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Ivor Cummins	00:00:23	Dr. Paul Mason, finally got to catch up with you - all the way from Australia.
Dr. Paul Mason	00:00:27	Pleasure's all mine.
Ivor	00:00:29	Excellent, yeah. I've been watching some of your videos and they're superb because you are going through all of the detail of the lipoproteins, but you've also got the clinical experience with patients many, many patients where you're getting to see this in real life play out. So maybe today we'll talk a little bit around these LDL-P and Lp(a) and some of these advanced lipoproteins and what they really mean.
Paul	00:00:51	One of my favorite topics!
Ivor	00:00:53	Right. So where do we start then? Well, I guess Lp(a) is one that's becoming very popular out there in the press and a few years ago you'd hardly hear about us. Now I've done quite a bit of research on Lp(a), but I think you've gone that step further. So maybe the context around Lp(a), when it's bad from the tie, when it may not be bad from the tie, kind of what it's all about for someone who gets a high Lp(a) reading.
Paul	00:01:18	Well, I guess my first thought on Lp(a) is that it's just a surrogate marker. And I guess what I mean by a surrogate marker is that it's there, but it's there by association, not by causation. So as you well know, when Lp(a) of the little molecule that Lp(a) uses to attach to the ApoB100 moiety. When that gets secreted, that gets secreted separate to the B100. And it only attaches to the Apolipoprotein B100 (ApoB100) when it's oxidized. So the existence of lipoprotein(a) by definition reflects the presence of oxidized LDL.
Ivor	00:02:10	So in other words oxidized ApoB100 particles, oxidized LDL particles.
Paul	00:02:16	Exactly! So, if you don't have oxidation on the ApoB100 moiety of the LDL particle, then the (a) will not attach.
Ivor	00:02:27	Right. So people with low Lp(a), it's obviously a good sign generally...
Paul	00:02:33	Yeah.

Ivor	00:02:33	People with higher Lp(a) indicates more oxidized lipoproteins, which is not a good thing. But interestingly too, for certain genetic peoples, like I think in Africa, Lp(a) does not associate with worse outcomes at all. And interestingly the Tsimane people with no heart disease really - their Lp(a) I noticed was higher than the Lp(a) in the heart attack men in the 4S Statin Trial. So there seems to be a lot of... it's still a very ambiguous measure, even though as you say it should indicate a problem.
Paul	00:03:11	Well, I think part of that just reflects that, I guess LDL and you know, “cholesterol full stop,” it doesn't give us a full risk profile. I mean, it's not the only factor that's going to be contributing to cardiovascular disease or stroke risk or something like that. So it's important that we don't all of a sudden start looking at cholesterol and LDL, oxidized or not in isolation. If you've got other risk factors going on, that's important too.
Ivor	00:03:39	Yeah. If you have many important risk factors in a good place, then having an isolated one may not really have any impact on the system, yeah?
Paul	00:03:50	Yeah. We're gonna look at the whole picture here, the whole package and I mean, that's what I guess mainstream medicine has tried to do with their risk calculators. You know, they say, “Well, how old are you?” “Are you male?” because that increases your risk. “Do you smoke?” And they pack all of these things into their calculator and they come back with a number. Now, unfortunately, a lot of what they put into their calculator is just erroneous. So I mean, they're looking at total levels of LDL and some of these other things sometimes, but the concept of a risk calculator is actually quite good. It understands that it's a multifactorial contribution to risk.
Ivor	00:04:27	Yeah. And in fairness, then you put together your factors of choice, and you get a much better risk projection than you would with any single risk factor for sure. Now, I guess, if you do a calcium scan, you're way better than the old risk factors and the risk calculator put together because it actually sees the disease.
Paul	00:04:44	Yeah.
Ivor	00:04:45	in the absence of getting a scan and actually finding out the disease level and the risk, the risk calculator can kind of fill a gap, yeah?
Paul	00:04:52	Yeah, all the present Lp(a), all oxidized LDL. But just understanding that, you shouldn’t take them in isolation.

Ivor	00:05:02	Absolutely. It's a multifactorial issue - and picking out a single factor is what a weak engineer might do!
	00:05:10	So Lp(a) then does reflect generally oxidized LDLs. I knew they were intimately connected to each other for some time. I also remember having a paper where most of the LDL involved in the plaque was actually of the Lp(a) type as opposed to classic LDL. So that would also tie in.
Paul	00:05:32	Yeah. I mean, I think this just reflects that oxidized LDL is the stuff that will penetrate through the endothelial lining. And that's the stuff that's going to form the plaque. If you have a healthy LDL particle that's not modified, and by modification, I mean either glycation where you have sugar attaching to the B100, or oxidation of the LDL particle, if you don't have either of those factors there, then it's just not going to end up in the atherosclerotic plaque. And the reason is because it travels there inside the macrophage. It resides there inside the macrophage, it doesn't actually travel there. And the only way it gets inside the macrophage is through a scavenger receptor on the macrophage, and those scavenger receptors have no affinity for a healthy LDL particle. It's not going to stay there.
Ivor	00:06:25	Right. And if you take it back a little further than, Paul in some of the work I've been doing recently, so if you take normal non oxidized, non glycated, non damaged LDL particles in your plasma there in your blood, and then you can of course have oxidized LDL's in your plasma in your blood. A million dollar question is, can ordinary LDL's go across the endothelium and become oxidized and become microphage-engulfed, contributing to the problem - or is it only oxidized LDL in the plasma, even mildly oxidized, that can really go across the endothelium and become part of the atherosclerosis process inside the wall?
Paul	00:07:06	So I think on the balance, I mean, it's almost always oxidized that would cross. But I mean, I would hesitate to say that, you know, non-oxidized could never cross. The point is if it could cross, it could come back again. And because it's not going to be bound up by macrophage.
Ivor	00:07:23	Yes, true. Though they do sometimes. Some lipidologists say, "Once they go in, they can come out - but they will get trapped on proteoglycans." Like the proteoglycans are trapping your healthy LDL to hold them and oxidize them. That's one viewpoint.
Paul	00:07:40	I'm not sure that's substantiated by empirical evidence.

Ivor	00:07:43	Yeah, I do agree. There's a paucity of evidence conclusively showing that. So oxidized LDL I think you can safely assume, and actually, Paul, I remember I had a few papers from Eastern European teams, not from American teams, where they took oxidized LDL (very mildly oxidized, not the hardcore macrophage level) - and they found that 40% of endothelial cells would die when exposed to these mildly oxidized LDL, but not when they use native LDL. And they also showed entrapment much higher for oxidized LDL, the native LDL. So I guess that would tie in with your belief that oxidized LDL is inherently a driver. A negative LDL is probably not so much something to…
Paul	00:08:32	Ah, for sure. And I think the we can take a step back, and it's glycation of the LDL which often precedes oxidation. So having high blood sugar levels, that means that you've got these LDL particles floating around in this soup and they're more likely to be exposed to the sugar molecules. And there's a process called non enzymatic glycation which basically means it's a concentration driven process. The sugar will attach. And that sugar attaching actually can generate reactive oxygen species. So the very process of glycation in some instances is enough to oxidize that LDL particle. But by being glycated, it also means it can't be taken out of circulation by the liver so the residency time in the circulation will be prolonged. And obviously, the longer it's sitting there, then that's also going to be more likely to be oxidized just on a time perspective. So it's the glycation and the sugar in the first place that does the damage.
Ivor	00:09:35	And that's certainly one agent of jack damage. And in the population nowadays, we know in America, around 70% of people are essentially diabetic. So that's going to be a huge driver of LDL damage in any case.
Paul	00:09:46	Yeah.
Ivor	00:09:48	There are other sources of LDL damage, I guess, but that would be the big one.
Paul	00:09:52	Yeah. Well, I mean, there's other risk factors that will increase the likelihood. So the omega-6 oils, polyunsaturated oils of the omega-6 variety, they're much more prone to oxidation. And we know that and there's some really nice studies out recently where they're actually looking at the structure of cell membranes, you know, comparing omega-3s and omega-6s, and it really does set it up. So, if you've got a longer residency time, and you've got these pro inflammatory omega-6s sitting in

