Dr. Gearoid O'Laoi Irish Pathologist - on strategies to achieve health - Podcast Ep14

Dr. O'Laoi:	00:00:00	He says this, that a biopsy here is he from the professor of pathology in New York, on a very well-to-do VIP - of his rectum and there's the letter. So it said, dear Basil, please look at this. It's very unusual, but I think this is carcinoma. So he showed it to me and he says, what do you think of it? And I said, it's not carcinoma – it's squamous Metaplasia, which is where the glandular tissue becomes squamous tissue and it looks very like cancer. He says, "Are you, he says, going to disagree with the professor of pathology and New York?" And I said "I sure am!" He says "he won't like it - but I like it. And I'm sure the patient will like it!" **Because I was right!**
Ivor:	00:00:47	Welcome to the fat emperor podcast. I am your host Ivor Cummins. We're supported by the Irish Heart Disease Awareness charity (www.IHDA.ie), which advocates a simple CT Scan to reveal your CAC score. So, Know Your Score and take action to prevent that premature heart attack. Everything you need to know, will be right here.
Ivor:	00:01:08	Okay. Today, we have the best of Irish, we have Dr. Gearoíd O'Laoí well known on Twitter and on other formats and he's a histopathologist, a consultant with massive expertise in autopsy and in histopathology. Delighted to meet you Gearoíd again
Dr. O'Laoi:	00:01:25	delighted to meet you over and we've met several times before.
Ivor:	00:01:29	Absolutely. I think in Iceland and in a few other far-flung places.
Dr. O'Laoi:	00:01:32	Yep - in Cork, even in Dublin!
Ivor:	00:01:34	Oh yeah. Crazy places like that. Well, you know what I thought I'd start off with, we usually start off talking about low-carb and weight loss and we're going to touch on that later. But one thing that occurred to me lately and has occurred to me many times, and it drives me crazy - is bias in science and in research, and the way that humans have this confirmation bias, and focus on what fulfills their beliefs rather than being excruciatingly honest and just looking at the data and accepting when it doesn't tell them what they want to see. And you had a few great stories from your pathology days...

Dr. O'Laoi:	00:02:09	We had an experience some years ago where a particular new marker was being assessed on a particular tumor to suggest the prognosis, etc etc And when we started doing it, we were getting a positive rate of 14% and other places rapidly began to report 25%. And all the literature said 25%. This is positive in about 25% of cases. So we discovered when getting our brains together with other Irish hospitals, that there was one other hospital who was getting 14%, and all of the others were reporting 25%. I went to meetings in England and 25% was what you did. And if you weren't getting 25%, you would go to special courses, which would raise your reporting rate to 25%. So we were left with this conundrum. Is it 14% or is it 25%? What we did first is we got one of our technicians to do 100 cases which had previously been reported as negative, to see if any of them were positive and they were to a complete extent all negative.
Dr. O'Laoi:	00:03:21	So then we discussed this myself, my two colleagues, what are we going to do? And we said, we've only one thing that we can do, we'll have to report what we find. We can't be making stuff up. So three years later I was at a meeting and an American who was an expert in this particular area said that in this particular case, the correct number of positives was 14%. So I stuck my hand up and I said, "come here a minute now mister" I said - well something to that extent: "how do you explain that the literature has said since the word go, that the correct numbers of positives was 25%, which everybody or most people are reporting as 25% - and it's now 14% which we were reporting [in our hospital] from the word go??" He says oh that's easy. He says "there was an initial misinterpretation of a seminal paper in this field, where it said that 25% of cases were positive, but these were all NOT general run of the mill cases. They were bad cases which had had recurrence, etc. And that's the explanation." So sometimes you have to go against the grain, you have to call the shot as you see it and not as everybody else thinks it should be. And this mentality is so essential in science
Ivor:	00:04:39	Absolutely Gearoid, and from my own career and my own experience, it's the same thing. A huge amount of engineers have this bias where they expect that factor x is causing the problem and they go and root out data to support the fact that it's x - and it gets reported and the bias is endemic ...many, many times. And I found myself that it is a temptation even for me, with my experience to actually...if I get data that conflicts with my belief and my belief is very strong, I have this instinctive desire to not dig too deep into that data.
Dr. O'Laoi:	00:05:15	It's a, it's an instinctive human thing. Now, of course, I have to overcome that and specifically go into that negative data that

conflicts with my belief even more than the data that supports. It's crucial, but it's not that common in research to see that behavior.

Dr. O'Laoi: 00:05:31 But you have to do that, because you may find that in a particular circumstance, this data is so, but in other circumstances it isn't. And that can explain how you get paradoxes. Like in particular peoples in the world, they can have a very high ApoB level in their blood, which would suggest a high risk of coronary artery disease. And yet they don't get it [Heart Disease]. So you have to explain why this is so on. What's overriding it. And this is the way we have to think.

Ivor: 00:06:04 Yeah, I think it was Karl Popper, the philosopher who spoke about the scientific method at length - and he was saying there's an "asymmetry of evidence" - that you can have 10 or 20 pieces of positive confirmatory evidence for your theory, but one piece of conflicting evidence carries complete power over all of the positive, and this, this is so important in engineering. But again, in research we don't see that - we see avoiding and creating paradoxes. Actually you have a few more paradoxes as we've talked about. So what one should do is when you have a paradox and as a piece of data that says your hypothesis is wrong - Instantaneously, if that data is credible and you're happy, it's real, obviously not of it's bullshit data, but if it's real, you at that moment have to destroy your hypothesis just briefly. And find out "how do I re rewrite my hypothesis to accommodate this data?" It doesn't mean the hypothesis is destroyed forever. You may have to say "this applies except when this factor is present", but you then have a new hypothesis. But that doesn't seem to happen often in the nutritional research world. The paradoxes are just used to keep your hypothesis and dismiss the conflicting data...

Dr. O'Laoi: 00:07:19 Exactly right. There's a phenomenon too, which you can, it's analogous to people having been to the moon and having samples, Moon Rock and having photographed the place and having all kinds of scientific measurements coming back to earth and uh, they become uncomfortable. Some of them become uncomfortable with these facts. So they start looking at the moon with a $20 pair of binoculars and see what they can find from that. And they draw scientific conclusions from that. This is equivalent to very weak observational associational, epidemiology - being allowed to supersede really rigorous, huge randomized control trials. Well, like for instance, the WHI initiative, which was a trial of 57,000 women, carried out for eight years at a cost of $700 million, which showed pretty conclusively that lowering the saturated fat in the Diet had no

benefit in health outcomes. And that eating extra whole grains and fiber and fruit, uh, likewise had no positive effect. But you go ahead and you do associations and say, "look, these five a day is showing up in this, they are good for health". But this is meaningless stuff. It's, it's just rubbish essentially.

Ivor: 00:08:37 And that that's actually a great way of putting it. You've got associations - you make a hypothesis, you then do the gold standard of an RCT, right? To really find out if the hypothesis is true. Then the gold standard experiment, which can prove cause says no - and then you actually slink back to your epidemiology weak data and say, "look, we want to believe this anyway."

Dr. O'Laoi: 00:08:59 Yeah, that's right. This is what's happening all the time with the "experts" at this, or Harvard, the Harvard something Chan School isn't it, or the Harvard School of Public Health. Chan is involved there somewhere.

Ivor: 00:09:13 Chan is the guy and I suppose Walter Willett. Yeah, they love epidemiology. What I hate about epidemiology is, well it's hypothesis forming. So when you see a correlation in engineering, we use Kepner Tregoe, which is a much more rigorous method for looking apparent correlations and distinctions and potential hypotheses. But it's always only "potential." So you use this epidemiology study, and you see a kind of a relationship. But for me with the human studies in epidemiology, it's the healthy user bias which really destroys them. So you have people who eat more saturated fat, let's say, and they tend to have some more heart disease. But when you look closer, the group that were eating more saturated fat also have more smokers. They have lower exercise level i...

Dr. O'Laoi: 00:10:05 They don't exercise at all I would say!

Ivor: 00:10:07 Probably - in general, probably not. But the killer is that you can never correct for the confounding that those people who ignore all of the official advice on health and go ahead and eat whatever they want, are hugely different people to others who heed the advice. And what they eat may have nothing to do with it. It's the fact that they have much less health focus. And then you get the results you want due to healthy user bias - and it's completely false science.

Dr. O'Laoi: 00:10:36 There's an example of where something was done properly, believe it or not, by Loma Linda in 1975. They had this hypothesis that a Vegan diet protected against bowel cancer, GI cancers in particular. So what they did, they did a proper

epidemiological study. They got Vegan doctors and I think they followed them up for seven years. Matched to non-Vegan doctors because they reckoned that doctors are pretty equal to doctors as regards social class and general behavior. And they discovered that they actually had slightly more GI cancers, all GI cancers than the doctors who ate a normal diet.

Ivor: 00:11:20 So, and that was, that was probably one of the better ways you can correct for healthy user bias. They did the right thing - and they're actually the Vegan or vegetarian organization?

Dr. O'Laoi: 00:11:30 Yeah, Loma Linda is the Vegan University.

