



**The Victory Summit® Virtual Event:
Motor Symptoms and Parkinson's**
Medication Management Strategies for Motor Symptoms
Davis Phinney Foundation

Polly Dawkins (Executive Director, Davis Phinney Foundation):
Welcome.

Aaron Haug, MD (Neurologist and Movement Disorders Specialist, HealthONE
Neurology Specialists):

Thank you. Thank you. I'm happy to be here. Yeah. I love talking about this. This is a conversation I have one on one with many patients every day, and it's nice to be able to try to lay out as much of it as possible, kind of all in one setting because there's not always 45 minutes to talk about all the medication options at every visit.

Polly Dawkins:

Well, that's what we have today, and we'll take questions from the audience. We have some slides to share, to help folks get sort of grounded in medications. But let's start off to get this right, medication management, and we heard that from Suketu as well, is really critical to living well with Parkinson's. We also know that some people choose not to take medication for a while and that others are taking sometimes a handful of pills, literal handful of pills a day. No matter where somebody falls on that continuum, I think it's important to understand the different types of medications that are available and to manage the motor symptoms. And we'll talk about the non-motor symptoms a different day. We have content on that for folks. So, let's start with the basic, how do we know when it's time to start taking medication?

Aaron Haug:

Yeah, it's a basic question and it's a big one. You know, when someone comes in and is first diagnosed with Parkinson's or maybe they've been diagnosed and have been wanting to wait on taking medications because they just have never taken medicines or they're already taking too many others. It's always a question of when do we start? And the answer that I, and most movement disorder specialists would give is that when your symptoms are interfering with your daily life, either how you feel, how you're able to work, how you're able to participate in your leisure activities and hobbies, anything that's having a negative impact on your quality of life, whether it's the slowness, the bradykinesia that it's hard to wipe a countertop or wash your hair, or the tremor that two thirds of people with Parkinson's will have at some point. If it's interfering with daily life, that's really the driving factor to decide to start medication.

Polly Dawkins:

And sort of a complimentary question. Some folks have said that they've heard that taking medication too early means that the meds will lose their effectiveness. Is that true? Or can you describe that issue?

Aaron Haug:

Yeah, let me speak to that. So, this is, I would say a common misperception, a common myth that's out there that medications, quote unquote, only work for five years or something like this. And I think two things are true. One is that the biggest factor in how well your medicines work is how long you've had Parkinson's, how advanced your disease is. And so, it's true that medicines work best. They kind of have the smallest hill to climb in the early years of the disease. But that, because we can't control how many years a person has had Parkinson's, it's not necessarily a reason to save it for a rainy day, so to speak because suffering through untreated Parkinson's symptoms for a few years can put you behind the eight ball in some ways with greater difficulty engaging in an exercise regimen and things like Dr. K was discussing the importance of.

The other thing that's true at the same time is that there are some medications that the more years that you're on them, the more complications can develop. And the medication induced complications are mainly two things, motor fluctuations, where the medicine works and wears off multiple times per day and medication induced dyskinesias. These are instead of the rhythmic tremor movement, more of an involuntary wiggling or fidgeting type of movement. And so, people that are diagnosed at a younger age might choose one medicine versus another to try to mitigate some of that risk of medication induced complications, but in terms of when to start medications at all, it's generally as soon as the symptoms are bothersome and this idea that medications stop working is not the case. Medications work for a person's whole life with Parkinson's, but the regimen may get more complicated as the years go by.

Polly Dawkins:

Got it. So how about we set the stage as well for folks about what the different types of medications that treat Parkinson's are and a bit of a primer for folks. And because I have read the Every Victory Counts® Manual many times, and your contributions to that I'm aware of maybe seven different categories or types of medications that work with Parkinson's. Is that about right?

Aaron Haug:

Yep. Seven categories.

Polly Dawkins:

So would you go through those, we've got some slides for folks to provide a visual background, would you go through each type of medication, how it helps reduce motor symptoms, again, today we're focusing on the motor and what the potential side effects are?

Aaron Haug:

Sure. So, here's the bird's eye view. These are the seven categories of medications and there's a follow up slide about each of them. I think that there's a lot to take in here obviously. I think that to simplify it, there are just a few of these medications that are used the vast majority of the time. There's also a little asterisk in the lower right-hand corner that says anything with an asterisk by it is the brand name only medication, which can sometimes create some issues around cost. But these are the categories. And so, I think, should I just kind of get into each one at this point, Polly? Okay.

