

**The Victory Summit® event: Newly Diagnosed
Living Long and Living Well with Parkinson's**
Recorded on Feb 20, 2021
Davis Phinney Foundation

Melani Dizon (Director of Education and Research, Davis Phinney Foundation):
First, I want to let you know that Dr. K is a movement disorder specialist at the Meinders Center for Movement Disorders in Oklahoma City. He received his fellowship and residency from the University of Texas Southwestern Medical Center. And he's American board certified in both psychiatry and neurology. So, let's get started. My question for you is, you know, who are you? How did you get into this work, in particular working with people with Parkinson's? And then what is your clinic like in Oklahoma?

Dr. Cherian Karunapuzha, MD, (Neurologist and Movement Disorders Specialist, Meinders Center for Movement Disorders):
Well, first off, I grew up all over the world. I mean, I grew up in the middle East, Dubai, Abu Dhabi, worked in India, studied in India as well, and then moved to America probably, gosh, it's been almost 20 years now. I've been practicing almost 20 years as well. Well, actually 21 now. Sorry, time flies. The reason I got into this line of work was there's always been a need. I've seen that over the years. I mean, I've seen some of my close relatives have very severe neurological disorders. Some of them with extremely severe debilitating diseases like polio. I remember most of my family members are still in India and we just eradicated polio you know just a couple of years ago. It's very hard just like how you guys are seeing with COVID. It's very hard to hit 80 to 90% of a population, which is a billion plus and eradicate a disease.

So, a lot of friends still would get the bad neurological effects of polio, which would be similar to a movement disorder, very, very bad form of a movement disorder in some cases and all of this sort of, you know, it just started working, you know, slowly, slowly in my mind, way back as to why couldn't we find better solutions for these folks, even as a kid. I remember my distant uncle who had one of these disorders was called scary grandpa by the grandkids because he looked pretty scary with all these movements, kind of like sometimes that we see with big, bad flailing dyskinesia in Parkinson's. And so, while he probably thought it was endearing because at least it's some sort of interaction with children that he gets, he could barely speak. But I kind of felt like why did he have to live with that?

What was there no medicine we can help with this? And strangely enough, now we have tons medicine options for that same individual, which I had seen like 30, 40 years ago. And so, these are the things which got me rolling in terms of joining medicine as practice as an occupation. So, I started med school when I was 17 and finished up and started teaching at the local medical school. And before you know it, I'm here in America. So, the one major constraint, which most moving disorder docs, I know some

of the other folks in this panel here as well, will echo the same thing is the fact that we don't have enough support because it's not a one man show, no matter how great you could be with manipulating medicines for this person. That's not it. As you guys just chimed in a little while ago, exercise, meditation, the way you think conceptually of yourself, and your family.

It's a very holistic approach, which we need to have for neurological disorders, especially a disorder like Parkinson's, which hits so many different circuits. And so, the one major thing which we strived for in Oklahoma was to build a center of excellence and many times a center of excellent for movement disorders and Parkinson's entails a whole bunch of people coming together under one roof, which made it structurally impossible, even for larger university setups because you have your physical therapist and your occupational therapist, and your speech therapist is sitting one block away in the allied health sciences building. You have your psychiatrist in another wing of the medical school. They're just so disjointed. We don't have a cohesive team. And so that's what we've tried hard, and with a lot of donor support, we were able to build the Meinders center, which is an integrated form of practice, where we have onsite physical therapist, speech, therapist, neurosurgeon, we have the whole team.

And when patients come in to see us, this is not just one-time eval, this is like every single time they show up, they're seen by the whole battery of people, not just my input that matters. I need to know what the speech therapist thinks of this person's speech or swallowing issues. You want to catch these things early and nip it in the butt, because a lot of times, what a lot of you guys who have been through this for a few years know, is that once you let a few things slide, then it's hard to recover back from that unless you've tried real hard. So, it's so much easier to nip it in the butt, kind of like an oil change, right? You don't wait for the car to break down and then do the oil change. You do it every year, preventative maintenance. That's the concept of our clinic.

Melani Dizon:

Great. So, Connie touched a little bit on this, but if you could let people know specifically, what is a movement disorder specialist? How are they different from a general neurologist? And then also, why is it so important to, even if you live far from one, and even if it's a bit of a challenge, why is it so important to make sure that they are part of your team, even if you only see them once a year, every couple of years?

Cherian Karunapuzha:

So, a movement disorder specialist is a general neurologist who is sub-specialized in one field of neurology, which is movement disorders, anything to do with funky movements, tremors, Parkinson's, funky postures, balance disorders. This subspecialty is handled by neurologist whose had extra years of training, usually one, two years of extra training. And this is all they do typically day in, day out. All they see is complicated movement disorder patients and they can see the earlier cases as well, but they have the extra know-how to deal with this particular disorder. So, a general neurologist deals with all elements related to the nervous system like your stroke, your migraine. So, he has information about all of it. So, when you compare your primary care physician to a

neurologist, yes, a neurologist is a specialist who could make a diagnosis of Parkinson's pretty easily, but then beyond him comes the movement disorder specialist, who knows more of the latest research, who knows some of the newer medications or maintenance when complications arise or the nuances of treatment in every Parkinson's patient.

