



## Transcript

### Welcome and Introductions

#### *Stephanie Paul*

**[SLIDE 1]** Welcome everyone and thank you so much for joining us today. **[SLIDE 2]** My name is Stephanie Paul, and I am the Senior Vice President of Development and Marketing at the American Parkinson Disease Association or APDA for short.

I'm pleased to welcome you to this Web teleconference education program designed for people with Parkinson's disease, care partners, family members, and healthcare providers. I would like to thank AbbVie Pharmaceuticals and Acorda Therapeutics for funding this important program and acknowledge their continued appreciation for the critical need to provide educational programs like this one to people impacted by Parkinson's disease.

APDA is the largest grassroots network dedicated to fighting Parkinson's disease and works tirelessly to assist the more than 1 million Americans with Parkinson's disease live the best life possible in the face of this chronic neurological disorder. Founded in 1961, APDA has raised and invested more than \$177 million to provide outstanding patient services and education programs, elevate public awareness about the disease, and support research designed to unlock the mysteries of Parkinson's that will ultimately put an end to this disease. APDA distinguishes itself as the national organization working one on one with the Parkinson's community to make each day better.

And now onto our program. **[SLIDE 3]** We welcome our distinguished presenter today, Dr. David G. Standaert, John N. Whitaker Professor and Chair of Neurology at the University of Alabama, Birmingham School of Medicine in Birmingham, Alabama. Dr. Standaert is also the Chair of APDA's Scientific Advisory Board.

Today we are delighted to have Dr. Standaert share with us the latest information about managing Parkinson's disease symptoms. We encourage everyone to complete the evaluation after the program because your feedback is instrumental in helping us plan for future educational offerings, including teleconferences like this and other programs.

It is now my pleasure to introduce Dr. Standaert.



## Presentation

**David G. Standaert, MD, PhD**

Well thank you, Stephanie, and welcome. I'm glad you all could join us to day for this discussion of managing symptoms on the Spotlight on Parkinson's Disease series, and I'm really pleased to have a chance to talk with you today about managing symptoms across the spectrum of Parkinson's.

As I put this talk together, I realized that much of what we're going to talk about today are things that I often discuss with my patients in the clinic. We spend a lot of time talking about managing different symptoms at different stages. Obviously, that's very individualized. Today we're going to try to cover the spectrum. We're going to talk about symptoms that arise early in Parkinson's and how they can be approached, and we'll talk about symptoms that arise later in the disease and how those can be approached and managed as well. So, I hope you get a sense for the breadth and the spectrum of different treatments and approaches to management that are available for this disease today and maybe a little glimpse of the future and where we're trying to go with the next generation of therapies and treatments for Parkinson's disease.

**[SLIDE 4]** So before I begin, I do have some financial disclosures here. I do serve as a consultant for a number of companies that are developing new treatments for Parkinson's, but I don't participate in any paid speakers' bureaus, and I have no equity in any of these companies.

**[SLIDE 5]** Parkinson's disease, at least as we know it or under that name, is a disease that was identified by Dr. James Parkinson in 1817; and what you're looking at here on the left is the faceplate from his publication. It's called "An Essay on the Shaking Palsy." The shaking palsy or paralysis agitans is the name that Dr. Parkinson gave to this disorder. And you can read there his description. He called it "involuntary tremulous motion, with lessened muscular power, in parts not in action and even when supported; with a propensity to bend the trunk forward, and to pass from a walking to a running pace." Now this is flowery language to describe what we recognize today as the symptoms of Parkinson's disease.

Parkinson's is a very common disorder that affects many people. Some of the very public figures who've been affected by Parkinson's are illustrated there on the right: The Pope, Linda Ronstadt, Congressman Udall, Michael J. Fox, Muhammad Ali, Robin Williams, and Davis Phinney up in the top corner. But these are only a few small representatives who stand in for the more than 1 million Americans who are affected by this condition.

**[SLIDE 6]** So let me talk a little bit about Parkinson's disease and the risk factors for Parkinson's, and the most prominent risk factor for Parkinson's is age. This is a disorder that becomes more common as one gets older. And as it says here, the good news is that we are living longer. Most Americans who are alive today can expect to live to be at least 80 years old, which is pretty remarkable, actually. Not a generation or two ago, it was much shorter than that. The downside to that, of course, is that the older we get, the more likely Parkinson's becomes. This little graph on the right illustrates this and shows the rate of Parkinson's, the number of people per 100,000 who will develop Parkinson's in each decade of life. So, under the age of 30, it's quite a rare disease. But as you turn the corner at 50



to 59 and then 60 to 69 and 70 to 79 and on upwards, the rate gets higher and higher. And this is important because our population is aging. The baby boomers are now crossing the age of 65. They're starting to enter this age of higher risk of Parkinson's disease, and so we're seeing more and more of it. I'm sometimes asked whether something is going on, people know or encounter more people with Parkinson's every day. No, there's nothing really magical going on that we know of; and there's nothing unusual about the change in the rate of the disease. It's simply that we have more and more people in this country over the age of 65, and because of that higher risk, you're going to see more people affected.

This graph also illustrates the point that Parkinson's is more common in men than in women. The reasons for that are not completely understood, and if there are questions about that, maybe we can address it at the end. But it is a condition that appears about twice as often in men as it does in women.

