Michael J. Fox: This is Michael J. Fox. Thanks for listening to this podcast. Learn more about the Michael J. Fox Foundation's work and how you can help speed a cure at michaeljfox.org.

Speaker 1: Welcome to a recap of our latest third Thursday webinar. Hear directly from expert panelists as they discuss Parkinson's research and answer your questions about living with the disease. Join us live next time by registering for an upcoming webinar at michaeljfox.org.

Dr. Rachel Dolhun: I am Dr. Rachel Dolhun, a movement disorders neurologist, lifestyle medicine physician, and senior vice president of medical communications at the Michael J. Fox Foundation. I'm also your moderator for today's webinar.

In this special Ask Us Anything webinar, we have a panel who will answer your questions about the gut and Parkinson's. We'll cover things like constipation, nausea, bloating, and other gut symptoms that can come with PD.

What we won't cover in detail is diet, but we have a whole suite of materials specific to that topic that you can check out at michaeljfox.org/diet. Before we get to your questions, we're going to do something a little different than our standard webinars. Earlier this year, I sat down with one of our panelists to learn more about the gut, brain, and Parkinson's. We'd like to play a video of that conversation to set the stage for our live conversation.

Wael, thanks so much for being here.

Dr. Wael El-Nachef: Thank you for having me.

Dr. Rachel Dolhun: So let's jump in because we've got a lot to cover. The gut. We might think about that and talk about it in different ways like I have a gut feeling or I've gotten upset stomach, but what actually is the gut?

Dr. Wael El-Nachef: So to me, the gut is a simple term to refer to the gastrointestinal tract, and that includes everything from your upper throat all the way down to the anus. The organs that are included in that include the esophagus, the food tube, your stomach, your small intestine and your colon.

Dr. Rachel Dolhun: And we think about it as far as digesting our food, but it does a lot more than that.

Dr. Wael El-Nachef: So the GI tract is amazing. It's why I got into the field. Aside from just absorbing and digesting food, it's the largest hormone producing organ. It's the largest absorptive service in the body. It's the largest community of bacteria in our body, and it's the second-largest neurological organ.

Dr. Rachel Dolhun: And that's second to the brain.

Dr. Wael El-Nachef: Of course.

Dr. Rachel Dolhun: And it's connected to the brain.

Dr. Wael El-Nachef: So although the intestinal tract can function independently, if you took it out into a tissue bath, it would have all these muscle contractions, et cetera. Really in order for it to function properly, it has to be wired to the central nervous system or brain. There's multiple connections throughout the GI tract and the brain. And this is really important because it's not just a one way communication. There are signals from the brain that go to the gut and the gut can signal to the brain.

Dr. Rachel Dolhun: And we experience this in our everyday lives. If I have an upset stomach, maybe I don't feel as well, and vice versa, we experience this brain gut talking to each other.

Dr. Wael El-Nachef: Absolutely. And a lot of people refer to the gut as the second brain, really. So there's really two brains talking to each other.

Dr. Rachel Dolhun: So sometimes in some people it may be a place where disease could, for example, start in the gut. We were learning that in some people, Parkinson's might start in the gut and actually then move to the brain. So that's one way that the gut and brain are really connected. But we also see it with a lot of people with Parkinson's experience things like constipation or other changes. So we certainly see how a disease that affects the brain like Parkinson's can also impact the gut.

Dr. Wael El-Nachef: So this brings up a really interesting advance in the research of Parkinson, and there's a growing theory that at least in some patients with Parkinson's, the disease first starts in the gut and then travels to the brain over many years. It's through those communications between the brain and the gut that this can happen.

Dr. Rachel Dolhun: And as we learn more about this, this could potentially be a way where we could learn how the disease is coming on, maybe even prevent it from spreading further.

Dr. Wael El-Nachef: So there's a lot of potential here. It's very exciting research, but it's still very early days.

Dr. Rachel Dolhun: And we'll talk a little bit more about what can go wrong in the gut with Parkinson's. But I want to talk about the microbiome for a second because so many people wonder, you mentioned all the important aspects of what the gut does for us. It also plays a role in our immune system, like fighting disease, making nutrients and vitamins. But the microbiome, tell us a little bit more about what that is and why it's important.

Dr. Wael El-Nachef: So yeah, the microbiome refers to the population of bacteria that live normally live in your intestinal tract.

Dr. Rachel Dolhun: In everybody.

Dr. Wael El-Nachef: And it's normal. It's not an infection. These are the bacteria that you have co-evolved with humanity over the centuries, and they don't live rent-free. They provide functions. Their byproducts can be absorbed and have beneficial effects and help us maintain a healthy life. If the population of the bacteria because it's not all the same bacteria, there's different types of bacteria. If that gets out of balance, that can lead potentially to harmful effects. And we refer to this as dysbiosis. You might see that term. In Parkinson's we've learned that and several studies have shown that the populations of bacteria in their intestines is different than what we see in patients who don't have Parkinson's. Whether or not this is cause or effect is still too early to say, but it's a very interesting potential.

Dr. Rachel Dolhun: And so exactly what you're saying is we don't yet know. We know there's differences in the microbiome and people who have Parkinson's, but we don't know if that's causing Parkinson's or it's from the Parkinson's.

Dr. Wael El-Nachef: Exactly.

Dr. Rachel Dolhun: And there are so many things that can affect our microbiome, whether we have Parkinson's or not, the foods we eat, where we live, whether we exercise, the medicines we take.

Dr. Wael El-Nachef: And it also depends on how the gut is functioning. So if the gut is slowed down, it's going to change how frequently you clear out your gut and that will affect which bacteria reproduce.

