INTERVIEW TRANSCRIPT

DISCUSSIONS WITH WORLD-LEADING EXPERTS

What Everyone With Migraine Should Know About Gut Health

Robert Bonakdar, MD
Pain & Headache Specialist
Scripps Center for Integrative Medicine
San Diego

Introduction (00:04): For many people living with migraine, gut issues like bloating, nausea, or sluggish digestion are just an everyday part of life. But until now, it feels like they've mostly been separated as individualized issues and not a part of migraine. Luckily, research is showing us that they all may be intimately connected through something called the gut-brain axis. The gut-brain axis is a communication channel that connects the trillions of microbes in our gut up to the nerves and pathways in our brain that control pain and inflammation.

Introduction (cont.) (00:23): Today, we're joined by Dr. Robert Bonakdar, a leading integrative medicine expert. He will help us understand what is the gut microbiome, what does it mean for migraine — and most importantly — how can we take practical steps to better improve our gut and brain health? Dr. Bonakdar, welcome back to the Migraine World Summit.

Dr. Bonakdar (00:52): It's a pleasure to be here, and your introduction was great as far as everything that the microbiome and the gut-brain axis has the potential to do.

Kellie Pokrifka (01:01): All right, let's start with the foundation. What is the gut-brain axis?

Dr. Bonakdar (01:06): Well, it's a term that's evolving. We know gut-brain axis is probably the easiest way to term it, but there's also other ways, including the oral-gut-brain axis, the oral-gut microbiome-brain axis, and others even bring in the immune system. So, it's really all about the various interconnections between multiple systems that influence the potential for migraine.

Kellie Pokrifka (01:35): That feels just as overwhelming as most of the advice we are getting from our doctors about how to take care of our gut to better improve migraine. So, where should we start? What makes up the gut microbiome?

Dr. Bonakdar (01:48): Yes. So, I think it's definitely a term that can be very complex, and when we start talking about microbiome testing, that's even more complex. But I try to simplify it as much as I can to say that it's more than just about the bugs in our gut, which as you mentioned, there are hundreds of millions or trillions. We actually have more microbiome or bacterial cells in our body than our actual human cells.

Dr. Bonakdar (02:11): So, we're more a host than we are actually human, which is mind-boggling, but it's actually more about those bugs. It's about what they do, the factory that they create and the neurotransmitters that they create, the vitamins that they actually create, which influence migraine that we'll talk about. It's also about the communication system. So, we sometimes talk about the gut as a second brain.

Dr. Bonakdar (02:42): Really, in many ways, it's the more prominent brain. Ninety percent of the signals from the vagal nerve go from the gut to the brain. Only 10% comes down from the brain. Ninety percent of the serotonin in our body is made in the gut. So, it's really a prominent organ that's more than just about the bugs. That's number one. And number two, I tell patients it's not all a bad thing. We usually talk about leaky gut, dysbiosis, all these terms about how the gut can make things worse.

Dr. Bonakdar (03:14): And in fact, there's many more ways that we can influence the gut to help us prevent migraine and other medical issues than it can cause harm. So, those are, I think, really important. And I think the third important thing is it's not all about diet. Obviously, what we eat influences the gut prominently, but there's so many other lifestyle approaches — sleep, stress management, even neuromodulation, exercise — that influence the gut-brain axis. So, there are many avenues to approach it, and it's not just about the bugs.

Kellie Pokrifka (03:53): How does this communication work? I know you mentioned something about how they work with digestion and they can influence the vitamins and minerals that we digest. How does that communicate back up to the brain, and how is that involved in migraine?

Dr. Bonakdar (04:08): Absolutely. So, we know that there are a lot of nerve bundles that communicate between the brain and the gut. The one that we're probably most familiar with that has been termed within the migraine literature, as well as just medical literature, is the vagal nerve. And the vagal nerve comes from the word “wandering,” because it's the longest cranial nerve, and it goes not just from the brainstem where all the cranial nerves sit into the neck and other areas, it goes all the way to the gut.

Dr. Bonakdar (04:41): So, that's why we know what happens in the brain can influence the gut. That being said, there are other nerves that also communicate. Most importantly, how the gut is feeling — whether it's stressed, whether it's constipated, whether there is gastritis or the early signs of an ulcer — all those things can influence the vagal nerve. And when the vagal nerve feels attacked or there's inflammation or other issues, it goes into retreat.

