Building a Resilient Gut: The Secret to Immune Tolerance and Brain Health Transcript

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Introduction to Gut Immune Tolerance

What our next discussion we're going to be talking about all things. Gut immune tolerance. How to build a resilient gut. And you help me do that is my good friend Kiran Krishnan.

Kiran is a research microbiologist and a health and wellness expert who aims to make complex information understandable to all. He has founded a number of successful health and supplement companies over the last 20 years, including co-founding and leading Microbiome Labs, the preeminent microbiome therapeutics focused brand among health care professionals.

He's currently a co-founder and partner in three other companies that aim to revolutionize wellness care. He has conducted and published several research studies in scientific journals.

He has published chapters in scientific textbooks, reference books, has global patents, and is a sought after speaker on human health and the microbiome.

And he's kind of my go to when it comes to gut health. So, Kiran, welcome. Thank you Jason, it's great to be here with you. So we were just kind of chatting a little bit beforehand about some of the things that we're finding in the health and wellness, in the food spaces and kind of this crazy place we're in where we have various perspectives on food.

And there's just seemed to be this mass confusion about aspects of food, components of food, what's good, what's bad. And I really feel for our audience out there because the messaging is just all over the place.

And and one of the things that you, you kind of brought up was this idea of fiber and how this is being attacked now. And generally what I see when it comes to something, whether it's, you know, Fitbits and lectins and fiber and sugars and what had there's a grain of truth, forgive the pun.

I guess there's an element of truth in there, but it gets mixed up in this just sweet of misinformation, ignorance, and just like a lack of real understanding of the mechanisms and how the body works.

Food Confusion and the Fiber Debate

And so maybe just give me your perspective on just kind of what I just said, just generally speaking, how are you seeing all these things that that we're attacking saturated fats and then we're attacking seed oils and there's like all this stuff out there.

What's your take and how do you process all that? Yeah, it's it's it's a really, really difficult area to navigate for consumers just because they don't have the background in these things and they hear people that they that they respect and believe having one extreme view of the other.

And I think part of the problem is that the pendulum just kind of swings too far on both ends. Right? And it's over corrections of things. Saturated fat has probably been unjustly demonized to a certain degree.

There are still some actual problems with saturated fat for certain people, but then the then the the pendulum swings all the other way where it's like plants have anti nutrients and this, that and the other.

And so plants will kill you. Right. And so people go nuts and they lose their mind. So if we take something like fight tapes for example like phytic acid which you hear a lot about like oh this phytic acid and it and it chelating minerals.

And so if you eat plants that are phytic acid in it, it's going to pull minerals off your bone. Well that that does not happen in humans, right. There's no connection at all.

Like maybe you can take in a petri dish. You can put a bunch of calcium or something in the petri dish and throw some phytic acid in there and then see it coagulating or chelating, if you will.

But that doesn't happen in the human body, right? The phytic acid has no chance of pulling minerals off your bone, because bone resorption, which is the process of releasing minerals in the bone, is a very controlled process and there are lots of different cells involved in it.

So it makes sense, right? Like that's a pretty important thing. It's a pretty important. Like how vulnerable would we be as a species if our ancestors are walking around and they're just eating whatever they could and some things are eating are just sucking minerals through bone, right?

And then they're just like falling apart and dying, and they just keep eating them and keep eating them for thousands of years, you know, exactly. Without learning a thing.

Right. And so, so yeah, I think people just have to use a little bit of logic in some of this and go, wait, some of these things have been around for thousands of years.

We've been consuming it were omnivorous. We eat lots of different things, and that's the basis of our diet. Then you look at literature and you look at the studies.

And the studies that are important are outcome studies, right? Mechanistic studies and all that are interesting to look at to understand how some cellular processes work.

But when you think about diet, you really have to look at longitudinal and outcome studies. The diet that is that is the most well studied with, with some of the best outcomes is the Mediterranean style diet, you know, and that's a very balanced, you know, quite diverse diet.

It's got good fats. It's got fruits and vegetables and lots of polyphenols and all of the things nuts and seeds and so on. Right. And that's the ideal situation.

So if you are extreme then you are off the charts on on what is what is determined by the research to be normal. Let's tackle fiber for a moment. I mean, I see too many carnivore people, you know, on this saying, not only do you not need fiber, but meat can increase diversity of the microbiome, and that fiber is unnecessary and can be harmful and so on. It.

I've seen it with a lot of people claiming that that it irritates this, this irritable bowel. Right. Like it creates inflammation. And again, I think, okay, maybe a grain of truth in that for some people in certain circumstances.

But we can't just blanket statement say okay, because that might cause irritation in some people with certain conditions. Right. You already a dysfunction going on.

