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

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Introduction and Guest Background

People just have to use a little bit of logic in some of this and go, wait, some these things have been around for thousands of years. We've been consuming it, we're omnivorous, We eat lots of different things.

And that's the basis of our diet. Then you look at literature and you'll look the studies. The studies that are important are outcome studies, but when you think about diet, you really have look long to known outcome study.

This is Dr. Talks. Well, in our next discussion, we're going to be talking about all things gut, immune tolerance, how to build a resilient gut. And to help me do that is my good friend, Karan Krishnan.

Karon 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 supplement companies over the last 20 years, including co-founding and leading Microbiome Labs, the preeminent microbiome therapeutics focused brand among healthcare 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 and scientific journals has published chapters in scientific textbooks, reference books, has global patents and is sought after speaker on human health and the microbiome.

And he's kind of my go-to when it comes to gut health. So Karan, 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 and the food spaces and kind There just seems to be this mass confusion about aspects of food, components of what's good, what bad.

And I really feel for our audience out there because the messaging is just all over the place. One of the things that you kind of brought up was this idea of fiber and how this is being attacked now.

Generally what I see when it comes to something, whether it's, you know, phytates and lectins and fiber and sugars and what have, 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 suite of misinformation, ignorance, and just like a lack of real understanding of the mechanisms and how the body works.

Diet 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 they were 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 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 respect and believe having one extreme view of the other.

And I think part of problem is that the pendulum just kind of swings too far on both ends, right? And it's overcorrections 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 pendulum swings all the other way, where it is like plants have anti-nutrients and this, that and the and so plants will kill you, right?

And so people go nuts and they lose their mind. So if you take something like phytates, for example, like Phytic acid, which you hear a lot about, oh, this Phitic acid and it chelates minerals.

And if eat plants that have Phtic acid in it, it's going to pull minerals off your bone. Well, that does not happen in humans, there's no connection at all.

Like maybe you can take in a Petri dish, you could put a bunch of calcium or something in the Petrie 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.

The phactic acid has no chance of pulling minerals off your bone because bone resorption, which is the process of releasing minerals from the bone, is a very controlled process and there are lots of different cells involved in it.

Which makes sense, right? Like that's a pretty important thing. It's pretty, 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 they are eating are just sucking minerals off their bone.

right and then they're just like falling apart and dying and they just keep eating them and keep beating 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 1000s of, years we've been consuming it we're omnivorous we eat lots of different things And that's the basis of our diet.

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

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

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

So if you're extreme, then you are off the charts on 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 thing.

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. I've seen it with a lot of people claiming that it irritates 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 with certain conditions, basically already a dysfunction going on, then we could just apply that to the lot.

Totally. 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 have two slipped discs.

Or broken leg. So for that person, squats and dead lifts is not a good idea, so then you can't go, well, for that person's had a good idea. So squats and deadlifts are bad overall, right?

And I'll even get more nuanced with that too. Like there's a genetic component where some people's, you know, certain parts of their legs are longer, they, et cetera.

And so for some actually squat may not be the ideal lift because of the way their body is structured and shaped. This is likened to food where it's like, we have genetic differences.

We have uniqueness. we had constitution kind of going back to Ayurveda and Chinese medicine. And so, and we're now doing this with the DNA company and various other genetic testing out there that we can start to tell, okay, this person doesn't digest saturated fats as well.

This person does better, right? There's all these little nuances where genetics come into play. Totally, yeah, absolutely. And just addressing the fiber issue, right?

So fiber is probably the most well-studied macronutrient there is, as a great example of that, so- Real quick, is that because it's easy to study? Or why do you think that is?

I think that is because you can quantify fiber intake easier than you could quantify protein and fat intake in people. Because fiber sources are somewhat limited and different cultures consume them at different levels.

And also 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 even further.