**[SLDIE 7]** A few of the basic facts that we teach the medical students about Parkinson's disease and the nature of the changes that go on in the brain before we talk about how to approach managing those symptoms. So, we have classically taught that there are a group of four symptoms that we look for to make a diagnosis of Parkinson's disease.

The first is resting tremor, so this is a tremor typically found, it usually begins on one side of the body. Usually it's asymmetric, so one side is affected more than the other. We actually look for that in the clinic. We look for that as a clue for the diagnosis of Parkinson's disease. Bradykinesia, which means slowness of movement. Many of you have probably had their doctor tap your fingers together. They're looking to see how quickly you can tap, how slow, or whether there's bradykinesia or slowness there. Rigidity, and that's something you feel in trying to move the arm or the leg. You can feel that it's abnormally stiff. And then postural imbalance. This is a tendency towards falling, which is a feature of Parkinson's as well. So, these four features are the classic four symptoms that we teach all of our students to look for in trying to make a diagnosis of Parkinson's.

These pictures illustrate a few of the other features. The top right there, in the yellow, those are actually sections of human brainstem from an autopsy; and the left shows a normal brainstem, and the right one shows one from Parkinson's disease. And the arrows are pointing to the area where all the black substance is gone. That substance is the substantia nigra, and this has degenerated; and in Parkinson's, it's very complete. Typically, 95 to 99% of those neurons are gone, and those cells make dopamine; and this is the fundamental defect in Parkinson's disease.

The pink picture in the center there, that round body is a Lewy body, and that's inside a neuron; and that's what we go looking for in the brain when we put it under a microscope to make a diagnosis of Parkinson's.

And the bottom set of four panels actually shows one of my patients who had a scan. It wasn't exactly DaTscan, but it's similar to what we use today, a scan called DaTscan, where we're measuring the dopamine function of the brain. You can see over four years this person's dopamine function declined, and that's something we can measure in patients as well. So, these are really classical features of the disease.



But I want to approach this a little bit differently to talk about symptoms. We're talking today about managing symptoms, and I want to break these symptoms out into three categories, essentially very early, early, and late symptoms and to think about them in this way because that's the way that people with Parkinson's disease experience this. There's a set of symptoms they experience early, there's a set of symptoms that come later after diagnosis, and there's a set of symptoms that come very late in the course of the disease. So, let's think about it that way a little bit.

**[SLIDE 8]** And there are a group of symptoms that occur in what I would call pre-Parkinson's. So, these are symptoms that we can find in people who don't yet have a clinical diagnosis of Parkinson's disease. And what this really reflects is that the changes in the brain are very slow, and there are changes in the brain and the body going on for years before the symptoms become recognizable as Parkinson's.

Some of these pre-Parkinson's symptoms include hyposmia, the loss of sense of smell. There's also a sleep disorder; it's called REM (rapid eye movement) behavior disorder. This is a condition where people act out their dreams. Often, they're thrashing around in the night. We hear that bed partners get hit. They're throwing pillows around, sometimes punching dragons in their sleep. It can get quite dangerous to sleep with somebody with REM behavior disorder if they're asleep and acting out these kinds of violent dreams.

It turns out that having this kind of sleep disorder predicts the later development of Parkinson's. At least 70% of the people who've developed this sleep disorder will have Parkinson's disease within five years, and it probably reflects early changes in the brain before the tremor, before the stiffness, and before the slowness.

Another feature that's very common early on is constipation. And, in fact, the presence of constipation turns out to be one of the strongest predictors of developing Parkinson's disease later. This was studied in a large group of men in Honolulu who were followed for over 30 years, and if they had constipation at the beginning of the study, 30 years later they had a much higher rate of Parkinson's. So, there are things going on in the body prior to the point where any neurologist would recognize it and call it Parkinson's disease.

**[SLIDE 9]** Then there are a group of symptoms that are common in early Parkinson's. Tremor is one of them. So, tremor is the most common reason that people go to see a doctor and get a diagnosis of Parkinson's disease. As I said, it's a very special kind of tremor. It's not just any tremor; it's a resting tremor, so when the hand is quiet, often when someone is distracted. I will often ask, "Well, do you get the tremor when you're watching TV, reading the newspaper?" These kinds of things bring it out. Most people with Parkinson's can suppress the tremor, at least early on. They can make it go away by thinking about it, and when their mind is on something else, it comes back. We've talked about bradykinesia, rigidity, and fatigue is a very common symptom of early Parkinson's disease.

**[SLIDE 10]** Then later in the game a different set of symptoms become more prominent. These I would call symptoms that go with advanced Parkinson's disease. So impaired balance is a late feature. You don't usually see impaired balance in people in the very early stage when they just have tremors. In the first few years, it would be uncommon. And, in fact, if someone comes in and says, "Well, my first symptom was falling, my balance was really terrible, that was my first problem, they



may not have Parkinson's disease. They may have another syndrome, perhaps a condition like progressive supranuclear palsy (PSP) or another condition, but it would be unusual to have balance and falling as the first symptom of Parkinson's; and that should be a reason to take a deeper look into the diagnosis.

In advanced Parkinson's, you also start to see the complications of the medication. So, wearing off of medicines, dyskinesia, and we'll talk a little bit more about these are complications of the treatments of Parkinson's. Memory problems become more prominent in advanced Parkinson's; although there can be some mild memory problems early in the game, this is typically a feature of later Parkinson's. And then hallucinations, seeing things that aren't there; and we'll talk a little bit about those and how you might approach those.