Dr. Bonakdar (05:14): So, in many ways, thinking about the communication going silent or going very low makes it hard for the gut and brain to communicate. So, a lot of what we're going to be talking about is how do we influence that communication system to be optimal so that all channels are open up and down so that if something good is happening in the gut, it's going to influence the brain positively to hopefully reduce migraine.

Dr. Bonakdar (05:35): The other question I think you brought up was the factory and how that influences communication. We know, for example, when the gut is working optimally and there's no leaky gut — meaning it's not overabsorbing or underabsorbing — it can actually create a number of our B vitamins. So, we've talked about riboflavin, we've talked about B12; it can actually create that in the gut with the cofactors that are there. But if the gut is, again, constipated and having issues, it can't make enough.

Dr. Bonakdar (06:07): So, yes, we can take those vitamins; yes, we can eat those in our diet. But a primary source is our own factory, our gut, to make those B vitamins. We also know the gut helps to absorb more magnesium. So, if the gut's working well, a lot of the work is already done. It's more about making sure that the gut is able to communicate and able to work as an optimal factory.

Kellie Pokrifka (06:37): Let me know if this is oversimplifying it. I know during a migraine attack, we know that the gut isn't really working that well. We try to avoid using oral medications because they might not be absorbed. Are you saying that the conversation between both the brain and the gut going both ways is influencing that during an acute migraine attack? And would you say that because our gut is not able to communicate as well, it's not able to tell our brain, "Hey, you're safe, we can end this attack," or is that a little too far off?

Dr. Bonakdar (07:08): I think that ... no, that's a good analogy. And we know for many folks dealing with migraine, when they have an acute attack, many parts of the body — as we're dealing with this threat known as a migraine — the parts of the body that aren't immediately working to reduce the migraine might reduce activity. So, the gut, for example, can quiet down. That's why sometimes the medications don't work as well because we're not absorbing; there's not normal peristalsis or movement of the gut.

Dr. Bonakdar (07:43): There's nausea, which can also increase inflammation and make it difficult to absorb. Obviously, that can go into full-blown vomiting, where we can lose our medication. So, if the gut is unhappy or feeling in danger — which often the signal from the brain down from the vagal nerve and other nerves is telling the gut, "danger” — then the gut also kind of quiets down and tries to just support the brain by not overdoing. That's one explanation that's out there.

Dr. Bonakdar (08:12): At the same time, the gut is also trying to support the brain by saying, "What can I do? What neurotransmitters can I support? What signals can I send to the brain with serotonin, GABA [gamma-aminobutyric acid], and some of the relaxing neurochemicals to help the brain calm down and de-inflame?" So, it's a constant triage where the analogy would be the ambulance from the gut is trying to get to the brain to support it and help the migraine reduce. But in many cases, there's a traffic jam and things are at a standstill. So, trying to go to other routes besides oral routes is why a lot of the medications in the migraine world are using non-oral routes to bypass it.

Kellie Pokrifka (09:02): Are there any other ways we can support the communication during an acute attack to make sure the gut can better support the brain?

Dr. Bonakdar (09:06): Yes. That's the background for vagal nerve stimulation as an example. What I tell patients is there are gentle ways to improve the vagal tone through deep breathing, relaxation, biofeedback — all the mind-body tools that you've talked about on the Migraine World Summit that we know help migraine. Part of that is it calms the gut and the brain to allow the vagal nerve to get back into the game.

Dr. Bonakdar (09:40): So, those are gentle ways to do it. Rest, sleep are also additional ways to do it. The vagal nerve stimulators such as gammaCore, which are FDA-cleared for migraine, I think of those as a CPR for the vagal nerve — literally going to the vagal nerve as it transcends from the head into the neck and into the body to basically do CPR on it to get it back into the game, to revive it.

Dr. Bonakdar (10:05): And that's another way we know not only does it allow the vagal nerve to help the brain to de-inflame and to improve communication of neurotransmitters, but it also helps the gut because the vagal nerve then can also do its job better in the actual gut. The vagal nerve communicates with CGRP and other neurotransmitters to modulate those, to help those also reduce migraine from the gut up.