That's probably the biggest reason for it. It's no different than why we have 8,000 studies on vitamin D because As early studies started coming out that vitamin D intake is beneficial, when researchers are starting to write 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 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. Um, and is this soluble and insoluble fiber?

It is, yeah. So it's a total intake of fiber. I think the typical average intake a fiber is around 70% soluble, about 30% insoluble. But if it is 50-50, it doesn't really make a huge difference, but predominantly soluable fiber, and that's the fiber that most people inadvertently even consume anyway.

And so what they found, 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 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 blood work and looking at all different things. In this case, it was 153 million person visit.

Wow. So massive cohort. Massive forward, right? So here's what they showed. They showed that for every 10 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 45 grams.

Fiber Intake, Supplementation, and Blood Sugar

So you could go from the standard American diet of inadvertent eight grams-ish of and take down your risk of all-cause mortality to 45% less by just getting yourself to forty-five grams of fiber, right?

If that was a compound, you know, if I discovered a component and I came out and said, hey, I got a compund that can cut your risks 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 have 200 studies, 153 million person visits. Oh, OK, great. What is this miracle compound and why isn't it a trillion dollar product?

Well, it's fiber. And it 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 these little compounds that from some mechanistic study might show something.

So it's mind boggling. I think it is disingenuous and it does a disservice to people in general. Yeah. I mean, humans are funny, right? Like we are really, really funny creatures.

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

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

So the boring things to think about for many people, there's no way to debate like. The form of walk and how you do it. Right. it's just, uh, just a walk.

And yet this is the thing that leads the same thing, all cause mortality, longevity, health and wellbeing, walking. And it's just so simple. Yeah. We know the data, 7,000 to 10,007, like the nice sort of like sweet spot that is, and if you get more than 7000 steps in a day, it is like all these benefits, right?

And we debate, oh, it was a high intensity interval training, or is it a Tabata workout? Or is like, okay, yeah, those are good too. You know, they have their place and like stick to the basics.

And it's totally 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.

That's great. Uh, by all means do those things, but don't do them in lieu of the basis of just walking. It's so simple. And the data on walking is way stronger than any of those other things.

And so is the historical context of it, right? Totally, yeah. That's the easy part for people to kind of wrap their head around, like what have we been doing historically and thereby what has our system adapted to requiring or working with in some way.

So again, 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 of those things myself.

Yeah, totally. But anytime someone is knocking some the basics, I think you have to be really suspicious of what they have say. So let's get into some of the nuance with fiber, right?

Because again, we mentioned insoluble and soluble. Maybe we can talk about the differences there. We have something like Metamucil, so if I hear, oh, fiber.

I'm just going to take MetaMucel or I'll take psyllium husk, or, I just stick to this sort of one strategy or philosophy when it comes to fiber is that going be different than eating leek and green beans and a 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're wander into the territory 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 and it's a healthy food.

You know, not many people complain about cucumbers, isn't it? Like they're not saying it said it to 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? Why is something so healthy that contains so much fiber? just absolutely wrecking me.

So we'll get, maybe we can get to that toward the end, but what's the difference in soluble, soluable? You know, how do we think about these things? Where are, where do you run into some, some danger or threat potentially?

where did they have it right? When they say fiber, you got to be careful with it. Yeah. Well, yeah, that's it, That's a really important thing to address.

I think a couple of areas, number one, so with, with fiber as important as it is, I you want to, You want be measured in, in ensuring you're getting adequate amounts, right.

And What are adequate amounts while I go to 40 to 50 grams a day? Because I know up to that point, it's a linear reduction in all-cause mortality. After the 40, 45 to fifty grams, 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 50-grams. There are days where I eat more than that. But that's my goal is to get to And one, one piece of advice here about how, cause people think, oh, I don't have 50 grams.

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 generally like a, what'd I take is a week.

Okay. I look at the content of, of a potato and whatever. Like, okay. So I get a rough estimate. Cause I dunno either, like I, you know, so, So you just kind of take that little study period and you go, Okay, this what, and then you, just have a loose feel, right?

