Danny Lennon:

It is my great honor and privilege to welcome Dr. David Jenkins to the podcast. Thank you so much for taking the time to come and talk to me today.

Prof. Jenkins:

Well, thank you.

Danny Lennon:

That the pleasure is certainly all mine and I don't say that lightly or just for entertainment purposes, to say it, it's genuinely and honor your work as people I'm sure we'll see in a few moments has not only been extensive, but has been pioneering in a number of different ways within nutrition science and has informed so much after that. So it really is an honor to be able to talk to you. So, but before I get into any of that specifics, I'm wondering, can we start with maybe some of the early part of your journey into the glycemic index as people now, everyone in nutrition science will, of course know this with great familiarity now, but you were at the forefront of bringing this into existence as an index in itself to describe what's going on. Can you maybe just give paint a bit of a picture for people of what things were like at that moment in time within nutrition science and how that work that led to the development of the glycemic index came about?

Prof. Jenkins:

Well, I suppose it was it's all, everything in life is complicated, becausethat's probably one of the more complicated parts of my life, but truly it was it was the fact that Denis Burkitt and Hugh Trowell had come back from Uganda to Britain and had made a major impact in terms of dietary fiber. They'd got the medical research council to decide that it was time that they should start working on dietary fiber. And I was lucky enough to be in the right place at the right time with the right friends. It's always the case of

who you know, and I was given a job very early on in my career to work with a medical research council on dietary fiber. And as we went through looking at dietary fiber it became fairly obvious that if that's a factor in terms of the rate of digestion of food, then it didn't matter how much carbohydrate was in the food.

Prof. Jenkins:

If you had a lot of fiber, it might make a difference. And so that was, that became important to us. And we started thinking, well, supposing if you take foods with say 50 grams of car hydrogen, and some foods have got fiber or some foods you've added fiber to, would they show a difference in glycaemic response? And they did. And so we thought, what happens is everything to do with fiber? And then we realized, no it wasn't to do with fiber, although that's what we were working on. And we always hoped that it would all to do with fiber, but it wasn't, it was many other factors. It was the way foods were, were put together. It was a potable size of the food that it was the other antinutrients in foods or nutritional factors that have a difference between foods and make a difference to the way you absorb those foods.

Prof. Jenkins:

So it really ended up being the rate of absorption that we saw as being important. And we did some studies with dialysis bags, spitting, gathering saliva from ourselves as Sali amla, and then putting these in dialysis bags with foods and showing that actually their blood glucose response related to the rate at which they were digested in Vire in others, in out of the body systems, the rate at which the food digested was suggested by human digestive enzymes determined the rate at which it would raise the blood glucose level. So he thought, well, that's interesting. we, if we want to use this, we better standardize it because obviously different people have different blood glucose responses. So you really want to standardize this. So we ended up as, as you just pointed out, putting together a glassy index, you know, was using glucose as the standard, and then seeing what percentage the food raised the black glucose by comparison with glucose itself, that was quite simple.

Prof. Jenkins:

So you could say it was either 60% of glucose, 70%, 80%, whatever. And that then allowed us to characterize foods because you could then use different groups of volunteers and they could, as long as they did glucose and then they did the food, then you can always express their food as a percentage of their, their glucose test result. And so we put together tables and lots of friends came together and did the studies on themselves for the first table? I have to say forweeks we just tested different foods spent, we didn't have a standard breakfast. You can imagine we had the breakfast, the food that was going to be the test for the day. So that was it. And we put these, these tables together and we sent it off to American Journal of Clinical Nutrition actually, sort of little paper. And it was it was accepted. I was surprised there was no other comment just accepted. I've never had a paper like that.

Danny Lennon:

<Laugh> If only it was like that more often.

Prof. Jenkins:

And and then it was published and nobody showed any interest for about a year <laugh> it was just, it was a published paper and that's it. And then fun enough. It, the reasons I cannot tell interest took off. And I think then it became a popular paper, but I have to say that it was a very, very quiet beginning

Danny Lennon:

As is often the case. I think with a lot of things that end up having a, a large impact. And certainly I think people listening when they hear some of that, they can see how some of that work and even those early hypotheses you were having in that area have essentially laid the foundation for many different types of, of work in current nutrition, science, and have splintered off into different ideas, whether that's indeed related to the glycemic index or whether that's in relation to specifically looking at fibers or we see, for example, like John Kerwin's group, looking at fiber or whole grains, or then we see other areas looking at well absorption rates and high fiber preload. So there's all these many different ways we can look at this work that might have some origins in some of these hypotheses, which I find is, is absolutely fascinating to see how it, how, how this idea essentially originally emerged.