So those are the kinds of things because that's all they do day in, day out. So, the more sub-specialized you can get with your physician, the more you're going to get out of that visit because they know much more about this disease than the general person, always in the same way you want to think about for all disorders, right? Your primary care doctor can manage your blood pressure and your heart problems, after a while they send you to the specialists, the cardiologists. After a while with the cardiologists, they go to the surgeon or the interventionists or the EAP specialist who puts in your pacemakers. So, everybody has a tear drop, because medicine is so vast, you can't learn everything. You can, but you can't keep practicing everything. You want to keep being good at it or on the cutting edge. So, the need for movement disorders comes to sort of have the overall game plan that in your disease course, okay, this is what we're going to plan for your disease.

This is more, we're looking at intensive milestones. This is very, we're thinking of probably starting X therapy or this or this is where you need this intervention. They make the overall plan, many times your local neurologist, if they're in good relationship with them, with the movement disorder docs, which usually is the case they follow through on that plan. Okay. We started you on carbo/levo, and we're going to gradually build that up. Your local neurologist is going to treat that and get it just right. We're going to start you on this medicine for your dyskinesia. And he's going to see in one, two weeks, what's going to play out in terms of side effects, any tweaking or adjustments. Okay. And it goes the other way too. The local neurologist might say, Hey, you know, I can't deal with this person's foot drawing in so excessively, it's very hard. What do we do about this? Ok bring him in, we can do some injections. So, these are the kinds of things, this back-and-forth relay between the two groups, it's like a tag team approach.

Melani Dizon:

Great. Yeah. One thing also that I remember somebody telling me was that one of the things that your movement disorder specialists would know that other people they might know about clinical trials, right? They might know about like the latest and greatest that's happening with Parkinson's. And for some people I know some people who did not have a movement disorder specialist near them, or they couldn't get in with them. They actually started on a clinical trial and they were getting much more time with the movement disorder specialist because the clinical trial was requiring that. So that's just something to look at, especially when you're new, a lot of the clinical trials require people to not have started medications yet or not to be having DBS yet or something like that. So definitely worth checking out. How do people get Parkinson's? How does it begin and even more so is there something, is there a clue of the way Parkinson's is manifesting in somebody that can offer a clue to how quickly or that it might progress or there are different types that you see?

Cherian Karunapuzha:

So, Parkinson's disease primarily is the damage of a circuit in your brain called the basal ganglia. And it deteriorates in a particular manner in which you showed very specific symptoms, which is slowness, stiffness and shaking, usually at rest starting in one body part, gradually making its way to other body parts over the years. And we're talking about a very long disease. If you dealt with this in your late fifties or sixties, we're talking 15, 20, 25, if you develop this in your thirties or forties, it's pretty much a lifelong disease. It's like you've got a chronic illness like diabetes, you just live with this all your life. These sorts of disorders, we know the end result, which is that the circuit is getting damaged. We know microscopically what this damage looks like as well. You look at these nerves, there are very specific protein accumulations within these nerves as well.

All of this is very classic. We can pick this up. What we don't know is what instigates this damage, because Parkinson's, doesn't develop in a day or two or in a month. It takes years, it gradually brews in your brain over years to slowly pick up and create the damage enough to manifest the symptoms. And so, we're talking five, 10 years out, or even 15 years out, you're probably starting to develop symptoms, which many times can be very subtle and many times non-physical. Why is it non-physical? Many times, to get to the Parkinson's circuit, there are so many other nerve bundles around it, under it, and so the theory is the disease can spread through all these different angles, towards the Parkinson's circuit. And so then, eventually the Parkinson's circuit gets damaged just right, and you start to show you symptoms. So, what could all those subtle symptoms be from other circuits being hit? Losing your sense of smell, constipation, starting to talk or acting out in your dreams, mood fluctuations, cause these are all the adjacent circuits around it.

So, you kind of have to hit them to get to this. So, in hindsight, a lot of y'all might start to think, you know what, I was talking in my dreams for the last five years. I was acting things out and mumbling saying stuff for like the last five years or, you know what? I started losing my sense of smell. I couldn't pick it up unless it was a really strong cologne or perfume. I couldn't really pick up the fragrances anymore. So, these are things in hindsight, which nowadays we are using to our benefit. Like you're using the lack of smell as a form of early identification many times. And we're trying to refine that. It's still not, what we call statistically speaking, highly sensitive or specific to use on a day-to-day basis. But that is one way of looking at, somebody had mentioned, I wish there was like a quick test where we could just quickly pick up, it is being refined.