Polly Dawkins:

That would be helpful.

Aaron Haug:

So, levodopa, carbidopa levodopa. This is the gold standard medication for the motor symptoms of Parkinson's. So, the carbidopa is there just as a transporter and the levodopa is there because it's a small enough molecule to cross from the bloodstream into the central nervous system. And it gets turned into dopamine, low dopamine as we know is the main problem in Parkinson's. And so, this is like putting gas in the tank. You're putting more dopamine back into the nervous system where it's needed. People ask, well, can we just make a dopamine pill? And that's basically what this is. Dopamine in a pill wouldn't be able to get into the brain, but levodopa can. And so, the reason this is considered the gold standard for most people with Parkinson's, this is the medicine that has the greatest benefit for the physical motor symptoms, the tremor, if you have it, as well as the stiffness and slowness. What about possible side effects?

These are going to be kind of effects, negative effects that we can see potentially with any medication, nausea and lightheadedness are near the top of the long list of possible side effects with most any Parkinson's medicine. And nausea is maybe a little bit more likely with L dopa than it is with some of the other medications. But these are usually manageable by either discussing the timing of the medication relative to food. Maybe using a slow-release formulation instead of an immediate release formulation. So, the side effects are usually something that we can work around, but this is kind of the cornerstone for most people's treatment regimen for bothersome motor symptoms is levodopa.

Polly Dawkins:

Great. May I ask a couple of questions from the audience about this specific treatment?

Aaron Haug:

Please.

Polly Dawkins:

So somebody is asking what's the difference between CR or controlled release and ER, extended release, if I've got those right, levodopa?

Aaron Haug:

There is no difference. This is just a terminology confusion. Some pharmacies call it controlled release, some pharmacies call it extended release, they are one in the same. There is one other difference which is extended release or controlled release capsules. And this is the brand name medication Rytary. But if we're talking about regular carbidopa levodopa, we'll sometimes call it the regular, usually yellow pills, immediate release IR, and then the other pills, which come in a few different colors and are either 25/100 or 50/200 milligrams. We call those kind of interchangeably CR and ER, so the language is just a little sloppy there.

Polly Dawkins:

And is that the same thing as slow-release levodopa?

Aaron Haug:

That would be a third thing that you could call the same thing.

Polly Dawkins:

Got it. So could you answer the question that somebody has about what is the benefit of slow release or ER or CR levodopa for some people? Why is that better for some people?

Aaron Haug:

For me, I find the main benefit to be tolerability because it kind of hits your system a little more gradually if there is nausea or lightheadedness, those side effects are often less with the CR, ER, slow-release formulations. There's theoretically, what it sounds like, a controlled release of the medication that maybe could prolong the amount of time that the medication works for you. If a person is having motor fluctuations and their medicine only lasts five hours when they're taking regular carbidopa levodopa, theoretically the extended release might extend that ON time to six hours. Unfortunately, it often doesn't pan out that way because the extended release sometimes has more variable absorption and some people find it overall less effective. And so, the main place that I find myself using it is either at night where it may kind of help a person get through to the next morning or during the day, if there are tolerability issues with the immediate release.

Polly Dawkins:

Ah, helpful. That's helpful. Tim in the audience asks, are there issues with only taking levodopa when you need it? And he mentions that he takes it in the morning and the afternoon when he is working, but he doesn't take it at night when he doesn't need it.

Aaron Haug:

Yeah. This is an interesting question. And it's an area that we have more hypotheses than we do evidence. A person without Parkinson's, their brain is releasing dopamine continuously, not two or three times a day. And so, the reason that most of us want our patients to take their medicine at least three times a day is to more closely replicate the biological pattern where the dopamine's there in a more continuous fashion. There's a theoretical concern that just taking the medicine once or twice a day, might by giving these large amounts of dopamine and then none for a while that it could potentially shorten the time horizon to when motor complications occur. But this is something that is more kind of hypothetical and anecdotal rather than something we have a lot of evidence to guide us on.

Polly Dawkins:

Got it. All right. Thank you for taking those questions in the middle of your slides. Let's jump into the next. So, we've talked about carbidopa levodopa...

