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Speaker 1: Navigating Parkinson's disease can be challenging, but we are here to help. Welcome to the Michael J. Fox Foundation Podcast. Tune in as we discuss what you should know today about Parkinson's research, living well with the disease and the foundation's mission to speed a cure. Free resources like this podcast are always available at michaeljfox.org.

Dr. Rachel Dolhun: Hi, and welcome to the Michael J. Fox Foundation's Podcast. I'm Dr. Rachel Dolhun, a movement disorder specialist, lifestyle medicine physician and Senior Vice President of Medical Communications at the Michael J. Fox Foundation. I'm also the guest host of today's podcast. In this episode, we're talking about a topic that's not typical dinner or casual conversation, and that's the gut or the digestive system and Parkinson's. We'll cover things like constipation, nausea, bloating, and other symptoms that can commonly happen with Parkinson's. And most importantly, we'll tell you what you can do about all these symptoms and where the research stands.

Now, one quick note on what we won't cover in detail, and that's diet, which is of course always a popular topic, but one that deserves its own dedicated resources. You can listen to our podcast, download a free guide and get other materials on diet and Parkinson's at michaeljfox.org/diet. So now on to today's podcast. Let's meet our panelists. First up we have Dr. Wael El-Nachef, who's a gastroenterologist or GI doctor, as well as a researcher. He's also the Founder of the Parkinson's Disease Gastrointestinal Clinic in Pasadena, California. Wael, thanks so much for being here.

Dr. Wael El-Nachef: Pleasure to be here. Thank you.

Dr. Rachel Dolhun: We're also joined by Sebastian Krys, a Grammy award-winning producer and engineer, as well as a member of the Michael J. Fox Foundation Patient Council. Sebastian was diagnosed with early onset Parkinson's in 2019 at the age of 48. He lives in Woodland Hills, California. Sebastian, thank you also for being with us.

Sebastian Krys: Great to see you guys.

Dr. Rachel Dolhun: So let's jump right in and let's start with you, Sebastian. Now, for a lot of people, as I mentioned, problems with the gut aren't really something we want to talk about with everyone, sometimes, not even our doctor, and certainly not on a podcast that thousands of people are going to listen to. So we really appreciate you being here and sharing your experiences with us. And with that, I'd like to invite you to just tell us a little bit more about your experiences with gut changes and Parkinson's.

Sebastian Kryz: Well, looking back at my diagnosis, I feel like now it was probably the first symptom that manifested itself, even as far back as 15 or even further years ago. I just noticed that I was just having unusual symptoms as far as constipations go, and something was off and I just kind of ignored it. And then after my diagnosis with Parkinson's, I had a couple of really bad constipation episodes. And when I say bad constipation episodes, I mean they would knock me out, basically my day was done. It wasn't normal, run-of-the-mill constipation.

Dr. Rachel Dolhun: Wasn't like feeling a little backed up. It was ...

Sebastian Kryz: No, it was something completely different. It was painful and it's hard to describe really. It's this whole issue of having to really go to the bathroom and really having no way of going. So the only thing you could do was lay down for a couple of minutes and then go and try again, and then this would go on for hours. But that only happened a couple of times and now it's become sort of my day-to-day. So I decided to see a GI a couple of months ago and my doctor suspects that I have gastroparesis from what I described. So now we're trying to figure out what the next course of action is.

Dr. Rachel Dolhun: Yeah, I'm sorry to hear that it's such a big part of your life and that it's so disruptive to so many things that you do. And we'll get into a lot of the things you talked about from constipation to what you mentioned, gastroparesis or gut slowing, and even just the fact that you mentioned it knocking you out, more about what that means and how it impacts your medication and your day-to-day. So thank you so much for setting the stage and giving us some background and we'll hear a lot more from you throughout the conversation. With that Wael, I'd like to turn to you and just ask the big question, why does Parkinson's impact the guts and how does it do so?

Dr. Wael El-Nachef: Yeah, so there's a lot of theories about that and in many ways it could be multiple avenues that are causing these sorts of symptoms. The first thing that we notice though in the GI tract in patients with Parkinson's who have GI issues is that everything moves sort of slowly. And when we talk about movements of the GI tract, we are referring to something called motility. So you might hear this term when you talk to your doctors. And then what Parkinson's patients experience is dismotility. And it's just a medical way of saying things are moving incorrectly. And in this case, slowly. In Parkinson's, the colon can move slowly, the small intestine can move slowly, and the stomach can empty slowly. And would be the gastroparesis that was referred to earlier.