Ivor: 00:11:33 Wow. And how do, I wonder how they, when we speak about bias, I wonder how they felt from the data began to come through?

Dr. O'Laoi: 00:11:39 Well they didn't like it, but they did publish it.

Ivor: 00:11:42 Well, big shout out there to Loma Linda for doing the right thing!

Dr. O'Laoi: 00:11:46 And another thing that's not widely known, but I've seen that a quotation of this, a professor in Loma Linda the years ago, a physician said that he had never seen a vegetarian reached the age of 100. Right. A vegetarian seventh day Adventist - but the chaps who ate fish etc. - did.

Ivor: 00:12:04 Yeah. And that's probably a nutrition thing, that you can make a healthy vegetarian diet, but the nutrient density is probably a challenge for the really long haul.

Dr. O'Laoi: 00:12:13 And also in Okinawa, the Japanese remarked that they hadn't seen any vegetarians in Okinawa reach a hundred

Ivor: 00:12:21 I think in that one if I occur recall correctly though. There were quite a few non-vegetarians who do go over a hundred...?

Dr. O'Laoi: 00:12:28 Oh yes many of them do. Yeah. Yeah.

Ivor: 00:12:31 So if you look at the entirety of the data and you're conscious of these biases and confounding, you could come to a reasonable conclusion on a lot of these questions. But I guess the conclusions you would come to are not popular - because we've had many decades of, of orthodox dogma - so reversing that now is catastrophically bad for reputations, and kind of...everything.

Dr. O'Laoi:	00:12:54	And for bank balances. Follow the money, honey! Well money is a big part of it of course. Yeah. And they, I guess there was so much collusion, well that's a strong word, collusion - but there's so much interaction between the food industry on the guidelines and you know it's, it's, it's a wicked web at this stage. There's no doubt about it. So a couple of other interesting ones - paradoxes we're just talking about - the Hong Kong one I think you particularly like...?
Dr. O'Laoi:	00:13:23	Yeah yeah - I kind of came across this, I think I was the first person to come across it. I came across the info that Hong Kong consumes more meat and more beef than anywhere in the world. Now people argue about that. But if it doesn't consume most, it's pretty well up there. And I've been in Hong Kong. I spent five days there about two years ago and I never saw so much meat in my life. If you ask for a plate of French beans in Hong Kong, there's beef mince mixed in with the French beans. There's meat everywhere. And these people are outliving the Japanese. And the Koreans. And they're living in a very polluted environment, um, and they are still managing to outlive the Koreans and the Japanese eating all this meat.
Ivor:	00:14:06	Yeah. And that is interesting that they do have the pollution and there's quite a lot of data has emerged around pollution being a driver of even atherosclerosis - not just, you know, breathing difficulties or asthma. So they have a lot of chips set against them, And yet they're, they're overcoming those chips living really long and yet eating a very high quantity of meat.
Dr. O'Laoi:	00:14:28	The French paradox is another one. This is my favorite because I've been there. I cycled once through the Dordogne area - the French call it a "Le Perigord". It's known as Gascony as well, but Gascony's a bigger area than Le Perigord. And I went cycling there for about 10 days with my wife once - exclusively in that area. And we got pure sick of eating Pate Magret de Canard (Duck Pate) that and Confit du Canard. That's what you could have. That's what they eat. They eat loads of cheese, loads of butter. Now statistically France together with Japan has the lowest incidence of heart disease in the world. But that area of Le Perigord has half the incidence of the rest of France, and they are the highest consumers of any size of an area in the world of saturated fat. Around 18% - same as the Kitavans do. And they're not getting heart disease from it. Their incidence of heart disease is a quarter of that, for instance, of Scotland.
Ivor:	00:15:35	Right. And I saw, I think it was Malcolm Kendrick's article about that - a quarter of the incidence with much higher saturated fat. And this is the fascinating thing. These things are called

paradoxes and then quietly pushed aside, I think the French, what's been used is the wine, and that's probably the main one...

Dr. O'Laoi: 00:15:56 Unproven. Unproven that it's the wine which is sparing them and the French have been cutting down their wine consumption quite considerably, and their heart disease rate isn't rising.

Ivor: 00:16:07 Exactly. Yeah. So the wine, I think we have enough studies on wine, that show tentative benefits, but nowhere near the four to six times difference that you're talking about. So the wine effect is an order of Magnitude off. Even if true is an order of magnitude smaller, then what could ever explain the paradox. But interestingly, the people who need that paradox - to allow them to continue their belief system - are happy to use it regardless of what I just said.

Dr. O'Laoi: 00:16:34 Yeah, I've, I've a theory about it. My theory is that saturated fat doesn't matter plus or minus, but that one of the reasons that the French have such a low incidence of heart disease is the very chilled out over eating and they'll spend two hours at our lunch so they get a good period of relaxation every day. And that has to be one of the drivers. If you watch Americans eat, it's actually a feeding frenzy. It's like, it's like the great white shark attacking seals off South Africa...! Whereas the French, the French man - he's like a gorilla picking up the odd grape while he's eating. And that's a difference.

Ivor: 00:17:15 Yeah, there are huge cultural differences for sure. Now on behalf of the Americans in fairness, not all are like that - but there's a general trend there towards that, and the modern life as well. It probably started earlier in America maybe than in Europe - of the fast life, you know - the busy job, multiple jobs, grabbing food, and the industrialized food supply in America started earlier than anywhere else. But now we're, we're well catching up. But yeah, these, these paradoxes. I don't know if there's any more before we move on to another topic. I think there was an Israeli one = was that around Omega six

Dr. O'Laoi: 00:17:47 Yeah, Israelis have a high, a high consumption of omega six and I think their heart disease rate is higher than they expect It should be. One of the best stories, which has been kind of lost to medical history - you seldom see a references to it now, but we were well schooled in that by our professor of social medicine who was professor John Corriden, who did not buy the lipid hypothesis at all. And he was an epidemiologist by training. Was the Yemeni Jews by Ahron Cohenn, uh, published I think 1967 around then in the Lancet - two or three papers. And the

upshot of it was that there was an early migration to Israel around the time of the foundation of the state by a population of Yemeni Jews. And these Yemeni Jews settled in Israel. And something like 20 years later, there was a second influx of the rest of them from Yemen and Aheron Cohen and his team examined the two populations and compared them.

Dr. O'Laoi: 00:18:48 And they discovered that the people who'd been 20 years in Israel had a 40 times the incidence of type two diabetes at the same age as the new influx from Yemen. This was a huge, huge factor. And when they looked into the diet, the only thing that they could come to was that sugar was very expensive in Yemen. So their consumption of sugar was very low, but they add a lot more fat in Yemen than in Israel. So he was one of the first people to really cement in his evidence - the case against sugar. And of course people conveniently forgot about it then. But it's very interesting to read the papers. I've read them.

Ivor: 00:19:34 Right - and that's epidemiology when you get, I think as per the standards of Bradford Hill - if you're two times or more the incidence, yeah, you can begin to think there may be causal relationship... so obviously this is a huge factor there. It reminds me actually of Reaven's study in 2002 not a sugar study, but it had one of the most impressive hazard ratios or risk multipliers I've ever seen. And he used steady state plasma glucose (SSPG), which is like an insulin clamp test. So it is really accurate. And the lowest third of insulin resistance people had zero disease or death seven years later, the middle third had 12 issues - 10 disease and 2 deaths - and the upper third of insulin resistance had 28 issues with 4 deaths. And the statistics were p zero zero out the Wazoo, right. Incredibly powerful...

Dr. O'Laoi: 00:20:23 I've read the paper - it was fantastic.

New Speaker: 00:20:26 Unbelievable. But the risk multiplier or hazard ratio for being high in the steady state plasma glucose was around 40 times. 40 times. And in the same study they happened to measure LDL and he had the decency to give the hazard ratio. So LDL for being high was a 1.001x multiplier. In other words, there was zero effect That said, I think the saturated fat thing, and it's interesting, there's a question mark around say ApoE4 people who are 17% of the population, you can get the genetic test for this, from www.23andme.com very cheaply - that ApoE4 people who have sustained damage from modern foods and are diabetic and have big heart disease, there's data out there that they may have some sensitivity to animal protein/fat combo in excess (particularly cheese). So that's probably, for me, it's kind of the exception that may prove the rule - that free living

humans who are not metabolically damaged, there's no problem. But there might be a subset of people that need to maybe just just keep an eye on their blood markers, and if they change their diet a lot and do something outlandish. Yeah.

Dr. O'Laoi: 00:21:40 Oh, I would agree with that. I mean, we're not all genetically the same. I mean, if you look at...in my park growing up I suppose there were 25 families. My father was the only fat man in the park. And he had been a great athlete and footballer when he was young, but all of his family were fat. Back when nobody was fat. When I was 23, I developed a fat stomach out of nowhere and I wasn't that much overweight. Maybe 7-10lbs But I had a stomach on me. So I had his genes. So we're different. We're insulin resistant to some extent. One of his brothers died of type two diabetes - died in about 1967 at the age of 67. And his mother died before World War II of type two diabetes. I don't know what age she was, but she wasn't that old. So,...

Ivor: 00:22:29 and you, you carried that weight through most of your adult life.