Prof. Jenkins:

We have to say, thank you for Denis Burkitt and Hugh Trowell fpr dietary fiber, because that was one of the big things. I have to say one of my colleagues came round and actually looked at our data Dr. McPherson, now at Ottawa, and she said, well, you know, you've been testing these foods and they've got these big differences. You really should make a focus on this aspect of your work because before we've been, I have to say, we've been looking at cholesterol levels and she said no, let's why don't you go and look at the glycemic effects. So she actually just in a friendly way as she passed through and looked at our data, gave us the comment. So we grateful for that too. I mean, yeah. Can I say it it's been the contribution of many people.

Danny Lennon:

Mm-Hmm <affirmative> of course, and certainly acknowledge that. And but I just do want to say, thank you on behalf of myself and others for, for your role within that. And, and indeed, I think I could spend a long period of time talking to you about specifically just about glycemia and postprandial glucose response. But nevertheless, with the time that we have, I did actually want to focus on another area of your work, which in itself has been very informative for many other groups. And I think originated back in the early two thousands with what people listening may now be familiar with seeing, as it's been mentioned on this podcast before, but more broadly this portfolio diet that was part of your work. And we can certainly get into some of the details with that. So the idea of can we come and create a dietary intervention that has a lipid lowering capacity based on what we know of different foods or different nutrients that seem to be able to lower lipids. And there's four main pillars that we we'll present, but I think maybe just to start off, I don't want to put words in your mouth. So when you are, and I'm sure you've been asked maybe 10,000 times at this point in your career, when someone asks you to describe at an overview level, what the portfolio diet is, what's the typical overview level that you would present?

Prof. Jenkins:

Well, I would say that the go back to the origins we'd been working for many years on specific foods DTRA fiber, obviously from the beginning and then on vegetable proteins, especially legume proteins. And we looked at soy and we looked at plant sterols, that you find in vegetable oils. And and we've been interested in working in nuts. We've been working with the the California Almond group who, who really have done a lot of basic work on nuts. And so we used to get nice little cholesterol reductions. It was, it was good, 5 to 7% reductions in serum cholesterol used to clap our hands and think that was a great study and then tell patients that they should go along and eat it. And my wife said, "you should stop playing around like this, why don't you go and do something important and put them together and get a

proper reduction in serum cholesterol level that clinical people will be interested in". <laugh> So again, following other people's advice, I followed her advice and that's what we did. We put them together into what we called in, in a joking way the dietary portfolio, as opposed to a financial portfolio where you are covering your potential losses and potential gains so that you put them all together and you hopefully maximize things. We thought it'd be good, because if you put everything together, you get a better effect. And you wouldn't have to give so much of anything that people got any sort of side effect from it. So we thought this is a great way to go. And we thought, well, we should be able to get a 30% reduction in serum cholesterol. And everyone said, that's nonsense. You can't get that with diet, but we said, theoretically, theoretically, we should. So we did the first study and that's, we got 30% <laugh>.

Danny Lennon:

And I think to put this in context for people for, at that time, when that study came out and remembering that this was, you had that compared to not only a control diet, but then also that of statin therapy at the time. And I think these were some of the first generation statins. So I think it was lovastatin that you had in that trial, particularly but to put that in context of the degree of lipid lowering, you were getting from this intervention relative to statin therapy was basically the same on this initial study, which as, as you suggest whilst maybe you had been able to forecast that maybe many people weren't imagining that magnitude of effect. Could you maybe put that in context for what was happening around that time?

Prof. Jenkins:

Well, I think the statins had come about in, in 1986, roughly, that was when lovastatin came out. And so you can say we were a bit late. We were 14 years following up doing comparison study. But before that time, before that time, we'd had tyramine, which was polysyrene with an aminated group on it. And it was like eating a sachet and sachet with a number of grams in the sachet , not just milligrams grams, and the stuff had to be mixed into a synthetic orange juice to try and get rid of the flavor because the flavor tasted light, the actual colystyrene, tasted like sawdust with a bad fish smell to it. So it wasn't a pleasant way of taking a medication.

Prof. Jenkins:

So that's why when statins came along in 1986, we didn't think they were going to be used too quickly. They were, they were used almost immediately. They just took over. And at that point everyone was being advised to go on a statin. So we felt at that point, it would be nice if we had at least something that transitioned people so that they could take it and they could take a statin, but they could also have an opportunity possibly. If they wanted to try diet before statins and to try diet that actually gave them a reasonable reduction in serum cholesterol. So if they, if they were clinically, it was necessary, they went straight onto a statin, but if not, this might suit people very well, and it was a plant-based diet. And so it was in sort of in keeping with literally the current view of of where darts should be going, which is more plant-based. And, and many would say that everyone should become a vegan anyway, for those who were, this diet was something that they could use asa support for lowering serum cholesterol.

