VIDEO_ Diet Doctor Podcast with Dave Feldman (Episode 8)

Dr. Bret Scher: Welcome to the DietDoctor podcast with Dr. Bret Scher. Today I'm joined by Dave Feldman from cholesterolcode.com. If you've been around low-carb circles for a while you've undoubtedly heard of Dave and all his amazing self-experimentation and what he's done to sort of further this concept of lipids in a low-carb lifestyle.

And are they different than lipids in general and the information we have specifically when in LDL cholesterol and LDL particle numbers elevated, what does that mean? And that's sort of a big cornerstone of a lot of his research and controversy. And we have to emphasize there's no answer to this. We don't know that the LDL elevation is harmful or not harmful in this specific subset and that's what Dave wants to explore so much.

So please don't construe any of this as medical advice, don't make any decisions based on this podcast. This is an exploration of what we know, what we don't know and how we can further this. Now a quick intro - cholesterol is all over our body; every cell in our body needs cholesterol.

We typically talk of LDL cholesterol as the bad cholesterol, HDL as the good cholesterol. Those are misnomers - cholesterol is just cholesterol. It's only good or bad depending where it ends up. But what's important is when we talk about LDL-C or LDL cholesterol, that's the total amount of cholesterol contained in LDL lipoproteins.

When we talk about LDL-P or LDL particles that's the number of lipoproteins. The way you can think about it is cars on the road. You've got a number of cars, that's the LDL-P, and then you've got the people in the cars that's the LDL-C. So you could have 100 people in one car or you could have 100 cars with one person. They're each going to have an LDL-C of 100 but the LDL-P is going to be either 1 or 100 in those scenarios.

And that's important because the literature does support that LDL-P, the particle number is a better marker than LDL-C. Now frequently people are going to use them interchangeably and for most cases that's okay, but I wanted you to understand the terminology because we throw that around a lot. We also talk about V-LDL, the very low density lipoprotein, which can be degraded into IDL, Intermediate Density Lipoprotein, and then down to LDL and that's an important path that we talk about.

And we'll explain more about that. As well as chylomicrons which are basically a collection of triglycerides coming straight from your intestines and being packaged so that they can circulate in the bloodstream. I think that's probably all the terminology you need to know to begin with. Hopefully we'll explain everything else as we go.

But as everything with Dave Feldman, this is a whirlwind of discussion with some great analogies and really focusing on this very important topic; how we can learn more about the subset of people and what the LDL means. So please enjoy this interview with Dave Feldman.

Dave Feldman, thank so much for joining me on the DietDoctor podcast.

Dave Feldman: Thanks for having me, Bret.

Bret: Well, you have had a whirlwind of a couple weeks I'm sure, you were recently on the Peter Attia podcast which has caused a lot of controversy, a lot of comments and I want to talk about that. But I think for the benefit of our listeners we actually should rewind a little bit and talk about sort of the building blocks of what got you to this point. And I know, between the two of us, we love this topic and we could talk all day on this topic so I'm going to try and summarize.

And you fill in as you think appropriate for this summary. And the basics is talking about LDL cholesterol, LDL lipoproteins, as an energy model that in people who are low-carb and burning fat for fuel and have potentially an increase level of their LDL particle number, that one hypothesis could be it is driven as part of an increased usage of the body of fat energy and LDL lipoproteins are a byproduct of that.

And as part of that you've shown with your inversion pattern that you can dramatically change your LDL particle numbers and your LDL cholesterol numbers either by fasting for three days and making the LDL number go up dramatically, or almost binging on high levels of saturated fat and dropping the LDL dramatically, things that really goes against conventional wisdom in medicine. Did you say that's an adequate summary of the building blocks of your work?

Dave: I think you did a very good job just stating it right there. I mean I would even go to say a little bit more simply, LDL cholesterol and LDL particles are very much influenced by the larger energy metabolism.

And much of my work especially in using myself as my own guinea pig is to find what those levers are, what are the levers that modify this energy metabolism both for fat-based energy and even for glucose coming from carbs. The more that I find I can play with these levers, the more I finally have the downstream result of altering LDL particle count and LDL cholesterol that of course is along with it.

Bret: So let's talk about the big picture for a second. Why is this important? Why do we care? **Dave:** Well, obviously a lot of people care about LDL cholesterol the so-called bad cholesterol. So we right now have a very large industry that of course sells medication in order for us to bring it down, because the assumption is the lower the cholesterol the better.

And I think you and I've had several conversations outside of this, for where we talk about, you know, we try to be cautious to not say that we know for sure whether the so-called lipid hypothesis which is the hypothesis that the more serum cholesterol you have the more cholesterol in your blood, the more at risk you are for heart disease in any context, that we know for sure whether that's right or wrong.

Because as right now I would say for the record I don't know for sure, but this does help to expose a context for which it may not only be not a concern but possibly even be an official to have higher levels of LDL particles because it may be reflective of a healthy lipid metabolism when you take other lipid biomarkers into account along with it.

Bret: And I think that's the key, that we're looking for a specific subset, we're looking at a specific subset not the general population and that can be a definite problem that we run into in medicine as a doctor in medicine guidelines, in medical research, that we try and apply our findings to the entire population. Because we have a study with 10,000 patients, therefore it must apply to everybody.

