#19 – DEEP DIVE SERIES: Hyperlipidemia (Why Cholesterol and Statins Aren’t the Villains You Think... Transcript

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Introduction to Integrative Medicine and Hyperlipidemia

[music] Welcome to the trip lab kitchen table conversations about integrative medicine and psychedelics. [music] I'm your host and attending physician Dr. Mariela Wood.

Hi everyone. Welcome back to another episode in our deep dive series. In this series, we are going to look deeply into the pathophysiology and the root causes of some of the most common medical conditions. Then with that understanding, we can better look how our traditional medications and holistic integrative therapies work to treat these disorders. If you're new to this podcast, integrative medicine is the field of medicine that combines evidence-based holistic practices with our traditional western model. So rather than only subscribing to one view or the other, we combine both in an evidence-based way to offer our patients more treatment options. And when I say evidence-based, I mean that these traditionally quote unquote alternative practices are now being studied so we can determine which ones are actually efficacious and which ones are not. If you want to learn more about how the divide between modern medicine and quote unquote alternative medicine happened and how that is changing, check out the intro episode to this series, episode number 15 called how big pharma deemed Eastern Medicine Alternative. But today we're going to talk about hyper lipidmia or high cholesterol. This is actually an umbrella term for elevated lipids in the blood mainly cholesterol and also triglycerides. This eventually leads to diseases like atherosclerosis or hardening of the arteries and plaque formation which eventually causes heart attacks, strokes and peripheral arterial disease. But let's start with the basics. What is cholesterol and why does it matter? We often hear cholesterol talked about like it's this villain that we need to eliminate. But cholesterol itself is essential. We actually need it to survive. It's one of the most important biological molecules in the human body.

So let's break that down. Cholesterol is a lipid, but unlike fats or triglycerides, it's a sterile. So a compound with a rigid ringlike structure. And that structure is what gives it its unique role in cell membrane dynamics. Every single cell in your body has a membrane made up of a phosphoipid billayer. Essentially a double layer of fats that form a protective bubble. But if that bubble were just fat, it would be too floppy and permeable. Cholesterol inserts itself between the fatty acid tails of those membrane lipids, regulating the membrane fluidity and integrity. So in cold environments, cholesterol keeps membranes from becoming too rigid. And in warm environments, it prevents them from being too fluid. It truly is what makes your cell membranes functional, not just structural. Cholesterol also clusters in regions of the membrane called lipid rafts.

What Cholesterol Does in the Body

These are specialized micro domains that serve as platforms for cell signaling, receptor activity, and intracellular communication. These are critical for immune function, hormone signaling, neurotransmission, and more. But beyond the cell membrane, cholesterol is also a precursor molecule for all steroid hormones. So estrogen, progesterone, testosterone, cortisol, eldoststerone, as well as vitamin D. So without cholesterol, your body literally cannot make these molecules. It's also used to produce bile acids, which help emulsify fats in the gut so they can be absorbed. So where does cholesterol come from?

Well, only 25% comes from our food. Our liver actually makes the other 75% of it. And normally the liver does do a great job of regulating how much cholesterol we produce. It uses enzymes like HMG COA reductase, which is what statins target. We'll get to that later. [snorts] Your body will ramp up or down cholesterol synthesis based on demand. So, the problem isn't that cholesterol exists. The problem is what happens when it's carried in excess or when it becomes damaged. Specifically, when LDL particles, especially the small, really dense LDL, become oxidized or glycated, they can penetrate the endothelium, which is the inner lining of the arteries where they actually trigger an inflammatory immune response. That's the first step in the development of atherosclerosis, which is the disease process behind heart attacks and strokes. This is why simply looking at a cholesterol number doesn't actually tell you the full story. So it's not about cholesterol being good or bad. It's about the context in which