Danny Lennon:

I think one of the really important points here is that it's not just a dietary intervention relative to anything that someone was eating a baseline. You have not only this trial, but other trials where the portfolio diet is given on a background of the NCEP Step II diet. And then in comparison to that, there

was actually the additional benefit over that. Can you maybe just explain that for people in the significance of that?

Prof. Jenkins:

Well, yes. I mean, we did try to make sure this was an add-on effect. So if you were on a good diet, if you were on a good diet, low saturated, fat, low cholesterol, you would expect to get a 10% reduction in your LDL cholesterol. And that's, that was our, if you like, that was our control. That was the controlled data. When you added these other foods to the diet, you would get an extra 20% because you have four pillars, each of around about 5%. There could be a bit more, could be a bit less, but around about 5%. [So] that gives you an extra 20. So that was our original calculation. We expect to get 30 good basic, and then addition an extra 20, and then compared with the statin, which is around about 30% in those days, as you commented was about 30.

Prof. Jenkins:

And, and so you put these, these foods together on the main background of a good diet, and that's what you get. If you had an even better diet, you could do better, obviously. And, and that's why we would say that if people were on a, basically a plant-based diet anyway, and then they enriched it with these other plant components or plant foods then you could do even better. And we did, in some cases give up to 35 - 37% reductions. But again, these are, I have to say that when we got the large reductions, this was for people who had all the food provided to them. So this is not for people who are going out and shopping at the supermarket. You know, I mean, buying food, that's a little bit different. We did a study like that; a multicenter study and what that showed was that we got half the reduction. So you've got about a 14% reduction in LDL cholesterol:still good, but obviously not the same as when people were taking everything. And so obviously if it's 14% as the mean reduction, then you can be quite sure some people got a lot less, but also some people got quite a lot more. So I think it's a range and it, and because it's a portfolio, you can invest as much as you wish in your portfolio. Right? So that if you invest a lot, then you get more.

Danny Lennon:

Yeah. And, and that's a really nice analogy; that "investment" essentially being the level of compliance that one has with the diet, the greater, the compliance, the greater level of lipid lowering that we're seeing. And of course that's probably unsurprising for people of that. The one of the main drawbacks is when we take an intervention and put it into free living people particularly with diet behavior change is always a big aspect there. Right.

Prof. Jenkins:

It's a very big aspect. In fact, if you say, what's my current headache, that is my current headache, getting adherence long term, really a real problem. And that's why I think very often when we want to show, something's likely to work, we have to go to a population study or a cohort study because it's very difficult to get someone to change and stay changed. I think, I mean, I think the Spanish, you been able to do it with the PREDIMED study that they've put together because everyone loves olive oil and nuts. And if you say, look, are we going to give you free olive oil? Everyone will take it. It's expensive. The extra Virgin is expensive. So if you, if you said, we're going to give you extra virgin olive oil every week, will you stay in the study? <Laugh> you say, "please!" <Laugh>

Danny Lennon:

Right. Yeah, I definitely want to circle back later to ways that this can get out into the population. And that might depend on when we're talking about specific nutrients. But when we're thinking about this, the diet more generally, I wanted to ask your thoughts on this importance of people remembering that, that the value of the portfolio diet, I suppose, is the fact that it is a composite of several factors that have this additive effect. Because I think that there's cases where people might take one of the aspects of one of these nutrients on their own, and then say, well, look, we can't really say this has a, a real clinically meaningful change. And at least some people may put that forth, but that's looking at something in isolation as opposed to a composite of several factors. I don't know if you have any thoughts that you would like to add in, in on that?

Prof. Jenkins:

Well to be honest, we did make it a portfolio. It's four at present. I think that my colleague John Sievenpiper , because we also did a portfolio on higher monounsaturated fat and got good effects on HDL, he's included that in the portfolio. So you could now say it's a chair with five legs to it. We could see a chair with six or seven or eight legs as things become more useful; proved and useful. Then they too would be part of a portfolio. And so we, we're saying that portfolio is a concept that can be expanded. It can be contracted. And if you hate oats and sort of the beta-glucan stickiness and you don't like okra, egg plant and these sort of foods, which are all rich in viscus fibres, if you don't want to take those, then you may have to take more soy protein or more, more of the other foods that we've got no more nuts, for example.

Prof. Jenkins:

So you can, you can vary what you, or if you're allergic to nuts, then you've got the other foods that you can take more of. And what we're saying is take more of all the foods. Remember that the 20%, the really big change that you can get comes with taking a healthy diet. So for heaven sake, don't go away from a very healthy diet with all your normal fruit and vegetables and whole grains, that's all part of, of what one sees in the diet. And you can do a good 20% with that. And then you add on these things to it. As Eugene's saying, we would like people to add all four, but if they want to add two or three, because some things they don't don't agree with, that's fine, but don't then expect to get the same effects.