But this is really the spectrum of symptoms of Parkinson's, going from the state really prior to diagnosis, when you can't make a diagnosis of Parkinson's, but the loss of smell is there, maybe REM behavior disorder is there, constipation is there. You can only put this story together, of course, by looking in the rearview mirror. Once you know that Parkinson's has developed, you can look back and recognize this pattern. But it's hard to see coming down the road at you, and this is an area where there's a lot of research going on to try and predict Parkinson's and maybe intervene because that's our hope for preventing Parkinson's in the future.

**[SLIDE 11]** Let me talk a little bit about how to establish a diagnosis of Parkinson's because this is a question I get asked about a lot. One of the things to know, as I said, is that the most common initial symptom of Parkinson's is resting tremor, at least 60 or 70% of patients who ultimately get diagnosed with Parkinson's, their first symptom is the tremor.

Other early symptoms though can be slow walking and impaired fine coordination. Just because tremor is the most common, that doesn't mean everyone has tremor. At least 30% of patients with Parkinson's disease do not have much tremor or have no tremor at all at the outset. So, making a diagnosis when the tremor is there and very characteristic is fairly easy. Trying to make a diagnosis when there's no tremor and there are other symptoms can actually be quite tricky, and you may need to find a physician who really has expertise to be able to do that.

So, when the tremor's there, usually fairly straightforward. When there's no tremor, it could still be Parkinson's. You've got to look for other features like slowness, bradykinesia, impaired fine coordination; and it may be a little more challenging to come to the correct diagnosis when there's no tremor.

It's a clinical diagnosis. So, at the end of the day, there is no test you can do while someone's alive that will give you a 100% answer as to whether Parkinson's is the correct diagnosis or not. But people with experience and neurologists who work in this area of movement disorder specialists can be very accurate. Their accuracy is 95% or more. But there really is no test that can be done in life that provides a completely certain answer. It's a clinical diagnosis.

And that's why we recommend consultation with a movement disorder expert. There are movement disorder experts at many major centers in the United States. One way you can find one is to work with the APDA. We have a network of so-called information and referral centers, and one of their



functions is to help people find connections with movement disorder experts; and so that's certainly a resource you can use. And you can find those in many areas around the country.

But consultation with a movement disorder expert is a good idea. Even if you have a community neurologist and you feel comfortable with them, you may want to make a one-time visit to a movement disorder expert just to be sure that the diagnosis is correct. And I have many patients who come to see me say once a year just for a second opinion, and they have a local doctor they work with, but they like to come and see an expert once a year; and I think that's a good idea because it helps you to stay connected with the latest discoveries and knowledge in the field which is constantly changing.

What about imaging tests? There is a scan. There's something called DaTscan, and this is a test of dopamine function. The way the test is done is we inject a radioactive dye in the blood, we have you wait about four hours, and then we put you in a scanner where we measure the uptake of this tracer, which binds to dopamine nerve terminals. And this can be very helpful in confirming a diagnosis of Parkinson's. Because the dopamine loss is significant, it's usually 70% at the time the symptoms are appearing, you should see loss of DaTscan uptake in people who have clinical Parkinson's disease.

Now does everyone need a DaTscan? No. If the diagnosis is clear from the clinical signs, there's no reason to get a DaTscan. It also doesn't really help to get a DaTscan if you have no symptoms at all because we really wouldn't take any action on that. The DaTscan is useful when you have symptoms but there's some uncertainty as to whether it's Parkinson's disease or not.

Just to give you some sense of this, at our clinic in Birmingham, Alabama, we see maybe 2,000 new patients a year who come for Parkinson's disease, and we do DaTscan on less than 100. So, it's certainly not a test for everyone, but it's very valuable when there's uncertainty about the diagnosis.

Another point about DaTscan is if you had a positive DaTscan, there's really no reason to do another one. They don't change that much over time, and they're not really useful for measuring the progress of the disease. They're useful for telling whether it's there or not in the first place.

**[SLIDE 12]** All right, so let's talk a little bit about treatment of early Parkinson's, and we said we were going to cover the spectrum here, so this will be a little bit brief because we have a lot of material to cover in our time here. But I want to walk you through some of the thoughts about how we approach treating Parkinson's in the earliest stages.

So, the first thing to appreciate about treating early Parkinson's is it doesn't always require medications. There are many patients who come to see us, and we make a diagnosis of Parkinson's disease. We discuss the implications of that with them, but they leave my office without a prescription because it's not necessary to treat every patient with medication. And that's an important thing to appreciate. You're not losing any ground by forgoing medication, there's no harm done by skipping medication in the early stages if it's not necessary, and many patients can wait months or sometimes even years before it's necessary to start medication for Parkinson's disease. So simply because you've made a diagnosis doesn't mean you have to jump right to a medical treatment at that point.



And the question of when to start and what medication to use is very individual, and it really depends on how bad the symptoms are and also their impact on lifestyle. So, I think the goal of treating Parkinson's disease is to enable people to go on to have a full and active and healthy life. And so, the medication should be used to try and reach that end. If the symptoms in early Parkinson's are maybe noticeable but not holding people back at all, there's no reason to jump in and prescribe a medication at that point.