Dr. Rachel Dolhun: So speaking of the gut slowing down, let's talk about that and how that happens in Parkinson's. Parkinson's can affect the gut in so many ways, and we often think about constipation because one of the most common symptoms. So let's start with that, but then talk about the other things that can happen.

Dr. Wael El-Nachef: Sure. So a lot of evidence suggests that the nerves in the gut itself can be affected by Parkinson's, and this usually results in things slowing down, meaning the contractions are slowed down or weakened and the movements are slower.

Dr. Rachel Dolhun: So just like our overall movements can slow down, our walking can slow down, our gut slows down too in Parkinson's.

Dr. Wael El-Nachef: Yeah, exactly. So this plays out in different ways depending on which organ in the GI tract is affected. So if it's in the colon, if it slows down, that leads to constipation. In the stomach, that can cause delayed gastric emptying or

gastroparesis. In the small intestines can lead to something called SIBO or small intestinal bacterial overgrowth.

Dr. Rachel Dolhun: And different symptoms with each of these different areas affected.

Dr. Wael El-Nachef: Exactly. And so if you have a gastroparesis or your stomach is emptying slower, then you might notice you eat a couple bites of food and you feel full immediately or you feel like there's a brick sitting in your stomach. This might prevent you from eating a full meal. If your colon is slowed down, constipation, if you have SIBO or small intestinal bacterial overgrowth, this can lead to bloating.

Dr. Rachel Dolhun: So all kinds of different symptoms also really impacts how well our medicine does or doesn't work.

Dr. Wael El-Nachef: So this is something that I've observed over time with patients and I think it's very important and also just interesting to think about it because it can lead to differences and changes in how we manage these problems. So what I often will see is a patient who has let's say gastroparesis or delayed gastric emptying. And this patient will also tell me that they've had increasing doses of their levodopa, increased frequency of their levodopa, but it doesn't seem to kick in as quickly. It doesn't seem to last as long. But once we address their gastric emptying, their absorption of levodopa improves.

And my theory, my thought on this is that we will often prescribe the levodopa and tell patients to time their levodopa away from their meals because protein in your diet will interfere with the absorption of the drug.

Dr. Rachel Dolhun: So they get absorbed in the same place so oftentimes if you take your levodopa with eating a big protein meal, we say that they might compete and you might not absorb as much medication. But what you're saying is there are other things that can happen that can impact how well our medicine is absorbed too.

Dr. Wael El-Nachef: So for example, when we tell a patient take your levodopa an hour before or after a meal, for example, we're assuming that their stomach is emptying normally. And the big problem though is if you have Parkinson's with delayed gastric emptying, your stomach may never be empty completely.

Dr. Rachel Dolhun: So taking higher doses or more often doses may not be the answer.

Dr. Wael El-Nachef: Exactly. And so they're always going to have this protein interfering unless we deal with the underlying problem, which is the slowed stomach.

Dr. Rachel Dolhun: And important to stress this doesn't happen in everybody. This interaction isn't a big deal in everybody, but in some people it really is.

Dr. Wael El-Nachef: Exactly. So it's always important to say this is for a subset of patients, it could be true. It's not universally the case.

Dr. Rachel Dolhun: And weight loss is another one that can happen in Parkinson's.

Dr. Wael El-Nachef: Yeah. So there's many reasons for weight loss in Parkinson's. It can be related to the gastroparesis that we discussed already, or having to take levodopa so frequently that there's literally no time to eat. Or for many patients, they attribute their GI symptoms to food and they start restricting their diet saying, "Oh, this food causes bloating, this food causes pain," et cetera, et cetera. And they end up just restricting themselves down to almost nothing and they're subsisting off saltine crackers. I've seen this many times and I think it's important in those cases for patients to take a step back and maybe speak with a specialist or a dietician to help them figure out what foods they do tolerate and to also importantly determine whether their symptoms are really due to the food or due to some of these other issues we've discussed.

Dr. Rachel Dolhun: And a lot of people understandably, will treat a lot of these symptoms with over the counter medications. We can get laxatives or stool softeners or any number of things to help us with a lot of these symptoms. And that's okay to a point. And then you want to seek specialist help.

Dr. Wael El-Nachef: Yeah, so I think it's always good to start with these over-the-counter measures because you can do this right away on your own and they're generally very safe. Stool softeners I'll say though, oftentimes are too small of a gun by the time if you have Parkinson's and constipation, I would probably not even bother with them.

But other medications like osmotic laxatives such as a brand named MiraLax or PEG is the generic that is extremely safe and very effective for many patients, and you can take this every day and it's totally fine if it works for you. A lot of patients ask me about stimulant laxatives. These are things like bisacodyl or Senna. These medications I think are fine to use, but they often cause cramping and other side effects. And so if you find yourself needing to take a stimulant laxative more than let's say once a week, then you should consider speaking to a specialist because they can help you find a regimen that's going to be better tolerated.

Dr. Rachel Dolhun: And don't wait. You're talking about these symptoms can really impact how medicine works, how we interact with other people, whether we go out to eat or just impact quality of life in general. So don't wait, talk to your doctor, see a specialist like you. There are even motility gut specialists that you can look for to help you with these problems.

Dr. Wael El-Nachef: Yeah, so I think patients will say, "When should I see a specialist?" And I always say, probably sooner than you thought because specifically with Parkinson's population, I feel that many patients may have psychologically accepted that

their life's just going to be hard and this is just part of the deal. And I think that's very unfortunate because there's a lot of things we can do for the GI symptoms and really we can oftentimes make patients feel pretty regular again. And so obviously if you're having red flag symptoms like bleeding, severe abdominal pain, if you're unable to eat food or drink water, those are all definitely need to see a specialist right away. But if you're having symptoms that aren't responding to over-the-counter therapies and you're still having symptoms, don't just accept that. Seek care from there.