cholesterol operates. And that context includes inflammation, oxidative stress, blood sugar control, nutrient status, and more. So we understand cholesterol a little bit more. Let's look into high cholesterol, hyper lipidmia. So high cholesterol typically develops from a mismatch between how much the body is producing, how much it needs, and how efficiently it's clearing it. That imbalance often starts in the liver, which is the central hub for cholesterol production and packaging. The liver will make these particles called VLDL, which stands for very low density lipoproteins, which then carry triglycerides and cholesterol through the bloodstream and to your tissues. As VLDLDL particles offload their cholesterol, they become LDL, which is the primary cholesterol carrying particle most people know. And when everything is working well, the system is tightly regulated. But in today's world, that regulation is often thrown off by insulin resistance, excess carbohydrate intake, and chronic inflammation. Notice that I didn't necessarily say fatty foods. I said excess carbohydrate intake. So when sugar and insulin levels are chronically elevated, which can happen of course from a diet high in refined carbs and low in fiber, but also from sleep deprivation, chronic stress or sedendary behavior, the liver actually ramps up VLDLDL production. This eventually leads to an overabundance of LDL particles circulating in the blood and especially those small dense LDL particles which are more prone to oxidative damage and arterial plaque formation. But still, high LDL alone doesn't cause heart disease. It's what happens next that really matters. To cause harm, those LDL particles need to actually penetrate the blood vessel wall. And this happens when the endothelium, which is the inner lining of the blood vessels, becomes damaged. So under normal conditions, that endothelium acts like Teflon. It's smooth, non-stick, anti-inflammatory.

But when it's exposed to chronic stressors like high blood pressure, elevated blood sugar, smoking, processed seed oils, or environmental toxins, it starts to lose its protective qualities. So, it actually becomes more permeable and LDL particles can now slip underneath the surface. Once LDL particles lodge beneath the endothelium, they can be exposed to a harsh biochemical environment.

How High Cholesterol and Atherosclerosis Develop

And if there's oxidative stress, meaning an imbalance between free radicals and antioxidant defenses, those LDL particles can become oxidized, which dramatically changes how the immune system responds to them.

Oxidized LDL is seen as a threat to our body. So when that happens, immune cells like macrofasages rush in to try to neutralize the problem. But in doing so, they engulf the oxidized LDL and turn into something that we call foam cells.

These foam cells accumulate in the walls of the arteries and form what we call a fatty streak which is the earliest stage of atherosclerosis. And over time that fatty streak grows more LDL, more foam cells, more inflammatory signals, which is why we can check inflammatory markers, which I'll get into later. But moving on. Next, the body tries to wall off this damage with a fibrous cap, creating a plaque. If this plaque remains stable, a person might not even know it's there. But if he becomes unstable and ruptures, it can trigger the sudden formation of a blood clot and that's what triggers heart attacks and strokes. But this I think is the most critical piece. This entire process is accelerated when the body is living in a state of metabolic dysfunction. [clears throat] So not just eating fatty foods but overall metabolic dysfunction. Insulin resistance not only drives over production of cholesterol particles but it also alters the way that those particles behave. It decreases HDL which is the quote unquote good cholesterol which is essential for clearing excess cholesterol from the arteries. It raises triglycerides which are inflammatory and further destabilize the lipid profile. And it also increases levels of small dense LDL which are more dangerous than the large buoyant ones.

There's other root causes other than insulin resistance that do this too. So, chronic inflammation from gut dispiosis, nutrient deficiencies in specific antioxidants like co-enzyme Q10 or vitamin E, poor sleep, elevated cortisol from chronic stress, and there's even certain genetic variations like LP little A, which we will talk about in a little bit, that increase risk regardless of lifestyle. So, when we talk about hyper lipidmia, we really do have to zoom out. It's not just a cholesterol problem. It's a whole body systems problem, a reflection of metabolic health, vascular integrity, immune activation, and lifestyle influences all converging. And this is where an integrative approach really comes in. Because instead of just focusing on the cholesterol number, we look at why the number is elevated in the first place. We support the body's ability to regulate cholesterol production, reduce inflammation, and repair the endothelium. In doing that, we're not just reducing the risk of heart disease. We're actually moving towards whole

system healing. So with all that, let's get a little bit deeper into lab testing. How do we actually assess damage? So most commonly physicians will order a basic lipid panel, which includes total cholesterol, LDL, the quote unquote bad cholesterol, HDL the good cholesterol, and triglycerides. Triglycerides are slightly different from cholesterol.

They store unused calories we can later use for energy. High levels though can start to thicken the arteries which we call arterioclerosis. And extremely high levels like 500 plus can cause inflammation and we often see this with pancreatitis. But let's go deeper besides the basic lipid panel.