Dr. O'Laoi: 00:22:33 I did.

Ivor: 00:22:33 So maybe if we hit on your story in brief, all of these phenomena and your discovery four years ago...

Dr. O'Laoi: 00:22:40 Well there are two, two or three things that are worked out. I believe you can do a lot of experimentation on yourself if you can reproduce it. And I got very keen on cycling when I was about 30 and I'd cycled all my life, but I got very keen on it as a form of exercise. And I began to cycle about 7,000 miles a year or more, which is quite a lot. I discovered that I was inclined to settle out at a weight of 15 stone 12, which is for Americans a hundred kilograms. Exactly. I'm 6 feet 2 inches in height. So my BMI was about 28.5. At that weight, I discovered that cycling a hundred miles a week had no effect whatsoever on my weight, eating the diet that I was eating at the time. I also discovered that if I cycled 200 miles a week, which is about 12 hours cycling or more, that I would lose two pounds that week.

Dr. O'Laoi: 00:23:36 So if I wanted to go on a bike tour, I would maybe spend two months doing 200 miles a week or more, and I would be quite light going to the mountains in the Alps. But when I came home and reduced the cycling rate it would all go back on, this happened time without number - always. I once went on a diet at about the age of 28 and I lost 42 pounds just by cutting down the number of calories - every, every waking minute was I was consumed with thoughts of food. And you can't beat that. The brain will just, what the brain does is it blanks out the fact that

you were ever on a diet and you just go back to eating the way you were. And I, had it all back on within one year. So I tried all kinds of things. I tried a high fiber diet. Believe me, it doesn't work. I ate all whole grains. I had nothing that wasn't whole grain, whole grain bread, whole grain rice, um, everything was whole grain, no effect on my weight whatsoever. And at one stage I was involved in an accident where I was hit off my bike and I couldn't drive because I had to have an operation in my hand. I couldn't cycle. So I was walking a big, big amount. I was walking 50 to 60 miles a week, including walking up to the Orthopedic Hospital in Cork, which is a very severe hill - that's about a 20% hill, two or three days a week. And I was walking this distance and I lost exactly zero grams in this 14 weeks. So exercise will knock weight off you, but just in super-normal amounts of exercise - and it's not practical. I established that beyond doubt. Then I came across something on the Internet where you sent this chap $50 and he gives you the secrets of losing weight.

Dr. O'Laoi: 00:25:28 So I did, and he's secret of losing weight was giving up sugar and doing some weightlifting. Now I hate weightlifting. So I decided that I would give up sugar. Right? Spent the $50, I gave up sugar, I lost 20 pounds in 20 weeks, but I was hungry. And 18 months later I started to slowly gain. So I said, this isn't working. Because I was, I was really hungry. And I'd come across, I had read John Yudkin's book, "Pure White and Deadly" about the dangers of sugar. I thought was a fantastic book, it was one of the best books I've read, scientifically. And I'd come across Tim Noakes' lectures on the web. And I said, "I'll give this a go." But I didn't give it a go for about two weeks. I kind of read everything I could about it. I realized that if you went on that, it's not going to work long term unless you stay on it.

Dr. O'Laoi: 00:26:22 So January the first 2014, I went on it and at the time I was about 12 pounds down on my original weight, which was mid 2012. So I lost 28 pounds in about five months. And I've kept it off for four and a half years. And, I've kept it off. No trouble. And there was a particular chap on the web, one of these gurus and knows everything - but actually doesn't really know anything. And he was poo-pooing the fact that I said that this is a very satisfying diet - and that's how it works. And I told him, "look, I eat as much as I want and all I do is I watch the the amount of carb I eat - and my weight is off for four and a half years." And he told me I was hilarious. This was his...response. But it's the truth.

Dr. O'Laoi: 00:27:13 All the people who would put the weight back on, I reckon are fooling themselves. They're eating more carbs than they think

they are. And I've been very rigid in approach to my diet. The approach is there is nothing as powerful as habit. So I don't break the habit. I will very occasionally have something sweet or tasty, but at this stage it's no temptation to me. It's not like having a Pringle.

Ivor: 00:27:39 Yeah. Now I would broadly agree with all of that Gearoid. You must continue deploying the diet in the first weeks and months. You're an enthusiast because the weight falls off on low carb. For me essentially in eight to nine weeks, I lost around 35 pounds. Yeah. And people were just shocked who hadn't seen me in weeks. So you're full of enthusiasm, you're very adherent to the diet. And, and it's fantastic, but exactly as you say, over time you can slip on unconsciously. And even shall we say, we talked about bias earlier, you can kind of fool yourself. You're still mostly doing it, but you've gotta be really careful that you really are.

Dr. O'Laoi: 00:28:24 The emotion I had when I reached the, it was disappointment. I said, this has been terribly easy. It has been terribly easy. I didn't have to fight hunger and I have learnt to eat as much as my body says to have, some days I eat a colossal amount of food and I find inevitably in the next couple of days, I'm just not hungry. And, I might've put on two or three pounds and a lot of it's probably fluid. It just falls off me. So I listen to the body. I don't consciously make myself hungry at all. I don't fast and there're some people who need to fast. My son fasts. He doesn't have any breakfast, but I don't fast. But here I am - it works. But you are remaining fully adherent essentially. I am. There was a big side effect that I had. I was very prone to depression for years. I'm very prone to depression, like I'd be semi-depressed most of the time and I'd get badly depressed periodically and I never went on any treatment for it - I learned how to cope with it with exercise and blah, blah blah. But I haven't been depressed since I went low carb. Now I didn't have that effect when I quit sugar because I was eating, eating starch. So I don't know whether it's weight loss, which is supposed to reduce chronic inflammation of the brain or - is it a more even blood sugar? My blood sugars are very, very, stable - my blood sugar would seldom go to 120mg/dL.

Dr. O'Laoi: 00:29:55 And it is mostly, it's pretty, pretty good. Or, is it a change in my microbiome? Because your microbiome is going to change depending on what you eat. Now what do I eat? I eat everything except what's bad. So I eat various veg, I even eat peas, carrots. I eat all kinds of meat. I eat yogurt, cheese, all that stuff that I actually really like. For breakfast this morning I had my usual three-egg omelet with about 40 grams of cheddar cheese in it

		and some white pudding (blood sausage) and it's grand and it's very cheap. People think low-carb is expensive, but if you know what you're doing, it's very cheap.
Ivor:	00:30:40	That's a great point. And I have repeatedly had to get in this argument or discussion, shall we say, but exactly. Because eggs were perceived as unhealthy, which by the way was one of the biggest disgraces in human history - that you could vilify an egg, which is almost the perfect, perfect food.
Dr. O'Laoi:	00:30:57	Yeah. Yeah. Perfect food.
Ivor:	00:30:58	But let's put that aside for the moment. The eggs because they were perceived as not so healthy - maybe "one a day" or less. The result is this is that the cost is actually very reasonable for the amount of protein and nutrients and choline and everything else is incredibly low for the cost...
Dr. O'Laoi:	00:31:16	And the dietary satisfaction is fantastic...
Ivor:	00:31:18	Superb - and appetite satisfaction following a few eggs, you know, you're good for the day. It's incredible. The other thing is the, the beef in Ireland, it's all pretty much grass fed, but I noticed that it's say $12 for a kilogram (two pounds) of the premium ground beef. The good stuff, but look at the label - the good stuff is only called "good" because it's very low fat - very lean. And the cheap stuff is approx. $5 for two pounds, and it is around 20% fat rather than 6 or 7%. It's high fat and it's called the "bad" stuff, but it's the best stuff...
Dr. O'Laoi:	00:31:57	It's also the the tastiest and you don't have to use any eggs or anything. And your hamburgers if you use the 18% high-fat is great because the fat sticks together. We use that. Another thing that's very cheap are things like chicken thighs or chicken, chicken wings, chicken thighs. You can get this thing in called Muslos, that's what they are called in Spain. My wife makes this dish in Spain where you get chicken thighs, you open them out, complete with skin - fry them and you make a casserole. It's completely divine
Ivor:	00:32:30	And skin included of course
Dr. O'Laoi:	00:32:33	And skin included and for nothing - dirt cheap. Like you'd have a meal for two, for $5.
Ivor:	00:32:37	Yes. And, and equally, if you go into the major stores in Ireland and I presume, it's not too much different than America, you

know, chicken cuts, they're really inexpensive. Now there might be some question I suppose - we have to acknowledge that in America, particularly with, you know, corn fed, maybe you know, these antibiotics and there is some question mark around the mass factory produced animals. The point usually made though, I think Dr. Eric Westman makes this point that, that if people can switch to a healthy low-carb regime - even if they're eating not the best quality of meats - they've still come a long way from how bad they were. Still a move forward.