As to why this is happening, this is still an active area of research, but it could be that the nerve cells in the gut are being involved by Parkinson's. A lot of people don't realize that there are as many nerve cells in your gut as there are in your spinal cord. And so it's a huge neurological organ and it can be affected by Parkinson's directly, but there's also a lot of nerves that go from your brain and send connections to your gut. And those nerves can also be affected by

Parkinson's. And if those don't communicate well with the gut, it can also throw things off. So there's a lot of ways to get these sorts of problems. And so regardless of the cause, there are ways we can deal with this and hopefully control the symptoms.

Dr. Rachel Dolhun: That's so helpful, and let's stay on that for a second because a lot of people have questions about things like inflammation or something we hear about with leaky gut. Can you tell us first of all, is inflammation playing a role in the gut in Parkinson's? And then after we talk about that, we'll get to leaky gut.

Dr. Wael El-Nachef: So yeah, inflammation, I'll say that the vast majority of the patients who, let's say they get an endoscopy or colonoscopy and biopsies are taken, that if their problems are due to Parkinson's, the biopsies are going to be normal. And so we're not going to really see inflammation on the lining of the colon. And it's more likely a neurological cause, meaning nerve cells in the gut or nerve cells communicating to the gut from the brain. If you have inflammation in your colon, it's probably a separate problem. Or it could be, sometimes we see something called ster colitis, that's a medical term, just meaning that you have really hard stool in the colon that's causing irritation of the lining of the colon. And so it's more of a secondary effect, the side effect of being constipated. It's not causing the issue really.

Regarding leaky gut, so this is a concept that's been around for a long time and for a while it had fallen out of favor amongst gastroenterologists, but it's beginning to pick up again with new research. Whether or not this is what's causing the issues is still very early to say. But the concept is the gut is a barrier and it's supposed to selectively allow certain things to be absorbed like nutrients and water, but it should also function to keep things out of the body that shouldn't be in the body. The idea with leaky gut is that we're absorbing things that we shouldn't absorb and that that's causing GI symptoms. And this is a very high level explanation, but whether or not that's causing the symptoms of Parkinson's is still being investigated.

Dr. Rachel Dolhun: So it sounds like we mostly think it's this slowed movement that happens in Parkinson's. Again, to just bring it high level, everything really slows down in Parkinson's, whether it's our facial movements or our general movement, how fast or slow we walk, and then that extends even to our gut, how fast or slow our stomach empties, our food moves through our intestine, all those kinds of things. And we think that's because of the nerves and the nerve cells primarily being involved, maybe less so inflammation or these other processes.

Dr. Wael El-Nachef: And again, these other questions about inflammation and leaky gut, these are things that are being investigated, but I think it's still very early to really hang our hat on that and we'll see how the research pans out.

Dr. Rachel Dolhun: And with that, Sebastian, I want to turn back to you and I want to get more into a lot of the symptoms that you talked about and that so many people ask about.

So let's start with questions on gas and bloating and nausea. Do those happen with Parkinson's? Do you experience those, Sebastian? And what do you think is causing all of that or contributing to all of that?

Sebastian Kryz: I definitely experience bloating. And again, it's not normal bloating. It's like, you become the Goodyear Blimp, kind of bloating.

Dr. Rachel Dolhun: You can't button your pants.

Sebastian Kryz: And a lot of that happens oddly enough after I drink a lot of water. So you're supposed to drink a lot of water with your medicine and it's a little bit of a catch-22 because you're hydrating, which is what you're supposed to do, but then it causes this tremendous amount of bloating. And then obviously going back to what the doctor said, part of the issue that I have is that since everything is slowing down, a lot of times I have failed doses from the constipation.

Dr. Rachel Dolhun: And just for our listeners, tell us what failed doses means.

Sebastian Kryz: I'll take my Sinemet in the morning and it just won't do anything.

Dr. Rachel Dolhun: It won't ever kick in.

Sebastian Kryz: Yeah, it'll never kick in. And then I'll take my next dose and that won't kick in. And then maybe by my third or fourth dose of the day, they'll all kick in at once. So then I have really bad dyskinesia because I'm at that point over-medicated. So that's a real challenge.

Dr. Rachel Dolhun: And Wael, is that common for people with Parkinson's? One to see a real big impact on your medication with these gut symptoms? And then two, let's talk about that, even water feeling like it's causing bloating. Does that happen and what can we do about it?

