

Dr. Mark Hyman

Coming up on this episode of The Doctor Hyman Show. We talk about fermented foods being so good for you like sauerkraut and kimchi and natto and miso.

Dr. Todd LePine

This is where these really good foods in someone who has histamine intolerance is like putting gasoline on a fire.

Dr. Mark Hyman

I'm getting worse. It's like, well no you should be getting worse. These are good foods for you.

Dr. Todd LePine

No, you have histamine problem.

Dr. Mark Hyman

Now before we jump into today's episode I'd like to note that while I wish I could help everyone by my personal practice there's simply not enough time for me to do this at scale. And that's why I've been busy building several passion projects to help you better understand, well, you. If you're looking for data about your biology, check out Function Health for real time lab insights. And if you're in need of deepening your knowledge around your health journey, check out my membership community, the Hyman Hive. And if you're looking for curated and trusted supplements and health products for your health journey, visit my website at [DrHyman.com](http://DrHyman.com) for my website store for a summary of my favorite and thoroughly tested products.

Dr. Todd LePine

Histamine is found naturally in the body. The body makes histamine. We also consume histamine and the interesting thing about histamine is it is also part, it's released by mast cells as part of our first response to offending organisms like

Dr. Mark Hyman

So mast cells are like a white blood cell.

Dr. Todd LePine

Exactly, yes. Like a white blood cell. Type of white blood cells, yeah. And the also interesting thing is that histamine actually works as a neurotransmitter. And when you think about this, this is really an interesting thing and as I was preparing for this, I sort of stumbled upon some things which I thought was really quite fascinating, is that when you take antihistamine, what happens to you?

Dr. Mark Hyman

You get drowsy.

Dr. Todd LePine

Exactly. So histamine, when it's at high enough levels, it stimulates the brain.

Histamine is actually involved in the sleep wake cycle.

Dr. Mark Hyman

Well, I mean, Tylenol PM or Advil PM, it's Tylenol, Advil plus Benadryl, which is an antihistamine.

Dr. Todd LePine

Right. So it's a balance. You know, too much histamine is bad. Too little histamine is also bad. So when you actually totally block histamine, you actually get sleepy.

It'll actually involve with the sleep wake cycle. And modafinil, is the drug that people take, that actually works on histamine. Provigil. Provigil, exactly. Actually part of that works on the histamine.

So it keeps the histamine levels higher, so it keeps your brain sort of awake, if you will.

Dr. Mark Hyman

Incredible. So most people are familiar with certain histamine conditions, right? If you get hives.

Dr. Todd LePine

Yeah.

Dr. Mark Hyman

If you have a peanut allergy. Yeah. If you have this condition we call dermatographia, which sounds weird, but essentially it's if you scratch your fingernail on your skin, it'll create a red welt.

Dr. Todd LePine

Yes. Yes. That's a that's a that's

Dr. Mark Hyman

a really write your name on your back and it'll kind of have raised like letters.

Dr. Todd LePine

And that's that's actually a poor man's way. And oftentimes we'll use that with patients to determine how much histamine they're having in the connective tissue because the mast cells are the type of white blood cells that are in the connective tissue of the body and when they have excess amounts of histamine in them or they release histamine too easily, you will get this thing called dermatographism where you can take your finger and stroke

Dr. Mark Hyman

on

Dr. Todd LePine

the skin and you will form a red line and it'll stay there and sometimes it'll get really wealthy and raised and that will tell you that there is a problem with excess amounts of histamine in the body.

Dr. Mark Hyman

Yeah, and it's something that we've all experienced. When you get a bee sting or something like that, you'll see this raised welt. But what happens for some people, they don't necessarily get the hives and they don't get these raised welts on their skin, but they do suffer a whole range of symptoms. So when someone walks in your office, what are the clues that alert you to the fact that they might have a histamine problem? Because by the way, most traditional doctors don't even know anything about this syndrome.

Yeah, if you have allergies, an asthma, but that's about it. But there's a whole host of problems that people suffer from that are mostly misdiagnosed, poorly treated and create so much suffering, which is unnecessary.

Dr. Todd LePine

Yeah. There's term out now which when I was in medical school, we didn't even have it. It's now called MCAS, mast cell activation syndrome.

Dr. Mark Hyman

Like it's a real medical diagnosis.

Dr. Todd LePine

It's a real medical diagnosis. Mean, we're seeing a lot of it now. And the question is, why are we seeing so much mast cell activation? And I've been puzzling on this myself.

Dr. Mark Hyman

Yeah, I never took that class in med school.

Dr. Todd LePine

I know,

Dr. Mark Hyman

right, exactly. But it's true, it's a big thing now.

Dr. Todd LePine

We're seeing a lot of it. It's not like there's one cause for mast cell activation. There are multiple causes. I actually even, when I deep dived into the literature, one of the things that I stumbled upon was the effects of EMF on mast cells.

Dr. Mark Hyman

EMF is?

Dr. Todd LePine

EMF is electromagnetic frequency.

Dr. Mark Hyman

Your cell phone, cell towers, WiFi.

Dr. Todd LePine

Absolutely. And there's some work by a woman, Johansen, out of, I think it's Sweden, who's done some work on the effects of EMFs on mast cell degranulation.

And there's some good studies showing that EMFs are one of the things in susceptible individuals that cause their mast cells to release more histamine that drives this allergic inflammatory response.

Dr. Mark Hyman

So that's fascinating. And so what are the sort of symptoms that you see people coming in with?

Dr. Todd LePine

Well, they oftentimes will react to every food. They're sort of the people who they can't, they have a more and more restricted diet because the more foods that they eat, it'll trigger, because lots of foods contain histamine or will get broken down.

Histidine is an amino acid and that when you consume foods that are high in histidine, things like meats have a lot of histidine, your body will actually break it down into histamine. Normally the body can process that, but when you have problems with either too much ingestion or too much production of histamine or not enough breakdown of the histamine, then you'll have problems with histamine intolerance. These are typically a lot of people who have food allergies.

And Mark, I think you've done this yourself. Yep. This is really interesting, is the old way of treating food allergies was what? Chromalin sodium. Yeah.

Right? Remember using that? It's actually a pretty good treatment for people who are really, really reactive to foods. And the way that chroma and sodium, because chroma is actually used for patients with asthma.

Dr. Mark Hyman

Yeah, you inhale, it's an inhaler.

Dr. Todd LePine

It's an inhaler, exactly. And it's a very effective drug. For really bad cases, chroma and sodium can be very, very helpful for patients who have severe histamine responses to foods.