Aaron Haug:

Yeah. So, the next, the second category of medicines to talk about is the second most effective category. So, these are the dopamine agonists. So, these are medications that are kind of like a synthetic dopamine. The most common of these are pramipexole, also known as Mirapex, ropinirole, also known as Requip and the Neupro patch, which is just available as the brand name. So, this is the second most effective category. The second most effective for tremor and stiffness and slowness. There are certain pros and cons or advantages and disadvantages of this family of medication. I alluded to the fact that some medicines are less likely than levodopa to cause motor fluctuations and dyskinesias over the course of time. And so, if I'm seeing a patient's maybe in their forties or fifties and they have pretty bothersome motor symptoms, we would talk about maybe starting a dopamine agonist rather than L dopa as our first line treatment, because less likely three, four years into treatment that they'll have those complications, including dyskinesias.

So that's the point that I made there. What are the disadvantages? It's mainly in terms of side effects, so young people who I just said might be more likely to benefit from the motor effects of dopamine agonists are also at somewhat greater risk of suffering this category of side effects that are the impulse control disorders. So, this is difficulty controlling impulses to do any of the things that humans normally are drawn to doing, eating, shopping, gambling, sex. And so, if any of those impulses are becoming kind of overwhelming, we call that an impulse control disorder and the family of medicines, the dopamine agonists are more culprit of causing those side effects than any of the other categories are really. Impulse control disorders are listed as a possible side effect on most every Parkinson's medicine, but it's in the dopamine agonist category that we think about it the most.

Polly Dawkins:

Do you find that there are individuals who are more likely to experience impulse control disorders?

Aaron Haug:

So, we know that it's more likely among younger patients and it's more likely among men.

Polly Dawkins:

Got it. Okay. Thank you.

Aaron Haug:

So, there are a couple of other idiosyncratic side effects that can occur to patients younger or older taking dopamine agonists. And these include sudden sleepiness or so-called sleep attacks. Again, this is listed on most every Parkinson's medicine as a possible side effect, but it's something that's seen frequently among the dopamine agonists and then also sometimes edema or leg swelling. And these are things that are more likely as you get to higher doses of the medicine but can occur kind of unpredictably. So, the dopamine agonists came around about 25 years ago and the pendulum really swung heavily towards them for a time and a lot of neurologists were using them instead of L dopa, at least in my practice over the last 10 years, and in the case of, I think a lot of movement disorder specialists, I think more and more of us are using L dopa, not to the total exclusion of dopamine agonists, but probably at a significantly higher frequency than the dopamine agonist because of some of these side effects that have become more apparent as the medicines have, you know, gained decades of use.

Polly Dawkins:

Super, all right, what's the third category?

Aaron Haug:

So, the thing I'm mentioning third here is the family called MAO-B inhibitors. So, MAO is a brain enzyme that we all have, and there's an A type and a B type. And these MAO-B inhibitors slow down and inhibit this B type of the enzyme. So, the enzyme's normal job is to recycle dopamine. And so, if we slow down the breakdown, if we use these MAO-B inhibitors, then your brain ends up with more dopamine. So, the medicines in this family are selegiline, rasagiline, which the old brand name was Azilect. And Zadago. So, all of these medicines increase dopamine. This family tends to be kind of mild and tolerable. So, the mildness is in terms of a mild benefit. I will sometimes estimate that if a L dopa regimen is 10 out of 10 effectiveness, it's the most effective medicine we have, that the MAO-B inhibitors are maybe somewhere around a four.

So, the benefit for tremor, stiffness, and slowness can still occur, but it's not as robust and remarkable as it can be with L dopa and the dopamine agonist. Because it's mild benefit and well tolerated, it's often used alone in people that are early in their course with Parkinson's. If someone has started on something else first, L dopa or a dopamine agonist, an MAO-B inhibitor may be added as the second or third medicine to try to smooth out fluctuations by prolonging and improving ON time that is achieved by any of the other kind of cornerstone medications that a person is using. I will mention also that there's a theoretical benefit with rasagiline that

came closer than any other medicine did to showing that maybe there's a disease modifying effect. That was not conclusive. And unfortunately, we don't have any medicine that's conclusively disease modifying, but the rasagiline kind of came close to showing that it might be.

Aaron Haug:

And so, if it can also be of mild benefit and most people tolerate it well, then for that possible disease modifying effect, it's something that we'll sometimes add in early for that reason. So, if you look at the side effects of selegiline or rasagiline and the side effects of L dopa and the dopamine agonist, it's almost the exact same list, but again, it's an issue of how likely are those side effects. And with most of the MAO-B inhibitors, the side effects are pretty unlikely. So selegiline, or maybe even more so rasagiline along with L dopa, those are about the only two medicines I'll use for people in their eighties, for example, because of the good tolerability.