Dr. Wael El-Nachef: Okay, so in terms of the medications, let's tackle that first. That is very common and that's something I only appreciated after seeing many patients. And I think the issue is, as Sebastian mentioned, is everything slowed down. And you might know that we ask patients to time their doses of levodopa based medications around meals because the protein in your food can interfere with the absorption. But when we give those instructions, we're assuming that the stomach is functioning normally. And that's a big assumption because many patients have delayed gastric emptying or slow stomach movements, also known as gastroparesis. And so their stomach may never be empty. And so they might follow the instructions to the T but there could always be some protein still residual in their stomach that might interfere with their absorption. And that's my theory and I've noticed that when we address the slow movements of the stomach, the drug absorption often improves. So yeah, I see this all the time.

Regarding the bloating with the water, I have to be honest, I haven't heard that specific complaint before and I might have some theories about why that might be.

But ultimately I think addressing the bloating, it would be the first priority, and then we could see if the water tolerance improves.

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Dr. Rachel Dolhun: Tell me a little bit more about these different symptoms. What causes them? How do you know if you have slowed stomach emptying that's causing your nausea and your bloating? All these kinds of questions are coming to mind for me, so I'm sure they're coming to mind for a lot of our listeners as well.

Dr. Wael El-Nachef: Yeah, so bloating is extremely common. I would say almost every patient I see has that symptom. And in my mind what I've noticed is that the most common cause of bloating is inadequately treated constipation. And then if we successfully treat the constipation, I would say over half of patients, the bloating gets better. Just that. And then I think people get very focused on the bloating, and I think common things being common, it's probably constipation related, especially in Parkinson's.

Another issue with bloating is that since things like gastroparesis, where the stomach isn't emptying well, can mimic the sense of bloating, and so that might be actually a symptom of gastroparesis. So that's something else to keep in mind.

And then lastly, I referenced before that the small intestine might be involved with Parkinson's, and that makes it move more slowly. And in I would say the minority of cases, if the bloating persists despite treating constipation and it persists despite treating gastroparesis, then we can start looking into things like small intestinal bacterial overgrowth. Though I found that this is often a red herring, but if everything else has been addressed and they're still bloating, then we can go down that path.

SIBO, small intestinal bacterial overgrowth, is not like an infection per se. It just means that the normal bacteria that are in all of our guts, in certain patients they might overpopulate, there might be too many of the bacteria in your gut. And this is a problem because bacteria normally produce gases as part of their metabolism. And if there's too many of them, there'll be a lot more byproducts of gas. And that can lead to symptoms like bloating, diarrhea or constipation, depending on what type of bacteria are overgrown. And the reason this happens in patients where the small intestine is moving slowly is because normally the small intestine sweeps out bacteria every so often into the colon and you expel them. But if things are moving slowly, that regular sweeping pattern of the small intestine doesn't happen as regularly, and that allows the bacteria more opportunity to divide. And that's the theory.

Dr. Rachel Dolhun: So it's more likely a consequence of the slowing down and everything else that's happening in Parkinson's, versus a potential cause of these symptoms.

Dr. Wael El-Nachef: That's what I've seen in clinic, that oftentimes it's a consequence of slowed motility, and you could even ... I've seen patients where I've just treated the motility issue, no antibiotics, and it gets better. It goes away. And so in many cases, I think it's just a side effect of Parkinson's. And I think there's an interest in examining whether these bacteria are causing the Parkinson's. I think that's a very intriguing idea, but in my experience it's most often the opposite.

Dr. Rachel Dolhun: And we'll talk a lot more about bacteria. Microbiome is always such a big topic and we want to get to that, but I want to say on constipation for a minute or two, because you mentioned that a lot of times constipation is the culprit for a lot of these other symptoms that happen, I guess, upstream or downstream, whichever way you want to look at it, whether it's nausea or bloating or those sorts of things.

So lots of questions on constipation always, but one question that comes to mind is, how do you even know you're constipated? Is there's some sort of definition that if you don't have a bowel movement every day, that means you're constipated, or you have to have one every other day. How do we think about that?

Dr. Wael El-Nachef: This is a tricky question, particularly in Parkinson's disease, and I think that this idea that one bowel movement a day means you're not constipated does not apply in this patient population. I've had patients who don't have bowel movements for days at a time, and that's constipation. I've had patients who have a bowel movement twice a day and they're constipated. I have patients who've had diarrhea, but they're constipated, or they have incontinence and they're constipated. And so it runs the whole spectrum of GI symptoms, and the issue is with Parkinson's, it can manifest in a lot of different ways.

Dr. Rachel Dolhun: Just to delve a little deeper on that, because it seems so weird to say I could be having a bowel movement every day, but I'm constipated. What does that exactly mean? The stool is not moving through in the right way and it's not clearing things out as you mentioned? Your food's not moving through, your not medicine's not moving through in the right way?