Dr. Mark Hyman

And it's true. People can come in with all sorts of weird symptoms that just are misdiagnosed. Have headaches, they can have migraines, facial congestion, sinus issues, fatigue,

Dr. Todd LePine

brain fog,

Dr. Mark Hyman

brain fog, digestive problems, menstrual cycle problems, nausea, vomiting. If it's

really severe, you can get really bad cramping, you can get edema, tons of fluid retention, palpitations, anxiety, your temperature regulations off, dizziness. So a lot of people come in with all these weird symptoms. Don't know what's wrong. I'm taking an antidepressant.

Dr. Todd LePine

Yeah, exactly.

Dr. Mark Hyman

So but but there is a there is a way to diagnosis. And so if you're suffering from any of these issues, it may be that there may be a chance that it could be a histamine issue. And when you have someone who comes in with all these symptoms and by the way, a lot of people have edema and food retention, you just stick your finger in their body, in their tissue because it's puffy and You can get edema in the legs. You can see just people carrying a lot of extra weight and fluid. There's often some type of histamine activation there.

Dr. Todd LePine

Well, sure. Because the mast cells, which are the cells that contain histamine, they're actually found in the spaces, the interstitial spaces in the connective tissue of the body. So that's why they get puffy because those are where those cells that are high in histamine reside.

Dr. Mark Hyman

And it can really be something that leads to chronic fatigue syndrome, this mast cell activation issue. It's a big deal. Most of the time it's just completely missed.

Dr. Mark Pimental

Yeah. I

Dr. Mark Hyman

mean, if you ask the average doctor, say, I think I have mast cell activation syndrome. Can you please get me the test and diagnose me? They're going to go, don't know. Yeah. You know, let me check your histamine levels.

So when you have a patient with this, how do you begin to think about diagnosing this? Because, you know, it can be a big it can be a big deal for people. And I want to share a case later. You're going to share some cases of some patients who suffered for decades, decades, and finally get better when we treat them.

Dr. Todd LePine

Yeah, well again we talked on the last podcast about the role of leaky gut in the microbiome. Interestingly, when you have dysbiosis, some of the bacteria will actually cause more of your body to produce excess amounts of histamine. So that's another thing where when the histamine is in excess in the digestive tract, that can be related to food consumption, which are high foods in the histamine, or the bacteria are actually causing the breakdown of histidine as an amino acid to go into histamine. So dysbiosis is one of the things that can trigger excess muscle.

Dr. Mark Hyman

And all the nasty gut thing again. We're always talking about the gut here on the Doctors Pharmacy podcast especially on our House Club episodes because it's such a fundamental thing and it's connected to everything. The microbiome is so critical in so many aspects of our health. And I remember when we started doing this, Todd, decades ago and we'd say, oh, people have a leaky gut or there's problems with their gut flora. They have dysbiosis.

They would just laugh at us. Literally, just doctors would just laugh at us and think we're completely crazy.

Dr. Todd LePine

Insane.

Dr. Mark Hyman

And yet it is now one of the most important areas of research in medicine is the microbiome and understanding leaky gut. And you see all kinds of papers and scientific literature using the term leaky gut. Wow. I literally remember sitting. It was in 1997 and I was at Canyon Ranch and I was having dinner with some guests and there were some doctors in the crowd and we were having nice dinner and we were I was talking about leaky gut.

And the woman this one was an allergist. Her specialty was allergy and things like histamine. And she looked at me and she's you're just completely nuts. There's no such thing as leaky gut. You know, this is just a bunch of you know what?

And I just was like, looked at her like, oh, boy, you know, and it's now, you know, twenty five years later. Yeah. And medicines really come along. It takes a long time, but people are still struggling. And I think the obvious, the worst sort of case scenario of a histamine reaction is obviously anaphylaxis.

Dr. Todd LePine

But

Dr. Mark Hyman

it doesn't have to be that. So talk about how we begin to diagnose it. We look at what tests besides a SIBO test,

Dr. Todd LePine

we look Well, you can measure histamine in the blood. You can also measure tryptase, which is another marker for mast cell activation. You can also measure, there's another test which in preparation for this, I've not measured, I haven't found the lab that does it, but it can be measured as N methylhistamine, which is a breakdown product of histamine. That's another one that can be done. And then, again, I think one of the tests for me is dermatographism.

I find that a very helpful clinical test to determine if a person's mast cells in interstitial spaces are overly reactive in releasing lots of histamine.

Dr. Mark Hyman

Yeah. And we also do a test for DAO deficiency.

Dr. Todd LePine

Yes. Yeah.

Dr. Mark Hyman

So talk about what that is. DAO is an enzyme, right?

Dr. Todd LePine

Yes, so DAO is a diamine oxidase. So this is an enzyme that our body has and it helps to break down histamine. So histamine has to be consumed, it's used, and then it has to be detoxified. And if this enzyme is lacking in a person for whatever reason, the enzyme may be turned off, you will have problems with detoxifying histamine, especially in the gut. And there are enzyme products that you can use, DAO enzymes, that you can use that patients respond very, very well to this.

Dr. Mark Hyman

Yeah, do that here at Telstra Wellness Center. We give people histiAO and enzyme support. It's interesting, there's a lot of things we do every day that block DAO production.

Dr. Todd LePine

Absolutely.

Dr. Mark Hyman

Alcohol, black tea, green tea, which is a good thing, mate, energy drinks, these all block DAO production. It's going to increase your histamine intolerance.

Dr. Todd LePine

Yeah, exactly. Yeah. Then you can use anti histamines. The other thing, we had another podcast earlier on migraines. I found this also very interesting is one of the things that is a histamine blocker is Butterbur.

And Butterbur is used in migraines. And the reason why Butterbur works in migraines is that it actually is working on an antihistamine level. Because you can get an allergic brain, if you will. We know about that where you get fuzzy in the head and you can get headaches and things like that. So excess amounts of histamine has an impact on the brain.

Dr. Mark Hyman

Yeah. And so when you see these patients, you can do some of the genetic testing, look for these DO deficiency issues. You can look at histamine levels. You can look at some of these byproducts. You can do tests for DO deficiency.

You can look at some of the other factors that might be causing it like leaky gut, food sensitivities. All that is really part of what we do here at the Ultra Wano Center when we check these patients history and we look at their lab tests. And then, so when they come in, sort of you have this suspicion because sometimes it's hard to diagnose, have a suspicion. It's pretty easy to sort of test and try different approaches that allow people to see if it's an issue. So what are the dietary things that we start?

Because a lot of histamine triggers are in the diet. And so we can have a low histamine diet. So what's a low histamine diet?