Dr. Rachel Dolhun: It doesn't have to be that way, and there's a lot of things that we can do.

Okay, we're back. I hope that you enjoyed the video. Here to add more are today's panelists. So first we have Dr. Wael El-Nachef, who you saw in the video. As a reminder, Wael is a gastroenterologist or a GI doctor as well as a researcher, and he's the founder of the Parkinson's Disease Gastrointestinal Clinic in Pasadena, California. Wael, thanks for being here.

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

Dr. Rachel Dolhun: We're also joined by Claudia Revilla, who's a member of the Michael J. Fox Foundation Patient Council and is very active in patient education and advocacy. Claudia was diagnosed with Parkinson's when she was 45 and back in 2010. She and her husband have two grown sons and they live in Houston, Texas. So Claudia, thank you so much for joining us.

Claudia Revilla: Thank you for having me. Good morning everyone.

Dr. Rachel Dolhun: And last but not least, we have Brian Duggan, who is founder of Citizen Science for Health. Brian lives in San Francisco, he's a participant in MJF's Landmark Clinical Study, the Parkinson's Progression Markers Initiative or PPMI. Brian lives with something called REM sleep behavior disorder or RBD, which is where you act out your dreams while you sleep. He was diagnosed with RBD eight years ago in 2015, and interestingly, this condition is linked to Parkinson's, so in some people it's the first or earliest sign of the disease. So Brian brings a really interesting perspective of somebody who is living with a risk for Parkinson's but has not yet been diagnosed with the disease. So Brian, thank you as well for being here.

Brian Duggan: Thanks, Rachel. Glad to be here.

Dr. Rachel Dolhun: So I want to say out loud before we start that we are going to have a very open conversation about things that we don't often talk about, right, because we're shy or we're embarrassed, and so we're so grateful to have Claudia and Brian here who are going to openly share their experiences. If that makes you a little queasy, put your lunch aside if it's that time of day. But Wael and I too, we're doctors, there's nothing we haven't heard, especially Wael. So we're here to

have a detailed conversation about this and to get to those questions that you may not otherwise feel comfortable asking.

So with that, I'm going to start with Brian and Claudia. Claudia you, I'd like for you to just give us kind of a brief overview of the symptoms that you experience related to your gut, how those have changed, maybe briefly how you treat them, how they impact your life, that sort of thing.

Claudia Revilla: Yes. Well, thank you for the opportunity to speak and I did have gut symptoms and I did not know they were related to Parkinson's so I had no idea. At a very young age, probably in my twenties, I started noticing that I had episodes of constipation or diarrhea. I was a very fit person. I used to go walk, exercise, and sometimes during my mid-walk I had to go to a neighbor's door knocking at their door because of very unexpected symptoms of constipation or diarrhea. And later when I was diagnosed with Parkinson's, it was in my early forties, and the doctors of course could not believe you're a woman at a different age, at a very young age, how can it be Parkinson's? And when I started investigating, I found the Michael J. Fox Foundation and the clinical trials, and then one really got my attention, got related issues with Parkinson's.

So I founded it in Fox Trial Finder. So what I did, I immediately contacted the site and I told them that I would like to participate. And then I learned a lot about this gastric issues. As my Parkinson's has been advancing, my gastric issues have been advancing too, and I've been seeing several gastroenterologists and sometimes you go to the ER because the constipation, it's so bad that you really need help. So I would suggest to anyone going or feeling issues with your gut, to start going to see a doctor, especially if you have Parkinson's. But when we go to the doctor for constipation, that is so severe, you will have to go the rest of your life with a special regimen and find what's going to hurt you or what will be good for you. It's a change, it's an eyeopener.

Sometimes you have your tremors or bradykinesia. It's very ugly when you realize that you also have gut issues and you need to be in contact with your neurologist and with your gastroenterologist

Dr. Rachel Dolhun: And learning and figuring out, like you said, what adjustments work for you and don't work and that sort of thing. It's a lifelong kind of experience.

Claudia Revilla: And every patient is different. So what works for me may work for somebody else. It's a trial and error basically.

Dr. Rachel Dolhun: Yeah. Thank you for sharing. And we are going to delve in further on specifically these topics of constipation and diarrhea and all the things that you mentioned. But before we get to Wael to do that, Brian, I want to turn to your experience. So what have things been like with the gut for you as somebody who's living with a risk for Parkinson's and also getting older like we all are?

Brian Duggan: Yeah, I'm struck by, as Claudia shares her story, that how we're all different. There's a whole spectrum of issues related to the gut and that a word like constipation, it means different things for different people and shows up different ways. As you mentioned, I have REM sleep behavior disorder. I live with a high risk of developing the motor symptoms of Parkinson's. Even though I don't have a Parkinson's diagnosis today, I'm seen as someone with an early stage of Parkinson's because I have hyposmia. And so I've been on the journey over the last eight years to try to prevent neurodegeneration and to avoid developing more serious symptoms. And right away, a couple of years into it, gut symptoms came up first, but not classic constipation. Not constipation of no bowel movements, but a sense of inability to fully evacuate my bowels or what I came to learn was called dyssynergia, I think, which is feeling like my muscles or my colon wasn't really coordinating with my sphincters correctly and I could no longer relax and move. So I had to go on a journey to find ways to deal with those kinds of symptoms, which as you say, all of us have gut symptoms to some degree. I mean, speaking on a webinar, I'm a little nervous. Where do I feel it? I feel it in my gut, right? So we all have these symptoms to deal with.