On the other hand, I think it's important to be thoughtful about what the symptoms may be doing to someone's lifestyle. I do encounter patients where they say to me, "No, these symptoms don't really bother me." But when I start asking questions and say, "Well, do you go out?" And they say, "Well, I used to go out a lot, but I don't go out anymore." "Do you do any activities?" They say, "Well, I used to play golf, but I gave that up too." And so sometimes people are not really aware that the symptoms are progressively holding them back and limiting their lifestyle. So, it's something you have to be a little bit thoughtful about and really try to understand how much these symptoms are impacting this person's lifestyle.

Another aspect of it, of course, is how demanding is their lifestyle or their work? If they're working and the tremor is causing problems with fine coordination, they can't use a computer mouse, that's a major problem. If they don't really use computers and they're retired, well maybe that's not such a problem. So, it's a very individual decision, and you really have to talk with your physician about how these symptoms are affecting you and help your physician to come to this question of when is the right time to treat them.

The other part of this is that everyone with Parkinson's should have an exercise and wellness program. Now this is true, even if you're not on medication. I think that exercise and wellness is at least half the treatment of Parkinson's disease; and this, of course, is good for all of us as we age, but it's especially important in Parkinson's. And everyone with Parkinson's really should have an exercise and wellness program, and we'll talk about some of the elements of that in a second.

**[SLIDE 13]** All right, but before we get to that, let me talk a little bit about medications for early Parkinson's. So, if you and your physician have decided that medication is right at this moment, what are the choices? And I don't want to get too bogged down in the details here, but the major classes that we would consider for early Parkinson's are here. There's a group of drugs known as monoamine oxidase inhibitors or MAO inhibitors. One of these is rasagiline. It goes by the trade name of Azilect®. And here I will try to use the generic names for these drugs as I go, but the trade names are so common and patients know them, I've tried to put them in there just to make the connection for you. But I will do my best to focus on the generic names and not the trade names so much, so it doesn't get too confusing.

So rasagiline is a MAO inhibitor. It blocks the breakdown of dopamine in the body and can be useful in early Parkinson's. It's something I would say has a modest effect but also pretty well-tolerated. If that's not enough, we often move off into this group of drugs called the dopamine agonists. And that includes drugs like ropinirole; pramipexole; rotigotine, which is the drug in the patch; and then, of course, there's carbidopa-levodopa, which is still the mainstay of therapy in Parkinson's. Carbidopa-levodopa is, in my mind, the miracle of Parkinson's disease, as discovered really in the 1960s,



became available for patients in about 1969 through the work of George Cotzias and others. And this drug is by far the single-most effective drug for Parkinson's. I don't think anyone would disagree with that.

There are many forms of carbidopa-levodopa, but in early Parkinson's, we tend to use what we would call standard Sinemet®, the 25/100 tablet is by far the most common thing you would see in early Parkinson's disease.

Now which of these is the right choice for you? That's a much more complex discussion. It really comes down to, again, what is the goal? What are we trying to achieve here? How much symptom control do you need? And how much potential side effect risk do you want to run because really the drugs that are more potent and more powerful are more effective but also run a greater risk of side effects. So, this is where you really need to talk with your physician about what your goals are, what you're trying to achieve, and how these medications may help you with that.

**[SLIDE 14]** Let me talk a little bit about exercise and wellness because I think this is critical in early Parkinson's especially. So, the first point about this is an exercise program, I think, is essential for success in living with Parkinson's disease. And as I tell my patients, I've been doing this long enough now to have the chance to watch people for 15 or 20 years with this condition; and those people who can adopt an exercise program and make it a part of their life early in the game do so much better than those who don't that it's just remarkable.

And I think that exercise in Parkinson's is essential, and the time to start is as early as you can. People with early Parkinson's usually have no restrictions. They can do whatever they want. They can engage in different kinds of programs. They have a lot of options and engaging in that and making that a part of your life early on will pay off. It's never too late to add exercise, but the earlier you do it, it's like putting money in the bank. The sooner you invest, the bigger the payoff; and I do think this is very critical.

So what kind of exercise is the best? And this is actually a difficult question in the field. I would say many different forms of exercise have been shown to have benefit. High-intensity exercise has been shown to have benefit but so has things like tai chi and yoga. Boxing is very popular these days. Bicycling is very popular, either on the road or stationary bicycles if the balance is a problem. Yoga, there are just a whole variety of different forms; and we honestly don't know which one is the best. But many different forms have benefit.

The key thing about choosing a form of exercise is this. It only works if you do it, and that may seem like a silly point, but it's remarkable how many people I talk to who will discuss exercise, but you have to get out there and engage and do it.

So, in my mind, the best exercise for you is the one you're willing to commit to and do. So, if stationery bike is what you like and you enjoy that, or at least willing to do it, then that's great. If you don't like that, then you really have an obligation to find yourself another alternative. You have to find something that you're willing to do and that you can do three or four times a week. I tell people to shoot for three or four times a week, maybe at least 20 minutes at a time as a beginning; and if you can go beyond that, great. But, again, it's really a critical part of the program.





All right, diet, I get a lot of questions about diet and Parkinson's. It should be a balanced diet. You want colorful fruits and vegetables. Fiber is very important. Constipation is a big factor in Parkinson's, and fiber and water are really the beginning of that.

