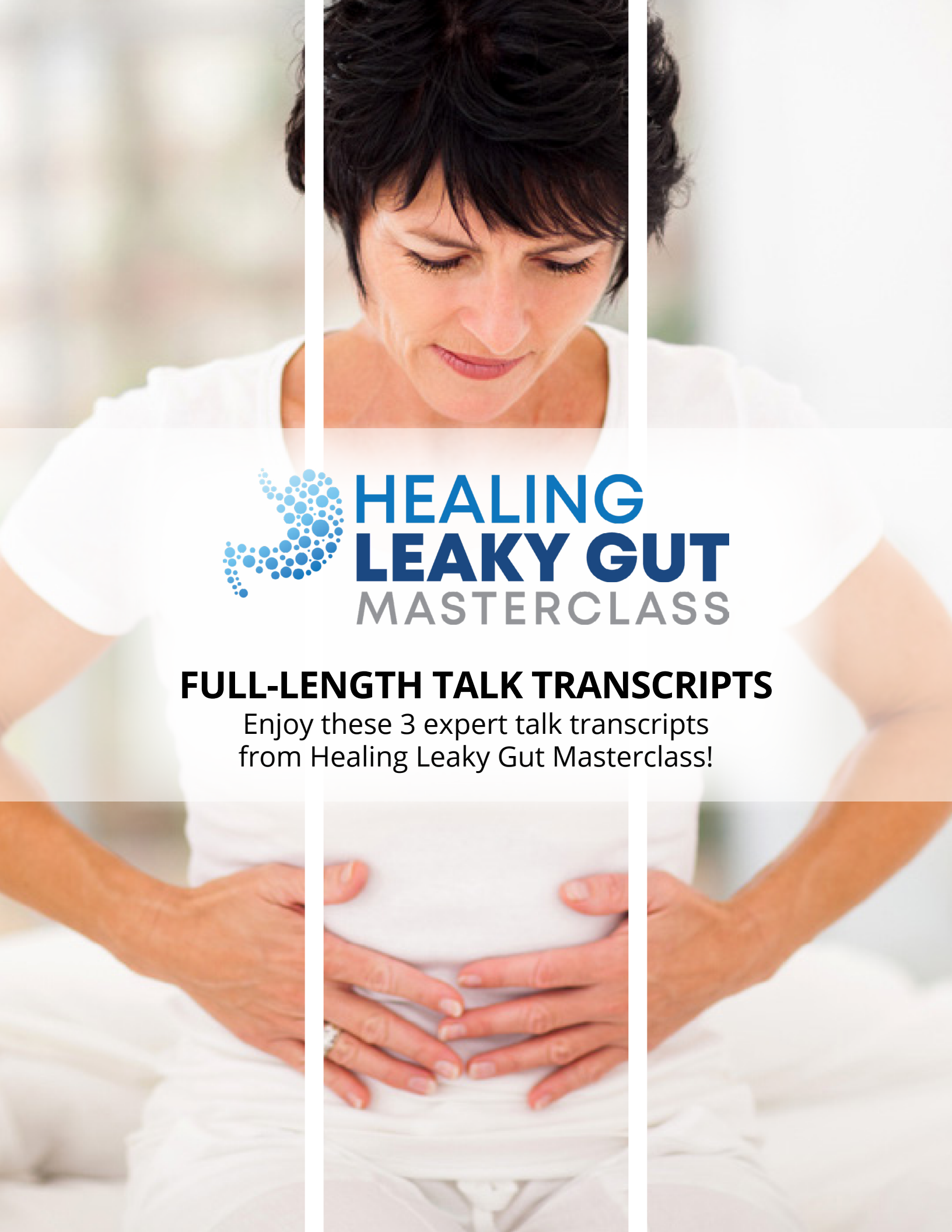

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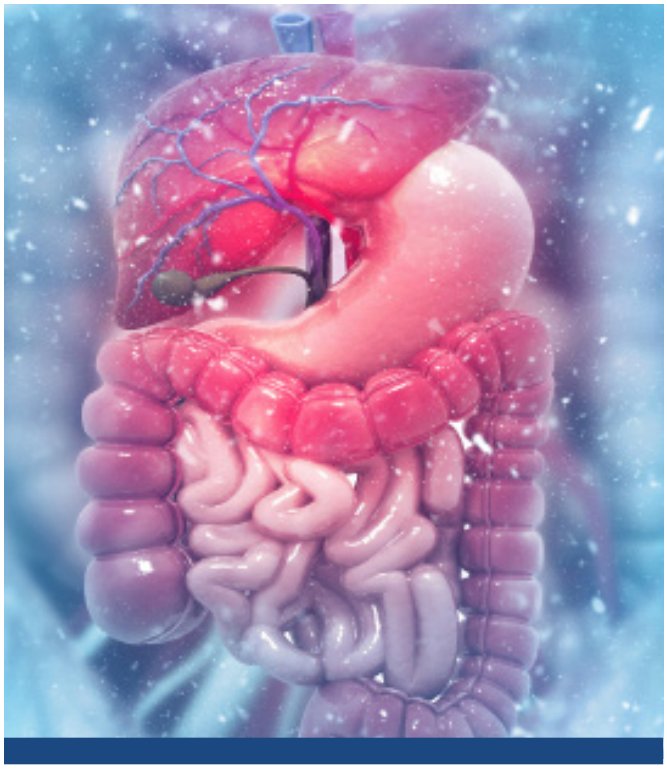

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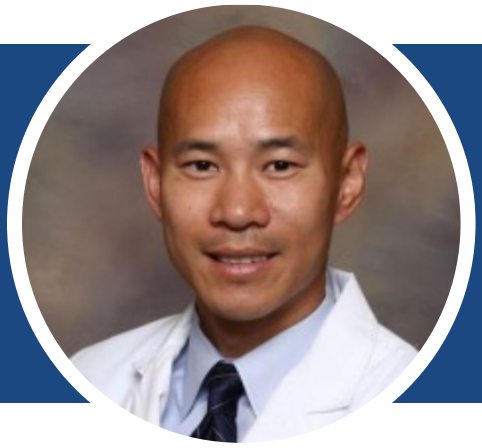


The Brain-Immune-Gut Axis, Vagal Tone, and Chronic Disease

Peter Kan, DC, DACNB, FAAIM, CFMP

Dr. Jockers: Welcome back to the *Healing Leaky Gut Summit*. I'm your host, Dr. David Jockers. And today, I'm interviewing my friend and functional medicine expert, Dr. Peter Kan. And we're talking all about the brain-immune-gut axis and its link to chronic disease.

A lot of times, when people have gut issues, it's actually a brain issue. We're going to talk about how the vagus nerve actually connects the brain to the gut and how oftentimes, when somebody has low vagal tone, when the vagus nerve is not expressing itself the way that it should, it manifests in a lot of digestive symptoms.

And oftentimes, people are taking different supplements to support their gut, but they're not addressing their vagal tone. They're not addressing what's happening in their brain and how their brain is communicating and connecting with their gut. And so, Dr. Kan is going to go through that in detail.

We're going to talk about the connection between the brain, the immune system, and the gut, what he calls the BIG idea. We're going to talk about how the blood-brain barrier compares to the blood-gut barrier and how leaky gut is oftentimes an issue with the brain and the immune system and tertiary downstream, so not the root cause, there's actually a gut component, but it's actually upstream getting to the root cause, we're dealing with brain and immune issues.

So you guys are going to love this interview. This is such fascinating information. I think for many of you, this is going to put a lot of pieces together, and it's going to give you functional strategies that really move the needle for you and your ability to get your health back, get your gut back in order, reduce inflammation in your body, and improve your overall health.

Guys, Dr. Kan, he is a chiropractic neurologist and a certified functional medicine practitioner. He's an expert in neurometabolic health, analyzing the relationship between the brain-immune-gut axis and how it impacts all of human physiology. He has a wealth of knowledge. He works with people all around the world.

You can check him out at askDrKan.com. That's A-S-K-D-R-K-A-N dot com. Guys, you're going to love this interview. Be sure to share it with anybody that you know that you care about. Get them signed up for the summit. This information is life-changing and lifesaving. Thank you so much for doing that, and let's go into the interview.

Dr. Kan, always great to connect with you, and I'm excited to talk about the brain-immune-gut axis and its link to chronic disease.

Dr. Kan: I'm excited to be talking about it, and thanks for having me, by the way.

Dr. Jockers: Absolutely, absolutely. Well, you're a world expert in this area, and I really love your take. Most people out there, most practitioners, both, certainly in conventional medicine, but then also even in natural health, if somebody has a gut issue, they're looking just at the gut, right? If their

symptoms are gas, bloating, acid reflux, they're focusing primarily and oftentimes only on the gut, and they're not relating it to other systems of the body.

If they have depression or anxiety, they're only thinking, okay, this person's got a mood disorder, but they're not thinking, what's happening with this person's gut? What's happening? Are they inflamed? Do they have inflammation that's affecting them? They're not connecting all these different areas.

And I know that that's something you do as a functional medicine practitioner. And you've also really highlighted this idea of how the brain connects with the gut through the immune system. And can you explain that in more detail?

Dr. Kan: Yeah, absolutely, David. So you are right. A lot of time, people come in with digestion issues, and almost like sometimes, it can be a low-hanging fruit. Hey, just give them some enzyme, and solves the problem. Or sometimes just L-glutamine, and that's it.

But oftentimes, people with chronic health issues, that may not be enough. And we have to learn to look beyond just the area of complaint and make, as I say, the BIG connection. And when I say BIG, to me, it's also this acronym called brain-immune-gut axis. Oftentimes people heard about the brain-gut connection or the brain-gut axis, or the gut-brain axis. Depends on who you talk to.

The gut people like to say gut-brain because they feel like the gut is more important. And the brain people will say brain-gut connection because they feel the brain is more important.

Really it's semantics because they're bidirectional. They all talk to each other. And my background is that I come from a background of board-certified chiropractic neurologist. And so I really had a lot of interest and a lot of clinical practice working with people with chronic brain symptoms.

Now, these brain symptoms people come into me for, it could be as serious as having MS, demyelinating disease. They have some type of disabilities that we're working with. Oftentimes though, they have these subclinical neurological issues, and that might be brain fog, that might be short-term memory issues.

They may have paraesthesia, numbness, tingling, but a lot of it is also cognitive issues, depression, anxiety. And what I noticed in the past, working as a board-certified chiropractic neurologist, I will do different type of brain-based therapy based on their localized region of dysfunction.

But then I'll notice that some people, they respond and other people don't. And the people that don't respond to these brain-based therapies were the one that had metabolic problems. So, metabolic problem, like blood sugar issues, like perfusion problems, like inflammatory issues, like gut issues.

So then, when we started to work with the people more than just the area of complaint and started connecting the BIG connection and connect the dots, our results just increased exponentially. So there's definitely a brain and metabolic components. So this is what I call a neurometabolic component, right? And when I say metabolic, that means everything related to metabolism, and metabolism is how your body break down and utilize energy.

But know that when you have metabolic issue, where you can't break down or utilize energy properly, it has a cascading effect that can create inflammatory problems, create hormonal problems, create problems with detoxification.

So now you have all these different other problems that balloon from that. And a lot of time, people are, again, kind of fixing the area of dysfunction, right? Oh, I need to detox, and that's all they're focusing on. And they're forgetting to set up, the prerequisites for good detox, or they just have digestion problem.

They're forgetting to look at what's upstream that could be causing digestion issue. A perfect

example of this, which is very common, is people with brain dysfunction that leading them to have gut dysfunction.

And so, we know that the cerebral cortex, okay, the cortex is an area where much of the brain processing occurs. So brain is basically a big old antenna. We take sensory input from the environment, and then the brain interprets that and gives an appropriate output. The output could be motoric output, generating muscle contraction, so we can move away from danger, but some of these are autonomic motoric output as well, so you can have blood vessel that constrict to get your blood pressure up. So different type of responses.

And one of those responses is motoric output to the gut, right? So then, if your cortex is not firing properly, and we'll talk about like why that might be, the cortical output, 90% of your cortical output you would think is for volitional movement, voluntary movement, like moving your muscle or thoughts that you're aware of.

Ninety percent of your brain's output is actually going to your autonomic nervous system, in your brainstem, pontomedullary area to drive autonomic function. So that's what your brain does 90% of the time. The other 10%--

Dr. Jockers: For the laypeople, that autonomic is the automatic part of our nervous system, where things that we don't have to think about, like blood vessels constricting, like muscle contractions in our gut that help move things through our bowels, we're not thinking about that, but the brain's constantly processing that 90% of it's energy or output has to do with that autonomic component.