And sort of what you're saying and what I agree a lot with is, "Well, hold on a second! Maybe this doesn't apply the same for everybody." So one of the main theories about why it would not apply for someone who is low-carb and burning fat is because our energy utilization is different. So talk a little bit about that. Why would we assume it would be different in someone who is low-carb?

Dave: Well, certainly a lot of the existing literature is focused on people who are on a mixed diet, such as having both carbohydrates and fat or even being carb centric, where they have primarily carbohydrates fueling them. So now we have a circumstance in which there are people who are specifically trying to be powered by fat. Both the fat they get in their diet and the fact that they have in their bodies.

Well, this is pretty relevant because as you learn more and more about these lipoproteins, lipid caring proteins, the more you find that actually it's a fairly complex system, but much of its primary purpose is to shuttle around these fatty acids that we're powered by.

And once you learn that, then you find out something pretty fascinating, which is these two larger classifications of these boats that kind of carry around these fatty

acids, our chylomicrons, and VLDLs very low-density lipoproteins. If you're getting direct delivery of fatty acids to your cells from one of these larger boats, you've got to know that the first one, the chylomicrons, they come from food you just ate.

And that the second one VLDLs they come from your liver, primarily from fatty acids that came from your adipose tissue, your body fat. Now why that's important is it explains this inversion pattern you just mentioned where if I'm going to have a whole lot of dietary fat, I'm just going to eat a whole bunch of fat, whether my body has less reason to release as much of these fatty acids from my own fat stores, my own body fat and therefore less and less gets made from the liver and packaged into these VLDLs.

That matters because these VLDLs, when they drop off their triglycerides, this form of fat-based energy, will remodel to LDLs. And the LDL particles are the ones that contain the so-called bad cholesterol, LDL cholesterol, which is a little bit of a misnomer as you well know.

Bret: Of course.

Dave: There's really only two kinds of cholesterol if you will, two flavors there, esterified and un-esterified, but basically speaking that's the cargo that ride-shares with these triglycerides in those boats. And so then the question becomes, "Is there a good reason and a bad reason for why you may have high LDL cholesterol?"

And I myself think that that actually is the case. I think there can be bad reasons you have high LDL cholesterol, but typically speaking the big hint is whether or not you have high triglycerides, meaning you're past your personal fat threshold, so you've kind of maxed out the amount of parking there is for the fat that you can stash.

And for that matter if you have low HDL cholesterol you have you have an engagement to where it showing that you're not utilizing your fat as well and a lot of that comes out in the literature as well. So the phenotype we're trying to look for as what they call it, is those people who have high HDL cholesterol, low triglycerides and high LDL cholesterol.

And thus far as you know I've been very active in social media trying to hunt down any and all studies I can that can show that that phenotype is at risk particularly for cardiovascular disease. Because it stands to reason that they should be if the existing lipid hypothesis is true.

Bret: There should be no exceptions really if all elevated LDL puts you at risk. So what you're saying is if you're not using fat for fuel you store it in your body, more

spills over in your blood and your triglycerides are therefore higher. And that's a measurement that you can use to say which camp are you in.

One that has elevated LDL for a bad reason or one that has it potentially for good reason. Now when you had this interview with Dr. Peter Attia who obviously knows a ton about lipids, one of the main issues-- well, there were a couple of different issues I guess. And he was not a big fan of your energy model. So let me ask you first, did you think it was disproven in this interview?

Dave: First of all I have a tremendous respect for Peter and I'm really happy they had me on. Disproven, no, I don't feel like it was disproven and I actually had a number of responses to a number of the points that he brought up from before. He had brought up kind of three in particular that he felt was disproving it.

The first one was mass balance. In particular he was interested in where were those cholesterol molecules coming from or going to or whether they were drawn from other pools. But as I brought up a lot in the podcast there's also a fourth one, which is how much they're recirculated. The liver can recirculate as many times as it wants any particular cholesterol molecule.

So if you were to look at a cholesterol molecule in an LDL particle you don't know whether or not it was synthesized that day, or if it was recycled yesterday, or if it was recycled a week ago. Or a month ago... there is no way to know. Unless you get into more complex tracer models which of course is something I would be interested if they would do, but that's how we know right now that there isn't as much synthesis.

Also there's been a recent paper by Volek and Phinney that further emphasized that a lot of these lean fat adapted athletes weren't actually having high levels of synthesis as he was... as Peter was postulating at the beginning of the podcast.

Bret: Yeah, let's talk about that paper for a little bit. So this came out recently, Phinney and Volek study, they looked at 10 competitive ultra-endurance runners and compared the 10 low-carb high-fat athletes to the higher carb low-fat athletes. And interesting what they found was LDL in the low-carb athlete of 161 versus 88 in the high carb. HDL of 102 versus 64, triglycerides of 63 versus 70 and in the low-carb athletes the LDL were the larger particles and HDL were the larger particles.

And interestingly what you're talking about they measured these other sterol markers, desmosterol and sitosterol, basically markers of synthesis or absorption, and you would expect that they would have been through the roof with an over twofold rise in the LDL, but they weren't. So how do you interpret that?

Dave: I definitely interpreted it as greater recirculation. Let's use a racetrack for an example, let's say that you were to ask what the mass balance of an empty racetrack is. And it starts at zero. But now you go ahead and add five racecars. Well, the mass balance has changed to where five more have been added. So we produced five more to add to the total.