Dr. O'Laoi: 00:33:19 Yeah - and a funny thing about carbs, I can honestly say I think people may be different in this regard. I could never get dietary satisfaction from carbs. I was never satisfied from eating carbs. I had a low fat diet for years. I had a low fat diet such that, although I did eat some chocolate or stuff like that and desserts, but I had no fat on my meat, I didn't eat a lot of meat. I had no eggs. I had no cheese for 30 years. And cheese actually, if you think that cholesterol is important, which it probably is in some people in certain circumstances, cheese usually will lower your cholesterol. And this is something that was published maybe 30 years ago by Moorefield, dairy research institute, which is near Fermoy in county Cork. And nobody believed it. And recently people in Dublin have repeated the same kind of experiment and cheese improves your lipids such as they'd be,

Ivor: 00:34:23 Yeah, I saw that came out in the web and a week ago and it seems like a pretty solid study and they got an actual lowering. To be honest for me, I think for some people it might go up a bit and for some people it might go down a bit and whether any of it means much is the big question. But still it's nice to see another misconception...

Dr. O'Laoi: 00:34:40 And the chaps in Gascony eat tons of cheese. In fact, I was cycling in France or last year, I've done a lot of cycling in France, but I was cycling in France last year and I noticed that there's a great treat available and most of their supermarkets, you can buy slices of all kinds of Terrine. You can buy Deer Terrine, Rabbit Terrine, uh, completely divine, fantastically tasty - great for cycle touring,

Ivor: 00:35:07 Yeah. Terrine. And for people who are not aware of what it is, it's very a very coarse paté really. And I love Terrines. When I'm in France or Spain, I go for it crazy. Because the smooth paté I, I eat them because it gives me liverr and nutrient density and it's great. I don't enjoy the smooth Patés massively, but Terrines are gorgeous. I love Terrines. Fantastic. So go get them guys. And we might circle now around to some familiar territory for you. You've been fixated, somewhat fixated about the process of

		Atherosclerosis and as a consultant pathologist for a whole lifetime career, you've been very close to the rock face.
Dr. O'Laoi:	00:35:49	I've seen a lot of it. And the thing that interested me about atherosclerosis is I did not believe the explanations for it. And because the evidence was very, very poor - there were kind of presumptions. Now you can't doubt the importance, uh, ecologically of hypertension in atherosclerosis. That's a given, right? If you have very high blood pressure, you're going to get a degree of Atheroma from it. There are people who think that there are two - a lot of doctors think that they're two sets people in the population: people who have no arterial disease, and people who have arterial disease. Believe me, most people have some arterial disease, even though it might be trivial. And some people are very unlucky. I saw a man die once because he had one plaque of Atheroma at the origin of his superior mesenteric artery - and nothing anywhere else. So you can be unlucky where you have it or you could have tons of it and not die of it. And you quite commonly do a post mortem on very old man and find that his coronary arteries are like bones - they are so calcified. And yet he has died of something else. I must tell you just a funny story. A term that was used for Broncopneumonia, which is a common kind of terminal event in old people. It used to be called the "old man's friend." And I remember a colleague of mine was teaching on the post mortem and the patient had died of bronchial pneumonia. And he had this student who was very Zany, very different - shall we say, slightly mad. And my colleague said, this man died of what's called the "old man's friend." You see what's there in his lung, what can you see? No nothing. I can't see anything. He says, well look, it's kind of a bit solid and so on. He says@ "the old man's friend, what do you think it might be?" "is it his dog?" said the student? You can't write these things when they happen.
Ivor:	00:37:56	Ha - and well, I'm sure that student grew up and went on to some good things....
Dr. O'Laoi:	00:38:03	No, he left medicine! They realized that he wasn't quite right.
Ivor:	00:38:06	Ah I see - maybe he did something more artistic?
Dr. O'Laoi:	00:38:10	Yes, that's right!
Ivor:	00:38:11	Yes. Well, and we were on the topic, oh, of course. Of atherosclerosis. So we've got this massive heterogeneity, if you will, where, ... I love that example of the guy with the one big Atheroma - and actually Dr. Scott Murray has some amazing

cases similarly in the UK. And one he had was, he had a twin, a homozygous true twin, who had an angiogram. And there was one specific area at a branch point in an artery where there was a very significant narrowing and an issue. And they went ahead and they may have stented it or whatever, but they were lucky in that six months later, his twin brother (who I think he lived in Germany), was over in England. They communicated and this twin brother brother agreed to go and have an angiogram in the name of science and perhaps in the name of checking himself, I think at the same time. And he had exactly the same Atheroma, in the exact same place. Now I chatted to Scott about this and asked about their bio-metrics. And of course they were both hypertriglyceridemia etc. So it wasn't that it was just a defect, but it was the same weak area in both these identical twins.

Dr. O'Laoi: 00:39:28 It was a physical abnormality that became atheromatous. If you have an abnormal angle or something like that, you can get Atheroma. And so you can be born with a physical defect that predisposes you to Atheroma in a particular place and you've got say turbulence there. Turbulence will be behind it.

Ivor: 00:39:45 Yeah, because when you've gotten a nice shear effect in straight sections of the artery, then very few atheroma. But in the junctions the endothelial cells are all arranged differently and also the nitric oxide release I think can be impaired - and all these other factors come together both. Even if you have all these weak points and most people do, many of them have - still some people may get really bad atherosclerosis, whereas some people have almost none - and that's environment mostly. One example might be, I mean I'm just guessing here, but you got a zero calcification score at the age of 65 - now that's, that's pretty ...it is interesting because you had genetics disposing towards at putting on weight and you would have had, you know, excessive insulin and other things during those decades where you are carrying the belly. You did offset though probably quite a bit of the damaging effect, with your are massive cycling.

Dr. O'Laoi: 00:40:46 Yeah. That's one thing. Another thing that I think is that, eh, until relatively recently, my blood pressure's always very low. Like my standard blood pressure would be 105 over 60. When I went on the low carb diet, I found that my blood pressure was more variable and I identified eventually by experimentation that if I overdid salt it tended to rise. So I'm salt-sensitive, but I'm not really hypertensive. So my blood pressure this morning, which I took just for your information, it's 109 over 60. So that's fine. But if I switch back in salt, which might not affect other people, it affects me. My blood pressure would rise.

Ivor:	00:41:27	But the key question is if it goes up to say 126 over 82, it doesn't really matter, or are you talking...
Dr. O'Laoi:	00:41:34	No - I'm talking about serious blood pressure. I've had a blood pressure of 180 consuming a lot of salt and two days later gone by just not eating salt. So what I do now is I eat a certain amount of food which has salt in it, like I'd eat some salami, etc. but I don't add salt to anything and that controls it.
Ivor:	00:41:55	And I think the literature in general would support that salt-sensitive hypertensives, you know for them salt is a factor but, but probably a lot of people, it's not really a factor. In fact, low salt might be an issue. So like many things I suppose in science and nature, there's kind of a, a hyperbolic kind of "very high can be bad for some" and "very low can be bad for others". So there is some variability.
Dr. O'Laoi:	00:42:20	Oh there is of course, and it's genetic. They've identified the gene that's involved in, I can't remember the explanation, but I've looked it up. 15% of people have a gene which predisposes them to develop hypertension on a high salt input, but not with a normal salt input. Like on seven grams of salt a day I wouldn't get... My blood pressure would be normal.
Ivor:	00:42:41	Oh, that's quite high though. You're, you're, this is great. For the listener though, you're talking super-high because the guideline is to stay down 2 or 3 grams of salt a day. While at 7 you're okay, which is massive salt.
Dr. O'Laoi:	00:42:54	Not really. Not, not really because I cycle - a lot. So if you exercise a lot, you lose a lot of salt.
Ivor:	00:43:02	Yeah, true. So you've got these interesting kind of...
Dr. O'Laoi:	00:43:07	There's a balance.
Ivor:	00:43:08	You're making it more, you're making it a more complex balance because you're going way over the guidelines, and yet maintaining, okay, blood pressure. But given that you're doing a lot of cycling and that's losing the salt. So it's a little complex. And then when you go super, super high and overshoot completely, you get the hypertension response. BUT, the other question is to go another level or question. Is your hypertension - through that mechanism - as problematic as someone who has hypertension because they're hyperinsulinemic eating a SAD diet and they've got everything gone to hell.

Dr. O'Laoi:	00:43:42	Yes but they have it all the time. Whereas I would only have it if I overdid the salt. And I discovered that through experimentation - by deliberately consuming salt and seeing what happens.
Ivor:	00:43:54	Transient, you have transient hyper tension, which when averaged over time is not high....
Dr. O'Laoi:	00:44:00	Yes - it's not "real" hypertension and that instance. But if I were in the habit for instance, of being on the standard American diet and putting salt on my food and eating salty food, I reckon I'd be in trouble - because for years I was eating close to the standard American diet, but I was using very low salt whatsoever, I wouldn't add salt to an egg even - but I didn't eat eggs anyway due to the low fat advice...but I didn't add salt to anything for at least 25 years, which, and my blood pressure was always low. But my dad, who died at the age of 96 died suddenly, actually at the age of 96.
Ivor:	00:44:30	He !had a friend!!
Dr. O'Laoi:	00:44:31	...which was a good move! But he always had a very low blood pressure. His normal blood pressure was under a hundred systolic right into his nineties.
Ivor:	00:44:43	Wow. That's amazing for a modern western male.
Dr. O'Laoi:	00:44:46	Yeah. I think it's as a gene.
Ivor:	00:44:48	So I either the genetics are enabling you to tolerate to an extent this poor diet and not go into the dysfunction of hypertension, which is basically an epidemic in the West - whereas the Kitavans or the Tsimane etc. don't have it. Or - let me just parse this out. Either you're protected from all of the dysfunction from these bad diets and you don't develop hypertension - or you just don't develop the hypertension "piece".
Dr. O'Laoi:	00:45:21	Exactly. Now - name me an animal - an animal who has this mutation?
Ivor:	00:45:26	I'm not sure actually
Dr. O'Laoi:	00:45:27	The bear - the bear gets metabolic syndrome, complete metabolic syndrome when he hibernates but he doesn't get hypertension because he has a mutated gene.
Ivor:	00:45:39	You're saying you're a bear?