Kellie Pokrifka (10:36): I've heard a couple of things when researching vagal tone that are things like if you hum or gargle, it can help. Is that something that, one, is legitimate at all? Or is that just a long-term strategy, or could that actually help us during an attack to try to help settle things?

Dr. Bonakdar (10:52): Anything that gives a signal to the vagal nerve that things are going to be OK — which is hard during a migraine attack — to feel like I'm going to hum a happy song because I'm miserable. That sometimes may work. I have had patients say, "I listen to music," and any signal that's relaxing can also allow the vagal nerve [to stimulate].

Dr. Bonakdar (11:11): But we do know when you look at vagal tone, which is often measured through something called heart rate variability — which some of the audience might be familiar with through their smartwatch or other ways where they can detect heart rate variability — that improves when we are doing enjoyable activities. When we're singing, when we're laughing, when we're with our favorite people, the heart rate variability improves. When we're exercising and doing things we enjoy, it improves.

Dr. Bonakdar (11:42): During a migraine attack, it can often be difficult to find those things. So, that's why more … not intrusive ways but medical approaches like vagal nerve stimulation in the neck — there are also vagal stimulators in the ear — and techniques such as humming, which kind of force the vagal nerve to come into the game. But those aren't as strong as the other interventions like the gammaCore to actually get the vagal nerve to be functioning optimally. So, it's not harmful to try those. Again, there might be some vagal stimulatory methods that I wouldn't endorse with a patient. I have heard some that may be not the safest thing to do — but humming, singing, and trying to just relax are all good ways to get the vagal nerve to do its job.

Kellie Pokrifka (12:35): Are there any you want to expand on that we should not try?

Dr. Bonakdar (12:39): There are ways where people put their feet in extremely hot water, or they're doing vagal massage in the area, which is not necessarily safe, especially if you have any carotid issues or heart disease. Those are more emergency measures when the vagal nerve and the body is not doing its measure — meaning vagal massage — so I would not recommend doing those. I would not recommend putting ourselves into any environments that try to jumpstart the vagal nerve that we don't feel comfortable with. That can often add to the difficulty of the situation. So, really focus on things that are going to calm the body, which are then going to signal the vagal nerve to kind of come back into the game.

Kellie Pokrifka (13:26): To add another aspect of our body into this, what is the oral-gut-brain axis?

Dr. Bonakdar (13:38): Yeah, that's one that's often underrecognized because we think about the gut, we think about stool testing, we think about what's happening in the gut. But the key factor is that what's happening in the oral mucosa directly impacts what's happening in the lower gut — the stomach and intestine.

Dr. Bonakdar (13:47): In fact, a recent study just this year that came out of *Neurology* — and hopefully some of those articles will be available for the audience — found that there are specific bacteria in the mouths of persons who are more prone to migraine that are likely nitrate reducers. Bottom line, they promote increased levels of nitric oxide, which we know can be both a trigger for blood vessel instability as well as migraine.

Dr. Bonakdar (14:25): So, you think about it genetically as well as environmentally. Maybe there's some genetics to that; we don't know. There's probably some environmental things over time that the mouth mucosa — the bugs that are in everyone's mouths — those folks with migraine already, just with what's happening in the oral cavity, are promoting migraine triggers, at least based on the early studies that we've seen.

Kellie Pokrifka (14:55): Is this related at all to when people say nitrates or nitrites are migraine triggers for them?

Dr. Bonakdar (15:01): That's a great connection. And we do know that some folks are extremely sensitive [to things] like beets and other high-nitrate foods, and some foods with preservatives that are nitrates can cause an immediate attack because of the blood vessel instability. So, there is some conjecture that in folks with migraine, nitrate foods are propelled towards that nitric oxide much more than in folks that aren't prone to that.

Dr. Bonakdar (15:29): So, it's not to say that nitrate foods should be avoided because some of these are very healthy — fruits, vegetables — but maybe not in an extreme amount because that might be a predisposition for some folks with migraine. And even in cases where it's not a high-nitrate food, if it even has a low amount, the conjecture is [that] the mucosa will also propel that to a point where it might cause a migraine. So, there's a lot more to learn.