Dr. Kan: Yeah. So only 10% of what your brain does is the stuff that you're consciously aware of. And that 90%, a big chunk of it goes to digestion, and that's mediated by the vagus nerve, right? So vagus nerve is cranial nerve number 10, and obviously, vagus nerve also controls muscles of swallowing, heart rate, innervate the lungs as well.

But a big chunk of the vagus nerve function is really digestion, is really the biggest part of what that nerve does. And so, the example here is that if you have poor cortical output, then that 90% of the brain's output goes to the vagus nerve, it's also going to be compromised. So therefore, you're going to have decreased vagus nerve output.

Now, the innervation to the gut, that motoric output, which is muscular contraction expressed in peristalsis and motility, is going to slow down. And when the motility slows down, then food doesn't go through your GI tract as well. So it kind of sits there.

Number one, you can have constipation. Number two, you can develop fermentation of just food and stuff sitting there, more likely to get bacteria overgrowth and candida overgrowth. So you get SIBO and candida overgrowth, and people again, kind of become stuck on, okay, I got to fix my candida. And 10 years later, they still have candida problem. Like, what happened to all these anti-candida herbs and wonderful stuff that you're doing? Why is it not working?

So when it's not working, you have to start asking BIGger questions, as the acronym goes. You got to go perhaps more upstream. And this is where the brain issue really comes in with digestion.

[9:55]

Dr. Jockers: And you mentioned the vagus nerve, and so, a term that I've heard a lot more in functional medicine, and something that I like to look at as well is vagal tone or the tone of basically the strength of what's happening and the effectiveness of what's happening through that vagus nerve. Can you explain that in more detail?

Dr. Kan: Yeah. So the vagus nerve, again, is one of your main parasympathetic outputs. And you'll obviously have other parasympathetic nerves and other nerves and other centers that control

parasympathetic function. For example, in your sacral plexus, you have the parasympathetic function in a sacral plexus that innervate your rectum and things like that.

And then you also have other areas where your sympathetic chain ganglia, these are a network of nerves that are in your spinal cord from T1 to T10 that really fires your sympathetic fight or flight response. And then, in a cranial nerve section, you have other cranial nerves that may innervate the eye to promote tearing. You have other cranial nerves that innervate other places on your head and neck.

But the vagus nerve is one that really has one of the biggest connection between the brain, and the rest of the body is controlled by that vagus nerve.

And we talked about the digestion and heart rate and other things, but the vagal tone is describing the strength, as you say, right? So vagus nerve kind of has that inhibitory effect on the body overall, but it depends on what you're inhibiting, right?

So if you're inhibiting an inhibition, it's kind of like a negative, and negative equals a positive. So if you inhibits something that inhibits, then you actually are activating something. So the vagus nerve, even though we say sympathetic nervous system fight or flight, is your gas pedal, and the parasympathetic is your brake pedal, but really, the vagus nerve is activating digestion, right? So it's not inhibitory in that sense.

So good vagal tone then will activate your digestive centers. And that includes not just motility that we talked about, also secretions, right? Digestive secretion of gastric acid, pancreatic enzyme output, biliary contraction, bile release, all of that is vital to good digestive function in various different ways.

And it can show up as symptoms in various different ways as well. For example, gastric stomach acid deficiency tend to manifest in very specific set of symptoms that are kind of different from if you have pancreatic enzyme deficiencies and also manifest a little bit differently than if you have biliary insufficiency.

So by really understanding the signs and symptom of these things, you can actually, just by symptom alone, be able to zero in pretty close to where the problem might be, and therefore, incorporate some natural medicine practices, either supplements, nutrient, herbs to really help restore some of these function.

I would say the digestive system is one area where natural medicine and functional medicine has a long history of providing a lot of help and tend to respond really well to things like we do.

For example, if you have low stomach acid, you can take apple cider vinegar or digestive bitters. If you have enzyme deficiency, you can take digestive enzymes. So these are things that we've been taking to in functional medicine and natural medicine for a long time with great results. So digestion is one area where this stuff really helps.

Dr. Jockers: Yeah. And digestive bitters, one of the reasons why they work well for helping stimulate digestive juice flow is they actually activate the vagal tone. They actually activate vagus nerve function.

Dr. Kan: Yeah. So bitters, by the sensory pathway, when you taste things that are bitter, it's got that vagus nerve stimulation. In fact, stuff that you do to your mouth have a vagus nerve stimulatory effect.

For example, a lot of the time, we advise our clients to do vagus nerve stimulation exercise. And these are typically things that we do with humming and gargling and gagging because we're activating the general motor efferent of the parasympathetic nerve function.

So we're basically activating these muscles of swallowing. When you gag and hum and stuff like that. You are basically activating these throat muscles, and therefore when you activate it by

a voluntary response-- well, the gagging is not necessarily voluntary, but gargling is. And what you're doing is you're basically sending a signal to the nucleus, the vagal motor nucleus, where all these motor signal goes in.

And when you fire that nucleus, then neighboring nucleus around that nucleus also gets fired. So then you have the vagal motor nucleus, but you also have other nucleus within that area where cranial nerve 10 fires down to the vagus nerve.

So then, that's how you can use these throat exercises to fire a neighboring center that drives some other function, which is the gut. That's why those things work.

Dr. Jockers: Yeah, it's really interesting, like strengthening a muscle and how that can actually benefit a lot of different movements. Well, it's kind of the same thing here. We're trying to get improved neuromuscular activation here, right? Where the vagus nerve is now the muscular component, now it's activating, for example, peristalsis in our gut.

But also, like you mentioned, those secretions also are like a cross. In a sense, you're getting both of those activations where it's helping improve the secretion component as well. So yeah, vagal tone is really key. What are some symptoms that you see with people that have low vagal tone?

Dr. Kan: People with low vagal tone, we might see digestive issues. So let's go with gut here, and what we might see digestive-wise would be you have trouble digesting carbohydrates and fat and protein, all of it. So like, why would that be? Well, remember vagus nerve, right?

If we're talking about digestion, it goes from north to south. So the vagus nerve's going to have a descending influence on all of the digestive organ, be it stomach acid, be it pancreas, enzyme release, and gallbladder.

So when you have decreased vagus nerve issue, then you may have decreased stomach acid, pancreatic enzyme release, and bile issues. So then you have all of those problems. Can't digest protein because you have low stomach acid, can't digest carbs very well because you have low pancreatic enzyme, can't digest fat very well because you have poor biliary function.

So that might be a clue to tell us that you know what? It's not that your gallbladder sucks and your stomach acid sucks, and your pancreas sucks. It's that you have vagus nerve that's not working, driving all of it. So that's one way you can tell.

Other things that you can tell is that remember the vagus nerve is one of the main parasympathetic outputs. And then the opposing force is the sympathetic, so if you are having a low vagal tone, then the opposite, the antagonistic force, will be much higher. It's like a teeter-totter.

So then, low vagus nerve function will cause a higher sympathetic response. This we might see in people with higher heart rate, higher blood pressure, perhaps more skin sweating, right? We might see a more dilated pupil. We might see people with even on physical exam paraparesis we might see.

Very interestingly, in functional neurology, then we're also looking for hemispheric balance, like left and right side, because sometimes you can have the right vagus nerve working less than the left vagus nerve. Just like you can have the right cerebral cortex work less than the left. So you can have this hemisphere imbalance that might cause where you might see blood pressure that's higher on one side compared to the other side.

So these asymmetries in a body that's related to sympathetic function and parasympathetic function really gives us a big clue about these autonomic nervous system function and if it's like a one-sided problem, and that'll allow us to direct specific brain-based stimulation to the appropriate side to kind of bring the function up.

Now, if it's just a general bilateral both-sided issue, then you might just think that it's a general

vagus nerve issue where you have a low vagal tone kind of across the board. Sometimes we'll see one-sided lesions or one-sided dysfunction. But that's really for you to see a functional neurologist to really have that checked out.

But I think for most people, if they're noticing a lot more these fight or flight responses, they're more stressed out easier-- and another sign of poor vagal tone is actually light and sound sensitivity, but the reasons for that, because when your sympathetic are firing, your pupils are more dilated.

That's one of the sympathetic response is your pupils dilate so you can let more light in so you can see better, so you can see threats better. If you are constantly having high sympathetic because of lack of vagal tone, then the pupil just dilate all the time, so then too much light is constantly bombarding your retina and bombarding your visual centers.

And some people just can't handle it. So then that light would just cause them to have migraines, they get sensitive to light, they just cause all kinds of problems. Sound as well. They'll be sensitive to loud noises, big bang. They'll just startle, where some people are just like, oh, that was loud. Then this person will be like, whoa, and then they'll have heart rate go up. They get all the sympathetic response.

The reason is because the light and sound processing, the sensory input all converges in the tectum, which is an area in the mesencephalon in the midbrain. And that midbrain mesencephalic area is also the starting place of your fight or flight response in the brainstem. So then we'll see a lot of these light and sound sensitivity as well.

Dr. Jockers: Yeah, I think a eureka moment, that was a eureka moment for a lot of our listeners here because a lot of people out there are dealing with these kinds of sound sensitivities, light sensitivities.

[20:00]

They're dealing with kind of a compilation of gut issues, maybe some anxiety, some depression, things like that. And they're not kind of putting it all together. So that was really, really powerful right there.

And what are some of the root cause factors for the average individual? Maybe they don't have-- like let's rule out like they haven't had a stroke, they don't have a brain tumor, things like that. What are some of the root cause factors for low vagal tone?

Dr. Kan: Well, as I mentioned earlier, you have to ask where it comes from, right? So the presynaptic input, the place where the signal came from that feeds into the vagus nerve, is your cerebral cortex. So if you have a cortical problem, then that might drive a downstream problem. So how do you know if you have a cortical problem? Well, very simply, do you have cortical symptoms? What are these symptoms? Brain fog, right? It's kind of the same list that we hear over and over again, but these are cortical problems.

So if you have brain fog, short-term memory issues, depression, anxiety, you can't focus, you have lack of motivation, lethargy, these are cortical issues. Now, sometimes you can have a very specific brain-based problem, like you have aphasia, where you can't speak, or you have some motor loss or one side of face droopy, that might be a sign of a stroke, and that's some medical emergency.

Well, we're talking about is this chronic issue that you're struggling with but you have no answers for, and the doctor says you're normal, but you are obviously having symptoms. The reason they say you're normal is-- and I oftentimes I hear people tell me, oh, I have brain scan and brain MRI, they tell me everything's normal. There's no tumor in there. So it's not my brain.

But you have brain fog and brain symptoms, don't you? Yes. So there's something going on in the brain. It's just not in the tumor because you can

have cortical problem that's a functional problem. So in functional neurology, we call it a functional lesion versus a hard lesion. A hard lesion is where you have a stroke. You have a bleed. You have a hemorrhage. We can see it on MRI CAT scan. Yeah, some kind of structural problem busted in there. That's pretty obvious. Okay. You can see it. That's a medical emergency.

A functional lesion is one where the imaging looks fine, right? The obvious structure looks fine, but on a functional level, the cells are not able to function, and the reason they can't function because there's a neurometabolic problem, meaning the way brain process energy has been compromised.

So what are some of these root cause of why the cortex would even be problem? Well, you have blood sugar issues. First place we start is fuel delivery. Can you deliver fuel to your brain? So that's why you and I, we talk so much about blood sugar.

Every time I interview you, we're asking about blood sugar because that really determines the function of how well your brain's going to be able to function, right? Blood sugar stability or using alternative fuels like ketones. And then along that fuel delivery conversation is oxygenation. Can you deliver oxygen to your brain?

Now, that's by the way of blood pressure. So, someone who's hypotensive, the blood pressure is suboptimal, not good enough to feel great, not bad enough to pass out, but not good enough to feel great. That can also cause inadequate blood flow to the brain, then the brain's just not getting enough oxygenation.

Now, you can also have anemia that can cause low oxygen, and that can impact the brain. Some people have small vessel disease. They have mini-strokes in the brain that they never knew they had. Well, a perfect example would be MRIs. You have MRIs, and doctors say, oh, we don't see anything abnormal. You just have age-related volume loss. And we see potentially some small signs of like perhaps some previous injury or something like that. They say, oh, it's fine.

But usually, when I see that, I see that as a chronic problem, chronic inflammatory problem with the brain that's built up to losing brain cell. Volume loss in the brain is no joke. That means your brain cells are dying at a faster rate than normal, and you're losing the size of the brain, and that's not a good thing.

And if we seeing like hyperintensities white spots in the brain, that means demyelination, and that also spells loss of brain function. So a lot of times, these are chalked up as age-related finding, but certainly, there are people who are elderly who don't have these findings, and they're doing great. And there's people who are younger who have these finding, and they're not doing so great. So it's not age-related. It's more how much inflammation do you have in your system.