Danny Lennon:

Right. And I think it's important that you reiterated there, that this is on the baseline of the healthy dietary patterns that we do know are productive for reducing levels of LDL-cholesterol or ApoB-containing lipoproteins probably most notably the, either the amount of saturated fat, or even the amount of saturated fat relative to polyunsaturated fat. As an example, if you have a sky-high saturated fat intake, it might not be worthwhile looking at, can I add in a certain amount of soy protein?

Prof. Jenkins:

No, I think it's for people who are interested in diet, to be honest. And I think, I think that's, that's the trouble Danny, that it's not going to be just for everyone. Some people just say, give me a tablet and that's it.

Danny Lennon:

Obviously in those initial years you've seen these really larger effect sizes. We we've talked about how there was a comparison with some of those early statins in terms of potential efficacy when there's high degree of compliance. And then since then, I think one of the, the big benefits of this idea of a portfolio

diet is the amount of work that has been done since then in order to replicate this and see this in different populations over time. I'm wondering, can you give us a summary of the trend since then of did the early promise, has that continued up to present day? And, and what have we seen in terms of more clinical trials looking at this type of dietary pattern?

Prof. Jenkins:

I think that the diet has become part of what many organizations are already recommending and a lot of the recommending these foods as a result, to be honest not a lot of trials have been done further, we're doing a large one now where we are looking, we are trying to look at whether we change the vascular system. In other words, whether we can using MRI, whether we can look at vessel wall volume and note that the vessel wall volume is reduced in others, you don't get cholesterol build up within the vessel wall. And the vessel walls are relatively thinner in terms of cholesterol plaque. We're doing these studies right now, and we will probably have the results in a year's time.

Danny Lennon:

Fantastic.

Prof. Jenkins:

It's been our last, our last volunteers and they're three-year studies. So that's the trouble. When you say how many services we done, lots and lots of studies know they take three to five years. If you're going to do an intervention study, you don't really want just to look at cholesterol, you really want to look at the endpoints.

Danny Lennon:

I mean, it's a thing across nutrition science, generally that we've talked about of the difficulty of getting controlled trials that are done well with hard end points is not a very easy thing to do. And only a few foods can probably do that.

Prof. Jenkins:

Won't find too many, you'll find a lot of drugs that they've done this on, but very few diet who say no foods.

Danny Lennon:

Yeah.

Prof. Jenkins:

Having said that, I think obviously the Spanish with their, their premed studies, they're, they're the group who've been doing these studies. And they're, I think the only group I know that have been successful in long term dietary trials.

Danny Lennon:

So I think at this point, I'd be interested in, in talking about some of those four or five legs of the stool or different pillars that we could talk about and maybe mention a few of the reasons why they are part of the portfolio to give people an idea of the initial work they are based on, or at least mechanistically why they're there. And we can maybe work through that. So if we start withy protein can you give an

overview of the, maybe either initial work that was based on, or, or mechanistically, what do we know about WHYY protein was, was chosen as one of the aspects of this portfolio?

Prof. Jenkins:

I think the work of Prof. Cesare Sirtori in Milan, who was the chair of pharmacology and was very interested in lipids, even though a pharmacologist very interested in diet <laugh>. And I think he looked at soy protein and saw that it was a particularly valuable source for lower serum cholesterol and with good pedigree in Japan and whatever where cardiovascular disease at the time that they were high soy eaters, which they were still to some extent, but they were high soy eaters and had far less cardiovascular disease. So he felt, let's take a look at this and let's look at the lipid levels that one sees when one sorts animal produce with soy, because it's a very useful food.

Prof. Jenkins:

And he's got a large at a large metabolic unit in one of Milan's major hospitals that fed these darts to patients in hospital and showed that it worked very well and published in the Lancet. I went over and spent some time with him, saw what he was doing and then was loaded up with food that I could take back to feed to patients. It was very generous. So I, one, realized that that that was the way to go. I have to say that he's followed this up and he feels that it's the 7S globulin fraction in legumes, in beans generally that does this. And soy is a, is a good source because it's a protein rich legume that's readily available and has been used as a protein source.

Prof. Jenkins:

So he did this, those work, and it looked as if from his work that it seemed to have a sort of HMG-coreductase inhibitor effect. And I was a little like a statin, very mild. So he showed that the, that probably was there was some absorption of the 7S globulin fraction in, in the human small intestine as such, and that this may have some, the effects on hepatic metabolism. So I think that that, that gave it sort of some credibility. And I have to say that many of us, many of us including my friend Dr. James Anderson who did a meta analysis for the New England Journal of Medicine way back in, I think in 95, in the last century showed that there were good reductions in serum cholesterol when you use soy in patient diet. And so of that, I think cemented it.