But it's not to the level where we can use it on a day-to-day basis. There are other approaches too, for example, you know, a lot of us will get a sleep study for various reasons. I'm snoring. I'm waking up fatigued as part of your sleep study. Many times this talking in your sleep, this acting out your dreams. That's what we call REM behavior disorder, gets picked up early. And so, while there can be other disorders, which can create REM behavior disorder, Parkinson's and similar disorders is a big chunk of that. And so, when sleep doctors pick up on that, usually they'll give us a call and say, Hey, do you want to just take this person on board and see if you can find the earliest hint of

Parkinson's yes or no, if not, you want to just keep following him or put them in a trial for early disease or send him for genetics, things like that. So, we're getting better at catching the disease before your first physical symptoms start. Four or five, six years out. We're starting to get much, much better.

Melani Dizon:

So, if let's say somebody is tremor dominant. So, when they finally figure out that they have Parkinson's, tremor is like their really big issue, their big motor symptom. Is there any evidence or let's say, you know, you have A, B or C as your primary symptom, and then this is usually a more progressive track of Parkinson's, is there anything like that? Is there anything for people that are like, oh yeah, some, some of these types of Parkinson's actually progress faster.

Cherian Karunapuzha:

So just to back up a bit for folks who didn't understand what that meant, tremor predominant, remember the three things which I talked about slowness stiffness and many times a resting tremor, starting in one body part. So, sometimes some of these symptoms are more prominent than the rest. And so, if you have a patient who has predominantly a lot of shaking, their hands are trembling, both sides. Their chin is trembling, their leg tremors, it's very evident. Sometimes even when they're doing stuff, their hand is shaking. We call this pattern more of a tremor predominant Parkinson's disease, as opposed to the other kind, which is more of a slowness and stiffness. The akinetic rigid, akinesia is a technical word for saying no movement. Rigid means that stiffness, it is the technical term for the stiffness. So, there's akinetic rigid forms, osteo-instability forms, tremor predominant forms, so there's different kinds. So, within this subset, we've seen traditionally that the tremor predominant kind tend to have a much more stretched out longer profile. Their milestones are much more stretched out. While they have very obvious looking tremors, they don't seem to decline in other fronts as bad as some of the other forms of Parkinson's. Why exactly this happens, we're still not fully elucidated on the whole mechanism of why that happens, but this is something which we've seen both anecdotally in my practice and shared by other colleagues within the movement disorder spectrum.

Melani Dizon:

Okay. So, carbidopa/levodopa is the gold standard of a Parkinson's medication. So, can you talk a little bit about what it's actually doing in the body and then what's it doing for symptoms? Like what sort of symptoms does it help?

Cherian Karunapuzha:

If you break it down, many times when you see this drug prescribed, it'll say carbidopa slash levodopa, of which levodopa is the main stuff that we really want. Levodopa is a precursor, meaning it is one step before the actual chemicals we are very interested in, it becomes dopamine in your nerve cells. So, meaning levodopa is taken up by your nerve cells, your nerve cells convert it using enzymes to dopamine. And dopamine is a neurotransmitter meaning... nerves, the way they talk to each other is, you know, electricity passes down a nerve and it comes to a nerve ending and there are other

nerves sitting around it. This nerve, as the electricity hits the end, a neurotransmitter is released. A chemical is released and that goes and connects to other nerves, kick-starting the electrical flow again. So, this is how nerves cross talk and in this particular Parkinson's circuit, dopamine is lacking and preferentially the nerves making dopamine or shooting out dopamine are getting preferentially damaged.

Whereas the guy receiving dopamine is relatively healthy, which means if I can introduce dopamine from outside or dopamine like medications from the outside, I can kickstart these nerves back up again because they are relatively healthy. This guy is getting damaged, but I'm going to just give it more fuel for the fire. That's it. That is in a sense what levodopa is all about. So, think of it literally like gasoline for these nerves. So, all you're doing is refilling the gas tank from the outside with external gasoline, external dopamine, that's levodopa. And all you're trying to do is keeping your nerves switched on throughout your awake hours. Kind of like if topping off the gas tank before it gets to empty, because when your nerves are switched off, they show all these symptoms, which we just talked about, slowness, stiffness, tremors, you start to shuffle, you lose your facial expressions, your speech pattern changes. There is a multitude of physical combinations of slowness and stiffness in different body parts. All of this starts to disappear as these nerves switch back on again. And again, that's what we want to try to keep. Our goal is to try to keep you in that state as best as possible throughout the day. Why do I need carbidopa if levodopa is the magic medicine? Carbidopa is the chemical compound, which let's levodopa go straight up into your brain and limits its use in other body parts. Remember dopamine is used in multiple body parts, not just inside your brain, outside as well. And so, I don't want to waste any of that gasoline. I want to let it all go up into the brain where I want it to work. So, adding carbidopa, along with levodopa, let's most of that levodopa go into the brain. This way, I don't get all of the side effects which come from levodopa being used elsewhere. What happens if levodopa is being used elsewhere? You get nauseous. You can get constipated, your blood pressure can drop, you get light-headed. There's a multitude of side effects, which come about, because dopamine is being utilized or being created artificially elsewhere in your body. This is why we made this combination.

