chest or abdominal CT scan shows some degree, even advanced, vascular aging either not mentioned in the report (I review the images on CD) or overlooked. A prior chest will show if the coronary arteries are diseased and calcified and this must be assessed and is often “free” additional information. This can be a very important in assessing the need for cholesterol lowering therapies. If there are no prior studies, a carotid thickness (CIMT) ultrasound is performed as it involves no X-rays, is painless, accurately identifies the health of important arteries, and can be repeated yearly to see if arteries are getting healthier or more diseased. The CIMT is much more valuable than a standard carotid ultrasound as it uses digital measurements that are very precise and objective. Other patients will also get a coronary artery calcium scoring (CACS) CT scan at a hospital or imaging center to identify silent heart artery aging. If the arteries are free of plaque, the elevated cholesterol may not need any therapy at all, as proposed by the SHAPE study, and now endorsed by the American Heart Association.

SEARCHING FOR SILENT ATHEROSCLEROSIS



ADVANCED LAB STUDIES

Over 20 years ago, a more advanced lab panel was introduced that was shown to be more accurate than the standard one measuring only the total, LDL, and HDL cholesterol and triglycerides. This advanced panel measures the number of LDL cholesterol particles called the LDL-p or LDL-particle number. In some patients with an unremarkable LDL-cholesterol, the LDL-p may be very high, something called discordant results. This is more common in patients that are overweight and have pre-diabetes or diabetes. The LDL-p is more predictive of future heart attacks and other events and is the measurement used in my preventive clinic. Other lab studies will be drawn like a high sensitivity C-reactive protein (hs-CRP) level to measure blood vessel (vascular) inflammation. The blood sugar will be assessed over the last 3 months with a HgbA1C level, homocysteine will be measured, and some genetics like apoE and 9p21 may be assessed.



LIPOPROTEIN(A): THE HEART'S QUIET KILLER

Often the most important lab value to assess risk for heart disease and need for therapy is measured for the first time at my clinic It is called the Lipoprotein(a) or Lp(a) level and is worth some additional detail. Lp(a) is a complex cholesterol molecule whose presence in the blood is determined by genetics, not diet. It is composed of an LDL-cholesterol particle, a sulfur bridge, and another lipid particle called apolipoprotein(a). If Lp(a) is inherited, levels in the blood will reach a plateau at around age two and remain high through adulthood. It is the most common inherited risk for developing premature cardiovascular disease. It is sometimes called the "sticky" cholesterol.

Lp(a) can cause several types of coronary heart disease, such as heart attack, stroke, peripheral arterial disease, aortic valve disease, and heart failure. The risk of heart disease from elevated Lp(a) will be even higher in the presence of smoking, hypertension, and type 2 diabetes. Elevated Lp(a) can influence the risk of blood vessel and heart valve damage from birth. According to a National Heart, Lung, and Blood Institute report published in 2018, an estimated 1.4 billion people globally have elevated Lp(a) levels, representing about 25-30 percent of the entire population.

Although measurement of Lp(a) is widely available, it is not yet considered a routine lab test and is ordered by an estimated 1% of physicians even though all labs measure it and it is inexpensive, In 2019 the European Society of Cardiology recommended drawing a level of Lp(a) once in a person's lifetime. In my practice, It is crucial to measure the Lp(a) level at least once before deciding on risk and therapeutic decisions.

Using Food to Lower Cholesterol Levels: The Portfolio Diet

Once this extensive evaluation is complete, often in just one visit, the role of diet in managing cholesterol is emphasized and patients are often given 2-3 months to work on their diet with a recheck before and other therapies are considered. Most patients have never heard of the Portfolio Diet, one we teach even if patients are largely or totally plant based. It is actually a “diet without being a diet”, as it was designed to work with any healthy food choices to lower cholesterol levels by keeping a focus on 4 food groups in most or all meals. Originally published by David Jenkins, MD and researchers at the University of Toronto in 2002. Dr. Jenkins noted that plant sterols (found in sesame and sunflower seeds peanuts, and avocados), soy proteins (found in tofu, edamame, and tempeh), nuts, and viscous fibers (found in oats, oat bran) were advised for cholesterol reduction but their combined effect had never been tested. His team evaluated eating a diet with this “portfolio” of added food choices and showed that LDL cholesterol fell by 29% in a month versus baseline levels. The reduction was similar to another group given a low dose statin medication, and most of the changes were seen as soon as 2 weeks.