Polly Dawkins:

Great. The questions just come in. If we could answer this one before we move on about dopamine agonist side effects. If somebody's gonna have a side effect from a dopamine agonist, will that show up early or is there a possibility that somebody could develop the side effect after like the sleepiness or the impulse control disorder after taking them for a while?

Aaron Haug:

Yeah, a couple things to say about that. One is that I wouldn't expect those side effects to occur right off the bat. There's something that, you know, when they occur, it seems to be after six months, after a year, a year and a half, and maybe that's because the dose has been gradually increased to better treat the symptoms. But some of these can be later and unpredictable. So, a person who's been on a stable dose of medicine could potentially develop, whether it's the impulse control disorders or the edema, or the sudden sleepiness, it could happen years into taking the medicine. The other thing that happens is that people are getting older, the more years that they've been on the medicine. So, while I'm pretty comfortable using dopamine agonist for people in their sixties, by the time people get into their seventies, the sleepiness in particular is maybe more likely just because people start to lose some of the functional reserve as they get older. So those are the two things to consider when thinking about when might those side effects occur.

Polly Dawkins:

Great. All right. Let's put your slide back up about fluctuations, I think it's a great visual to help us get grounded in some of these some of the questions that are about wearing off.

Aaron Haug:

Yeah. So, what we're looking at here is a typical day. And at the left-hand side of the screen, a person is waking up. They maybe haven't taken medicine since the night before. And so maybe they feel off, they feel stiff and slow and maybe shaky. And then there's the arrow that shows

where a person is taking their medicine. And then we start to go up the curve, the symptoms start to be alleviated. A person feels more ON, and then later the symptoms begin to return. We call that a wearing OFF period. There are a couple of medications that have been approved recently, specifically for the treatment of OFF periods. And so, people have seen ads or commercials for some of these medicines and they come in and they say, am I having OFF periods? And the answer to that question is almost always, no, usually people that are having OFF periods know it because they say, oh yeah, four hours and 45 minutes after I take my carbidopa levodopa, I start to feel worse like I need another dose.

And so, if you're wondering whether you have OFF periods, then it's quite likely that you do not, and that's good. Those may develop as the disease advances and that's a bridge we can cross down the road. But if a person is wearing OFF and feeling that their medicine stops working, or isn't working as well after eight hours or after six hours or after three hours, then that's where we can start to use some of these multi medication strategies where it may not just be a matter of increasing the dose of one medicine, but maybe dosing that medicine more often, or using some sort of booster medication to try to prolong and improve the periods of ON time.

Polly Dawkins:

Great. All right let's move to the fourth category.

Aaron Haug:

So, the COMT inhibitors are a booster. So, the MAO-B inhibitors that I mentioned just a minute ago could also be considered a booster but can also be used by themselves. But the COMT inhibitors are different. COMT is a different enzyme and what it does is recycle levodopa. And so, this is a medicine that is only ever used in combination with levodopa. And so, there's three mentioned here, entacapone, formally known as Comtan and then tolcapone and Ongentys is a newer one. And so, by slowing down the breakdown of L dopa, you can extend and improve your ON time from each dose of L dopa. As I kind of alluded to just now COMT inhibitors are only used in combination with carbidopa levodopa. If a person with Parkinson's takes entacapone by itself, it doesn't do anything because it's only there to improve the effect of the L dopa. Entacapone is the most widely used of these Comptan was the old brand name it's available as a separate pill.

It's usually kind of an orange oval, or it's also available in combination as a single pill, carbidopa levodopa entacapone, which comes in five or six different strengths, which can be nice to make adjustments. A couple of side effects to be aware of with entacapone as a COMT inhibitor. I mentioned that most of the medicines have the same list of side effects, but entacapone has one special side effect, which is maybe about 5% of people get diarrhea from it, from causing kind of an immune reaction in the gut. It's not dangerous. And I have a couple of patients that use this strategically to treat their bothersome constipation. But if diarrhea is bothersome and it coincides with when you start entacapone, the medicine may have to be stopped. The pills

are orange, as I mentioned, and they will stain things. So be careful if you're like leaving it on your counter, and it will also turn some of your bodily fluids kind of an orangey color. So, if you're urine turns orange, it doesn't mean you're dehydrated. It's just a side effect of the medicine and it's not worrisome.