Dr. Rachel Dolhun: And thank you. You and Claudia both mentioned first of all, the difference between all of us as individuals with or without Parkinson's. But then second of all, the broad array of symptoms that can happen in our gut. So we mentioned constipation, diarrhea, this big word you mentioned called dyssynergia or incoordination essentially. So Wael, I'm going to turn to you to really start to break those things down for us. What does constipation actually mean? What are all these other things that can happen in Parkinson's?

Dr. Wael El-Nachef: Yeah, so in Parkinson's, far and away the most common GI effect is constipation. And you can look in a textbook or look at different professional societies, see their definitions or attempt to define it, but it's really tricky, particularly in Parkinson's. And some of the other panelists mentioned or alluded to this, but I'm going to just give some scenarios. Let's say you have a patient and they have no urge to have a bowel movement and they really only have one bowel movement a week and they feel uncomfortable. That's pretty clearly constipation. But then I also see patients who have the urge to have a bowel movement, they go to the toilet, they cannot pass the stool or maybe a little bit comes out and they have this urge like five, six times a day. And so on paper they're having six bowel movements a day, but they're also constipated.

Or then you have patients who are passing liquid stools periodically, and the reality is that they have an impacted or partially blocking stool in their rectum, so backed up that only the liquid stool can get through. And so even though they might tell you they're having diarrhea, they're actually also constipated. And so it's not very easy to fit people into one box of a definition and you really have to take the whole clinical story and try to make sense of it and also take into account that they have. And so there's even other presentations I've seen. I don't want to go on and on about this, but to answer your question, it's very difficult to give one definition of constipation.

Dr. Rachel Dolhun: It's a change from prior though. I think sometimes we talk or doctors will say like, "Oh, it's less than three bowel movements a week" or something like that. But maybe that's normal for you is to have three bowel movements a week, but if suddenly you go from three to one every other week or something, then something's wrong so it's a big change from prior. But then also the importance of what you were talking about where someone might think even like they're having diarrhea, but really it's constipation so it really speaks to the importance of having a conversation with your doctor, but also really being descriptive and open about what you're experiencing.

Dr. Wael El-Nachef: Just to jump in real quick, this is one of the biggest issues. I always start off my clinic visits saying, you need to just speak explicitly. This is not the time to worry about my delicate sensibilities. I'm a GI doctor and just tell me exactly what you're experiencing. No euphemisms, just plain English.

Dr. Rachel Dolhun: So tell us a little bit more. I want to get back to constipation, lots of questions about how to treat constipation. But before we get to that, tell us a little bit more about what Brian was mentioning, which a lot of people probably aren't familiar with or haven't heard of before, which is this dyssynergia or dyssynergic defecation, these big words that, like I said, we've probably never heard of, don't know what they mean, but can really be a problem for a lot of people.

Dr. Wael El-Nachef: Yeah, absolutely. This is very common by the way in Parkinson's. And I think we might have a slide. I just want to warn you. There's going to be some images in here if you're eating just et cetera, be prepared. But this is a look at some of the anatomy and it helps describe what's going on. And essentially what you're seeing here is a side view of the body. And you can see on the top, I don't know if you can see my mouse, but there's the spinal cord, the spinal column, and then the sort of pink organ is the rectum. And then you see a sling of muscle. This is the puborectal muscle. It actually keeps the rectum sort of kinked, and that's to have continents. And this is when you're not trying to have a bowel movement, this is how things look. And then below that you have your anal sphincters. There's the external and internal ones.

So essentially this muscle called the puborectal, which keeps the rectum sort of kinked. When you're trying to have a bowel movement, it needs to relax and straighten out the tube of the rectum in order to have a bowel movement. You also have to push, give some force to move the stool out of the rectum, and also your sphincters have to relax both the internal one and the external one. And this is a very coordinated, somewhat complicated action. And so you can imagine there's a lot of ways where this could fall apart. If one of these things don't happen and at the right time in the right sequence, then you're going to have difficulty passing a stool. And so you can imagine in Parkinson's where there's issues with the nerves in the actual intestinal tract and issues of the nerves going from the brain to the intestinal tract, that there's a lot of ways this can go wrong in Parkinson's particularly.

And so if a lot of patients who have this problem do have the urge to go have a bowel movement, they sit down and they often describe it as pushing against the closed door, for example. They have that sensation or that they have to really push hard to get things through. Sometimes they have to use their fingers to help things along, et cetera. I also noticed that patients with this problem respond particularly well to things like suppositories, even ones without medication in them, just the glycerin suppository because it helps initiate the reflex and it helps stimulate the right movements.

So we diagnose this through something called manometry where a little catheter, probably the thickness of my pinky is inserted into the rectum and there's a balloon on the end of it that gets inflated and they can take measurements of the different muscles involved in this and help make the diagnosis. And we can talk more about that in a moment but that's just a quick crash course about dyssynergic defecation.

Dr. Rachel Dolhun: Just a quick point on this, so some people who have constipation might have this dyssynergic defecation as part of the problem, not everyone, but so how do you know what is causing your constipation if you have constipation and Parkinson's?