Dr. Mark Pimental

Foods would

Dr. Mark Hyman

what actually are Put it this way. What are the foods that have the highest histamine that we should be avoiding?

Dr. Todd LePine

Yeah. So basically the way to think about it is bacteria produce histamine. So if you have food that's old, you have food that's sitting in the refrigerator for a couple of days, guess what happens? The bacteria actually break down histidine, the amino acid into histamine.

Dr. Mark Hyman

So no leftovers for

Dr. Todd LePine

Leftovers, exactly. Oh that's leftovers, exactly.

Dr. Mark Hyman

I really want leftovers. Or maybe just like the next day.

Dr. Todd LePine

And then fermented foods. Fermented foods are fermented by bacteria. So anytime we have food that's old or fermented, things like Parmesan cheese, aged meats, etcetera. Chured meats. Chured meats, etcetera.

They have high histamine and that's part of the fermentation process.

Dr. Mark Hyman

And yet we talk about fermented foods being so good for you like sauerkraut and kimchi and natto and miso and Exactly.



Dr. Todd LePine

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Dr. Mark Hyman

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these really good foods in someone who has histamine intolerance is like putting gasoline on a fire. And they'll and they'll

Dr. Mark Hyman

well, I'm getting worse. It's like, well, no. You should be getting worse. These are good foods for you. No.

Dr. Todd LePine

You have histamine problems.

Dr. Mark Hyman

What is that saying? It was good for the geese and good for the gander. Right? I think I think this is so so critical what we're talking about here, Todd, because functional medicine is personalized medicine.

Dr. Todd LePine

Absolutely.

Dr. Mark Hyman

Yeah. It's precision medicine. It's not like medicine. It's precision nutrition.

Dr. Todd LePine

Yeah.

Dr. Mark Hyman

So it's really important to understand that even though this way of eating may be great for some people with fermented foods and eating avocados and having delicious shellfish.

Dr. Todd LePine

Bone broth.

Dr. Mark Hyman

Bone broth.

Dr. Todd LePine

That's another one.

Dr. Mark Hyman

Right. We think all these are great foods, but you might be killing yourself. Of course, alcohol and beer and all that is a problem. Wine. But but, you know, we are we're we're really here focused on what is right for you.

Yeah. And I think dietary dogma really interrupts personalization approach to nutrition. Some people do great on vegan diets. Some people do terribly. Some people do great on keto and some people do terribly.

Yeah. So there's no one size fits all approach. And what really frustrates me, Todd, and probably I imagine you too, is that, you know, there's all these people out there on the web and Internet and promoting this and that approach and this and that diet, and they're not seeing patients. Yeah. And the thing about seeing patients is it's incredibly humbling.

If you've seen tens of thousands of patients, you know, you can't be dogmatic.

Absolutely. This is the way you have to be vegan or you have to eat meat or you have to eat fermented foods or it's like you go, wait a minute, everybody's different.

And what works for one may not work for another.

Dr. Todd LePine

One man's food is another man's poison.

Dr. Mark Hyman

That's right. Even good foods, we're talking about good foods. I think this is a really important point, particularly people who have histamine issues, which is a lot of people at some level or another, they should consider trying a histamine free diet and also other other foods that we think are also great, maybe triggering histamine like papayas and chocolate. Oh my god, chocolate, which I love. It would be terrible to get this condition.

Yeah, dried fruits or nuts, food dyes, additives, wheat germs, health food, tomatoes, bananas. All these things may really cause increased histamine production. Sadly, in order to get this under control, sometimes you need to be restricting some of these foods for a while for a while for body to It's not forever.

Dr. Todd LePine

That's the thing is, I think you're absolutely right. Like an elimination diet is not something that you do forever. And a low histamine diet is also something that you don't necessarily have to do forever. And I think that the key thing is really working with a really good, well trained, experienced functional medicine nutritionist who can help you navigate all of the nuances of what to eat, what to avoid, what to take in terms of supplements can be very, very helpful.

Dr. Mark Hyman

Absolutely. You know, and the things that we want to focus on if you have a histamine intolerance or foods that are low in histamine, fresh, really fresh food is the key, right? Not old food, like you said. Yeah, fresh meat, freshly caught fish. Now, fish has been sitting around for a while or canned fish is not as very good fruit.

That's not citrus fruits. Eggs are great.

Dr. Todd LePine

Yeah,

Dr. Mark Hyman

not gluten grains. Get away from the gluten, but quinoa and and black rice, not dairy. Avoid dairy, but you can have coconut milk or almond milk, lots of veggies, but no tomatoes, avocado, spinach or eggplant. Right. So you've got to be smart about this. And it's a little complicated and often you need help with the nutritionist. Yeah, all the good oils and fats that we like. Those are all great. So, know, it's pretty much how I eat. I mean, I do eat avocados and certain things, but I really pretty much eat protein vegetables.

And it works so well for these patients. So, Todd, when you see a patient like this, tell me about a case that you might have had where it sort of kind of got you thinking about this and allowed you to to really drive down into really the diagnosis and the treatment?

Dr. Todd LePine

Well, you bring up an interesting thing because, you know, as I have seen more and more patients, and I think we are seeing more patients who have, you know, histamine intolerance, call it mast cell activation syndrome, to what degree, is there are certain individuals who can be a little bit more predisposed towards this. So people who have Ehlers Danlos syndrome, you know, the hypermobile people can actually have, for whatever reasons, have a higher incidence of histamine intolerance. The other thing in the case I recently had was a patient who came into me with severe mast cell activation syndrome. It was on a bunch of different medicines, including chromium, which we talked about earlier, decrease food reactions to histamine. And I saw the patient and he gave a very interesting history.



He had this skin lesion, which sort of like morphed into this almost like a scarring type ulcerated lesion on his back area. He saw multiple dermatologists, had a biopsy, had part of the area removed, and was ultimately diagnosed with some type of form of a scleroderma, sort of like a malignant scleroderma, which is sort of interesting and like, that related to? But he was also having all of these histamine type reactions. And then when I asked him a bunch of questions, you know, I started thinking about, well guess what? Lyme disease is also associated with histamine intolerance because Lyme bacteria resides in the connective tissues in the body, sort of hides there.

And that in turn can actually activate those mast cells, which mast cells are the first line defense, or one of the first lines of defense against infectious agents. And when I asked him, because he had a lot of fatigue and brain fog type symptoms too, but maybe that was related to something else. So I asked him about potential exposure. So lo and behold, he ended up having a low CD57 count, which is oftentimes a It's not diagnostic of Lyme, but it tells you that the immune system is not working so well. And when I did advanced testing on him, he had actually had conventional lab testing.