So again, fuel delivery, inflammation, anything that can cause inflammation, which will be toxins, which would be infections, and then stress hormones. So these are the common--

Dr. Jockers: Trauma may be like a head trauma or something.

Dr. Kan: Oh, yeah.

Dr. Jockers: Concussion.

Dr. Kan: So leave it to the functional neurologist to leave out head trauma. So concussion, absolutely. Now, the thing about concussion is that it builds up over time. Meaning the more concussion you've had, the second hit, the successive hit, it creates more and more of a decreased threshold for your body to handle successive concussions. And then it can get to the point where you don't have to hit your head anymore. All you got to do is eat gluten or get stressed or get an infection, and that can drive this inflammation in the brain even without the concussion.

And sometimes, the term that I call is called chemical concussion. You're literally chemically reconcussing yourself every time you eat gluten, every time you get exposed to chemical because once you have that concussion, your brain is primed for more inflammation.

Dr. Jockers: Because your immune system, and in your brain, your microglial, which are kind of the immune cells in your brain, are hypersensitized, right? They think you're at risk, so they're like cops out with their guns drawn, ready to shoot. So when they see something that looks a little suspect, boom, they're firing.

Dr. Kan: Yeah. This idea of the primed microglia is really important because I don't think many people know that once you have a brain injury, these microglial cells literally can go through a morphological change.

Meaning they literally change into a different type. They go from M1 to a M2 type of macrophage or glial cells. And what happens is one of these types of-- once you hit your brain, you have concussion, you have brain inflammation, these glial cells can shift into a more inflammatory type. And then, for the rest of your life, they stay as an inflammatory type.

So that means that kind of, like you say, they're primed and ready to attack anything that comes now where before you can tolerate things and now you can't tolerate as well. That's why these people get more sensitive to chemicals. They're more sensitive to inflammation. Some of these people they can't handle oxidative stress. So they exercise, which produces oxidative stress, which is a good thing, but then they're already inflamed so that extra oxidative stress from the exercise will just make them have brain fog and make them fall apart.

So these are things that we manage, right? We're managing all these variables. The brain-gut connection, the gut-immune connection, all of it is kind of connected.

Dr. Jockers: So we all have a certain threshold for stressors. And when somebody has a cortex problem like you were talking about here, they have a lower threshold, right? Meaning that like what they could handle when it came to a-- because obviously, we're dealing with stressors and toxins from a lot of different contributing factors.

But the overall threshold of what they can handle now is significantly reduced. So they may have been able to handle a certain amount of exercise, certain amount of stress, and now their level of resiliency to that is much lower. So that same level of stress now overwhelms their system and sets off this vicious cycle of inflammation that impacts them, and they have a myriad of different symptoms.

Dr. Kan: Absolutely. And this is the reason why we detox. This is the reason why we try to get rid of underlying infections. This is the reason why we clean up the diet so that there's not so much of these inflammatory contributors to add to this background already elevated level of inflammation. So then the body can just take a breather and say, ah, I'm not inflamed anymore. I can take a break.

And so it gives your body to come back to homeostasis, which allows you another chance to build more resiliency because you can put stressors in the system which builds resilience, but if you're always stressed, then you're never coming back to balance and never get a chance to kind of bounce back and build that resilience.

Dr. Jockers: Yeah. Now, in our gut, particularly our small intestine, we only have one cell wall that's kind of connecting it. And obviously, depending on different factors, we can have a level of permeability in that gut lining. Now, what are the similarities, and how does that impact-- what's happening there with that gut lining? How does that impact what's happening with the blood-brain barrier? Like, what's their relationship?

Dr. Kan: Yeah. Can I say the old saying? I guess you hear a lot these days that you hear the brain's on fire, the gut's on fire, or vice versa. And then we say this, and this sounds really catchy, and it is actually true, but how does that happen?

And the reason that happens is because the intestinal barrier, that one cell layer lining, the cytoarchitecture of that intestinal lining, like the way that intestinal lining is structured with actin and myosin and claudin and zonulin, that's exactly the same way your blood-brain barrier is structured.

So like in your blood-brain-- and people say, what's blood-brain barrier? Is that like a net in there? Well, the blood-brain barrier is actually the blood vessels that supply blood to your brain. That's what the blood-brain barrier is. It's blood vessels.

[29:55]

And all the blood vessels in your body have the endothelium, which is the inner lining of your blood vessel. And then the blood-brain barrier, that inner lining, have the same type of protein as you do in a small intestine. So some of these proteins are claudins and occludins, and zonulin.

So if you've develop antibody to claudin and occludins and zonulin in the gut, well, these antibodies are going to circulate by blood, and when it gets to the blood vessel in the brain, the antibody then will prompt an immune response against the same protein claudin, occludin, zonulin in the blood-brain barrier, so thereby causing inflammation of those tissues. Now we have more permeability of the blood-brain barrier allowing chemicals that normally doesn't get through.

Remember, the brain is an immune-privileged site, which means that it's protected from the rest of the body because the brain is mission-critical. So then once it becomes permeable, then it just raises havoc because you're going to have antibodies, you're going to have things that can come in and out.

Really the biggest problem with that, David, is that once you have blood-brain barrier permeability, you have more likelihood of things getting into the brain that is not supposed to. That triggers the glial cells and other immune actions to create more inflammation in the brain.

Anytime you have inflammation, that's like your body throwing a grenade to blow something up. In this context of an infection, that's great. Blow the bad guys up all day. But if you have inflammation against self tissue, then you're going to have like cellular debris floating around.

So if you have cellular debris of your brain floating around due to brain inflammation and then you have leaky blood-brain barrier, those cellular debris of the brain can leak out through the blood-brain barrier into the systemic circulation.

Now it has a chance to get presented to the lymph nodes, to the TMB cells in the lymph node, and you can build antibody against neurological tissue. Now you're going to have the more likelihood of getting neurological autoimmunity.

And this is, again, a big problem because you can-- if you have thyroid problem, you can remove the thyroid gland. If you have a brain problem, you can't remove your brain. We want to keep it.

Dr. Jockers: And we haven't done brain transplants yet, right?

Dr. Kan: That'd be interesting. But yeah, so this is why the blood-brain barrier and leaky gut is really a very common occurrence. Doesn't mean everybody with leaky gut is going to have leaky blood-brain barrier, but it definitely sets it up so that it can be a very high likelihood.

Dr. Jockers: Yeah. That's really interesting how that connection works. And you mentioned how like we have this brain-immune-gut, and so you're talking about-- obviously, we talked a lot about the brain. We talked about leaky gut here, how it impacts the blood-brain barrier, and you talked

a lot about inflammation, which is an immune component.

Let's tie all that together with like that immune system you've got in the middle of your BIG acronym, and so, can you connect the dots there?

Dr. Kan: Yeah. This is where that vagus nerve again has a really big immunological component. So the vagus nerve actually has connections to your spleen and your liver. And when you have good vagal tone and vagal outflow, it actually, through that vagus nerve pathway, inhibits macrophage activation in the spleen and the liver.

And what that means is that it can dampen inflammation in those area, and that has a systemic effect. So this where if you have decreased vagus nerve output, right away, you're going to have a more inflamed system because macrophages are these immune cells that are big eaters. They basically go eat up pathogens, but they can also eat up cellular debris.

If the macrophages are overactive too, activating too much, potentially it can damage self-tissue. You're going to just basically activate a lot of cytokines and create a lot of inflammatory response.

So that's a mechanism for how the vagus nerve directly contribute to inflammation. Now, also from a brain perspective, this is really interesting that your left brain is typically the part of the brain that kind of makes you-- just like the sympathetic and the parasympathetic, everything in the body has a gas pedal, brake pedal, right? So this is how we can achieve homeostasis. Your left brain typically is kind of seen as your go brain. It's more dopamine-driven.

Dr. Jockers: More gas.

Dr. Kan: Yeah. Makes you more like want to approach things and motivated, want to go look for a food and mate, while your right brain is more of your brake pedal. Makes you kind of, whoa, let's pay attention to our environment. Is there bad guys? Is there something that's really bad for me? So that's a general description. Okay. It can be seen that way.

Well, your left brain is a gas pedal, also tend to push your immune system. It tend to stimulate specifically T helper 1 immune response. And then, the right brain tend to push the T helper 2 immune response. So T helper 1 is a part of immune system that go kill things. T helper 2 is primarily the immune system that make antibodies.

So sometimes we'll see people with a very left-brain dominant or right-brain weakness having more inflamed body because the T helper 1 response may be too overexuberant, causing more inflammation. On the other hand, if we see someone with a right brain activation and then left brain that's insufficient, it's all about balance, right? It's not like everybody's perfect.

Some people are just more of a right brain person, the more the artist type, some people more the accountant type, but when it's too much, that's when it becomes a problem. So in the right brain active situation and left brain deficient situation, you might see someone with more asthma and allergies, which is more of a Th2 response.

So this is where the brain hemispheres can contribute some of these patterns that we see in people as far as immune system function.

Dr. Jockers: Yeah. Interesting. And is there certain toxins that somebody might be exposed to that could push one of those systems more than another?

Dr. Kan: Yeah. So, in the literature, definitely environmental toxins like BPA and these environmental toxins, they tend to promote a Th2 dominance. So toxins tend to have a Th2 promoting properties. So then this is why it can cause someone to be more asthmatic, more allergic, having more of these allergic type of sensitivity on the skin or in the lung or otherwise.

So toxins can do that.

And we also know not just toxins but infections can also drive Th2 response. For example, pathogen that are too big for engulfing, for phagocytosis, pathogen that are too big for phagocytosis are typically handled by the immune system with eosinophils and mast cells with histamine and these mediators because they basically spill enzymes on the bad guys that's too big to engulf to kind of bleach them to death.

So then, these eosinophils and mast cell responses are typically a Th2 response. So then, what would be a pathogen that's too big to engulf? Well, parasites. So, if you have parasites, you have mold, these things can drive-- they're classic Th2 drivers, and so is environmental toxins.

So these are the things that we're looking for as a pattern. And if we see this person, yeah, asthma, allergy, always have some kind of sinus infection, and then also, this person may have more of a left brain dominance where they're very nitty-gritty about little things or watch too much device, electronics.

Kids with ADHD and autism tend to be more left-brain dominant. So that's why they love their electronic, and we should be limiting electronic exposure for those kids with ADHD because they have a decreased right brain activity and too much-left brain.

So when I see an example here, autistic kid having allergies and asthma and then having like this autism left brain driven, can't pay attention. And the right brain also is bodily sensation, so they can't feel their body, they can't embody themselves, they also can't read body language, that's all right brain deficit, so that's an example in that population of this left brain-right brain imbalance that's connected to an immune system problem.

Dr. Jockers: Right. Wow. Yeah. Really great stuff, Dr. Kan. And you have several different programs where you walk people through kind of how to understand these things and then also how to improve their neurometabolic health. Can you explain some of your programs and obviously we'll send people, send some traffic that way.

Dr. Kan: Thank you so much for letting me share. Yeah. So we have a neurometabolic digital program, and basically, it's a course hybrid coaching program. And it's a 16-module course. It's really comprehensive because what I wanted to do is teach people how to address all the different factors that can impact brain, immune, and gut.

So the modules include things like how to help balance blood sugar, perfusion, support gut health from north to south. We talked about vagus nerve, stomach acid, pancreatic enzyme, bile, like we have a module on each of those, and then leaky gut and then addressing parasites, mold, toxins, detoxing.

And then very detailed modules on brain. In fact, there's three modules on brain and then hormones. So it's very comprehensive. This is great for someone who like to learn, who's interested in the mechanisms and the why, but then also want to have like very concrete steps. Okay, what do I do with all this knowledge? So it's not just like, okay, here's all the stuff. It's actually okay, step by step, what would you do first? What would you do second?

Now keep in mind it's not cookie-cutter because everybody's different. So that's why we include a coaching component so we can kind of explain to people and talk them through it so that they can have more context of how to apply that information to a specific situation.

So, yeah, people really love it. And I think again, it's not for everyone. It's for people who just love to learn. They want to get really deep into it, and they really need help at the same time to solve really complex problems. And they may need just a lot of components to be all brought together.

[40:00]

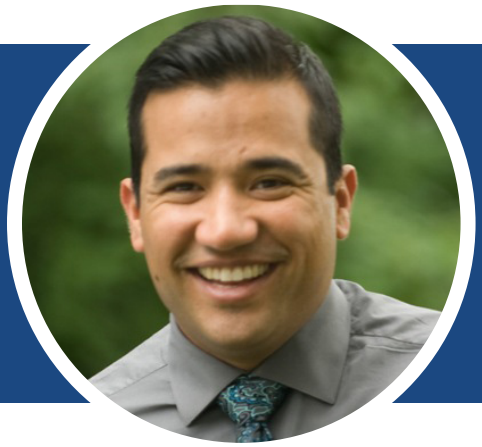
Some people maybe just have leaky gut, and that's it. That's awesome. But some people might need more, so this is an opportunity for them to dive in.