Polly Dawkins:

So now, I'm gonna quiz you, Aaron, how do you pronounce the long word that's COMT.

Aaron Haug:

Oh, the enzyme?

Polly Dawkins:

Yeah.

Aaron Haug:

Catechol-O-methyltransferase is the whole name.

Polly Dawkins:

Very nice. I can see why we say comt, C-O-M-T. Alrighty. Let me just check our chat really quickly and see if there are any questions about COMT inhibitors. I don't see any right now, so let's move on to the next category.

Aaron Haug:

So, the adenosine receptor antagonist, this is a new category. There's only one medicine in it. It's called Nourianz. It's only available as the brand name and this works on kind of a side pathway, adenosine and dopamine are kind of in balance with each other. And by blocking adenosine, you're kind of relatively getting more dopamine function. So, we think that's how it works is by increasing dopamine signaling. Currently, this medication is approved only as an add-on, a booster to levodopa, although unlike the COMT inhibitors, which even theoretically can't possibly help without levodopa, Nourianz theoretically could. And so there may be a day where Nourianz can be taken as a standalone medication as well.

Polly Dawkins:

Are there any side effects to this medication?

Aaron Haug:

So, same list of possible side effects. Interestingly, one of the selling points of this category of medicine is that maybe it's less likely to cause dyskinesias than just increasing your levodopa would be, but at the same time, dyskinesias is listed as the most common possible side effect. We think that the adenosine pathway is maybe a little bit more involved in tremor. And so, if someone has tried a couple of other medicines for tremor, this is something that we potentially could try to treat tremor that has remained bothersome despite some other attempts.

Polly Dawkins:

All right. Okay. Thank you. Next one.

Aaron Haug:

So, amantadine is a special medication. It's been around for a long time. It's a fairly powerful medicine for the motor symptoms of Parkinson's and it also has a special role to play, which is that it's the only medicine that you can take more of and get less dyskinesias. It's the only medicine we know of, that's an effective therapeutic tool for dyskinesias. So that sounds well and good. Some people will start this maybe even as their first medication or added in somewhere along the way. But kind of, like I mentioned with the dopamine agonist, as people get older, some side effects become more likely and so dry eyes, dry mouth worsening, or causing constipation, or even causing hallucinations are more common with amantadine. So, I find it a lot more helpful when people are in their fifties and early sixties, I start to use it not very often by the time people are in their seventies and eighties.

Polly Dawkins:

Isn't there a longer release amantadine available?

Aaron Haug:

So yes, I'm referring here to kind of generic amantadine. There are two brand name only formulations of amantadine that only need to be taken once a day, instead of maybe twice a day, like the amantadine, these are called Osmolex and Gocovri. And it's nice to not have to take medicine quite as often. That's kind of one of the advantages of those. But because they're available only as a brand name, I tend to use the more inexpensive amantadine.

Polly Dawkins:

Got it. Okay. And is there one last category?

Aaron Haug:

The last category, the anticholinergics. So, these medicines like trihexyphenidyl and benztropine only work on tremor. They don't help stiffness. They don't help slowness. But if someone has a lot of tremor, and is fairly young again, then this is a category that we might use. So those same side effects that I just mentioned about amantadine we actually call those anticholinergic side effects, dry eyes, dry mouth, constipation, hallucinations. And so, this family of medications is called anticholinergics. So expectedly, the anticholinergic side effects are potentially an issue here, but for bothersome tremor and a younger person, it's a medicine that we'll sometimes think about. So those are the seven categories and they kind of each got an equal amount of face time here. But I think you can maybe, or I'll emphasize that levodopa for most people is kind of the cornerstone of the foundation. And then maybe we increase it a little bit, or we take it more times a day and maybe we buttress it with an MAO-B inhibitor, like rasagiline or buttress it with a COMT inhibitor like entacapone. And if someone's developing

dyskinesias, we may be add in some amantadine, but for most people, levodopa is at the heart of it.

Polly Dawkins:

Somebody in the question we have about, seven minutes left together and so many questions. And so, I'd like to try to get through some of those, if you're willing?

Aaron Haug:

Absolutely.

Polly Dawkins:

Somebody has asked if there is a future technology that would be implanted where it could understand, whatever the technology would be, could understand how much dopamine you have and how much you need and release it accordingly. Do you know of anything like that coming down the pipe?