I think we talked about that in another podcast, how regular conventional lab testing for Lyme disease is not that helpful. But I did a specialized T cell Eli spot test on him, and his Lyme, Eli spot test lit up like a Christmas tree.

Dr. Mark Hyman

Wow. Right. So he had Lyme disease.

Dr. Todd LePine

He had Lyme disease, which was actually triggering a lot of his mast cell activation type symptoms. So I've been working with him for a while, and he did very well. I put him on a supplement which is a combination of quercetin which can help with

Dr. Mark Hyman

It's like a natural antihistamine.

Dr. Todd LePine

Natural antihistamine.

Dr. Mark Hyman

It turns out it's really good for COVID too.

Dr. Todd LePine

Yeah, exactly. Very powerful phytochemical. And he did very well by adding nettles along with quercetin in supplement form. He also worked with a nutritionist, got on a low histamine diet, dramatically made a huge, huge improvement. His brain was working better and his energy was better, but he still wasn't 100% better.

So that's where I went to the next level, and he's currently actually being treated for Lyme, and it's in the medical literature. I sort of stumbled upon this because I had this patient come into me and she had the same thing. She had severe mast cell activation. She was on injections for

Dr. Mark Hyman

It was like \$20 a year.

Dr. Todd LePine

Yeah, \$20 a year. \$20

Dr. Mark Hyman

a could control the histamine, which could be controlled by diet and these other things.

Dr. Todd LePine

Exactly. And her condition actually turned out to be the same thing. It was actually

undiagnosed Lyme disease. And this is, I think, one of those things where you have to think about it. Not that Lyme disease causes everything, but Lyme disease is such a tricky condition that you've got to be thinking about it.

Anybody who comes in- The great masquerader. It's like syphilis, exactly. It's like the great masquerader, and people can come in. I've seen people with Parkinson's symptoms. I've seen people with brain fog.

I've seen people with rheumatoid, you know, seronegative rheumatoid arthritis.

Dr. Mark Hyman

Chris Christofferson at Alzheimer's, quote Alzheimer's, and Lyme Exactly.

Dr. Todd LePine

I had one patient with fibromyalgia who was, quote unquote, fibromyalgia, whatever that means. It means you're hurt all over. So Lyme can actually mimic fibromyalgia.

So you really gotta think about it, and it doesn't present as one neat little boxed diagnosis. It's really, you got to really

Dr. Mark Hyman

Well, that sort of speaks to the one of the foundational concepts of functional medicine is that one disease can have many causes.

Dr. Todd LePine

Yeah.

Dr. Mark Hyman

Right. Like histamine intolerance could have many causes. Yeah. And one cause like Lyme disease can create many diseases. Yes.

Can create like, you know, Lyme disease can cause neurologic issues and joint issues and skin issues and chronic fatigue and Alzheimer's and mast cell activation syndrome and, you know, know, POTS and all these weird diagnoses that doctors treat as if they're the thing, but actually it's something else.

Dr. Elizabeth Boham

Like some symptoms of histamine intolerance will include things like headaches or migraines, congestion, congestion after you eat, especially digestive issues are really high on the list. Abdominal pain and bloating, diarrhea, constipation. We talked about the rashes that can happen, urticaria, hives, rashes that can happen. And, but we also know that histamine intolerance or high levels of histamine can cause a lot more systemic things as well. So, or other systemic symptoms.

So, things like low blood pressure, heart palpitations, dizziness, vertigo feelings, anxiety. So, sometimes people will feel more anxious when their histamine levels are high, chronic fatigue. And so, you know, histamine intolerance.

Dr. Mark Hyman

You get a lot of nasal congestion, right? And sometimes even asthma symptoms and

Dr. Elizabeth Boham

Absolutely. Right? Absolutely.

Dr. Mark Hyman

People who have Brain fog and it's like everything, right? So it got me dismissed as, you know, people don't put the dots together and the doctors don't often put the dots together and these symptoms are often seen as disparate or not connected, but they're all really connected, right?

Dr. Elizabeth Boham

They are, right, they are. And it is, you know, to be honest, I've often not put the dots together, right? So it is not always easy. We're always like, oh, this person has headaches, why are they getting headaches? Or they're having digestive issues.

Then all of a sudden you go, oh, this is all related and I've gotta be thinking about And so, know, we've learned a lot over the years too, and to be able to help people as well. So I think of mast cell activation syndrome, systemic. There can be a lot more things going on. And, you know, when we say the word histamine intolerance, we're really thinking a lot about that, you know, that reaction that happens from eating a food and that histamine reaction or that histamine imbalance that occurs after a meal where there is just too much histamine around and the body's not able to break it down. And, but you know what, it's often a clinical diagnosis, right? So, it's it's often based on looking at that person's story and understanding, you know, really understanding their timeline and what their symptoms are and looking for those interconnections that can really help us to determine if this is what's going on for them. Because the testing is imperfect.

Dr. Mark Hyman

Yeah, that's right. I mean, like in terms of traditional medicine, what would be the traditional, approach to diagnostics, testing, and then treatment. And then let's sort of talk about how we would approach this from a functional medicine perspective.

Dr. Elizabeth Boham

Right. So, you know, you can measure histamine levels, right? So, whether you can measure histamine levels in the blood, so you can measure something called histamine and tryptase in the blood, and you can measure histamine in the urine. It's called a methyl histamine urine test that's done. And that test is often done both functionally and conventionally.

And it can be helpful if the levels are high. So if the levels are high, you go, Oh, this person has an issue with histamine. But, but what's a, what's, what's a problem with this test is that the levels fluctuate a lot during the day and depending on what you just ate and the amount of food you ate and what, you know, how, we'll talk

Dr. Mark Hyman

about this Right. It's not, it's not super reliable,

Dr. Elizabeth Boham

It's no, it's not. And so a lot of times, these tests come back negative, meaning they look normal, but that doesn't mean the person doesn't have issues with histamine. So, just because these tests are negative, it doesn't mean, Oh, you can check that box and say, Histamine's not an issue. So, in addition to those tests, you know, we're always looking a little deeper. So, we can measure things like, we can now measure things like DAO levels.

So, you can actually measure that enzyme level, which is many times helpful. We can look at things like, is there increased intestinal permeability? You know, by doing some tests that look at antibodies against Zonulin and lipopolysaccharides, because that can give us an indication that this may be an issue. And we also-

Dr. Mark Hyman

Zonulin is like the gluten marker for excess gluten and lipopolysaccharides are toxins that bacteria make that create inflammation. So those are bad things that happen in your gut and that can trigger this.