Dr. Wael El-Nachef: Yeah. And so, even if you're having a bowel movement, it might not be a complete evacuation. And so it might be every day, but I think the main thing that I look for is if the patient's having other GI symptoms. Like if they're having bloating or if they're having nausea, things like that, let's take a look and see if treating constipation will fix those problems.

And so that's my usual starting point. And part of the problem is, in Parkinson's, there's obviously the motor issues, the motility issues, but there might be some sort of sensory issues in the gut as well. And there have been studies showing

that patients might have a very large amount of stool in their colon and they don't sense it, when an average patient would definitely sense it. So it takes a lot for the alarm bells to go off for a Parkinson's patient. That's why you might catch something when it's already pretty far along.

Dr. Rachel Dolhun: And I want to talk much more about treating constipation, because that's obviously always a really common question, but, Sebastian, let's turn back to you. And what are you hearing in this conversation that's resonating with you? Or you're going, "Yep, that's my experience." How did you approach managing constipation when you realized this was an issue for you?

Sebastian Kryz: Well, I mean the first thing that resonates with me is, I guess the first question is, is it treatable? And then, is the treatment a medical treatment? Is it diet? Is it a combination of those things? Is it different for everybody? Is there something you can do right away to help alleviate some of these symptoms? Which I'm sure a lot of the people listening, probably their head went right to the same place because you want to obviously try to get some relief. And I find that with Parkinson's, the two big things that you want to try to treat in order to have a better life is sleep and gut health. And then those things fall into place, then a lot of things will fall into place.

Yeah, I mean, as far as symptoms go, definitely I've experienced both those things. I've experienced having being to go to the bathroom and still feeling very constipated immediately after and feeling like it was just sort of round one, let's say, of whatever battle goes on that day. And I've experienced the other extreme of not going for five days.

Dr. Rachel Dolhun: And as you mentioned before, this can be so extremely disruptive to your life. It can impact your schedule, how you take your medicines, if you want to eat, if you want to exercise. So it is critical to talk about it and to treat it, and your really well-put-together questions of what can we do.

So Wael, we'll go back to you, what can we do? Whether it's over-the-counter medicines, things we're eating, sleeping, diet, you name it. What are the top things we can do if this is an issue for us?

Dr. Wael El-Nachef: Yeah. Well, first I want to say that there is treatments, and it does vary depending on what's going on. And so, Sebastian, don't worry, there's things that can be done and hopefully you'll get well very soon. But I think it's important to remember that there's not just one type of constipation. In Parkinson's there's two main things that I see, it's when the colon is moving slowly, which we call slow transit constipation, and that's treated one way.

And then there's also dyssynergic defecation. And so dyssynergia refers to synergy, and so in order to have a bowel movement, you have to have a coordination of several different muscles. The anal sphincter has to relax, the pelvic floor muscles have to relax as well, and you have to push. And that has to

all happen in the right sequence and with the right force, et cetera. And that's very commonly abnormal in patients with Parkinson's as well. And that's treated a different way compared to slow transit. And the reality is, about half of Parkinson's patients have both problems, and so that's something we have to keep in mind too.

And so I want to take a step back. When you were first describing your symptoms and you said things like, "It really knocked me out." And you used, and I wouldn't say vague terms, but for me, I think the point I want to make is when you talk to a doctor about these, you have to be explicit with the symptoms you're experiencing. And don't be shy, especially if it's a GI doctor, you're not going to make them blush. They've seen and heard everything. And so I've had to ask patients, and it comes out later, "Are you having incontinence? Are you having leakage, even when you're not on the toilet?" Things like that. And so that will really help us understand what type of constipation you're dealing with, what your problem is. And I'm not saying you have to detail these over a podcast right now, but just I'm saying in general, things that you should talk to your doctor about and mention.

Now going back to your question, what can we do to treat this? If you're having occasional constipation, and I think maybe in Sebastian's case this might not apply because I think your case might be a little more severe, but for the occasional constipation, I totally recommend trying over-the-counter medications to just get things back on track and get some comfort and regularity. And so, one of my favorites is something called MiraLAX or PEG. It doesn't matter if it's generic, they work equally the same. And you can mix that with water, juice, coffee, whatever liquid you want. Has no taste, no scent. It's super safe. Really the worst side effect I've ever seen is diarrhea, meaning that you just decrease the dose. And that's something you can take every day. And it works just by ... You can think of the MiraLAX powder granules as little sponges, and they draw water into the colon and help move the stool that way. So it's super safe, super gentle, no cramping. And so that's something that I would start with.