Dr. O'Laoi:	00:45:40	I'm a bear. Excellent. Bear face cheek!
Ivor:	00:45:44	Bare-faced science.
Dr. O'Laoi:	00:45:45	This is, yeah.
Ivor:	00:45:46	You know, now you've rung a bell. I do remember this. Yeah. The bear gets into the Metabolic Syndrome in the late autumn or whatever - builds all the fat in fairness, is not even an insulin-sensitive obese because actually does develop the hyper insulin but not the hypertension, which is a massive sign of dysfunctional processes...
Dr. O'Laoi:	00:46:08	They've identified the mutation. I remember reading this because fundamentally all these fat people you see walking around the place are hibernating. Well, they've got a hibernation reaction essentially. And what turns on the hibernation reaction? Two things - maltose, which you get from beer - and fructose, in excess, in calorie excess fructose causes production of uric acid. And I think uric acid is the actual trigger. It is the thing, that signals the body to start storing fat
Ivor:	00:46:46	Lustig I think went through some of this - in some of his lectures. And then uric acid also predisposes to gout - kind of a sugar related disease and, and many other negative things.
Dr. O'Laoi:	00:46:56	I think it's been deemed by the guy who did it, an American professor - the obesity trigger - Uric Acid. That's turned on by fructose.
Ivor:	00:47:09	Right. And that goes down to ATP. And the way the fructose is processed and all. The jury is still being debated on, on the sugar in general. If you're eating a low-carb, very healthy nutrient-dense diet, you can probably have quite a bit of fructose without kicking in those kind of processes. And in fact I only found out relatively another thing recently, and it was interesting. We always think of the fructose as "all has to go to the liver and it cannot be taken by the cells as glucose can". But relatively recently a paper came out, which explains that in normal fructose intake, in reasonably healthy people that the gut actually converts a lot of fructose to glucose...
Dr. O'Laoi:	00:47:45	Yeah, I read that one too.
Ivor:	00:47:47	Which is interesting. There's all this new data coming out. Even if you're thinking you have some things down pat, and even in the body, of course in the liver you can switch the fructose to

three-carbon glucose, and if you're not high on glucose intake i.e. in a healthy diet - a lot of the fructose just becomes some glucose. So there's all these myriad dependencies. Speaking of dependencies and context. If we get back to Atherosclerosis, we've got of course the LDL theory and you know, mainly LDL particle-based now or LDLp - it used to be the classic LDLc concentration. It's mostly now, well it's the particle count being higher and that's fine.

Dr. O'Laoi: 00:48:22 Or as they say in Dublin, "the pe-articles"!

Ivor: 00:48:24 Yeah the pe-articles - often "the effing pe-articles" in fact. So we've got the particles being higher and interestly, I've been a a person who quite publicly has questioned aspects of the cholesterol hypothesis as have you and many other people. But I will hand - or I have from all my research and awareness that if more particles get trapped in the Intima, they are part of the inflammatory cascade that leads to Atheroma. They are part of it. So in a sense it is true that the particles of LDL are part of the cause. The question is the dependency and the context. So in engineering, eh, my analogy, which is quite trite is the aircraft one. So in an aircraft, a rotor, or older actuator fails, and the rudder goes hard to the right. The pilot can't control it now, the plane crashes but doesn't completely explode. But the fuel goes on fire and the people who would have survived - a lot of them - but because of the fuel fire - they're all burned to death. It's a tragedy. Now obviously the root cause there is not the fuel - it was the rudder - but there's a sense with the cholesterol hypothesis that people want to call it primary root cause - when it's really an interacting factor...?

Dr. O'Laoi: 00:49:44 it's an amplifier.

Ivor: 00:49:44 And that is one way of looking at it, yeah, and we used to call them "interactional variables" and the weaker engineers would kind of fall in love with an interactional variables, but the the more experienced guys would know: "well, yes, when it's higher, things are worse" - but that's not the cause that we can address, the one that's most close to the real causal chain.

Dr. O'Laoi: 00:50:05 Well one would imagine. Now I'm not an expert on statistics or that - my attitude towards medical statistics is ask somebody who's really good at it because he'll know. But one would imagine that were LDL to be the primary cause of Atheroma, that the lifelong level of LDL, or even the more recent level of LDL, would line up with Coronary Artery Calcium scan results are post-mortem evidence of Atheroma, but it doesn't. And some people say, "oh, well that's because it's a lifelong thing."

Well, they have lifelong LDL's in a lot of people with familial hypercholesterolemia and in them the extent or otherwise of Atheroma does not line up with their LDL cholesterol either. So you'd say, well, what does line up with? Well, what does line up with it is, proxies of insulin resistance like triglycerides over HDL or whatever you want to do or measure the insulin resistance - they line up. So that would suggest to somebody who didn't have a bias that maybe the insulin resistance is the primary cause. It's what's facilitating the Atheromatous effect of LDL. And that when you take out the insulin resistance, then the incidence of heart disease falls. So you would say, is there data on this?

Dr. O'Laoi: 00:51:34 There's buckets of data on this. If you read things like the Quebec heart study, or Framignham - or any of it, all of it shows this, but people don't want to see it. All of it shows that if you have low markers of insulin resistance, then you were very much protected against heart disease.

Ivor: 00:51:54 Yeah. It's, it's a far more dominant driver. So if you're 50 or 60% higher in, in LDL particle counts, there's a slightly higher, you know, incidence of heart disease - but the insulin resistance / hyperinsulinemia is far more important. It's probably important to note that you can be insulin resistant in a physiological way when you're eating a very low carb diet. But that's not pathologic.

Dr. O'Laoi: 00:52:17 No, it's not.

Ivor: 00:52:19 Rather tt's pathological - exactly - when, when you're hyperinsulinemic and insulin resistant together, peripheral leak together, As doctor Kraft said "hyperinsulinemia and insulin resistance. They are not combatants. They are one and the same." And he meant that for, for pathological states, you have the two as two sides of a coin. But yes Insulin Resistance is a much more dominant driver and we haven't even gotten into the many other drivers besides cholesterol.

Dr. O'Laoi: 00:52:41 But one of the weaknesses, uh, in the, in the knowledge, in general of doctors in this area is they don't realize that when you diagnose somebody as having Type 2 Diabetes - that's late diabetes - they're diabetic for maybe 20 years beforehand. If you use tests of sufficient sensitivity, you can show this. And it's probable that in America and places like California anyway, that 50% of people are diabetic. And you would include people who have, um, so-called prediabetes - that is diabetes in its effect on the kidneys, in its effect on the other organs, whatever...and heart disease etc.

Ivor:	00:53:27	Exactly. And the actually the figures, the latest CDC figures I got - for over-45's in American adults. And that's where most heart attacks occur. For over-45's, it's technically 64% of American adults, over 45 years old adults are prediabetic or diabetic, which you correctly say is all diabetes. And then there's, there's some more who do not fulfill the criteria for prediabetes. But if you measured insulin, you've get more. So you get 70 or 80.
Dr. O'Laoi:	00:53:59	We all know it is, I mean this is a giant iceberg yet there's very little of it over water.
Ivor:	00:54:07	It does - there's a lovely diagram of metabolic / insulin resistance syndrome with an iceberg and it shows all of what's going on underneath. So this is a huge driver. And there are older drivers, we probably won't get into that e.g. if you're low on critical elements like vitamin D and nitric oxide. But recently I've been looking a little deeper, and coming up now I'm going to be giving talks with this content, into WHY cholesterol may or may not be a problem. And I knew, as we said at the start, if you have more particles, technically more will get into the arterial wall - to some extent, we don't know exactly. But more will get in and more in there if you have an issue is going to give you more of the issue. So it's not rocket science. So we agree in principle. However, I wondered about what mediates or or governs how many get from your blood into your arterial wall and how many get stuck and become oxidized - and you get the, the catastrophic cascade into atherosclerosis. I wondered what decides how many get in, besides the number in your blood because you rightly said, we know there are populations with higher numbers than the Americans - populations with nearly no heart disease, you know, with higher particle numbers in their blood and we know those the opposite also. So we know those there's a problem in the logic. And what I discovered was the glycocalyx is an incredible structure that has a sieving effect on the inside wall of your artery, and also the endothelial cells transfer cholesterol particles across them in a very governed process, and also LDL leaks between the endothelial cells and can transfer - and there is science on all of this going back 30 years. And when you get inside the artery wall, your proteoglycans that trap the particles and can to a greater or lesser extent caused them to get oxidized. The activity and the affinity for those proteoglycans to trap the LDL's depends on whether you're a diabetic or not diabetic and what your blood's like in terms of health - whether have small dense particles or not etc. So there's three layers of what controls, how the particles may command and may cause a problem. And all of these are independent of your practical count. And they're all, unsurprisingly (there's science on all of this) - connected to