Now if those five racecars make a circle around the track the mass balance actually hasn't changed, they've just circled the track. And until they leave can we say that they've been distracked? Well, if you go ahead and add five more racecars, you've increased it five more but the five that are already on the track are still added to the total.

Now there's 10. And they can continue making loops as many times as they need to. Well certainly for those people who are going to have higher levels of LDL cholesterol or LDL particles in their circulatory system there's some amount of synthesis to add them.

But as far as constantly recycling them they will continue doing it as many times the body seeks to do so and rather effortlessly in comparison to actually constantly making them and degrading them or destroying them in some fashion, sending them back out the other side. There is no good reason for the body to just go ahead and re-create cholesterol especially as expensive as it is to do so biologically.

Bret: So I guess one way to think about it then would be the timeframe in which these lipoproteins and the cholesterol concentration increased, because if it happened in a day, maybe you need to dramatically increase your absorption or production for that to happen... If it happened over six months or a year that can be more of a slow minimal increase in production, but a continuous recirculation. Is that one way to think about it, or am I sort of saying that wrong?

Dave: For me, again I'm coming from network engineering, it's all a pool. And how much of it is a pool that's in circulation versus how much is in the liver at any given time? The only thing that really matters at the end of the day is just how much is needed and whether or not that's easily achieved. And as far as this circulatory system goes, I mean literally is a circulatory system, it is like a racetrack, a fairly complex one, but that's basically how it's going to work.

Bret: Okay so let's take your inversion pattern for a second. With those three days what would you expect the absorption and production measures to be? Would you expect those to be significantly different?

Dave: I was talking about a hyper-responder on a low-carb diet versus somebody in a typical diet.

Bret: Right, who does your three-day protocol and sees their their LDL increase dramatically with fasting?

Dave: Or the other way around.

Bret: Who sees they fast and the LDL goes up?

Dave: Correct, if they fast their LDL goes up.

Bret: So would you expect the production markers in the blood to be much higher under that circumstance? Or again is still recirculating because it's coming from your fat stores so you would expect a change in your production or absorption?

Dave: If we were to set a hypothesis I would say it's a little of the former and a lot more of the latter. I think that there may be some degree of an increase in production, but I highly doubt that it's a 100% increase in production to match what we then see as the increase in total LDL particles. I think more likely we're going to see a greater recirculation against the pool that the liver already had resident.

Now to one degree the liver is also making use of the cholesterol for other purposes, going on in the bile or being used for sex hormones and so forth. All of these things are of course a little bit tricky to track, but the larger question is will it make more if it needs to? Certainly. When you actually look at the total quantity and capability of what it can make versus what's actually in the circulatory system at any given time, it's actually quite daunting, it really has enormous amounts of control.

But again I'm still thinking about this from the mechanistic standpoint of is it worthwhile to constantly make and degrade it in a rapid rate? For the most part I don't find that the engineering of the system itself reflects that. It seems to be very greedy about its cholesterol. It wants to get ahold of it and keep ahold of it as long as it can for what purposes it can use it for.

Bret: And let's be clear, just because it's there does not by default make it dangerous. Yet that's sort of what the lipid hypothesis would assume. And even Peter agreed there are other factors; inflammation, vascular injury, being two of the most important ones.

So what about this concept though that it's just a diffusion gradient? That the more there is, the more it's going to get in the vessel wall and the more damage is going to come some? Some would say that will counteract your hypothesis.

Dave: I think if it worked that way, they would be right and this is effectively what Peter was kind of advancing. That it's kind of like fire and oxygen that it's a-- I often

like to call this the accelerant hypothesis. As in sure maybe it takes a spark to ignite the flame, but the more would you have, the bigger the flame.

However I have yet, and this is part of why I brought up the challenge that I've had on Twitter and that I circulated on social media... I have yet to see what I would consider to be probably the template of a healthy lipid metabolism.

And how it's reflected in these lipid numbers, showcase the same gradient, showcase that as people's level of LDL-C or LDL peak at higher that there is a correspondingly higher level of atherosclerosis. Something I was trying to bring up in the podcast at the time and as I'm sure you're well familiar with, I have been getting a carotid intima media thickness test on both my left and right carotid arteries, they are the arteries around the neck.

And it's an ultrasound which will capture both your intima and your media together. Basically it's capturing its thickness. Now I've been getting it about every six months since I went on a low-carb diet and for the first two years outside of a few experiments I'd pretty much averaged in LDL-C of above 200 mg/dL which is very high and an LDL-P, the particle count, of over 2000 nmol. And that is something that without question most doctors... most doctors, you probably personally know, wouldn't let me leave the office without at least two drugs.

Bret: Absolutely.

Dave: Statin police would be right around the corner for me. So during that period of time both my left and my right carotid arteries regressed whereas there were supposed to stay the same or for that matter progress and get thicker with my age. They had actually regressed on both sides. And the left side was actually a bit better and dropped by around 50 nm. In the right side around 150, it started out a lot thicker.

Bret: Interesting.

Dave: And it wasn't until I did a recent experiment where I actually intentionally gained weight for my research... that's a bigger story, that I saw it reverse, hit the other direction, it actually shot up on both sides.

Bret: And what were you eating to gain weight in that time period?