Dr. Wael El-Nachef: So, I would say the reality is, so the average Parkinson's patient who has constipation might have an element of dyssynergic defecation, but also will also have slow movements of the colon. So it's a one two punch. So that's when they've done studies on this about more than half of patients with constipation have both. And so I think the pandemic was very instructive to me as a clinician because we could be very aggressive about testing and doing all these sorts of workups and it'd be very interesting. But because of the pandemic, I found myself trying to limit testing. I didn't want to bring patients in unless they had to come in, remember those days. And I found that if actually we just treated what... We did something called empiric treatment, meaning trying a treatment and seeing what happens. I found that oftentimes the majority of the time I'm able to get patients regular with their bowel movements without having to undergo a lot of treatments. And usually I don't do the manometry unless the treatments I've tried don't work because oftentimes if you're able to speed up the colon for example, you can more or less get pushed through the dyssynergia.

If the patients still have problems, then we do the manometry because then there's different treatments and it's almost more like a physical therapy sort of treatment.

Dr. Rachel Dolhun: So I want to bring Brian and Claudia back into the conversation, but before we do that, lots and lots of questions even beforehand on how do you treat constipation. So many people experience it and want to know what's kind of the order of how we look at these things. Talk to us about over the counter things.

Are those safe to take every day? And then kind of, like I said, the order of how you go through and actually treat constipation.

Dr. Wael El-Nachef: So I usually don't bother with things like stool softeners like Colace or docusate because I think especially by the time a patient sees me, they're beyond Colace being helpful. And usually I don't use it even in my non Parkinson's patients. I would say that a real go-to a place where every patient starts, and even patients on the stronger medications, they still also take MiraLax, that's the brand name, also known as polyethylene glycol or PEG. But MiraLax is way easier to say because this medication is very safe and you can't really overdose on it. You might get diarrhea.

Dr. Rachel Dolhun: It's okay to take it every day.

Dr. Wael El-Nachef: You can take it every day. It doesn't get absorbed into your bloodstream. It stays in the gut. So for me, a lot of benefits, a lot of pros to that medication. And it's gentle. It's not a stimulant and the patient can adjust it on their own. And so I think that's also huge because it gives them a lot of control and a lot of say, but essentially it's a white powder, has no taste, has no scent, and you can mix it with essentially any liquid like water, juice, even coffee. So it's very easy to take too. And it works like little sponges that draw in water into your colon and helps soften the stool and makes it easier to pass. So that's where I start with everybody.

I don't want to go on too long. I'll be a little more abbreviated with the other ones, but the next step usually for my patients, if that's not sufficient, which oftentimes if they're seeing me it's not going to be, is I recommend they continue taking the MiraLax and they can take it even twice a day every day.

And then I add on some sort of a stimulant laxative, something like Senna, which is available over the counter derived from natural products. A lot of people like that aspect of it and it's safe and it's something I usually recommend you take at bedtime and it should help produce a bowel movement in the morning. And this works differently than MiraLax. It works by increasing contractions throughout the GI tract, specifically the colon. And so what I see is that if you do both the MiraLax and the Sena, they're synergistic. It's like a one two punch. And so that would be the over-the-counter approach to treating constipation, especially more milder forms that I think anybody with Parkinson's who's having issues can start with.

Dr. Rachel Dolhun: And we mentioned we can take MiraLax every day. What about the Senna or the stimulant laxatives? Can you take those every day? Is there risk of getting dependent on those or needing them then to have a bowel movement?

Dr. Wael El-Nachef: So in the old days, there was concerns about that, but as they've done studies on these sorts of laxatives, it hasn't really borne out, and so my feeling, my recommendations that it is safe and that it's okay to take them. My only thing

though is that they're not the most ideal medications to take daily because sometimes they can cause cramping or stomach discomfort. So if you find yourself needing to take it every day, then probably you need to try something else, something stronger that's going to be better tolerated. The recommendation is that you can find something that's better tolerated, not that it's not safe, but I think, just for your quality of life.

Dr. Rachel Dolhun: Well, and also if you're getting to the point where you need MiraLax and Senna every day, make sure you're talking to your doctor at the same time so that we're making sure we know what's happening. And like you said, if there are better, more effective treatments we can add on or switch to.

And so Brian, you raised your hand a long time ago, so I apologize it's taking so long to get to you, but tell us your take on this and what's worked not worked for you.

Brian Duggan: What Wael was showing in terms of the anatomy, totally matched my experience of what is this thing called dyssynergia, and it was like a switch one day and then I had to go out to find the new normal, which for me did take physical therapy and some biofeedback work to get to something that was a new kind of balance. So I appreciate you alluding to those.

Another quick question about treating constipation. What about magnesium supplements? That's something that I found was useful, but is that generally regarded as a good thing overall or it just happens to have some benefits?

Dr. Wael El-Nachef: So I would say I see that a lot. I think it's very familiar laxative for a lot of people. Things like milk of magnesia, et cetera. I think that it's safe to use occasionally, but my concern is especially in older patients or if you have kidney problems that the magnesium can build up in your system and that can be a problem. So if you're finding yourself using it every day, I wouldn't recommend it. I would say if you're using it once a week or even less, that's totally fine. But if you're looking for a regular regimen, like a daily regimen even, it's not something I would... I would not recommend that.

Dr. Rachel Dolhun: And again, just speaks to the importance that even things that are available over the counter, it's important to be talking to your doctor, to your pharmacist about what's okay, what's not okay, what might interact with your other medications. Claudia, please.

Claudia Revilla: Yes, exactly. I was just about to say that the moment you realize that you're having trouble, it's uncomfortable. It's not a nice talk to your doctor or to anyone, but it's a problem that it's going to grow probably if you leave it unattended. So if you can start with the MiraLax, if you notice that you have certain issues, start small. If you don't find relief, things are getting worse and you continue feeling bad, just talk to your doctor. Don't leave it. Common sense tells you that something's going on down there and rather than going to the ER

one day because you are impacted, it's easier if you start going to see your gastroenterologist.