Like. I'm sure you're not every day counting and measuring and tracking and spreadsheeting. And right. So you just get it. But for most people, it just takes up a little bit of like, what do these foods contain?

And then getting a sort of. Yeah. And I mean, you can use chat, GPT and AI to help you. So the way I do it is, and you shouldn't go from your normal standard American diet of eight grams per day to 40 grams the next day, right?

You want to taper it up. My recommendation is usually adding somewhere around four to five grams for each day for a week. Meaning if I'm getting 10 grams a day regularly, then for the week I am doing 15 grams.

seven days, let my body get used to managing the fiber and utilizing it properly. Then the next week I'm getting 20 grams a day, then 25 and so on. The way I do it, because I want to ensure that I am 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 that tend to have fiber in it.

I ate a good amount of nuts and seeds, a lot of broccoli, beans. So I just looked a few things that And I gauge with the help of chat GPT approximately how much fiber is in my standard bowl that I have at home.

And you can actually just scan or take a picture of it and then upload it to chat and ask it assume how many fibers in it. It can absolutely do that. And it's, and it.

Ballpark, right? Like that's the main ballpark. Yeah. Keep in mind that the studies, when you look at those studies and that many, you know, that mini person visits and large scale of a cohort, they're not measuring this stuff like precisely.

It's all rough, it plus or minus 15, 20% here and there. it is 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, 28 grams one day and 40 grams the next day, and 30 grams, it doesn't matter. You're getting it in and you're accumulating the benefit there.

So I averaged out and to me, I'm getting about 20, 25 grams a day from just the regular stuff I eat. And so what I decided is that, okay, I'm going to then supplement 20 grams a day.

So that between what i normally eat and the supplementing, i know i'm getting around 40-45. Some days it's higher, some days a little less. And the way I supplement, and this has another benefit, is even just basic psyllium husk.

I look for fiber products that may have a small variety of fiber. Maybe it has some acacia fiber in it, or some inulin, but the easiest thing is psyellium organic India version of it because it's just super clean.

There's nothing else in it but silly musk, right? And I do about 10 grams of in water before meal, drink it down.

Immune Tolerance and the Microbiome

It's not a great experience because there's no flavor or anything to it, but you just drink down and you do that about ten to fifteen minutes before you eat and then you'll eat.

Now, the other side benefit of that is it acts like a GLP-1 agonist. It slows down gastric emptying and makes you eat less food. It flows 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 look at taking fiber before the food, taking the fiber after the even something as insulinogenic as, like for me, bananas are actually very insulinagenic, even more so than like a donut can be.

And so I started using bananas and I would take like 10 grams of fiber before the banana or, and then another time do it without the fiber and you'd see like, I will blunt the glucose response by 40, 50%. Right?

Quite dramatically. Just from kicking that 10 grams of fiber. So I know then I'm fighting against insulin resistance. I've been improving my metabolic health.

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

And fiber, we'll talk about why, but fiber plays a very important role in the next thing we want to talk, which is immune tolerance. And the loss of immune tolerances, and I actually 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, but also what parts- Yeah, and real quick, Karan, maybe you can just define immune tolerance for those who maybe aren't quite familiar with what that is.

Sure. Yeah. And just 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. You're immune cells are born out of your bone marrow or your thymus. Those are the two parts of the body that produce immune.

Now, when immune, cells of born, they're born with capabilities, but not with any knowledge, your immune 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 Midwest, we actually have different antigens, different viruses, and different thing that could harm us even in same country just being a couple thousand miles apart.

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

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

How does it do that? It is born with capabilities. The analogy I give is, imagine your immune system is an army that has all the tanks, all of the missiles, guns, helicopters, everything it needs, but it has no general, no plans, it doesn't know who the enemy is.

