Dyslipidemia - Part Five

Ensuring adequate levels of glutathione and glutathione peroxidase activity is an important part of cardiovascular disease prevention, especially in those with inflammation and oxidative damage. Glutathione levels can be increased by both food and supplements. The amino acid glycine is an important building block for glutathione, and glycine is found primarily in the skin, cartilage, and bones of animals, so an optimal source of glycine, and thus an important glutathione precursor, is bone broth. I suggest consuming at least a cup a day of homemade beef, chicken, or fish stock, and this could be either consumed in the form of soup or used as a base in sauces or even consumed straight as a beverage.

I'd also recommend eating fattier cuts of meat rather than only lean cuts to get extra glycine, and that's presuming the patient is not a hyper-responder with very high LDL-P, in which case that may not be a great idea because the fattier cuts of meat contain higher amounts of saturated fat, if they are saturated fat sensitive, so they could take perhaps glycine as a supplement. Fresh raw fruits and vegetables are great sources of glutathione, and then finally raw dairy products when they are obtainable—in some states, they are legal—are an excellent source of glutathione. Unfortunately, pasteurized dairy contains almost no glutathione, so they are not interchangeable.

Image credits: https://www.seekinghealth.com/optimal-liposomal-glutathione-30-servings

Of course, you can also supplement to increase glutathione levels, so a high-quality, grass-fed, non-denatured whey protein powder is a really good option for increasing glutathione if patient is tolerant of whey. Then, of course, you can supplement with glutathione itself. For many years, it was believed that oral glutathione was not well absorbed and doesn't raise intracellular levels of glutathione in the body. Some recent research has contradicted that and found that oral glutathione may be effective in some cases. I have found that the liposomal form of glutathione, as is often the case with other nutrients, seems to be the best absorbed, the best tolerated, and leads to the best clinical effects, so that's the form that I use in my practice.

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Curcumin and turmeric extracts exhibit anticarcinogenic, anti-inflammatory, antioxidative, anti-infectious, hypoglycemic, and hypocholesterolemic activities, so this is why you see curcumin popping up in so many different therapeutic areas. For our purposes in this presentation, curcumin increases the LDL receptor MRNA sevenfold. In the apoE LDL receptor double-knockout mice, which would be a mouse that is extremely prone to developing super-high cholesterol because they have both of the genetic mutations that lead to familial hypercholesterolemia, curcumin demonstrated anti-atherogenic effects despite no change in lipids, so it wasn't actually lowering the cholesterol, but it was mitigating some of the potentially harmful effects.

One study of curcurmin in humans found a significant decrease in the level of serum lipid peroxides by 33 percent, an increase in HDL cholesterol of 29 percent, and a decrease in total serum cholesterol of 11.6 percent. Some studies have shown that curcurmin increases glutathione levels also. The forms of curcurmin used in these studies were not the most bioavailable, so it's possible that the results would have been better with more bioavailable forms. Both CoQ10 and curcurmin have also been shown to reduce oxidative stress and inflammation, so you can use them when inflammatory markers are elevated on the True Health Diagnostic panel and when CoQ10 levels are low.

Fish oil is highly controversial in heart disease. The most recent large study suggests little to no benefit, and some have even suggested harm. I've written about this extensively, and I'll link to a recent article and podcast in the resources section. That said, cold-water fatty fish consumption is consistently linked with lower risk of cardiovascular disease, and I think patients, particularly those who are at risk for heart disease, should aim for between 12 and 16 ounces of cold-water fatty fish a week.

At one point, it seemed that some subgroups such as those with metabolic syndrome may benefit from fish oil more than others, but again, recent evidence is pretty mixed on this. Some studies do show benefit. Some show no effect, and others even show harm. The safest course, in my opinion, is to just advise our patients to eat fish, particularly low-mercury species of fish, but if you have a patient who can't or won't eat fish, I would probably suggest a low dose of cod liver oil, such as one teaspoon or a half-teaspoon a day, because it not only contains moderate doses of EPA and DHA, it also contains vitamins A and D, which many patients don't get enough of in the diet.

The next is dietary fiber. Research is incomplete here because most studies focus on the effects of fiber on total cholesterol and LDL cholesterol rather than LDL particle number or Lp(a)-P. The few studies that have looked at the effects of fiber on particle number in addition to cholesterol showed mixed results. In some, only total cholesterol and LDL cholesterol dropped, and apo B or LDL-P stayed the same. In others, both decreased. In my practice, I've seen some reductions in particle number when fiber is used as part of a comprehensive strategy, but of course, it is difficult to know if the fiber has any impact on that, or if it is the other things such as the tocotrienols and the pantethine that are having that impact.

Also, in the National Health and Nutrition Education Study, the NHANES study, 407 subjects were followed for more than 19 years, and those with the highest quartile of dietary water-soluble fiber intake had a relative risk of 85 percent, 0.85, for coronary heart disease and 0.9, or 90 percent, for cardiovascular disease event, so a 10 percent lower risk for cardiovascular disease and 15 percent lower risk for coronary heart disease in those in the highest quartile of water-soluble fiber intake.

Now, of course, you know by now that this does not establish causality. It could be that those who were eating more fiber were also engaged in other behaviors that are protective against heart disease because fiber is considered to be healthy, but given what we know about how fermentable

fibers such as soluble fibers affect the microbiome and how the microbiome influences cardiovascular disease risk, there is certainly a plausible mechanism here.

Note that only fermentable fibers have this benefit, so this is another reason to focus our efforts in this area. You can use fibers such as glucomannan, partially hydrolyzed guar gum, acacia, or other supplemental soluble fibers that we've talked about in the gut unit, or just increase your intake of these fibers in food.