Dr. Bonakdar (15:52): When I read that literature, my first thought is: What can we do to help the oral mucosa of those who are prone to that to reduce those "bad bugs," so to speak, to not be able to promote nitric oxide? Are there mouthwashes? Are there oral probiotics? There are all kinds of tongue rinsing and scraping. There's no evidence in humans that that makes a difference, but it does create the potential that if you have good oral hygiene, that it potentially has some benefit in preventing migraines. There's still a lot to study, but it does bring up some interesting questions.

Kellie Pokrifka (16:32): What are microbial signatures in pain disorders that you've described?

Dr. Bonakdar (16:38): Oh, yes. So, we know that with the vast increase in microbiome studies and stool analysis that's out there, especially in research facilities, there are signatures for different

conditions. One of the first studies that really got me interested in the whole topic of the microbiome was actually in fibromyalgia, folks with fibromyalgia. They basically looked just at the microbiome analysis of — blinded — patients with fibromyalgia versus healthy controls. And what they found is with almost a 90% accuracy, just by looking at the specific microbes — the bugs that were heightened in one and lowered in that population — you could detect, you could diagnose who has fibromyalgia and who doesn't, which is mind-boggling that not knowing anything about the person, just the signature of what's in their gut tells me that they have fibromyalgia.

Dr. Bonakdar (17:33): And over the years, we've had the same with migraine, in neuropathy, and even other types of pain. So, when we look at migraine signatures specifically, we know that there are lower amounts of some of the anti-inflammatory species. So, we've all heard about acidophilus and the families they belong to like Lactobacillus; acidophilus tends to be lower in some studies of migraine. Bifidobacterium is another family that's beneficial that tends to be lower.

Dr. Bonakdar (18:06): And then there's heightened amounts of some of the inflammatory bugs that can go on to cause more inflammation [and] more difficulty for the vagal nerve to do its job. So, if you do a stool analysis, typically, the studies show that you will see these signatures of things that are beneficial are lower, things that are inflammatory are a little bit higher — not in all cases — but that is a signature that's there. Which is why some people say, "Well, I want my microbiome tested to see if I have that signature and whether I can shift it with some of the diet and probiotic interventions." It's an interesting thought, but there are a lot of details that unfortunately don't make it that easy today.

Kellie Pokrifka (18:51): When we're looking at these different signatures, are they different in different regions across the globe?

Dr. Bonakdar (18:55): That's a really interesting question. And absolutely, we do know that because diet is very different around the world, one of the things we see, for example, is that in other parts of the world, there's a lot more intake of fermented foods. Almost every culture has their version of kombucha, their version of yogurt, kimchi, etc. In the U.S., it is actually much less likely to get fermented foods on a regular basis in our diet. It's changing. We are seeing the benefit of fermentable foods.

Dr. Bonakdar (19:31): So, if you look at the gut microbiome of folks in Asia and other parts of the world where there's more fermented food, you're going to see a much more diverse population of species. And that's one of the key things — not just with migraine, but just in general — more fermentable foods in the diet means more diversity. More diversity is good in preventing not just migraine, but a lot of chronic illness. So, we do see a lot of regional changes.

Dr. Bonakdar (19:52): As far as changes in migraine populations in different parts of the world, you do see changes as well based on what's prevalent in that region, because there's also an environmental [factor] — who I live with affects my microbiome, as does the microbiome of folks with migraine based on who they live with, where they work, or what type of environmental exposures they have.

Kellie Pokrifka (20:18): Can you tell us about the different animal studies about transplanting sick microbiomes onto healthy mice or other animals?

Dr. Bonakdar (20:26): Absolutely. That's one of the other lines of study that's really compelling. And I think for folks getting into the microbiome literature and research, it's eye-opening because multiple conditions — but we'll talk specifically about migraine — basically they take the stool of somebody with migraine and then they transplant it into what are called germ-free mice. These are mice that basically have an environment where they don't have any microbiome and they are suddenly the proud owners of the microbiome of someone with migraine.

Dr. Bonakdar (20:51): What's really interesting is study after study has shown that when you do that, typically the mouse will begin to have animal traits that are representative of migraine. So, they'll have trigeminal sensitivity. They'll be sensitive to their environment, to lights, to touch, things that we see with trigeminal sensitivity in humans. So, the migraine equivalent in animals happens not immediately, but over time. Once the microbiome sets in and begins to communicate with the animal brain, the animal brain changes and it can create that migraine.

