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MJFF: 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.

Jimmy Choi: Well, hello everybody. How are you? And thank you guys for joining us today. My name is Jimmy Choi. I have the pleasure, and of course, the honor of being your moderator today. I'm a member of The Michael J. Fox Foundation Patient Council, and I've been living with Parkinson's disease for over 19 years. Today, our panelists will discuss autonomic issues in Parkinson's disease. We will talk about autonomic nervous system and how it's affected by Parkinson's. We will also cover symptoms such as low blood pressure, bladder problems, constipation, and sweating. And of course, we will discuss ways to treat them both medically and through changes in lifestyle. So we've got a lot to discuss today, so let's get started. So let me first introduce our distinguished panelists joining us today. We have Bret Parker. Bret is the co-chair of The Michael J. Fox Foundation Patient Council, and he is also the executive director of the New York City Bar Association.

Jimmy Choi: Bret was diagnosed with Parkinson's disease in 2007 at the age of 38. We also have Dr. Anna Hohler, a movement disorder specialist, a chair of neurology at St. Elizabeth's Medical Center in Boston, Massachusetts, and she regularly sees people with Parkinson's in her clinic. And she also does research focused on autonomic dysfunction. Finally, joining us from all the way across the Atlantic Ocean, please welcome Dr. Ray Chaudhuri, professor of movement disorders and neurology at King's College Hospital in London. His research specializes in non-motor symptoms of Parkinson's disease. So, let's start from the top, the autonomic nervous system. Dr. Chaudhuri, if you can, please describe to us the autonomic nervous system.

Dr. K Ray Chaudhuri: Hi Jimmy. Thank you. Thank you for having me to this fantastic program and thank you to all listening in. Autonomic nervous system is an ubiquitous part of our body. It helps us breathe. It helps us sleep. It helps us open our bowel, our bladder. It helps us having sex, and also most importantly, it helps us maintain our blood pressure. It is the reason the normal autonomic nervous system prevents us from fainting when we stand, for instance. So, it's basically a control system, a very complicated and complex control system within the body. It has a peripheral component, which are the sympathetic and the parasympathetic nerves, which innovate virtually all our internal organs. The sweat glands, the skin, and so on. And then it spreads to the spinal cord, the connections to the spinal cord, and from therein it stretches to the brain. So there are important centers within the brain, particularly the lower part of the brain, the brain stem, that ultimately gives us control over the system.

Dr. K Ray Chaudhuri: Now in your slide, you'll see a network of nerves that are controlling blood pressure, bladder, heart, temperature, digestion, sexual function. The origins really come from the brain stem control, which is then further controlled by the brain, the cerebral cortex. And as we know in Parkinson's, it is the brain stem and the sense area of smell, the olfactory bundle, that are affected pretty early and therefore involvement of the autonomic nervous system is very common in Parkinson, and can actually predate the clinical diagnosis of Parkinson.

Jimmy Choi: Wow. Thank you for that, Dr. Hohler, can you tell us why autonomic issues can happen in people with Parkinson's?

Dr. Anna Hohler: So, patients with Parkinson's disease, as Dr. Chaudhuri just mentioned, can have dysfunction in certain areas of their brain that are impacting the autonomic nervous system. So, they can have disease pathology developing in the brainstem and then spreading to other portions of the brain itself, which can then contribute downstream to these difficulties. We do believe that a lot of patients with Parkinson's disease develop issues such as constipation, for example, before they actually develop motor symptoms, such as tremor, stiffness, slowness, and gait dysfunction. We also see a progression of autonomic dysfunction throughout the course of patient's Parkinson's disease, so that people who might not initially have obvious Parkinsonian and autonomic issues may develop worsening autonomic function over time. Oftentimes that is impacting their bladder. As mentioned here, it can impact their blood pressure, the constipation, as we mentioned, and sweating. There are a host of other issues that can be impacted by the autonomic nervous system as well.

Dr. Anna Hohler: The interesting part is that some of the Parkinson's medications can also further impact some of these autonomic issues. So, some of our Parkinson's medicines can drop the blood pressure further. So, it's important for people with Parkinson's to understand these autonomic issues, so that we can monitor these patients and understand the impact of autonomic system for these individual patients and how that can interplay with their medications. Alpha-synuclein, which is misfolded in Parkinson's, is felt to play a role in this process.

Jimmy Choi: Yeah. You know, whenever people talk to me about Parkinson's, they immediately go into the motor symptoms, right? I think the general public, to them, Parkinson's is just what they see, which is tremors, rigidity, and other motor symptoms. And I always tell them, at least for me, tremors are like 15 percent of my problems. You know, we're dealing with a lot of these things that could be invisible to the eye from first observation. So, I'm wondering, Bret, if you yourself had any personal experiences with that, or even with any of the symptoms that we've already listed.

Bret Parker: So, thanks Jimmy, and thanks to everyone for being here. So, as you mentioned, I was diagnosed in 2007, so it's been about 15 years. And like Dr. Hohler mentioned, my first noticeable symptoms or diagnosed symptoms were the traditional ones: tremor, rigidity, very minor, not very noticeable. And it sort of stayed that way for several years. It was only further into my disease that I started to notice some of the other symptoms that we're going to talk about: sweating, constipation. And for me, even just very more recently, blood pressure issues. So, the beginnings were the sort of the more physical ones, but it probably, if you look back, the autonomic issues were there as an early sign, I just didn't know them.