Dr. Rachel Dolhun: And you can start with your Parkinson's doctor. Sometimes Parkinson's doctors can manage well enough if it gets to a point, they can refer you to a gastroenterologist, a specialist. And then even from there, if you need somebody who's even more specialized like Wael, you can look for a gastroenterologist who's also what we call a motility specialist. So you can look for that. Your doctor can give you a referral, you can look at major medical centers. You can also look online for these doctors, like many, they're in short supply, but they are out there. So important as you said, Claudia, to make sure that you're advocating for yourself, you're bringing this up.

Lots of questions, and Claudia, I'm going to start with you and then Wael ask you to fill in. But lots of questions about do gut symptoms get worse when my other Parkinson's symptoms get worse? So if I feel slow or I feel tremor, does it make sense that my gut symptoms or my constipation will get worse as well? Do you experience that?

Claudia Revilla: Yes, definitely. But I feel that whenever I have constipation or gut issues, my Parkinson's gets worse. It doesn't matter. My medication doesn't get absorbed. My carbidopa levodopa doesn't work as well. Sometimes I have to take an extra dose and that's when I say, "I think that something's going on" and I think I pay attention. So listen to your body. It's telling you something. When your Parkinson's medications are not working or are slow at work, check what you're having. You can either have UTI or you can have a constipation issues, you can be getting the flu or something. Or sometimes when you have constipation, that also affects the absorption of the carbidopa of your medications because there's a backlog there and you need help. If you don't get help, it's just going to get worse and worse and worse and trust me, you don't want to wait until the end.

In the beginning I was completely reluctant. I said, "No, the doctors are wrong. I don't have constipation. I have Parkinson's, but I don't have constipation." But trying a trial and error medication, MiraLax timing prove me wrong, and I am supposed to be a well-educated and well aware patient. This is not anything nice, not something that you'd like to admit, but as our Parkinson's advances or sometimes as the first symptoms of Parkinson's show up, they come with gut issues. It's just a matter of timing.

Dr. Rachel Dolhun: And Wael, Claudia did such a nice job of summarizing why Parkinson's symptoms and gut symptoms go hand in hand, but give us a little bit more of a level of finer detail on that. What's happening and why when the gut isn't working right, why is that impacting our Parkinson's?

Dr. Wael El-Nachef: So I think this could be from multiple... There could be multiple explanations for that. One of them that I see a lot is that when the gut slows down, it's going to affect your absorption of your medications for Parkinson's. I've noticed that

when my patients are treated successfully for a slow moving GI tract, their Parkinson's meds seem to work better, longer on times, less dyskinesia, et cetera. And so sometimes I even have to warn the patients that they might not need to take their meds as frequently once they get their motility of their GI tract back to normal. That's happened a few times for sure.

There's also though some studies that suggest that perhaps if this is somehow related to the microbiome, et cetera and there have been attempts at testing that with fecal microbial transplant. And we're still very early in this research. Some very early studies have suggested that maybe the motor symptoms improve with fecal microbial transplant. More recently there was a controlled trial, it's still a small one, which showed the constipation of Parkinson's improved but not the motor symptoms. And so I think we're still at an interesting and exciting era to look into those sorts of connections, but it's a possibility.

Dr. Rachel Dolhun: Lots of questions about fecal transplant. So you're saying that it's under investigation, but early days still whether that could help constipation as well as potentially Parkinson's, other symptoms?

Yeah. Lots and lots of questions on specific treatments. So two of very much interest, one is Metamucil and the other one is pre and probiotics. So Wael, tell us about those.

Dr. Wael El-Nachef: So I would say Metamucil in general, just saying in the general patient population, it's great. It's a naturally occurring fiber. Fiber has so many other health benefits and it can be used for constipation and also be used for diarrhea actually. It works by sort of jelling up the stool into a soft consistency regardless of what you're starting from. And so for us, that's like a silver bullet as a physician. It'll fix either problem.

The issue with Metamucil though is that in some patients it can cause a lot of bloating and this is particularly true if you're starting this medication in the setting of pretty severe constipation. And so in the case of Parkinson's, the patients I see usually they're quite constipated. And so throwing Metamucil into that mix can oftentimes be really unfavorable, let's just say and the patients are extremely uncomfortable with bloating. Even though it might help with bowel movements, it might not, I usually don't start off with Metamucil or any fiber supplement for that matter. And I try to get things moving if the patient is interested in either adding in, supplementing in more fiber or trying to replace some of their MiraLax with Metamucil instead after they've gotten some good control, that's something we try.

And I often will work with a dietician or nutritionist to really drive that conversation because that's usually their wheelhouse in terms of, because it's not just about the Metamucil, it's also about the fiber in your diet too. You want to try to get fiber from your dietary sources.

Now regarding probiotics and prebiotics, so I get this question a lot too, and there's a lot of data out there and it is quite confusing. It's not a clear cut case as to whether all Parkinson's patients should be on prebiotics, probiotics, et cetera.

And for me, I don't have a strong recommendation about it. I don't think it's going to be harmful, but I'm not convinced it's going to necessarily fix any problems that you might be having. And I often see that these supplements can be expensive and it complicates pill regimens. You already have enough medications in your life, why are you making this more complicated? And usually I just recommend trying to get these prebiotics in your diet. I think I might've mentioned it in the video, but essentially there's foods that we can eat that promote the good bacteria in your gut. And these foods are usually quite healthy anyway, so it's good to eat those. So I usually don't recommend pre or probiotics, but I'll recommend dietary changes.