Recently, the impact of the Portfolio diet was assessed from dietary records in 123,330 women in the Women’s Health Initiative study from 1993 to 2017 at the Harvard School of Public Health. Heart disease outcomes were assessed and the impact of adhering to the Portfolio Diet was measured in an average follow up of 15 years. Adherence to the Portfolio Diet was associated with a lower risk of all heart events (11% lower), heart attacks (14% lower), and heart failure (17% lower). The authors concluded from this non-randomized study that “higher adherence to the Portfolio Diet was associated with a reduction in incident cardiovascular and coronary events, as well as heart failure”.

When Diet and Lifestyle Do Not Reach Goal Cholesterol Levels: Treatments

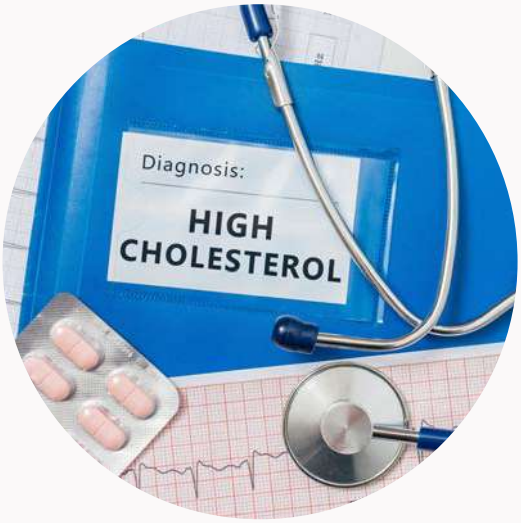
Cholesterol goals may need to be quite aggressive in patients proven to have significant cardiovascular disease, even if asymptomatic. The prior goal in heart patients of lowering LDL-cholesterol to <100 mg/dl was dropped to <70 mg/dl after new research was published. Most recently, the most advanced disease patients are often treated to lower the LDL-C to <55 mg/dl and supplements and Rx medications are usually needed in addition to lifestyle therapy. While decisions are personalized and take into account, all the data available, the “menu” of choices used in my clinic include list below and more.

Statins

Since 1987, drugs ending in “statin” have been available including the most popular atorvastatin (Lipitor) and rosuvastatin (Crestor). Studies with 100,000s of patients indicate that those with atherosclerosis may benefit from statins. Although most patients do not have side effects, the risk is real and includes aching muscles or weakness, elevated blood sugar, and some cognitive decline. I combine statins with the vitamin coQ10 to restore depressed levels of coQ10 to normal. People without atherosclerosis on CIMT and heart CT studies usually do not require statins.

Ezetimibe

Although less well known, ezetimibe (Zetia) has been available for nearly 20 years as a prescription. Unlike statins which lower cholesterol in the liver, ezetimibe lowers cholesterol in the intestines. It has an excellent safety profile, and several large studies demonstrate reduced risks of heart attacks and strokes. Ezetimibe can be combined with statins at low doses resulting in excellent cholesterol levels without side effects.



Bempadoic Acid

A new drug class came on the market in the last few years. It is called bempadoic acid but is sold as Nexlotol. It required years of basic science research and large clinical human safety and efficacy trials to get FDA approval. It lowers cholesterol in the same pathway as statins but only in the liver and at a different enzyme point. Because it does not act in the muscles, muscle aching is less common, in fact, rare. It can be added to statins, to ezetimibe, to PCSK9 inhibitors, or used alone. There is a version with ezetimibe combined together called Nexlizet. It has proven to be a very useful option for those not tolerating statins or not reaching LDL-cholesterol goal on other medications. The safety profile so far is high. It is not generic and requires pre-authorization from most insurance companies.