Dr. Bonakdar (21:41): So, that's been shown in multiple studies and really brings up the point of, well, if a migraine signature can cause that, could we also put a nonmigraine or a healthy signature to transplant? Not in the United States — I'm not familiar with any studies here — but in other parts of the world, they have used healthy "super microbiome donors," very healthy subjects who don't have medical issues, and their stool is utilized in a sterile fashion for folks who have very severe disease. Often, it's things like C. difficile and severe G.I. [gastrointestinal] issues, but it's being used in more and more conditions.

Dr. Bonakdar (22:25): So, I wouldn't be surprised within the next five years or so that we're going to see some research institutions actually doing fecal transplant in refractory cases for neurological conditions.

Kellie Pokrifka (22:37): If I have that gut microbiome signature that is susceptible to migraine, does that mean that during an attack it's flaring, it's getting worse, or does it just mean there's more inflammation? How does the gut signature translate into an active migraine attack?

Dr. Bonakdar (22:56): That's something I think we're learning more about because we know that the microbiome is incredibly sensitive to what's happening around us. There's actually been some studies looking at the microbiome pre- and post-international air travel. So, not a migraine attack, but just as an example, we know that even within that realm — where you're stuck with a lot of other microbiomes, maybe an environment that's not the most desirable but not necessarily a medical issue — you get on the other side of that, your microbiome has already changed.

Dr. Bonakdar (23:09): And then when you look at an actual migraine episode, we do know that with the gut slowing down, that also changes CGRP levels, [which] can go up, which can influence migraine. We know the vagal changes — vagal tone changes — that can also influence the species. So, whatever signature is there during an acute attack, many aspects of that are heightened. So you get more of the inflammatory bugs; you get less of the beneficial bugs. Your body's always trying to shift to help, but during an attack, it's hard for it because everything is slowed down. And slowing down in general is not good for the gut and influences more dysbiosis or leaky gut.

Kellie Pokrifka (24:16): Do events like traumatic events — whether it's physical or emotional — do they impact our gut microbiome?

Dr. Bonakdar (24:21): Yes. You'd be surprised to know that there's been literature on many aspects of trauma as well as just even suboptimal lifestyle approaches. So, there've been studies showing acute stress — taking the microbiome into the wrong direction with all the things we talked about. We know that sleep deprivation in a lab can also change the microbiome towards a negative. We know excessive exercise — not beneficial exercise, but to the point where there's severe exhaustion or overexertion — can also influence the gut negatively.

Dr. Bonakdar (24:54): So, pretty much anything you think of that's an adverse way to affect the body beyond diet can also influence the microbiome to go in the wrong direction, which again, I try to talk to patients about how do we optimize those things? Because there's also research that if you optimize sleep or stress management — there's actually a study of long-term meditators demonstrating pre- and post-changes, beneficial changes, in the gut. So all those things can actually go in either direction depending on lifestyle.

Kellie Pokrifka (25:34): So, if we are continuously having frequent migraine attacks, is that actually making our gut microbiome worse?

Dr. Bonakdar (25:39): Conceivably, by slowing down the gut and increasing inflammation, yes, each episode could accumulate more negative potential for the gut. At a certain point though, I think the migraine signature is going to be pretty set. The microbiome does try to recover. So, between episodes, it's always trying to go towards a signature that's going to improve inflammation and improve nutrient uptake.

Dr. Bonakdar (26:06): Unless it's chronic all the time and there's no changes for the better, the gut is always trying to recover. And the mucosa, the lining of the gut, is incredibly dynamic. So how we eat is always helping it to recover. Things like a healthy diet — fruits, vegetables, fiber — all those things are trying to counteract the effects of an acute attack. So, I think that's the hallmark of our gut; it's always trying to recover and help us. So how we can enhance that is the key.

Kellie Pokrifka (26:49): So, with people with more episodic migraine attacks, does that mean that either the days leading up to an attack, during an attack, a couple days afterwards — are they all separate? Or even during the interictal stages where they're not having attacks, does their signature look different than when they're actively in an attack?

Dr. Bonakdar (27:07): Yeah, that's a great question. I think we don't know the exact answer to that because it's really hard to do microbiome testing through all the stages of a migraine. But we do know in general, as it's building up, all the things that create the migraine are also negatively affecting the gut based on inflammation, reduced communication, etc. So, all those things are probably trying to go in the wrong direction.