No strategy at all, right? It doesn t know where the borders are, what s good and bad. It just is ready to go. The way we've developed is the immune system gets its instructions largely from the microbiome.

The microbiomes is outward-facing component of the system, right? So the micro biome is sitting in the mucosal tissue. Most of inside part of your body, most of you orifices are all lined with the mucusa.

This would be like military intelligence, it's like the first people to get information and then relay that down to the ones that are actually going to take action.

Yep, exactly. It's your first line of defense there. Some of them can fight for you, many of whom don't. Like you said, informants, if you will. Imagine you had a neighborhood watch.

That's often the analogy I use. Your microbiome is the neighborhood's watch, meaning they're all watching out the windows and keep an eye on what's happening in the neighborhoods.

Then they will signal to the cops or the military when something bad is going on. In fact, they help the immune system understand what to attack and what not to.

A loss of immune tolerance means that that relationship and the tutoring and communication between the system and 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 hay wire. It tends to up-regulate inflammatory mechanisms.

I can explain that for a bit. 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, and let 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 system is in you gut, but what does that actually mean?

Well, that means that about 70, 80% of you immune sampling tissue is 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.

In your gut in one way or the other, right? If I'm walking around and I breathe in a virus, a cold virus that's out there, the virus is going. To go into my upper respiratory tract, it's going get trapped in the mucus in my.

Upper respiratory track. And then that mucus is going to get sloughed off by something called a mucociliary elevator, and then it's going push it down to the back of my throat and I'm going swallow it.

So that virus with the mucous is gonna end up in my gut. If things going through your eyes, your ears, all of that drains to back your throat through the eustachian tube, right?

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

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

In the mucous layer, you have got all the microbes living, and then that mucuss layer has a certain thickness to it. And the bottom part of the mucous layer is very few microbes in it, Most of the microbes live in the top part of mucus layer.

That mucous layer in a 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 form the final barrier before things enter your actual circulation.

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

You have to imagine this is our barrier. This is out gate system. If the Bobby is a fort, this the walls of fort and sitting on top of walls the fort which is the top the mucus layer are the informants of neighborhood watch.

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

Now, the reason they're called Dendric cells is because they have these dandrites, which look like little tentacles that can extend. You've got the intestinal epithelial cells sitting shoulder to shoulder.

On top of that is the mucus layer. In the mucous layer are the microbes. everything that comes into your body comes in to that mucus layer with the microbes there.

The dendritic cells are actually on the other side of the intestinal epithelium, but their little dandrites can sneak in between your intestal epitelial cells and go into the mucous and start sampling things, right?

So it's sampling like, oh, what is that? That's a food antigen, or that's an environmental particle, that a bacteria. That's a virus, right? Now, while it's sampling things, the commensals 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, dandritics cells know that those antigans are tolerant antigens.

We don't need to attack it, right? So they're getting that signal from the microbiome. The microbiomes sitting next to, let's say, a peanut protein that comes in, and the dendritic cell is sampling the peanut proteins, the micro biomes essentially going, hey, you don t have to 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 to tolerate this peanut protein, so the immune system needs to learn about this.

Well, how does it teach the rest of the system, anywhere you see peanut proteins don't attack it, is that T cell then activates a B cell that makes an antibody against at that protein.

And that antibody typically is called IgA, right? It's not an IgG or IgM or Ige, which is a hypersensitivity response. It is an 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. But that whole process basically happens with foodborne antigens, with environmental particles, bacteria, viruses, and all of that, that the microbiome teaches the immune system not to attack.

So then you look at what happens when you lose immune tolerance. 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 secretorial fluid.

So anything that's coming in, it's just binding and neutralizing and teaching the immune system, oh, this stuff is neutralized. Don't worry about it. You don't have to attack it, and when IgE binds to something, It doesn't elicit an inflammatory response.

It elicits a tolerance response, No. And that's one of the things that we can test too. It's a, it's often a really good test and a gut test because if it, if its low, well, we get a problem.