Dr. Elizabeth Boham

Right. And then when the body makes antibodies against them, that means that there is increased intestinal permeability. So it's a test that we do to give us a sense of is there increased intestinal permeability and is that where we need to work to help improve this person's health? And we also look at genetics. We look at genetic markers all the time, you know, that can influence how well you make that DAO enzyme, as well as how well you break down histamine through methylation.

So there's a bunch of different genetic snips we will evaluate for that will also give us some information about like how much is this person at risk for having issues with histamine.

Dr. Mark Hyman

Yeah, it's interesting. And you know, I think, you know, people have even weird symptoms like dermatographism where you kind of scrape your skin with a fingernail and it'll just like wealth up and look at. So, or you can write stuff on your skin and it's like graffiti.

Dr. Elizabeth Boham

Right.

Dr. Mark Hyman

But these are really a whole host of really disparate symptoms. And again, this is a spectrum, System intolerance, mast cell activation syndrome, they're all part of a continuum of dysfunction of your immune system, overreaction of the allergic response in the body and triggers all this cascade of downstream symptoms. The problem is traditional medicine doesn't do a very good job of this and throws a lot of medication at it. Antihistamines, things like Allegra, Claritin, Zyrtec or what we call H2 blockers, another histamine receptor like Pepcid or Tagamet. And then they use, you know, mast cell stabilizers, which actually I think are can be helpful like cromol and sodium, which we which we use and you can take it orally as a as a liquid before you eat to kind of decrease any reactions to food.

I find that extremely helpful during safe medication. There's more serious ones like Singulair for liquid trying inhibitors which are which are, you know, strong medications, steroids. So that's really kind of the the toolkit. And it's a very limited toolkit and often doesn't really solve the problem, just masks the symptoms. So the beauty of functional medicine is that it helps us really start to think about the symptoms.

And as you mentioned, we do a deeper dive. Look for things like leaky gut, for food intolerances, we look at dysbiosis, what's happening in the gut. We also look at mold and environmental toxins and hormone levels and all the things that we know really are relevant when it comes to sort of trying to understand the root causes of overactive histamine response. So I think it's an area I think we have a lot of success with and a lot of different approaches than traditional, you know, healthcare. I think the, you know, the interesting thing about, you know, histamine is that, you know, it also is in food, right?

So people have to eat. You know, you make histamine in your body, but you also get histamine from various foods. And maybe you could sort of share, you know, what an initial approach would be from a functional medicine perspective. You know, we do with the deep diagnostics, as you mentioned, you know, look for leaky gut, look for dysbiosis, look for hormone imbalances, toxins, look for food sensitivities, look for mole issues. Do, you know, genetic testing to look at histamine related enzymes like TAO and maybe even urinary histamine levels.

So we do a whole range of tests. But then once we find out someone has this, what's kind of the general approach they would take, to dealing with the root causes?

Dr. Elizabeth Boham

So, we want to calm down the body and calm down this reaction, this overreaction that's happening in the body. And so we will often do a trial of a low histamine diet And it can be very effective as I mentioned with this patient with migraines and how effective it was. But what's important, I think really important to just start off with is this is not a lifelong diet because there's a lot of really healthy foods that have

histamine in it, right? That or even can cause histamine to be released in somebody's body. So what we ultimately want to do is decrease the body's reaction to these foods and heal leaky gut.

But let's start talking about this low histamine diet because it is a really great tool that we are using often and just for a bunch of reasons. One, to see how much is histamine related to this person's symptoms and then how can we help start to calm down the body's immune reaction and then over time we work to relax the diet. So, what we always do is we do phases, so we're not overly restricting foods. And it's, you know, because it's important to recognize that the amount of histamine in a food varies significantly depending on how long that food has been sitting there, how long that food is, you know, how long it's since it's been picked or or caught and, or prepared. We know that foods that have been the longer they've been, sitting there, they will histamine levels will go up.

And so it's important to think about a lot of different things when we're doing a low histamine diet. So, terms of the phases, what we start with first is removing alcohol, especially beer and wine and champagne. Those as you mentioned earlier are foods or drinks that are high in histamine and they also block the body's ability to break down histamine. So, we pull those away first And, we also work with people to make sure that they are not keeping a lot of leftovers around. They're eating foods that are fresh, very newly prepared.

If they if they do have leftovers, they wanna freeze those foods right away because the longer the food is sitting there, the more histamine it will produce. For example, we also know like with fish, for example, you wanna try to eat fish thirty minutes after it's been caught. Well, you know, because that will have

Dr. Mark Hyman

the lowest level of fish Exactly.

Dr. Elizabeth Boham

That's so hard to do. So a lot of times people will have frozen fish, which is good because those fish are often frozen very quickly after being

Dr. Mark Hyman

Oh, that's interesting. Yes. That's interesting.

Dr. Elizabeth Boham

And they're gonna be lower in histamine, but the key is when you defrost your fish, you wanna prepare it right away and consume it right away because, the longer it's being defrosted or the longer that, you know, if you eat that food two days after you prepared it, there's going to be higher levels of histamine in it. So, all of that can be really complicated. So, I will always recommend, and, you know, we do this at the Ultra Wellness Center, you know, we have what, seven nutritionists now? You know, I always recommend

Dr. Mark Hyman

people who with nutritionists.

Dr. Elizabeth Boham

Work with a nutritionist because it can be such a complex process to figure out and to remove, and you wanna do it in a healthy way where you're not overly restricting, but it can be really helpful. So, you wanna have fresh foods, minimally processed foods, and, you want to have foods without those additives in it, like sulfates and MSG, things that can trigger more of a histamine response in the body.

Dr. Mark Hyman

No, it's just like, you know, the aged cheeses, fermented foods, alcohol, those are all really full of histamines. You have to be really careful with those in.



Dr. Elizabeth Boham

Absolutely. We put a lot of those in phase two. So if phase one isn't enough to calm down the body, then we'll move and pull away the canned and smoked fish, anchovies, which unfortunately that's one of my favorites. But again, this is not a lifelong meal, food restriction. Processed and fermented meats we pull away, aged cheeses, pickled and fermented foods, which like sauerkraut, kimchi, yogurts, kefir, mustard, ketchups, vinegar, soy sauce.

You know, a lot of these, as we talked about earlier, are really healthy foods. So, we wanna be able to add them in in the future, but sometimes again, we pull them out for a period of time to see how much that helps somebody's symptoms improve. And they typically will see improvements in two to four weeks. So, it's like a two to four week removal to get a sense of how much things calm down in the body. There is even a phase three where we have to restrict even more and pull away some plant foods like avocado, spinach, tomatoes, pineapple, citrus foods that can also trigger some histamine reactions in some people's body.