Dave: I was eating a lot of bread and just a lot of starches. I actually tried to avoid sugar and fructose in its many forms and for the most part I just had a lot of starches.

Bret: So did your HDL and triglyceride also change in that timeframe?

Dave: They did.

Bret: So you were no longer in that phenotype that you're describing and that's when he saw the carotid intima media thickness increase in your tests?

Dave: Right. Now as you all know the CIMT is often used as a proxy in many of these different studies as a risk marker for atherosclerotic burden. Now the reason I was trying to bring this up with Peter and the reason trying to bring this up with everyone is that it is commonly known that a risk factor for having higher and higher levels of CIMT is LDL particle count.

Yet here I am in the 90th percentile in what I would consider to be theoretically a very well-functioning lipid metabolism that sure had high LDL-C but also had very high HDL-C and low triglycerides.

That phenotype continues to impress me with how many other people I know turn around these incredible cardio metabolic markers in spite of having these very high levels of LDL. And in that regard I do have a lot of difficulty believing that it's as simple as fire and oxygen because it seems to be that there really is more to the mechanism itself.

Bret: Now I'd suggest to touch briefly on the CIMT test. It has gone a bit of a bad wrap, because it doesn't have the same predictive value as a calcium score when compared head-to-head. But the point is that's a one-time test. Now its greatest value I think is exactly how you're describing it.

You can quickly measure small degrees of progression and regression and the data you have there is pretty powerful to say the LDL is certainly... an elevated LDL is not harming the test for you and I think that's pretty powerful. Now of course it's not outcome data, of course it takes years in larger studies and I want to get to talk to you about that a little bit more, about how we could potentially design a study that would answer that question.

So we talked a little bit about the mass balance and I think we can kind of move past that one now. The other one though was this concern about the VLDLs and how they are so low and if you are having a higher production of VLDLs for energy that they should then be higher in the blood. I mean wasn't that one of the arguments as well?

Dave: Yes, so let's actually kind of impact that a little bit. So we've kind of talked about this a little bit earlier in that VLDLs are those lipoproteins that can come from the liver with... I would argue is their primary purpose as to distribute energy from fat and in particular their cargo is coming from your fat cells for the most part.

So with that in mind after they've dropped off these fatty acids then they remodeled to LDL. Now your triglycerides is measured in a fasting cholesterol test. Are going to be almost entirely the cargo of VLDLs, because chylomicrons get cleared relatively quickly. So with that in mind it does seem to be a rather basic conclusion that if you're making more of these VLDLs you should therefore have more triglyceride cargo.

And this was the point Peter was making and actually a point there was further reinforced by Dr. Thomas Dayspring who also went through the transcript and made a note of that as well.

That if the energy model that I'm proposing is correct and that people who were on a low-carb high-fat diet were actually secreting more VLDLs, but in particular this phenotype we're talking about, people who are very, very lean, very fit, seemed to have very high demand and therefore a lot more turnover, that they should therefore have higher levels of triglycerides to match what is theoretically the higher levels of VLDL.

And this I was trying to explain on the podcast and I'll explain once again, this assumes that there is the same rate of turnover of VLDLs across all of these different profiles of people, which I definitely would argue against. I think that VLDLs obviously can drop off their cargo at different rates of speed and I think it has a lot to do with where you are on your personal fat threshold.

So to kind of simplify it a little bit - do your fat stores have a lot of parking available? Because if they do then they're going to pick up a lot of these triglycerides at a fairly rapid rate. And it's fine because the whole point of your fat cells is especially to provide fat-based energy to nearby tissues like the muscle tissues in the same area.

That's why it's a good thing to have adipose tissue that's nearby the muscle tissue to constantly give it resupply. So in many ways VLDLs are just repleting it, they are kind of like the wholesaler, if you will, that's providing. I'm stealing that one from Siobhan Huggins by the way.

Bret: So if you are a fat burner and you are utilizing your fat stores, you're going to have more fat parking available, so a higher turnover of these VLDLs. So even though more being secreted you're still not going to measure more because you're getting rid of the triglycerides out of your system quickly. They're not sticking around in your system because you utilize it.

Dave: And the VLDLs are transforming rapidly to LDLs. So that's why... I can't emphasize this enough, once you get a better sense of the energy model, it's hard for me as an engineer to come to the conclusion that your LDL particle count or your LDL cholesterol count are truly deleterious to a high degree if in fact your triglycerides

are so low, it suggests that you probably needed that many of those LDL particles because if they were originating as VLDL particles you needed that much traffic to deliver that much triglyceride back to your adipose tissue and of course to fuel your muscle tissue and other non-adipose tissues.

Bret: That makes a lot of sense. Now another thing that was brought up that may have been a new topic for a lot of people was this concept of a ApoC-3. So all these lipoproteins have proteins on the outside of them that come with awful names like ApoB-100, ApoB-48, it's a little confusing, ApoC-3 being one of them, but this is thought to be sort of one of the worst ones you can have.

One of the most harmful proteins you can have, because it increases the residence time of the VLDLs. It makes them stick around for longer where they can then be potentially pro-atherogenic. But that only happens really in people who are insulin resistant, diabetic, have high triglycerides. So how does that even play in to this phenotype or does it at all?