And then the last point about this is it's important to stay well-hydrated, especially in hot weather or with exercise. So, if we're going to work hard or exercise, stay hydrated. That's a critical factor in success here.

**[SLIDE 15]** All right, so let's talk a little bit about some of the symptoms that develop in more advanced Parkinson's disease. So, we'll begin with "wearing off" because this is a very common symptom. So, what is wearing off? Wearing off means losing the effect of medication at the end of the dose interval.

For example, if someone is taking carbidopa-levodopa three times a day, they're probably taking it about every six or seven hours. And when they first start on this treatment, they may find it works all day. It works day, it works nighttime. They don't really have any interruptions in the response. But after several years they'll find that, well, these pills just don't last as long as they used to. I'm running out of gas at five hours, and my next pill isn't due for six or seven. And that's wearing off, loss of effect at the end of the dosing interval.

It's pretty common. You'll see it in at least 50% of people who are on levodopa after five years of treatment. And when it's mild like that, it's not so troublesome. But over time it can become more annoying.

As I said, it's most often seen with carbidopa-levodopa. It can be seen with the other drugs, but by far the carbidopa-levodopa is the most frequent cause of this. Now, it's also the most effective medication. As I said, about half of patients will have wearing off after about five years of treatment with carbidopa-levodopa, and it tends to worsen with time. It starts out mild but then becomes very annoying. And when it reaches the point where the wearing off is sudden and sometimes unexpected, it's difficult to go out. You can't go out to a store if you're afraid your medication is going to suddenly wear off and leave you stranded somewhere. So, this is a problem that creeps up on people. It starts off as a mild issue, and it gets more troubling over time.

**[SLIDE 16]** So what do you do to manage this symptom of wearing off? What are the options for managing wearing off? A lot of the options for managing wearing off are different manipulations of medication, and I'll take you just briefly through a few of these different alternatives.

One is to change the timing. So, obviously, if you are experiencing wearing off after six hours, well, you could move the doses closer together. You could go from three times a day to four times a day. You can go from four times a day to five times a day. But, of course, there's a limit to this. Once you get up to taking pills six or seven times a day, it gets quite inconvenient and hard to keep track of. So, changing the timing, moving the time around can help; but there's a limit in how far you can take that.

What about extended release? If the problem is that the medications are wearing off, can you stretch out the effect of the medications? And there are a number of different ways that have been derived to do this. And if you're using carbidopa-levodopa, one way is a combination called Rytary<sup>®</sup>, which is a



slow-release form of carbidopa-levodopa. There are also long-release forms of ropinirole and pramipexole, so these are extended-release pills that release the medication slowly over 24 hours.

Another way to go is to slow the breakdown of the drugs in the body. So, if you can make the drug stay around longer, particularly the levodopa, which is the drug that really has the biggest effect, you can reduce this wearing off. So, there's a class of enzyme inhibitors called COMT (catechol-O-methyltransferase) inhibitors. These include entacapone; that's the drug that's in Comtan<sup>®</sup>. It's also in Stalevo<sup>®</sup>. It gives you a longer action. Rasagiline can also slow the breakdown of levodopa, and then a newer drug called safinamide also works to slow the breakdown of levodopa. So, all of these are useful for wearing off, for extending the duration of the pills.

Well, if that's not working, what else is there? There are so-called rapid treatments. These are treatments that you might use if your drugs have worn off and you're stuck, and you need to get moving quickly. One which has been available for quite some time is apomorphine injection, also called Apokyn<sup>®</sup>. And then there's a brand new one. This is an inhaled levodopa formulation called Inbrija<sup>™</sup>. This is so new that we don't even have it yet available in our clinic and, honestly, have not used this in a patient yet. The clinical research looks promising, but it's just come on the market. So, these are two strategies for very rapidly getting medication in your system to get going when the medicines have worn off.

And, lastly, it is important here to mention diet. I said in early Parkinson's the diet is typically a healthy balanced diet with fiber is okay. What you find in people with more advanced Parkinson's is that there are some people where dietary protein is a problem, that they find if they eat a high protein meal, their medications no longer work, particularly the levodopa. And this is a competition between the protein that you're eating, which is made up of amino acids, and the levodopa, which is an amino acid. And they can compete with each other to get into the blood and into the brain. You can recognize this if you find that you have a high protein for breakfast. You have eggs for breakfast and the morning medicines don't work, that's a clue this could be a problem. And if so, you may want to work with your physician and a dietitian to redistribute the protein through the day to try and improve this. You, of course, can't live with no protein; so that's not an option. But you can change the timing of the protein and the kinds of meals you eat to try and help with this.

How common is this? It's not that common to see this dietary interference with protein. I would say it's less than 10% of the patients that I see. But when it happens, it can be quite annoying.

**[SLIDE 17]** Let's talk a little bit about dyskinesia. So, this is another complication of advanced Parkinson's disease. So, what is dyskinesia? It's a form of chorea. So, chorea is a word which means dance-like. So, it's a writhing, continuous movement; and sometimes patients confuse this with tremor. I've had a lot of people come and say, "My tremor's bothering me." But really when you look at it, they're not having the kind of rest tremor or slowness, stiffness that they had before they were on medication. Now they're having abnormal, involuntary movements, they're writhing, they can't sit still. And this is dyskinesia. This is most commonly seen actually when the medication level is too high in your system.