And so, so so again, we do it in phases, and we can, you know, we can attach this handout, I think, right, Mark, to the for people?

Dr. Mark Hyman

Yeah, in the show notes, we'll put a handout on on the different phases so people can listen in and actually figure out, you know, what to do by looking at this handout that we have provided the Ultra Wellness Center. Put a link to it. And I think I think it's kind of a good guide on how to get started on your own. But but, you know, one of the challenges is that even if you do all that stuff, you know, I always, you know, I always say, you know, we need to figure out not, you know, what you're sensitive to, but why you're so sensitive. Right?

And that's sort of the next phase. You can get people immediate relief by removing histamine and by giving them, you know, DL enzyme and maybe some other things that sort of are mitigating symptoms, you know, whether it's antihistamines or chromaline or whatever you're going to give them. But at the end of the day, to really resolve this, have to dig deep into the root causes and to try to deal with those things that we really are good at in functional medicine but are not so great at in traditional medicine. And, you know, and that involves everything from optimizing and fixing the gut, whether it's bacterial overgrowth, fungal overgrowth, leaky gut, inflammation, healing and repairing the gut, which, you know, we have a whole program four and five hour program in functional medicine. I've done many podcasts on the gut.

Optimizing nutritional status that affects their immune system, whether it's vitamin C, B6, magnesium that support histamine metabolism, also the stress reduction part, which is really key because that activates everything, getting regular sleep, exercise, but then also diving see, well, do you have mold? Do you have environmental toxins? Do we have heavy metals causing this? Do we have something else going on that we need to treat directly? And how do we up regulate your detoxification system?

So we really treat both the histamine syndrome itself, but also then dive into root cause treatment so that people don't have to suffer with this their whole life.

Dr. Mark Pimental

We now believe that, and you sort of brought this up as part of the introductions, is that we now believe that food poisoning starts the whole process. So you and eating is part of it. You know, back in the day, meaning like forty, fifty years ago, when we were in, kindergarten, we would sit in a sandbox and eat the sand. Now we eat salad out of a bag until we go to club med. And for the first time in our life, we



see salmonella or, you know, we go somewhere and we, we get travelers diarrhea or we get food poisoning or whatever.

We start to explore the world of food. But food poisoning triggers this. And, and we now have identified the toxin in food poisoning, the CDTB toxin that trips off some antibodies in the human body that then cause your nerves of the gut to fail or to be, impaired. And so when the flow of the gut is slowed by this impairment, bacteria build up and there's two bacteria that just flourish when it's a little more swampy. So, I used to watch Survivor shows on TV and Discovery Channel.

You probably watch those and they always say

Dr. Mark Hyman

I like The Lost. I used to watch Lost, which was kinda like Survivor. Yeah.

Dr. Mark Pimental

It's a little bit different. It's a little more there's a little more raunchiness story. With Survivor, you're just kinda trying trying to make it to a road somewhere. But, the point was that he he always this this guy on the survivor show would always say, if the water's not moving, don't drink it. If the water's flowing fast, drink it because it's cleaner.

And the same thing with the small bowel. If the small bowel stagnates, it becomes swampy bacteria grow in it. And the same thing is happening in the human small intestine. And so it's a sequence. So food poisoning, the antibodies, and then you develop the bacterial buildup.

Dr. Mark Hyman

So you're almost saying it's like an autoimmune disease of the nerves of the gut that develops that kind

Dr. Mark Pimental

of makes So

Dr. Mark Hyman

this is a kind of a radical idea that irritable bowel is an autoimmune disease, isn't it? I mean, is kind of not what most doctors typically think of when they think of IBS. They think of IBD or inflammatory bowel disease, but they don't think of, you know, irritable bowel being autoimmune.

Dr. Mark Pimental

But the interesting, the interesting thing about contrasting IBD to IBS, so the antibody that we discovered is an autoantibody that is directly related to the pathology. So the higher that antibody is, the sicker you are. The antibodies in IBD are markers of IBD. They're not directly implicated in the pathophysiology. The antibody to vinculin that we discovered is directly related to the pathophysiology.

We can make rats have IBS just by giving them this toxin. And so that, that's very, cool because it allows us to study new drugs and new therapies coming

Dr. Mark Hyman

into future. Not so cool for the rats though. So this is fascinating. So you were saying there are different kinds of bacteria. Can you explain, you know, what are the kinds of bacteria?

And then and then what, type of food poisoning? Is it any? Like if you get giardia or if you get salmonella, shigella, campylobacter, or Entamoeba, or like, you know, what, what are, are the kinds that typically cause the problem?

Dr. Mark Pimental

Well, the four horsemen of the apocalypse of IBS are Campylobacter, Salmonella, Shigella, and some E. Coli, food poisoning type of E. Coli, pathogenic E. Coli. Giardia can do it too.

It turns out it has vinculin in its structure. And so maybe that's how you get the antibodies from, from Giardia. The viruses are, are less likely to precipitate IBS. So the four horsemen, Campylobacter, Salmonella, Shigella, and E. Coli.

So that's, that's, and, and it occurs about, starts to occur about three months after you get sick. Patients will remember, some don't remember and they'll say, well, you know, they have a couple of days of diarrhea and they don't pay much attention to it, But they remember going on a trip to Hawaii and they end up in the hospital with bloody diarrhea. And then ever since then, nothing's been the same.

Dr. Mark Hyman

I have heard that story so many times. You know, I went to Thailand or India or, you know, Jamaica and like, and sort of tripped the whole thing going.

Dr. Mark Pimental

Yeah, or the taco truck in Venice. Yeah, so.

Dr. Mark Hyman

Taco truck.

Dr. Mark Pimental

Lot of possibilities.

Dr. Mark Hyman

Wow. So, so this explains like sort of 60 you say, but you know, not all of it, Right?

That's right. What are the other things that may be driving irritable bowel syndrome?

And are they also related to SIBO or is it, is it all, something else?

Dr. Mark Pimental

Well, so based on culturing the bowel, we've been able to isolate that sixty percent of IBS is SIBO. The other forty percent is a mixed bag. So for example, and you probably talk about this now, Ehlers Danlos syndrome, Potts syndrome, We're starting to recognize those illnesses as characteristically GI centric, at least in their early presentations as well. So some of the leftover forty percent have Ehlers Danlos syndrome or POTS, or some of them are celiac that we've missed. Some of them are food sensitivities.

Some of them are histamine sensitivity, some of them. So it's a mixed bag of, a number of other disorders and some of them are fungal overgrowth. We see that in about six to ten percent of that hundred pie. So, there's still more to unpackage.

We're not ignoring the other forty.