Melani Dizon:

Okay. I want to talk about ON and OFF in just a minute, but what are the downsides of taking carbidopa/levodopa? A lot of questions are from people who are newly diagnosed. What are the downsides, if any, to taking them?

Cherian Karunapuzha:

So, all we're trying to do is recreate the dopamine levels, which were previously there naturally in our brain. The problem with trying to give levodopa from the outside or dopamine from the outside is our nerves, you know, when they shoot out dopamine and the other fellow receives it, it goes and recycles back into this nerve. And again, it's shot out. So, it's a very smooth release. The way it's released is very fine tuned in a normal circuit. But when this nerve is damaged, and we're trying to get dopamine from the outside, it's more in waves that it goes. So, there's a surge of gasoline. There's the dopamine in form, and then you switch on and then it wears off. So initially these nerves

are relatively healthy to where they can pull back some of the dopamine it shot out and recycle it.

So, I don't have to dose the dopamine that often. Over the years, they get more clunky, they get more deteriorated. And so, the levodopa or the dopamine doesn't stay for very long. It doesn't recycle well. So basically, these nerves leak out the dopamine faster. So you notice that you're still getting the same kick like you used to, but it's getting shorter and shorter. It doesn't seem to last as long. And that happens because you to get progressively deteriorating those nerves. Now, if you gave a person levodopa excessively, this person has Parkinson's, and you gave this person levodopa way more than what this person's requirement was very aggressively, early in the disease. You can instigate these sort of fluctuations earlier and earlier into this person's disease. Naturally, this person will fluctuate. We'll start to yo-yo every four hours, every three hours, if you let this disease progress and he's taking a little widow, but naturally he is going to progress because those nerves are going to get more clunky, but that takes five, six, seven years, slowly builds up as you take levodopa.

So, as you progress through the disease, the more deteriorated your nerves get, you're naturally going to show this. You can pull that earlier into the picture by aggressively dosing, a whole lot of levodopa, and there are many cutoffs or numbers, which are coded by literature. Currently, you know, the magic number seems to be around 400 milligrams a day after which there is a higher risk of bringing on these fluctuations and dyskinesia earlier and earlier. So that is one theoretical possibility that that can happen. But the way I look at levodopa is, as long as it's judiciously used, it is fuel for your brain. It is what keeps you moving. And so, if I can achieve that movement, that smooth movement in you throughout the day, with whatever dosing that I need, pretty gradually inching up, whichever level I get to which achieves that, I get to keep you on that for a long stretch.

So, I don't feel afraid in using levodopa early at all. It was a very old concept where we want to save ourselves from levodopa. We don't want to use levodopa early because then you start to fluctuate. You start to have the dyskinesia like Michael J. Foxx if you've ever seen him on TV, but that's no longer true. We now know that the most common reason why you start to fluctuate or develop those excesses is disease progression. Your nerves are the reason why that same medicine, the same two tablets you were taking three years ago, now that's something completely different. That's you, your brain, not the pill. That's your nerves getting more clunky. That engine is getting more and more damaged. So, it responds to the gasoline very differently.

Melani Dizon:

Okay, great. So, let's dive in a little bit more on the, ON and OFF, and what's happening in people's brains, obviously, but it seems to be, like, it's so different for people, right? Like there'll be some people that are, Oh gosh, I've got to take it every, you know, couple of hours and people ask, do I double? Like, if I'm breaking it up, why don't I just take more throughout the day so that I don't have to deal with off times? But then that's not helping them either. And so, what is going on when somebody is OFF and ON, and

you can talk a little bit about all the different types of OFF, like a delayed ON and that kind of thing. And what are some things that people can do about it? And maybe talk a little bit about also drinking and eating and how it relates to taking this med.

Cherian Karunapuzha:

So, as you progress through your disease, let's say about five, six years into your disease, your nerves are starting to get clunky enough to where, as I said, it doesn't recycle your prior dose for longer stretches. So, when you first start off taking something like, levodopa, you take it, the nerves switch on, and then it keeps recycling and shooting it out, recycling and shooting it out, meaning it's buffering itself with the old batch of medicines, even though you're giving you a second in the afternoon, you're not really feeling a dip. You're pretty smooth because the previous dose is still kind of cycling. You're just stopping up the gas tank and keeps you smooth. But as the years go by, that recycling in your brain is getting more and more poor because those nerves are dying. They're not as effective in recycling. So, they leak out faster.

That's when you start to catch the initial dips, meaning the way you would notice that is you switch on with your medicine, whatever dose that works for you. And then let's say about five, five and a half hours, you start to gradually wear off with your symptoms. So, meaning, it's not all of a sudden, you're switching off your symptoms. You gradually return that little bit of tremor starts to come back in that left hand, or you start to feel slower in the way you plant your feet. It's a very gradual dip down, it's sliding down to zero, and you can usually catch it before you go to zero, because your next dose is from roughly about 20 to 30 minutes later. This is how many times catch your initial OFF. This ON and OFF fluctuation is a gentle, wearing off. This is the most common way in which people manifest.