Here are some more tests that we actually do have in traditional laboratories. So no functional medicine testing needed to check these ones. First, we have Apo B, which truly is one of the most important markers we now have for cardiovascular risk. And it actually is finally starting to make its way into conventional guidelines. So, let's understand it. Every aogenic particle, which means BLDL, IDL, LDL, LP little A carries exactly one apo molecule on its surface. So what that means is measuring apo B gives you a direct count of how many of those potentially damaging particles are circulating. This is much more precise than just measuring LDL cholesterol which does tell you the amount of cholesterol within the particles but just not how many particles are present.

So higher apo means more particles means more opportunity for those particles to enter the endothelium and form plaque. And this is pretty validated. In fact, several large-scale studies have found APOB to be a stronger predictor of cardiovascular events than LDL, particularly in people with insulin resistance or metabolic syndrome, where LDL particle size and density are often altered. Now, on the flip side of that, we have apo A1. So, this is the main structural protein of HDL, the so-called good cholesterol. APO A1 is responsible for reverse cholesterol transport. So, it'll take excess cholesterol out of tissues and blood vessels and deliver it back to the liver for disposal.

So, a low APO A1 can indicate impaired HDL function, even if your HDL number looks normal. That's important because we now know it's not just how much HDL you have, but how well it works that really matters. So with APO B and APO A1 we can actually calculate the APO B to APOE A1 ratio which provides a nice snapshot of the balance between aogenic and protective lipoproteins.

In newer studies that ratio was more strongly related to risk of a heart attack than either smoking or diabetes and individuals with a high ratio had three times greater risk of having a heart attack. This is huge because currently our ASCVD risk guidelines take into account smoking and diabetes as major risk factors, which they are, but this ratio seems to be even more telling when assessing risk. Next, we have lipoprotein A, also known as LP little A, which is a genetically inherited and highly aogenic form of LDL. So it has an extra protein, lipoprotein A, that makes it more likely to stick to damaged vessel walls and promote that plaque formation.

Advanced Lipid Testing and Cardiovascular Risk

It also interferes with the body's ability to break down blood clots. So it actually adds a thrombotic risk on top of atherosclerosis. What's wild is that it's estimated that one in five people actually have elevated LP little A and most people don't know it because it's not included in standard labs. If it's elevated, it doesn't mean you're doomed, but it does mean that you'll want to be more aggressive about other risk factors, especially inflammation, blood sugar control, and oxidative stress. Unfortunately, statins don't lower LP little A. There are new therapies that are being studied, but they're not available yet. But beyond those cholesterol tests, we are also looking at inflammatory markers, which I mentioned earlier. Specifically for cardiovascular risk, we look at high sensitivity CRP or C reactive protein.

So this measures lowgrade systemic inflammation, the kind that damages the endothelium, makes LDL more likely to oxidize and fuels plaque instability.

Elevated high sensitivity CRP levels are associated with higher cardiovascular event risk even in people with normal cholesterol. From a functional medicine perspective, it also gives us a useful window into chronic inflammation, but it is non-specific. So, it's a piece of the puzzle, but not the whole picture. Last, with testing, we do need to talk about the coronary artery calcium score, the CAC score. So, this is a low radiation CT scan that we can do to detect calcified plaque in the coronary arteries. It gives you a direct look at how much plaque has already built up, something that a blood test can't do at the moment. So a CAC score of zero is associated with a very low

short-term risk of a cardiac event. We often say you have a quote unquote warranty period of about 5 to 10 years. A higher score, you know, ranging from 100 to 300 correlates with progressively higher risk. This test is particularly useful in people who fall into the gray area. So maybe their ASBD risk is borderline or their cholesterol levels are mildly elevated and they're hesitant to start a statin. [snorts] A CAC score of zero might give reassurance, but a higher one could prompt earlier intervention. But there is nuance. It's not a perfect test. It only detects calcified plaque. It does not detect soft, inflamed, or unstable plaque, which can still rupture. So, this means that it actually can be falsely reassuring in people with rapidly progressing disease, but little calcification.

It still is definitely a useful tool, especially for risk reclassification, but it's not perfect. So, all of these advanced tests can help us decide how aggressive we need to be about lowering cholesterol to prevent a heart attack or a stroke. More traditionally, that means helping us decide whether or not we need to start a statin. Now, this is a hot topic, so we are definitely going to dive into statins a little bit deeper before we get into our integrative approaches. I have seen so much in the media and I've had so many patients coming to me saying that quote unquote statins are evil, which is a really bold statement. So, let's break down what they do, what the concern is, what they can help us with, what they may not help us with. Let's just break it all down.