		the membrane, or sitting within the particle (or even in the circulation) you're going to set yourself up for trouble.
Ivor	00:10:36	And that's pure synergy, yeah. So you've got a combination of vegetable oils excess, which ironically, the heart organizations push, combined, still, amazingly, if you're listening out there, but also then the excess of glycation from hypoglycemia and postprandial sugar spikes from the kind of sad diets our people are eating. So you've got this terrible synergy to damage LDL particles and have them be comparative…
Paul	00:11:04	And then as you said, then they can also damage the endothelial cells.
Ivor	00:11:08	In turn. So we've got this…
Paul	00:11:11	… cascade
Ivor	00:11:12	… cascade and self-reinforcing loop I think in some cases. It's shocking.
	00:11:17	So, the other thing is I remember a paper where the LOX-1 receptor in the endothelium, and it also takes part in many parts of the…
Paul	00:11:27	I'm sorry, is that the LOX-1 on the macrophage?
Ivor	00:11:29	Also - same thing. So, I have a paper which I was fascinated by and it basically says that oxidized LDL is the problem and not native LDL. A 2009 paper. But what they showed was the LOX-1 is on the macrophage, the LOX-1 is on the endothelium, taking oxidized LDL from the plasma into the wall - and it's also involved in around four other places including the macrophage. So LOX-1 is involved everywhere.
Paul	00:11:56	Well, not necessarily. I think there's actually six separate scavenger receptors on macrophages, LOX-1 being only one of them.
Ivor	00:12:03	Yes.
Paul	00:12:03	And I think there's another one or two that might actually be able to be involved in that process.
Ivor	00:12:07	Oh, true. There are many and it's very complex. But I think what this team was saying that even just looking at LOX-1, it comes up in so many parts of the atherosclerotic cascade. But our real point was that it illustrates that oxidized LDL even in the plasma,

not just trapped on the wall, is a fundamental part of atherosclerosis and native LDL, they basically pushed aside and said, not relevant.

Paul 00:12:33 Exactly. And it's probably also worth pointing out here that the reason oxidized LDL is so bad because it can generate something called reactive oxygen species, which are basically unbalanced valence shells electrons, that will then basically go and they'll do damage to what they come in contact with. And there's really neat evidence that antioxidants can actually reverse or prevent some of this damage. Not reverse at once you scrambled an egg, It's a bit hard to undo that.

00:13:06 One of my favorite examples is something called Gilbert Syndrome, which in medical school, that's an Australian pronunciation, Gilbert (zheel-BAYRS) Syndrome. It's French.

This is actually a condition where you have elevated levels of bilirubin in the circulation, which is a potent antioxidant. And we call this a syndrome, we say, "You've got Gilbert syndrome," but if there's any one syndrome which I could have, it would be this because it's actually associated with a significantly reduced risk of cardiovascular disease. Significantly reduced. I think it's in the order of 50% or something like that. Massive reduction. And purely because I'm surmising here is the antioxidant potential of the bile going around is probably undoing some of the damage of the oxidized LDL particles possibly before they damage other structures.

Ivor 00:14:03 Right. And Gilbert's is not particularly problematic in itself. I don't think there's a lot of morbidity.

Paul 00:14:09 No, it actually reduces mortality. That's the whole point. Your chance to having a heart attack if you have Gilbert Syndrome is a hell of a lot less than if you don't. As I said if there's a syndrome I could have, that would be it.

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Ivor 00:14:20 And you know, an irony, God, the irony is going to fly here. The irony is [name removed] went to a low carb diet because he was scanned to a fatty liver and his gamma glutamyl transferase was up over 100. And I told him, that's fatty liver, right, "That's diabetes." He went on a low carb diet for just four to six weeks, collapsed all of his bad markers, GGT and I think ferritin, and everything looked fantastic. The doctor got a shock, but it's bilirubin that've gone up significantly.

Paul 00:14:50 Yeah. If you're under less oxidant stress, then you might not be depleting it as much. Obviously, there's other pathways involved in bilirubin circulation.

Ivor 00:15:00 Yeah, but I guess it seemed to be when it goes up it's a bad thing.

Paul 00:15:03 It's a little bit like uric acid. I mean we always associate uric acid as being deleterious because it's associated with gout, etc. etc. But uric acid is also an antioxidant. I'll tell you some other ones is, melatonin is a powerful antioxidant and there's nice evidence there that actually can reduce damage.

Ivor 00:15:24 Now, absolutely, I've heard of that. Now, with good sleep cycles and all, you probably optimize your melatonin compared to shift working and all the other negative effects of bad sleep. But, all of the antioxidants you're talking about now they're endogenous, internal made by our body antioxidants which can be very powerful. I think though the external antioxidants, that industry portion, nutraceutical I think they have very limited effectiveness compared to endogenous. What do you think?

Paul 00:15:52 I think I have to agree. But I would probably extend something a little bit further. So rather than talking about antioxidant, we will talk about antiglycation. And there is a substance. I don't know if you have heard carnosine. Now, that's kind of sine with an "s" - not carnitine. Everybody confused it to. That's actually been shown to be a glycation inhibitor and it can actually reverse glycation as well. And it's been shown to lower HbA1c in type 1 diabetics, and it's also been shown to reduce kidney damage. It has all of these benefits, the downstream benefits is by interfering with the glycation on LDL particles, and it has been shown to interfere with glycation of LDL particles, then you prevent the downstream effects of the oxidation and the subsequent damage.

Ivor 00:16:39 Wow, the whole cascade, you caught it off at the knees so what?

Paul 00:16:42 And I guess that is an exogenous supplement, which I occasionally, if I've got a patient who I consider particularly high risk and I see a hell of a lot of glycation oxidation when I have a look at their lipid profile, then I often do recommend substances to inhibit glycation and to inhibit oxidation while they're in a high risk phase.

Ivor 00:17:04 Excellent. And you know what, it immediately rang a bell there because several months ago I met a couple from England who they're promoting an Eastern European developed scanner. I think it connects to your ankle and elsewhere. But they were saying that exactly that the carnosine in high doses, higher than the recommended doses has a dramatic antioxidant effect. And I was meeting with them quite briefly. And I thought afterwards, "Did they mean carnitine?" But I said, "No, they did say "carnosine" and I intended looking it up but I never got a chance.

Paul 00:17:38 Yeah. Well, it's two amino acids complex together. It's pretty simple substance.

Ivor 00:17:42 Oh, yeah. But carnitine is the one that always brings to mind than carnitine shuttle and all that stuff.

Paul 00:17:47 Well carnitine is actually... I mean, I'm a sports medicine physician, so what gets me out of bed in the morning is you know, training athletes and trying to optimize their performance. And we're actually mocking around a little bit at the moment seeing if we can just eat a little bit of extra fat metabolism out in some of our elite athletes by using carnitine.

Ivor 00:18:07 Oh, carnitine.

Paul 00:18:08 Carnitine, yeah. Because I mean, once you get up to about the two grams a minute, you basically top out of your fatty acid oxidation. So we're just trying to obviously, if we can enhance that, then you can run along at a higher VO2 for a little bit longer.

Ivor 00:18:23 Excellent. Well, that sounds like really interesting work.

Paul 00:18:25 That's a bit of a digression.

Ivor 00:18:27 Well, it's inherently safe as well. But carnitine, to something else but carnitine… oh, it escapes me now, it'll come back to me later. So carnosine is the supplement. Then there's glutathione, the body's primary antioxidant.

