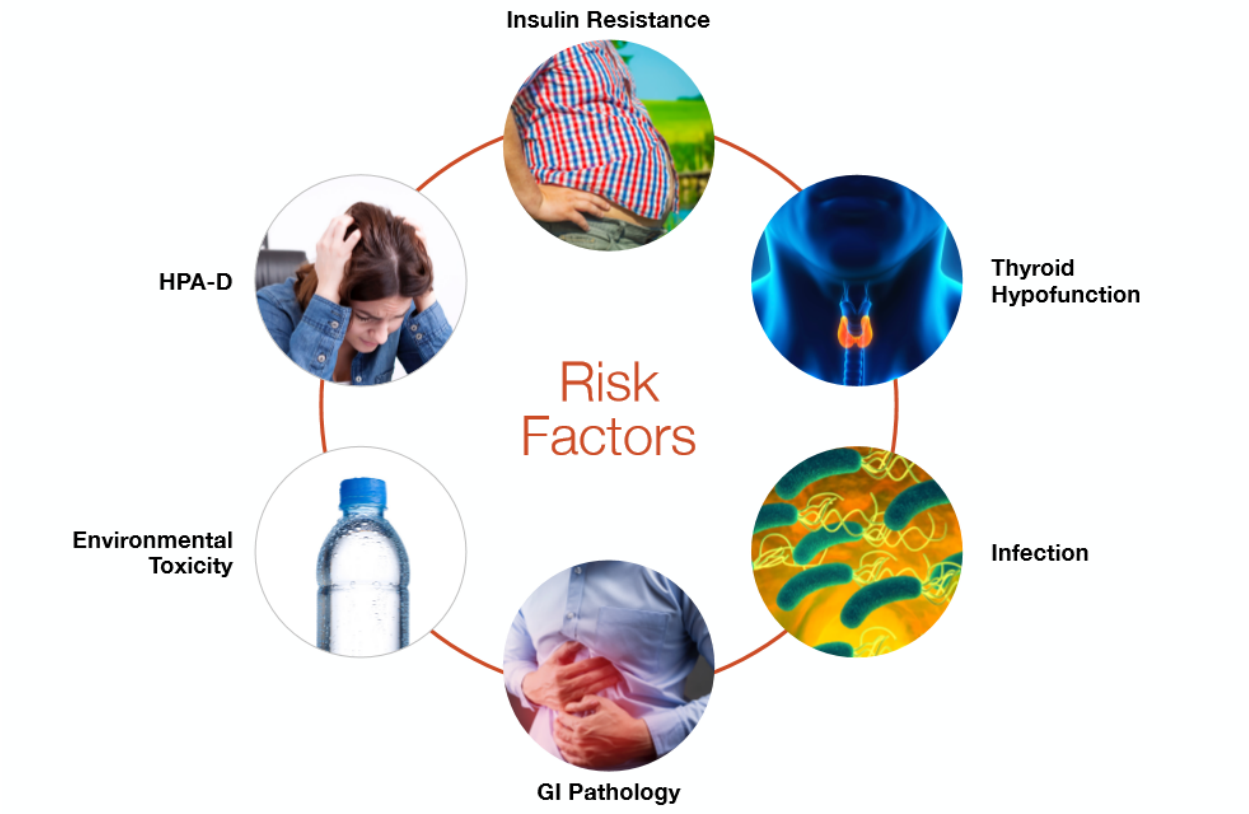
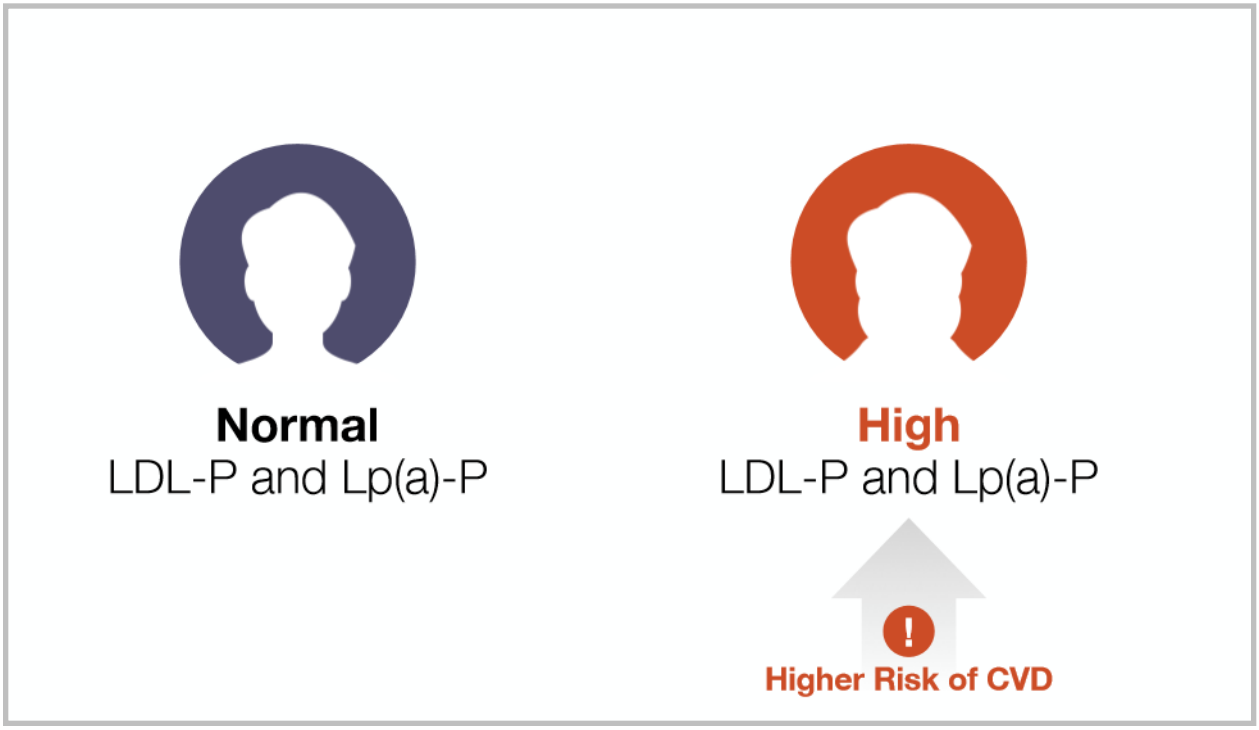
Dyslipidemia - Part Four