Dr. Bonakdar (27:33): That being said, we do know that a number of the treatments that are often used for migraine can help the gut. Again, we're talking about vagal stimulation; anything that reduces the migraine attack typically also helps the gut and the vagal nerve get back into the game. So, it's kind of a constant battle between good and evil, so to speak, to try to get the gut to do its job and to help the brain reduce the migraine potential.

Kellie Pokrifka (28:06): All right. So, until we can have the fecal transplants where we can just get everyone's really good ...

Dr. Bonakdar (28:12): Maybe don't sign up yet, right?

Kellie Pokrifka (28:14): What are some practical steps that we can actively take right now to try to help?

Dr. Bonakdar (28:18): No, absolutely. There are many things we can do. I'm very lucky to have a registered dietitian in my office who takes the discussion and who looks at how much the diet is a potential trigger — meaning are we following the Standard American Diet, which might not have a lot of fiber, may have some inflammatory fats, may not have enough hydration. All those things, if we shift it towards a more health-promoting diet — things like the Mediterranean diet, the DASH [Dietary Approaches to Stop Hypertension] diet, the Healthy Eating Plate diet, a higher omega-3 diet. All those things — my thought, and again, a lot of researchers agree — the reason they help migraine is multifold. But one of the ways we believe is that it's helping the gut — because we know for every 10 grams (g) of fiber you increase in your diet, the study shows there's about a 10% reduction in migraine potential. So, just by shifting more fiber into the diet, that helps.

Dr. Bonakdar (29:21): Fruits and vegetables also have a lot of phytonutrients and antioxidants, which we know can reduce the oxidative stress or inflammation in the gut while also affecting inflammation in the brain. So, starting with regular hydration, consistent meals, and staying away

from the Standard American Diet, going towards more of the healthy diets — which we have multiple studies that show they help migraine. We don't know exactly all the pieces of that, but part of it is the phytonutrients and the higher fiber. So, that's a good starting point before we go to nondietary approaches or supplements.

Kellie Pokrifka (29:58): When you were saying fruits and vegetables, how dramatic is that impact?

Dr. Bonakdar (30:02): Oh, it's very strong, especially in populations where we know they're not getting a lot of fruits and vegetables. One example of that is the pediatric and adolescent population with migraine. We know that population in general is not eating a lot of fruits and vegetables, is not getting a lot of fiber, so they're depleted of that. So, again, the average American ... we're trying to go 25 to 30 g of fiber. The average American is at about 12 to 15 g.

Dr. Bonakdar (30:31): The average teenager is probably in the single digits. So, if we can get those single digits closer to the 20 g, we're going to already see some benefit. But in one study looking at pediatrics, increasing fruits and vegetables with the input of a dietitian and monitoring increased the potential for migraines to decrease. So saying that again, overall migraines decreased by 50% to 70%, which is better than almost any medication we have.

Dr. Bonakdar (31:03): So, arguably, one of the biggest tools we have is shifting diet, especially if we know that there are gaps. And we know fiber and fruits and vegetables are a gap. I think the latest study said over 90% of the American population does not get the recommended dietary allowance of fruits and vegetables in their diet. So, that's a great place to start.

Kellie Pokrifka (31:24): What supplements would you suggest for someone who is just starting, they're a little bit lost, they have no idea — they've tried so many different diets. What supplements should we be trying to try to improve this?

Dr. Bonakdar (31:31): Yes. I think supplements do make an impact. And in some cases, diet's already been tried, or diet's been difficult. There may be areas of dietary sensitivity or folks who are just tired out of another diet for their migraine. We totally get it. Supplements do have a place. I don't go right to probiotics, and I'll talk about that in a second, but a great place to start is actually just fiber supplements.

Dr. Bonakdar (31:59): There are a number of ones out there, like your Metamucil, Sunfiber, etc., that help you get that extra 10 g a day if you're having difficulty doing that in your diet. I would start slow, maybe 1 or 2 extra grams per day. If you're having a difficult time adding that to your diet, putting fiber supplements into your diet might be a good place to start. You can also just start with fiber foods, adding things like flaxseed to your salads, to other parts of your dietary intake — your yogurt, for example — to get more fiber. So, that's a supplement I like.