But then there's other classes of laxatives, things like Dulcolax, which is bisacodyl, or senna, and those are more stimulants. And typically I don't recommend these on a regular basis because they can cause cramping and they often will cause diarrhea. So this is something, if you need it more than once or twice a week, then you probably need to change your regimen and talk to your doctor, figure out what's going on.

People often ask me about things like psyllium fiber, brand name is Metamucil, for example. And I think that's great, I think it's very safe. There's other health benefits of fiber, but my caution for that in a patient who's already constipated is that it can exacerbate bloating. And so if you're extremely constipated and you take psyllium, you're going to be unhappy. So I would say that's something more, once you're on a maintenance regimen, you can add that in. Or you can

start at a very low dose, like a teaspoon once a day and see how that goes for a week or two, and then you can go to two teaspoons. I think eventually you'll need to be on a tablespoon or two, but-

Eventually you'll need to be on a tablespoon or two, but starting very small is probably the best.

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Dr. Rachel Dolhun: Yeah, it's a really good point. It's like if I sprained my ankle, my treatment at that point wouldn't be to strengthen my calf, it would be to ice my ankle, take anti-inflammatories, and then ultimately strengthen my ankle muscles and my calf so that I don't sprain my ankle again. So it's kind of the same idea, right? When we're constipated, we don't want to add something on top of it, but the fiber in the long term can potentially help keep us regular. So something to get on and stay on if you're not constipated. And then if you are, think about clearing out that constipation, getting on a good regimen, including fiber, once we're back on a normal routine.

Sebastian Kry: Dr. What about Gas-X for the bloating? What's your view on that?

Wael El-Nachef: So I never prescribe it. I think many of my patients come to me and they're taking it and I think they might get some benefit from it. Some of it, I think, might be placebo. But once we've addressed their underlying GI issues, whether it be slow transit constipation or gastroparesis or dyssynergic defecation, they usually just stop taking it on their own. I don't even have to ask them to. They're like, "Well, I don't need it anymore." So, in my mind, it's like we should treat the underlying issue and not just try to mask the symptoms with a medicine like that. I don't think it's harmful. I think it's okay, but I don't usually recommend it, basically.

Dr. Rachel Dolhun: It's like a bandaid, until you can get to the actual thing that's underneath all of that stuff.

Dr. Wael El-Nachef: Yeah.

Dr. Rachel Dolhun: And on the treatment, still staying on that for a minute, are there people who shouldn't take these over-the-counter medications or are there other things you would tell people about, when we're in this trial and error process, and we're standing in the pharmacy aisle, and we're overwhelmed by all the options of what there is for stool, how can we think about navigating that?

Dr. Wael El-Nachef: So, I mean, first of all, all of this is being mentioned with the assumption that you're up-to-date on your colon cancer screening and then most of the constipation that you see in Parkinson's is not colon cancer. So I'm not saying everyone should panic about that, but obviously, you should get your routine colonoscopies, et cetera, as anybody would because you're not immune from

getting colon cancer. And it would be a shame to miss that, because we just assumed it was due to Parkinson's. So just make sure you're up-to-date on that. And then the other things I would say is, if you have red flag symptoms, which mean symptoms that are concerning for something serious like bleeding or weight loss or even I would say mucus coming out, I would also talk to a GI doctor to make sure you're not missing anything either. And in terms of being overwhelmed with options, again, I did mention a few things about maybe just starting with MiraLax and just going with that, as a starting point, and go from there.

Dr. Rachel Dolhun: And, of course, always talking with your doctor. It's okay to try some of these things, that's why they're there. But ultimately, the idea that making sure that you're talking with your doctor so that we are all on the same page about what's happening and when we need to move to something stronger than those over-the-counter medicines. So talk to us about that. When we're in Sebastian's spot and these aren't working for us, what do we do then?

Dr. Wael El-Nachef: Yeah, so usually I meet patients after they've worked with their primary care doctor, they've worked with their neurologist, and many of them have seen a couple of gastroenterologists and they've been scoped up and down. There's nothing else really to explain their symptoms in terms of a physical visible lesion or a problem. And so by this time I see them, they've already tried the over-the-counter medications and they're not working. And in a case Sebastian's, where there's appears to be symptoms of gastroparesis with medication malabsorption, as well as constipation, I'll often talk to them about prescription type medications that are a little stronger.

One of them is called prucalopride. Brand name is Motegrity. This medication's been around for a while and it works by increasing the contractions in the GI tract. It's specifically approved for constipation, but it also affects and improves the motility in the stomach and the small intestine as well. So, for a Parkinson's patient, especially with these sorts of symptoms, it's a great option. There are side effects that I need to discuss with the patients and make sure they understand, but most patients tolerate it really well and they respond really well to this medication.