Paul 00:18:42 Yeah, yeah.

Ivor 00:18:43 That's pretty central, right? That's kind of the central processor of…

Paul 00:18:47 Yeah, well, this is an antioxidant. And I mean, this just leads to so much. It's involved. Vitamin C is involved in the production of glutathione fine as well. And funnily enough, there's a strong relationship between need for vitamin C and your oxidant state, possibly due to the need to generate more glutathione.

00:19:09 We could divert here and talk about a condition called favism, or intolerance of broad beans. It is a genetic condition where people have broad beans and they have so much oxidants stress, they deplete all the glutathione and essentially, they destroy their red blood cells.

Ivor 00:19:27 Wow…

Paul 00:19:27 so I mean you can see what happens if you don't have enough glutathione. And it's not that it's a deficient state of glutathione, it's just that it just ran out.

Ivor 00:19:36 It's essentially running out, and then all the reason I got into biochemical research and all this six years ago was I had a very elevated gamma glutamyl transferase. And that of course creates glutathione and it can also break down glutathione. So if you've a high GGT, it's a screaming indicator that you are depleting or overly needing like glutathione and deliver damage that often ties into many of these issues. So there are a lot of these measurements and things that people aren't really aware of because there's too much talk on cholesterol.

Paul 00:20:08 I mean, we could spend an hour just talking about the different liver enzymes. I mean, they all have different functions, they all mean different things.

Ivor 00:20:14 And they're all really important, but they're undervalued.

Paul 00:20:16 Yeah, well, if you understand what the different patents mean, I mean, it's really valuable information. And it depends on the patient too. So if somebody comes in and they like to have a bit of a tipple, that's significant because GGT is an enzyme. It's what we call inducible. That means that if you're having a lot of alcohol, the amount of GGT will actually increase as a part of the body's need to process that alcohol. Whereas at some of the other liver enzymes, if we have a look at AST and ALT, then they're actually contained within hepatocytes and they get released into the circulation when the

hepatocytes dies. Think of it bursting open and the chemicals released into the blood. So a lot of the enzymes, that we actually test for, we actually were looking for an increase and we infer that if they present in the circulation at a higher level than they ought be, then the cell that was originally containing that has died.

Ivor 00:21:13 So cellular damage increases in the liver and you get these elevated liver enzymes essentially.

Paul 00:21:18 Yeah, yeah.

Ivor 00:21:19 And it's very important. Yeah, GGT was classically used for a long time to find alcoholics or check whether they were back on the wagon.

Paul 00:21:27 I still use it as a flag.

Ivor 00:21:28 Yeah. The irony is though, even with no alcohol XXXXX for instance, practically doesn't drink. He was over 100 in his GGT, and it was his fatty liver so it's…

Paul 00:21:37 … oxidant stress though. And when he took away the oxidant stress, his bile went up. Funnily enough...!

Ivor 00:21:41 Absolutely!

Paul 00:21:42 Because less need to use the antioxidant capacity of the bile.

Ivor 00:21:47 Exactly. And he was eating a lot, and actually watching movies and television, he was eating a lot of ice creams and he was eating a lot of chocolate and he was a devil as we say, a devil for fruit juice. He drank a ton of fruit juice and he thought it was healthy. He thought it was five a day. This misinformation is out there on so many foods.

Paul 00:22:08 Ah, it’s amazing. The funny thing is, even doctors, just because we go to med school, it doesn't mean we not talk about any of this. We literally don’t. We have no training in us.

Ivor 00:22:26 No, but your personal research to the databases, the publications and your patients. you've generated an enormous amount of knowledge in fairness. But as you say, how much of that really came from medical school? It sounds like.

Paul 00:22:40 Well, I'm actually look, I've just finished the fellowship a year and a bit ago. That's a four-year specialization on top of when you finish your earlier training. And that's one of the only two specialties in Australia that has a formal nutrition component. And I can tell you without a shadow of doubt that what I learned was out of box. I'm currently in conversation with the seniority within the college to actually rewrite some of their curriculum, which was for a specialist medical college. To be honest, I'm not holding my breath, but if we could have a low carb friendly medical curriculum within a specialist medical college, I mean, that'll be a real feather in the cap.

Ivor 00:23:26 Wow, it would. Congratulations! That's a huge movement. But what you're saying is bollocks. I mean, they're essentially giving out the same old food pyramid style nutritional belief system, which is less than worthless.

Paul 00:23:40 Yeah. Look, there is some movement towards where the evidence is, but it's sort of like, you know, two steps forward one step back and being dragged along, kicking and screaming. There's certainly not a wholesale embrace of the literature. And I've been… it was just actually last week, I had a few more emails, it's inviting me to review the curriculum for them. And I guess I'm sort of testing the waters a little bit and saying, "Well, how keen are you to actually…" because you know what I'm going to say. Is there the political will there to actually change things if they do need to be changed? And that I'm not so sure about.

Ivor 00:24:23 We'll see what happens. Well, anyway, this is always going to be challenging, but it's great to see some movements within it. So why don't we jump to now, just to be a real jumper around it. LDL-P maybe, the particle. That's very topical.

Paul 00:24:35 Well, that's topical and I think it's as the conclusion you'll come to and we had a pre broadcast conversation, I think it's absolutely correct. All it is if you understand you have the LDL particles in circulation, and they're healthy, and when they've delivered all their cargo, dropped off their triglycerides where they need to be, then they go back to the liver. So you've got this receptor on the outside called ApoB100. And that binds to the LDL receptor in the liver. It's a doorway, it's like a security spot goes back into the liver, take it out of circulation.

00:25:10 Now the only thing that will stop it from leaving the circulation is if that ApoB100, that security SWAT card is damaged, and that can be damaged by glycation. And so essentially, if you damage it by glycation, your LDL particles will accumulate in the circulation. But they won't be the big ones. Because, as you know, when you glycate an LDL particle, it actually changes the size just fractionally to the point of where it's called small dense. So it's a very slight kind of reduction. And as well as that, it's the LDL that's already delivered its cargo. So it already started out as a smallest of physiological LDL particle would be and then you might have a little bit smaller with glycation.

00:25:57 So if you actually were to take all of these LDL particles that are accumulating and building up and put them in a glass jar, they wouldn't actually take up that much volume because they're all small. So that's why the LDL particle count is actually a better marker than total volume of LDL, of LDL cholesterol.

Ivor 00:26:18 Yeah, just for people watching, the classic LDL measure was LDL-C where you smashed up all the particles per unit blood volume and found out how much cholesterol molecules are inside them. But the LDL-P as you say is counting the particles…

Paul 00:26:31 The particle number, not… yeah, so if you just get them on and smoosh them in a jar and said it takes up this much room, that's the total volume of LDL. Nut that that's not useful because the LDL particles might be really big. They might be carrying a lot of cargo, and they might be undamaged.

Ivor 00:26:48 And most crucially as that latter point , they may be on damaged or they may be damaged LDL. So if you have a guy who's got a 2200 count, and another guy is a 2200 count, orthodox medicine I fear sometimes thinks, “Well, they're both high score, they both have a high risk.” One guy has no damaged LDLs, and his glycocalyx and endothelium is all in great shape, blah, blah, blah. And his HDL is working fantastic, the efflux, any that get into the wall, right? The other guy beside him, everything could be in a mess. One guy is really high risk, one guy is not high risk. But if you just look at the number, you don't know.