Then we can just apply that to to the ballot. Totally. It's it's no different than like, hey, weightlifting is great right? Like go and do deadlifts and squats.

That's fantastic for you. But if you're if you have two slipped discs, including so for that person. So it's a deadlift is not a good idea right. So then you can't go well for that person it's not a good idea.

So squats and deadlifts are bad overall right. That's and I'll be I'll even get more nuance with that too. Like there's a genetic component where some people's, you know, certain parts of their legs are longer.

They they break, etc.. And so for some people, actually squat may not be the ideal lift because of the way their body is structured in shape. And so this is likened to food where it's like we have genetic differences, we have

uniqueness, we have a constitution kind of going back to Ayurveda and Chinese medicine.

Why Fiber Matters for Longevity

And so and we're now doing this with, you know, the DNA company and various other, you know, genetic testing out there that we can start to tell, okay, this person doesn't digest saturated fats is what this person does better.

Right. There's all these little nuances where genetics come into play. Totally. Yeah, absolutely. And and just addressing the fiber issue. Right. So fiber is probably the most well-studied macronutrient there is as a as a great example of that.

Right. So it's also quite sad because it's easy to study. Or why do you think that is. I think that is because you can you can quantify fiber intake easier than you can quantify protein.

And fat intake. I think people because fiber sources are somewhat limited and, and different cultures consume them at different, at different levels. And also when, when you have certain studies that show real great promise, in terms of the effect of a nutrient, whatever it may be.

Then it's easier to get grants to study that and then further. Right. That's probably the biggest reason for it. It's no different than why we have, you know, 8000 studies, vitamin D, because as early studies started coming out, that vitamin D intake is beneficial when when researchers are starting right, grants grant offices are much more likely to give them money because they're like, yes, this is a really interesting scaling topic.

We want to learn more about it. And so it's easier to get grant money to do that. And so, you know, so so here's the latest meta analysis on it. Right.

So we're talking about a 2019 published meta analysis that looked at roughly 180, almost 200 published studies on fiber intake. And this had a wide variety of the types of studies interventional studies, longitudinal studies, and so on.

And is this soluble and insoluble fiber? It is. Yeah. So it's a total intake of fiber. I think the typical average intake of fiber is around 70% time, about 30% insoluble.

But if it's 5050, it doesn't really make a huge difference. But but predominantly soluble fiber. And that's the fiber that most people inadvertently even consume anyway.

And so what they found and the total number of person visits. Right. This is an important number, because when you look at how strong is the cohort of data in any given meta analysis, you want to look at either number of person years, which makes up the data or person visits.

Right. So among all of the studies, how many visits were there to the lab getting the bloodwork and looking at all different things? In this case, it was 153 million person visit.

Wow. Right. So same massive cohort mass report right. So here's what they showed. They showed that for every ten grams of fiber that you add to your daily diet, you reduce your all cause mortality that's dying from any disease by 10%.

And that was up to almost 45g. So you could go from the standard American diet of inadvertent eight grams ish of fiber and take down your your risk of all cause mortality to 45% less by just getting yourself to 45g of fiber.

Right. If that was a if that was a compound, you know, if I discovered a compound and I came out and said, hey, I got a compound that can cut your risk of dying from anything by 45%, right?

Number one, the first question people would ask is, well, that's a huge claim. So you must have huge data to support that. And I go, yeah, I am doing 200 studies, you know, 153 million person visits.

Oh, okay. Great. What is this miracle compound and why isn't it $1 trillion product? Well, it's fiber, you know, and it's it's just so fascinating to me that that kind of level of data is ignored.

And then people pick on small things like phytic acid and, you know, these little compounds that from some mechanistic study might show something is so it's it's mind boggling.

It's I think it's disingenuous. And it does a disservice to people in general. Yeah. No, even the funny. Right. Like we are really, really funny creatures.

Like, I've really discovered this in the sort of the health field, right, between the integrative practitioners. I know between the clients and patients that I've seen.

It's like we're just really funny. You know, it kind of reminds me, you know, what you're saying from like of walking, right? Walking is like the most boring thing to study.

It's the most rewarding thing to think about for many people, there's no way to debate, like the form of a walk and how you do it. Right. It's just it's just a walk.

And yeah, this is the thing that leads that same thing all cause mortality, longevity, health and well-being, walking. And it's just so simple. And and we know the data 7000 to 10,000, 7000 like the the nice sort of like sweet spot that is.

And if you get more than 7000 steps in the day, it's like all these benefit to it. I know we we debate those high intensity interval training or is it a Tabata workout or is it like this in UK?