Dr. Rachel Dolhun: And just to be clear on that, so probiotics are like the good bacteria we want in our gut. Prebiotics feed that good bacteria.

Dr. Wael El-Nachef: Exactly.

Dr. Rachel Dolhun: And we can get both through our food as well. And I think it's kind of unclear, as you said, it's a little bit conflicting whether those are very helpful in Parkinson's. It's also not clear yet which specific bacteria, how much of that bacteria. And so when you look at pro and prebiotics, there's different strains of things. So where we can trying to get that from our food.

Lots of questions, and Claudia and Brian-

Oh, Brian, you've got your hand up.

Brian Duggan: I was just going to just jump in as somebody who's experimented with different probiotics, prebiotics. I haven't been able to find some magic bullet there. I mean, like you said earlier, it's very early days on all of this stuff relating to the microbiome. Obviously it plays a role, all these microorganisms, but how to get them to be better. They're testing out there where you can get your microbiome tested. I've done some of that, but it's a lot of noise and not a lot of signal. Maybe I'm working with a naturopath now at UCSF. Maybe we're finding some ways forward to learn more, but it's still very early days. So I tend to have gone back to food, eating some fermented foods or eating some starch foods and that seems to be a clearer way forward, but it's all experimental at this point I think.

Dr. Rachel Dolhun: Go ahead Claudia.

Claudia Revilla: It goes back to common sense. We all know what foods makes us bloated. We all know what foods makes us constipated or they are very dry. We need to drink a lot of fluids and sometimes even having a regular bowel movement and

everything's building up, building up and starts putting up pressure in there. There was a time that I strongly believe I had appendicitis. I show up to the ER and the doctor said, "Yes, you have appendicitis. You are so sore. Well, just to make sure we're going to go and try a CT scan. Are you constipated?"

"No doctor, I'm been good, and I have a bowel movement every day." So when they run a scan, they come back and they said, "No, you are backed up. You really need to improve your gut health. You need to take MiraLax every day. And of course reduce the foods that we all know that cause a lot of gas or that make you back up." Common sense and communication with your doctor help a lot.

Dr. Rachel Dolhun: Yeah. And you mentioned too, gas. That's a problem for a lot of people and we're getting a lot of questions about that. So Wael, tell us a little bit more what makes that happen? How can we manage that?

Dr. Wael El-Nachef: Yeah, so that's a common complaint and also this sort of segues with what Claudia is saying. And so basically you see three images showing a person without Parkinson's on the left and they have a normal-sized colon and they're not constipated and they feel well. And then the middle image is a patient with Parkinson's who is constipated but is not complaining of symptoms, and you can tell that the amount of stool in the colon is much more than on the left.

And on the right is someone with Parkinson's who is symptomatic. They're saying, "I feel bloated, I feel constipated," and they're extremely constipated. So part of the study was looking at is essentially that there's an issue with the sensation of what's going on in the GI tract that it takes quite a bit for someone with Parkinson's to feel like something's off.

And so by the time a patient comes to me saying, "I feel constipated," they're probably very, very constipated. And so kind of what Claudia was explaining, this is very common, I see that all the time. The segues to the bloating issue and oftentimes I always say bloating, the three top causes of bloating in Parkinson's is constipation, constipation, constipation. And so the patient might not experience a sense of being constipated, but that's the first sign that they feel. And so usually my first approach is to just treat them for constipation and see if the bloating goes away, and the vast majority of the time it does. And so if the patient is reluctant to accept that they might be constipated, I'll often even get an X-ray just to say like, "Hey look, you really are constipated." And this helps the patient maybe piece together the other subtle symptoms that they're having that might not fit with the traditional conception of what constipation is.

Another mimicker of bloating per se is gastroparesis. When the stomach is emptying slowly, it's not moving well and food just sticks there and patients will often describe that as bloating, but it's a totally different problem and we treat that differently.

And then lastly, and this is one the patients are often asking about, but it's less commonly something that I'm pinning it to is something called SIBO or small intestinal bacterial overgrowth. And that is often because the small intestine normally has some bacteria in it, but because it's not moving quickly, it's not cleaning out the bacteria periodically as well, those bacteria are allowed to multiply a lot and therefore it's not an infection per se, it's just too many of them. And so that can cause bloating as well. And if that happens, there's tests to look for that and we can treat that but usually it's constipation.

Dr. Rachel Dolhun: So Wael, some people are asking what does bloating actually mean, and is bloating the same as excessive gas or flatulence?

Dr. Wael El-Nachef: So bloating usually is gas within the GI tract and that can lead to excessive flatulence and belching and stuff like that so they go hand in hand.

Dr. Rachel Dolhun: And lots of questions on nausea. So nausea can be related to Parkinson's, to Parkinson's medication. Just tell us more about nausea and Parkinson's, what it can be from and how we can manage it.

Dr. Wael El-Nachef: So nausea that I often interact with is related to, again, constipation or gastroparesis and usually treating those underlying issues resolves the nausea. There's always the concern. You can get nausea as a side effect from the Parkinson's meds and that is tricky. There's some medications we can try to treat with to counteract that. Some of them like Zofran or Ondansetron, those can be helpful. There's also domperidone that medication I don't use very often because it has black box warnings, but historically has been used for nausea in these situations, but I try to avoid that.

Dr. Rachel Dolhun: Brian, you had your hand up.