So, first, how do statins work? They are a class of drugs that inhibit an enzyme in the liver called the HMG COA reductase, the key rate limiting step in cholesterol synthesis. So by blocking this enzyme, statins reduce the liver's production of endogenous cholesterol. In response, the liver then upregulates LDL receptors which pulls more LDL particles out of circulation. So end result lower LDL cholesterol in the blood. But statins don't just lower LDL, they also have plyotropic effects, which means they reduce inflammation, stabilize plaque, and actually improve endothelial function. These effects are part of why statins reduce cardiovascular events in people with modest LDL elevations. So what does the evidence actually say for their effectiveness? For secondary prevention, meaning people who already have cardiovascular disease, statins are unequivocally beneficial. They reduce the risk of heart attacks, strokes, and cardiovascular death. This has been shown across multiple large trials including 4S, HPS and prove it for primary prevention. So people without known heart disease but do have risk factors. The data is a little bit more nuanced.

Statins do reduce events cardiovascular events like heart attack strokes but the absolute risk reduction is smaller. For example, in a metaanalysis by the cholesterol treatment trialist collaboration, statins lowered LDL by about 39 points and reduced the relative risk of major cardiovascular events by about 20 to 25%. But relative risk is not the whole story. For someone at a low baseline risk, that relative reduction might translate to a very small absolute benefit. I'm talking like one to two fewer events per a thousand people per year. For high-risisk individuals, the benefit is more substantial and often outweighs any of the risks which we'll talk about. So that is why most guidelines use risk calculators like the ASCBD 10-year risk score to help us determine whether a statin is appropriate. So let's get into it. Why all the fear? Why do statins have such a bad rap outside the medical community? There are potential side effects like muscle damage, cognitive effects, maybe we'll talk about that, diabetes risk, and just general distrust of big pharma, I think, is all playing a role. But let's break all those down and let's look at what the data actually tells us.

So, first we have the muscle damage. This is certainly the most common concern people have with statins. Muscle pain, muscle damage, and this is where the data and real world experience don't actually align very neatly. Studies show that statin induced myopathy, meaning actual measurable muscle damage, is very rare. We're talking a true incidence of less than 0.1% in large randomized trials. In fact, several placeboc controlled studies, including the well-known stomp trial, found that the rates of muscle pain in statin users were actually no different in those taking a placebo. But there is sort of a catch. In clinical practice, patients do report muscle symptoms and not infrequently.

Statins: Benefits, Evidence, and Side Effects

These symptoms typically include aching, stiffness, weakness or fatigue, especially in the large muscle groups like the thighs or the shoulders. And this phenomenon is now what we often call statin associated muscle symptoms or SAMs. And the medical community believes that at least some part of it may be due to the no SIBO effect where the expectation of side effects actually creates or amplifies them. However, we can't dismiss all symptoms as psychological. While true status myopathy like actual muscle damage is rare, it can occur and in these cases we can often detect elevated creatinine kinace or CK levels which is a marker of muscle breakdown.

In rare cases, there is a more serious form of muscle injury called statininduced meioitis or eventually rabdtomyis, which involves significant muscle breakdown and can even affect the kidneys. But this is even more rare, typically seen at really high doses with other drug interactions or people with certain genetic predispositions. So the bottom line with all the muscles, true muscle damage from statins is rare but not impossible. Muscle pain or weakness is seen more commonly, but it doesn't usually reflect actual harm. In people who are sensitive, we can try switching to a different statin, reducing the dose, use alternate day dosing if appropriate, or sometimes supplementing with co-enzyme Q10 can help too, which we'll talk about the integrated fragments later. And checking a CK level can be useful if someone is having symptoms and you do want to rule out the significant muscle injury. Okay, so the next big concern, the one that I hear a lot as well is the cognitive side effects like memory loss, confusion, or brain fog. So, this all came out because in 2012, the FDA added a label warning to statin medications, citing quote unquote rare cases of memory loss, forgetfulness, and confusion that appeared to be non-serious and reversible once the medication was discontinued.