Soluble vs Insoluble Fiber and Practical Intake

Yeah, those are good to you know, they have their place and like stick to the basics and it seems like. Well and people will spend, you know ungodly amounts of money on getting themselves a cold plunge system and the sauna and that red light and all that, and that's great.

You know, by all means, do those things, but don't do them in lieu of the basics of just walking, you know, and it's so simple. And the data on walking is way stronger than any of those other things and those the historical context of it.

Right? Yeah. And that's the easy part to for people to kind of wrap the head around. Right. Like, what have we been doing historically and thereby what has our system adapted to requiring or working with in some way.

Right. So so again, you know, not like all the biohacking in the world. You want to do perfectly fine. I have no issue with that. And I love saunas and I do some, some of the same fights.

Oh right. Yeah. Totally. But but anytime someone is knocking some of the basics, I think you have to be really suspicious of what they, what they have to say.

So let's get into some of the nuance with fiber. Right. Because again we mentioned insoluble. Insoluble. Maybe we can talk about the differences there.

You know we have something like Metamucil right. So if I hear oh fiber, I'm just gonna take Metamucil or I'm gonna take psyllium husk or, or I just stick to this sort of one strategy or philosophy when it comes to fiber, you know, is that going to be different than, you know, eating leek and, you know, green beans and you know, of wide variety of plant sources of fiber.

How should I think about that? And then maybe you can work in and we'll kind of maybe after that we'll wander into the territory of, of loss of immune tolerance because I can maybe hear somebody, some people listening to this already and saying, well, I try to eat this one food that has tons of fiber.

It's a healthy food, you know? I mean, not many people complain about the cucumbers, isn't it? Like they're not saying it's a it's an unhealthy food. And yet there are I've met people that they cannot eat a cucumber without, you know, having dramatic symptoms.

And so this is the case actually with a lot of plants in the vegetable family, is that people will eat them and they say it just absolutely wrecks me.

Like there's just no way I can eat that. So how can I argue and benefit? You know, why is something so healthy that contains so much fiber just absolutely wrecking me?

So we'll get maybe we even get to that toward the end. But what's the difference in soluble soluble. Now how do we think about these things. Where are where do we run into some some danger or threat.

Right. Potentially. Where do they have it. Right. When they say fiber you got to be careful with it. Yeah. Well yeah that's that's a really important thing to address.

So I think a couple areas. Number one so with with fiber as important as it is I think you want to you want to be measured in in ensuring you're getting adequate amounts.

Right. And what are adequate amounts. While I go to 40 to 50g a day. Because I know up to that point it's a linear, a reduction in all cause mortality after the 40, 40, 45 to 50g, it the line starts to flatten out in terms of its impact on all cause mortality, meaning that there's probably some degree of diminishing return.

So I don't see the need to go beyond 50g. There are days where I eat more than that, but that's my goal is to get to that point now. And one piece of advice here about just people think, oh, 50g, how do I measure that? Right.

And what I've learned with this is like whenever it comes to protein or fats or sugars or whatever, I'm trying to like gauge is that there's like general like a what I take is like a week and it's okay.

I look at the content of a potato and whatever. I'm like, okay, so I get a rough estimate. I don't know either. Like, you know, so so you just kind of take that little study period and you go, okay, this is what I'm getting.

And then you just have a loose feel, right? Like, I'm sure you're not every day counting and measuring and track and spreadsheet thing and. Right. So you just get it.

You wait for for most people, it just takes up a little bit of like what these foods contain. And then getting a sort of sense. Yeah. And I mean, you can use ChatGPT and I, I totally so it's oh easy these days.

So the way I do it is and you shouldn't go from your normal standard American diet of eight grams per day to 40g. The next day. Right. You want to taper it up?

My my recommendation is usually adding somewhere around 4 to 5g for each day for a week. So meaning that if I'm getting ten grams this a day regularly, then for the next week I'm doing 15g.

You know, seven days. Let my body get used to managing the fiber and utilizing it properly. Then the next week I'm getting 20g a day, then 25, and so on.

The way I do it, because I want to ensure that I'm reaching my goals, is I did exactly what you suggested, which is I took about a week's worth of eating and looked at some of the common things I eat.

The tend to have fiber in it, so I eat a good amount of nuts and seeds. I eat a lot of like broccoli, you know, beans. So I just looked at a few things that I eat and I, and I gauged with the help of ChatGPT approximately how much fiber is in my standard bowl like that I have at home, like, you know, and you can actually just scan or take a picture of it and then upload it to chat and ask it to, assume how much fibers in it. Wow.

It can absolutely do that. And it's and it's in your ballpark. Right. Like that's the main ballpark. Yeah. And keep in mind that the studies when you look at those studies and that many, you know, that many person visits and that large scale of a cohort, they're not measuring this stuff like precisely.