Dave: Well, this is where I was a little surprised that early on in the podcast Peter had said ApoC-3 typically follows insulin resistance or maybe it was the other way around, that you tend to have less ApoC-3 if you have more insulin sensitivity. But the point being as that obviously if you can change your level of insulin resistance you're changing what is probably going to be the detected level of ApoC-3.

And also with that same subject matter I was saying, "Well, I'm actually very interested if an assay does get generated for which I can track ApoC-3, I believe it'll be dynamically determined." Because I believe again as I was sort of stating early in the podcast, I believe in something that has a composite response and that a lot of these things like the Apo's, these little snaky bumps you're talking about that are on the outside, they're kind of like metadata.

They are actually... for those people who... I'm going to speak to software people, for these people who are familiar with the emails they're kind of like headers. And so headers will tell an email about where it's going to go and it's used with packets and so forth because they're like address labels on a package. And in a way what ApoC-3s do is they allow for not only binding to some other things, but they help to kind of reduce the likelihood of clearance.

Now again if you already start with the lipid hypothesis being effectively fact, then of course you'll think ApoC-3 is just a terrible thing to have on there because anything that increases residence time is a bad thing. But we find lots of things particularly in the immunological response of LDL particles that suggest they actually are probably a

lot of good things that can come from having more exposure of LDL particles in the system.

So for example a lot of people don't realize that they carry antioxidants, alpha-tocopherol for example, a lot of people don't realize they can bind the pathogens to help clear it. So one of the things that-- it's an anecdote, one of the things that I can't help but notice, and I was just talking about this last night dinner, was that since I moved to Las Vegas 10 years ago I've gotten the flu three or four times, I've gotten a cold almost every year and I've gotten bronchitis three times in Las Vegas in the desert of all places.

After I'd gone keto I have not gotten any of those. I was excited at one point because I thought that I might be getting sick and immediately went and rushed to get blood work because I had not once gotten some sick blood work and I wanted to see the difference.

Bret: You are one of the few people actually excited to get sick. That says a lot about you Dave.

Dave: Absolutely but virtually anything that was infectious disease related, not even like a persistent cough... I just didn't seem to get anything. And I tend to find this is reported a lot by the Facebook group that we have for this phenotype, which is you know I typically refer to as lean mass hyperresponders.

They often report just getting sick less. Well this happens to match those people who have the genetic disease that can result in higher LDL particles known as familial hypercholesterolemia, which is you know is a genetic disease that can result in higher levels of LDL particle count, therefore higher LDL-C.

And they have of course seen many different studies and it's been suggested that this was an advantage before the 20th century when there was more risk of dying, mortally from infection. And so this was one of those things where if you had it, it was actually a little more than immunological benefit even if as it was assumed there would be a greater risk of cardiovascular death.

Dave: And in literature today at least what literature we have, which be honest is not great, suggest that if you're not one of those people who has premature cardiovascular disease that you actually do get some benefits possible for longevity which could be related to hypothesis, decrease risk of infectious disease down the road.

And it was always curious me how we can identify those people who are going to be a greater CVD risk with FH and those who don't, because it's not clear across the board.

And that brings up this concept of Mendelian randomization or the genetic studies that look at genetic reasons for higher LDL associated with increased cardiovascular death risk and genetic reasons for low LDL associated with decreased cardiovascular risk.

And people will like to point to that to say, therefore it proves high LDL bad, low LDL good. But again it doesn't necessarily address this specific circumstance. So why again with this circumstance be different and not necessarily correlate with those Mendelian studies?

Bret: Actually I am glad you brought this up because this is probably one of the most interesting subjects I think in that from a distance it seems like such an excellent piece of evidence for the lipid hypothesis. I mean how great would it be if we could just randomly pick a bunch of people in the population who would just magically have higher levels of LDL particles and therefore higher levels of LDL cholesterol and then just see with their risk of death is especially by cardiovascular disease.

And that's what the Mendelian randomization trials are attempting to do. Peter Attia actually had a great illustration of this as kind of a hypothetical in his series, The Straight Dope on Cholesterol. And he describes as a wand, like what would be cool is if we could get say 100,000 people and wave a wand and then those people would to have more LDL particles in them.

And then have another cohort and it's like less than that, and another cohort that's less than that and then just track them lifelong. And that's what Mendelian randomizations are attempting to do. But early on I realized that there were a number of issues that I was having with the SNP's, that's the single nucleotide polymorphisms that they were tracking and a lot of them had to do with... the kind of term is lipid malabsorption.

Effectively if a cell, any cell in the body, needs what it needs, it has something known as receptors, receptors that can extend that can effectively actively pick what it wants. In fact the way these receptors bind is almost like a key in a lock. So with that in mind it seemed pretty obvious to me that if you are depriving a cell of its capability to get what it wants... so if I were to say, you get the cells that don't have a receptor, that can either gather lipids or lipoproteins... You are inhibited from that.

Especially if they are endothelial cells, which endothelial cells line your vessel walls. Well, then my concern is that could cause a dysfunction. And again without question this is somewhat theoretical but even so, why not just go ahead and exclude those? Why not focus on those SNP's that result in high LDL particle or high LDL cholesterol

but don't actually impact the health of the cells specifically, particularly in regards to lipids or lipoproteins?