Prof. Jenkins:

And then later on there was a health... The FDA allowed a health claim for soy, which I think was key. They've got that under review right now. I hope they don't do anything unwise. I hope they keep it there because it is a useful thing. it's a small, a small effect, but very consistent in so many studies. So all, all the meta-analyses that have been done for the last 25 years, quarter of century have shown the same thing. So I think that soy: small effect, but useful, and what we did, and it was professor Penny Kris-Etherton, when she looked at the data she looked at the data and said, well, it's not just the innate effect of soy itself in lowering serum cholesterol, but you've got the reduction of if you like the beef effect or whatever it is, the beef and saturated fat effect that you are actually removing. So you shouldn't be just looking at how much the soy does it, but how much it actually does in the diet. And with that you'd probably get a few more percent increase in Indo increase in reduction as greater reduction of probably five to seven to 6, 7, 8%, depending on the person's diet, who's done the substitution. They've substitute into a bad diet, they're now improving their diet considerably, they'll get a better reduction. So that we felt was a very useful food, because it was, it was a food that not only had some benefits of itself, but also changed the diet to be a better diet overall.

Danny Lennon:

Yeah. I just think that's a really important point about nutrition science generally, that you just made that I think is worth emphasizing the people of that. We can't just talk about a food in isolation, because if you add something to the diet by nature, you're typically putting that in place of something else. And in this context, when we think of how people use most soy based foods, they are going to now be replacing something that's likely higher and saturated fat. If they're replacing, let's say fatty cuts of meat now with tofu or whatever else or dairy with, with a soy based milk. Now they're changing them out of saturated, fat and other components of the diet. And now we're seeing that there's a potential extra benefit for some of the aspects of soy. And you notice particularly within the soy protein there's a component there and soy in general seems to be interesting because you have a really interesting nutrient profile with other aspects, for example, like the isoflavone content, which is also talked about in other areas of cardiovascular disease. So it becomes really interesting then when we think from looking at one particular mechanism to then zooming back out and thinking about changes in dietary patterns of different food groups and what type of effect there will be, you know,

Prof. Jenkins:

Well, that's right. So you're quite right. And that's one of the things I think is we underestimate is the displacement value, and that's not found for all things we take, because some things we take because they're small, small calorie volume doesn't make a big difference, but I think soy does make a difference in displacement because it is a protein food, it's a calorie food. And so it does displace those foods which are associated with things you may not want to have a lot of in your diet.

Danny Lennon:

One thing I want to circle back to that, you also mentioned that might be an interesting point for people is you, you did mention that the FDA did approve this health claim in relation to soy and its ability to reduce heart disease risk through this lipid lowering effect, I think in 1999. And you noted that it's now currently in review and I suspect that that decision to review that claim might be one of the reasons why you and some of your colleagues have done this cumulative meta analysis that I think was published in 2019. Can you maybe first of all, let people know just what, what you found with that meta analysis, what that was that indeed based on some of the FDA looking into this review and then importantly, just as a side note for those interested what accumulative meta-analysis actually tells us?

Prof. Jenkins:

Well, I think what we tried to do, what we did we were worried and the FDA, I don't think, I think the FDA taking this very seriously cause they have, they've delayed their decision for, it must be two or three or four years. I'm not even sure how long it is. I've forgotten. <Laugh> how long this debate's been going on, but it's probably the near part of four to five years while they've considered, whether they should. And I think the reason why they thought they should is because they wanted things to have bigger effects. And what we were saying is, no, don't worry about the big effect. becauseif you portfolio something, then it's a valuable effect and therefore don't try and diminish your portfolio, try and build up those foods, which could fit into a portfolio. Anyway, I think we did have discussions with them.

Prof. Jenkins:

I have to say I, I went down from, from Toronto to to see them in Washington and cause I hadn't got certain papers with me. We had to, had to meet the FDA in the cafeteria <laugh> well, their offices they're very good. They came down, we had a chat about the issue and I think that they're, they're

looking at it in a way. So it might be the claim might be somewhat softened, but I don't think they would take the claim away. I don't hope they won't take it away. It may soften it. Just because it's a, it's a smaller effect, which is, I think is fine, but cause of all these things and cause we were worried about the, the concern that, so I may be ignored and that the vacuums in cell themselves should be, will be ignored.