It's all rough, right? It's possible -15, 20% here and there. It's about the consistency and the cumulative effect of doing it over time. That's really where the big benefit comes from.

So if you're like 28g one day and 40g the next day and 30g, it doesn't matter. You're getting it in and you're accumulating the benefit. There. So so I averaged out and to me it was about I'm getting about 20, 25g a day from just the regular stuff.

I eat.

Understanding Immune Tolerance in the Gut

And so what I decided is that, okay, I'm going to then supplement 20g a day so that between what I normally eat and the supplementing, I know I'm getting around 4045 some days a tire, some days it's a lot less.

And the way I supplement and this has another benefit is even just basic psyllium husk. And I look for fiber products that may have a small variety of fiber.

Maybe it has some acacia fiber in it, some inulin, some psyllium husk. Right. But the easiest thing is psyllium husk. And I use the organic India version of it because it's just super clean.

It's there's nothing else in it but psyllium husk. Right. And I do about ten grams of it in water before meal. Drink it down. It's not a great experience because there's no flavor or anything to it, but you just drink it down and you do that about 10 to 15 minutes before you eat, and then you eat.

Now the other side benefit of that is it acts like a GLP one agonist, right? It slows down gastric emptying and made to eat less food. It slows down and blunts the glucose response, which I actually tested on myself for a three week period that I had a CGM, a continuous glucose monitor.

I looked at all these foods and I looked at like taking fiber before the food, taking fiber after the food. And I would do like, you know, even something as is insulin genic as like for me, bananas actually very insulin genic.

Even more so than like a donut can be. And so I started using bananas and I would take like ten grams of fiber before the banana or, and then another time do it without the fiber.

And you'd see like I would want the glucose. The glucose response is like 40, 50%, right dramatically just from taking the ten grams of fiber. So I know that I'm fighting against insulin resistance.

I'm improving my metabolic health. So it has all of those benefits, along with the fiber going down and then feeding the microbes in the in the large bowel and then them converting it to really important compounds that my body needs to fix and repair things, you know, and maintain structures, especially the barrier system and also immune cells needing it.

Right. And and fiber. We'll talk about why. But fiber plays a very important role in the next thing we want to talk about which is immune tolerance. Right.

And the loss of immune tolerance. And I actually just just produced a white paper on this because we're developing some products to really look at, revamping immune tolerance, because it's becoming clear that loss of immune tolerance is at the root of so many chronic conditions.

Right. And not only because your immune system is now inadvertently attacking things it shouldn't attack. Yeah. And also, maybe you can just define immune tolerance for for the issue, which maybe aren't quite familiar with what

that is.

Sure. Yeah. And just the, the way to really understand immune tolerance. Is this your immune system is of course, the only system in your body designed to defend you.

Right? That's a defensive system. Your immune cells are born out of your bone marrow or your thymus. Those are the two parts of your body that produce immune cells.

Now, when immune cells are born, they're born with capabilities but not with any knowledge. Right. Your immune system is a very important system that needs to learn how to adapt to your environment, because everyone has different things that their immune system needs to defend them against. Right?

You are all the way in the West Coast. I'm in the Midwest. We actually have different antigens. We have different viruses. We have different things that could harm us even in the same country, just being a couple thousand miles apart.

And so your immune system has to adapt to your environment. My moon system has adapt to my environment. That's why biologically, the immune system is designed to not have any sort of ingrained or inbred memory as to what's bad and good.

It's supposed to learn on the fly, right? If I get up right now and I moved to India, it's going to have to adapt to that crazy environment compared to this crazy environment.

Right. And so how does it do that? So it's born with capabilities. The analogy I give is like imagine your immune system is an army that has all the tanks, all the missiles, all the guns, all the helicopters, everything it needs.

But it has no general and has no plans. It doesn't know who the enemy is. What's a no strategy at all, right? It doesn't know where the borders are. It doesn't know what's good and bad.

It just is ready to go. It needs instructions the way we've developed is the immune system gets its instructions largely from the microbiome. The microbiome is the outward facing component of the immune system, right.

So the microbiome is sitting in the mucosal tissue most of the inside part of your body, most of your orifices are all lined with the mucosa in that this would be like military intelligence, right.

It's like the first people to get information and then relay that down to the ones that are actually going to take action. Yeah, exactly. It's it's the it's you're like first line of defense are some of them can fight for you.

Many of them don't. Some of them are just like like you said like informants if you. Well. Right. So imagine you had a neighborhood watch. That's that's often the analogy I use.