But this decision to label that was not based on randomized control trials. It actually stemmed from postmarketing surveillance reports, which are essentially anecdotal reports submitted by clinicians and patients after the drug was approved. There weren't thousands of cases, but there was enough that the FDA felt it was worth including on the label to increase awareness and encourage more systematic study. So, let's think about this a little bit more. Why and how could statins cause cognitive issues?

Well, cholesterol is critical for brain health and about 25% of the body's cholesterol is actually in the brain. It's essential for the myelin sheath formation, syninnapse integrity and neurotransmitter signaling.

So the theoretical concern is that statins, especially the lipopilic statins like sveastatin or tobvisatin which can actually cross the bloodb braid barrier might interfere with central nervous system cholesterol metabolism. The next piece of the puzzle is that we do know statins lower co-enzyme Q10, which is essential for mitochondrial energy production.

Statins inhibit the same pathway that produces both cholesterol and co-enzyme Q10. And some researchers speculate that the reduced CoQ10 in the brain could impair cognitive function, though this hasn't actually been definitively proven yet. Last, statins may alter lipid rafts in neuronal membranes. So these are those cholesterol-rich zones that cluster receptors and signaling molecules. So in theory, disrupting these could affect how neurons communicate. But all of this is still very theoretical. So what does the research actually say? A 2013 systematic review by the FDA itself, which included both randomized trials and observational studies, concluded that there was no evidence of statin associated cognitive decline. In follow-up randomized control trials, statins have also not been shown to increase the risk of dementia or cognitive decline. And some trials have even found protective effects, particularly in patients at high cardiovascular disease risk. The Prosper trial, which looked at pravisaten in elderly patients, found no significant difference in cognitive outcomes versus placebo. More recently, a 2021 meta analysis from the Journal of the American Heart Association looked at over a thousand patients and found no evidence that statins negatively affect cognition. And again, some studies suggested actually a protective benefit, especially in preventing vascular dementia. That being said, individual responses can vary. There are occasional case reports of reversible memory loss or brain fog that resolve after discontinuation.

These tend to be idiosyncratic and difficult to study, but they're not entirely dismissed. If a patient reports cognitive symptoms while on a statin, it is reasonable to consider switching to a hydrophilic statin like pravisaten or rzuatin, which are less likely to cross the bloodb brain barrier. We can also evaluate for other causes of cognitive symptoms like sleep, thyroid, B12 deficiency, medications, and we could consider a trial off the statin if it's safe, if the patient is low risk and the symptoms are significant. So again, we come back to the theme of this episode, personalized root cause care. Not everyone needs to be on a statin, and not everyone who experiences symptoms should be told it's all in their head. We really need to listen to the patients, look at the data, and individualize our plans. Okay, one more thing to talk about how scary statins are, why statins are quote unquote evil. Another concern that's gained traction, both actually in the literature and among patients, is whether statins can increase the risk of developing type 2 diabetes. So, this one actually is not just internet fear-mongering. This one is real. It's a well doumented side effect, but it's one that needs to be put into context. So, let's start with what the data actually shows. Large metaanalysis have shown that statin use is associated with a modest increase in the risk of new onset diabetes, particularly in people who already have risk factors like metabolic syndrome, pre-diabetes, central

obesity, or sedentary lifestyle. One of the most cited analysis is from the Jupiter trial where statin therapy ruastatin specifically was associated with a 27% increase in diabetes incidents.

But what's important to note that was in people who were already at high risk. When you zoom out to larger populations, a 2010 meta analysis in the Lancet found that statin therapy was associated with about a 9% increased relative risk of developing diabetes. So in absolute terms, this only translates to about 1 to two new cases of diabetes per a thousand patients per year on statin therapy. So yes, there is an increased risk, but it's relatively small. And in patients with high cardiovascular risk, the benefits of statin, aka reducing heart attacks and strokes, generally still outweigh the small increase in diabetes risk. Okay, so we've been talking about statins for a while now. Let's just recap and move on to our integrative treatments.

So the bottom line, statins are effective at lowering LDL and reducing cardiovascular risks, especially in high-risisk individuals, and they can be an important part of an integrated treatment plan. Side effects like muscle symptoms, cognitive concerns, and slight increases in blood sugar are real, but relatively uncommon and often manageable.