Now as it happens there are actually such diseases that result in this. In fact one that I'd like to talk about is glycogen storage disease. The reason I'd like to talk about this one is because glycogen storage disease is... there's many different versions of it, but particularly one version for which you have low levels of glycogen, there can be very high levels of lipids, in particular lipoproteins, and yet they're dumbfounded because these people don't have high levels of atherosclerosis.

In fact study after study they tend to find that they have they call it an athero-protective-- I forget exactly how they state it, but effectively they somehow have a protective measure and they've tried to isolate with special mineral or nutrient of some kind that they must be higher in levels of, in order to protect against these high levels of lipids that they have at the same time.

And naturally the first thing I gravitated towards was well maybe this time around these people don't likewise have these SNPs associated with lipid malabsorption. And therefore why not go ahead and find as many things as you can like glycogen storage disease, whether it was for or against the lipid hypothesis, as long as it doesn't impact the health of cells and their ability to uptake lipids or lipoproteins.

Bret: Interesting, but if they have some protective mechanism it wouldn't necessarily be the same one you're talking about, because it's not that their energy demands are higher or actually since they aren't burning that glucose as well, yes, their energy demands are higher, I take that back, right.

So they can't burn glucose, they can't use glucose as efficiently for fuel so maybe they are transitioning to using the fatty acids more so their energy demand is higher so they do sort of fit. Now I got to remember, I remember looking at this, but do they have low triglycerides and high HDL?

Dave: No, they tend to have higher levels of triglycerides. But this doesn't surprise me that they are still having lots of carbohydrates in spite of being effectively being pushed in the direction of having a high-fat metabolism.

Bret: Right, because the treatment generally is very frequent carbohydrate meals, so you're constantly replenishing your glucose supplies since you can't metabolize it as well, you need more in your system.

Dave: And that's why I theorize that actually-- I realize this may be a controversial position but I'm just following the logic as it follows, that those people that have

glycogen storage disease may benefit substantially from being on a low-carb high-fat diet.

Bret: Right, absolutely. So at this point I want to take a slight detour here to talk about the sort of the problem with all this though, because one of the points I think Peter made very well is I have a patient sitting in front of me and I need to know what to do with that patient and there's a lot of theory here, there's a lot of hypothesis and it makes a lot of good sense to me, but we don't have the proof.

And one of his big points was I need to go where the majority of the evidence is and where I think the highest probability is. So talking in terms of probability and address my patient that way. So did you see a fault in that type of logic in the way he approaches his patients?

Dave: You know, I want to answer with a little bit of an anecdote. While I was in college I had a friend, we were really close and he was very much a pro-science guy. Whenever we would be doing tests he would talk about much he was an atheist and how I can believe all this religious nonsense etc. but when midterms or finals came around he would bring his lucky rabbit's foot.

And I would get surprised by this and the first time I sort of let it pass. The second time I said, "Why are you bringing that? I thought that you didn't believe in anything superstition related?" And he said, "Well I could use all the help I can get." And I think that there are a lot of people understandably so, we've grown up with this, our whole lives, who would say, "Look I hear you, it's still theoretical.

All I know is I can't help but recognize..." and this is true, "...that the vast majority of doctors still very much believe in this." And so for me it's a little bit difficult to overcome, a lot of people will just say, "I'll feel better just having my LDL lower." And for what it's worth we could be right in our cautious optimism and it could still actually be better for people if they can bring their LDL down if it actually makes them less stressed.

Bret: That's a good point.

Dave: It's an important point because at the end of the day if you don't feel comfortable with where things are at metabolically, but you can still feel good at a different level by making some changes, a lot of times just your overall peace of mind can be just as valuable as anything else. And I think that that's something that even on the low-carb side of the fence we should take note of.

So I will have a little bit of an issue again being somebody who likes to look at just the hard numbers as they stand and somebody is saying, "You don't know for sure on this

phenotype "even though you have studies that you can show that show it's low risk "when I feel like so many of the doctors I know will insist that it's dangerous," it still makes me feel bad that that's going to do it enough for me personally, for Dave Feldman.

But I can totally understand if other people want to take a different route if they feel and judging the evidence for themselves they come to a different conclusion, and not only can I respect that, but at our blog, cholesterolcode.com and the Facebook groups I want everybody to respect their decision to do so.

Everybody's on their own health journey and that's super important to emphasize. So while this is very exciting, it's absolutely true. You can say the evidence isn't quite there, but by the same token I'm going to push back a little bit to say that the evidence is there on the other side.

Bret: Well, and you can look back even to the Framingham data and say that low HDL was more predictive than high LDL and certainly when LDL was elevated with an elevated HDL, there was a lower risk in that situation.

The pushback would be, well those were the smaller patient population in the group, but still they were not having the same degree of atherosclerosis and someone sad it was LDL-C and not ApoB, but we don't have evidence to say it's different. We don't have evidence to say with the high LDL and high HDL there is an increased risk. That doesn't exist either, does it?

Dave: No, and look, let's call a spade a spade here. It's not just about whether or not the evidence as it stands right now. The two studies I was pointing to substantiate the theory that I'm advancing that this can in fact be a healthy metabolism and that they are at low risk when they have high HDL-C and low triglycerides.

I'm surprised that there's not as much genuine interest in the field right now to test this immediately. I mean certainly it's one of the things I was hoping for going on the Attia podcast, it's certainly something in which I'm pinging lots of pro lipid-lowering experts. I'm saying, "Help me disprove my theory, help me do that." Help me get ahold of MESA data, help me get ahold of PURE data, help me get ahold of Women's Health Study.