Like your, your, your microbiome is the neighborhood watch, meaning they're all watching out the windows and keep an eye on what's happening in the neighborhood.

And then they will signal to the cops or the military when something bad is going on. And in fact, the, the, the immune system understand what to attack and what not to attack, right?

So a loss of immune tolerance means that that relationship and the tutoring and the communication between the immune system and the microbiome is disrupted.

And as a result, the immune system goes a little bit haywire and it attacks all the things it shouldn't attack. And that would be food particles, environmental antigens, of course, your own tissue in the case of autoimmune conditions.

So it's going haywire. And and it tends to upregulate inflammatory mechanisms. Right. And I can explain that for a little bit. Now let's maybe let's get into how your immune system samples the environment and how it does so in the

context of the microbiome.

Right. So you've got let's and let's take the gut because that's the largest site of sampling in your body. And I think most people listening have heard this term like most of your immune system is in your gut. Right.

But what does that actually mean. Well, that means that about 70, 80% of your immune sampling tissue is in your gut. That and there's a good reason for that, because most things you encounter in your environment are going to end up in your gut in one way or the other.

But if I'm walking around and I breathe in a virus, a cold virus that's out there, right, the virus is going to go into my upper respiratory tract. It's going to get trapped in the mucus in my upper respiratory tract, and then that mucus is going to get sloughed off by something called a mucus elevator.

And then it's going to push it down to the back of my throat. And I'm going to swallow it. So that virus with the mucus is going to end up in my gut. If things going through your eyes, your ears, all of that drains to the back of your throat, through your Eustachian tube, right?

So everything virtually, unless it's trauma and penetrates through your skin, is essentially going into your gut. Of course, the biggest introduction of foreign materials into your body comes from food and drink.

And so all of that, of course, is going to your gut. So your body's designed to have the largest immune sampling site in your gut. So the way that structure is, is set up is you've got this mucus layer in the mucus layer, you've got all the microbes living.

And then that mucus layer has a certain thickness to it. And the bottom part in the mucus layer has very few microbes in it. Right. Most of the microbes live in the top part of the mucus layer.

That mucus layer in the small intestine sits on top of what we call the intestinal epithelial cells. These are the single cell layer cells kind of sitting shoulder to shoulder that that form the final barrier before things enter your actual circulation.

Right in the first part of the circulation is what we call the interior circulation, where things, most of the things actually go to the liver, but from there they're going to go throughout the body.

So so you have to imagine this is our barrier. This is our gate system. Right? So if the body is a fort, this is the walls of the fort. And sitting on top of the walls of the fort, which is the top of the mucus layer, are the are the informants are the neighborhood watch.

Right. They're sitting then watching what's coming in. So they're sitting up there now the the first and the most active immune cells that are constantly sampling things are cells called dendritic cells.

Now, the reason they're called dendritic cells is because they have these dendrites which look like little tentacles that can extend. Right. So you've got the the cells the Intel.

So until your cells sitting shoulder to shoulder on top of that is a mucus layer in the mucus layer of the microbes. And everything that comes into your body comes into that mucus layer with the microbes there.

The dendritic cells are actually on the other side of the intestinal epithelium, but they're a little dendrites can sneak in between your intestinal epithelial cells and go into the mucus and start sampling things.

Right. So it's sampling like, oh, what is that? That's a food antigen. No, that's an environmental particle. That's a bacteria. That's a virus. Right now while it's sampling things the commensal around it are activating certain receptors called toll like receptors.

When they activate toll like receptors and kind of present antigens to the dendritic cells, the dendritic cells know

that those antigens are pollen antigens.

We don't need to attack it. Right. So they're getting that signal from the microbiome. The microbiome is sitting next to let's say a peanut protein that comes in right.

And the dendritic cell is sampling the peanut protein. The microbiome is essentially going, hey, you don't have to attack that, right. So we need to build tolerance against that.

So the dendritic cell learns that. It then goes and activates T cells. And then it activates T cells to say hey T cells we need to tolerate this peanut protein.

So the immune system needs to learn about this. Well how does it teach the rest of the immune system anyway? You see peanut protein don't attack it is that T cell then goes and activates a B cell that makes an antibody against that.

That protein and that antibody typically is called IGA, right. It's not an IGA or IgG E, which is a hypersensitivity response. It's a IGA antibody. Then that antibody secreted into the mucosa.

And then anywhere that that peanut protein is seen, it might bind to it and kind of neutralize it. But the peanut protein bound with an antibody indicates the immune system that, hey, this thing is tolerant.

We don't need to attack it, right? But that's that whole process basically happens with food borne antigens, with environmental articles, with bacteria, viruses and all of that that the microbiome struck at the microbiome teaches the immune system not to attack. Right.