Paul 00:27:26 Yeah, that's true. That's true. I mean, I've really like… I do a couple of tests. I do a liquid subfraction, where we basically fractionate it. It's pretty simple. You put the

substance in a gel and use centrifuge it through and it will travel down through the gel based on its density basically. You can do electrolysis, where it separates up based on charge, but I just like the density when the particles get separated out by size. In addition to that, I can do a special test for oxidized LDL using monoclonal antibodies that will bind to the antigen or the epitopes on oxidized LDL. So I combine those two tests and I also, you know, I've got the benefit, I can do ApoA1 which is found on HDL, I can do B100. And I can do LP(a). So, I'm so lucky, as a medical doctor, I can actually have a patient come in, and I can do a complete analysis. And I'll be honest so, most of the time I have people seek me out. They know I'm relatively knowledgeable about cholesterol, and they say, “My GP wants to put me on a statin and I need you to reassure me. I need you to do all these testing on me.” Nine times out of 10 I say, “You can do the testing, it’ll cost you this much money, I don't recommend it.” And the reason is because we can usually infer enough. That people that seek me out are usually on a healthy diet, they usually ketogenic they usually got a triglyceride that's as low as you like, and a HDL that's outside the normal range being high. We can run the metrics there and we can just play probabilities and we can say, “Oh my, certainly your profile is going to be okay.” A lot of people come in, they just say, “Look, I understand the theory, but I just want the comfort that I get from seeing a pretty colored graph,” you know or what have you and will often do that. But usually, I actually recommend people not to do it simply because that'd be better off spending that money on a massage.

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Ivor 00:29:24 Indeed. Well, I mean, some people, they really want to see all the numbers, they’re enthusiasts, and they’re may be particularly paranoid about heart disease or might have something in the family so although near sure they're healthy, they're low-carbers, their trig:HDL ratios are gold, you can never say never so they like to dig deeper.

Paul 00:29:42 Yeah, and you're a metric kind of guy.

Ivor 00:29:45 To a point, but equally I think it can be overdone. In my personal thing and obviously I worked on behalf of Irish Heart Disease Awareness to promote calcifications gone from middle risk middle aged people, but again, that's not for people who are really low risk in the bloods. And it’s not for people who are really high risk in the bloods because to be honest those guys, you have to assume they have a problem coming. But for the big middle-risk group, where the

bloods are ambiguous and it's not certain, that group you'll find the huge disease people, or the zero-disease people.

Paul 00:30:16 Yeah.

Ivor 00:30:16 So that's what I would say is just get a scan. It's $100 and find everything…

Paul 00:30:21 Yeah, I actually do use the CAC, the coronary…

Ivor 00:30:24 Oh? In Australia it's not that common.

Paul 00:30:26 Oh, I use it a lot.

Ivor 00:31:04 Excellent!

Paul 00:31:05 But it's interesting because if you actually have a look at the way it's calculated there's a much more accurate way of getting a calcium score, but the algorithm has actually been patented. So it's actually if you have a look at the literature, if you've ever wondered why, if people have a scan, maybe in close sequence for whatever reason and the numbers jump around a little bit, there's a lot of random noise down the low levels of the coronary artery calcium score, and that's because it takes a pick at calcium and then it multiplies it by a certain area and that could be soft plaque or whatever. And it doesn't truly - at low levels I think, sensitively reflect calcium change. And I think in terms of risk prediction, I think it's worthwhile having a coronary artery calcium score because you want to know if you're super high or quite low. But if somebody is quite low, I will then monitor their progress with CIMT rather than with a coronary calcium score

Ivor 00:32:49 But your other point though at the calcification, true, it's really, "Are you a zero or very low." "Are you open to hundreds, depending on your age?" "Are you like substantial?" "Are you really high?" They are the guys who want to catch. So in fairness, the CIMT to monitor your month to month progress, calcium more every couple of years for a highly diseased person or every 6, 7, 8 years for someone who's low. So it's a much longer term.

Paul 00:33:19 Well the point is you don't have the noise in the CIMT that you do in the Coronary Artery Calcium score and that's just because of how it's calculated.

00:33:29 I'm a little bit disappointed that the better algorithms are actually patented. What can you say?

Ivor 00:33:36 I know, but this often occurs in medicine and you know, business - how to make its money I guess. People should be getting the volume and density as well from the calcium scan. Often they just get the Agatston, the rolled up score…

Paul 00:33:50 And that's the standard report that we have. We just get the Agatston score really and very rarely where we actually get a graphic.

Ivor 00:33:58 Yeah. I believe nearly any scenario, you can actually ask for the volume and density and generally get it. The CIMT, there are papers out there, very recent ones that the predictive power of CIMT for future events appears to be very weak. Generally.

Paul 00:34:20 Yeah, and that's why I do it to monitor progress and not…

Ivor: 00:34:24 Relative.

Paul 00:34:25 Yeah, so compared to where you were before, rather than as an initial risk predictor. I think the Coronary Artery Calcium is the best for risk prediction if you're looking at an investigation tool like that.

Ivor 00:34:37 Yeah. But the CIMT is a really dynamic kind of, "which way are you heading in a dynamic way?"

Paul 00:34:43 Well, that you should only use certain sonographers. Now it's actually quite easy. I've got an in-room ultrasound and that you can see how it's easy to make mistakes. So what you want to do, you want to find a landmark like the carotid artery bifurcation and then you go up say three centimeters, an absolute fixed point and you have to zoom, in you have to measure it, you have to be meticulous that you're in the exact same location and you come in on the same angle. And you have to use the calipers on the screen to market precisely. I mean, I actually… look, so I've got in-room ultrasound and I occasionally do it in rooms if I'm not running late. The sonographers I use for it, guys who I trust.

Ivor 00:35:26 Yeah. You have a very special scenario where you're taking your error and tightening it really tight. On average CIMT people wander into a hospital, get a CIMT, I

mean, the operator is clicking where he sees the borders, it's gone up…

Paul 00:35:40 If you have the same person do it every time, even if there is an error, it systematizes the error. So it makes it reproducible, if not entirely accurate.

Ivor 00:35:50 Yes, exactly. So you, to be quite honest, Paul, you're a very special advanced application of CIMT from what you described there compared to the generic. If someone walks in the door and gets a CIMT, you know, in "ACME CIMT Company" - God knows what you'll get....

00:36:08 So we were talking about… oh LDL-Ps. So the LDL-P then, you would have this massive range of markers you're measuring, the size, the density, the sub fractions, you're looking at the whole picture as we described earlier. So to our hypothetical person with a 2200 LDL-P who's healthy, versus the 2200 person who's seriously unhealthy, you're going to be able to tell one from the other with all the other measurements you're looking at.

Paul 00:36:37 Well theoretically, yeah. I mean, yeah, you just plug that in. So let's take HbA1c as an example measure where you really need to interpret it in context. So a HbA1c is where you have hemoglobin that has sugar attached to it. And we know that that's, you know compared to cholesterol, it's probably a better marker of cardiovascular disease because it reflects glycation. But every so often, you'll see one that will be really high or really low. And it'll be in congruent with the rest of the risk factors. And in that situation, what often happens is I go looking and I'll come up with a reason why the HbA1c will be wrong.

00:37:18 So for instance, if you have really rapid cell turnover, if you have a condition, a lot of oxidation in your body causing hemolysis, (destroying of the red blood cells) then you've got a fresh population of red blood cells that haven't had time for sugar to attach so your HbA1c will be lower. Or if you have iron deficiency, or what we call hematinic deficiency where the turnover of red blood cells is slower, well, this is something that we often see in thalassemia condition. So, people from Middle East or Mediterranean region ancestry. Their cells turnover is slower so the HbA1c will be artificially high. And you only know that by you have a look at these other markets in their blood, you say, "Oh ferritins, good. ILT is nice and low." You know, "Your uric acid is doing this" and you have to look at the whole profile of their biochemistry and then you

say, “No, I disagree with that HbA1c.” But I mean, because it is such a powerful marker, we sometimes have to resist the tendency or the urge to put all our balls in one basket.

Ivor 00:38:24 Yeah, I think A1c is great, but as Dr. Kraft said, it failed its component in the sense that it can be misleading in certain times compared to a postprandial insulin result.