Jimmy Choi: Yeah, it's just, it's strange, you know, just looking back, right? Hindsight's always 20/20, you know. Living with Parkinson's for almost 20 years now, I even look back into teenage years and I can recall some of these things that, "Oh, maybe that was due to Parkinson's." But Dr. Chaudhuri, Bret already talked about some of the issues that he's dealing. We've talked about the bladder issues, the blood pressure, constipation, et cetera. What are some other examples of autonomic issues in Parkinson's?

Dr. K Ray Chaudhuri: Thank you, Jimmy, and bright as well. I think it's important to emphasize that Dr. James Parkinson, who described this condition from my city here in London, literally five kilometers away, in his original essay in 1817 mentions his autonomic problems. He mentions splatter problems in his patients. He mentions sleep problems. He mentions constipation. He mentions dizziness on standing, but somehow, as you both said, I have a program. In fact, we've written a two volume book called, The Hidden Face of Parkinson's, which is basically non-motor aspects. And autonomics dominate those non-motor problems. And some of the key problems we see, and we did a big study across Europe and US and Japan in 2010, actually. When we looked at the prevalence of these non-motor problems, using a standardized questionnaire, which we had developed, which actually is used through the Fox Finder, the non-motor questionnaire.

Dr. K Ray Chaudhuri: And we found that in over 50 percent of medical consultations, non-motor symptoms are never discussed. The focus is on motor symptoms, tremor, that stiffness, the falls, and the difficulty of movement. Of course, they're crucially important. And, in specific answer to your question, Jimmy, I would say bladder problems are one of the primary issues, and bladder problems include urgency. When you have to go, when you feel like you have to pass urine, incontinence in some cases, but most importantly, also nocturia, getting up at night to pass urine. It becomes a real problem in many, many patients and is a symptom that we see often early in Parkinson. Then low blood pressure, particularly blood pressure dropping in response to standing suddenly, blood pressure dropping after you've had a big meal, a big carbohydrate meal. And in some patients we have shown blood pressure drops after we exercise. Supposed exercise, hypotension.

Dr. K Ray Chaudhuri: This can be quite significant because it can make people faint, feel faint, feel dizzy and become posturally intolerant. Constipation, sweating issues, particularly hyperhidrosis. Some people get drenching, sweating, slip sweats at night, which can wake them up. And that can be a problem in some. So these would be the key part of the autonomic problems, but there are many others, of course. There are bowel-related problem aspects of dribbling of saliva could be autonomic in nature. Aspects of vision could be autonomic in nature. Aspects of sleep could be autonomic in nature. So it has got a very wide footprint. A lot of it is remains hidden, and I still think we need very much increased awareness amongst our doctors and nurses so we can help all people with Parkinson's with these symptoms. And many of these are treatable.

Jimmy Choi: Now, it's already been mentioned, multiple times already today, that these things are happening even before motor symptoms are visible to your average person observing. So, you know I... And Dr. Hohler, should people who are experiencing these things individually, should they be concerned that "Hey, one day I might be diagnosed with Parkinson's?" Or, how do we know that we should check with our doctors about this?

Dr. Anna Hohler: So it's a good question. And I think it's hard to know before a diagnosis of Parkinson's, per se. Some people are at higher risks for developing Parkinson's disease, perhaps because they have a family member who has Parkinson's disease. And those people may know to monitor for some of these issues beforehand. I think public education about 10 early signs of Parkinson's, some of those being related to autonomic, that's been very important in terms of getting information out to individuals who may suffer from constipation or even problems with blood pressure before their motor symptoms. But one of the biggest things, I think, is once somebody has some of the motor features clearly, is that we need to be monitoring at each visit for autonomic issues. And then individually at home in between visits. One of the things I think is so helpful is to be able to, in a visit when you're going to see your movement disorder specialists, have your blood pressure taken, sitting and standing.

Dr. Anna Hohler: And if possible, laying, sitting and standing to see if you are having changes in your blood pressure, that could suggest that, even before you may notice, you are developing some of these autonomic issues. We did some research in terms of our moderate to severe Parkinson's patients, and found that 70 percent of our patients did have drops in their systolic blood pressure of 20 points or more, in doing this testing or diastolic of 10 points or more, but only 50 percent of those patients actually felt lightheaded. So, your blood pressure may be fluctuating more than you realize if you're just waiting to feel lightheaded. Some people can get a little bit of tightness in the back of their neck when they have drops in their blood pressure. Some people can have leg weakness. So, it's important to monitor blood pressure. And definitely if you've been diagnosed as having blood pressure fluctuations, having a blood pressure cuff at home can help with this as well.

Jimmy Choi: Yeah. I mean, that's important to know all these things, because sometimes you just don't know these things are happening. You know, some of the... When it comes to blood pressure or sweating, now we're getting into, and even, sexual functions, now we're talking about some pretty sensitive and personal issues, right? And to be honest, I myself was, it was tentative and even embarrassed to bring them up with my doctor or even my wife. Bret, is this something that you deal with as well? If it is, how do you make sure that you address these issues with your own care team?

Bret Parker: So, Jimmy is, as you know, I don't have a very big filter. So, there's pretty much nothing that's off-limits. And for me, talking about all this stuff makes it easier, and it not only puts me at ease, but it puts my care team at ease. And it doesn't mean I'm not uncomfortable, because it's awkward to talk about sweating. And I we'll talk a little bit about that, but it's an awkward symptom, but it's actually something you need to talk about with your physician and with your care team. Even my doctor, sometimes doesn't always raise these issues. It's interesting that my blood pressure, for example, is normal during my morning visits with my doctor, but it's at other times that I experience it, and my wife can experience me with dropping blood pressure.