Prof. Jenkins:

And they're very valuable food cause of that. We we've done a series of meta-analyses. We did one in 2010, which came out in BMJ Nutrition. And then more recently, as you said, we've done two more. And the last one came out in in the Journal of the American Heart Association. And that was the cumulative meta-analysis where you look since the time that they allowed the health claim, when they made the health claim, you say about 1999, right? The way through to the present, we added in sequentially, all the studies that had been done since then. And then the ccumulative meta-analysis allows you to look and see whether there's any inflection: Did it go down? Did it go up? No, it stayed pretty much the same, right? The way through. So I know, and we've got, we've discussed with FDA, they say yes, but we've changed our regulations. Well, that's fine. So the reason they're doing it is because of their regulations, not because anything's happened to soy. I think that's probably the important thing to say. And that's the reason why we published it. Because we want to say nothing has really happened to soy. It's just the regulatory change in FDA, a regulatory change that I think they could unregulate again.

Danny Lennon:

Yeah. But we're, we're seeing good consistency with, with some of those findings in relation with soy. So, so maybe if we take a turn to look at fiber and particularly viscous fibers, which are part of this the portfolio, can you maybe outline for people who are maybe unfamiliar or maybe unsure of what that term means? What exactly we mean by a viscus fiber

Prof. Jenkins:

Viscus fibers, fibers that have, that are sticky. In other words, things that are sticky that have got some viscosity to them so that if you put them in water, they don't just sort of slop around in the water and they thicken the water. So it becomes thicker and anyone who's, anyone who's ever cooked oatmeal and made porridge out of it will understand that as, as the thing heats up and cooks, it gets thicker. And part of that is the starch, but a large portion of it is the beta glucan, which you've got in the oatmeal and those substances. And you could, you can use the gums like pectins and these sort of things that found in fruit, you thicken your jams with. All these things are viscous types of fiber. They thicken, they thicken the fluid that you put them into.

Prof. Jenkins:

And they also probably thicken the contents in the gastrointestinal tract. That means that the bile acids that you secrete from your hepatic system into the gut, along with bile, that goes into the gut, along with pancreatic juice that those bile acids, which you've got there that normally emulsify the fat, you normally reabsorb, certainly by the terminal ileum, you reabsorb your bile acids. Bile acids are made from cholesterol so that if the bile acids actually leak out through the ileocecal valve, into the colon and then out into the pot, as it were when you empty your, your bowels, then you actually empty out cholesterol as biles acids, straight out. So that's basically what the viscus fibers do. They increase the thickness of the unstirred water there. And certainly when it gets to the terminal ileum, you're reabsorbing bile acids, a greater proportioned bile acids are going to get lost from the body. Therefore

the liver has to draw in more cholesterol to make bile acids out of that cholesterol. And so it lowers the blood levels. So the more you wash out more bowels, you wash out in the feces, the more the liver has to suck the cholesterol out of the blood to make more bile acids, to secrete into the gut. Because you broken the entero-hepatic circulation of biles acids through the gut, through the liver, and then back again. So you've broken that you put them out in the pot, so you've lost them. So that way it's, so if you like, so viscous fibers in a way are way of losing cholesterol from the body as bile acids.

Danny Lennon:

So you mentioned the beta cans. You mentioned some of the gums and pectin, psyillium. These would be the type of things we refer to as these viscous fibers. And we have this mechanism by where they're binding to bile acids, which is a way to essentially excrete cholesterol for, for lack of a better term. And that leads in the liver needing to produce more bile acids and use new cholesterol instead of recycled cholesterol, essentially. So we have this net loss of cholesterol. I did want to ask then on that, there's been some looking at the role of some non viscous fibers, for example, i[inulin-type] fructans, that seem to maybe potentially have that the same type of effect. Would they be working by a similar type of mechanism? Would they have a similar type of effect or is that still an unknown question?

Prof. Jenkins:

I would say that we've used inulin, and I have to say... You're right, Some people seem to say they get a cholesterol reduction with inulin and the fructans.We've not got any, any major effects. So I really don't know what they do. And, and I think a lot more studies need to be done. And I don't know any meta-analysis of inulin, or, or inulin-like products from the artichoke that have shown the effect. So, I mean, please give me a meta-analysis, let me see some more studies.

Danny Lennon:

Great. so let's talk about nuts. And I think this is a, a really interesting food group in general, and a really interesting case study for nutrition science, because the epidemiology on, on not intake is really positive across a whole range of different outcomes. And so if we look at nuts in particularly this ability to lower blood lipids, what is the main mechanism or mechanisms by which we suspect it's having this potential effect?

Prof. Jenkins:

Well, I think it's nuts are different. So if you take walnuts, they've got polyunsaturated fats and you would expect the polyunsaturated fats to have an effect on lowering cholesterol because poly the P:S ratio is, is one of the one of the drivers of LDL cholesterol got a, if you've got a low P:S ratio then you are going to get a, a different response in terms of about losing. You've got a high P:S ratio, so the more polyunsaturated fat, the lower so that's that, that, but almonds, for example will be mostly monounsaturated fat. So what does it do? For monounsaturated fats seem to have some small effect on, on LDL cholesterol, but a much bigger effect on HDL cholesterol maintaining the healthy cholesterol as it were. So you, you may get more of an LDL reduction with with walnuts and more of an HDL increase with almonds.