And that's because the recycling is getting more and more poor. As the years go by, one more variable comes into play. So, we've understood the problem, which is happening within our brain, which creates this sort of fluctuation. As the years go by that interval gets shorter and shorter. So, we get that part. But one more issue is the fact that other circuits in your brain are also getting damaged, including your autonomic nervous system. These are special kind of nerves, which control the automatic stuff in your body. The stuff you take for granted, not the pain, touch, temperature, kind of guys, this stuff you don't think about, like your bowel movements, your bladder, your blood pressure, your sweating, your secretions, your drooling. I'm not thinking about pushing food down my throat always like, "keep it out," it's happening automatically in the background. This stuff starts to get damaged. And as I said earlier, many times way before your Parkinson's symptoms start, you start to get a bit of damage in your gut. That's why the slowness happens. And you start to get constipated. So about five, six, seven, eight, nine, 10 years into the disease. If you go further and further into the disease that constipation, that lack of motility in your gut goes all the way upstream to your stomach.

Why is that so crucial that her stomach doesn't move? Sure. It doesn't move. It's like sludge, whatever you eat, it's slowly moving its way down using gravity. So that

levodopa medicine is absorbed only in the first part of your intestine. This is extremely crucial to understand. Most people think the minute I put this medicine under my mouth it is getting the job done and the clock starts again. No. It has to go down your food pipe, into the first part of your small intestine before it gets absorbed. So that's why you start to feel a lag in the medicine kicking in. It's like this medicine takes 30, 40 minutes to kick in. I mean, I took it and this is why very specifically, what starts to happen is when you gut slows down, these pills get stuck in transit. They get stuck in the folds of your stomach and it takes you half hour, one hour to push through or many times what happens, it does go through to your intestines, but food comes along behind it and pushes it through too fast. So, you don't get a full absorption of the medicine. So, scenarios can play out that way. One, we talked about, a delayed ON, or no ON, like the medicine failed, a dose failure. These are scenarios where the tools take a long time, a delayed manner in which it starts to kick in, or it doesn't even kick in, like 60 minutes later, it still hasn't kicked in because it's somewhere stuck in your food pipe or in the folds of your stomach. So, this is one scenario. Another the scenario is what we talked about, too quick of a transit, where it's not getting a full absorption. What happens there? Half the medicine, I'm just making this up, half the minute kicks in, a partial ON. So usually when I take two tablets I turn ON, I know my arms move up and down, my tremor gets better completely. And I walk faster this time round. When I took my dose, my tremor got better, I'm kind of half loose, but I'm still kind of shuffling. Partial ON. It's the same two tablets I've been taking for the last 10 years. What happened? Why did this third dose of the day decide to do this? So, your gut is no longer your friend and it becomes this second bottleneck other than the deteriorating nerves in your body. So, these two variables create a more of an aggressive, OFF and ON. Unpredictability starts to seep into your fluctuations. Previously it was very predictable. I got used to this. For about six years into this, I started to feel like, yeah, I start to differ on five hours, and I start to differ on four hours. I plan my day. I know how to take my pills. I'm good. But now randomly, my third dose fails.

My first dose of the day takes one hour to kick in. I can't predict when and how these pills are going to kick in effectively. So that's your stomach. This is why we have certain simple tricks that we use. Don't always work, but always good. Number one make sure you have a bowel movement every day. Why? Because it's like railway carriers. These pills have to get to that spot every couple of hours, every four hours, it has to get there for absorption. If you're backed up for three, four days of not pooping, you're going to have good days in a week and bad days in a week in terms of medicine response, simply based on whether you pooped or not. If you have not noticed this, look at this for the next two weeks and you will see how this matches your site. And so, you have cleared the bottom end. But what about the top end?

Remember, I said, it takes time to get to the first part of your intestine. How can you accelerate that process? Make sure you take the medicine on an empty stomach so that there's no blockage with a tall glass of water to flush it through kind of like a toilet. You're going to flush it through way past the stomach to the first part of your intestines, you can get there fast, it dissolves the medicine quickly and gives it enough time to absorb the pill before food comes along. Why do I keep harping about food? Because

the protein in your food messes up the absorption of the medicine. This is why we like to say right, spare at least one hour before a meal or two hours after a meal when you decide to take your medicine, that's the ideal recommendation. If you can spare 30 minutes to an hour, that would be great, but make sure tall glass of water, you're chugging it down, so that it gets there quick enough. And it stays there long enough for full absorption before food comes along with it. And you're pooping every day, so that everything transits like railway carriages, smoothly. These two things, it sounds extremely silly, but you do this for two weeks. You will see a dramatic difference in the way your Parkinson's feels even without adjusting your meds.