Dr. Jockers: Yeah, for sure. We always pat ourselves on the back when it's like, you just give somebody Betaine HCL, and they get better or probiotics. But the reality is that there's a lot of people out there that are listening to this conversation that, unfortunately, they've tried the probiotics, they tried the Betaine HCL, the glutamine, and all that kind of stuff, and they're not any better. And if that's you, you're that person that really needs what Dr. Kan has to offer. And is the best place for them to find that at askDrKan.com?

Dr. Kan: That's our main website. That's a starting place. Yes. We also have websites directly related to that program called the bigmasterclass.com. Usually, that's through launches. So, by the time you watch this, we probably will be in the launch. We're also going to consider turning into an evergreen offer so that people can jump in at any time.

Dr. Jockers: Well, send me over a link so I can put it in the show notes as well so we can send people there. Thanks again for your time, Dr. Kan.

Guys, definitely check him out. I know you guys love this interview. This is really, really good content. And give him some love. Check him out on social media and also, of course, his website, askdrkan.com. Thanks so much, Dr. Kan, for your time, and we'll see you guys in a future interview. Be blessed, everybody.



From Toxins to Trouble: The Vicious Cycle of Endotoxemia & Leaky Gut

Kiran Krishnan

Dr. Moore: Hello, and welcome back to the *Healing Leaky Gut Summit*. I'm your cohost, Dr. Jaban Moore. Today I'm here with Kiran, and he is an absolute expert in the gut. He's a co-founder of Microbiome Labs. He is a published author in two peer-review journals and a researcher in the microbiome specifically. So there's not many people that could know more about this topic than him. Thank you for joining me.

Kiran: It's my pleasure. When I heard that you were doing a program on leaky gut specifically, I mean, I've almost dedicated most of my career to leaky gut as a microbiologist. So this was a perfect opportunity to get to share some of the most critical information. So thanks for having me.

Dr. Moore: Yeah. And I know when we were talking, you wanted to get into endotoxemia, which is a topic I don't hear a ton about. So what is it?

Kiran: Yeah, it's, in fact, what happens once you have leaky gut, and it's arguably the worst consequence of leaky gut, right? So basically, leaky gut means that your intestines are becoming unusually permeable. Your intestines are permeable to a certain degree, and they're going to be permeable throughout the day from time to time.

And the reason for that is because that's also where you absorb a lot of your nutrients. So we need some permeability in the intestines. And biologically, the intestines are designed in such a clever way that the physiology slows down the permeability and then creates certain checkpoints.

I can actually show this schematic that might help people understand. So if you look at your typical intestinal lining, you've got these two distinct mucous layers here. So you've got this light color mucous, which is called mucin-1, and then you've got this darker blue mucous, which is called mucin-2.

Now, the darker blue mucous is actually a thicker gel-like structure. This top layer here in a healthy microbiome is more of a thin layer of mucus, which is where most of the organisms tend to live.

So you have most of your microbiome in this top layer here. And then this bottom layer here that sits right on top of the lining cells of your intestines tends to be relatively sterile. So you don't have a lot of microbes there at all.

So this area is a very important checkpoint because anything that's coming through here, when you eat something, it comes up in this layer. This is called luminal area, and then nutrients and everything else have to move down this way past the intestinal cell lines and then into circulation. So down here is circulation.

Now, basically this part, this thicker part slows down the movement of objects. And then, when objects get into this area, they have to either go through these cells or in between the cells. And then, between the cells is a space called tight junctions.

These cells have to deliberately open up gaps in between them to let nutrients in, or there are nutrients that can move through the cell indiscriminately. And those are typically things like minerals, calcium, magnesium, those that kinds of things can just move right through the cell. Our body gives those things full carte blanche access to the circulatory system. That way, we can absorb them effectively and get our level of nutrients that we need.

Now, when we're talking about things like toxins and bacteria and viruses and environmental toxins, all the kinds of things that would create havoc in the body, all those things get caught up in this mucin layer.

And if they happen to make it through this mucin layer, they get caught up even further in this thicker mucin layer. And then finally, these cells here, these intestinal epithelium cells, will have to sit and decide whether it's a thing that they're going to let through or not.

And if it's not a nutrient that they recognize, then they will tighten up their spaces in between, and they won't let them through the cell or in between the cell. At the same time, they'll alert the immune system that's down here to show up on this side and neutralize and deal with whatever's up here.

So this is how the intestines can be permeable and also not permeable at the same time. Now, you see on this side of the diagram, what happens when the intestines become super permeable, and we'll get into this part. So you see a loss of this mucin-2 area. The darker blue is no longer here, the lighter blue has basically spilled in, and then you see all this inflammation going on on the lining cells. So keep this picture in mind, and we can talk about that.

So basically, what happens is when you lose that thicker mucin-2 layer, you lose a key component of the geographic and physical barrier to things just leaking through, right? Our digestive system is the biggest exposure we get to the environment around us because, of course, food and drink brings in lots of foreign things, but a lot of your system up here, your nose, your eyes, your ears, everything you breathe in, everything you experience in the environment all drain into your gut, right? That's how it's designed to do it.

When you breathe in something that's irritating your lungs, your mucus in your lungs traps it, and then you have these beautiful little hair-like structures called the mucociliary elevator that moves that mucus that's trapped, the toxins up the lungs, and then you end up swallowing that every single minute of every single day.

You don't even realize you're doing it, but it's actually an automatic thing. Things that enter your eyes will drain into the back of your throat. Things that enter your ears or any other part of your sinuses will drain into the back of your throat. So everything is getting sampled in the gut.

So the gut has to act as this major sampling site and major site of restriction for things that can enter into your blood, right? So if you have the normal structures that we talked about, the dark blue layer, the light blue layer, the intestinal cells that are tight against each other, then the body can make decisions as to what goes through and what does not.

If you lose that middle layer, that darker blue gel-like structure, then things start to just flow through. Now, to answer your initial question, which seemed like probably 20 minutes ago, the endotoxemia is basically the movement of toxins from the top layer, the mucous layer where all the microbes live, into the blood non-specifically, so flowing right through.

And the thing of it is, about 50% or more of the microbes that live in your gut are called gram-negative bacteria. That means these bacteria have a unique structure to them where they produce an endotoxin that sits in their cell membrane structure and their cell wall structure-- sorry, cell membrane structure. They don't have cell walls.

So their cell membranes have this toxin sitting in there. Now, if it's in the cell, it's not really causing a problem for us or neither for them. But bacteria are dying all the time in the gut. They're dying. They're lysing. They're blowing open. That toxin gets released. And typically, it's supposed to get trapped in this upper layer right here. But if you lose this below layer, then this upper layer is constantly flowing through, this toxin is going to constantly make its way through into your blood system.

So the word endotoxemia means an endotoxin, which means a toxin that's derived from within. So it's not something we can get away from. Like an exotoxin is like a mold toxin in your house, and you're like, oh, my God, it's making me sick. You can either remediate the house or move. An endotoxin is one you can't get away from. So it's constantly produced in the gut, and then the -emia part means it's in the blood, right?

So that then becomes the most profound outcome of leaky gut. Other things are going to leak through as well. In a leaky gut, you're going to get viruses and environmental particles and other things. But the thing that really creates a massive amount of problems, and we can talk about why, is the movement of that bacterial endotoxin across the lining and into circulation. That becomes a foundation of the vast majority of chronic illnesses.

Dr. Moore: Got it. So because we have bacteria normally in our digestive tract, that's what Microbiome Labs that you talk about all the time, so is this necessarily pathogenic bacteria that's causing this problem, or is this normal gut flora where these endotoxins are coming from?

Kiran: Yeah, and that's a really important question because it's actually not always pathogenic microbes. In fact, lots of your beneficial commensal microbes happen to produce this endotoxin, right? So the bacteria use it for other purposes.

The bacteria use it for communication with other microbes. They use it as a binding receptor. They use it as a way of reading their environment. So it's really for the bacteria at the end of the day. But when it's not in the bacteria, and it's by itself, it triggers massive amounts of inflammation in the body.

And the reason why it does that, there's an evolutionary significance to it, right? So I would venture to guess about 70% of that endotoxin is produced by normal commensal bacteria in your gut. They should be there. They're always there, even in a healthy individual, they're there, and they're producing this endotoxin, right?

And then about 25% to 30% probably are from either opportunistic pathogens, meaning they're not always pathogenic. They're only pathogenic under certain conditions or direct pathogens, which are always pathogenic. So it's a much smaller amount that's coming from pathogens. It's typically from your own commensal bacteria.

The thing is, because there's so many microbes that exist in the gut that make this toxin, your immune system has basically evolved to recognize this component of the bacterial cell wall or cell membrane as a way of recognizing the presence of bacteria in general because your immune system needs to find little structures on different microbes to identify different microbes and viruses and so on.

[10:00]

Because remember, we don't want our immune system to attack everything. We want it to be able to make judgements because lots of your commensals, all the trillions of bacteria that are living in your system, which are everywhere in your blood, in your brain, in your eyeballs, in your gut, and everywhere else, you don't want your immune system continuously attacking all of these microbes. You'll be sick nonstop. You'd be 24 hours every single day of your life, you'll be sick.

So there's a tolerance level that's developed with your immune system where it recognizes commensal-friendly microbes, and it doesn't attack them. It has a relationship with these microbes. But it's come to over time, over the course of evolution, to recognize this endotoxin that's present on certain bacteria as being a bacterial source of a biological component.

Now, the reason why it really wants to know this, and the reason why it keeps monitoring this significantly, is because when you undergo bacteremia or septicemia, that's blood poisoning, which is a very scary, very difficult condition, and I would imagine that a lot of people through the course of evolution were dying from bacteremia because it doesn't take much, right? It takes a little bit of trauma on your arm or somewhere on your body for it to get infected.

And then you're breaking the barriers so you can get blood poisoning or in the case of internal infections and things like that, where you end up with blood poisoning, your immune system has learned to recognize this LPS in your body as a potential signal that there's too many microbes in circulation.

So anytime it recognizes a presence of this endotoxin, which is called LPS, in the blood, it takes it very seriously because it's anticipating that maybe you are bacteremic, right? And that's the kind of thing that would kill a lot of people before the day of modern medicine.

Now you have a chance of surviving if you become septicemic. If you end up in a hospital, they can take care of it, but you can be walking around perfectly healthy and then be in death's doorstep in 24 hours when you undergo bacteremia. So that's the natural protection against it.

So when that leaks through and ends up in circulation, your immune system takes it very seriously. And everywhere it encounters this endotoxin inside the body, it elicits a massive inflammatory response.

Dr. Moore: So this can explain why so many people that end up with leaky gut, then that leaks through, and now we have this immune response where you have GI symptoms in some cases, but not every case, right? So if your immune system doesn't capture it immediately upon getting into the gut and it circulates to a joint or to your brain or to other tissue types in your body, you could have leaky gut that isn't eliciting gut symptoms but is eliciting fibromyalgia, body pain, brain fog, and all of these other-- so that explains why leaky gut is not just a gut problem.

Kiran: No.

Dr. Moore: But as you were going through this, I'm thinking to myself, okay, so you can test for LPS, right?

Kiran: In the clinic, it's very hard to test for LPS accurately. We can do it in research settings. And the reason is because in order to understand how much LPS is in circulation, you have to pull out blood and spin out the serum because you look for it in the serum, and then once you pull it out of the body, it only has about a four-hour half-life, which means you have to get it to the lab and get it analyzed within that time, which is just not practical in a normal clinic setting.

So in research, what we can do is either A, we can test it that quickly because the labs are right there, or you can freeze it to minus 80 degrees Fahrenheit, and then it's stable for a long period of time, right? So normally, what we do is we collect all the samples, freeze them all, and then run them all at the same time when the study is completed.

So in the clinic, you really can't do it. Well, you can do surrogate markers or indirect measures. There are some labs that do that, but they're just not accurate because they haven't used those in research papers.

Dr. Moore: Got it. So then what would allow for, as you were talking about, you've got our three layers. What is allowing for that middle layer to go

away? What's causing that to happen?

Kiran: Yeah, that's the critical question, right? So in order for this middle layer and the top layer to be made, you've got these cells in here called goblet cells, right? These are our own cells that produce this mucin layer, and it produces this thicker version of the mucin layer, so it's constantly producing it from the bottom and pushing it up.

Now, there's this defined separation between the thicker layer and the thinner layer up here. Now, the way the thick layer becomes a thin layer as it moves up is there are microbes that live on this very edge that can start to digest this thicker layer and make it more liquidy-like.