Paul 00:38:35 And most people don't understand. And I mean, I try and control for it, I do a surrogate marker, it’s just fructosamine, which is looking for glycation of protein and the most dominant protein in the serum is album and obviously, that's got a half life. I think about 21 days. So you compare that to the red blood cells, so that will give you more immediate red glucose levels over the shorter period. But the trouble is the reference ranges. We use in Australia from my lab just absolutely horrible. So I've actually got to sit down, I've probably got 1000 of them now or something like that. And I really need to sit down and try and work out my own reference ranges because I can't trust what's in the literature.

Ivor 00:39:14 Right. You need to know what's good, bad and indifferent. But at least you're triangulating the A1c the fructose and getting to a better judgment. That's what it's all about, always using…

Paul 00:39:25 … multiple data points.

Ivor 00:39:26 … triangulate. Yeah, that’s the way to go. Of course, the continuous glucose monitors and postprandial measurements of your blood glucose is another good way to guess it whether you've got the highest spikes…

Paul 00:39:41 Game changer. That's been an absolute game changer. It's absolutely fascinating. I mean, we could talk for hours just about that. But for people understanding the personal effect on their metabolism, in terms of blood sugar levels of the food they're ingesting, I mean, a lot of people come in and say, “How many carbs? Can I have 20 grams or 30 grams?” But I tell you what will find out is the blood glucose monitor.

00:40:08 And it will also show us a couple of other interesting points. So I mentioned before that glycation leads to oxidative stress. It can lead to a generation of reactive oxygen species. So we know that fluctuations in your blood sugar level are far more deleterious than a stable blood sugar

level. And that's even true. If you have a flat blood sugar level that's higher, that's potentially less harmful than somebody who's got an average blood sugar of lower but it's spiking all over the place. And that's where a CGM will give you information that an HbA1c will not.

Ivor 00:40:46 Yes. Even though the two are loosely related by equations, that one is much more dynamic and showing you what's happening.

Paul 00:40:53 So I want stability and sometimes occasionally what we see, and I don't fully know the reason that I suspect it's in athletes because of their need for sugar for anaerobic exercise, especially the anaerobic athletes, when they go on a healthy diet, their sugars will flatline but it will just tend to kick up a notch. And I'm not concerned about that.

Ivor 00:41:19 Exactly. And there's many people are going keto and low carb. Their A1cs are okay but are often getting fasting blood sugars fairly high...

Paul 00:41:28 Well, fasting is the least useful I think in glucose measures.

Ivor 00:41:32 True, but there's a lot of excitement and force about running a blood sugar that's a little higher than the idea low one. But that phenomenon occurs a lot with people who are eating really healthy, low carb diets. They don't have the glucose spikes.

Paul 00:41:46 You want them to be flatlined. If they might start out at a five or something, sure, but if they don't go beyond 5.5, and I have a male, couldn't really care.
Ivor 00:41:57 That's it or even if they're averaging at 5.4, but It only goes up to 5.8 after a meal. It's the postprandial spikes that are the main problems.

Paul 00:42:05 Yeah.

Ivor 00:42:05 And also the beauty of the HOMA Index, if your blood glucose is a little higher but stable, as you say, you really got to look at your insulin. If your blood glucose is a little high but stable and you're running really high insulin, you've got a problem and the higher glucose maybe something to worry about. But if you're running a really low insulin and you're this type of person, a healthy person with a higher but flat blood w glucose, it's okay.

Paul 00:42:31 Well, I have to be honest, several years ago, I was using the HOMA, it was actually the HOMA2-IR.

Ivor 00:42:38 It's noisy.

Paul 00:42:39 But I've actually found it not that useful, I think. So I do a modified craft I'd say on on most of my patients. I've got about 500 of them now. It's relevant for us because craft was described using 100 gram bolus of glucose, and in Australia, we just do 75 grams, so it's actually being quite interesting to come up with our own normative data on our patient population.

Ivor 00:43:06 And is that working with Catherine Crofts or you're doing by yourself?

Paul 00:43:10 Well, I will liaise with Catherine. I mean, we've had conversation about sharing our data with her and letting her control the numbers. As far as I know, of, in as least in Australia, I don't know if anybody else has done more than more than we have.

Ivor 00:43:25 500, that's a lot and you're doing when you say modified, you're not doing the full five hour. It's let's say two hour?

Paul 00:43:31 Two hours is enough. Two hours is enough. I think you can distinguish between all the different profiles within two hours of data. But what we also do, and it's really important is you thrown a half an hour measure, because if you're healthier, your insulin peak will be closer to half an hour, even 20 minutes. And obviously, the insulin peak, the worst metabolic health you have then that gets pushed back.

Ivor 00:43:56 Yes. So that first phase sharp insulin response is actually quite meaningful.

Paul 00:44:01 Oh yeah! If they have a big spike at half an hour and it drops by one hour, hey, that's nice. You've got a good release, a bolus stools of insulin and good capacity and then you're back to normal. And you very rarely have overshoot.

Ivor 00:44:13 Yeah. And that's crafted and focus so much on that particular phenomenon. He focus more on the 1,2,3,4 or 5 hours. The way he put up was, if you're ambiguous at two hour, if you're between 30 and 40 micro units, then

maybe the third and fourth hour can help. But I don't think he focused so much on the first hour.

Paul 00:44:31 One thing that I really actually do like is I get patients to wear a continuous glucose monitor. I think after two hours, I don't really care about insulin so much but the glucose, because you will often see a delayed reactive hypoglycemia. And that's not uncommon at three hours. And we pick that up on the CGM trace.

Ivor 00:44:49 Yeah, that's nice. Now of course, if you do a full insulin, I'd say you're going to pick it up too because you're gonna do three four or five hours glucose and insulin assays. But who wants to do that?

Paul 00:44:56 Nobody wants to do that.

Ivor 00:44:57 Yeah, it's too much.

Paul 00:44:58 Yeah, when I say, "Ah, you got to take care two hours out of your day," most people look like I've just eaten their lunch or something.

Ivor 00:45:04 Exactly.

Paul 00:45:05 "You just what?"

Ivor: 00:45:07 Yeah. Meridian Valley Labs in the US, they have a blotter where you can do a full five-hour test, but you can just do it in the comfort of your own home with a blotter.

Paul 00:45:15 Okay.

Ivor 00:45:15 You get your insulin glucose on blood drops on a cardboard sheet. That is pretty sexy and I think it's pretty cheap. But you're right, no way you're going to hook up to a machine for a few hours.

Paul 00:45:26 You know, universal health care in Australia, I mean, this is all you know, if it's medically indicated, which most people come into me with metabolic arrangements it is, that's covered by Medicare. That's fantastic.

Ivor 00:45:36 Hey, hold on a minute. We're sitting in America as we talk. We're in Boulder, Colorado. You sound like socialist.

Paul 00:45:43 I'm not trying - I am actually.

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Ivor 00:45:58 So this Continuous Glucose Monitor, a massively powerful tool and the watches are coming out now and people are getting CGM and the hackers/bio hackers.

Paul 00:46:06 What you've got, you've got this little device where you actually get push measurements too from the CGM. So rather than having to swipe, that will actually push it to your phone every five minutes. So you don't even have to swipe.

Ivor 00:46:18 All right. So if you drop a filthy kebab, you know…

Paul 00:46:22 … there's no hiding. Well, I love the continuous glucose made up because there's no hiding from it. So I had a patient a little while ago, and... you know, I get my patients through food diaries and I can try and understand their patterns and also looking at their bloods. And I was looking at a food diary, and and my filter in my brain was working. It said, you know, "Just be careful what you say. Don't call her a liar." And I'm just sort of saying, "So, I'm just having trouble reconciling your results with your food diary." And I just had a puzzled look. And she looked at me like I was an idiot. And she said, "I've been doing a food diary for 10 years, and I'm the only person who ever sees it. And I still lie on that food diary. What makes you think I'm going to be honest on a food diary that you're going to see?" I thought, "You know what? That makes perfect sense.