Dr. Rachel Dolhun: And, Sebastian, you're listening so intently. Come back into our conversation and tell us what you're hearing, what kind of things ring true in your experience, what this is making you think about you wish you would've talked about with your doctor or you will talk about with your doctor?

Sebastian Kryz: Yeah, I mean with Parkinson's and with GI issues and any of the issues that we have, it feels sometimes like a game of whack-a-mole. And it's just really trying to get to the point where your life just feels consistent, no pun intended. I just now started the journey of talking to a GI and really addressing this. And I would just encourage people to do it sooner, because it is really disruptive, especially when you have those failures, and it can really just throw your life for a loop,

whether it's travel or work or whatever it is that you have to schedule. It's very difficult when you have to change your entire life because of these issues, and I've found myself with that problem, where it's really affected my work and my daily life schedule.

Dr. Rachel Dolhun: And I think for a lot of people, that becomes their new "normal" and they feel like this is just the way it is with Parkinson's or the way it has to be. And while I know this is a big point you want to reinforce to our audience is that this isn't necessarily what you have to live with. There's a lot that we can do about this and it is so important to talk with your doctor or get to a GI specialist if that's for you.

Dr. Wael El-Nachef: Yeah, I mean I have a very, maybe biased view of what patients go through, because I only see the patients with Parkinson's who have GI issues. But I can tell you, of those patients, it's the GI issues that are really the problem in their quality of life. The motor symptoms, they're a nuisance, but they're manageable. But it's the GI issues that are keeping them from living their life, that are keeping them from leaving the house, even, and so it can be really devastating. It can be very alienating and, the patients, they feel that they're isolated.

Dr. Rachel Dolhun: So can treating a lot of these gut symptoms actually help other symptoms of Parkinson's or help medication work better?

Dr. Wael El-Nachef: So I can say that, from my experience, I've noticed that many patients have improved absorption of levodopa-type medications, to the point where I have to warn them that when we start a medication that improves motility, to watch out for dyskinesias because you might need to lower your dose or reduce the frequency.

Dr. Rachel Dolhun: Because you're used to having to take much more or have ... yeah, interesting.

Dr. Wael El-Nachef: Yeah, I've had patients who come to me and they're taking Sinemet every couple hours. It's like it's nonstop and doesn't work very well, et cetera. And then, suddenly, their stomach's moving and it totally changes the dosing pattern for them. And so that's something to keep in mind. I've had a couple patients referred for me who didn't really complain of GI symptoms, but they were referred for me because of the absorption issues. And then when we dug in, we found out, "Oh yeah, it does sound like you have gastroparesis because of the way you're eating, because of how you're spacing out your meals, you're eating small amounts."

This is the allegory of the frog sitting in the pot of water going up by one degree at a time. And the issue is that these symptoms didn't happen overnight for patients. This is, as Sebastian mentioned, this probably has been building up over many, many years. And so I think a lot of patients have learned to tolerate a lot. Unfortunately, they shouldn't have to. But just to keep in mind that ...

maybe compare yourself to someone without Parkinson's and see what their quality of life is in these regards, and that should be your standard. Don't lower your expectations.

Dr. Rachel Dolhun: It's such a good point. And two more questions on constipation. Then I want to move on to microbiome, because I want to make sure we get to that really very popular topic. So on constipation to what you're talking about, a lot of times we just think this is just Parkinson's. But are there other things we should be thinking about that can cause or contribute to Parkinson's, whether it's our Parkinson's medications or other medications, the foods we eat, the exercise we do. What are other potential contributing factors to constipation that there might be something we can do about?

Dr. Wael El-Nachef: So definitely making sure you're hydrated is helpful. There's also a lot of support for the idea that moving around will help you stay regular and there's a lot of benefits to exercise, and just moving in general, aside from GI health and aside even from cardiovascular health, I understand, for Parkinson's in general, exercise is really important. In terms of diet, so there's no one-size-fits-all recommendation I make in terms of diet. But, obviously eating a diet that's rich in fruits and vegetables and natural sources of fiber, are going to help with your gut health. And so that's things you can do. Oftentimes, though, if it's really severe constipation, it's not just about eating an extra apple or something like that. So I wouldn't blame yourself if you have severe constipation. Obviously your diet can help, but in some cases it's not going to be sufficient no matter how you eat.