Brian Duggan: I just wanted to say hearing why I'll go through this, how important it is to seek out a specialist for help in these areas and to not be shy about it. I mean it's just on my journey and the gastroenterologist that I got connected with was actually as part of a clinical trial. So some of it's through just going through your Parkinson's doctor and getting to a specialist. Some of it can be through research and through the many research options offered by the Michael J. Fox Foundation and others. But getting connected to specialists because it's such a specialty area with so many varieties to it. That's what I'm just struck by as you give all the details on this. And so I want to encourage people to, even though it's a sensitive area, reach out to a specialist.

Claudia Revilla: Dr. Yes.

Rachel Dolhun: Well that's what I was going to ask as. Wael, with so many things and you're saying, "Well, bloating could really be your stomach not emptying fast enough and constipation can cause bloating." How do you work with somebody to figure out what's causing what and how to treat it?

Dr. Wael El-Nachef: So it depends on the patient. You have to hear the story and really understand what they're experiencing. And oftentimes these, I'll try medications and it's not just for a treatment, but it gives me a lot of information too to see how they respond. And that can often give me a better idea of what's going on.

If there's still lack of clarity, there's a lot of testing available that we can do for gastroparesis, there's gastric emptying studies, et cetera. But I don't necessarily just jump to that right away. I think we can spare our patients a lot of this going through the ringer, just make them feel better sooner.

Dr. Rachel Dolhun: Claudia, you were going to add something.

Claudia Revilla: Thank you. Yes. I think it's accepting that we have a problem and acknowledging going through the doctor. It's a humbling experience. It's embarrassing due to the nature of it, but it's better to end up asking for help. I did not believe I had such big of an issue until I thought that I had appendicitis and the doctor show up and said, "No, look it's just poop."

And it's like, "Oh my gosh, I'm never coming to the ER again." Just go to see the doctor. A little thing can turn into a big thing in no time if you let it go.

Dr. Rachel Dolhun: It can feel embarrassing, but this happens for everybody. We all poop, we all have... So it doesn't help anybody to be embarrassed about it or shy. And it's Wael, what you've been talking about too is being open and that's how you help your doctor figure out with you what's happening is not just saying, "Oh, I'm backed up" or "I'm a little bit whatever." It's like being graphic and very descriptive and open about what you're experiencing.

Dr. Wael El-Nachef: And then I also want to say, even if you're not having symptoms, if you're due for a screening colonoscopy, this is my little soapbox here, make sure you're up-to-date with your colon cancer screening. Just because you have Parkinson's doesn't mean you're immune from everything else. So if you're due for screening, get it done.

Dr. Rachel Dolhun: Yeah, an important reminder that we can, just because we have Parkinson's doesn't mean we can't have other things happening and that we shouldn't get our regular screening for other things. Wael, lots of questions about enemas. So tell us what those are and if they're okay to use on a regular basis.

Dr. Wael El-Nachef: So enema is essentially inserting fluid into the rectum and it helps, first of all, it kind of works like a suppository in the sense that it helps initiate the reflex but also helps wash things down, wash things out. I think they're fine and sometimes in certain situations I recommend them, but I don't think they're very convenient. So this is a once in a while sort of intervention. If you find yourself using enemas frequently, then probably you should talk to your doctor to find a better regimen. But they're safe, especially if you're using water, you

can just use straight water in your enema. And so it's useful but not the most convenient option.

Dr. Rachel Dolhun: And one last question for you is maybe you can tell us some tips for if we have more milder conversation, and I'm even thinking about things like what fiber or foods or Squatty Potty we hear about. Are those things helpful in addition to all the other treatment options we talked about? And then also talk to us about when constipation gets really severe and significant, if you have tips for people who are in that part of their journey.

Dr. Wael El-Nachef: So for the milder side, like the Squatty Potty, I've heard a lot of patients say that helps them. I think it's probably best in the patients who have some element of dyssynergic defecation that we just discussed because it helps align your anatomy better and also that's how we are naturally built to use the bathroom. In terms of on the more severe side of things, there are medications that our prescription and much stronger, but there's different types though and they have different mechanisms.

So you might've heard of things like Linzess or Linaclotide. And so the truth is I'm not a huge of using this in Parkinson's. This works by making your intestines secrete a lot of fluid. And I've noticed this is just anecdotal, but I've noticed that Parkinson's patients who take this either have zero response or have extreme diarrhea and it's the type of problem where they can't leave the house. And so it's hard to find patients who just Goldilocks response to it. And I'm not sure why this is the case in Parkinson's. In other patients it's great.

There's also a medication called Motegrity is the brand name or prucalopride. This medication works by increasing contractions throughout the GI tract. And I've noticed this is very effective for patients with Parkinson's who have constipation or slow stomach movements and it's not responding to other medications. And so this is something I use quite a lot.

Dr. Rachel Dolhun: Thank you so much. I can't believe we're already at one o'clock. We have to finish the discussion. I wish we could probably talk for three or four more hours. So thank you Wael for all of the information. Thank you Brian and Claudia for being so open with your experiences, and I'm sure there were many who identified with what you are going through, have gone through and it's been so helpful to hear all of your perspectives.

Before we end, two quick things. One is just a mention of PPMI, the study that Brian is participating in. This is the Michael J. Fox Foundation's landmark clinical study that's looking at following people over time to see if and how Parkinson's comes on. No treatment that's tested, but really just sharing your data and your experiences to help researchers understand how Parkinson's progresses from its very earliest stages. So you can learn more about that and join if you're interested through the resources in our resource list.

For more on this specific topic on gut and Parkinson's, including the video we watched as well as a blog by Dr. Wael, you can visit michaeljfox.org/guthealth. And if you want to learn more about diet, as I mentioned, more resources at michaeljfox.org/diet.

So thank you again so much to our panelists and to you for being with us today.

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