		hyperglycemia, hyperinsulinemia and all of the other primary root causes we talk about. It appears that all of these primary root causes sit and govern how leaky all those junctions are. I went on with a rant just there, but it just stuns me that even the particle LDL theory is utterly governed within the theory itself off of them getting into the wall - is governed by all the things we talk about.
Dr. O'Laoi:	00:56:53	Yeah, yeah, yeah. Yudkin in his book stressed that, if anything, he said, relates to myocardial infarction in tests -it is the blood serum insulin level. He established that and that's the 1970's - all the patients who got a myocardial infarctions as far as he was concerned, had raised insulin levels.
Ivor:	00:57:17	Yeah, exactly. And we're, we're hardly measuring insulin - so it's amazing he was even able to get that data, but Yudkin was a truly great, incredible...
Dr. O'Laoi:	00:57:24	Brilliant credible scientist.
Ivor:	00:57:24	Yeah. And so decent as well. Unlike his opponent, Ancel keys. But we won't go down that one. But so Yudkin observed that but also the EuroAspire study in 2015 was published, and they looked closely at all of the CAD or coronary artery disease victims across Europe, ages 18 up to 80 - and 25 countries. So that's a perfect engineering pull - you unbiased, grab everyone who has the problem and then look closely at their glucose, not even their insulin. And it turned out over 70% had glucose dysregulation. So they were essentially diabetic - over 70% - and they didn't even measure insulin. And the most recent EuroAspire from a colleague in the UK is coming out for the UK. Same thing. Diabetes seen in 65%. I mean, wow. It's incredible.
Dr. O'Laoi:	00:58:18	We were right, we was right man!
Ivor:	00:58:23	So we just slap ourselves to the back and go home. Well No, we continue getting the message out there. So it is multifactorial - atherosclerosis. But even in that brief discussion, there's a whole array of hugely important drivers and root causes. And then kind of on the side interacting with with these drivers is the cholesterol reality, the particle reality. So you don't need to deny it. You just need to say it's so peripheral, that why would you really so much on that when you've got so much bigger fish to fry...
New Speaker:	00:58:51	I've always said on Twitter or whatever, uh, I don't believe that LDL cholesterol is insignificant, but I think that there's a much

		bigger driver, which is insulin resistance. That's always been my stance. Looking at the data, one of the things you learn from, I mean, I've made a hundred diagnoses a day for 30 years, one of the things you learn is you've get a kind of gut feeling about diagnosis and it's usually pretty good. Like you... can I give you an instance of a case? I got a liver biopsy from a lady and she had some kind of a lesion on her liver and there was lymphoid tissue and that. I said, gosh, this is difficult. So I sent it to Dublin. I sent it around Ireland to about seven pathologists saw it - and they all thought it was lymphoma, and the consultant says to the consultant in charge of the patient, what do you think? I said, I think it's reactive - it looks like lymphoma, but I think it's not, but seven people say it's it's lymphoma. We'll watch her, he says - and nothing ever happened to her. That's gut, and I use my gut a lot now, gut can be wrong, but it's more often, right? It's 95% right.
Ivor:	01:00:10	Absolutely. It depends on the person who's using the gut and how truly experienced they are. Of course. So you can't, you can't universally say trust your gut because some people's gut is completely up their ass...
Dr. O'Laoi:	01:00:24	You have to let that one in - you have to let that in!
Ivor:	01:00:27	I knew what I was saying...!
Dr. O'Laoi:	01:00:28	Ivor has a part time career as a proctologist!
Ivor:	01:00:32	There you are. I'll get my Clyster pipes there. Actually, there's Clyster pipes. That's an unusual reference. Are you familiar?
Dr. O'Laoi:	01:00:39	What are Clyster pipes?
Ivor:	01:00:42	Well, I did Othello the Shakespeare play when I was very young, and we studied it and Clyster pipes are ancient proctologist's instruments. And actually the character Iago in the play refers to another character who's, who's handling an object where this Guy Iago has framed him, set him up - he's handling an object that will make an older person think that he's involved with his wife. So he says "see how he plays with the handkerchief - would it were Clyster pipes for his sake." In other words, he's handling something that going to be big trouble for him, but Shakespeare of course had his humor. I mean, I think proctologists they had a little Satchel and they, they were able to put these probes and the rectum and check things - Clyster pipes. So anyway, that's an aside.

Dr. O'Laoi:	01:01:27	Remind me to never have that examination!
Ivor:	01:01:29	Yeah. Yeah. I don't think proctology would be for me. Uh, but we were, you were giving actually these stories of diagnosis and I know we're going a bit off from atherosclerosis but we'll, we'll circle back in a moment. But examples of those over your massive career - of making calls where others hugely experienced, made incorrect calls. I think you had one which involved a senior guy. He was getting a diagnosis or a very wealthy guy?
Dr. O'Laoi:	01:01:56	Oh yes. Um, well I worked for Basil Morton who was subsequently Sir Basil Morton, fantastic pathologist rated the world's best gastrointestinal pathologist. He worked in Saint Mark's hospital in London, which is purely a large bowel hospital. It's now part of the, Harrow unit. But he had written, he had published only 120 papers in his career, but they were all magnificent. And he had the ability to look at something, as if nobody else had looked at it before and get a sort of independent view of it. But one day he called me and he says "there's a biopsy here from the professor of pathology in New York on a very-well-to do VIP - of his rectum. And there's the letter. So it says, "dear Basil, please look at this. It's very unusual, but I think this is carcinoma." So he showed it to me and he says, what do you think of it? And I said, it's not carcinoma, it's Squamous Metaplasia, which is where the glandular tissue becomes squamous tissue and then it looks very like cancer.
Dr. O'Laoi:	01:03:05	He says "are you going to disagree with the professor of pathology in New York?" I said "I sure am." He says "he won't like it - but I like it. And I'm sure the patient will like it!" Because I was right. So you just have to, you have to learn to to call stuff. You can be wrong too. You can be wrong. But many times you're right. If your gut says something isn't right, something isn't right.
Ivor:	01:03:35	Absolutely. And again depending on, in the context of your experience, on your skill and talent and all those things. Pathology is interesting because usually one would think when you've got a slide and a sample and you look at it, oh, that's carcinoma. That's a cancerous cell. And no, this one has no cells - but it's not that simple, there's a huge interpretation involved.
Dr. O'Laoi:	01:03:58	There's a visual interpretation. There's also another matter involved, which is, for instance, if a pathologist gets a cervical smear and examines it really, really carefully, they can show using instrumentation that when he's examined that as carefully

as he can, he's only seen 11% of the cells. The way the brain works. So when you flick your eyes, the brain doesn't register what you see between the flick and the end of the flick. And now it's very difficult to overcome this and the microscope because of the design of the microscope. But this is a phenomenon that's known to fighter pilots and the motto they have fighter pilots have is "use your head or you're dead." Because if a fighter pilot is flicking his eyes from side to side, he doesn't see between the flicks. So they don't do that. They move their head. But you can't do that with a microscope because the microscope would have to move with your head and you just can't do it. So that's an interesting thing. It's physiology.

Ivor: 01:05:03 And of course it is. Yeah, if you try to move your eye across the wall. It moves in jumps - with dead zones. But we as hunters, as we evolved our eyes can track a moving target fluidly

Dr. O'Laoi: 01:05:15 That's right. The movement attracts attract you. Like if you look down at a pavement and there are ants on it, even though you can't see anything out of the corner of your eye - if it's moving, you can see thousands of moving ants. If they all stopped moving, you wouldn't see them.