Prof. Jenkins:

So both of these things are ideal because you, they they're both useful in terms of improving the blood lipid profile, but the effect on LDL cholesterol with almonds will be relatively small unless you take a large amount of them, but you still get the benefit with HDL and some small effect in terms of LDL. So

we think the lipids in the, in the, in the nuts have a big effect probably the protein has some effect as well. The fiber may have a little effect where we don't think too much. It's not, it's not so much viscous, but also things like phenols and other things that one finds in the nut itself. Cause it's, if you like to poly-pill, it's got lots of components to it. So any of these components going to make a very small effect. And if you say, well, prove it, we can't It's too...

Danny Lennon:

Small, right. That that's, it, the effect in, in general for the food group is small. And then nevermind if we reduce that further to a specific component

Prof. Jenkins:

To what it is within we're in trouble.

Danny Lennon:

Yes. And, and I think that's a, a big problem when yeah. People try and apply that level of, of scrutinies to nutrition specifically, without understanding the nuances of looking at food groups and the complexity of a overall food matrix. And I suppose one of the other aspects that that could be part of the picture with nuts is indeed the phytosterol content of some of them. And indeed another pillar of, of this portfolio that you do mention is indeed plant sterols. This may be one that people are familiar with because they're now appearing in various different products that are produced by industry where that's spreads or yogurt drinks, et cetera. But they've seen these, these plant sterols and even stanols that have been aimed at reducing blood lipids. Again, can you maybe just give a, a quick primer for people on how that mechanism works and then the level of consistency and confidence we have in that area of literature?

Prof. Jenkins:

I think, well, the first thing, I think we've got a fair amount of confidence in that area because we've had many studies, many, and they all show about sort of 10% reductions for one to two grams of of plant sterol in the diet per day. We did a plant-based diet to be honest we called it the Simian diet. It was, we thought it was what the apes would've been eating and the gorillas and what have you. And we managed to increase our plant sterol intake just from regular foods to one gram a day. So that's that that's higher at high end of of what one might be able to consume one a more plant-based diet. They're found in oils, they're found in leafy vegetables. They're found in they're found basically associated with plant foods with high oil content.

Prof. Jenkins:

So that's, that's where you find them. So you'll find them obviously in oils and plant oils of various sorts how do they work? Well, interestingly, they work they're complimentary to the to the viscus fibers in a way, because they take out the actual cholesterol, not as bile acid, but cholesterol. And in your bile, you are secreting sort of 50% of bile acids, and 50% of your cholesterol is cholesterol as such. So even if you're not eating a lot of cholesterol, even if you're not even you're on a low cholesterol diet, they will still be effective, because they will take out your body's own intra circulation cholesterol in this case, not bile acids, but cholesterol in this case and take that out into the outside world. So that's, that's basically what they do. They block, they block cholesterol absorption.

Prof. Jenkins:

So they block cholesterol absorption in the same way, in many ways, similarly to the drug azetimibe, which we use. So you've got the, you've got the vis fibers, which are almost like cholestyramine you've got you've got sort of the soy proteins, which almost like almost like an HmG statin. You've got the plant sterols, which are like azetimibe and you've got nuts, which are like a combination of it all. So I think those are the, that, so basically it's reducing cholesterol absorption. Even if you haven't got a lot of cholesterol in the diet, cause it takes out the Ary cholesterol, which is your major cholesterol in your gut, the major cholesterol in your gut doesn't come usually from the diet, it comes from yourself, so that's why it's always useful.

Danny Lennon:

So we have even from a diet that is trying to focus on these, we might be able to get to something around a, a gram, one gram of these sterols. And then if someone is using some sort of supplemental form from these other products there's been trials that oftentimes look at two grams per day. One of the things that gets discussed and is about within that context of, let's say two grams a day where the timing and frequency of that comes in of is there a benefit to placing that alongside bigger meals versus not, or having it across the day versus in one go, et cetera? What we know in relation to the timing of this

Prof. Jenkins:

There haven't been, as I know of standard studies looking at this, so we haven't said you will take it all in the evening, you'll take it all in the morning and you'll take it throughout the day. Let's see what happens after three weeks or four weeks or five weeks. We haven't done that study. So that's a good study we done. It's not been done, but I have to say looking at our patients, who've been participants in trials. It doesn't seem to matter. They tend to take it with meals. They tend to take it easily. In the initial days, we looked in Marrin for example, and if they took it in margarines, mostly at breakfast time, not much at lunch, perhaps a little at dinner, it didn't seem to make any difference whether they did that or spread it out throughout the day. So we, we didn't, to be honest, it didn't become a major interest for us. sure it should be. It should be because they always say we take a statin at night. That's best because that's when you are synthesizing cholesterol in the liver most. So statin, take it in the evening, but we've not done the study.