Bret Parker: And as I mentioned to you, when we're preparing for this, I actually fainted twice from low blood pressure from standing up too quickly. So, to answer your question, I think honesty and candor is the best policy. Your care team, whether it's your significant other, your family members, they may observe some things that you're not observing in yourself. And it's important to listen to them and include them in the conversation and not be embarrassed about the... The more we take away the stigma by talking about it, the less stigma there'll be.

Jimmy Choi: Yeah. I love that advice. And Dr. Chaudhuri already mentioned that more than half the time, right? More than half the time in doctor visits, these issues aren't brought up. And I think it could be because that it's embarrassing topic. So no, that's great advice, to be open and honest with people. But these, we're going to get into a little bit more on these symptoms, and more specifically how, what we can do to treat them. But for more information on symptoms and factors that can precede a Parkinson's diagnosis, those of our audience members, please check out a new educational guide called, Better Brain Health, and there's a link for it on the.

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Jimmy Choi: Better brain health, and there's a link for it on the resource list on your screen. Understanding how these factors may precede a Parkinson's diagnosis is important, not only for early detection, but also, change the course of treatment for each individual. That's one thing that I wish I had known almost 20 years ago.

Jimmy Choi: But did you guys know that the Fox Foundation's landmark study, the Parkinson's Progression Marker Initiative, also known as PPMI, follows both people with and without Parkinson's over a long period of time to learn how the disease starts and it evolves along the way. Now PPMI is recruiting volunteers, and people who are recently diagnosed with Parkinson's can play a critical role. Once again, click on that resource link to learn more about that.

Jimmy Choi: Last thing I'll say about the PPMI is that it aims, really, to change everything about how Parkinson's is diagnosed, treated, and potentially even prevented. PPMI is open to anybody, with or without Parkinson's. I can't stress that enough. It is not just a study for people with Parkinson's, but it's anybody, people with or without Parkinson's. So you, your family members who are part of your care team, please, everybody is welcome to participate. Anybody that's over the age of 18, living in the United States, it all starts online, you can get started in the study today by clicking that get started button in the take action box on the bottom right of your screen.

Jimmy Choi: So, let's center ourselves and let's come back and talk about ways that we can treat some of these issues. Now, recently, I joked that I didn't know if it was age or if it was PD, that my wife and I had recently switched sides of the bed so that I could be closer to the bathroom. Now it could be both, right? But, last time I checked my friends who are my age, they don't have to get up to go to the bathroom two or three times a night. So Dr. Chaudhuri, what are some things that we can do to treat bladder issues?

Dr. K Ray Chaudhuri: So, bladder problem, as I mentioned, is consistently listed by people with Parkinson's, as you've said yourself, Jimmy. It is one of the most troublesome, and because it can be socially embarrassing and also has profound impact on sleep, and some people, if you're getting up three, four, five times at night to pass urine, for instance. So I think you can go by, firstly, the common sense approach, which is essentially lifestyle and diet. It's quite important that nearing bedtime, and I'm thinking most people will be looking at the nighttime, limiting the amount of fluid intake that you do. At the same time, be aware that dehydration is not good in Parkinson's. You've got to drink about 1.5 to two liters a day, at the same time limit it before nighttime. And caffeine, which can also precipitate urination at night. I would also add to that possibly also alcohol, at nighttime, pre-bed, is not a good thing.

Dr. K Ray Chaudhuri: Then, you need to schedule bathroom breaks throughout the day, that helps with keeping the bladder urge under control. And bladder strengthening exercises actually are very much understated. They are relatively easy to do, you can do it yourself once properly trained up, and is incredibly useful as we age. And this would really be useful for holding the urine when the urge comes so that there is no accident, so to speak.

Dr. K Ray Chaudhuri: And then, of course, comes medication. I think medication wise, I always look at bladder problems and medication to be two ways. The ones, as in the slide, are medications to relax the bladder, and that could be through drugs, such as Oxybutynin, there is Tolterodine, and the one where there's really good evidence, where the Movement Disorder Society would advocate the use of that drug based on level one, which is randomized controlled trial evidence, is Solifenacin. More recently, Mirabegron has also become effective, it works not just to relax the bladder, but also to prevent some of the urgency related urges, and then the Darifenacin. So these are all similar group of drugs. One thing to be careful about these drugs is they have some anticholinergic effects, and they can cause some anticholinergic side effects, and the doctor and the nurse, with the person themselves, need to be conscious of those and make appropriate management strategies.

Dr. K Ray Chaudhuri: Then there are, of course, drugs which can also help empty the bladder, and there are several of them that are listed there, and some of them can be used in a very specific, personalized manner. One size doesn't fit all. In addition, I also think there is also another option for bladder, which is dopaminergic drugs. We often don't talk about that. Remember that there are five dopamine receptors in the brain, and the dopamine D1 receptor has a specific action on bladder.

Dr. K Ray Chaudhuri: So drugs, dopamine drugs, that works on D1 receptor are effective for bladder, this is a developing area. Currently there are two big clinical trials coming up, which will be looking at D1 active drugs and bladder function. But already we have some drugs such as Rotigotine transdermal patch, and even Levodopa, which have some action at the D1 receptor. But more, what is very interesting is D1 active drugs, which are called PAM, which are allosteric modulators at these receptors. We will look forward to those in future.

Dr. K Ray Chaudhuri: And finally, in terms of nocturia, if you have to get up at night, it would be really good to have a well-lit path to a bathroom so that there are no falls, there are no accidents, particularly if the blood pressure drop might be there. And in some cases, in some cases, not in all, we might have to use a catheter to drain so that there is no incontinence in the bed or in the bed area, because that itself can lead to its own complications. So you can see, management really needs well thought out, common sense pathway, it might need lifestyle changes, and of course there is the therapeutic pharmacological options, and there are some new drugs currently being developed, particularly in the dopaminergic arena.