And this is how this whole mucous elevator keeps pushing up, right? And then, when it gets to the top here, it sloughs off through defecation. So this topmost layer is now getting pooped out basically every day.

So think about your goblet cells are making this thick layer. It's moving up in this boundary between the thick and the thin layer. There are microbes that are basically converting the thick layer into the thin layer, and this whole thing just keeps moving up and pushing toxins and everything through.

Now that's in the homeostatic environment. So there are microbes that are well designed to be able to eat that thick layer, and there are beneficial microbes that do that on purpose.

So, for example, *Akkermansia muciniphila*, it's a mucin-loving bacteria that's a very important keystone species, and it lives just slightly deeper in that thick layer, and it metabolizes the top part of that thick layer, making it more liquid. When it's doing that, that's actually giving a signal to the goblet cells to produce more of the thick layer.

So the action of that Akkermansia is all about maintaining a constant flow and rebuilding of that mucus layer, and maintaining the structure and integrity. Now, let's say you've gone through a couple of courses of antibiotics. Akkermansia's growth levels are way low.

Other egregious bacteria can start also doing the same thing, eating away at that mucin layer, but they do it without stimulating the goblet cells to produce more, right? So dysbiosis, which is a term we use just to generally describe imbalance and leaky gut, which is driven by bacterial imbalance, is most simply explained as having an imbalance of microbes that eat away at that mucin-2 layer versus microbes that rebuild it.

And what happens then over time is you get a net loss of that mucin-2 layer, and then this mucin-one layer, which is more like liquid, will just flow through too close to these intestinal epithelial cells.

And then within the intestinal epithelium that's aligning cells of the intestines, there's lots of immune cells as well. It's loaded with immune cells. Almost every four or five cells in that structure is an immune cell because it's constantly reading these environments up here to translate signals to the rest of the immune system.

So these immune cells here, when they recognize that too many microbes are coming too close because this top layer is sloughing down into the lining of the gut, they start eliciting a massive immune response because these cells are anticipating septicemia.

These cells are thinking, holy crap, there's trillions of microbes floating in too close. The barrier is gone, right? So the wall is down. Now all you have is a chain link fence, which is essentially what these intestinal epithelial cells are like. And now they start recruiting all of these immune cells to this region, and the immune cells come here and start bombarding and just carpet bombing that area with inflammation and so on, trying to kill everything here, right?

And then this is how your intestinal epithelial cells first get attacked, and they are the ones that

suffer the most damage in the beginning. But the problem with that is actually makes the gut even more leaky because now that chain link fence is down as well, right?

And then, all of this inflammation can translate to the rest of the body. So leaky gut absolutely starts with something that drives an imbalance between the microbes that eat away at the mucin layer versus microbes that rebuild it.

Dr. Moore: Brings so many questions to my mind as you're going through this because, first of all, what can damage that process? Is it some sort of H. pylori? Is it Clostridia? Is it parasites? Is it stress? Like, is there a top five or something that comes to mind that you can tell people like these are some of the major causes that you see?

Kiran: Yeah, I would say yes, there's absolutely top five. So pathogens, you'd be surprised, are probably-- maybe there's one pathogen in the top five because pathogens, in general, can't really elicit their function unless the microbial ecosystem is already weak, right?

Because think about the microbiome. A healthy microbiome has 40 trillion microbes in there. So even if you send in a pretty egregious pathogen, it has a lot to contend with, with all this competition in there for it to actually cause infection and be able to grow to a level that it can cause a problem. So pathogens are actually less of a problem in terms of the initial start of the dysfunction, right?

So I would say the top five things are, number one, is constant exposure to low levels of antibiotics, right? And in our world, so you can have, of course, a major course of antibiotics, that's a high dose of antibiotics, that's actually number two, but number one is the constant exposure to low levels of antibiotics.

[20:00]

So what I mean by that is all our food and our agriculture and all that is completely loaded with antibiotics. The most popular one being Roundup, for example, right? Roundup is an absolute antibiotic. The patents filed by Monsanto are for an antibiotic. And in fact, when you look at the studies behind it, it's one of the worst kinds of antibiotics because it selectively kills good bacteria.

A lot of the opportunistic bacteria like the Klebsiella and Pseudomonas and all that. They actually have mechanisms around how Roundup harm cells. But a lot of the good bacteria, the Lactobacillus and Bifidobacteria and Ruminococcus, they get wiped out to very, very low levels from the exposure to Roundup.

And Roundup is at small levels every single day that you consume your food and drink and all that, right? So over time, that has a very profound effect on your gut. So that's probably number one.

Number two are major courses of antibiotics, right? For ear infections, sinus infections, whatever they may be. Most kids by the age of four have had at least two rounds of antibiotics. Most adults, you take any adult on the street, has probably had a dozen rounds of antibiotics in their life, right?

Antibiotics knock down your microbiome and create massive dysbiosis. Not to villainize antibiotics because there are times when you need them, and they will save your life, but we likely overuse it. Even the CDC, which is very conservative about this stuff, estimates that at least 50% of the antibiotic prescriptions are unnecessary, right?

They're given for viral infections and so on. So there's an overuse of antibiotics. And then in that antibiotic number two is the use of antibiotics in our food, meaning our meats, our cattle, and chicken and pigs are all fed antibiotics, right?

And there's something like 90 different types of antibiotics that are actively used in animal farming, and most of them have not been checked for safety in humans, but we're getting those antibiotics indirectly through these animals.

So I think those are two things.

The third thing is a significant reduction in the diversity of our diet, right? So in North America and the Western world, our diets are so narrow. Most people will eat about 10 or 12 different types of foods on an annual basis, and if you think about the people that eat all the processed foods and all that, most of those have the same base in it, right?

They're either wheat-based, meaning everything in there is wheat flour, or they're soy-based, or they're corn-based, right? So those are all just this one category of food. Even though it looks like you're eating a bunch of different things, it's all either wheat, soy, corn-based, and then we're getting some protein and some fats from time to time.

But if you look at our ancestors, and the anthropological studies show that our ancestors ate upwards of 600 different types of foods annually, right? They foraged. They gathered. They hunted. They ate seasonally. They could only eat what was there during that season. So their microbiomes were super diverse.

And the reason why diversity of foods makes a difference is that different carbohydrate and protein structures and all these different types of foods dramatically change which microbes can metabolize them, right? So a diversity in your diet feeds a diversity in your microbiome as well. So that's three.

The fourth one is our divorcing ourselves from microbes in general, right? We are designed to be a product of the natural environment. We were evolved as an osmotic being within the environment, right? Our ancestors ate, slept, and drank in the land. They ate dirt. They drank waters out of rivers and streams. They picked and dug and foraged for things.

So everything they consumed was loaded with microbes all the time. And we incorporated some of those microbes in our gut. We excrete some microbes out into the environment. We're constantly exchanging microbes in the environment.

And the studies are very clear. People that, for example, live in a rural environment, tend to have healthier, more diverse microbiomes than people that live in an urban environment, right? So we are designed to be exposed to microbes constantly.

And the vast majority of people aren't anymore because we live in relatively sterile environments, homes, cars, offices, and so on. So our exposure levels are dramatically reduced. So that's four. The last one is stress. And you had mentioned that earlier.

Stress is probably one of the bigger dysbiotic drivers in the gut. So, if you think about the constant exposure to low doses of antibiotics from things like pesticides, herbicides, and all that are all over our foods, so those are coming in, and they're creating a dysbiosis in the gut. They're starting to kill off beneficial bacteria, allowing dysfunctional bacteria to prevail to a certain degree.

Now, what happens when you undergo stress is a lot of those dysfunctional bacteria I mentioned earlier are opportunistic bacteria, right? They don't necessarily express all their toxins and virulence factors and all that all the time. They actually sit and wait for the right opportunity to be able to do that.

Many of them have evolved to read the host stress hormone levels as a trigger for them to express their toxin genes. So what they do is they sit around, and the moment our cortisol levels are up, our epinephrine or norepinephrine levels are up, they go, okay, the host is under stress, which means the host's immune system is suppressed. This is the opportunity for us to prevail and express our genes and start multiplying.

So not only is that low level of antibiotics creating this now imbalance, a stressor, an external

stressor, whether it's work or life or whatever it may be, will then give the impetus to those opportunistic bacteria to really explode their growth.

So the combination of those two are really, really powerful in over time, driving a significant amount of dysbiosis, eventually leading to more microbes that eat away at the mucin layer versus rebuild it. And it's important to keep in mind with leaky gut. Remember, your intestines are 26, 27 feet long, right? So it's a very long intestinal tract.

You could have leaky gut in like a six-inch section of your gut, and it's causing some problems. It's causing some systemic inflammation in your body, but it's subclinical, right? You wouldn't notice it. There's no symptoms associated with it, and so on. And we've measured this in lots of young people.

For example, our first leaky gut study that we published were average ages 23, normal body weight, no history of any illnesses, weren't on any medication, and we tested 50% of them had severe leaky gut, right? But it was subclinical still because it was only a portion of their gut.

Now, as that 6 inches becomes 12 inches, 18, 24, and so on, then the pathology becomes more profound. And that's when you start to see symptomology, which, of course, can be completely distal from the gut. It doesn't have to be gut symptoms like you had mentioned. It can be in your brain, anxiety, stress, Alzheimer's, Parkinson's, dementia, all of those are leaky gut conditions.

Heart disease, obesity, diabetes, skin conditions like eczema, psoriasis, autoimmunity, all of them are leaky gut conditions. All of those are also endotoxemia conditions, more specifically. And I'll conclude this part to say that there was a 2015 publication in a journal called *Frontiers in Immunology*. And this was a meta-analysis publication, meaning it was a study that looked at all the studies on the topic.

So it provided us some scientific consensus on all the data. They concluded that stress-induced leaky gut was the number one cause of mortality and morbidity worldwide. Number one killer worldwide was stress-induced leaky gut and endotoxemia, that's a translocation of endotoxins.

So we cannot overstate the importance in people paying attention and understanding this process because if you can stop leaky gut, then you're profoundly improving your overall health outcomes.

Dr. Moore: After dropping a fact like that, number one cause of death, I say I know listeners are going to want to know what can we do about it? So when we've lost this middle layer, when endotoxemia is coming in, it's like, okay, well, if you're not producing the mucus appropriately, what do we do?

Kiran: Yeah. And that's the beauty of it, right? It can all be reversed at any point. It doesn't matter if you're 98 years old and your gut is leaky, you can absolutely reverse it at that point. If you're one years old and your gut is leaky, you can reverse it so it's never too late, which is great.

It always starts with rearrangement of the microbiome because now the reason you have all these problems is because your microbiome is off kilter. You've got too many microbes that eat away at the mucin layer versus ones that rebuild it. So that's the first place of focus.

Number one, we have to remove or try to reduce the drivers that keep driving the dysbiosis, right? So instead of eating all these processed food and foods that are not organic, where you're getting huge amounts of exposure to things like glyphosate and Roundup and all that stuff, you need to try to go more clean with your diet, right?

So you want to reduce your exposure to those low levels of antibiotics that you're getting all the time. You want to filter your water better. So you want to get a good water filter at home, a carbon filter, or an RO filter of some sort so that the water

you're drinking is cleaner, the food you're eating is cleaner. So that's step one that we have to kind of clean up our environment.

[30:05]

Step number two would be to send in microbes that can help readjust the balance. So we've been working with the spore-based probiotics since 2012, and we've published a number of studies on the MegaSpore, the probiotic with the five strains of spores. We've published at least two papers showing that the spores can alleviate leaky gut and endotoxemia in as little as 30 days.

And one of the powerful reasons why they can do that is they do something called quorum sensing. Quorum sensing is the ability of certain microbes to go into the environment and read the signatures of all the other microbes in that environment. And when they find these egregious microbes that are eating away at the mucin layer or producing toxins, they'll sit around them and bring down their levels by producing antimicrobials or competing for space and nutrients and so on.

They also produce other postbiotics or prebiotics to grow your beneficial microbes. So what we were able to show in one of our published studies was when you add the MegaSpore, for example, to a dysbiotic gut, a gut that we had inundated with antibiotics and was completely off-kilter, what it's able to do is restore the growth of those keystone species like Akkermansia.

That's the key one that really stimulates the rebuilding of your mucosa and brings back a lot of the other beneficial microbes and dramatically brings down all of the dysfunctional microbes and increases the diversity of the gut, right?

And that happened in as little as three weeks in that particular study. So introducing the right kind of probiotics, the spore-based probiotics, reducing exposure to things that drive dysbiosis, managing stress becomes a really, really important thing, right?

And there's a couple of different approaches to managing stress. Number one is you can do mindfulness work, so meditations. There's apps you can use. There's exercise. Weightlifting is a very powerful way of reducing stress-related hormones.