Image credits: http://www.integratedhealth.com/probiotics-enzymes-foods/prescript-assist-probiotic-90.html

The next is probiotics. Both animal and human studies have documented a modest but significant reduction in serum lipids with long-term consumption of oral probiotics. In human studies over a period of four to six weeks, reductions in total cholesterol ranged from 4 to 12 percent, LDL from 5 to 8 percent, and triglycerides about 10 percent. Most studies, unfortunately, have not looked at the effect of probiotics on LDL-P or Lp(a)-P.

If you understand the mechanisms, though, for what causes elevated LDL-P, which we talked about earlier, you know that GI pathology is one of them, so anything that we can do to improve GI

function should help lower LDL-P. I mentioned a couple cases before where we fixed the patient's gut, and their LDL-P did go down significantly, sometimes 30 to 40 percent.

Diet and supplement interventions can reduce **Lp(a) by up to 30% in some cases.**

What about diet supplement interventions for reducing Lp(a)-P? Very little is known about this, and again, the conventional wisdom is that there aren't any. Also remember that so far there is little convincing evidence that lowering Lp(a)-P actually improves clinical outcomes. I think in this case lack of proof is definitely not proof against, and given the strength of the association, the precautionary principle applies. Despite the lack of evidence on the effects of diet and supplements, my anecdotal experience suggests that these interventions can have a significant impact on Lp(a)-P. The case study I showed you earlier demonstrated a 35 percent reduction from an Lp(a)-P of 219 to 143. There are some studies on single interventions that have shown benefits. For example, a study in 1998 found that taking 2,000 mg of hexaniacinate, which is a time-released form of niacin or B3, for almost two years lowered Lp(a) by 39 percent. Another study found that 2 g per day of L-carnitine lowered Lp(a) by about 20 percent after six months. Note the very long duration on each of these cases.

Linus Pauling hypothesized that Lp(a) might be a surrogate for vitamin C in humans. He did some additional studies in animals that found that when vitamin C was low, Lp(a) levels were higher, and there was a higher risk for heart disease. Supplementing with vitamin C along with lysine and proline, which also play a similar role, could lower Lp(a), but do note that research investigating that claim has not supported it so far. The studies that have been done looking at the effects of vitamin C on Lp(a) have been unimpressive, but those studies that were done did use a somewhat lower dose of vitamin C than Pauling recommended, so it's possible that higher doses of maybe 4 to 5 mg a day to bowel tolerance could be effective.

Treatment matrix

Presentation	Diet	Supplements
High LDL-P / Lp(a)-P without inflammation	Mediterranean Paleo	Tocotrienols, pantethine, RYR, fiber, probiotics; niacin & L-carnitine (Lp(a)-P)
High LDL-P / Lp(a)-P with inflammation	Mediterranean Paleo	Tocotrienols, pantethine, RYR, fiber, probiotics, CoQ10, curcumin, glutathione; niacin & L-carnitine (Lp(a)-P)
High LDL-P/Lp(a)-P with metabolic syndrome	Low-carb Paleo	Tocotrienols, pantethine, RYR, fiber, probiotics, CoQ10, curcumin, glutathione; niacin & L-carnitine (Lp(a)-P)
Normal LDL-P/Lp(a)-P with inflammation	Paleo	CoQ10, curcumin, glutathione

Here's a treatment matrix. We'll go through this with each category of patient. If you have a patient with high LDL-P and/or Lp(a)-P without inflammation, the diet approach would be Mediterranean Paleo and then supplements tocotrienols, pantethine, red yeast rice extract, soluble fiber, probiotics, possibly niacin, and then L-carnitine if their Lp(a)-P is high.

If you have a patient with high LDL-P and Lp(a)-P and inflammation, the same diet, the same basic lipid-lowering supplements, but then you could add CoQ10, curcumin, and glutathione for the inflammatory component.

Then, if you have a patient with high LDL-P and Lp(a)-P and metabolic syndrome, low-carb Paleo would probably be a better approach, at least as a starting point there, and you would give them the same lipid-lowering and anti-inflammatory supplements as with the previous case or category.

If you have a patient with normal LDL-P and Lp(a)-P who has inflammation, you could use a standard kind of Paleo approach and things such as curcumin, glutathione, and CoQ10 and, of course, addressing the source of the inflammation. In that case, there is no real need for a special diet or lipid-lowering supplements because they are normal.

What about statins and other medications? I've written a lot about statins over the years, and I'll provide some links in the resources section. I've argued that most research suggests that the only population statins extend lifespan is in middle-aged men with pre-existing heart disease. That said, this may be in part due to the fact that most clinicians are treating to LDL-C instead of LDL-P and Lp(a)-P. It's possible that results of studies would be different if treatment targets were updated. However, higher doses of statins would likely be required, which, of course, would increase the risk of side effects.

I'm doing a bonus interview with Dr. Peter Attia that I'm going to make available to you as part of ADAPT, and he has a different take on statins and is much more aggressive in treating high LDL-P and Lp(a)-P than I've been, so you can listen to this and get his perspective. We'll also be talking about new drugs such as PCSK9 inhibitors, which increase the lifespan of LDL receptors and thus remove LDL particles from the circulation rather than blocking synthesis like statins do; and then apoA antisense drugs, which are not available yet but will be shortly, which prevent the liver from making apoA, which in turn would effectively prevent the liver from making Lp(a) out of LDL and apoA. They are remarkably effective, as you would expect, at reducing Lp(a) and currently appear to be relatively well tolerated with relatively few side effects.

At the end of the day, as we talked about earlier, it's an individual decision, and it should be based on their family history, their health status, their risk tolerance, and then other risk factors for heart disease.

Okay, that's it for now. See you next time.