Melani Dizon:

Yeah, I think that's great. I remember that from the time that we talked earlier, and we've had several people, we were kind of sharing that piece of the interview about drinking water and people have said it's game changing for them. And I think the really interesting thing about the water is, you know, to visualize it, you can visualize drinking that water and having it go through and the pill, moving, otherwise, how's it gonna move? You need to get it to move. Right? The other thing that you talked about is constipation. Well, water can help with that. That's one of the things that water can actually help with, but what are some other things people can do? Because constipation is such a big problem.

Cherian Karunapuzha:

So, you want to divide it out into a couple of ways in which you want to tackle constipation. You know you've got a slope, right? We just talked about it. It's like sludge in there. You're using literally gravity to get it to go down. So, you want to add liquids, meaning water so that the consistency is looser. You want to add things in your diet, which actually holds water in gut, lets it stay in the gut. This is what we call fiber, roughage, right? So, you're green, leafy vegetables, your dried fruits, like your prunes, figs, raisins, raisin water. Any of these things, the cocktail you can come up with where water stays in your gut, so that it lubes the gut. Basically, you're lubing the gut. So, this is two ways in which you can use what you intake to make a difference.

Number two, as I said, it's gravity. What can help a whole bag of intestines in your stomach, contractions from the outside, meaning you exercising, you getting up and doing some cores, some small workouts. You'll be, it is very dramatic. You will see this. If you exercise every day enough of your truncal muscles, your stomach muscles, you do little bit of a crunches, small things like this. It makes a big difference. Along with your diet in helping you keep everything. This is very dramatic. Then comes to the medicine options. Within the medicine options. We think of laxatives. We think of prescription laxative, and prescription medicines, which add more fluid into the gut. Within the laxatives, again, conceptually, you know, when we take a laxative and we occasionally get constipated, whatever, we think of probiotics, we think mild stuff. We think we'll be doing it as needed.

You see the problem with doing something as needed, especially when you've got this completely clamped down or if you plugged up already for two, three days, is that the bottom half is still pretty plugged up the top half where you started to introduce a laxative today, it's loosening up. So, you're floating on the top and you're tight on the bottom. And it eventually goes through. What happens, you cycle between two, three days of constipation, then you decide to take a laxative like Miralax® or Milk of Magnesium. And then you have a bout of diarrhea for two days. Cause all of that backup stuff. And then you cycle back and forth. And so, you never get rid of it. So, the way I like to say this is once you get a bowel movement going, once you've evacuated yourself, you start yourself on a daily dosage of something.

It doesn't matter what, whatever works for you. Milk of magnesium, Miralax, it's usually stuff like this, which lets fluid built into your intestine. Those are the kinds of stuff, daily. You don't have to follow the full instructions and do a full cap. You can do a half cap, whatever works for you, but consistently. It is not an as needed option there. That's what gives you rhythm. You've got obviously, we talked about diet, exercises, all of that. Other than this, there's also a couple of other prescription medications like Amitiza®, Linzess®, which we can use for gut options as well. Some people try to get onto this spicier diet. It works for some like, you know, eating more spice, like peppers and chili on kind of irritate. So many times, if you take the stomach lining, you have a bowel movement, you know this, when you eat a spicy taco, you've been through this. And so, the same approach in using a little bit of chili or pepper in their diet that gets them blowing a double shot of caffeine coffee. They all have their baggage's. Remember if you do a whole lot of coffee, your tremors can get more active. So, there's plus and minus to this. So whatever works for you, but that has to be part of your daily regimen, it is not an as-needed thing that you just think about once every two weeks.

Melani Dizon:

Great. All right. Thank you. I'm going to look over for some questions now. Since we've had a bunch coming in, and I just want to let people know that if it's super specific we can't answer it. And Dr. K can answer, you know, general presence, but he doesn't know all of your details. So, he's not going to be able to tell you how much medicine to take or how many milligrams or things like that. So definitely talk to your doctor, if you have a specific question like that. Is Sinemet neuroprotective or just a treatment of symptoms?

(technical difficulties)

Cherian Karunapuzha:

As far as we know, it is just purely helping the nerves operate at its normal pattern. Then this is all we're trying to do with Sinemet so far. We have no data indicating that it is neuroprotective. There were some old signs where we thought perhaps it was actually toxic for the brain or for the nervous system, but that has since been kind of washed away.

Melani Dizon:

Okay. People that are allergic to Sinemet, is that a common thing? And what are some things that people can do?

Cherian Karunapuzha:

So first, most allergies to a drug comes from many times from the inactive components within the drug or many times the actual dye of the tablet. Okay. So, in my experience I can tell you, it's mostly to the yellow dye in the most standard form of carbidopa/levodopa that is available which is the immediate release, which we kind of call it by its old brand name is Sinemet. So many times, the strategy which I play is switching to another formulation of carbidopa/levodopa, which doesn't have the yellow dye. So, you can use the CR formulation, you can use Rytary®. You can even use it 10 slash 100 carbidopa/levodopa where you have less carbidopa in. I prefer not to go that N slash 100 route because it's less carbidopa. We just talked about why carbidopa is so crucial for helping us prevent some of the dopamine related side effects. So, taking less makes not much sense to me, unless these are reasons that are kind of manipulating.