Dr. Rachel Dolhun: Yeah, and always talk with your doctor about your medication list. Ask if there are medications you're taking that might be contributing to constipation. To your point, if you can see a dietician, maybe it's a trial and error about what foods might be working better for you or not as well for you and all those kinds of things. The last thing I want to ask about constipation is, again, something we get asked about a lot and that's fecal transplantation. This is in the news a lot. There's a lot of research going on around this. So tell us what it is and where the research stands on this as a potential treatment for Parkinson's and Parkinson's constipation.

Dr. Wael El-Nachef: So fecal transplantation is basically you're taking a stool sample from one individual and inserting it into the GI tract of a patient. And this can be taken orally, it can be taken through enema, or it can even be administered via colonoscopy. So there's a lot of different ways to deliver the transplant. This has been studied for many conditions, not just Parkinson's. The best evidence is for a type of infection called *Clostridium difficile* or C. diff. And this causes diarrhea oftentimes in hospitalized patients and can be very difficult. And we've known for many years that doing fecal transplant can solve this problem. It's been explored for things like inflammatory bowel disease, a lot of autoimmune conditions, and now being explored in Parkinson's.

There have been some studies to suggest that doing fecal transplant in Parkinson's could be helpful, but these are very early studies and we need to start looking for researchers to do what we call double-blind controlled study. So right now they're sort of taking all-comers, giving them the transplant, and saying, "Do you feel better," and doing measurements, et cetera. But it needs to be controlled. So for us to really make a conclusion at this point, the data we have is exploratory, meaning maybe this is a good topic for us to explore further. So I don't think we're ready for prime time with that. And so a lot of patients are interested in this stuff.

Dr. Rachel Dolhun: Lots of ongoing work, but as you said, not quite ready for everybody to get this treatment.

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Dr. Wael El-Nachef: Yeah.

Dr. Rachel Dolhun: Sebastian, I'll turn back to you as we turn to the microbiome. So I don't expect you to answer the complicated technical questions on it, but I guess I'd start with you and ask, what's your understanding of it? What questions do you have about it? And then we can turn to Wael to fill in all the gaps for us.

Sebastian Kryszewski: I would ask him to fill in all the gaps for us, honestly, because a lot of this is new to me, as it is to many patients that are just... I'm four years into my diagnosis, and what I'm dealing with now versus what I dealt with two or three or four years ago is very, very different from a treatment standpoint.

Dr. Rachel Dolhun: And you said earlier that, but when you feel that your sleep and gut health are the big things for you, so you're alluding to the microbiome there. And this is where I think there is so much interest because people do experience this and feel this and want to know how is my gut and my gut bacteria specifically playing a role in my Parkinson's, my symptoms, how I feel. So, Wael, let's turn it over to you and just give us the high-level primer on the microbiome and its role in Parkinson's.

Dr. Wael El-Nachef: Yeah. So the microbiome refers to the bacteria. We've talked about the gut microbiome. It refers to the bacteria that are in your intestinal tract. Everybody has bacteria in their gut. We've co-evolved with these bacteria since our very early beginnings. And so it's normal to have bacteria in your gut.

The issue that comes up is whether these bacteria, if there are bad forms of bacteria that can cause diseases, if things get out of balance in terms of the populations of different types of bacteria. This has led to an explosion of research. And there have been some very intriguing results in animal models, specifically with regards to Parkinson's. But again, I think this is very early

stages. This is related to the fecal transplant discussion we just had a moment ago, but end of the day, I think it's very early to say whether or not the bacteria in our gut could cause Parkinson's. I think it's an interesting concept, but I think it's also very likely that the imbalances of bacteria that we do see in Parkinson's patients are more likely a side effect of a slow-moving gut.

Dr. Rachel Dolhun: So just to put a finer point on that, we've all got this bacteria in our gut. It's different for different people in some regards, the amounts and the levels, but we also are starting to see that the microbiome, the bacteria, are different in people with Parkinson's versus people who don't have Parkinson's. But to your point, we're not exactly sure why that is. Is it because of the Parkinson's? Is it because of the medications that you take? Is it specific foods you eat or don't eat that are outside of Parkinson's? So it's really hard to know what's what here. But tell us a little bit more specifically about why are these bacteria here? What do they do for us? Do they help us? Are they good for us? Are they bad for us?

Dr. Wael El-Nachef: Yeah. So the bacteria in our gut usually do a lot of functions for us. They produce metabolites that, many times, can help maintain our gut health. Sometimes they're absorbed into our bodies and have other functions. And so, like I mentioned, we co-evolved, and so they're getting benefit from living within us, but they don't live rent-free and so they're doing stuff for us too. Now the question is if the wrong bacteria take hold and they're producing things that are bad for us, could that cause disease? And that's a very interesting theory, and I think we'll see how the research pans out as we extend these studies more into humans.