Dr. Bonakdar (32:37): I also like omega-3s. We don't think of them as a gut-brain axis supplement, but we know that increasing omega-3s not only helps the brain because it is a place we need more omega-3s; we know omega-3s also improve the gut by increasing the Lactobacillus [and] Bifidobacterium, as well as they promote short-chain fatty acids like butyrate. So, omega-3 helps the beneficial bugs fully do their job by using that as a cofactor to create more things like butyrate, which we know is beneficial for migraine. So, that's another supplement I like.

Dr. Bonakdar (33:17): Then when we get to probiotics, I don't have a go-to — there's not a go-to probiotic for migraine, unfortunately. There've been a number of studies, and some have been positive, some have been neutral or negative. So, we don't have one to hang our hat on as sort of the hero probiotic. We do know in general things with Lactobacillus and Bifidobacterium that we get in yogurt and kombucha are not bad. They likely are beneficial if you're not getting enough of that. But there's no positive migraine signature probiotic to try.

Dr. Bonakdar (33:51): That's one of the reasons my research team is doing a randomized trial right now using a probiotic which had signals of migraine benefit in a separate trial in those with IBS (irritable bowel syndrome). Those populations improved their IBS [and] saw some signals of migraine reduction.

Dr. Bonakdar (34:10): So, we're doing a randomized trial, meaning half the group gets the probiotic and the other half gets placebo. We're doing microbiome testing pre- and post-[trial]. We're also looking at blood levels of your typical B vitamins and magnesium to see if those are shifting based on feeding the gut the probiotic versus placebo, and if that's the reason why some people benefit from probiotics and maybe others don't. So, there are a lot more questions than answers with probiotics in my opinion. So I don't usually use probiotics right off the bat, and I focus on the other supplements.

Kellie Pokrifka (34:44): Are there any medications that either are for migraine or treat a lot of the common comorbidities that may be beneficial or harmful to our gut when we're trying to improve it?

Dr. Bonakdar (34:57): We have to think about that because we're taking it for the migraine. Unfortunately, we do know that some of the common over-the-counter treatments, like anti-inflammatories — your ibuprofen, your naproxen, which many folks with migraine have to rely on — actually are not great for the gut, either short-term or long-term. If you're using those over a period of time, they're more likely to cause leaky gut and make it more difficult for your body not to hyper- or under-absorb things that can cause inflammation.

Dr. Bonakdar (35:16): We also know that they can go on to things like early ulcer formation, which we know is also not good for the gut. So, in general, trying to minimize NSAIDs is important for many reasons, including other effects on the kidney, etc., but the gut is really where we want to focus on. What we sometimes do is add an acid blocker to the anti-inflammatory — your proton pump inhibitors [PPIs], etc. — to help the ibuprofen not affect the gut as much. That can help, but the proton pump inhibitor, by reducing acid, also makes it difficult for our body to absorb really important nutrients for migraine, such as [vitamin] B12, magnesium, zinc, and iron.

Dr. Bonakdar (35:47): So, if you're on those chronically ... There are many reasons to be on that — if you're trying to heal an ulcer, there are many medically valid reasons you should stay on and not stop it cold turkey. But if you've been on it long-term and there's not an ongoing reason to be on it forever, talk to your doctor about tapering that. Or at least checking your nutrient levels — [vitamin] B12 and things like that — to make sure you don't need a replacement to replete that nutrient. There are other drugs that do that, like metformin.

Dr. Bonakdar (36:39): So, with any drugs that you're on chronically, it's good to do a check. Talk to your doctor. Are there any nutrients that I may be prone to have a deficiency in that I should be taking, especially ones that may affect my migraine? So, those are the common ones. Migraine medications tend to be overall neutral, especially if they're bypassing the gut.

Dr. Bonakdar (37:02): The one caveat would be some of the CGRPs are prone to cause constipation; and anything that causes constipation — whether it's a CGRP, a tricyclic antidepressant like amitriptyline, or any other constipating drug — also can affect the microbiome negatively. So, one of the key things we do in our migraine history is: How prone are you to constipation or diarrhea? They're both obviously things we would want to balance out, but constipation tends to be more difficult for the microbiome. So, we want to try to get that gut to be regular, which helps everything work properly.