We're trying to figure the rest out, but it's, it's a little bit harder to unravel.

Dr. Mark Hyman

So let's pause there for a minute. Cause you just said something that I think might slip by, which is this whole idea of fungal overgrowth, or what often is referred to as CFO, small intestinal fungal overgrowth, you know, and in, in my coming of age as a functional medicine doctor, basically people would laugh when we talked about yeast overgrowth or anything like that and candidiasis, and it was just like a quacky alternative concept. But it seems to me, you know, now understood as potentially playing a role in some of these cases. Can you talk about the current understanding of this and actually some of the treatment? And then I'll sort of loop back to that. How do we start to treat and think about IBS differently?

Dr. Mark Pimental

Yeah, I mean, Satish Rao, Doctor. Satish Rao in Georgia has done a lot of the seminal work in this, But, more recently, we've done shotgun sequencing of the small intestine, and we've been seeing these this fungal overgrowth.

Dr. Mark Hyman

But that doesn't mean you that doesn't mean you shoot somebody in the gut with a shotgun.

Dr. Mark Pimental

No. Shotgun sequencing means we sequence every single piece of DNA we can find, and then characterize it and see what organisms it represents. Yeah. And it represents fungus about ten percent of the time. And that when the fungus is higher, you're you're the patients are experiencing more abdominal pain and more diarrhea. So there is a subclass of these patients that it is fungal, but it's smaller than some would like to believe, but larger than those who are naysayers, as you've probably heard. And so it is there, it's real, and, but it's a little more challenging to identify. There's no breath test for it. You got to go in and chase it. And that's the, that's the challenge.

Dr. Mark Hyman

Chase it by doing stool cultures or?

Dr. Mark Pimental

Well, chase it. It could be by stool, but if you want to find small intestinal fungal overgrowth, you've to get into the small intestine and that's, that's really

Dr. Mark Hyman

Saphylate. Because you have

Dr. Mark Pimental

to have endoscopy and all of that. That's how Doctor. Rao identifies it.

Dr. Mark Hyman

Yeah. And, and any particular species of fungus or is it sort of a broad array?

Dr. Mark Pimental

So what we found in this quote shotgun sequencing is *Candida albicans* is a big part and a little bit of *Candida glabrata*. And there's a few other *malassezia* and all these other organisms that are very minor, but they generally aren't at a high number that we think are as consequential as the first two I mentioned.

Dr. Mark Hyman

Yeah. No, I definitely have seen that on cultures and, you know, you know, in my experience, maybe it's not universal, but it tends to lead to more constipation. And so people tend to have more constipation. And also I can tell because they might have other fungal symptoms. They might, you know, eat tons of sugar and starch. They might actually have fungal rashes on their skin or dandruff or other kind of clues that they have kind of a yeasty kind of situation going on. But I think it's important that it's been identified. And going back to kind of the treatment of that, how would that normally be treated?

Dr. Mark Pimental

Well, yeah, generally in, in, allopathic medicine, try an antifungal. There are natural antifungals as well, and I, you're probably better versed in those than I am, but we, we do use fluconazole, we do use nystatin, occasionally we use more radical, more advanced antifungals, but, but those are the typical first two choices.

Dr. Mark Hyman

Yeah. Sometimes you can take what we used to call amphotericin, which is a horrible first generation antifungal, but it's not absorbed. So if you take it orally, it's not absorbed and that can tell you exactly. Yeah. Oh, yeah.

You know, and then, and in terms of the bacterial stuff, you know, talked about these three different bacteria, right? You've got methane producing, hydrogen producing, sulfide producing, and they all are a little bit different. And you said the methane

producers are not really bacteria, they're archaea. But, you know, for simplicity's sake, let's call them bacteria. And I don't think most people know what archaea is. It's arcane, right? It's archaea. Yeah. So what is your approach to starting to kind of differentiate these? And then how do you determine what the right treatment is for a patient?

And can kind of kind of guide us through what to do both in terms of, you know, lifestyle, diet, any kind of supplements that might be helpful and medication?

Dr. Mark Pimental

Yeah. So, first of all, we helped develop the first three gas breath tests. So just full disclosure, but it's changed my practice because there are patients who fell through the cracks without knowing hydrogen sulfide. So unpacking each, the hydrogen positive breath test patients are generally, we actually just published this paper, it came out literally yesterday. There are two bugs, that's it, that cause the hydrogen overgrowth.

It's *Escherichia coli*, the non pathogenic one, and *Klebsiella pneumoniae*. Those two characters, when they come into town, everybody leaves, because they're so opportunistic and bullies, and we think they produce even toxins to the other bacteria around them to try and get rid of the the inhabitants. So it's like you've got a gang that comes into the small town and everybody leaves. So it's a disruptor of the microbiome and and and then they rise very high in number. So that's the hydrogen one.

The second category is the methane or methanogens. And those characters live both in the colon and the small bowel. And we have a paper coming out showing exactly where they're living and it's pretty universal in a lot of these patients. So hence we call it intestinal methanogen overgrowth and not SIBO methane because it's not just the small bowel, it's colon also. And when they produce methane, it gives you a lot of constipation, a lot of gas, and you can't pass the gas and it's these people are quite miserable.

And then the third is the hydrogen sulfide, which is the new kid on the block, which has changed my practice because some of those patients we didn't know, breath test is normal, everything looks fine. And then the hydrogen sulfide's positive, we get rid of it and all of a sudden they feel better than they have in their life. And, and for some reason, when you get rid of hydrogen sulfide, it doesn't come back so quickly, which, which is beautiful. I have patients who've gone a year, just one treatment and they're done. And so I'm really excited about that.

So, I mean, I could talk about the treatments if you like now or

Dr. Mark Hyman

Yeah, yeah, yeah. Go through the treatments because they can be real different. And this is important to understand for people because, you know, just because you have a real bowel, it's not like a one size fits all approach. You've got to differentiate what type it is. And, and these tests that, Doctor.

Pimenton developed, the tests for anti CDTB and anticonvulin antibodies are really important. And then the the breath test that allows you to look at hydrogens, methane, and sulfur. So, can you talk about what are the, you know, what are the different treatments for each of these?

Dr. Mark Pimental

Yeah. So, I mean, if I have an IBS patient with diarrhea or a patient with diarrhea and bloating, my practice now, I do the antibodies because I want to be able to say, was it food poisoning or not? And if the antibodies are really high, it makes it harder to

treat, But also you travel, you better take prophylaxis because you could get into further trouble with these antibodies going higher. I universally do Really?

Dr. Mark Hyman

Like prophylaxis, like what? Like Xifaxan?