So resistance training and movement is a really important thing. Getting outside in nature not only can reduce stress but it also exposes you to more microbes, which actually can help diversify your microbiome. So go out for walks, runs, hikes, these things will make a difference. Go downstairs to your gym or to the local gym and lift some weights, right? You don't have to be a bodybuilder at the gym for an hour.

You can go for 10 to 15 minutes and do some basic things like lifting a dumbbell over your head and, of course, be safe, and hopefully, you know what you're doing to some degree, but just some degree of resistance training, and creating that triggers on your muscles.

There's something called the muscle-mitochondria-gut axis. It actually starts to change your microbiome and reduce your stress hormone levels. And then the last thing is getting diversification of your diet and getting more prebiotics in and more resistant starches in your diet because the mucin layer is predominantly made by the production of butyrate.

Butyrate is an important short-chain fatty acid in your gut that some microbes produce. Butyrate becomes the primary fuel for those goblet cells to reproduce mucin, right? And then the building blocks of the mucin are amino acids, are proteins. And so, you need to take in adequate levels of protein.

So think about this simple shift in your lifestyle. You want to modulate stress. You want to get adequate amount of sleep because a lot of that repair is going to happen when you're sleeping. It's not going to happen during the day when you're constantly eating, and things are constantly

moving into your bowel, right? It's going to happen when you sleep.

So if you don't sleep enough, you don't have enough time to repair it. You're going to want to get in the right type of probiotic. The spore-based probiotics have been shown to be able to do that. You want to increase the diversity of diet, especially getting in more prebiotic foods and resistant starches.

And then finally, if you can get out and do some exercise. Those kinds of things will really help. And sorry, last thing is reducing the things that drive dysbiosis. All of these sound relatively simple, but I promise you if you add them all up together, they're incredibly powerful for revamping the lining of your gut. And you don't have to do anything too complicated. It's just these little changes added up together will absolutely change the leakiness in your gut.

Dr. Moore: Well, that was an incredible wealth of knowledge from a topic that-- endotoxemia doesn't get talked about enough. Leaky gut being the topic where you're doing here, which are so interconnected to the causations of it, and then all the way down to what we can do to start to work our way out of it.

As you said, go lift a dumbbell above your head, exercise. Some of them are easy and can be implemented immediately. So I really appreciate your knowledge, your research, all that you've done for the health of the world with your research and company. So is there anything else that you'd like to add today?

Kiran: Yeah. So I mentioned that stress is one of the most prolific things that drives leakiness in the gut, drives endotoxemia, and then also drives neurological inflammation. So one of the new mechanisms that's well understood, and in fact, COVID drove this to a certain degree, and this is where long hauler syndrome comes in, is in the central nervous system, what's supposed to happen is tryptophan, which is an amino acid that you get from your diet and so on, and it's a precursor to the production of serotonin, which is your happy hormone and melatonin, which is a sleep hormone, and serotonin beyond being the happy hormone, also helps with bowel movement and it's anti-inflammatory, does all kinds of other wonderful things.

And same with melatonin. Besides the sleep component, it also helps circadian rhythm, anti-inflammatory, antiviral capabilities, and so on. What tends to happen when you experience lots of stress, and you have endotoxemia, you have LPS leaking through, is tryptophan starts getting converted into something called quinolinic acid instead of melatonin and serotonin.

So now your central nervous system is producing this compound. Instead of the happy hormone, the sleep hormone, which are anti-inflammatory, it's producing this compound that's neurotoxic. So it keeps you in this state of neurological activation, of sympathetic activation, which is a flight-to-fight response of neurological symptoms like nerve pain and fibromyalgia, and all of the symptoms related with long haul COVID, for example, are all based on tryptophan metabolism that's now becoming quinolinic acid.

So all of that is really, really a profound pathology that exists in large numbers of people in the Western world. We tend to have this tryptophan dysfunction, a lot of it driven by stress and other things that we experience in life.

Psychobiotics, these are probiotics that have an impact on the central nervous system and in the brain. The right type of psychobiotics have been shown to be able to reverse that tryptophan switch. So we launched one called Zenbiome, it's a Bifidobacterium longum 1714.

And what we've been able to show, and I think now eight published studies is when you take a psychobiotic like this, it actually shunts tryptophan metabolism back to serotonin to melatonin, which then actually dramatically reduces

stress response, cortisol levels, epinephrine, norepinephrine levels, and all of the inflammation that goes along with stress.

So another really effective tool for people because we live in an incredibly stressful world, where anxiety and all that is an epidemic, we have this tool of psychobiotics that can really help. So that's a very exciting area of microbiome-related research. It's the gut-brain axis and the utilization of psychobiotics to help with some of these really profound problems that people struggle with.

So that's the last thing I'll leave you out with that there's awesome hope, lots of cool things coming down the line that can really help people in a significant way.

Dr. Moore: So after dropping those little factors, where do people get a hold of information or understand more about these psychobiotics and everything else you're researching?

Kiran: Yeah. Come to our website at MicrobiomeLabs with an S dot com. You'll find all kinds of information on mechanisms and products and webinars and resources so you understand how these things work a little bit better.

Reach out to me on Instagram. My handle is KiranBiome, K-I-R-A-N-B-I-O-M-E, and I post a lot of my talks and research and things that we put out into the atmosphere to educate and empower people. I do a lot of that on Instagram as well. So feel free to reach out there.

But there's a lot of really, really exciting tools coming out and are already out, and I think it's going to really change humanity over the next 10 years because we're going to have a much better handle on these chronic conditions that are plaguing people right now, and destroy families and livelihoods and all of that stuff and make for terrible quality of life. We will have a very significant handle on that.

And a lot of it starts with being empowered with knowledge, right? So thank you for doing a program like this because these types of programs are a key thing to empower people with information. When you know better, you can do better, right? So being educated on the subject is really important. So thanks for the opportunity.

Dr. Moore: Absolutely. Love to have you on. Wealth of knowledge. Thank you so much. And if you're listening, make sure you go to Microbiome Labs. Learn more about the microbiome that also leads to the gut-brain connection, and now the brain-biome or whatever you're going to call it. Thank you so much.

Kiran: Thank you.

How Menopause Affects Digestion and the Microbiome

Michelle Sands, ND

Dr. Jockers: Welcome to the Healing Leaky Gut Summit. I'm your host, Dr. David Jockers. And today, our topic is How Menopause affects the Microbiome with Dr. Michelle Sands. What we're going to cover in this interview is what is menopause, what's perimenopause and what's happening to the female's body during this period of time?

What's happening to estrogen, progesterone levels. How that impacts gut health. How that impacts leaky gut, intestinal permeability. How that impacts the unique species of bacteria in the gut. And we're going to talk about the top strategies to improve gut health to set you up for success during perimenopause, during menopause.

So many women are having major symptoms like hot flashes, low libido, weight gain, vaginal dryness, headaches, a lot of different issues, dry skin as they go through the perimenopause-menopause transition period. So we're going to cover that and we're going to talk about the importance of good gut health, a healthy, balanced microbiome as you set up and then go through the perimenopause and menopause solution.

And we're going to ask this question. Is hormone replacement, is estrogen-progesterone replacement a good strategy for someone going through a number of symptoms associated with menopause? So you guys are going to get the answer to that in this interview. You're going to love this.

Dr. Michelle Sands. She is a number one international bestselling author, licensed naturopathic physician. She's a co-founder of Glow Natural Wellness and a highly sought-after female hormone and anti-aging expert. Her book and programs have been featured all over major media outlets. You can find her website at glownaturalwellness.com.

And Dr. Sands, she sees women from all over the world and has a remarkable track record for improving health and happiness with her proven proprietary system, The Glow Protocol. And she offers women going through the perimenopause and menopause transition, accessible, affordable, and safe options for hormone restoration through her widely popular Healthy Hormone Club. She has a free hormone restoration masterclass we're going to talk about as well.

You guys are going to love this interview. So without further ado, let's go in. But be sure to share this with the people that you know and that you care about because it can make a big difference in their life. Thanks so much and let's go into the interview. Well, Dr. Michelle Sands, thanks so much for joining us today.

Dr. Sands: Thank you so much for having me. It's

a pleasure to be here.

Dr. Jockers: Absolutely. I know you're a female hormone expert and you work with a lot of women that are going through perimenopause and menopause. So let's talk about some of the major symptoms that women experience as they're going through this transition in life.

Dr. Sands: Yeah. There are tons of symptoms. The ones that we talk about the most are going to be hot flashes, night sweats, insomnia, vaginal dryness, and mood swings. Those are really the ones that everybody attributes to menopause. But there are actually 99 symptoms of menopause. Everything ranging to ringing in the ears to soar joints, to high cholesterol, and of course gut health issues ranging from bloating, gas, constipation, diarrhea, leaky gut. It goes on and on.

And the hormones are so much our chemical messengers of our body. So they're involved in pretty much every aspect of our life. And then every aspect of our life, from everything we eat, everything we think about, how we sleep, the environment we interact with, that all interacts with our hormones.
So they're very sensitive. It seems like they might be scary to balance hormones, but everything you do to have a healthier heart, everything you do to have healthier bones, everything you do to have a healthier gut also helps your hormones too.

Dr. Jockers: Yeah, for sure. Hormones are such a key player in our overall physiological processes. And so what's actually happening to a woman's hormones as she goes into perimenopause and then into menopause?

Dr. Sands: Women's hormones cycle throughout the reproductive years, so starting at puberty, we start having fluctuating levels of estrogen and progesterone. Our testosterone increases. And then as we reach our end of our reproductive life, which is our perimenopause stage where we're kind of winding down, our ovarian production of our estrogen and progesterone is starting to slow.

We're not releasing eggs every month and we're not getting that bump of progesterone estrogen each month. So we start to notice symptoms. The first symptoms that usually happen are associated with progesterone decline. That's usually the first hormone to drop. Because when we don't release an egg, there's no need for progesterone to increase.

And so symptoms like anxiety. Symptoms like insomnia. Constipation is another big one with low progesterone. Most women don't put two and two together, but progesterone really helps with gut motility. And so even women before perimenopause, women who are cycling may notice that right before their period, they start to get a little constipated.

And then when they get their period, they might get what's referred to as the period poops where you have a little bit of diarrhea. And women will notice this all throughout their reproductive years but a lot of women don't put two and two together to know that it's actually our hormones that are fluctuating and not necessarily something they ate. So that's really interesting.

So progesterone is the first one to fall. Then we have estrogen. And when estrogen falls, estrogen is so important for the female health, for our brain, so brain fog kicks in. We start to get loss of collagen. So starting at whatever age you enter menopause, the average age is 51 but most women will enter perimenopause five to seven years before that, so this can be as early as the thirties for some women. Average is in the forties.

But your collagen will start to drop. So you'll start to notice more laxing in your skin, wrinkles, fine

lines, and things like that. Also, joint pain because estrogen is a lubricator. So it's really important for lubricating your joints and you may notice you start to have joint pain, stiffness. Estrogen is also very important for not only your brain health, but bone health and heart health.

And then, of course, there's the vaginal dryness, painful sex, all the issues around the vaginal microbiome, including urinary tract infections because estrogen is so important for supporting our lactobacillus. Which is important for our gut health, but also our vaginal microbiome as well. So those are some of the big ones. As I said, there's everything from tinnitus to high cholesterol to hair loss. There are so many symptoms of menopause, but specifically for gut health, our hormones are so important.

And a lot of women notice as they reach their forties, they start to notice they can't eat as many foods as they used to eat. They start cramping or bloating or digestive issues once they have their meal. And a lot of women will actually cut out whole food groups because they're afraid of what's going to happen to their digestion. And then also, a lot of my clients will say they actually avoid some social situations because they start to have a lot of uncontrollable gas. And it is really a quality of life thing that making sure we have that balance is so important. There's a lot that we can do.

Dr. Jockers: Yeah, for sure. So you mentioned three hormones, estrogen, testosterone, and progesterone. And so as women are going through this transition, you mentioned progesterone's dropping, estrogen's dropping. And oftentimes, even though it's kind of normal and natural for these hormones to drop, oftentimes, progesterone drops more, right? A kind of a greater-

Dr. Sands: It drops first. Yeah.

Dr. Jockers: It drops first. Okay.

Dr. Sands: So progesterone drops first.

Dr. Jockers: So there could be a larger gap between the estrogen and progesterone, and that can be a player in some of these symptoms as well, right?

Dr. Sands: Absolutely. Hormones are all about balance. And so when our estrogen and progesterone is balanced with our testosterone as well, for women, we don't talk about testosterone a lot, but women have a good deal of testosterone in relation to the rest of their hormones. We just don't make quite as much as men. But it's so important for our bodies.