Jimmy Choi: Yeah, that's one of my takeaways from that, but thank you. My takeaway from that is there are some certain things that we can do on our own immediately, like those lifestyle changes, right? These are things that we can do on our own to help better the situation. But for me, just looking at the list, I really got to get better at clearing my own pathway to the bathroom. Usually it's my dog, she's in the way, I always try not to kick her. But, regardless, I'm going to revisit this and then see if I can reclaim my far side of the bed back from my wife one day. But, regardless of which side of bed I sleep on, getting out of bed could be a challenge too, on its own, right?

Dr. K Ray Chaudhuri: Yeah.

Jimmy Choi: Sometimes I stand up too quickly and then I get lightheaded. Bret, you already mentioned this, you mentioned that a couple of times already that you've fainted. Do you mind sharing a little bit more detail about those experiences?

Bret Parker: Now, sure, Jimmy. I had normal blood pressure. I have normal blood pressure. I exercise when I can, and never experienced it, but I did notice a little bit of standing up, and sometimes it's a balance issue, sometimes it's blood pressure, but standing up, I felt a little lightheaded. Twice in October, and I've never passed out of my whole life, and so I was in my living room and I stood up too quickly, and the next thing I knew I was on the floor. I could hear myself hitting the floor, but it was very out of body. And my wife, who saw it, she said, "You just collapsed." And it happened again a few weeks later, so I went to see a cardiologist, actually, and he prescribed a medication for low blood pressure, but only to take, basically, three times a week.

Bret Parker: My blood pressure is generally fine, but it's when I stand up too quickly, or at certain moments when I obviously I have a dip. And so you see on the slide, he prescribed, I'm going to get this wrong, Fludrocortisone, for me. I know everyone's got to take their own drugs and I'm not giving medical advice obviously. But for me, just that little bit of slight increase in my blood pressure three times a week was enough to keep my blood pressure basically at normal. I'm still very careful when I stand up. I mean, I make sure I don't stand up too quickly. The big meal thing is an important tip because I realized that when I passed out, I had just eaten dinner and stood up too quickly, so double whammy. But for me, it's now very manageable. I haven't felt any of the low blood pressure since this happened in October, and everything back to normal on that front.

Jimmy Choi: Well, I'm glad you're feeling much better about that. Dr. Hohler, this is a serious one, right? Because someone can seriously get hurt. Bret I'm glad... You took a tumble, but I'm glad you're okay. So, Bret already mentioned a couple of things on the slide that we can do to treat low blood pressure. What are some other things that we can use to treat low blood pressure?

Dr. Anna Hohler: Thank you, Jimmy and Bret, thank you for letting us know about the experience you had, which is very similar to many experiences of our patients. Our goal is to hopefully prevent episodes like this from happening, and by having a good understanding of the autonomic system, and then implementing those things that you've done already, into an individual's life, improvements can be made that are very significant. So what are the issues with, why is low blood pressure a problem? We hear a lot of media attention about blood pressure being too high, and risk for heart disease and risk for [inaudible 00:25:57] equally problematic because it can result in other things as well.

Dr. Anna Hohler: So we did a study looking at individuals who were having low blood pressure in Parkinson's, and those individuals were at higher rates of developing cognitive problems and walking problems. And so you can imagine, then, how low blood pressure, abnormally low, or big drops in your blood pressure could impact your daily life, put you at risk for falls and injury, and also, cause problems in terms of your day to day living.

Dr. Anna Hohler: So there are many things that we can do to try and mitigate this issue. The first one is optimizing your lifestyle in terms of your dietary changes. So hydration is so helpful in terms of stabilizing blood pressure, having a consistent amount of hydration in your system. And there are ways to do it that can improve blood pressure without causing as much trouble with urinary difficulties, particularly at night. So what we try to have people do is concentrate their hydration in the beginning part of the day and the first half of the afternoon, as much as possible. Blood pressure tends to be lowest in the beginning of the day, and then come up a little bit naturally over the course of the day. So, start hydration early when the blood pressure tends [inaudible 00:27:11] have the most bang for our buck.

Dr. Anna Hohler: Oftentimes water, with electrolytes, can help as well, in terms of keeping the fluid in the vascular system, rather than having it get processed too quickly through the kidneys and then out through the bladder. So what we can advocate for is about 50/50, 50 percent of your good fluids we often advocate for as being electrolytes, for low blood pressure or blood pressure fluctuations, otherwise known as orthostatic hypertension. In addition, heat, in terms of hot beverages, and also hot external temperature, can also lower the blood pressure, so trying to avoid those. And then alcohol can also reduce blood pressure as well.

Dr. Anna Hohler: We've talked a little bit about meals, and the impact on of meals on blood pressure. What happens is when we have a large meal, particularly a large carbohydrate meal, a lot of our blood from our system goes to our stomach and our digestive system to work on the digestive process, which takes it away from other areas and often contributes to this low blood pressure phenomenon. So what we want to encourage is smaller, more frequent meals so that we don't have this, what we call a postprandial, or after meal, issue, where our blood pressure may drop significantly.

Dr. Anna Hohler: In addition, there are some lifestyle changes that can be helpful. So for example, exercising regularly, and particularly working on strengthening legs, and leg muscles, can be very helpful. So for people with orthostatic hypotension, we often advocate for them to do exercises such as biking and rowing, and so those can be useful. If people do want to exercise and have low blood pressure, there are things we can do, such as hydration, and sometimes medications that they can take before exercising to help bring their blood pressure up to a good range in order to be able to participate in exercise.