Dr. Mark Pimental

So I give Xifaxan prophylaxis. That's what I do in my practice. And a lot of the GIs now do that. Because if the antibody goes higher, the damage to the nerves of the gut is more intense or the effect on the gut is more intense. And at least that's what we're seeing in our clinic.

So we're very careful with those patients who have the antibodies positive. When it comes to then, then we do the three gas breath test, in all of our patients. And if it's hydrogen and you, we all know Rifaximin got FDA approved for IBS with diarrhea on the basis that IBS was in part of microbiome disease. And now we understand that microbiome condition is SIBO. So I give Rifaximin for that.

If it's methane, we have one double blind study that we can lean on and it's Rifaximin plus either neomycin, which is what the double blind study covered or rifaximin and metronidazole. And then the third category is hydrogen sulfide and we give rifaximin, but we give it with bismuth, because bismuth is an anti, it blocks some of the synthetic functions of hydrogen sulfide in the sulfate reducing bacteria. Point is the hydrogen sulfide goes down, the bacteria are reduced and therefore the patient's normal bacteria take over and things get better more permanently in that group it looks like.

Dr. Mark Hyman

And that's basically Pepto Bismol

Dr. Mark Pimental

and Pepto Bismol.

Dr. Mark Hyman

Interesting. So in terms of diet, is there a different approach to each of these in terms of what you would recommend from a food perspective?

Dr. Mark Pimental

We haven't sorted out and or had time to sort out the different diet approaches, but I envision smarter people in me and diet will come up with a way. What we do now is what we call low fermentation eating. So, we don't use low FODMAP in our practice because you can't do it indefinitely, but low FODMAP will reduce the amount of calories you're providing to bacteria and therefore they'll ferment less and that might help. But long term low FODMAP hurts your microbiome and can cause nutritional deficiencies. So you can't stay on the full low FODMAP indefinitely.

Dr. Mark Hyman

And FODMAP is like fermentable oligosaccharides that

Dr. Mark Pimental

basically fermentable oligosaccharides, monosaccharides, etcetera. And, and, and basically it's too restrictive, but you've probably, most people have probably read about low FODMAP diet. It's very popular, in the last few years, but we use what's called low fermentation eating, not as restrictive. And the philosophy of that was with a low fermentation diet, you can go to any restaurant in the country and you'd find a meal. So it's, you know, you don't want to be the person at the table just because you have IBS that spends ten minutes with the, with the, you know, ten minutes, trying to explain your dietary restrictions on a low FODMAP diet.

So, you know, that that's part of the reason we want our IBS patients to feel as normal and as, socially non isolated as possible. And that's part of it.



Dr. Mark Hyman

What is a low fermentation diet?

Dr. Mark Pimental

So it's basically restricting, restricting non digestible carbohydrates. So low fiber, no dairy, and then none of the artificial sweeteners, because of course they're easily fermentable and then, spacing your meals. So you don't eat for five hours between meals because the damage of the nerves, we talked about that earlier, the damage of the nerves causes a reduction in cleaning waves of the gut. So the cleaning waves only occur when you're not eating. So your gut is sort of like got two computer programs, eating mode, cleaning mode.

If all you do all day is spend time in the break room, taking a bite of a bagel that's in the break room, you never go into cleaning mode. So, so in addition to the construct of what to eat, we tell you when to eat, and to try and space your meals out. So anyway

Dr. Mark Hyman

Was it interesting, you know, the the typical dietary recommendation when I was in medical school for IBS was more fiber, Metamucil, basically. What you're saying is that you want to restrict soluble fibers that are digestible. And that, and, and low, low fiber diets seem to be con- you know, it seems like a contrary notion when you want to create a healthy microbiome because good bugs also live on fiber. So how do you, how can you navigate that?

Dr. Mark Pimental

Well, you know, I may be punished for saying something like this, but everything has fiber in it now. Even Cheerios, they put fiber in it because it prevents colon cancer and its colon health and all this stuff for twenty years. How many, how much have we heard about colon health and fiber?

Dr. Mark Hyman

A lot.

Dr. Mark Pimental

And what have we, what have we got now? We've got colon cancer happening in the forties and we're doing screening colonoscopy at 45 now. I'm not saying it's fiber causing that, but all the fiber we've been pounding and the cardboard we've been eating hasn't really done as much as we thought it might. So I'm, I'm a little unclear about fiber, but from the point of view of bacteria, you put more fiber, you're gonna have more of the bacteria. If you had bad bacteria to begin with, there's gonna be more of them.

And for a healthy person whose microbiome's healthy, no problem, but not for these patients with these microbial conditions.

Dr. Mark Hyman

Now, if you've gotten, you know, these antibiotic treatments, you know, you've gotten diagnosed, you've gone through the testing, you've gotten the personalized treatment, you do the course of antibiotics. What prevents the bacteria from coming back? And in my experience, it often does. So how do we manage this sort of recurrence that occurs? Because you don't want to keep giving people antibiotics because intuitively people go, wait a minute, antibiotics are bad for the gut. So why are we giving antibiotics to someone who's got a gut problem? It seems counterintuitive.

Dr. Mark Pimental

Well, I can answer that in two or three ways, but I'll, I'll try to touch on a little bit of each. We looked at rifaximin before and after treatment, the small bowel. And when



you get rid of the bullies in the town, all the inhabitants of the town come back. So it goes opposite of what people think. We're not, you know, being cataclysmic. It's getting rid of the E. Coli and the klebsiella and SIBO that allows the regular bacteria to re flourish, repopulate, and take over again for a period of time. But remember, the problem is those cleaning waves are not working. So it is possibly going to come back. It depends how badly damaged.

And that's where that antibody comes in. Cause if the anti vinculin, which is that auto antibody for the autoimmune disease of IBS is very high, the neuropathy is more high or more intense, and you're going to relapse or reoccur more frequently. So that's where we were able to have some further strategy. But first of all, take the antibiotics. They actually repopulate the town counter to what you think.

We've never seen antibiotic resistance to Rifaximin so far, knock on wood. It's a very unique, chemical drug. And then we get them on the low fermentation eating diet. That's what we do. And for those where the antibody is high or those who relapse, we do put them on a prokinetic.

So they space their meals, everything's going right. But we want to stimulate those cleaning waves at nighttime because that's the longest time you're not eating, and make you clean up as much as possible at night so that the bacteria don't have a chance to come back. So we don't do all three things for everybody. It depends on, you know, if somebody relapses in two years, we don't need to put them on a drug every day to prevent. But if they relapse every three months, then we can stretch it out to a year by adding the prokinetic or doing more aggressive diet strategies.