So, there are other ways I would try to do carbo/levo and see if they still have this allergic reaction. Most of the allergic reactions, which I've seen tend to be dermatitis, itching, or some sort of a skin eruption is the way I've seen it. Very rarely have I seen the asthmatic reaction where you feel like the tongue is swelling up and things like that. Now a second scenario comes whereby you're allergic to carbidopa. This happens. And so, we can find alternatives. Unfortunately, not here in America, but we can get the medicine procured from, let's say, Canada and elsewhere, where you can have other formulations of levodopa, which doesn't have carbidopa in it. There'll be another chemical, very similar to the it's mechanical action, which is not carbidopa. And so that's the many times the second step of what we try, is using other formulations, which doesn't have carbidopa in it to try and treat the person.

So, the few patients that I have who consistently have this recurrent allergic reaction, we do this. The third thing is we get the dermatologist on board, which by the way, every Parkinson's patient needs one dermatological exam once a year for their melanoma screening. Remember melanoma kills two in one year if it goes undetected. So, you always need a normal screening once a year with the dermatologist. But the dermatologist may help you work through the allergic reaction with medications, which they give themselves. So sometimes we take a drug holiday where the person doesn't take the carbo/levo for a while, they get them on the right kind of medicines, which suppress your immune system. And then we bring back in the carbo/levo.

Melani Dizon:

Great. So, the really valuable piece of advice for that is don't give up. And if it's not working, work with your doctor, and if your doctor isn't willing to work with you to find out this, then find another doctor because there are solutions. So, don't give up.

Cherian Karunapuzha:

Correct. And that, this is specifically what I mentioned before, the nuances, which your movement specialists would be savvier, cause they've seen this, you know, this is not a common problem. And all of a sudden, if you say I'm allergic to levodopa, sometimes a physician might think, levodopa's natural in your body. I mean, you make this stuff. How can you be allergic to something you make yourself? So, many times, they don't think it through. And so, because we see enough of this, we know how to kind of mess around with it.

Melani Dizon:

Can you talk a little bit about dopamine dysregulation syndrome, what's happening?

Cherian Karunapuzha:

Dopamine dysregulation syndrome is where, so, you know what happens when I introduce this dopamine? We talked about get dopamine into the brain and the circuit will switch on. But unfortunately, I can't tell levodopa to take a left and then go take a right and go straight to the Parkinson circuit alone. It goes everywhere. It goes into your mood circuits. It goes into your thinking circuits, your sleep circuits. There are so many circuits that use dopamine. So many times, we can artificially manipulate your mood circuits as well, and remember, dopamine is used in your addiction pathway. You can get compulsive, you can get addictive behavior, kind of rev up with dopamine and dopamine related products. And so, dopamine dysregulation is a phenomenon whereby you start to have a craving dopamine. You need more and more dosings of dopamine to kind of feel like you're switching on, even more so than what you need.

And every time you dip down on your dopamine levels, and this is a vicious cycle, you keep needing higher doses. The more you take, the more you have these big drops where you feel like your body's going through an off. And when we look at the person, the person is too mobile, doing well, no tremors, if anything, he's just flailing dyskinesia because you're taking so much of levodopa, but they feel like they're OFF. They're coming off a high almost, and a high can feel like a mental high. I don't feel cloudy. I feel elated. I feel kind of down in the dumps, I feel too anxious. Sometimes it's a physical dip like, Oh, I'm cramping up. I feel pain coming on. And this keeps perpetuating the more and more and more you do for that. If it escalates out, there are certain subtypes or people who we typically end up seeing this in younger patients, this can happen more frequently.

The older, more senior women tend to get more dyskinesia. And also, they also end up kind of going through this sort of dopamine dysregulation. It's tricky, but it can be managed if caught early. And actually the, the treatment is kind of like, you know, when you get high on illegal drugs, what do we do? We actually slowly back them off. We get them on smoother, long formulations. It's an initial toughing out for a month or two, but they will thank you after two months, once you can get them down down down. Sometimes you have to go more aggressive, and we offer non-dopamine options like DPS, et cetera. Just to give them the more control they need.

Melani Dizon:

So, some people said something, and I also just want to remind everybody that Dr. Aaron Haug is going to be here, and he is going to be talking about medications and lots of different types of medications. So, we'll hold some of those questions. Let's see, people are talking about swelling. Some people have mentioned, is that a side effect of drugs, is swelling part of Parkinson's or what's going on there?