Dr. Anna Hohler: In our studies, getting a systolic blood pressure at least of 100, in terms of sitting and standing, helps in terms of blood flow and ability to participate in normal activities and also exercise. We want to change positions slowly, and Bret mentioned this before, in that when he jumped up too quickly, he was having trouble with getting more lightheaded. So slow position changes are helpful, you don't want to stand still with your knees locked for long periods of time, such as being in line when you're doing Christmas shopping, that's a high risk activity for fainting. You want to make sure your legs stay moving, particularly when you're upright.

Dr. Anna Hohler: Compression hose can be very helpful, and in fact, many of my patients wear compression hose, particularly ones in the lower portion of their legs, from their ankle to below their knee. They find these comfortable and they also can do their activities with these. The more compression, the better. So the higher the rate and the more coverage over the legs, the more benefit you get, but there's obviously a balance between comfort in daily activities and high compression, high coverage modalities. This is something you can discuss with your movement disorder specialist, it can be very helpful.

Dr. Anna Hohler: In addition, as I mentioned, the blood pressure can be lower during the day, and then it can get higher during the course of the day. And as we lay down, the blood pressure can be higher than it is when we're standing up. Sometimes the blood pressure can get too high, and that's called supine hypertension, more commonly seen in the evening or at night. That can also cause problems with headache or flushing in the face, you can get confusion from this as well. So there are times when monitoring blood pressure, not just in the morning, but in the evening, can be helpful, and adjusting medications in the evening time to lower blood pressure, or raising the head of the bed so we're not so flat, can be useful.

Dr. Anna Hohler: I mentioned before monitoring blood pressure, having the blood pressure cuff at home can be very useful in terms of teasing out an individual's patterns of blood pressure fluctuations. We are also very fortunate to have medications that can be used for low blood pressure, so particularly designed and FDA approved for Parkinson's is Droxidopa. And then medications also that can help for blood pressure that are not specifically for Parkinson's but do help stabilize blood pressure, include Fludrocortisone and Midodrine. They have different mechanisms of action, so sometimes they're used individually, sometimes they're used in combination, and it can be very useful, particularly in terms of the timing of the medicines. Some individuals, like Bret mentioned, may only need these infrequently. Some patients need these medications multiple times a day, if they have more serious or more complicated autonomic issues.

Jimmy Choi: Thank you, Dr. Hohler.

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Dr. Anna Hohler: Complicated autonomic issues.

Jimmy Choi: Thank you, Dr. Hohler. Just looking at this list I learned something new for myself today. I'm big with exercise. Exercise is my jam, so to speak and my pre workout drink every morning is a hot coffee. Maybe I should change that up a little bit, maybe a little bit more water, like my wife's been telling me for years and avoid the hot beverage before working out. Because I think the most of the times that I do experience low blood pressure is post workout. So hopefully that'll help me out a little bit, but so far we've talked about bladder issues and blood pressure issues, man. I mean, these are some crappy symptoms, right?

Dr. K Ray Chaudhuri: Just to amplifying that point, it's really an important point that animate. Exercise induced blood pressure fall is actually well recognized phenomenon in autonomic dysfunction. And it's been shown in many studies and taking water before exercise is actually really important so that you don't precipitously drop your blood pressure even up just after the exercise. It's a really important point.

Jimmy Choi: Yeah. Thank you. One more piece of ammo for my wife to yell at me.

Larry Gifford: A landmark study that could change the way Parkinson's disease is diagnosed, managed and treated is recruiting participants now. PPMI or the Parkinson's Progression Markers Initiative needs people with and without Parkinson's, especially people age 60 up who have close relatives living with the disease. Take a short survey today at michaeljfox.org/ppmi to see if you're eligible. That's michaeljfox.org/ppmi.

Jimmy Choi: Now let's talk about something that's not so pleasant, right? Let's talk about constipation and also sweating. So Dr. Chaudhuri, what are some things that we can do when it comes to constipation and sweating?

Dr. K Ray Chaudhuri: Yes, the constipation is another of those symptoms that in fact, we now recognize this as a prodromal feature. In other words, it can present. There was a paper by Professor Schrag from here in London, in *Lancet Neurology*, and she showed constipation can be present anything up to 10 years before a diagnosis is made and more recent work. In fact, using The Michael J. Fox Foundation PPMI database have shown that people with severe constipation will then go on to develop Parkinson, might have a high risk of developing some other complications of Parkinson. So management of constipation is actually really, really very important. And the other thing to remember about constipation, it can be caused by various things. It can be caused by commonly caused in Parkinson's by dehydration. So one general advice for any person with Parkinson is crucial attention to hydration, particularly in hot weather times.

Dr. K Ray Chaudhuri: And that would be about 1.5 to 2 liters of water a day. And although it might make you paradoxically go to the toilet a bit more to pass urine, but it's actually very important for the general hemostasis, for blood pressure, preventing the blood pressure drop and also constipation often that would clear the bowel out quite nicely, but other things are quite standard. Lifestyle changes like eating, regular dietary changes like fiber to the meals, having a high fiber diet, eating smaller meals on a regular interval to also help the postprandial changes that might occur after a large carbohydrate meal for instance. The exercise we've already talked about regularly can help with constipation quite significantly. And more recently we are certainly advocating probiotics, because the gut microbiota is substantially changed in Parkinson and the bad bacteria overcomes the good bacteria and probiotics, but not just any probiotic, probiotics that reach the large gut. And there are some of them usually liquid ones. They are quite good at restoring that normal dynamics of the gut.