So then you look at what happens when you lose immune tolerance. So so here's what happens. And that's also how you produce lots of secretory IGA. Right.

Which is really important because secretory IGA acts as like the first line of defense in all your secretory fluid.

How Loss of Tolerance Drives Inflammation

So anything that's coming in, it's just binding and neutralizing and teaching the immune system up. This stuff is neutralized. Don't worry about it. You don't have to attack it.

And when IGA binds to something, it doesn't elicit inflammatory response. It elicits a tolerance response. Now. And that's one of the things that we can test too.

It's it's often a really good test and a good test because if it's if it's low, will we get a problem? Like that's not good. We need the body to be using, you know, stigma or secretory IGA if it's really high.

That also indicates that that's a good sign. The body's producing it, but it indicates dysfunction. There's something going on. There's an alarm bells going off that we're producing a lot of this stuff.

So something something's happening that we need to be aware of. Right. So yeah, it's really like those, those two extremes that indicate something's actually off.

Totally. Yeah. And it's a great marker because it's a marker of like your body's immune system functioning the way it should. And there is another player in that whole game, which I didn't mention is something called a regulatory T cells.

The regulatory T cells are the T cells that monitor this whole interaction. And and as long as this tolerant response is happening, it's happy. And it's just sitting there monitoring it right now, let's say, you know one of your dendritic cells kind of goes haywire.

Doesn't get the right communication from the from the microbiome and takes that peanut protein and goes, oh, this is an enemy and presents it to the T cell, the the helper T cell as an enemy to get the helper T cell to elicit an immune response against, then that regulatory T cell comes along and goes, no, no, no, no, no, you messed up right.

That's not a enemy. You need to dampen that down. Now, that whole process is so important that that was the Nobel Prize in medicine in 2025. The discovery of the regulatory T cell and its mechanisms was awarded to three individuals who played a significant role in discovering that over the last ten years.

And that was the Nobel Prize in Medicine this year, which is fascinating. That's how important it is. Right. And so and the microbiome is at the core of that whole mechanism.

So let's say you've got a dysfunctional microbiome. You've had poor lifestyle choices, antibiotics, whatever it may be. Your dendritic cells are still they're sampling right with their little dendrites everywhere.

But it's sampling things without the microbiome effectively sitting next to it and saying, hey, don't this is fine. This is tolerant, intolerant. So it starts this sample things as if those things are problematic.

And so then it pulls those antigens in to process called phagocytosis. It eats the antigens of you well, takes it to T helper cells and presents it to T helper cells in a different way than it would have if it saw that antigen in the context of the microbiome.

And then as a result of that presentation, the T helper cells activate a whole bunch of other immune responses, like your killer T cells and natural killer T cells and so on.

And then those cells come in to that area, go, oh shit, we got to attack this thing and it starts attacking at the same time, because it's not a tolerance response, because it's not seeing the antigen in the context of the microbiome, you're not getting IGA being produced against it.

Then there's another part of the immune system that senses that, hey, you are low IGA. What does it do in response to that? It upregulate IGI, right? So people with histamine intolerance, mast cell activation, you know, allergies, asthma, all of this overreactive inflammatory hyperactive immune responses tend to have more IgG in their secretory fluids in IGA because your body's going we need some antibodies in this in this in secretory fluid which is our first line of defense.

We're not getting the signals to make IGA because the microbiome is not providing those signals. So we're going to make IgG instead. The problem with it is when IG binds an antigen it recruits cells call it Sana fills in basophils which then release histamine and all kinds of stuff to create this hypersensitivity response.

Right. So then what is effectively happening is because the microbiome is not present in the right way to facilitate the tolerance response to all of the common things that your immune system shouldn't be attacking.

Your immune system then starts to perceive those things as things that should attack. And on top of that, it's creating a blanket inflammatory response by up regulating IgG response everywhere else.

Then you have this other danger of call. It's called a bystander effect, right? The bystander effect is where any time you've got inflammatory responses against things and inflammatory responses are facilitated by the early part of the immune system, called the innate immune system.

The innate immune system is kind of the analogy I was used is like, imagine you had a window open and then you had a bunch of you had a bunch of mosquitoes coming into the window and you're like, oh God, I got to kill the mosquitoes.

You run into the room and you start bloating the whole room, right? And you're going to kill the mosquitoes. Absolutely. But you're you're going to burn the wall a little bit and you're going to burn to break the windows,

probably. Right.

So that's what the innate immune system does. It goes, oh shit, something's there. We don't know what it is. They're just going to come to that area and bombard everything, right?

And then they're supposed to then hand off the process to the adaptive immune system. And they in my analogy, the adaptive immune system would be the more reasonable.