Again, it's something you don't see early in Parkinson's. Even with high doses of medicine, dyskinesia doesn't generally appear in the early years. But five years and later, you'll start to see



dyskinesia; and usually it's obvious when the medications are high. So, if you take carbidopa-levodopa, that drug is going to get in your system maybe an hour later. It's going to hit a high level, and that's when the dyskinesia is going to appear.

Mild dyskinesia doesn't necessarily have to do anything about it. Some people actually prefer the feeling of a little mild dyskinesia to the feeling of the medicines being too low, leaving them stuck and slow. So mild dyskinesia doesn't really necessarily need to be treated. But, obviously, if it gets severe, it can really become disabling; and this can become a major problem.

Medication timing is very important in dyskinesia, and so looking at the timing, how much medication are you taking, what are the different times that you're taking can be really helpful in sorting this out and trying to alleviate dyskinesia.

If that doesn't work, there are medical treatments for dyskinesia. The main one is a drug called amantadine, and this is an old drug. It's been around for many years, since the 1950s. Actually, it was developed to treat the flu originally; and so-called standard amantadine has been around for a long time. There's also now a once-a-day extended release amantadine that goes by the name of Gocovri™, and both of these are useful if you're trying to suppress the dyskinesia that you can see in advanced Parkinson's.

**[SLIDE 18]** Let's talk a little bit about beyond medication. So, if you have wearing off and dyskinesia, and you've tried all of these things with the medications and it's really not doing the job, what are your choices? Well, there are some options that can be very effective. One that's been on the market now for more than 15 years is deep brain stimulation (So, this is a treatment where we implant an electrode in a certain region in the brain called the subthalamic nucleus or sometimes the globus pallidus. There's a pacemaker-like device in your chest, and we treat the Parkinson's electrically.

This is potentially useful for all the symptoms. It can help the tremor, the stiffness, the slowness. It can suppress dyskinesia, and it's particular good at suppressing tremor and dyskinesia. So often these are hard to control in other ways, and deep brain stimulation can be useful.

There's a new generation of deep brain stimulation devices coming as well, so we've been using pretty much the same device since this technique was invented; but coming on the market now are a bunch of devices which are newer, which are smaller. Some of them are rechargeable so you don't have to change the batteries. So there really is a revolution going on here and better and better deep brain stimulation techniques. And you'll see this happening over the next few years.

There's also a technique called levodopa gel intestinal infusion, and this takes advantage of the idea that the problem with levodopa is the medicine wears off. So, if wearing off is a big problem, you can put a tube. It goes in through the stomach, and it threads out to the intestines. You have a pump, and you infuse this levodopa gel which goes by the name of Duopa® usually 18 hours a day. And this is very useful for wearing off as well. So, if your medicines are wearing off and you go to a continuous infusion, that can certainly have a major benefit in terms of reducing or perhaps eliminating that wearing off.



Probably get a lot of questions about focused ultrasound. This is a technique that is a way of making a lesion in the brain. So, it's a technique there, you're actually creating a hole in the brain using ultrasound waves. Now there's a surgery required that waves go right through the skull and are focused on a spot on the brain and produce a hole in just the right location.

This has been FDA-approved now for several years for treating essential tremor and now has FDA approval for treating tremor in Parkinson's. At least as currently used, focused ultrasound is primarily useful for the tremor. I don't really expect the current approach to be that helpful with the other symptoms, but sometimes tremor is the main problem in Parkinson's; and this may be a useful new approach. It's still a fairly limited availability, and only a few centers are offering this at this time.

**[SLIDE 19]** All right, well let's go a little bit farther and talk about just a couple of other late complications of Parkinson's disease. One of these is memory problems, and I will make the point that mild memory problems are very common in Parkinson's. So just having trouble coming up with a name, being a little slow with a word, this is very common in Parkinson's disease and usually not necessarily a sign of worse problems to come. But it is true that up to 30% of Parkinson's patients may develop more severe problems to the point where it really does limit their life and they have difficulty taking care of their affairs and interacting with their world, and this can be a serious problem in perhaps up to a third of Parkinson's patients.

What do you do when memory problems are developing in Parkinson's disease? Well, I think the first step is actually to try to look at factors that might be contributing and see if you can change them. One of them is medications. So, some medications can definitely worsen memory. One that is notorious is this drug trihexphenidyl, also known as Artane®. It's often used early in treating Parkinson's for the tremor, but sometimes what happens is people stay on this for years and years and eventually contributes to memory problems. So, when people complain to me about memory difficulties, I always look for this; and if you're having memory difficulties, you probably should come off this medicine. It really does aggravate memory quite a lot.

Infections can cause memory problems, bladder infections, lung infections. And another thing that really is important to look for is sleep apnea. So, people who are snoring at night, they're pausing in their breathing, waking up with sudden starts and gasping may actually have sleep apnea; and they aren't getting enough oxygen to their brain, and sometimes just fixing that can have a big benefit in memory in Parkinson's.

If you have looked at all these things, what else can you do? There are drugs. There's this drug called rivastigmine, which is a drug originally developed for Alzheimer's, but it is helpful to a degree in Parkinson's and these enhance acetylcholine function, so these may be a useful option too.