And there are things that are associated with low testosterone. One of the major things associated with low testosterone is going to be loss of energy, loss of sex drive, but also testosterone is really important for reducing inflammation specifically in our gut. And so low testosterone, can actually lead to leaky gut, increased intestinal permeability, which then down the line can lead to increased risk of autoimmune conditions and much bigger issues down the road.

So having healthy testosterone levels is so very important for women. But in addition, even if your testosterone levels stay strong, IF those are high in relation to your estrogen and progesterone because they've now dropped, now you can have issues like acne, hair loss, belly fat, and things that you don't want as well.

So we don't want to have high testosterone in relation to our estrogen and progesterone. We want everything to be balanced. Same thing with estrogen. We don't want estrogen dominance. We want a balance of our estrogen, progesterone, and testosterone that hormones need. It's like Goldilocks and the three bears. They need to be

not too much, not too little, but just right.

Dr. Jockers: Yeah, that makes sense. And also, when women are younger, high testosterone is associated with PCOS, polycystic ovarian syndrome as well. That's not what a woman's going to experience as she goes into menopause.

Dr. Sands: But it could be a similar scenario because with PCOS, women generally are having anovulatory cycles, meaning that they're not ovulating, and that's causing them to have significantly decreased progesterone. And progesterone opposes testosterone. Kind of keeps it in line.

[9:55]

And so these women are kind of experiencing on a smaller scale, actually on a larger scale for them but on a smaller scale in perimenopause, it's a similar scenario for a lot of women as their progesterone drops, but their androgen stay level.

It's different. It's really unique for a lot of women because you can have a woman who is 40 years old and she can have very, very low testosterone, and her progesterone estrogen haven't dropped yet. But conversely, you can have a woman who has very perfect testosterone but her estrogen and progesterone have dropped so low that now she has those PCOS-like symptoms.

Dr. Jockers: Yeah. Now, you touched on the way that some of these hormones impact the gut, the microbiome, and just the gut junction itself. You mentioned with estrogen, I heard you mention how that has a beneficial effect on lactobacillus, which a lot of the different species of lactobacillus are healthy bacteria that are in our intestinal tract as well as you mentioned in our urinary tract. Right? So they play-

Dr. Sands: Exactly. Yeah. The urinary and vaginal microbiome is so important to keep that in check and it is very much related to our gut microbiome. So usually, if you have an issue in one, you're going to have an issue in another, especially if it's due to the lack of estrogen. So it's not just the lactobacilli though, it's also the bifidobacteria as well.

So those are two big, huge species of bacteria that not only do we need those in order to have good neurotransmitter synthesis and good absorption and digestion of our food. But also, those two bacteria species, they also help to keep the balance of your bad bacteria tamped down. So a decrease in estrogen can harm the levels of your good lactobacillus and bifidobacteria. But also, it can cause an increase in the more harmful or less preferential bacteria to have in a gut.

We need all of the bugs in our gut to have environmental diversity, but you want them in certain levels. So the more harmful bacteria, when they get higher and you have less lactobacillus and bifidobacteria, then you're going to have digestive issues. You might have cramping, bloating, constipation, diarrhea difficulty digesting foods. And so you really do want that optimal balance.

And there are things that you can do besides replacing estrogen, of course. Eating a healthy diet. Having fiber in your diet. Taking a probiotic. Eating fermented foods. Having prebiotic-rich foods. So it's not just about replacing hormones. We do do that in our practice and a lot of women will want to do that for all the other symptoms of menopause as well. But it's really important to know why these things are happening to you.

It's not that you did something wrong. It's just the human body. The female body wasn't really designed to live past 50-something years old. So our systems kind of shut down. Now, we have the technology and we have the sanitation and

we have the lifestyle where we can live to 100 years old. And so that's why for a lot of women, replacing hormones is an option because now they can live vibrantly until that hundredth year.

Dr. Jockers: Yeah, for sure. And let's come back to replacing hormones. But first, let's talk about, you mentioned estrogen, how that impacts the gut. How about progesterone? What's its impact on the gut microbiome?

Dr. Sands: Before we move on to progesterone, I also just wanted to add in, with estrogen, it has a huge impact on our bile production and our digestion of fats. So our gallbladder stores bile. Bile is produced by the liver. It's a digestive flu that helps to break down fats and when estrogen levels drop, we actually make less of this bile. And so now it's kind of more concentrated when it empties into the digestive system. And so that can make digesting fats extremely difficult for women.

Dr. Jockers: By more concentrated, you mean more sluggish.

Dr. Sands: It's more sludgy. Yeah. It's not as free flowing. It becomes more kind of like sticky sludgy.

Dr. Jockers: Cholesterol-rich.

Dr. Sands: Yeah, exactly.

Dr. Jockers: Bile is made up of bilirubin, which is a breakdown product of red blood cells, cholesterol, and specific salts. And so it's going to have a higher concentration of cholesterol to salt, which makes it more sluggish there.

Dr. Sands: Yeah, exactly. Exactly. Sluggish is a perfect word. And when that happens, you're going to have a harder time digesting your fats, but also, it can put you at risk of developing gallstones and gallbladder problems as well. So it also has a direct relation to estrogen and so it's an important part-

Dr. Jockers: And that's so key too because bile, not only is it key for digestion, but it actually helps to sterilize the small intestine.

Dr. Sands: Yes. Yes.

Dr. Jockers: To get the bacterial levels under control. And a lot of people are dealing with small intestinal bacterial overgrowth, and that can be related to poor bile production.

Dr. Sands: Yeah. And we do see increase in SIBO in women as they enter perimenopause and menopause. And it's higher in women than in men all over. So it's a huge distinction that we often don't think of. A lot of people aren't pointing to estrogen and progesterone when it comes to gut issues, but I think it is really important to take note of that.

Dr. Jockers: Yeah, for sure. And then there's also a marker, beta-glucuronidase, that I know that you look at. My health coaches look at when we're looking at people's stool analysis and looking at hormone balance. What is the role that plays with estrogen metabolism?

Dr. Sands: Yeah. So up until now, we've been talking about the effect estrogen has on the microbiome, but the microbiome also has a huge effect on our estrogen circulation in our body. So there's a part of the microbiome that we call the estrobolome. And part of what that does is it reduces the enzyme called beta-glucuronidase.

And this enzyme, what it can do is it can take estrogen that you've had circulating through your body and then you've metabolized it and now you're getting ready to excrete it out, the used estrogen, it can actually reactivate the estrogen and send it back through the circulation. And this can create estrogen dominance issues for women.

Even women with menopause symptoms, you don't really want that recirculating estrogen going back through the body. So you have to have the right amount of beta-glucuronidase so you can actually excrete the used estrogens.

Dr. Jockers: Yeah. And I see a lot of people that have elevated beta-glucuronidase and so as we get into solutions, we definitely want to touch on that. What they can do to help bring that down.

Dr. Sands: Absolutely.

Dr. Jockers: Now again, because we've talked a lot about estrogen and it, its impact on the gut and how the gut impacts estrogen levels, how about progesterone? What is its impact on the gut?

Dr. Sands: So progesterone's major impact on the gut has to do with gut motility. So estrogen is really important for helping moving your food through the digestive tract. When progesterone levels decline, this can actually slow gut motility, and this can contribute to gas and the petrifying foods releasing harmful gas, and discomfort, bloating, distension, constipation.

And then you can also kind of re-toxify your body. Because when you're excreting stool and urine, you're actually getting rid of toxins. And so when you're constipated, you can actually send those toxins back up through your body. Just like with the estrogens recirculating, you can have toxins recirculating as well. And a lot of people can feel kind of sicky, sluggish, uncomfortable, tired, fatigued. And this is a direct relating to progesterone.

Dr. Jockers: Yeah. I always say you got to pee and poop your way to good health.

Dr. Sands: And that's the elegant way to put it. Yes, exactly.

Dr. Jockers: Yeah, for sure. And so we've talked a lot about these hormones, how they're impacting gut function, and that was really interesting. I didn't know that progesterone had that impact on motility. So, so critical. So estrogen playing a really big role again with bile production so that way we're able to sterilize the small intestine.

Digest and absorb fats and fat-soluble nutrients like vitamin A, vitamin D, vitamin E, all these key nutrients, omega-3 fatty acids, all these really key players in overall physiology and immune health, hormone health, all that stuff. And then you mentioned testosterone playing a big role in keeping inflammation under control. So you can kind of see how all three of these hormones in balance really work to keep that gut working just right. Keeping that microbiome in balance.

Obviously, as a woman goes through perimenopause and menopause, there's going to be kind of a teeter-totter where it's like there's going to be times based on her stress levels, her sleep, things like that where things are out of balance. And ideally, if you're out there and you're listening, you know what you need to do to get back in balance. But you may not, and that's what Dr. Michelle is here for. So let's talk about that. Things that we can do to create balance with these hormones.

Dr. Sands: Yeah, so balance, that's the perfect word. I mean balance for your hormones, but also balance for your lifestyle. We live in a very hard-charging, do it all kind of lifestyle. And that attitude of just trying to get things done all the time and not taking time for rest, that's one of the main contributors to one, hormone imbalance, but two, the gut issues associated with hormone imbalance.

Because one thing we didn't talk about was when your estrogen and progesterone decline, your cortisol can increase because of stress. So we

just have a lower ability to deal with stress when we have a decline in our estrogen progesterone. Partly because there's more inflammation, but we're more sensitive because of the neurotransmitters that are affected.

[20:00]

And so when cortisol's up, it just makes you more heightened stress response, which takes you out of the rest and digest response. It's opposite. The relaxation response helps with digestion and repair where the stress response is going to be more the fight or flight. You're not going to take the time to digest as much. You don't release as much digestive enzymes into your system. You don't release as much hydrochloric acid.

And so that's really key is taking the time out to have a practice, whether that be breathing, yoga, meditation, walking outside in nature, reading a book, painting, doing something that you actually enjoy that may not be productive but does something for you. Taking time out. That's like number one for me over supplements, over hormone replacement, over anything else you can do. That's definitely number one is stress reduction practices every day, non-negotiable. For sure, that's going to help your digestion.

Also, speaking of that, when sit down to eat a meal, not eating on the go, taking our time to chew our food and chew our food really well. Because chewing actually is like the beginning of your digestion. It mixes with your saliva and it helps your body to have that pre-broken-down food going into your digestive system. And that's going to be huge. Also, it's mindfulness with your food. You're going to feel fuller faster. You're going to be more satisfied.

So chewing your food. Taking the time to eat. And then, of course, for food diet, and eating a diet that's rich in fiber but also diverse in fruits and vegetables, but also animal products if you eat those. Because the more diverse your diet, the more diverse your microbiome and you're going to have the ability to feed all of your microbes in your body.

Fiber is going to help with the motility, it's going to help move things through. So that's very important. A lot of people don't get enough fiber. In the United States, we don't eat enough fiber. So just trying to make sure that you're getting fiber, including fermented foods. Things like yogurt, sauerkraut, and kimchi, those are all going to help promote the growth of your good bacteria.

If you can't eat fermented foods, you don't like them, consider taking a probiotic supplement. I like spore-based supplements, but you can find one that you like and works for you. If you've never taken a probiotic before, you may have to work your way into it slowly with a quarter dose or a half dose just because it can cause a little digestive issues at first if you don't have what you need to accommodate it, but it will help.

Staying hydrated, really important. Hydration is going to help with your digestion. It's going to help with your elimination. So drinking your water, super important. Also, eating foods that help to support your bile production is going to be great. Things like artichokes are going to be super important because those help with just supporting bile production as well. I just want to see what else, I said fiber.

Getting sleep. Sleep is so important for our digestion. So making sure that you take the time and get seven to nine hours of quality sleep at night. When we're sleeping, this is when our body repairs itself. This is when your liver actually helps to clear out and that's going to be important for your hormone balance. And so sleep, very important.

And then like just for some remedies, if you are having digestive distress or bloating or gas, ginger tea and peppermint tea are great to have on hand to just sip on. It really helps with gas and bloating and gut motility. So I think that those are great options as well.

Dr. Jockers: Yeah. It's a lot of really good strategies right there. Kind of a good foundation to start with. Now, when you're seeing a woman, let's say a woman's doing all those things, but you look at labs and she's got high beta-glucuronidase going back to that compound that the gut microbiome produces that causes the estrogen levels to recirculate.

Particularly, estrogens we should be breaking down and metabolizing and excreting. Now they're elevated up in the bloodstream. And oftentimes, a very, very toxic estrogen compound is being elevated. What should a woman do if they see something like that on a stool test or whatever-

Dr. Sands: Yeah, we'll typically recommend supplementing with something like calcium D-glucarate, which helps with that. And then also DIM, which helps your body detox estrogen. And then, of course, exercise, healthy diet, sauna, and other things that help with detox like red light therapy. These all can be helpful in getting the harmful estrogens out but also going back and healing that gut.