Dr. K Ray Chaudhuri: And there've been some brilliant piece of work on this shown from workers from Helsinki and Finland, who've done the work. So that's the general advice. Then medication wise, yes, of course you can go for over the counter softeners and laxatives. And in some very significant cases, we would use enemas. Often when we have people who are coming in for advanced therapies like apomorphine, like [inaudible 00:37:02] infusion, we would definitely do an abdominal x-ray because often the bowels are quite dilated and that would... Constipation can affect your oral tablet absorption. And what we would do in that situation is provide the patient with an enema. Usually that clears out the bowel and it improves your tablet absorption quite substantially.

Dr. K Ray Chaudhuri: So that's a really important part to think about. In terms of prescribing, you can use stool softeners, you can use pro-peristaltic drugs, and there are many in the market. One where the evidence space is the strongest is volatile and glycol or macrogol that probably the commonest laxative that's used. But in addition, there are reasonable evidence to suggest some of the other drugs which have been listed here, but particularly Amitiza (lubiprostone), which is often used [inaudible 00:37:58], which is used particularly for female patients with Parkinson's and it's used quite commonly in some countries. I'm not totally sure about its availability in the US. In terms of lifestyle changes further, I think the other thing to remember about is the constipation it's link with incontinence. And again, if that happens, bowel incontinence or a inability to a feeling that your bowel emptying is not complete, that's also an indication when you should discuss that with your medical specialist, but drinking enough fluid a day. I can't overemphasize the importance of that.

Jimmy Choi: But since we're drinking, talking about taking in fluids from a perspective of sweating now, what are some things that we can help with people who are dealing with sweating issues.

Dr. K Ray Chaudhuri: Sweating is probably the least explored area in terms of what we know and how we can manage. Sweating in Parkinson occurs under various different scenarios. One of the commonest one is when people get fluctuations. So motor fluctuations, you're going from on to off period and off periods. What often we don't recognize as non-motor fluctuations or non-motor off periods. So that can be often associated with the burst of sweating. And in that situation, when the sweating is associated with the levodopa or the drugs wearing off, perhaps the best remedy for that disturbing sweating is to get rid of the off period as much as possible with whatever strategies, either using longer acting gluconic drugs or using an enzyme inhibitor like a COMT inhibitor or perhaps using injectable preparations of dopaminergic drugs. So that's one area where we can definitely help, but also generally speaking, if a person has a problem of hyperhidrosis and we often see this at night, the drenching sleep sweat problem, it would be really good to limit and identify the sort of food and drinks that might trigger this in the commonest one [inaudible 00:40:24] very spicy food and people who might not be particularly used to it.

Dr. K Ray Chaudhuri: And in some cases, antiperspirants might be useful and there are drugs such as Clonidine, and so on have been used. But a word of caution because these drugs can also sometimes shut off sweating, which can be detrimental to a central core temperature. So you've got to be careful about that if it becomes excessive, yes. And then simple advice like wearing loose fitting clothes, it's very hot in London today. So wearing fairly loose shirts, it's also can be [inaudible 00:41:02] depending upon the time and place you are in and cotton socks rather than a nylon and another nonabsorbent socks, basically absorbent socks. And one thing that I think is relevant to sweating, but not just sweating, also postural dizziness is avoiding standing if it's really hot outdoors for any long period of time, because that can also precipitate a faint. So I think those would be the practical aspects that might go in with the sweating issue.

Jimmy Choi: Yeah. Both of these constipation and sweating hits close to home for me personally. How about you, Bret? What do you think? Are there some things that you do to help ease situations? Because I mean, you work in high pressure situations, right? And I imagine that in some situations [inaudible 00:41:52]

Bret Parker: If you've ever seen a broadcast news with Albert Brooks, that's what it's like for me sometimes I could be about to give a speech or give talk at a meeting and the sweat, it just comes pouring out of all everywhere. And so I follow a lot of the tips that we've talked about. I always try to have an extra shirt around an extra undershirt around, I went to a concert recently and I knew I'd be sweating from that. I had a change of clothes afterwards. So it's embarrassing and it's uncontrollable at times. And so these are great tips for those sort of lifestyle changes. The constipation. I feel like, I was destined to have constipation because for many years I was so regular and I would sort of brag to my wife about how regular I was.

Bret Parker: I'd go every day, like clockwork in the morning, I was like a well oil machine. And then my constipation started to kick in, instead of going every day I was going every other day and now it's every three days or sometimes longer. And so I've tried some of the dietary things, although not all of them, which I need to follow. Water is something I need to take more of. And I've tried some of the stool softeners over the counter products. And let's just say that my wife's now getting the last laugh at me because I'm now sweating like she does. And I have constipation like a lot of women do and there's some justice in the world, I think it's a... But all joking aside, these are all symptoms that I've now talked to my [inaudible 00:43:20] doctors about because not talking about them is not going to help them.

Jimmy Choi: Yeah. One big difference between men and women is that men are big giant babies. So we tend to cry and complain about it more. But that brings up actually a very good point, Dr. Hohler, there are many women living with PD who are in their late 40s and early 50s. Right? So how can you tell the difference between sweating that's related to Parkinson's versus the menopausal sweating?

Dr. Anna Hohler: Jimmy, thank you for this question. This is a very important area that we're exploring in more detail now in terms of how perimenopause and menopause impact people's Parkinson's symptoms. So I have a number of women who present the clinic who discuss issues with night sweats or sweats in general. And the question is often is this related to what I'm going through in terms of my hormonal changes, is this related to Parkinson's and how do we tease it apart? So we do a variety of things to try and better understand that some of it is taking details about the history when the episodes are occurring. Is there some kind of pattern that might be more related to Parkinson's medication doses and the wearing off that Dr. Chaudhuri mentioned, or is it more of a time of day or fluctuations with kind of the time of the month, for example.