Ivor: 01:05:32 And if you look at an individual ant, your eye, you can track that ant wherever he goes continuously and smoothly. Yeah. But if you try and move your eye across the surface, it will only go in these discrete digital jumps. That's what, that's what happens. Yeah,

Dr. O'Laoi: 01:05:45 Yes that's, that's the problem. And another problem too is that what your brain sees is not exactly what your eye sees, because your visual system tries to simplify what you're looking at. So you may flick over some cells and the brain fills them in from the surrounding area. So you don't see them at all, this is the problem you're up against. We know this from science that it's been done on vision. So doctors get condemned for missing something, but the degree of misses is very reproducible between people. For instance, an area of difficulty is reading Barium enemas, Barium enemas where you do an x-ray of the gut using a contrast - is the Sigmoid colon, which is a twisted bit of colon and above the rectum - and it's easy to miss something there. And they've got top, top radiologists to look at x-rays of Sigmoid colons - and they miss a third of them in the Sigmoid colon. They miss ones where you could afterwards easily point at them and say "look there it is" and they then say, "oh gosh, yes". They miss a third initially however. If you get two

		radiologists looking at it, they miss 15% the two of them. So he will never reach perfection on that.
Ivor:	01:06:58	Right? Yeah. There is some natural inborn error
Dr. O'Laoi:	01:07:01	There's a natural error rate. There's a natural error rate in everything.
Ivor:	01:07:05	So all you can do with that really is design in redundancy. Yeah. They you do multiple layers of inspection...
Dr. O'Laoi:	01:07:11	This is why, for instance, in screening they do repeats. And one of the ironies of the ironies of cervical screening is that if there's an actual cancer of the cervix, it all kind of swells up - so that you get fewer cells in the malignant ones, then you do in the benign ones.
Ivor:	01:07:34	Uh, so that's, that's kind of tragic - they "hide"
Dr. O'Laoi:	01:07:36	They kind of hide yeah,
Ivor:	01:07:38	They haven't evolved to hide of course. It's just a bit of luck for the cancer, and bad luck for the person. And I think when you, when you are trying to register something as well, it will depend on, on your own personal frame of mind or pattern recognition ability.
Dr. O'Laoi:	01:07:51	Yes - also, if you know that the person has cancer, you will find the cells.
Ivor:	01:07:55	That actually, I just have an analogy popped into my head. We had an enormous issue many years ago in the high volume manufacturing where I was and I had to lead it for my sins and it, it, it cost a huge amount of money in the end. So it was the biggest ever issue. And we fixed it, we root caused it. But there was a defect of a delamination, which you could only see on the highest-power optical scopes and you have to use diffraction lenses to create a diffraction pattern so could see the lamina and it was only one microscope setup that could do it. It had been missed for 6 or 12 months because all the high-powered scopes were not set up in a very specific way.. But the thing was when I got into that issue it was so huge, the responsibility was so huge. I became ultra-focused on seeing these defects and I found that the slightest glance, and I would see it because I was obsessed over I mean my whole brain was wired to see these defects.

Dr. O'Laoi:	01:08:50	You programmed yourself to see it.
Ivor:	01:08:52	I think so, unwittingly you were just programmed because there was so much at stake. But you can't of course be able to be like that for every myriad different thing when you are looking at stuff as a pathologist, you'd go insane. So it's maybe only specific, special things where you can become hyper, almost survival-obsessed at and maybe enhance your ability to catch things.
Dr. O'Laoi:	01:09:13	Sometimes it's just luck. When the first cases of Legionnaire's disease appeared in America, they took all of these bacteriological samples and they spent ages looking at them, loads of people and they saw nothing. And one of the pathologists who'd been looking at them came in one night and jus took one slide, put it down and there were the bugs. Luck, just luck - that's what it was.
Ivor:	01:09:36	And once they are observed, then it's a state of the art thing - then you find them. Actually legionnaires, and again we're going rolling all over the place here, but a couple of months ago a guy died in the UK - and the legionnaires is of course - if you've got moisture in vapor phase, not pure liquid but tiny droplets, um, you get these particular type of bacteria with warmth and you can inhale them in a mist. I don't think that you can't drink them - inhaling them is the problem. This guy in England had a hose, looped up on his veranda and it had got very hot and warm over the weeks in the summer. The temperature of the water went up and the particular bugs were in it - and what did he do? Unfortunately, instead of pouring liquid flow into his plants, he turned the spray nozzle on - and killed himself. Just a rolled up hose at the right temperature and using a spray nozzle.
Dr. O'Laoi:	01:10:24	I think 63 degrees kills them. I know somebody who got it and he was on a respirator for three weeks and he came out of it, but they have no idea where he got it. They couldn't explain...
Ivor:	01:10:43	A bit like that Wiel's disease. We can get it from rats , but sometimes people get and they're just not sure how. Yeah. So many diseases out there. On an interesting note though, I have a general belief that's built over the years that if you eat a nutrient dense diet and you do all the correct things to be healthy, your ability to deal with infections is not "magically amazing". But it's better, it's, it's substantially better and I think that's one of the side benefits of a low-carb, high nutrient dense eating, lots of really great food.
Dr. O'Laoi:	01:11:14	It's got all your vitamins too..

Ivor:	01:11:16	you get all your vitamins, you're getting magnesium and getting potassium and chloride. You're getting old. What you need to make the human chemistry set, which is massively complex - you're making it hum - and as a result a nice side benefit is you know the common colds and other maladies. For me over the last five, six years, the rate has collapsed impressively compared to the previous years.
Dr. O'Laoi:	01:11:36	I got a run off them about a year ago, but I've had none for a year...
Ivor:	01:11:41	Yeah but on average you can do a timed test average over multiple years. Rolling average. I see striking difference. Neurological health as well. You mentioned at the very start and that is quite striking that when you change your diet, yes you lose weight. I looked at the time course of events as I lost all that weight though. And I noticed that in the first days before I lost any measurable weight effectively - my blood pressure started going down a steep incline. And I made the mental note at that time because it was quite dramatic. I was generally 140 over 90+. Hypertensive significantly - when I was doing triathlons and massive training, it would drop right back down to 125 over 80. But I noticed in the first few days when I switched knife-edge to low carb, before I lost weight, my blood pressure started heading down units a day. It was extraordinary, uh, after a few weeks I was coming down to triathlon levels. Even though I was doing no exercise, the weight was coming behind the blood pressure collapse - and it just shows that it's the fuel going into the system and the metabolic health of the system that is driving a lot of the issues, the weight loss is almost a "side thing."
Dr. O'Laoi:	01:12:58	You get the same, you get the same improvement in diabetic, um, parameters before you lose weight. If you go on a low carb diet that's well established by Volek and all of them.
Ivor:	01:13:10	Oh yeah. And perhaps, I mean if you just measured the visceral or the ectopic fat in the organs, sure. That's going to go down rapidly and line up with the improved metabolic parameters. But the general obesity is it, it's a side order. I mean it's, you know, it's a bit of a vanity involved - it's nice to have it low but, but hell, much of the adipose tissue all around you is harmless. Yeah. So we'll have to circle back to atherosclerosis because we were, we were at that point of, you know, we've got the factors and we've agreed that overwhelmingly the important factors are kind of outside the cholesterol interacting one. That said, if someone changed our diet in a significant way and their cholesterol shot up, it would behoove them and be the smart

thing (and any engineer would do this) - is make sure that all of the other markers are all in a good enough place that you can choose to not worry too much about that cholesterol. But to ignore a biomarker like cholesterol shooting up would be stupid. So I think that's probably a fair point to make. But, but let's say we move then into the process itself and calcification particularly, which is a later stage of Atheroma, but it happens soon enough that it acts as an incredible measure of risk...

Dr. O'Laoi: 01:14:27 Yeah. Well what you are going to get is you, you're gonna get some Atheroma and some of them would calcify and there's a rough proportion to how much calcifies. So it's very good, it's a very good flag for the presence of Atheroma if you've got this calcification. Now there, there are two terms that are used: 1. calcification where you ought not to get it is called "ectopic calcification", which means calcification in the wrong place. That is divided into "metastatic calcification" - and metastatic calcification is what you get if you have an abnormality of calcium metabolism, like you've a parathyroid adenoma or something of that nature. Then what you get is you get calcification in normal tissue. And the other type is called dystrophic calcification. Dystrophic calcification is calcification in abnormal tissue or diseased tissue or scar tissue. So that's what it represents. It really is a repairing thing or a reparative phenomenon at least in part - it braces the tissue. There is a paradox that statins are thought to increase calcification in Atheroma, but they don't seem to make the result worse. So this could be a somewhat beneficial effect, I don't know. But it, they say "queers the pitch" as regards diagnosis - and one mustn't have a queered pitch.

Ivor: 01:15:57 No, especially when we're dealing with science and people's lives. But it is an interesting one and I think I heard the same explanation and I don't think there's any really deep mechanistic papers explaining it and I wouldn't have had the time to get into them, but it's a reasonable enough thing that statins do have a benefit. What's debated is the degree of benefit and what's causing it. The pleiotropic versus the cholesterol. But to be honest, we're happy enough in general people in my world that lowering cholesterol particles with statins may not be the main benefit that is seen or observed. But at the same time as we agreed earlier, if you lower the number of particles and they're an interacting part of the process, you may ameliorate the problem , which is fine. Also, if you lowered the number of particles, there's going to be small dense and oxidized LDL and problematic LDL reduced. Interestingly, oxidized LDL in the plasma, I've just been studying papers recently, has a dreadfully bad effect on the endothelium

and it causes attraction of monocytes and immune cells and causes corruption of the internal layers that sieve LDL. So, so everything's interconnected. But yeah, the statins may be consolidating calcification and getting a benefit while making the CAC value go up slightly. Yeah. Which is fine.

Dr. O'Laoi: 01:17:47 Now I'll give you an instance of something that has a huge effect on the outcome of coronary artery disease. If you've got somebody who smokes, who's had a coronary. If they quit smoking, they double their chances of long-term survival. Statins won't do that. Double is a big effect.