But slower individual that comes into the room and goes, okay, let's turn off the blowtorch. Let's use like a little flyswatter and let's close the window properly.

Right. So that's a more adaptive gentle response. But the innate system gets there faster. The blood guy gets there faster. So he's going to blow some stuff up.

And so during the innate immune response your own cells are going to get damaged. Right. So debris from your own cells are in that area. Macrophages and dendritic cells which are called antigen presenting cells come to that area and start eating up everything that's in that area for two reasons.

One is to start cleaning things up. Number two is to start presenting potential antigens to the next part of your immune system, which is your adaptive immune system, to try to tell the immune system what was the culprit.

Ultimately, right. It's kind of the idea is like something bad happens, something caused a issue. We're going to come and bomb this area, and then we're going to look through the debris and go, what was that thing?

And that's the job of the dendritic cells and macrophages in that role. They come in, eat up everything, start presenting antigens to the T cells and B cells.

Now the regulatory part of the of the immune system, the T right part observes that whole presentation. And when it sees things that you shouldn't be presenting like your own tissue accidentally, it stops it.

But if you don't have a healthy microbiome and you're not up regulating the T rag, and the T rex system is very dependent on your microbiome, then you're going to get an accidental presentation of your own proteins.

Then your immune system goes on. That's one of the culprits, and develops this whole antibody response against your own protein. That is an autoimmune process which is autoimmune, right.

So this is how you can go from intolerance being kind of an annoying thing. Like, oh, there's certain foods I can eat I want to stay away from that is my ever yeah, just stay away.

Just avoid them. Just, you know, because I don't tolerate them. If that keeps continuing in your body, you'll become less and less tolerant of more and more things, including your own body.

At some point. Right. So so it is it. This goes back to an early part of our discussion where it's like, oh, there's all these plans and things that I can't eat.

And I, it doesn't agree with me. Well, it doesn't mean you just avoid all of that because it's a strong indication that your system is moving in the wrong direction, and it's only going to get worse.

Right? Absolutely. Yeah. And so we have a few more minutes here. Caron, I want to be mindful of your time, you know, and what I want to kind of remind people of is you mentioned the microbiome being a central, playing a central role in sort of regulation of the immune system there.

You know, what comes to mind for me is poor digestion, lack of hydrochloric acid production, poor vagal tone, inability to move the food through the GI tract, sets up purification, sets up fermentation starts to throw off the microbiome can't break down a proteins and other peptides.

Now those are being sampled and peptides or long chain proteins are viewed as as a foreign body instead of amino acids. So you know, we're not we're not breaking down the amino acids in our brain is not working as well.

We're not producing dopamine, serotonin, acetylcholine, etc., etc.. So it's to me, I think about the dysfunctions that happen, right? Head injuries, lack of sleep, poor food choices, antibiotics, birth control pills, you know, not chewing our food thoroughly, eating at the wrong time of day, eating too much.

Right? Like there's there's all these things that probably many of us have partaken, in, in our, in our life, especially in childhood, when we just don't know better.

Right. Or for me, it was pre-internet, like I didn't know anything. Right. And so there's a lot that can go on there. So maybe you can kind of just give me in the last few minutes here, what are some things that people can focus on?

What can they do to kind of rebuild this system and gain that tolerance? Yeah, really, really easy. And, really quite important. And I want to make one quick connection because we, I know the program overall is about toxic brain with the toxic gut and everything we talked about with loss of tolerance.

Right. What that ends up doing is constantly activating the innate immune system, causing inflammatory responses to things that shouldn't be creating inflammatory responses.

Now, those inflammatory responses that start in the gut end up going throughout the periphery, including the central nervous system. This is big. Like right? Like that has been active.

Five Pillars to Rebuild Gut Resilience

It's massive. This is like the foundation of the vast majority of chronic illnesses, which is why they were given the Nobel Prize for discovering this tolerance issue.

Right. And when you have this constant inflammatory activation because of loss of tolerance, you also get the same inflammatory activation in the central nervous system through something called micro glial cells.

These are like the macrophages and dendritic cells of the central nervous system. So now stuff you eat and things in your environment that shouldn't be causing inflammatory responses, are causing inflammatory responses in your gut.

And then moving up your central nervous system. Now your brain is inflamed and your brain is getting damage. Your body's always as microglia like when those get activated neuron fire, they're combined to turn off. It's actually really hard.

I remember learning this from a function and they're all just like, you know, once those are on and they're going crazy, that's difficult. It's very hard to regulate them because the Treg cells that we talked about in other parts of the body, they don't work as well or as efficiently in the brain. Right now.