PCSK9 inhibitors

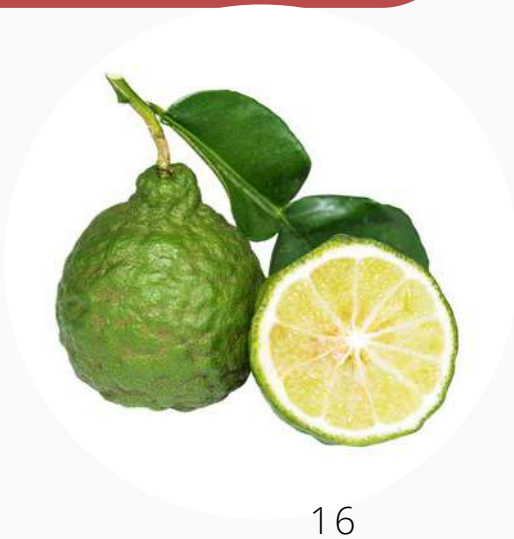
Over 5 years ago, 2 new cholesterol medications were introduced in the USA after extensive testing. They are the brand names Repatha and Praluent and are injected every 2 weeks. They are known as PCKS9 inhibitors. They are very powerful in lowering the LDL-cholesterol and may also lower the Lipoprotein(a) level. They are expensive and usually insurance authorization is required demonstrating that statins and ezetimibe either causes serious side effects or were not effective. Their safety seems very favorable.

Red yeast rice

Red yeast rice or RYR is a natural agent in a capsule that lowers LDL-cholesterol with a mechanism similar with statin medications. RYR is available in health food stores. In an adequate dosage, RYR can lower cholesterol on par with a statin. RYR is usually well tolerated. Several large studies involving thousands of patients demonstrate that RYR can reduce the risk of heart attacks and strokes.

Citrus Bergamot Superfruit

Citrus bergamot superfruit grows in southern Italy that has been studied for its ability to lower cholesterol and blood sugar. It is in a tablet or capsule form and is very safe. It can used alone or in combination with statins, ezetimibe, or RYR. Studies have shown that bergamot helps reverse plaque in carotid arteries.



Niacin (vitamin B3)

Niacin is vitamin B3 and has been used to lower cholesterol for over 50 years. It has a distinct ability to cause a flushed feeling about 30 minutes after taking a dose. Niacin lowers LDL-C, raises HDL-C, and can lower Lipoprotein(a) cholesterol. Niacin has fallen out of favor combined with statins, but it is used alone or with other agents in patients with an elevated Lipoprotein(a) level.

Aged Garlic

Aged garlic, white or black, is odorless and is available in tablet or capsule. Studies demonstrate that aged garlic lowers cholesterol and blood pressure. Several studies from UCLA also show that aged garlic can reduce the amount of plaque volume in heart arteries which is amazing. Garlic can be combined with other agents, is safe, and is inexpensive.

Conclusions

Considering what to do with cholesterol and lowering the risk of heart attack and stroke is not as simple as it seems if precise recommendations and safety considerations are of primary importance. Simply put, patients with the most atherosclerotic plaque, whether symptomatic or silent, need the most aggressive lifestyle, supplement, and prescription therapies, often combined to reach very low LDL-c levels. Lipoprotein(a) is enormously important, and treatment can be adjusted to lower levels, the topic of my most recent book. Even those following a whole-food plant diet naturally low in calories from fat may have elevated LDL-c or Lp(a) and other risk factors and should not assume they are “bulletproof” to heart events. Fortunately, the ability to precisely diagnose, measure, and treat heart disease risk factors has advanced enormously and the future is bright even when heart disease is present.

ABOUT DR. KAHN

Joel Kahn, MD, FACC of Detroit, Michigan, is a practicing cardiologist, and a Clinical Professor of Medicine at Wayne State University School of Medicine. He graduated Summa Cum Laude from the University of Michigan Medical School. Known as "America's Healthy Heart Doc", Dr. Kahn has triple board certification in Internal Medicine, Cardiovascular Medicine and Interventional Cardiology. He was the first physician in the world to certify in Metabolic Cardiology with A4M/MMI and the University of South Florida. He founded the Kahn Center for Cardiac Longevity in Bingham Farms, MI in 2015.

Dr. Kahn has authored scores of publications in his field including articles, book chapters and monographs. He writes health articles and has 6 books in publication including Your Whole Heart Solution, Dead Execs Don't Get Bonuses and The Plant Based Solution, and Lipoprotein(a): The Heart's Silent Killer. He has had appearances on Dr. Phil, The Doctors Show, Dr. Oz, Larry King Now, and the Joe Rogan Experience. He has been awarded a Health Hero award from Detroit Crain's Business. His podcast, Heart Doc VIP, is listened to worldwide.

Dr. Kahn can be found at www.drjoelkahn.com