Dr. Rachel Dolhun: And are there things that we can do in our day-to-day to help promote a healthy microbiome or things that we're doing that might be doing the opposite?

Dr. Wael El-Nachef: A lot of patients asked me about probiotics. There have been a couple of studies that have suggested that that might be helpful in Parkinson's. I don't think there's enough evidence for me to make a strong recommendation to do it. I think the issue with probiotics is also that they're not FDA-regulated, so it's not really clear what you're getting when you're buying them at the store.

And so my real recommendation to patients who are motivated to do something like probiotics is just to obtain the probiotics naturally through the foods they eat. So foods like yogurt, kimchi, sauerkraut, kefir, like those sorts of things definitely have probiotics, and you could try that. If you feel better, then continue to try eating those foods. If you don't feel better, then save your money.

Other issues too is this concept of prebiotics. And so this is the idea that instead of trying to ingest bacteria and put the bacteria in our gut that way, we should ingest food that the good bacteria want to eat, that will promote the good bacteria that are already in our guts. And so that's a whole nother discussion,

but just essentially, foods with fiber, fruits and vegetables, those will often serve as prebiotics.

Dr. Rachel Dolhun: So those are the good things that feed the good bacteria. What are the things that might impact our microbiome in a negative way, things like constipation or antibiotics or?

Dr. Wael El-Nachef: Unnecessary antibiotics is something that can really throw off your microbiome.

Dr. Rachel Dolhun: The key there's unnecessary. So we oftentimes do need them but-

Dr. Wael El-Nachef: So obviously, even the antibiotics that you really need can still throw it off, and we'll just have to deal with the consequences. But I think the main thing is not taking a Z-Pak every time you have the sniffles and just making sure that you're only taking antibiotics when it's really, really necessary because that can throw off your microbiome big time. So there's been questions about could certain Sinemet-type medications throw off your motility in your microbiome. I think that's unclear. Some of the research is conflicting, whether the motility changes in the colon or in the stomach, but essentially, you need these medications, and we just have to deal with the outcomes and we can manage them.

Dr. Rachel Dolhun: And last question on microbiome. We're starting to see these over the counter or mail-in kits where you can get your microbiome analyzed. Should we do that? Is that a good idea? Will it tell us much? What do we know now?

Dr. Wael El-Nachef: So I've seen this a couple times. I think, when I see these reports, honestly, I'm not sure really what to make of them. And so I think the problem is when you do tests, they have to be validated, and we have to understand what we're testing for and what do we do with the information once we have it. And I would say, be wary of those sorts of tests. I would only get my microbiome tested if a doctor prescribed that test for me or if I was part of a research study, but to just do it on my own, I'm worried that you might just be losing out on money and you're not going to get much benefit from the results.

Dr. Rachel Dolhun: Your money's better spent on apples with fiber in them or exercise or whatever it is. So I want to give you both a chance to just leave our audience with what you'd want them to know. And Sebastian, I'll start with you. If it's something in your experience that you wish you would've known or what you want to empower the audience to do, what would you tell them?

Sebastian Krys: Just listen to your body and definitely talk to your doctor about all of the issues that you're having and put them in an order of priority, because I do feel like a lot of this is a domino effect. And I agree with the doctor; I refuse to believe that this is as good as I'm going to feel for the rest of my life. I feel like you can always do something to improve the way you're feeling, your quality of life.

Dr. Rachel Dolhun: Yeah, that's right. And Wael?

Dr. Wael El-Nachef: I think, along the lines of what Sebastian's saying, don't settle for these sorts of symptoms. Hold your standards high in terms of GI issues, because there's a lot that can be done. You just need to find the right GI physician who can get control of those symptoms. So oftentimes, that might mean someone who specializes in motility. And most academic centers will have a motility center, and those physicians are really accustomed to dealing with the type of problems we see in Parkinson's. That's what I would recommend.

Dr. Rachel Dolhun: So there's a lot that can obviously happen, but there's a lot that you can do, and it's important to just not feel embarrassed. There's books about everybody poops, right? This is okay. This is normal. This is okay to talk about. You have to talk about it in order to find out what's going wrong and what you can do.

We're, again, so thankful Sebastian and Wael for you both being here, sharing your experiences and your knowledge. For more on this topic, including a video and a blog with Dr. Wael El-Nachef, you can visit michaeljfox.org/guthealth. And if you want to learn more about the best foods for your gut and for brain health, you can check out our library of diet resources, which you can find at michaeljfox.org/diet. So thanks for listening. Thanks for being here. And until next time.

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