So rather than rejecting statins outright, integrative medicine looks at the whole picture. So we can optimize metabolic health, address root cause concerns, and use medications when it meaningfully reduces risk. So what are those integrative treatments? What we often forget is that up to 80% of cardiovascular disease risk is modifiable through lifestyle changes.

So, of course, let's start with the most foundational intervention, food. Food truly is medicine. And the nutrition plan that has the most evidence to lower cholesterol is definitely the Mediterranean diet or Mediterranean nutrition plan. So, this means eating foods rich in vegetables, fruits, legumes, whole grains, olive oil, nuts, and fish.

Following this nutrition plan has been shown to reduce LDL by up to 15%. And reduce cardiovascular events by up to 30%. And it's not just lowering cholesterol, it's reducing inflammation, improving insulin sensitivity, and protecting the endothelium.

Alongside the Mediterranean diet, we have the anti-inflammatory diet, which in my opinion really is just another take on the Mediterranean approach that also emphasizes colorful polyphenol rich produce and anti-inflammatory spices like turmeric, ginger, and garlic. All of those which help reduce oxidative stress, which is a key driver of LDL oxidation and plaque formation like we discussed earlier. But within both of those food plans, let's also call out some specific nutrients that have direct LDL lowering effects.

First, we have soluble fiber. So, examples of these being oats, beans, lentils, flax seed, and psyllium. So, 5 to 10 g can lower LDL by 5 to 10%. And they work by binding bile acids and promoting cholesterol excretion. Plant steriles, you need around 1 to three grams a day, block intestinal absorption of cholesterol and can reduce LDL by around 10%. Garlic is another big one, can reduce LDL by 9 to 12%. And this one also improves triglycerides, too. Next, we have to talk about exercise. I do want to do a whole deep dive episode on movement and exercise soon because it truly is proving to be one of the most important things you can do for your body and your mind, especially with longevity medicine and research on the rise.

Exercise doesn't just help you quote unquote burn calories. It actually rewires your metabolism at the cellular level. For cholesterol, regular physical activity improves lipoprotein metabolism, increases LDL receptor activity in the liver. So that means help pull more LDL out of circulation.

It can increase HDL, the quote unquote good cholesterol production.

Integrative Approaches to Lower Cholesterol

It enhances insulin sensitivity, which is tightly linked to lipid balance like we discussed earlier. And it also reduces inflammatory cytoines and supports our vascular endothelial health, meaning that your blood vessels stay more flexible and less prone to damage. So, when it comes to cholesterol specifically, here's what the research shows what it can do for us. Moderate to vigorous aerobic exercise, which includes things like brisk walking, cycling, swimming, or jogging, can lower LDL cholesterol about 5 to 10% on average and can increase HDL by around 3 to

6% depending on the intensity and duration. A meta analysis published in sports medicine found that aerobic exercise alone led to significant reductions in total cholesterol, LDL, and triglycerides even without weight loss. Resistance training around two to three times a week adds another layer of benefit. It improves muscle mass and glucose uptake which lowers triglycerides and improves the lipid profile indirectly. The greatest benefits that we're seeing are when we combine aerobic and resistance or strength training especially when done consistently over months or longer. Longer the better. So, the general recommendation is to aim for at least 150 minutes per week of moderate intensive activity or 75 minutes per week of vigorous activity plus 2 days a week of strength training. I would argue the more the better to an extent. You know, you can burn yourself out. But the truth is any increase in daily movement matters. Even light activity, walking after meals or breaking up long periods of sitting can significantly improve metabolic function. What really is powerful here though is that exercise doesn't just change your cholesterol numbers. It changes the entire system that produces those numbers. Okay, next let's get into supplements and botanicals, which seems to be everyone's favorite part of integrative medicine.

First, we have red yeast rice, which is the closest natural alternative we have to a statin. It actually contains a compound called monolon K, which is chemically identical to lovaten. Because of this, it works by the same mechanism.