Like that not good. We need the body to be producing, you know, SIG-A or secretory IgA. If it really high, that also indicates that that, a good sign, the bodies producing it.

But it indicates dysfunction. There's something going on. An alarm bells going off that were producing a lot of this stuff. So there's, something, some things happening that need to aware of.

Right. Yeah. Its really like those, those two extremes that indicate something's actually off. Totally. Yeah. And it's a great marker because it is a marker of like your body's immune system functioning the way it should.

There is another player in that whole game, which I didn't mention, is something called the regulatory T cells. The regulatory t cells are the t-cells that monitor this whole interaction.

As long as this tolerant response is happening, it s happy and it 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 microbiome and takes that peanut protein and goes, ah, this is an enemy and presents it to the T cell, the helper T-cell as an enemies to get to helper to elicit an immune response against it.

That regulatory T cells comes along and it goes no, no you messed up, right? That's not a enemy, you need to dampen that down.

Gut Sampling, IgA, and Autoimmunity

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 10 years.

That was a Nobel prize in medicine this year, which is fascinating. And the microbiome is at the core of that whole mechanism. So let's say you've got a dysfunctional microbiom.

You've had poor lifestyle choices, antibiotics, whatever it may be. Your dendritic cells are still there sampling with their little dandrites everywhere.

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

Then it pulls those antigens in through a process called phagocytosis. It eats the antigins, if you will, takes it to T helper cells, and presents it T-helper cells in a different way than it would have if it saw that antigen in the context of the microbiome.

As a result of that presentation, the T helpers cells 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 into that area and go, oh, shit, we got to attack this thing. At the same time, because it's not a tolerance response, cause it is 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 your immune system that senses that, hey, your low Ig A, what does it do in response to that? It up regulates IgE. So people with histamine intolerance, mast cell activation, allergies, asthma, all of this overreactive, inflammatory, hyperactive immune responses tend to have more IgE in their secretory fluids than IgA because your body's going, we need some antibodies in this secretori fluid, which is our first line of defense.

We're not getting the signals to make Ig A because the microbiome's not providing those signals. So we're gonna make IGE instead. The problem with IgE is when IgG binds an antigen, it recruits cells called isonophils and basophil, which then release histamine and all kinds of stuff to create this hypersensitivity response.

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 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 IgE response everywhere else.

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

The innate system is kind of- the analogy I always use is like, imagine you had a window open and then you got 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 blowtorching the whole room. And you're going to kill the mosquitoes, absolutely, but you are going burn the wall a little bit and break the windows probably.

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 come to that area and bombard everything.

Then they're supposed to then hand off the process to the adaptive immune systems. And 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 fly swatter and let us close the window properly, right? So that is a more adaptive, gentle response. But the innate system gets there faster.

The blow torch guy gets their faster, so he is 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 cells in that area, macrophages and dendritic cells, which are called antigen presenting cells come to that air and start eating up everything that's in the area for two reasons.

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

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

And that's the job of 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 immune system, the Treg 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 upregulating the treg, and the rreg system is very dependent on your microbiomes, Then you're going to get an accidental presentation of your own proteins.

Then your immune system goes out. That's one of the culprits and develops as whole antibody response against your on protein, which is auto immune presentation, right?

So this is how you can go from. intolerance being kind of an annoying thing like, oh, there are certain foods I can't eat. I have asthma. Oh, just stay away from them because it's whatever.

Yeah. Just stay way, avoid them just 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.

This goes back to an early part of our discussion where it's like, oh, there's all these plants and things that I can't eat and it doesn't agree with me.

Well, it does it mean you just avoid all of that because it it is a strong indication that your system is moving in the wrong direction and its only going to get worse.

Right. Absolutely. Yeah. And so we have a few more minutes here, Karan. I want to be mindful of your time, you know, and what I wanna kind of remind people of is you mentioned the microbiome being essential, 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 putrification, sets up fermentation, starts to throw off the microbiome, can't break down on proteins. So now they're peptides. Now those are being sampled.