Ivor: 01:18:23 I remember many, many years ago, I used to smoke a long time ago and I remember being really impressed by the linkages to mortality, primarily true cardiovascular mortality. I know lung cancer is a terrible one that's 25 times the chance if you smoke, but relatively speaking, not a huge amount of people get it. But the cardiovascular was amazing - and one thing I noticed that ties in with that is I got the charts, and if you stop smoking - then rapidly your cardiovascular excess risk begins to fall away. Yeah, which makes sense because the smoke is damaging your endothelium, damaging your Glycocalyx. It's oxidizing your particles. It's doing stuff that when you stop it, you can recover fast. But interestingly, when you stopped smoking after a long period, your cancer risk does not drop so fast. Which also makes sense because that's more longer term cellular damage. Very slow. Yeah. So I love how these things all fit together beautifully. So the smoking - yes smoking is a big risk factor for heart disease. Of course.

Ivor: 01:19:30 There was a study actually with calcium scanning and smoking reminds me, which was stunning and they had smokers and nonsmokers and when they looked at… I shouldn't be laughing, but this is totally insane. When they looked at the non-smokers with a high calcium score, versus the smokers, I mean real smokers of similar age with a zero CAC score. Well the non-smokers were six and a half times more likely to have a heart attack (with a 100-1000 initial CAC score) - than the smokers with a zero CAC score. And it actually made me realize something - if you scanned all of the smokers and nonsmokers, you'd find out the non-smokers who are going to have heart attacks. And you'd also find the smokers who are actually probably going to be fine. Not to say smoking's okay of course - but the calcification scan and CAC score would actually allow you to sort the wheat from the chaff?

Dr. O'Laoi: 01:20:40 Yeah, there are two peoples who smoke a lot. The French and the Japanese - and their incidence of heart disease is only

		marginally increased by smoking. Unlike us. Now, they don't know why. It's something that they're not eating. Probably. What did the French have in common and with the Japanese? They both eat about 70 pounds of sugar per capita per annum, whereas the Americans eat 140 - in Ireland we eat 130 - so big difference. I reckon it's the sugar - there is a critical amount of sugar. They know, I'm looking back historically from when sugar and white flour came to the missions and doctors were there studying the populations - that 70 pounds - if you give population 70 pounds or more of sugar per annum for 20 years, they start getting diabetes and heart disease. That's the, that's the threshold. There's almost a threshold value. There is a threshold value,
Ivor:	01:21:41	So all of your analysis of sugar would really need really accurate sugar figures - accurate per person and be mindful of a threshold, potential effect to properly analyze. But I think most of the science and sugar we see is kind of all over the place and there's probably commercial and political historical reasons...
Dr. O'Laoi:	01:21:59	There is no probably about it!
Ivor:	01:22:20	Yeah. The smoking thing, there was also the Scottish, the Scottish - there's a massive hazard ratio for smoking versus non-smoking, like 2.8x or something more heart disease if you smoke. But you've just reminded me the French, in Lyon I think a study showed that the hazard ratio for smoking was only 1.3x and I think you're right that everything is synergistic and interacting. So if you do everything correct, like say the Kitavans, you can do one thing that's questionable and get away with it. And this actually is not a surprise because all technical systems, when we have multi-factor complex problem in say high volume manufacturing, the same kinds of things apply. If you have many factors set to the right place, you may have excellent yield, and you may be able to have one factor, you know, as the bad factor in the wrong place, but you're okay because the other good ones carry it. This is not a surprise and all of these causes of heart disease are similar. If you're doing enough things right, you'll get away with one sin or two sins. Like we say, particle counts and all. If you're doing everything else right, that may not really be an issue at all. If you're doing quite a few things wrong - rapidly everything starts getting to be a problem and that's where we get the catastrophic early deaths. It's a way of looking at things, but it makes sense in the technical arena,
Dr. O'Laoi:	01:23:40	It is right I'd say.

Ivor:	01:23:40	it is right almost by definition, from the world I came from. But some people seem to struggle to intellectually just grasp it. It seems to me quite transparent - and to you of course, because you're brilliant too! So we'll, atherosclerosis then. It is the world's biggest killer. Do you have any stories on atherosclerosis from the pathological side in your experience - you mentioned about this guy who had just one plaque - and also the inventor of the calcium scanner Doug Boyd professor of physics - he told me a story that, not a story, it's a fact. Back in the early days, decades ago, you could have a very small percentage with a zero calcification score who have an event and that was understandable because they could have rapidly progressing arteriosclerosis where they have an - as yet uncalcified plaque, not having significantly calcified yet. As perhaps in rapidly progressing Diabetes - you might fall before you show up in the scan. But this is rare, mind you. And if you got a scan the day before you have their heart attack, you'd probably have seen calcium - it's just that the scan was done too long before the event. And also in the other extreme there's around 1% who get super-high calcification and Professor Boyd called them, "ceramic coronary arteries" people - and they have no events and they have scores in the thousands...
Dr. O'Laoi:	01:25:11	I've seen them, they calcify rapidly enough and the reparative process is rapid enough - that they actually stave off any events and they get to the end of the line, without problems. They used to speak, um, of a phenomenon called Monckeberg's Medial Sclerosis where you got sclerosis, that is fibrosis and then calcification of the "media" of the artery - not the intimate where you don't have plaques. And that I think that's actually a rear a real but a rare enough entity. And I think some of them must be that they don't know what causes it conquer burgs medial. It's lyricists, right? I think I heard a doctor Bernstein speak of that or I might be mixing it up, but it's unusual. He had sclerotic arteries in his legs, which gradually came to normal on this diet after years. I remember reading that one of us in his book, he's an extraordinary man, incredible less doctor Bernstein. Think the bridge Bernstein, Richard Bernstein. He was an engineer originally and he became a doctor after discovering the crucial nature of being low carb.
Ivor:	01:26:13	He was a type one diabetic, fixed all his diabetes and in frustration that no one would listen to him. He went into medical school and became a doctor. Of course, he promptly found out that no-one would listen to him then either! Because his paradigm was against the dogma. I think he's, is he 82 or 83 years old? Maybe 86. He's still, he's had diabetes type one for something like 56 years or more, which is almost unique, uh, to

survive that long with type one diabetes. He had some residual complications of it, which he was unable to reverse, but they haven't progressed. So he has no complications at the moment, and everything is perfect. Exactly. In his eighties, he's doing YouTube instructional videos. The Diabetes University, if anyone wants to Google it, Bernstein, diabetes university, anyone with type one diabetes - these 25 short videos explain every aspect.

Ivor: 01:27:12 It's an incredible result, incredible man. And basically overwhelmingly, I know there's lots of steps and interventions he recommends, but inherently it's simply low carb, you know, and, and it's a little higher in protein. And there is his "law of small numbers" that if you eat big bunches of carb at all, your ability to control the insulin swings afterwards gets nearly impossible. It's an engineering fundamental mathematical thing. If you bring the carb in your diet right down, you now have a low amplitude and it's really easy to control. And because you're keeping the insulin, exogenous insulin and the glucose both down, you, you don't get the pathologies of type one diabetes essentially. It's incredibly simple in some ways. Yeah, it's somewhat frighteningly simple. It's effing crazy.

Dr. O'Laoi: 01:29:02 I wanted to tell the story now, which has a bad word in it. And it's very Dublin. And I told the person who was referred to by this remark about it and he said it as straight out of James Joyce. We had a post mortem room technician called Ben when I was working in Dublin years ago and he was the real Dublin accent character and he had a coolness with the professor who ran the ward, and the professor is aware of this. So the Professor is out at the Christmas party. So he bought Ben four pints of Guinness at the Christmas
party. So anyway I met Ben in January after the party and I said "how did you enjoy the party, Ben?" "Oh, Jaysus", he says "you can say what you want about auld professor, but he brought me down four big black pints - un-suh-fuckin-licitated!" I think Joyce would have written that!

Ivor: Ah, Joyce. Yeah. Joyce was amazing. I tried to read Ulysses, but I just kinda said, I don't know – maybe not for me. He had the biggest vocabulary of any human being

Dr. O'Laoi: And he loved compound words. I have a liking of writing big long compound words myself. Hmm. I'm no Joyce thought.

Ivor: Ah, well that's a hard act to follow. And Cormac McCarthy. Actually, one of my favorite American novelists - he sometimes creates sentences that go on half a page, and sometimes he's brutally terse- but mostly he's got those really special style -

long rambling, descriptive, great. And he's still alive. Great books. So I think we'll probably, we'll probably roll to a close because you got to get back down to down to the territories, you know, out in the boonies.

Dr. O'Laoi: Or as a chap I worked with in Dublin said years ago, "the provinces, the provinces."

Ivor: Yes. And as I used to joke with friends from the country or outside of Dublin, because I'm a Dublin guy, I used to say, you know, it's "the parochial areas. I also like the provinces though. I like that too. We're going to have of course, as is customary after any of these podcasts, we're going to have a big bloody ribeye on the charcoal grill. I hope that's acceptable to you. You're not a Vegan, no?

Dr. O'Laoi: No - I don't have to have a Vegan cell in my body. I mostly eat meat!

Ivor: Very good. Thanks a lot Gearoid.

Dr. O'Laoi: Thank you very much. I really enjoyed it.

Ivor: Thanks for tuning in guys. If you're watching on youtube, you can see my subscribe button in the middle of the screen, a free viewing of the widowmaker movie on the far right and myself and Dr Gerber's book, each rich live long on the left. Otherwise, please do subscribe to the audio podcast. Thanks.