Okay, now let's talk about treatment. I'm going to sound like a broken record here, but except in the highest-risk patients, those maybe with LDL-P above 2,500 who are middle-aged, who have already had a heart attack, people who may be at imminent risk for another heart attack, I think it makes sense to address underlying mechanisms first and see if we can bring down LDL-P and Lp(a)-P that way. If we retest and the markers are still high, then the question becomes, is treatment necessary? I talk about this in much more detail in the High Cholesterol Action Plan, but I want to at least cover it briefly here, and my thinking has evolved slightly since I put the High Cholesterol Action Plan together.

The truth is, we have very little data on the significance of high LDL-P in a population that has no other significant risk factors, is consuming a healthy, nutrient-dense diet, and is living a healthy lifestyle. The studies that show an association between LDL-P, Lp(a)-P, and heart disease are done in the general population that is following a very different lifestyle, one that probably has many more inflammatory factors in it. We know that nine of 10 people who have high cholesterol and go on to have a heart attack have at least one other significant risk factor for heart disease. It is at least possible that high LDL-P and Lp(a)-P in the context of a really healthy diet and lifestyle and in

the absence of other risk factors only confers slightly increased risk of heart disease or maybe no increased risk at all.



However, it is also true that atherosclerosis is a gradient-driven process, at least as we understand it today, and all other things equal in two people, the one with higher LDL-P and Lp(a)-P would theoretically be at higher risk for heart disease if our current understanding of heart disease pathogenesis is complete. Of course, it may not be. There have been many revisions of our understanding over the years, but at least with what we know today and what we understand of the pathological mechanisms, they fit the data pretty well.

From this perspective, it makes sense to take action to normalize LDL-P and Lp(a)-P, but how aggressive that action is and whether it involves only diet, supplements, and lifestyle change, or those things plus medication, depends on a number of different factors, including the individual's family history, other risk factors for heart disease, and quite simply their risk tolerance and their desires. Some patients are completely opposed to the idea of taking statins or other drugs and are comfortable with the uncertainty of a higher LDL-P. There is nothing as clinicians that we can do about that other than just provide them with education and recommendations based on our understanding, whereas others are more concerned about the risk and want to do anything they can to optimize their markers, including medication.

In my practice, I'll typically address the underlying mechanisms first. Then, if the numbers are still high, use diet and lifestyle to further lower them. If the numbers are still elevated after that, we'll have an open conversation with the patient, explaining what I just explained on the last slide, ask

them what they want to do, and I find that this collaborative approach works best. With that in mind, let's talk about diet and supplements.