I mean it would be great if I could get LDL particle count, but heck even LDL-C, that would be great. However as you well know there's a lot of firewalls you got to walk through to get to these larger data sets. But if the evidence has been there this whole time, shouldn't we take a look at it?

Bret: So it seems we should have some sort of study to look at this. And do you think a lot of the people who are ingrained in the lipid hypothesis feel this isn't even worthy of their attention and that giving it attention will only sort of fuel the fire even more?

Dave: You know, I kind of turn that around if you feel as a lipid-lowering expert, somebody who firmly believes in lipid hypothesis, that there are a number of people that are not acting on this advice because they hear this energy model and it feels somewhat compelling and that perhaps there is something to be said for having the higher HDL cholesterol, the lower triglycerides as being beneficial, then if I were one and I believed the lipid hypothesis, I would be all that much more of an advocate in trying to find and unearth this data to disprove it.

Because after all I'd rather disprove that it could be impossibly beneficial, that in fact having high LDL as bad in any context. Because that is in fact what the lipid hypothesis is.

Bret: Right, that's a very good point. I hope we'll have something soon because this question I think does need to be answered clinically. Because the discussions about the specifics, about the different theories back and forth can get very confusing and it doesn't address the fact that this is a different physiological set up, this is a different way of being where we are using a different fuel. So a lot of the arguments and part evidence doesn't apply and that's what can make this so confusing.

Dave: Absolutely and I mean at a minimum I don't know how many reasonable persons can say, "Let's find out."

Bret: Well, I'm sure we could talk on this for a few more hours, but let's not. Instead I want to ask you about one of your more recent experiments and you are no stranger to experiments, you and Siobhan are the king and queen of self-experimentation in lipid manipulation, so tell us about this latest bread experiment that you did.

Dave: Well to be fair we like to call the tandem drop experiments the first time that my colleague Siobhan Huggins and I-- she by the way helps to run the cholesterolcode website with me, we both did a different version of an experiment at the same time.

For her she had a keto shake generously provided by Ketochild by the way that had dropped her LDL cholesterol throughout the entire time she'd be drinking it, because she was invoking the inversion pattern by having a very large caloric amount of it. I think getting somewhere close to like 5000, 6000 cal a day. She is not very tall like I am so that's like a fairly large amount.

Bret: It's a lot of calories for her.

Dave: Yeah, definitely a lot of calories. And sure enough her LDL-C dropped like a rock and you can read more about that on the blog cholesterolcode. It's actually tomorrow, at the time that we're recording this I haven't revealed this yet, but tomorrow I'll be revealing that in fact I was on a different diet at the same time and I guess I'm revealing this to you for the first time.

I actually went the other direction. I dropped off of keto and went high carb low-fat. And I intentionally chose-- I wanted to demonstrate the energy model by choosing food that nobody would ever provide in any diets or recommend. So it was white bread and processed lean meat.

Bret: Wow!

Dave: That was the only two things that I ate over and over and over again.

Bret: For how long?

Dave: I want to say 10 to 11 days.

Bret: How did you feel?

Dave: Horrible.

Bret: I can't believe you do this to yourself. I'm glad you do, but I can't believe you do this to yourself.

Dave: Now it gets even more interesting, at some point I'll get a chance to post the graphs, but I have a continuous glucose monitor match this time around. So you can see the first continuous glucose monitor like almost a straight line while I was on keto. In fact you couldn't even tell when I ate meals because I had almost no response. And as I like to joke on this experiment it was the Alps.

You could actually just see these huge rises in my glucose and honestly the CGM I have to say that is a really powerful device continuous glucose monitor, because it can pick up your rises and falls in glucose especially postprandially. And it made me not want to fully engage the experiment as I had planned just because watching this moment after moment was so daunting.

Well sure enough I saw the fastest drop in my LDL cholesterol, but before I talk too much more about it, I have to insert a quick warning. I knew that this would be a drop because I knew I was switching from a fat-based metabolism over to a carb centric metabolism. And I knew that also I would be filling up my glycogen stores which is also a part of my theory as to why it is that the body would feel less need to mobilize as much fat for fuel, but on top of that I'm inducing a state of hyperinsulinemia.

Needless to say, Bret, as with the prior experiment I did with the weight gain, I want to tell any of your listeners who is listening right now, this is actually not something I'd recommend for that matter. It's something I discourage anybody from doing. As I say with many of my experiments, I do them so you don't have to. This is absolutely one of those.

Bret: Thank you.

Dave: I don't want anyone to go, "This would be a great way to lower cholesterol." This is not a great way to lower cholesterol in my opinion. But that said it was one that I felt confident would work, which is why I actually filmed a video that I posted to YouTube privately and I'll be actually making public by the time I do the public presentation of this, where this is exactly what I predicted.

That not only would it be the fastest drop that I'd ever had with my LDL cholesterol, but then I would actually break my own record. And sure enough I did, I brought it from around 300 mg/dL and in seven days I brought it down to 82.

Bret: Oh my goodness. 382!

Dave: That's right.