**[SLIDE 20]** All right, let's talk a little bit about hallucinations. Hallucinations can be a major problem in Parkinson's as well. They are more common in advanced Parkinson's disease. Often, they have a bit of a progression. Patients often first see simple things like the curtain looks like a waterfall, a shadow is moving, a tennis ball looks like a mouse – these kinds of things.

Then you get small furry animals and other critters, sometimes people are in the room. They see people and perhaps people they recognize or don't recognize. And then the later stage of this, they



can become quite disturbing. People see things that are frightening, that are disturbing, and they may act on them. I've had patients run away from hallucinations and really injure themselves. So, I think this again is an individual kind of question. If you're talking about very mild symptoms of just a shimmering of a curtain that might be a waterfall for a split second or something like this, maybe you don't need to overreact to that. But when patients are frightened by their hallucinations, concerned about them, or acting on them, that's a very serious problem and really needs to be addressed. So, again, it's an individual solution. But if you get the sense that you are seeing things that aren't there or that your person that you're caring for is, it's very important to talk to the physician about it because it will have a big impact on what drugs they might treat them with and how they might change their treatment.

Hallucinations are often aggravated by the dopamine medicines that we treat Parkinson's with. So, when this is a problem, thinking about can we cut these back, especially the dopamine agonists, the pramipexole, and the ropinirole is an important step.

There is a drug that's specifically approved for treatment of hallucinations, a drug called pimavanserin. So, this can be used. You'll also see a drug called quetiapine used. This does not have specific FDA approval, but many practitioners in movement disorder also use this for treating hallucinations in Parkinson's.

And there's some drugs you should stay away from. Haloperidol is one of them. There are other drugs. These all block dopamine and will make Parkinson's much worse, and there's a list on the APDA website of drugs to be avoided. I recommend that all my patients carry around a copy of this list of drugs to be avoided because sometimes you might go to a small medical facility, and they're really not aware of it. It's important to have this information.

**[SLIDE 21]** Lastly, I want to touch on a tool that you can use to help track some of these symptoms. The APDA is working to develop this. This is a new healthcare communication graph, and you can find this on the APDA website as well. And this is something that you can use to track some of these troublesome symptoms and help share them with your doctor. We all know that doctor visits are too short. You only get a few minutes to make your points and get your information across; and if you can put some of it together in advance in this way, I think your physician will find it very helpful.

**[SLIDE 22]** So with that, I will make one more point here which is the future of Parkinson's treatment. So, we've talked about treating symptoms, but really the future here is trying to prevent the progression of Parkinson's. And this graph illustrates this idea. It has a line above it labeled Normal Aging, suggesting we do see some decline in our function over time with aging. But in most people, it stays above the purple zone. It doesn't enter the zone where we can recognize neurodegeneration.

In Parkinson's, something happens, we turn the corner, there's a more rapid progression, and you see the symptoms of the neurodegenerative disease. And what we're all after is a treatment that would change this downward slope. And if you could protect the brain from the process of Parkinson's, you could either slow the progress or perhaps if you can apply it in this pre-Parkinson's period, you might prevent the actual symptoms of Parkinson's from appearing. And so, I think this is where much of the energy and research is, and I hope this is the future we're going to.



**[SLIDE 23]** So my concluding points here, the symptoms of Parkinson's change continually; and you have to adapt your strategy accordingly. So, it is a process of continual change.

Exercise, balanced diet, and hydration are important at every stage of Parkinson's disease. This is really an essential part of the plan.

In early PD, when to start the medication is often the biggest issue. It's not so much which medication but when to start is the biggest question.

In advanced PD, you really have to have strategies that fit the different symptoms you may be experiencing, and this is really a process of working with your physician and adapting to these different developments. And as I said, periodic consultation with a movement disorder expert can be very valuable in this process.

So, with that, I will conclude my remarks and will be happy to take some questions.

## Question & Answer

**Stephanie Paul**

**[SLIDE 24]** Thank you, Dr. Standaert, for your very detailed and informative presentation today.

It's now time for the Question & Answer session.

**Stephanie Paul**

Okay, we'd like to begin with a Web question, and this comes from Nalene, and the question is, "How does Parkinson's affect cardiac heart rate?"

**David G. Standaert, MD, PhD**

So, Parkinson's can affect cardiac heart rate, and Parkinson's affects the so-called autonomic nervous system which controls all the autonomic functions of the body – the bowels, the heart rate. One of the things you may see early on is a loss of heart rate variability. So normally the heart rate goes up and down. But if there's a loss of innervation of connection to the heart because of Parkinson's, the heart may just stay at a steady rhythm. That is really most troublesome when you're exercising. You may find it's difficult to get your heart rate up because of Parkinson's. The other issue is that Parkinson's can cause low blood pressure. It tends to lower the blood pressure, and the medications make that worse. So, staying hydrated is very important.

**Stephanie Paul**

Okay, we have our next question from the Web. This comes from Douglas. "How about yawning fits?"



**David G. Standaert, MD, PhD**

How about yawning fits. So yawning is a very interesting phenomenon. Obviously, all of us yawn. But one of the things that can trigger yawning is dopamine drugs, and so I've noticed a number of times I've seen patients with this. Some of the dopamine drugs, particularly pramipexole and ropinirole, can be a trigger for yawning and excessive yawning. So that's at least something to look at if you're having that problem.