Dr. Anna Hohler: There are also test that can be done to look at hormone levels, which can help to tease out whether somebody may be premenopausal as well. So we use a lot of that information to try and get a better sense and then management in conjunction with these lifestyle change, management things that we talked about for Parkinson's. There may be some other over the counter therapies that can be helpful for individuals who may also be perimenopausal. So we talk about that with our patients. We also collaborate closely with their GYN doctors, in terms of collaborative medication management. It's definitely an area that we are looking into more now to try and best answer the questions for those patients.

Jimmy Choi: Well, thank you very much. You shouldn't thank me for the question, Bret [inaudible 00:45:30] it up really good. The transition was perfect for that. So thank you Bret for that. So Dr. Hohler, your research focuses on autonomic dysfunction. Perhaps you can tell us more about research and maybe how it's leading to new therapies.

Dr. Anna Hohler: Yeah. Exciting time for autonomic dysfunction. When I was in medical school, there wasn't much discussion about the autonomic nervous system, but now when the medical students and the PA students and all of our learners, nursing students come through our clinic, we spend a lot of time talking about this, not just related to Parkinson's, but also with other disorders as well. There is definitely a big emphasis on autonomic because it impacts individuals quality of life, the course of their disease as well. We do know that those individuals who have more poorly because we're not able to stabilize the autonomic so well, then they might have more quick progression of their disease, for example, because they might end up getting more problems with constipation. Their meds might not work as well. They might end up having more complications in terms of falls and other things.

Dr. Anna Hohler: So understanding the autonomic system, understanding how to stabilize it over the course of the disease over the course of the day, understanding as Dr. Chaudhuri mentioned the brain gut connection and the gut we talk about as being the central portion of success with Parkinson's. If we can get our gut functioning and trying to have a bowel movement every day, we're more likely to get good absorption of our hydration. We're more likely to get good and effective use of our medications. They're more likely to be consistent in terms of their absorption and their impact on our system. And as a result, if we can potentially impact the gut microbiome long term, we might be able to slow progression of the disease or potentially even look towards cures down the line as well.

Dr. Anna Hohler: In addition to diagnosis and monitoring new therapies like continuous infusion therapies for Parkinson's patients or deep brain stimulation therapies, which allows us to use lower doses of medications, which potentially can also contribute to drops in blood pressure. So as we know, carbidopa levodopa, for example, can drop blood pressure, particularly when it goes through our gut. And so that also might be something that we have to factor.

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Dr. Anna Hohler: That also might be something that we have to factor in when we're talking about the management of our patients. So there's a lot to be learned in terms of autonomic, there's a lot we can do in terms of stabilizing autonomic symptoms for our patients and improving their quality of life and mitigating the progression of autonomic degeneration is one of our big highlights in terms of therapeutic intervention as well.

Jimmy Choi: Thank you, Dr. Hohler, and thank you, Dr. Chaudhuri and Bret for your insights as well. I wanted to make sure that we have some time left for questions. We're about 10 minutes left. We've been receiving a lot of questions already, but it's not too late. If you have any questions, just a quick reminder for our audience to please type it in the Q&A box, and we're going to get to as much of them as we can in the 10 minutes remaining. So I'm going to go ahead and... Since we're on the topic and actually Dr. Hohler, you just talked about this real quickly and how carbidopa-levodopa impacts can impact blood pressure. Maybe it's a question for both you and Dr. Chaudhuri, but what are some ways that people can manage that better? I mean, if we know that if we know that the side effects is causing the low blood pressure change, what are some things that we can do to manage that?

Dr. Anna Hohler: I think one of the first things to know is that when you take your carbidopa-levodopa, it should be taken with a big glass of water. That helps to reduce... Stabilize the absorption. So it's absorbed a little bit more continuously rather than in an uneven manner. And then it also helps to mitigate some of the drop of blood pressure that we might see. If taking the carbidopa-levodopa does cause a big drop, and it's not alleviated by the compression stockings, hydration, electrolytes, sometimes changing the timing, reducing perhaps the dose itself, changing the timing, those things can help. And also other medications can be used for Parkinson's if people are having a significant problem with carbidopa-levodopa as well.

Dr. K Ray Chaudhuri: I totally agree with that. I think changing the timing here because levodopa of course, is the gold standard for Parkinson's and once you are on levodopa, likely you'll be on it for the rest of your life. So changing the timing, particularly, I advise people to take it actually before any meal, often an empty stomach, the effects are less obvious than you might have it with a meal and the meal related vasodilatation or dilatation of blood vessel that occurs. And, also in addition, avoiding too much supine standing activity immediately after taking the tablets often help, because what happens is if you take levodopa it starts becoming active in about 25, 30 minutes. And if you're doing a lot of physical activity standing at that time, you might aggravate the blood pressure drop. So you can take some simple steps to see if you can counteract this. Along with this, as was mentioned, in some situations, a lot of compression stocking and so on, if it's not helping keeping the fluid intake going. And I often add in a vitamin C tablet per day, and that also seems to have a beneficial effect, although it's not evidence based. So these are sort of some maneuvers you can do, but you know, you have to carry on with the levodopa. And so one has to find a way.

Jimmy Choi: Thank you. So, here's a question for, for both of you again. We talked about how to tell the difference between menopausal changes and Parkinson's sweating. So here's a question that's more related to the men, is that how can we distinguish differences between urinary changes in PD versus say an enlarged prostate for men. Dr. Hohler we'll start with you.