Ivor 00:47:12 Human nature.

Paul 00:47:12 People can lie to themselves, but you can't lie to a CGM.

Ivor 00:47:16 No. And anyone who comes in with a high calcification score and in CAC scan, or has serious heart disease, become symptomatic, or any other reason, one of the first things they should do is get a CGM, because I know they're going to get certain meds and all and they're going to change their diet. And hopefully they understand low carb as needed or keto along with many other things. But a CGM is the first thing that a person with heart disease or a person who suddenly got a really high CAC score needs.

Paul 00:47:46 100%.

Ivor 00:47:47 Yeah, it's a no brainer.

Paul 00:47:49 It's a clinical utility. I mean, for me, it's absolutely been a game changer. And I've actually steered away from pushing ketone testing as much, because what happens? What happens? If you have somebody come in and they have a one hour insulin of say 200 or if it was 300, but you know, very, very insulin resistant, how likely are they going to be able to enter ketosis, even if they're on 20 grams a day? Not on God's green earth. They're not. But they can still lose weight by being lower carb. So it becomes more important. And if we have the goalpost that they're striving for being ketosis, they're going to become dissatisfied. If we set the goalpost to something they can achieve, and that's a flat blood sugar, then that's something that they're actually much more in control of.

00:48:36 Now there's some circumstances, some people have a horrible dawn phenomenon. And some people they have autoimmune diseases. I mean, you know, the difficulties in people on prednisone or other corticosteroid medications. It's absolutely amazing. I should show you some of the traces. I mean, in medicine we get taught, "Oh, they make it much more low, make it harder for you to get blood sugar control ra, ra, ra" that when you actually see it. So you might be on 10 ground milligrams of bread and it might be pushing your blood sugar up to 15 for five hours a day or something.

00:49:10 You know, the changes you see are just huge. And I think, I certainly as a doctor, I had no concept that it was so massive. And I mean, we blame you say, "Well, you're going to have to just try a little bit hard and a on steroids to control your sugar." "Maybe, you know, do a sliding scale a bit more often." Bollocks! It's never going to work.

Ivor 00:49:33 So you need to get them off these agents or ideally…

Paul 00:49:36 Well I've got a patient at the moment. She came to see me on 40. I had an email because I'm sharing her care, she's actually not from Sydney, and she's down to 15 so far without any flares. She's got a condition called polymyalgia rheumatica, which if you if you drop it down too quickly, you'll get a big player and not a pleasant state. But, you know, even the drop from 40 to 15, it's made a big difference, but the residual 15 is still causing her a hell of a lot of troubles.

Ivor 00:50:04 So ideally, by adopting the optimum diet and beginning to fix all of the dysfunction that's going on there, then you can go lower later on maybe in those meds?

Paul 00:50:16 Well what it is, so I'm actually, I'm a big fan now of I guess what's more commonly known as autoimmune protocol diets using restriction of lectins. So we see often, and do establishing that kind of diet and these people actually allows us to accelerate the dose reduction a little bit quicker than what would otherwise have expected.

Ivor 00:50:41 Now that's a fascinating topic in and of itself. Actually, I was just chatting, I did a podcast this morning with Mikhaila Peterson. We had a great chat, obviously an extreme case of autoimmune. But autoimmune is everywhere and cardiovascular disease now essentially can be looked at as an autoimmune disease. There's so many more disease, as you mentioned Alzheimer's. So maybe let's talk about autoimmunity catastrophe in the world today and the types of foods that can help trigger it.

Paul 00:51:10 But before we do, let's just talk about the craft test in lectins.

Ivor 00:51:15 Right.

Paul 00:51:17 Lectins, and a lot of people don't realize this, so say wheat germ agglutinin (WGA), can actually bind to the insulin receptor. And it binds to it in a way that it activates it for a lot longer, a prolonged duration compared to just straight insulin. So if you've had people who, I've got lots of patients who have been on a keto diet that's heavily plant based, you know, a few lectins in there, and when they've gone and cut out a lot of those lectin sources, they've lost a hell of a lot of weight upwards of 10 kilos, effortlessly.

Ivor 00:51:56 20 pounds, 25 pounds, yeah? American units.

Paul 00:51:59 Yeah. I think this impact of the lectins on the insulin receptor. Also the lectins have been shown to create leptin resistance.

Ivor 00:52:13 There's the big issue.

Paul 00:52:14 So if you combine activation of the insulin pathways and leptin resistance, then you can see how these lectins can be so problematic.

Ivor 00:52:23 Lectins. Now, they also directly attack the lining of the arteries, the glycocalyx and many other things. Maybe speak a little on that.

Paul 00:52:32 So the definition of a lectin is it's a carbohydrate binding protein. And on the surface of our cells, we actually have little what we call proteoglycans, so little proteins with sugar on the tip. And as you know, sugar is a carbohydrate. So if you're a carbohydrate binding protein and you see a sugar that's attached to the surface of the cell, what you're going to do? You're going to attach to it. And I mean that obviously requires the correct receptor binding affinity, so not every lectin will bind with a proteoglycan but a lot of them will. And this process of attaching to it damages it.

00:53:07 We can have a look at what it does if it attaches to the glycocalyx. We can have a look at what it does if it attaches a glycocalyx in the blood vessel. Either way, both steps of attachment will damage that lining.

Ivor 00:53:21 And they could be extremely deleterious, not just a mild impairment or problem but really severe damage to crucial membranes and component.

Paul 00:53:29 Well, let's take the gut. So leaky gut syndrome. So a lot of people don't realize that gluten, or wheat germ agglutinin (WGA) is actually a lectin. That will induce leaky gut that will allow the lining of the intestine to become more permeable towards content. So if eat these lectins and you have intestinal permeability, then they'll be able to cross into the circulation and meet the immune system. Bacteria in the gut that are normally, that are normally confined to the gut will be able to enter and meet the immune system.

00:54:03 And here's the problem, and this is where autoimmune disease gets triggered is that the immune system will identify a fragment of a bacterial capsule or a lectin and it will will amount an immune response against it because it's a foreign pathogen. That's fair enough. And then you have these what I called antibodies. They're sort of like little, think of it like a search like you know, in a bombing raid and you just want to lock onto it, and these lectins will identify something for destruction or these antibodies will identify something for destruction. Now, what happens if the antigen or the particular molecular pattern that the immune system is identifying on a lectin, what happens if that is replicated on the surface of a healthy tissue cell?

Ivor 00:54:54 Yeah, like in type 1 diabetes.

Paul 00:54:55 We then have something called molecular mimicry and you end up initiating tissue destruction of a healthy cell. And that's the basis of autoimmune diseases.

00:55:07 You basically need to have three things lineup. You have to pick the wrong parents. You have a genetic susceptibility. And that's a big one. That's quite important. You need to then have increased intestinal permeability. And then you also need to have passage of substances across the intestine like bacterial fragments or lectins that will induce this molecular mimicry type response. You have that, and then depending on what particular antigen you mounted a immune reaction to, your immune disease could target the bitter islet cells in the pancreas, it could target a nerve sheath cell, it could target a kidney cell. There's a manifestation which is absolutely "protean".

Ivor 00:55:55 Absolutely. And of course, although the genetic component is important, if you remove the environmental one and that never occurs, chances are you'll never develop the autoimmune condition.

Paul 00:56:07 Yeah.

Ivor 00:56:07 Do you think it's requisite to have the environmental insult that triggers the molecular mimicry? In other words, no one is genetically predetermined to get the autoimmune. Or at least very few.