For patients with high LDL-P and normal metabolic function, I suggest what I call a Mediterranean Paleo diet. This is a Paleo-type diet that favors monounsaturated fat over saturated fat, and it minimizes added fat. Fat as it naturally occurs in food is fine, but not adding a half stick of butter to a sweet potato, for example. Suggest a more moderate-carb and moderate-fat approach rather than a low-carb, high-fat approach. This is especially true for those patients who saw a dramatic increase in their total cholesterol or LDL cholesterol and/or LDL-P when they switched to a low-carb Paleo diet.

In patients with metabolic syndrome, however, a lower-carb Paleo approach is often better for lowering LDL-P because the pathology in that case is insulin resistance. Whatever you can do to promote weight loss and improve insulin sensitivity will tend to lower LDL-P in people with metabolic issues.

Other dietary considerations include emphasizing tree nut consumption, ensuring adequate intake of EPA and DHA, consuming fermented foods and fermentable fibers, eating a broad spectrum of colors, and maximizing intake of antioxidant-rich foods.

There are over 25 compounds that have been shown to prevent and treat vascular disease by more than 38 different mechanisms, but we're going to focus on those that have the best evidence behind them as well as the fewest side effects. Several studies have looked at each of these compounds individually, but only a few studies have looked at them in combination. That said, those studies have shown pretty promising results.

A combination of natural remedies decreased LDL-P by 35%

For example, in one study using a combination of pantethine, plant sterols, green tea extract, tocotrienols, Phytolens, and a red yeast rice extract, total and LDL cholesterol fell by 34 percent. LDL particle number dropped by 35 percent. VLDL dropped by 27 percent, and HDL increased by 10 percent. These improvements are quite remarkable, and in fact, they are comparable and even greater in some cases than what is typically observed with statin drugs.

Image credits: http://catalog.designsforhealth.com/Annatto-Tocotrienols-with-Black-Cumin-Seed-Oil-60-softgels

Alpha-tocopherol is the form of vitamin E that most people supplement with. However, studies have shown that alpha-tocopherol not only doesn't reduce the risk of heart disease, it may even increase it. Tocotrienols are naturally occurring derivatives of tocopherols with much more potent antioxidant activity than the tocopherols themselves. Studies have shown that tocotrienols are more effective in reducing total and LDL cholesterol, but this is only true if the formula does not contain more than 20 percent tocopherols. The other important consideration is which isomers of tocotrienols are included. Studies have shown that a combination of the delta and gamma isomers is the most effective at reducing total cholesterol, LDL, and triglycerides. The recommended dose is 200 mg of delta and gamma tocotrienols in purified form, preferably from the annatto plant, with 90 percent delta and 10 percent gamma tocotrienols taken at night with food. Tocopherol should be less than 20 percent of the total vitamin E consumed per day. Otherwise it will inhibit the cholesterol-lowering effect of tocotrienols. Many multivitamins contain alpha-tocopherol or mixed tocopherols, so these should probably be avoided during treatment.

Image credits: http://www.jarrow.com/product/247/Pantethine

Pantethine is a naturally occurring derivative of pantothenic acid, which is vitamin B5 and a precursor of coenzyme A, or CoA. Human studies have shown significant improvement in lipid profiles with pantethine. Total and LDL cholesterol and triglycerides are decreased, and HDL is increased without any known adverse effects. Pantethine works by increasing the bioavailability of CoA, which in turn reduces the synthesis of fatty acids by about 50 percent and cholesterol by 80 percent. Pantethine enhances the removal of arterial cholesterol as well, which reduces plaque formation, endothelial dysfunction, and thickening of the arteries. Pantethine has been shown in some studies to reduce the oxidation of LDL, which is important since, as you likely know, that is one of the major driving factors in heart disease. Finally, pantethine is one of the few natural products that increases HDL in addition to reducing LDL and triglycerides. There is no single pharmaceutical currently known that has this capability. The average dose of pantethine in clinical

trials was 900 mg per day, either 300 mg three times a day or 450 mg twice a day. I prefer the 450 mg twice-daily dosing for convenience. It's really important to understand that pantethine does not work overnight. You have to give it at least four months to see significant results, but in some studies that lasted longer, there was a continual improvement in lipids for up to nine months, so this is something you really have to communicate to your patients if you're going to prescribe this treatment, is that they should be on it for a minimum of four months and perhaps even nine months or longer to see the optimum benefit.