Kellie Pokrifka (37:34): If we experience constipation or diarrhea during an acute attack, is there something we should be taking during that acute attack? For example, if we took a laxative or magnesium to get things going, would that help the gut acutely to try to calm down the migraine attack?

Dr. Bonakdar (37:53): That's a great thought. We do know that when we are constipated, there's slow motility with a migraine, which is very typical. Things that help it have been used. Probably the most common one is magnesium, both because it's readily available and because taking a G.I.-positive-movement type of magnesium — your magnesium citrate, sulfate, or oxide — those tend to propel and can actually help in some regards, as well as increasing your magnesium which is depleted during a migraine.

Dr. Bonakdar (38:26): Other medications like Reglan also are used in folks that are especially prone to constipation during migraines to help things move and help them absorb medications. On the flip side, from a nausea standpoint or when things are going too quickly, there are things that help with slowing things down. Things like ginger are sometimes used because ginger has been shown to reduce leaky gut, improve how the gut absorbs, and also reduce nausea. So, anything that helps the gut get back into a normal working state — which isn't always easy during a migraine — is also a good idea for the microbiome.

Kellie Pokrifka (39:16): All right. Before we wrap up — I know we could talk about this for hours — do you have any last advice for people who are trying to go through this and trying to improve as much as possible, either acutely or long-term?

Dr. Bonakdar (39:26): Yes. I would say there's a lot of push to do microbiome testing because that's seen as sort of the quick diagnostic fix. Like, "We're going to do a microbiome test, it's going to show low X, and we're going to take more of X, and suddenly the migraines are going to go away." Unfortunately, it's wishful thinking. I think we're learning a lot about microbiome testing, which is very complex, very data-heavy.

Dr. Bonakdar (39:52): So, number one, I would say if you're thinking about that, work with a clinician to make sure it's a good idea and also a clinician who can help decipher the results. Don't necessarily do an over-the-counter version or direct-to-consumer because in some cases, you can get suggestions — they will give you suggestions many times for the supplements they have in connection with the kit — but they're not necessarily things that you really need.

Dr. Bonakdar (40:18): I would say backing up, think about how is what I'm feeding my gut? And I mean that in a larger sense of not just what I'm eating, as well as my supplements, but how am I feeding my gut with my mindset, my exercise, my sleep pattern, my stress management. And if there are any areas that have a gap, those are the ones I would start with.

Dr. Bonakdar (40:39): It could be in the diet — maybe I'm not eating enough fiber. There are ways to do that by shifting my diet, talking to a dietary expert, maybe use a fiber supplement, increase my omegas, do stress management, etc. Those are the places to start, and no headache specialist is going to argue with you when you tell them, "I'm going to try to improve my sleep hygiene, get to bed on time, reduce my stress, do biofeedback, and exercise more working with trained professionals." Those are all good things for migraine and they're good things for the gut. I would start there.

Dr. Bonakdar (41:09): And secondly, I would say the gut can be your friend; it's not a scary thing. We talked about fecal transplant and very complex things that sound very scary. I would say we need to back up and say the gut can be our friend and a lot of what we do in our daily pattern — what we eat, drink, how we communicate, how our environment is — [that is] where to start to optimize our gut, which over time we know can also go on to optimize our potential for migraine.

Kellie Pokrifka (41:48): I know I have had a very difficult time trying to figure out reputable sources and everything like that. And I know our audience definitely feels that way. Where can we follow your work so we can learn more and know that we're going in the right direction?

Dr. Bonakdar (42:02): Absolutely. So, I blog on migrawell.com, and there is discussion of nutrients and other approaches for the gut. There's also a section on neuromodulation devices, including vagal nerve stimulators. So there is a lot of discussion in that area. For folks who are on the West Coast, in California, who might have episodic migraine or be interested in being in a clinical trial, we would love for you to follow the link to see if you can qualify to be in the study. And those are some areas.

Dr. Bonakdar (42:40): And I think I provided a number of articles that help decipher the microbiome literature — the glossary of "What is diversity?"; "What is family?"; "species"; etc. We're all learning about the microbiome. I learn a lot from my patients. So, I think there's more to be discussed here, and hopefully, I'll be able to come back and let you know how our trial looks.

Kellie Pokrifka (43:04): We absolutely need that. Thank you so much for being on the Migraine World Summit.

Dr. Bonakdar (43:08): My pleasure. Have a great day.