Dr. Anna Hohler: So I can start with that one. I think both of us probably have some ideas on that.

Jimmy Choi: Okay.

Dr. Anna Hohler: So again, some of it comes from the history in terms of, has it been related to progression of disease, progression of medication usage at certain times. Some individuals also can benefit from an exam to find out whether or not their prostate is enlarged in terms of exam with their primary care doctor, for example, that can help in terms of exam findings. In addition to that, there are additional evaluations of the bladder that can be done that can help tease this out as well. So there's history taking, and then there's different testing that can be done to help with this.

Dr. K Ray Chaudhuri: Yeah, again, totally agree. I think it's key is the history and examination. And I always say there is an issue in Parkinson's that often other physicians, not neurologists, maybe when they see a problem in Parkinson's, they always blame the Parkinson's. So I think it's really important that you dive deep into it and ensure that it has been seen by urologists to have been examined. And the prostate, as you just said, Anna is examined and there is no obvious prostate malady, but of course we have to remember that both might coexist as well. So it's a complex situation, but I think clinical examination, by a suitable specialist in certain areas, along with history taking will absolutely be the key as you said.

Jimmy Choi: So the next question comes from an audience member who is... We talked about sweating, right? So, and this is an intriguing question for me too, because I know there are a couple, multiple studies out there around odor and body odor and PD. So is foul body odor linked to Parkinson's? Do we have any more information on that?

Dr. K Ray Chaudhuri: It's very interesting this question, because I don't know whether the audience is familiar, but there have been research studies where people have been looking at the possibility of body odor being a predictor for people developing Parkinson's. In fact, in the UK, there are at least two studies where especially trained dogs have been used in studies to detect out people with Parkinson's. It doesn't necessarily mean a malodor, but it means a particularity in the odor, which might be associated with the dopamine metabolism and some of the metabolites and how the sweat is excreted to the sweat glands. So it is a very interesting area. And one that can be perhaps be used in ongoing research in future, I'm not aware of the final data from that study, but certainly one study was ongoing about the dog. And I know a friend of mine from Seattle had sent me some information on that, about a similar project going on there. So, Anna, I don't know whether you know more about this.

Dr. Anna Hohler: So this is exactly the study I was going to be bringing up as well. So the work with the dogs, and dogs can be utilized in a variety of different medical issues in terms of diagnosis, they have an acute sense of smell and may perceive things that as humans, we are not able to to such a degree, there is some speculation about whether or not it is related to the dopamine receptors, the breakdown of certain systems in the body, in terms of how the sweat is processed in the patients with Parkinson's as well, whether or not it's higher levels of sweating in certain portions of the body that may contribute to some of the body odor as well, or the actual metabolism in the sweat glands, and whether that may be impacted by Parkinson's. So it's a fascinating area, but it is an area where we want to spend more time and energy, because if it is something where we can have a simple test to evaluate individuals, perhaps without having to examine them physically, et cetera, or in addition to that, that might help give us clues about Parkinson's. We're all very interested in this.

Jimmy Choi: Great. Thank you. We have just about two minutes left. I think we're going to take one last question. I think this is an important question and I want to bring this up because nobody really wants to talk about, because it might be an embarrassing topic. So of course, question actually has been several questions about sexual dysfunction due to autonomic symptoms. How do we go about that? Where do we start? You know, is, do we start with our doctors or where do we go? Dr. Hohler we'll start with you.

Dr. Anna Hohler: Yes, this is obviously a very important issue and it affects not just the Parkinson's patients, but obviously the family dynamic as well. So we try to ask about these non-motor symptoms in all of our visits. And I know Dr. Chaudhuri has developed a wonderful questionnaire that goes through a lot of these non-motor issues that can be useful, and an individual can take this questionnaire, or they can go through it with their specialists to be able to tease out issues. So, so sexual dysfunction patients can be very profound in terms of being able to have the energy for sexual activity, or actually not being able to perform in terms of different functions of sexual activity. So oftentimes we need to get good history about what's happening and determine whether or not the autonomic system may be impacting it. There does seem to be some data that if we can stabilize blood pressure and try and reduce these low blood pressure episodes, then people may be able to preserve their sexual functioning perhaps a bit longer. But this is being worked out in quite a bit of detail right now.

Dr. K Ray Chaudhuri: Yeah. I think again, Anna, you're absolutely spot on and in answer to your question, Jimmy, I think it's an obligation. We, as physicians working in the field, have to help our patients with particularly these problems. Certainly it's been my area of interest for so long. And I do find the non-motor question are very useful because people may not want to discuss it openly often would tick those questions, like two questions on sexual function. And that just leads you to a discussion. Now that discussion may have to be with you, or maybe some people might feel it better to do it with a nurse specialist or somebody of their own gender. It also varies amongst different cultures, different races, different backgrounds, and so on. It's a very complex area, but in terms of management, we can do a lot because sexual dysfunction can not just affect the person with Parkinson's. Anna said it can affect the carer. It can affect relationships, et cetera. Then we have impulse control disorder, which can also manifest to some extent with sexual dysfunction and so on. So it's a huge area and one that we really need to focus on and develop more transparency and management strategies in future.

Jimmy Choi: Yeah. Thank you guys. Thank you very much. Actually, I didn't even think about that right. About the com the compulsion or the needs and the wants of human thoughts that around this. But unfortunately, guys, we are out of time. I want to thank you again for being a part of our community and for joining us today, everybody. And once again, thank you to our panelists for sharing your time and expertise with all of us. I hope you guys found all of this to be very helpful. Thank you very much and have a great day. Everybody take care.

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