Paul 00:56:21 I don't look, but you can get a damn big reduction. I'll pick a condition, Parkinson's disease. So this is a disease of the neurons in the brain that secrete a neurotransmitter called dopamine. So that is actually likely to be caused by lectins. This sounds like a crazy convoluted story. So what happens is you actually have these lectins say, pass through the intestine and they end up from the stomach. They can actually enter a nerve called the vagus nerve which travels all the way up to the brain and they can ascend up the nerve to the brain, to the brain cells that secrete the dopamine and essentially caused Parkinson's disease. And that sounds like such a ludicrous kind of explanation.

00:57:15 There would be an easy way to test it, right? So you'd cut the vagus nerve. That's the highway that these lectins are using to ascend to the brain. So if that were the case, you could just simply cut that and you shouldn't get

Parkinson disease anymore. So, the Danes did a study. It was between, I think it was 1972 and 1995. So everybody who had this operation called vagotomy where they cut the nerves, and they put them into a registry and they compare them to an equivalent control group for the rate of Parkinson's disease, and they followed them like over 20 years. And they found that the rate of Parkinson's disease was reduced by 47%. When they've actually done studies in animals, I think it might have been dogs. They actually gave them lectins and something else to increase their intestinal permeability. And they actually labeled these lectins so they made them traceable so you could actually see them, and then they euthanize them. And when they biopsied the brain, they could actually see this P lectin that had fed them was now sitting on the dopamine secreting neurons in the brain.

Ivor 00:58:23 Cross the blood brain barrier.

Paul 00:58:24 Yeah. Well, here's the thing. So very similar, the same pathway that intestinal permeability is caused by its up regulation of something called Zonulin which then releases tight junctions so the proteins that hold the cells together in the gap. You know Zonulin works in the brain as well? You know that can work on the blood brain barrier?

Ivor 00:58:47 Right. So even the BBB is subject Zonulin, loosening the junctions?

Paul 00:58:53 Yes.

Ivor 00:58:54 Wow! I wasn't actually sure of that at all. So lectins are a huge problem but in plant foods, there are many lectins spread throughout the whole plant world. So who knows which person is going to get an autoimmune problem relating to which plant world food.

Paul 00:59:08 Luckily, so there's over 119 plant sources of leptins described at last paper I read, there's probably more. But you know, that's still a lot. I mean, quite a bewildering variety. But we know where a lot of the harmful ones come from. So peanut agglutinin, and wheat germ agglutinin, soybean agglutinin, fat agglutinin, and that's a particularly good one, that's from red kidney beans. You know what, if you feed a rat 1% of raw kidney bean for two weeks, you'll kill it?

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Ivor 00:59:46 I did hear from what's his name, Dr. Gundry, his book, "The Plant Paradox." He came out very strongly and even study human, if you take a handful of these kidney beans, you don't cook them which kind of you know detoxifies them, you can die. And the threshold limit value, the 50, TLD 50…

Paul 01:00:05 I don't know if it's ever been described in humans, but what has been described is that consumption of four kidney beans could almost be enough to put you in hospital with serious gastrointestinal distress, vomiting, diarrhea, dehydration.

Ivor 01:00:18 Yeah. And I think he went further to talk around actual toxicity leading to death, only no one does it because they all boil them. But I always say to people, what do you think of the food that if you don't boil it, it can put you in hospital with only a few beans? Or even kill you. Does that sound like a good food?

Paul 01:00:37 Have you heard of ricin?

Ivor 01:00:39 Yeah, well, I know the subway poisoning incident in Japan - and it's extracted, ricin sen is extracted from?

Paul 01:00:44 From castor beans.

Ivor 01:00:46 Ahh, that's it! Yeah, yeah. I heard. Go ahead.

Paul 01:00:49 So this is, that's the most (toxic), I think that's the most toxic natural substance known to man. And it comes from a bean!

Ivor 01:00:56 Yeah, but…

Paul 01:00:57 They use it for nerve poison.

Ivor 01:00:59 True. Now, there are pretty exotic extractions to get the ricin purified…

Paul 01:01:03 Oh yeah. Nobody is going to be eating castor beans.

Ivor 01:01:06 No, no. True. But even the other one like the beans we just talked about, four or five of them uncooked could end you up in hospital.

Paul 01:01:14 Yeah.

Ivor 01:01:15 I mean meat, fish, eggs and all these things when you eat them, they're never going to put you in hospital.

Paul 01:01:20 No.

Ivor 01:01:20 So all of the challenging foods appear to be in the plant world. that's not to be "anti-plantfoods", there are a lot of good plant foods that caused no issue.

Paul 01:01:28 Well, there's a study I like to talk about, and they actually… so reflux is actually can be caused by lectins as well because the lectins can… there's a cell called a mast cell, and it's got these two little molecules. IgE molecules, lots of them. But if a lectin grabs the outside of these molecules which are attached to the mast cell, they do what's called cross linking and they lead to release of its contents which is histamine. And if you release histamine in the gut, you then subsequently get the release of acid.

01:02:01 And they've done studies where they've actually had people go on a low carb diet for six days and actually put a probe measuring the acidity down into their esophagu. And they found a significant reduction in acidity within six days. Basically, you know, reversing reflux. And this is lectins which will do that.

Ivor 01:02:25 Right. So a low carb diet particularly…

Paul 01:02:27 … because it cuts out the grains.

Ivor 01:02:29 Yeah.

Paul 01:02:29 … and it cuts out the lectin rich foods.

Ivor 01:02:33 So then if you, and we'll have to curve into closure now. I know we went expansive and now we go down to kind of conclusive. And, the lectins, you really should find out well, which of the vegetable world or plant world things I should eat that are truly safe?

Paul 01:02:50 Well, I say that, sorry, the point I was about to make is that this study they looked at 16 lectins for their ability to cause histamine release. And there was 4 that really stood out for having stonking great levels of histamine

release. And that were all plant based lectins. So I think that talks to your point that the plant based lectins, and it doesn't obviate animal source lectins from causing any harm at all. But the most deleterious ones, by far the most problematic ones are plant based.

Ivor 01:03:21 And it's understandable, the old cliche plants can't run away and we know they make lots of toxic compounds for antibacterial…

Paul 01:03:27 That's not a cliche. I mean, that's a fact.

Ivor 01:03:30 Well, I mean, it's almost so much a fact that it's almost cliched. It's almost becoming obvious.

Paul 01:03:34 So do you know what they do now? Genetically modified organisms - so wheat germ agglutinin is such a powerful pesticide that they're now creating crops, tomatoes and things like that, that have been genetically modified. They've had the sequence for wheat germ agglutinin put inside them into corn, for instance. So you might be saying, "Oh, I can't have wheat products. I know that does something bad. Look, give me a tomato instead." Good luck!

Ivor 01:04:03 Yeah. But the WGA from wheat, the wheat germ agglutinin, which is on the most problematic part that we eat, is finding its way…

Paul 01:04:09 Yeah, is now found in some GMO foods like tomatoes and corn.

Ivor 01:04:13 That makes things challenging indeed. So yeah, but let's glide in gluten, wheat germ agglutinin, and a couple more things in wheat. So wheats are no go. But from the plant world, what are the most…

Paul 01:04:26 … the bad ones?

Ivor 01:04:27 Well, I even thought "what are the safest, most generic ones?" I mean, for me, it's broccoli, cauliflower etc. which were bred in the 15th century. They're generally seem to not have much reaction in humans...

Paul 01:04:40 Yeah.

Ivor 01:04:40 ... for your classic veg. Maybe some of the root vegetables., above ground leafy green vegetables generally seem to be relatively benign. I mean, what were the

selection of vegetables for most people? Not for all, but for most people, a selection of vegetables that you can depend on to be on likely to cause a major issue?

Paul 01:04:58 Yeah. So…

Ivor 01:04:59 Tough.