Because we don't want to just treat the beta-glucuronidase because it's part of the whole environment. So looking to see, do you have a good balance of your good bacteria? If you're looking at labs, you're going to be able to see this. Do you have a possible parasite, mold, yeast, anything like that?

And really, gut health as you know, because you're the expert here, it's so important for every system in your body. So if you are noticing any issue with your gut, chances are there's another issue that also needs to be worked on. But beta-glucuronidase is a great supplemental thing that you can take to help with that. Beta-glucuronidase calcium D-glucarate helps with beta-glucuronidase to get it to its balance. But looking to find out why that's happening, it is probably even more important.

Dr. Jockers: Yeah, for sure. Yeah. Calcium D-glucarate is probably the most well-studied compound for getting that beta-glucuronidase under control, but I found also that adding in more of the bitters, is right.

Dr. Sands: Yeah, definitely. Bitter greens.

Dr. Jockers: And you mentioned artichoke, ginger. Things like that can be helpful. Milk thistle actually can be really helpful.

Dr. Sands: Yes.

Dr. Jockers: Oftentimes, there are issues going on with the liver related with—

Dr. Sands: Absolutely. Absolutely.

Dr. Jockers: Yeah. So that can be really, really helpful supporting that as a whole.

Dr. Sands: Exactly.

Dr. Jockers: What are some other things that you're seeing perhaps on labs? First off, what are the key labs? Do you do a DUTCH test? What are some of the key labs you like to look at?

Dr. Sands: So we always look at a DUTCH test because that's going to give us not only levels of hormones, but also we can see how those hormones are breaking down. Which pathway for testosterone. That's super important,

especially for women. Because we can see as your testosterone breaking down the more androgenic pathway where if we added testosterone, you might suffer from hair loss, facial hair, belly fat, and things like that. So that's really important to look at.

But for estrogens it's really important to see, is your estrogen breaking down the pathway that can cause DNA damage, or the healthy pathway, or a great kind of split of all three pathways, which is nice. And then the DUTCH also is nice because it's going to give you cortisol. Four points during the day so you can see what your cortisol rhythm is like. You can see your metabolized cortisol, which can give us some insight into thyroid.

And then we can also see some other markers like melatonin and oxidative stress markers as well. So it's really nice test. It's a little expensive so we do have an alternative. We also do saliva and blood spot testing if someone just wants to see if their estrogen, progesterone, and testosterone are not where they need to be.

That's a great way to kind of spot-check and that's like a quarter of the price of a DUTCH test. So it depends on what you're looking for and how much information you want. and in a perfect world where tests didn't cost any money, I definitely would recommend the DUTCH test, but we also offer other testing as well.

Dr. Jockers: Yeah. And the DUTCH stands for Dried Urine Testing for Comprehensive Hormones. And like you mentioned, it's got a lot of biomarkers so you can really see a lot and help customize a plan. Doesn't necessarily mean you need to get that to start. However, especially if you're hitting plateaus and you're doing a lot of things Dr. Michelle's been talking about, then that would be a really good strategy to look at because that can help fine-tune things.

A lot of times for women, they'll just take something like DIM and say here are all the press about how Diindolylmethane is so good for estrogen levels, but sometimes that's not their issue. That's not going to impact the pathway that they need help with.

Dr. Sands: Exactly. Now, for a lot of women in my demographic, they not only have the fat problems, but they also have hot flashes and vaginal dryness and all the other things. So they are looking for hormone replacement. In that case, we actually don't use the Dutch test because the Dutch doesn't give you an absolute level of progesterone. It gives you an inference based on the metabolites. So we do like to use the saliva or dry blood testing when we're looking at replacing those hormones and we're just looking at absolute levels.

But yeah, it's definitely an option. So you have so many options. You can start with lifestyle, with diet, exercise, stress reduction, sleep supplementation, but if that doesn't do it or you also still have other symptoms besides the gut issues, then yeah, hormone replacement therapy is available. Bioidentical hormone replacement therapy is absolutely safe, especially when it's topical.

There's really zero side effects. And their only side effects are living longer. So it's not a taboo thing like it used to be. And menopause itself is no longer taboo to talk about either. Oprah is talking about it. All of the celebrities are talking about it now. So it used to be that women were embarrassed about menopause or embarrassed about digestive issues, but now, we're all talking about it. And so you don't need to be embarrassed. It happens to everybody and there's no reason not to get help.

Dr. Jockers: Yeah. And what's the difference between bioidentical hormone replacement

therapy and conventional hormone replacement therapy?

[30:00]

Dr. Sands: So conventional or synthetic hormone replacement therapy, the difference is the substances that you're putting in your body are similar to the chemical structure of the hormones that your body makes, but not the same. So they might have a little extra hydrogen or carbon or a little extra thing on there, but the bioidentical hormones are absolutely identical to the hormone. Chemically structured to the hormones that your body makes so your body can't tell the difference.

Some of the synthetic hormones are still considered safe. However, oral hormones for estrogen, particularly oral estrogen, whether it's bioidentical or synthetic actually can cause some problems with clotting and some other issues. So I never recommend oral estrogen, whether it be bioidentical or synthetic. And I'm a naturopathic physician so I'm always going to try to do everything as close to nature as possible. And we're always going to opt for if it's available, why not opt for the hormones that are identical to what your body's expecting?

Dr. Jockers: Yeah, for sure. Bioidentical obviously is, is the identical structure of the hormones that our body's naturally producing. And then you mentioned a topical approach, right? Topically, it can cross into the bloodstream transdermally through the skin. Why is that a more effective strategy than oral?

Dr. Sands: Because orally, it has to go through your digestive tract to your liver, be metabolized, and then go into the bloodstream. Whereas topical, that hormone is going into the bloodstream in the first pass. So it doesn't have to be metabolized by the liver first. And when it's metabolized by the liver, it's changed a little bit. You also lose a lot of hormones when it has to go through your digestive tract. So you have to use a much higher dose to get the same effect when you're doing oral versus topically.

Dr. Jockers: Yeah. And so based on specific testing, you could see if a woman might need a little bit more progesterone, a little bit more estrogen, a little more testosterone, or sometimes women need a little bit of all three. Is it one or two?

Dr. Sands: Yeah. Yeah, everyone's different. So we look at test results, and there's a range. Testing is not a perfect number. There's from this level or this level, it's considered normal. So we also look at symptoms. Because every woman's going to be different. Some women like to be at the top of the range for testosterone. Other women feel better in the middle or the lower end of the range. And so we're always going to look at symptoms.

We look at like 100 different symptoms, self-evaluated by the woman, combined with their test results to see are you in the range? Are you below the range? Are you right where you need to be? Do you need a little bump to feel a little better? And so we'll do that. And it's not a perfect science. So we retest every four months. We re-evaluate symptoms and we dial it in. And every woman's going to be a little bit different.

And then also, depending on the stage of her life, if she's in perimenopause, it's going to fluctuate a little bit because she's still making hormones sometimes. And if she has a stressful environment, if she gets sick, then things can fluctuate as well. So you always have to be rechecking and re-evaluating.

Dr. Jockers: Yeah. It's really good to know. And I know just clinically, I've seen a lot of women do amazing when they get the right amount of

hormones. It's life-changing for them. And I'm sure you're seeing this on a regular basis.

Dr. Sands: Yeah. It is life-changing. Unfortunately, some doctors will give you mega doses of hormones, which we never recommend. We only recommend physiological doses. What the body would expect. But there are some clinics, anti-aging clinics out there that they want you to get a vague result right away. So they give mega doses, which feels really good at first for a lot of women and men, but then what happens is you start getting symptoms and it starts not working as much because your body is just rejecting the mega doses.

Dr. Jockers: Do you get a receptor downregulation? Is that what happens? Almost like if you take a high amount of insulin, you create more insulin resistance.

Dr. Sands: It's not quite the same. The mechanism's kind of uncertain because you don't get so much a receptor down your regulation as you get the symptoms of too high hormones. Like I said, it's Goldilocks, right?

Dr. Jockers: Yeah.

Dr. Sands: And it takes a while to reverse those symptoms, and some of them, especially for women, it can take a long time to reverse. Their voice can change with too much testosterone. Clitoris can get larger. And these things can take a long time and maybe never change back. So it's really important to work with someone who is looking out for your best interest, that understands the whole body holistically.

And they're not just handing out hormones in a clinic because that there are some people that do that. And it might work for some people, but it's, it's not a good idea in the long-term. We always want to look towards long-term health and what's going to help you now, but what's going to make you feel better in 10 years, 20 years, 30 years as well.

Dr. Jockers: Yeah, for sure. And I know that you guys, you have a free hormone restoration masterclass as well that women or men, or anybody can go to really discover more about what's happening with their hormones if they're dealing with any of these perimenopause menopause symptoms. For men, low testosterone issues. And they can learn more about it. How do people access that?

Dr. Sands: Yeah, you can go to fixhormones.com and you'll just put your information in and you can choose when you want to watch the class. If you don't find a time that works, you can just click any time and we will send you the replay right afterwards. And it's great because it's going to dispel all the myths and misconceptions. And there's a lot of confusion around hormones, hormone replacement, who it's for, who it's not for. Will it help you? Will it hurt you? I explain it all in really simple, easy to understand terms, and then you can also ask questions as well.

Dr. Jockers: Yeah, that's wonderful. This is going to be a really great solution for a lot of women out there. And let's go back to testosterone. What are some key strategies beyond what you mentioned earlier for testosterone? When I think about it, I think weight training. I think resistance training. And most a lot of women, I shouldn't say most, but a lot of women are, are concerned about weight training. They think they're going to get bulky. But really, one of best things-

Dr. Sands: I think that's turning around the corner. I feel like that is changing now. I think when I was growing up, women were supposed to be skinny, but now, everyone wants to have a booty. Bigger is considered healthier.

Dr. Jockers: Yeah. Strong is the new skinny, right?

Dr. Sands: Yeah, exactly. So I'm really excited to see that. But, yes. there was actually a study showing the most testosterone-boosting activity that they've ever found was chopping wood with an ax. But you can stimulate that with kettlebells or those they have those sledgehammer things in CrossFit. But lifting heavy weights, yeah.

Heavy weights for one person is going to be different from heavy weights for another person. Some people, that might be a bodyweight squat if they've never done squats before. But it's where it's hard for you after eight to 10 reps and then you rest and you go again. That's great. Sleep. Lack of sleep is one where primary reasons for low testosterone, believe it or not. Huge importance. And then also nutrient deficiency. Not getting enough magnesium.

Dr. Jockers: Zinc. Zinc is really key.

Dr. Sands: Not getting enough zinc. Yeah. Not getting minerals and then also not getting enough protein is really important. So one thing I didn't mention is magnesium is actually a really good mineral for people who have constipation, bloating, sluggishness. Magnesium can help with relieving gas, relieving constipation, and so that's something very easy that women can take.

If you take too much of especially magnesium citrate, you might get diarrhea. So just be careful with it. But also eating magnesium-rich foods can be helpful as well. Spinach, beet greens, sweet potatoes, things like that are going to be great. Dark chocolate. We all love that. And then Epsom salt baths can be also awesome because you absorb it through your skin.

Dr. Jockers: Yeah, that's so good. And magnesium's also good for helping calm high cortisol, as well, as a common effect.

Dr. Sands: Exactly. It's like the stress mineral, right?

Dr. Jockers: An adaptogenic effect. Yeah.

Dr. Sands: Exactly. Exactly.

Dr. Jockers: Yeah. Super key. This has been a great interview. We've covered a lot of great information here. I know that the listeners are going to really enjoy this. Again, that site, what was it, fixhormones.com that people can go to?

Dr. Sands: Absolutely. Absolutely. That's where you can watch the masterclass and then I'm always answering questions. I have a team of hormones, specialists, doctors, and nurses, and we love answering your questions, so don't be shy.

Dr. Jockers: Wonderful. And your normal website also is glownaturalwellness.com as well?

Dr. Sands: That's correct, glownaturalwellness.com and then Fix Hormones you can find in the masterclass.

Dr. Jockers: Awesome. Thanks so much, Dr. Michelle. This has been a wonderful interview. I know listeners have learned a lot. Any last words of inspiration here for our audience?

Dr. Sands: Yeah. So since we're talking about menopause and perimenopause, I just want to let women know that your final period is not the end of your story. There's a whole other chapter. There's much more to go. Never let anyone write you a prescription for the rest of your life. You write that prescription. And the things that you're learning in the series from Dr. Dockers and the other experts, these are the things that are going to help you thrive. So just know it's not the end. It's a beginning.

Dr. Jockers: Awesome. Thanks so much, Dr. Michelle. Go check out fixhormones.com guys and we'll see you in a future interview. Be blessed everybody.

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