Danny Lennon:

Okay. So maybe before we start finishing in terms of future work in this area of for either your group, other groups, people listening in, in terms of this area of potential lipid lowering via the diet. What interesting questions do you think still remain that hopefully over the next number of years can be looked at in terms of research? What are those outstanding research questions that, that you'd like to see some more data on?

Prof. Jenkins:

Well, I think my colleague, Dr. John Sievenpiper here in Toronto has got a big study going it's it's a study basically looking at cardiovascular disease, you know, you have a large study, it's going to be difficult, one to run, but it's going to be very valuable. It's going to show whether people who take the diet get less cardiovascular disease significantly than those who don't. And to what degree do they get less? In other words, does it give them the same sort of reduction as you get from taking half the statin dose? Because we only expect to get about half the reduction in cholesterol. So can we then make the direct comparison, say yes it will do them good and they will get half or will they get more? Will they get more

of a reduction in cardiovascular events than you even expect for the cholesterol? I mean, we don't know, but I think that's important. And because there are going to be many people as you know, who won't, whose adherence won't be that great. Right. even if they get a small reduction in cholesterol, will that actually sharp the benefit in terms of cardiovascular outcomes over the years? So he'll be looking at high-risk people and following them over over years

Danny Lennon:

So maybe to finish the final question, we'll leave it on an overview, pragmatic-type question. And in lieu of us not being at a point yet where everyone can just get easy, low cost access to our PCSK9 inhibitors and be done with it for those that are thinking about attempting to lower their lipids via diet, what would be the quick overview that you would give of number one, the foundations of where to start, and then just a quick recap of the elements that we've discussed today.

Prof. Jenkins:

Well, I really think my, my number one is take a plant-based diet, because that's going to cover you off in so many areas that we are not covering you off at present. So a plant-based diet, obviously get B12 levels checked so that you know, how, how you're doing. I think that's important. But then I think certainly portions of nuts, a handful of nuts a day, mixed nuts. These are fine. I think take soy. Soy products are good. Also supplement that with with peas, beans and little so that you can increase your total protein intakes quite comfortably. I mean, take viscus fibers, take oats, take oat bran, take take barley soups you know, with vegetables, these sort of things. So a vegetable barley soup with okra, to increase the viscous fiber and with some tofu slices to spice it up as it were, will give you protein, your viscus fiber and will give you many of the things that we want you to have and, you know, don't make it miserable for yourself as a breakfast with with sort of with fruit on the top of the oatmeal with some soy milk on it, it's really quite pleasant.

Prof. Jenkins:

You don't have to sort of hold your nose and just take it down. Do you know what I mean? it's quite pleasant, so you can make life very pleasant for yourself. And there, there are a number of of of helps that one can get in this area to start oneself on a do and try those. I know that Neil Barnard in Washington has got a group who've been putting together a lot of menus and ways of helping people to take these sort of dance therapeutically. And they're, they're very useful. Our patients have tried them and find them very good. So, I mean, I think that try and make it enjoyable. My advice is to, if you haven't tried any of these sort of foods go to a good vegan restaurant, if you've got one locally near you and just see how, what their foods are like, I mean, you know, try and go and see what the professionals are like when they're actually making these foods and they're pleasant.

Prof. Jenkins:

So make it enjoyable with yourself. And I think also think closely about the planet and think why you're doing this. It's just for your own health. Yes. But it's also for planetary health. And I do think that if people actually take some thought about a better planet and realize that that's how that that's the way you are eating, then I think that may encourage adherence more than just thinking, well, can I do a little bit more of this or a little bit less of this, which one always trends do as well tries to get rid of the diet. But if you actually have a sort of almost a religious goal that you are actually saving the planet then you don't tend to think as much. Can I do a little more of this or a little less of that? You actually do the things that should be done and you benefit from it.

Danny Lennon:

Thank you so much. Dr. Jenkins, not only for giving up all this time to come and talk to me today about your work, I've really, really enjoyed it. But more so at a grand scale for your contribution to the field. I know it's been incredibly insightful and enjoyable for me to read through your work over a long period of time. And I, like I said, I'm very honored and privileged to have to talk to you about that today. So I want to thank you for that and for coming on and talking to me to today.

Prof. Jenkins:

Well, thank you, Danny. And I hope it's useful. I hope I hope it benefits.