Paul 01:05:00 That's really tough because I mean, you can look at anything. So you can look at FODMAP content which is fermentable, polysaccharide, disaccharide, monosaccharide, and polys. And certain vegetables, they're really high and if you're subject to irritable bowel syndrome, you can't have those fiber, excess fat. So there's a hell of a lot of fiber in cauliflower and that causes… so fiber causes constipation.

01:05:22 That's probably news to a lot of your listeners. But I'll just very briefly talk about the mechanism. So the problem in constipation is you're trying to pass something through a small hole. So how does making that something bigger solve the problem? This is analogous to adding extra cars to a traffic jam to try and clear the traffic. So fiber, and they've actually done some, the best study they've done on it has actually looked at varying levels of fiber, and they showed 100% resolution in all symptoms of constipation on a zero fiber diet.

Ivor 01:05:59 Yeah, I saw that one. That was based on a whole bunch of patients. 170 you had severe constipation?

Paul 01:06:04 No, I think in the 60s, they had 67 in the whole trial and I think the arm that went in ended up going on the no fiber was 41 patients.

Ivor 01:06:12 All right. It was even smaller than the recalled.

Paul 01:06:15 But the statistical significance was 0001 or something like that, because it was such a, it went from 100% symptomatic high to zero percent symptomatic low. The P value was just insane.

Ivor 01:06:31 I did get a shock. It was the first human trial I'd seen for anything (never mind nutrition) that had 100% response, massive response in the intervention group. 41 out of 41 went from three days between bowel movements to one. But then they gave them back half the fiber they were eating and they got half as bad as they were before. So they put a cherry on the top of that.

01:06:58 Now, those people had constipation. They had severe issues and I think the team did say, “Well look, this fiber, this generic fiber, not soluble fiber (I think it was more your classic brand wheat type fiber maybe.) But what they made the point was fiber attracts water and bulks in your body. And everything about fiber should make it make constipation worse. So they went ahead and did the experiment and they actually demonstrated, “Well, that's what happens.”

01:07:25 But then what about for healthy people? A little bit of vegetable and fiber? The “biome” etc.

Paul 01:07:29 Well, that's the thing is I mean, it depends on the individual. There's a threshold that people have. I guess I'm reluctant to answer your question, what vegetables and what plant foods I would recommend, because if you pick the wrong individual, you'll have a problem with most any plant food. Now some people will tolerate certain things. I mean, let's take blueberries. So first of all, they're loaded with sugar. They got 12% sugar, which a lot of people don't realize, but they've also got a lectin-like compound in them. And they're also very high, they’re a FODMAP-type food, very high in fiber.

Ivor 01:08:06 Yeah.

Paul 01:08:07 Let's look at nuts which is another staple on a low carb diet. They are loaded with fiber and they cause… they’re frequently responsible for constipation and gastrointestinal distress. So I mean I have a lot of difficulty and I guess my response is well if you really want to have a plant food, it's going to be a matter of trial and error.

Ivor 01:08:28 Yeah, I guess. If you if you eat meat, fish, eggs and healthy ancestral foods along with after you check herself for bad reactions, more benign types of plants and vegetables, bring in some nutrients, some nuts, I mean, Brazil nuts bringing a lot of magnesium, and you know there are…

Paul 01:08:47 Well they have promoted heavily for the selenium.

Ivor 01:08:50 And selenium as well, yes. And magnesium as well, I believe and selenium, actually Brazil nuts…

Paul 01:08:54 But they always have to wonder about the availability of nutrients within nuts.

Ivor 01:08:59 Well, if you've got firm nuts of course, I mean, I believe the magnesium was because the nut tree goes deep and it draws magnesium up and the modern, shallow planted, the modern mass-produced vegetables, the soil is depleted.

Paul 01:09:11 Yeah. No, they're not technically a nut, but cashew nuts.

Ivor 01:09:16 They are legume, are they?

Paul 01:09:17 Yeah. Like peanuts. You know how they say that you can buy raw cashew nuts. You know, sometimes you have raw cashew nuts or roasted nuts? That's a lie. You can't buy raw cashew nuts. And the reason is, because they're so incredibly toxic if they're not already cooked. Workers, when they're shelling them, they have to wear gloves because of the damage that the lectins will do to their skin.

01:09:43 Some of these things that people…

Ivor 01:09:45 I didn't know that one.

Paul 01:09:46 I'm very reluctant to make a recommendation which in my heart of hearts, I feel will be harmful to somebody somewhere around there. I mean, I just don't want to wear that.

Ivor 01:09:58 No, no, and and that's fair enough Paul. I think in the coming years, all of this will get understood more. People will have CGMs and will understand their own body more, what they can and can't do. I think people are going to get more awareness around the challenges with plant foods.

Paul 01:10:16 And I think GMO is an issue, is the conversation that hasn't been had properly. I think the trouble is that people oppose it almost instinctively but without an understanding of why it should, why it should often be opposed. And I think certainly, you know, crossbreeding a wheat germ agglutinin into a tomato. And if people understood the effects and the deleterious nature of wheat germ agglutinin, I think they would be a lot more opposition than there currently is.

Ivor 01:10:49 Yeah. You're talking about things that have a certain complexity that the average public will never… you're right, there's a luddite rebellion in some sense. A lot of

the people who are against GMOs don't really know why, they just know it's new, it's genetics.

Paul 01:11:02 If you can articulate an argument, it's hard to gain traction.

Ivor 01:11:06 Yeah. And to be honest, I stay out of a lot of stuff. Because I stick to my focus, which is cardiovascular disease and some of the major problems we've talked about with a cholesterol and insulin, all the rest. GMO was a bridge too far for me.

Paul 01:11:20 To be honest, me too. I mean, I look at it and it's something that I think is concerning from a public health perspective. Because it doesn't affect me personally.

Ivor 01:11:30 No, and I think you have enough fish to fry with the fundamentals you've talked about here actually, that if we can get a lot of those CGMs and understanding insulin, understanding the problematic nature of certain plant foods and many other things, and understanding cholesterol properly to put it in context. I think we get all locked on the next five or 10 years. You know, we can move on to the mad stuff later.

Paul 01:11:54 Yeah. I think we're still taking baby steps. We're dealing with the "low-lying fruit" at the moment. I mean, it still sounds crazy, but we're still trying to just remove excess sugar from the food supply. I mean, that's the lowest lying fruit of all.

Ivor 01:12:09 So the baby steps first for all of us, you may be massively advanced ahead of the average doctor but you're still going to be forced to take the baby steps to start fixing population health before we get on to the sexy stuff.

Paul 01:12:21 Yeah. I mean public health is public health. I mean, it's archaic.

Ivor 01:12:26 It is, but that's what we're all out to transform in the following 10 years. All of us, right?

Paul 01:12:31 Yeah. And I mean, people like yourself. I mean, I have to be honest, I'm a little bit of a stalker. I listened to a few of your podcasts and you're doing an incredible job. I mean, the advocacy that you're able to do. You're driving more change than a doctor and I can honestly say, with each single

podcast you're doing, you're probably helping more patients than most doctors will in their careers.

Ivor 01:12:55 Wow! Well, thanks a lot, Paul. I hope that's true. I noticed an element of true. We're certainly trying really hard and of course, we're promoting the calcium scans of those disease, people who are at massive risk. Maybe they're thin outside, fat inside. They don't know, they'll find out.

Paul 01:13:09 But important thing is you're promoting the solution.

Ivor 01:13:13 As well. It's a two hander, as we always say, identify the people at risk, not just the overweight smokers, but also the slim TOFI's - but then they need to know what to do. And it's not just a medication, they need everything we're talking about.

Paul 01:13:25 I thought you're gonna say knock them out, man.

Ivor 01:13:29 I'm Irish, but I'm not that bad! Thanks a lot, Paul.

Paul 01:13:33 Thank you. I had fun.

Ivor 01:13:34 We'll do another soon.