So, it inhibits HMG COA reductase and lowers LDL production in the liver. Studies have shown that red yeast rice can lower LDL by 20 to 30% and in some cases up to 42% when combined with the fish oil pill. So, those numbers are actually a statin level result without a prescription. What's even more interesting to me, some patients who've experienced those statin associated muscle symptoms have actually successfully transitioned to red yeast rice without the recurrence of side effects, even though it's chemically identical to lovaten. This makes me think that being an herbal supplement, there's other compounds in it that can help be productive. One important thing I do want to note about red yeast rice, though, and truly any supplement, but for this one specifically, quality really matters. Some cheaper brands may contain citrinin which is a potentially nephrotoxic damaging to the kidneys contaminant. So it really is important to stick with vetted options from companies. Next we have bourberine which is a plant alkoid found in herbs like barberry and golden seal. This one I think is pretty fascinating. So it acts on amp K which is a metabolic master switch. So think of it like activating your body's internal metformin.

Bourberine improves insulin sensitivity. It lowers blood glucose. It actually naturally produces GLP-1 release, which also supports weight loss and appetite regulation. And for cholesterol, it has been shown to lower LDL by 10 to 20%. And it's especially effective in people with metabolic syndrome or insulin resistance. But for this one, the important note is that there actually is a long list of drug and herb interactions with this supplement. alone, it's pretty safe and pretty well tolerated, but it does interact with a lot of things, so it's especially important to talk to a healthcare provider before using this one. Next, we have artichoke extract, which is another botanical with pretty solid evidence behind it. It contains polyphenols that inhibit cholesterol synthesis in the liver and reduces the absorption from the gut. Studies have shown that it can lower LDL by about 5 to 15%. And it does have additional antioxidant benefits that support liver health as well. Next, we have garlic, which we talked about earlier in the food section, but people can actually take it as a supplement form as well. And it has measurable effects on lipids when taken at those higher therapeutic doses. So, standardized garlic extracts can reduce LDL and triglycerides by about 9 to 12%. Next, we have omega-3s or fish oil pills, which I really wanted to highlight because these are commonly thought to lower LDL, but they actually don't work on LDL alone. They work by reducing triglycerides. However, if you do combine this with other interventions, then they can help support LDL reduction.

My general rule of thumb for patients is this. If you eat 3 to four servings of fish a week, which I know is is up there, you don't need a fish oil supplement, but if you don't, then maybe considering a supplement a couple days a week could be a great option. Okay, last but not least, we have co-enzyme Q10 or CoQ10. While this supplement doesn't lower cholesterol directly, it does support mitochondrial energy production, it lowers oxidative stress and can reduce blood pressure actually by up to 10 points. And it's especially helpful in patients taking statins because as we talked about earlier, statins actually deplete co-enzyme Q10 as they're depleting cholesterol. So that's what we have for supplements. There are more, but that was just a quick overview. One last aspect of integrative medicine but arguably in my opinion one of the most important aspects is actually mindbody medicine. So very often we think of cholesterol as purely a metabolic deficiency or a dietary issue. But the reality is that chronic stress, emotional dysregulation and autonomic balance all directly affect lipid metabolism, inflammation and cardiovascular risk. Stress impacts cholesterol in a huge way. When you're under chronic stress, whether psychological, emotional, or

physical, your body releases cortisol, adrenaline, and other stress hormones. Over time, those hormones eventually increase glucose and triglyceride levels. They also promote visceral fat accumulation, which worsens insulin resistance, and they alter lipid metabolism in the liver. They also increase systemic inflammation, which we know now is a key driver of endothelial damage and plaque instability. And research actually shows that mindbody interventions, including meditation, yoga, taichi, and breath work, can measurably improve lipid profiles and reduce cardiovascular risk.

A 2022 systematic review and meta analysis found that mindfulness-based interventions significantly reduced total cholesterol and LDL cholesterol compared to the controls. Even short-term meditation interventions have shown to improve heart rate variability, reduce blood pressure, and lower inflammatory markers like CRP, which we talked about earlier, which directly impact cardiovascular risk. These interventions result in a 5 to 10% reduction on average. Additionally, the downstream effects on autonomic tone, vascular health, and inflammation really are profound. Okay, so that was a lot, but I do want to end this episode with this.

When we really look at the pathophysiology of disease, we see that every treatment and recommendation should be very nuanced and tailored to the individual person. We can combine holistic therapies with traditional medical therapies to reduce risk short-term and long-term.

Thanks for listening to the trip lab. If you liked this episode, please subscribe and share so we can get the conversation started about integrative medicine and psychedelics to destigmatize it and fully explore what this could mean in the world.

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