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

We're producing dopamine, serotonin, acetylcholine, et cetera, etc. To me, I think about the dysfunctions that happen, right? Head injuries, lack of sleep, poor food choices, antibiotics, birth control pills, not chewing our food thoroughly, eating at the wrong time of day, Right?

There's all these things that probably many of us have partaken 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 anything. 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 people can focus on?

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

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

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

When you have this constant inflammatory activation because of loss of tolerance, you also get the same inflammatory activity in the central nervous system through something called microglial cells.

These are like the macrophages and dendritic cells of this central nerve system. Now stuff you eat, and things in

your environment that shouldn't be causing inflammatory responses are causing inflammation responses in you gut, and that's moving up your central nervous system.

Now your brain is inflamed and your is getting damaged. Your gut is also- And by the way, those microglia, when those get activated and are on fire, they're hard to turn off.

It's actually- Really hard. I remember learning this from a functional neurologist. Once those are are and they are going crazy, that is 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.

The brain has its own immune type of system. Yes, that is where this loss of tolerance and toxicity in gut directly impacts the And that is one, the microglial activation and inflammation in the central nervous system is central to anxiety, depression, neurodegenerative conditions and all that.

One quick example of that, is take tryptophan for example, right? Tryptophane 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 nerve system, tryptophan is not converted to melatonin and serotonin.

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It's converted into something called kinurenin, and quinolinic acid, which are both neurotoxic. and enhances anxiety and depression, right? So the precursor to your happy hormone is now being converted to something that makes you depressed and toxic to you brain.

So that's just how impactful inflammation is. 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 in each of these five pillar.

If you skip two or three of the pillars you're really not going to get the same response, so you want to become conscious 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 get enough fiber, enough polyphenols in, and enough lean meats, good healthy fats, olive oils and all the good stuff.

Fresh food like they have enzymes in them, like real live foods. 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. I mentioned earlier that your micro biome is required for all this tolerance effect.

Not only is it the presence of a microbiomes, 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 diet is number one. 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 got 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 affected against your gut and your brain. Number three is lifestyle factors. And

the most important lifestyle factor to me are adequate movement.

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

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

And then the other thing is that myocines also reduce cortisol and stress, right? So, so pillar number three, which is weightlifting and movement actually helps pillar.

Number two, Which is stress. Right. The other in pillar, number in the lifestyle is sleep. Right. 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 that stuff.

You need six, seven hours of sleep and it varies from person to person. If you're using things like the aura, it can tell you what your sleep efficiency is and all that.

I think people really need to get much more focused on their ability to sleep. Number four, pillar number four is exposure. What I mean by that is, exposure to good stuff like in the outside environment, getting out, moving, going through hikes and touching dirt and rocks and then also reducing your exposure things that kill your microbes.

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? So, then with supplementations, probiotics, like the spore-based probiotic, prebiotics, good fish oils, polyphenols, you know, the 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, Karan. It's always amazing. I love talking to you. But I feel like we could geek out on the microbiome and the immune system and all things health for a long time, your wealth of information.

So tell people where they can find more of the work that you are doing today. Yeah, you know, I post a lot on my Instagram, which is the handle is at Kiran Bayoum, K-I-R-A-N, B- I-O-M-E.

And one of the things people will see out there is I also offer a microbiome course called Build Your Resilient Gut. If people want to take a course and understand it deeper and I understand more action items and things they can do for themselves.

Then if you put my name in YouTube, we'll find lots of interviews that people have done that have, and they've kindly uploaded them to YouTube as well.

So lots information in all these places. Amazing, Karan. Good to see you as always. Thank you so much for coming on. My pleasure. Stay connected, stay healthy, and join us next time on Doctor Talks, real talks from real doctors on the issues that matter to you most.