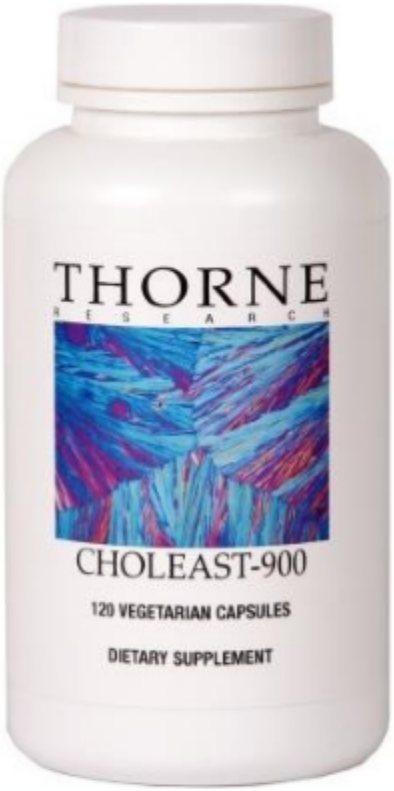


Image credits: https://www.thorne.com/products/dp/choleast-900

Red yeast rice extract is a fermented product of rice that contains compounds called monacolins that reduce cholesterol production by inhibiting the HMG-CoA reductase enzyme. If this sounds familiar, you're right. It's exactly the same mechanisms by which statins lower cholesterol, and this

is not a coincidence. Lovastatin, which is also known as Mevacor, was the first statin introduced to the market, and it was isolated from red yeast rice. Lovastatin, which is also known as monacolin K, is the main active ingredient in red yeast rice. Two capsules of Thorne Coleast-900 contain about 5 mg of lovastatin, which is analogous to taking a very low dose of a statin. However, red yeast rice extract has a far lower incidence of side effects than statins. For example, in one study in 2009, published in the *Annals of Internal Medicine*, only 7 percent of statin-intolerant patients experienced muscle pain when they switched to red yeast rice extract. This is a group of people who already had demonstrated intolerance to statins, and only 7 percent of those people experienced any side effects when they switched to red yeast rice extract, so we could expect that in the general population, the incidence of side effects would be much lower because not everyone in the general population is statin intolerant.

Note that the brand of red yeast rice extract that you choose is extremely important. Please be aware of this. The levels of monacolin K, which is the active ingredient, can vary tremendously in most products, so you never know what dose the patient is getting. For example, in a recent peer-reviewed study of 12 commercially available red yeast rice products, the dose of monacolin K ranged from 0 to 10 mg, with an average of 2.5. The other issue is that some varieties of red yeast rice extract may contain citrinin, which is a toxic byproduct of the fermentation of the rice. Citrinin is a mycotoxin that has been shown to be toxic to the kidneys. In the study that I just mentioned, five out of the 12 products that they looked at had detectable levels of citrinin. The Thorne product has been shown to have a consistent dose of monacolin K and to be free of citrinin. There are a couple of others than have come on and off of my list, but the Thorne product has been the most consistent.

Image credits: http://www.jarrow.com/product/448/QH-absorb

Although the research is somewhat mixed, some observational and clinical trials suggest that CoQ10 can partially but not completely reverse myopathy and other adverse effects that can be caused by statins. One reason for the mixed results in the studies may be that the bioavailability of CoQ10 supplements on the market varies considerably. Some are much better absorbed than others. It's possible that if highly bioavailable forms of CoQ10 were used in all studies, the results would be more consistent. The Kaneka form has been used in the majority of the higher quality CoQ10 trials in the past 30 years. This is the form that Jarrow uses in its QH-Absorb formula, which I've used with good results. The typical dose is 200 mg once a day. Since ubiquinol is fat soluble, it should always be taken with a meal that contains fat for optimal absorption, and since some patients find it to be stimulating, I typically recommend that they take the CoQ10 with breakfast.

People with low glutathione and low HDL **are 6 times more likely to die from CVD.**

Studies suggest that people with low levels of glutathione have higher levels of oxidized LDL and a greater risk of heart disease. For example, one study found that people with the lowest levels of glutathione peroxidase activity had approximately 2.3-fold greater risk of death from cardiovascular disease compared to those with the highest levels. This difference was exacerbated in those who had both low glutathione peroxidase activity and low levels of HDL. Those individuals had an approximately sixfold higher risk of death from cardiovascular disease.

Now, to put this in perspective, people with this combination appear to be at greater risk for heart disease mortality than that attributed to moderate hypertension, type 2 diabetes, smoking a pack of cigarettes a day, or having an LDL cholesterol in the 200 mg/dL range, so that's a pretty significant risk profile.

In another study, researchers found that glutathione was severely depleted in the heart tissues of patients with coronary artery disease when compared to healthy controls. Also, studies have shown that polymorphisms in genes controlling glutathione production are associated with an increased risk of heart disease. Finally, a meta-analysis of 42 case-controls in three prospective studies found an inverse association between circulating levels of glutathione peroxidase and coronary heart disease.