The brain has like its own immune type of system. And so, so yes, that is where this loss of tolerance and toxicity in the gut directly impacts the brain.

And and that is one the microglial activation and inflammation in the central nervous system is central to anxiety, depression and neurodegenerative conditions and all that.

One quick example of that is take tryptophan for example. Right. Or tryptophan is the precursor to serotonin and melatonin. You need that and you need to make your sleep hormone and your happy hormone in your central nervous system.

But when you have microglial activation and inflammation in the central nervous system, tryptophan is not converted to melatonin and serotonin. It's converted to something called new renin and colonic acid, which are both

neurotoxic and and enhances anxiety and depression.

Right. So so the precursor to your happy hormone is now being converted to something that makes you depressed and toxic to your brain. So that's just how impactful inflammation is.

So let's break down quickly what people can do. I actually break it down to five pillars, and you have to do at least one thing that each of these five pillars.

And if you if you skip 2 or 3 of the pillars, you're really not going to get the same response. So you want to become conscious of being of having this cumulative effect.

Pillar number one is food, right. Like we talked about earlier, you want to try to increase the diversity of your diet. You want to get enough fiber, enough polyphenols in enough lean meats, enough good healthy fats, you know, olive oils and all the good stuff that no fresh food.

Like they have enzymes in them, like real live foods. Yeah, exactly. Bitters. You want to get your digestive bitters in to help with the digestive process.

And so food is one of the most impactful things on your microbiome. And I mentioned earlier that your microbiome is required for all this tolerance effect.

Not only is it the presence of the microbiome, but a byproduct that they produce from digesting fiber called short chain fatty acids, acetate and butyrate are two short chain fatty acids made from fiber digestion that are critical for this whole immune process to occur, to build tolerance and make IGA right.

So so a diet is number one. And number two is stress management. So stress is one of the biggest drivers of dysbiosis. Every bout of stress you have is like taking a small dose of antibiotics.

Stress creates dysfunction in the gut microbiome. Makes the gut more leaky. And of course put your brain in an inflamed state as well because it activates the HPA axis, the hypothalamic pituitary adrenal axis, and puts you in fight or flight.

So stress can be very profoundly effective against your gut and your brain. Number three is lifestyle factors. And the most important lifestyle factors to me are adequate movement.

So the simple walking we talked about right. And resistance training if you can do it which is would be fantastic because when you lift weights against a resistance and your muscles contract against the resistance, they release compounds called myo kinds.

And myo kinds have a profound effect on sealing up the lining of your gut and improving the balance within your microbiome. So myocarditis can act as like a your endogenous, your endogenous, you know, prebiotics if you will.

Almost. And then the other thing is the major kinds also reduce cortisol and stress. Right. So so pillar number three which is weight lifting and movement actually helps.

Pillar number two which is stress. Right. The other thing, and pillar number three in the lifestyle is sleep. Make your gut microbiome is a diurnal system.

It needs that rest period because that's where it does all of the housekeeping stuff and repairs the lining and all of that stuff. You need 6 or 7 hours of sleep and varies from person to person.

If you're using, you know, things like the aura, it can tell you what you see, proficiency is and all that. And I think people really need to get much more focus on their ability to sleep.

Number four, pillar number four is exposure. And what I mean by that is exposure to good stuff like in the outside

environment, getting out, moving, going through hikes and all that touching dirt and rocks and all that, and then also reducing your exposure to things that kill your microbes.

So, you know, really strong household cleaners, personal care products that are loaded with antimicrobials and all that. And then the last one and it's deliberately last is supplementation.

Because if you don't do anything in these four, you can't out supplement all of those other bad habits. Right.

Where to Find Kiran Krishnan

So and with supplementation probiotics like the spore based probiotics prebiotics good fish oils polyphenols in a basic things you don't have to get super exotic with your supplementation.

If you're doing all four of those things and add some basic supplements to it, that cumulative effect will have a profound outcome for you over time. This is great promises. It's always amazing.

I love talking to you. I feel like we could geek out on on the microbiome and and the immune system and all things health for a long time. You're a wealth of information, so tell people where they can find more of the work that you're doing today.

Yeah. You know, I post a lot on my Instagram, which is the handle is at Huron Biome. Kiren bio on me. And one of the things people will see out there is I also offer a microbiome course called Build Your Resilient Gut a.

People want to take a course and understand it deeper and understand more action items and things they can do for themselves. And then if you put my name in YouTube, you'll find lots of interviews that people have done that have, and they've kindly uploaded them to YouTube as well.

So lots of information in all these places. Amazing. Karen, good to see you as always. Thank you so much for coming on. My pleasure. Thank you. Jason.