Bret: So if someone who is firmly rooted in the LDL hypothesis saw this, they would say, "Fantastic! You have improved your health dramatically." Yet you felt terrible, your blood sugar was spiking like crazy, your insulin was through the roof... Is that really improving your health?

Dave: Well, we're leaving out two other markers. What are those two other markers I like to look at in the lipid panel?

Bret: I don't know, I can think of a lot though... CRP is that one of them?

Dave: HDL cholesterol and triglycerides. My HDL dropped to around 48, I had to double check.

Bret: From?

Dave: From the 60s. But my triglycerides were a lot more interesting. They bounced up above 200.

Bret: Really?

Dave: Yes.

Bret: So from like the 60s up to 200! Fascinating.

Dave: It almost was a flip-flop, it's almost as if my LDL-C switched with my triglycerides. Because my triglycerides were nice and low when I started and my LDL cholesterol was very high. It then got all the way down to 82 and my triglycerides have gone much higher.

And I've seen many different YouTube videos and read many articles that say once your LDL-C is nice and low particularly if you can get down there around like 70s or below that you're basically bulletproof. That you don't have to worry about cardiovascular disease at all.

And that even if your triglycerides are high and your HDL is low, it doesn't matter. Again no oxygen for the fire.

Bret: Right.

Dave: But as I'm sure you and I both know Tim Russert had actually a very low level of LDL cholesterol unfortunately when he passed. He had very high levels of triglycerides and his HDL was not in a good shape either.

So for me again I want to look at the whole picture, I want to look at the whole lipid metabolism and I want to see in particular those people who have high LDL-C when matched with high HDL cholesterol and low triglycerides. Obviously I would rather not be on the profile that I was on at the end of that experiment.

Bret: Right. Just as a quick aside, did you measure LP(a) with this experiment?

Dave: One of the issues was because-- in order for me to be able to track this day after day I actually wasn't able to get a lot of blood test due to the traveling, because this was over the time in which I was in LA at the National Lipid Association Conference.

So it may have been that I got it in the two lab test that I got throughout, but actually most of these were tracked on a cardio check, which is a device from PTS Diagnostics. It's not as good as a lab draw, but I then did a further lab draw at the very end of the experiment as well. Now one of the more fascinating things is even though I brought it that low, it started to rebound toward the end.

My LDL-C actually started going up a little bit as my triglycerides started going down a little bit. And this actually makes somewhat sense because of course this will be impacted, LDL-C gets impacted by the Friedewald equation.

But the larger question is would I continue if I wanted to keep playing with it to see if I could get my LDL-C lower and lower? Probably could've, but I didn't want to. By that

time I was very unhappy with the experiment and very happy to be leaving it and getting back to my ketogenic diet.

Bret: You must have a very patient wife to deal with your mood swings as you go through all these dietary changes. This is a tough episode to wrap up because we've talked about a lot of different things but what you think the next step needs to be?

Dave: Well, obviously I'm a bit biased, but I do feel the discovery of this phenotype with lean mass hyperresponders may hold the key to really unlocking whether there really is a strong validity behind the lipid hypothesis. And I think it may actually be one of the most important things for the low-carb community to determine.

Again I'm biased but I feel pretty strongly about that. If there are a number of people who we see who get this phenotype and they feel just amazing-- I mean this Facebook group, I can't emphasize this enough, the most common statement we get incoming is people saying, "I don't know what to do because I feel so great. All my markers look fantastic but my doctor is freaking out. My LDL-C is so high... what I do about this?"

And we don't really have a short easy answer, but I can say anecdotally and with some reservation that a lot of these cardio metabolic markers coming back and looking good is part of what fuels my optimism. But what we really need is a study, a long-term follow-up study on those people who are lean mass hyperresponders to actually see whether or not this is a risk factor. And while I'm cautiously optimistic I've got to hold my strongest reservations out until I can get to that point.

Bret: And so I think, an important point to lead this with is we are not advocating, neither you nor myself are advocating to ignore LDL, we're not saying that this is proven to be safe. We're saying this is a fascinating topic worthy of a lot more exploration. And if you are in this phenotype you can learn a lot online, but the ultimate decision has to be made by you and your health care provider about what to do about this.

Because it still is very individualized, even if you are in this phenotype that we are talking about with a high HDL, low triglycerides, that still has to factor in your other risk factors, your family history, what the rest of your health is like and if you've had any other tests like calcium scores or carotid intima media thickness test.

So still very individualized so don't take this as any medical advice. This is just exploring a fascinating field which you have done a tremendous job in spearheading and bringing to the limelight and I'm very thankful for you doing that. So where can people learn more about you?

Dave: Obviously the blog cholesterolcode.com. We try to answer as many questions as we can for people who bring their labs there or have questions themselves. There is also a Facebook group for this phenotype lean mass hyperresponders. You can actually do a search for lean mass hyperresponders on Facebook.

And of course we're very active on Twitter. I'm @Daveketo. And you can find Siobhan Huggins also on Twitter as well. And overall we're just very happy with how many people have helped to carry us through this journey, as we also have patrons where people have been very helpful with the hard costs of our blood tests, so I got to give a shout out to them as well. It wouldn't be possible without our patrons being able to give us support, to each of our patrons.

Bret: Dave Feldman, it has been a pleasure and I look forward to hearing more about more experiments that you're doing and helping further this field so thank you so much for joining me.

Dave: Thank you.