Cherian Karunapuzha:

So, I'm assuming swelling usually in your feet or in your legs. Several reasons as to why you swell out in your legs and feet. The most common reason why we swell up in our legs is because your plumbing, your circulation is not very effective. Okay? So, meaning the organ which helps pump blood into all your different body parts and sucks it back up is not working well. Meaning heart failure or impending heart failure is the most common reason why you get leg swelling. And the same way, the stuff which filters your circulation, the dosing part, your kidneys. If they don't do a great job, pushing out sodium and water, you're going to pack a whole lot of fluid in your bloodstream, which eventually seeps out. So, heart and kidneys are the two major things we always look at because in that age group, it's like in your sixties and seventies, you are losing warranty on many other organs too.

And so those are the first things, you can't blame everything on Parkinson's always. First thing, we connect you with your primary care doctor. You see one more person in that tag team as, Hey, can you just run some battery of tests and get an echo? Can you just do a blood work? Just to see if her kidneys are working. Okay, these are the two things. Then we go down the track of actual mechanically in those limbs. Is there any restriction in the outflow of blood, which helps create a pooling of blood? You know, you have clots in your legs, DVP, or deep vein thrombosis, and they do an ultrasound of your legs. These are the kinds of things we look for, or if you're diabetic, or if another reason why you start getting infections in your foot, is it a local inflammation or cellulitis is what we call it.

So, these are things we look for from outside of Parkinson's standpoint. Then you come into Parkinson's as to why, why am I developing leg swelling? Especially very advanced patients who are bed bound or chair bound that they're stuck in certain angles and orientation. When you sit in long stretches for long periods, you start to get more fluid accumulation in the most dependent, meaning the most rested part of your body, which is why on a very long car ride, if you're not the one pressing the gas pedal, everybody else starts to feel like their shoes are getting tighter and tighter. Your shoe is getting more and more uncomfortable because the leg is slowly swelling up. The same phenomenon happens in very advanced Parkinson's patients. Then you get medication. There are a couple of meds, I'm sure Dr. Haug is going to talk about this. Amantadine is a common culprit and number two, Nuplazid®, your psychiatric medicine for psychosis. These two guys can cause leg swelling. So, these are common things. When we pick up on this, your dopamine agonists, like Mirapex® weekly, Neupro®, all those guys can give you the same thing. So, we always will check. Sometimes primary care is like

pulling their hair out, going, why is this person's leg swelling? So, this is why tag teaming is so crucial because it interconnects many, many specialties together.

Melani Dizon:

Okay. So again, with the tag teaming, and I think it's just a question that comes up a lot. If somebody does not have the access to a movement specialist, they have a primary care physician. What are some things that those people can do to get the most out of their time with their primary care physician? If that's the only doctor they're able to see.

Cherian Karunapuzha:

Exactly. So, if you're limited and we talked about possibilities, like let's say telemedicine approaches to connecting with a specialist, sitting in New York or sitting in Oklahoma or where, I mean, I have patients connecting from South Dakota and all the different States across the country. So now we have an access. Let's say you don't have that access. We gave your insurance. Doesn't pay for that. You're in a rural setting. You don't even have access to our new roads. What can you do best? Kind of what you're doing right now, educating yourself. Why does that help? Because the more, you know, the more savvy you are about your disease, you start to understand the nuances yourself. Like this medicine is useful for this, or this is what I'm going to OFF on. And sometimes going educated to a practitioner when you have 15, 20 minutes with them, and you're saying, look, I'm very OFF, I've read about this. This is motor fluctuations. And typically, this is what happens, can you work with me on this? So, going informed, is number one, going with a plan like doc, can you help me tackle my tremor? Can you help me tackle my constipation, I'm trying to regulate my dates. What do I do? Do you want me to try Miralax? Is there a better pill for that? So, things like this, the more educated, keeping a diary and a quick summary list of what you want to talk to with your physician, usually, they open up, they hear, and they go, okay, let's try to tackle this, or let me call a friend who I worked with, you know, and just ask him over the phone.

Curbside is what we call it, among our physicians. I get curbside, from New York, from God knows where all the time. But hey, you know, we don't have a guy here, he's on sabbatical. Can you help me with this? Very easily they can work with this, but you need to be the motivated patient, which you are, because that's why you're here today.

Melani Dizon:

Yeah, absolutely. That's great. That's great advice. And also, you can always, we've had a lot of people who take their every victory counts manual to their primary care doctor and say here, a little light reading. They, you know, they might appreciate it sometimes.

Cherian Karunapuzha:

To be honest, and not just because we're doing the seminar today, I have read through most of the manual, and it's the most easily accessible from a patient perspective. So, it is a great reading tool for you guys.

Melani Dizon:



Yeah. Thank you. Thank you. So, all right, well, we're gonna wrap this up. I know there are a lot of questions. A lot of them are medication related. So, Dr. Haug will have a chance to answer some of those. And then we have some exercise questions. Dr. Mike will be to answer some of those. We wish we could have Dr. K with us for another three hours. I know that we have enough questions to satisfy that. But we have to let you go. So, thank you so much for being here and we'll be in touch soon and, and definitely really appreciate your time today.

Cherian Karunapuzha:

Thank you so much. Please be safe out there. Guys go get the vaccine and have a blessed new year. Thank you.

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