Aaron Haug:

Yeah, that's a great question. For medicine, I think the answer is no. There are devices for continuous delivery systems of levodopa. There's the Duopa pump, which involves a small surgically inserted tube, but it's an open system. You just program it to deliver however much, it's not detecting how much you need. And in the next year or two, there may be subcutaneous delivery systems of either a dopamine agonist or levodopa that are also come available. In the deep brain stimulation space, potentially in the next few years, there may be a closed loop system where the DBS device can detect what's going on in your brain and can increase your stimulation as needed. So that's something that we may be seeing in the coming few years.

Polly Dawkins:

Super. And I think I've heard about a subcutaneous continuous that's not a surgery for delivery of levodopa.

Aaron Haug:

Yeah, that's right. So possibly in the next year or two, that may be a reality.

Polly Dawkins:

Super. Somebody has asked about some of the rescue meds and all. I think we're gonna leave those, like Inbrija, we're gonna leave those for the conversation that's coming up about OFF. So, for those of you who are hoping to hear about that, we'll come back to that. One question that we get quite a bit, and I'm sure you do as well is about a slow emptying colon. And how do I'm sorry, I'm losing my track here. How can we take medication when the colon isn't emptying? Do you have strategies or thoughts about the slow gut and slow emptying?

Aaron Haug:

Yeah, so constipation is a highly prevalent condition among people with Parkinson's as most of us know, and for some people it's their most bothersome symptom. And so, some people have slow gastric motility, and unfortunately there's not directly a way for us to treat that exactly because the main medicine that's used for that called metoclopramide or Reglan can make the symptoms of Parkinson's worse. So probably the best we can do is try to not be constipated, try to have a bowel movement every day. And by keeping the gut moving, because levodopa is absorbed in the first part of the small intestine, if the colon's cleared out every day and you're able to keep things moving, then that will improve the efficacy of the medications. In that same note, taking each dose of, especially carbidopa levodopa, with a full eight ounces of water to kind of wash it through the stomach on into the small intestine where it's absorbed is a good idea.

Polly Dawkins:

You've done some work with us on constipation, which we can share with everybody. In a really readers digest format, what do you recommend for your patients who are experiencing trouble, some constipation, to sort of keep regular so that their meds work better, water, you said?

Aaron Haug:

Yeah. So, lifestyle management is first, plenty of fluids, exercise, dietary fiber. If we're doing all those things, then over the counter medications can be quite effective. If the bowel movements are hard, then docusate also known as Colase is a stool softener, and that's sometimes enough by itself, but usually people will need a laxative as well. And a so-called osmotic laxative like Miralax, polyethylene glycol can be safely taken every day and can be quite helpful. So, it's the mush and the push strategy with a stool softener and a laxative that some people need.

Polly Dawkins:

That you take one thing away from this today, the mush with the push.

Aaron Haug:

Memorable.

Polly Dawkins:

Memorable. Yes. We do need little memory help here. Alright. So many questions. Is there a problem with taking half the prescribed dose twice as often? And I don't know what this person was referring to, which medication, but I'll probably assume levodopa.

Aaron Haug:

I would assume so too. So, there's not a problem with it, except logistics. It's just hard to do, to remember, to take a half tablet six times a day, instead of one tablet, three times a day. It may be a little better to fractionate it in that way to take less, more often, because it's a step closer to what our basal ganglia normally do where they're kind of putting out the dopamine on demand continuously throughout the day. But at the same time, life is hard enough. I'm not

gonna try to make anybody take their medicine six times a day, especially right out of the gate. But if someone's having bothersome dyskinesias or motor fluctuations, then a strategy of fractionation where you take less, but more often, is something that we'll often try.

Polly Dawkins:

I can imagine that gets complicated with eating as you're supposed to have a fairly empty gut when you or empty stomach, when you take your meds.

Aaron Haug:

Yeah. So, the empty stomach issue. So, levodopa, we have always said works better on an empty stomach. Some people say 30 minutes before a meal, some people say an hour after a meal. Some people say, wait at least an hour. Some people say two hours. If you're taking medicine six times a day, there's not enough hours in the day. It tends to be the case that for a lot of people, the med timing separate from meals is maybe not so critical, but it's more the people that are having a lot of fluctuations where separation from meals, especially separation from protein is important. So, it does create kind of a logistical conundrum.

Polly Dawkins:

Yeah. I can imagine. Oh, my goodness. So many things to think about so many questions out there. We so appreciate you here and the work that you're doing in our community, it shows how much passion you have for this work. Thank you.

Aaron Haug:

Thank you for having me happy to be here.

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