**Stephanie Paul**

Okay, thank you. We do have a caller on the telephone, so if we could please take that question.

**Operator**

Our first call is from Ellen from Ohio. Ellen, please state your question. Your line is now live.

**Ellen, from Ohio**

Is parkinsonian diagnosis the same as Parkinson's diagnosis?

**David G. Standaert, MD, PhD**

Okay, so the question is whether parkinsonism or parkinsonian symptoms are the same as Parkinson's disease? So parkinsonian symptoms or parkinsonism means that you have at least two of those four symptoms I put up on the slide – tremor, slowness, stiffness, postural imbalance. Does that mean that it's Parkinson's disease? No, because there are other causes of parkinsonism. I would say most people who have parkinsonian symptoms turn out to have Parkinson's disease, but other causes are drugs, like medications like haloperidol can take a normal person and make them look parkinsonian. There are also other degenerative disorders, such as PSP and other rarer conditions. So, this is part of the process of going from symptoms to diagnosis that a movement disorder expert can help you sort out.

**Stephanie Paul**

Okay, thank you, Dr. Standaert. We have another Web question, and this comes from Christina. "Are there any types of exercises that actually have shown to slow the progression of a particular symptom?"

**David G. Standaert, MD, PhD**

Well exercise has definitely been shown to improve symptoms in Parkinson's disease, so there have been nice studies on high-intensity exercise; but even things like Tango dancing has been shown to reduce falls in Parkinson's disease. So, all of these have been shown to have benefit in terms of symptoms.

Now what we'd all like to know is whether these exercises also benefit the brain. Do they slow the underlying disease process? And there is some evidence that this is true in animal models. So, if you



exercise rodents modeling Parkinson's, you can actually slow the rate of degeneration. This has never been shown in humans yet, but it is of a lot of interest.

So certainly, it makes the symptoms better. Whether it's actually changing a degenerative process in the brain for the better as well remains unknown. But I recommend exercise anyway because it will certainly improve your symptoms, and it may well slow the process in the brain.

### ***Stephanie Paul***

Thank you, Dr. Standaert. We have another Web question coming from Merriam, and the question is, "Do you recommend taking taurine or other dietary supplements to maintain cognitive abilities?"

### ***David G. Standaert, MD, PhD***

Right. So, the question about dietary supplements for cognitive abilities, and taurine is one that has been used over the years. I think the trials in Parkinson's have, unfortunately, been not that convincing. Most of these dietary supplements we've not really been able to show a clear effect. And those that we've tested really rigorously like vitamin E clearly, most unfortunately, have no benefit in Parkinson's. So, I don't really recommend dietary supplements beyond, as I said, a healthy diet, colorful fruits and vegetables, which tend to be rich in antioxidants.

### ***Stephanie Paul***

Okay, so along the lines of that question, there is another question from the Web from Shahir, and the question is, "I would like to know more about the role of natural supplements such as velvet bean and green fava beans in controlling PD."

### ***David G. Standaert, MD, PhD***

Well, those are very interesting. So those beans, particularly one that goes by the name of *Mucuna pruriens*, what those beans have in them is levodopa. So those are a natural source of levodopa, which is the same compound that's in Sinemet. The downside to the beans, I find, is that the amount of levodopa in them varies a lot. And so, patients have trouble with them because one batch of beans doesn't have very much. The next batch of beans has a really large amount of levodopa. It's unpredictable. They, obviously, aren't measuring this in different batches.

So, yes, there are many people who've noticed that beans from this family, the fava beans and *Mucuna pruriens*, will see that they get at least a temporary benefit in their symptoms from the beans. But over time it becomes hard to manage because of the unpredictable dosing that's going on. So generally, it doesn't work out that well in the long run, and they're better off with a Sinemet tablet which isn't very expensive and is a measured and known quantity.

### ***Stephanie Paul***

Terrific. Thank you, Dr. Standaert.

We have a question coming from the phone. If we could please take that.





### **Operator**

Our next call is from Rose from California. Rose, please state your question. Your line is now live.

### **Rose, from California**

Hi, good afternoon. I have a question. I have dysphasia, which is not being helped by my Sinemet. Are there any medications I can take to address this?

### **David G. Standaert, MD, PhD**

Right, so the question is about dysphasia, which is a problem in Parkinson's disease. People do get swallowing dysfunction. But I think you have to dig a little deeper into the cause of the dysphasia. There are a number of different problems that can trigger dysphasia, some of them related to vocal cord problems, others are motility of the oral pharynx. And usually Parkinson's alone is not really enough to get people to the point where they can't swallow at all. So usually when this arises, I recommend seeing an ENT (ear, nose, and throat doctor) and usually getting a video study of the swallowing to really understand what the nature of the swallowing dysfunction is.

### **Stephanie Paul**

Okay, terrific. Let's now go to a Web question, and this comes from Karen. "Along with being in early stage PD, I have severe gastroparesis, and I'm unable to take meds for the PD because of how sick they make me as well as lowering my blood pressure. Any suggestions for alternatives for me as my symptoms are escalating?"

### **David G. Standaert, MD, PhD**

Right, well, having difficulty tolerating medications is a big problem because most of the medicines we have for Parkinson's disease are oral medications. Now the one approved medication we have, which is not a pill, is the rotigotine patch; and I have had some patients who simply couldn't tolerate any oral medications at all and have had some success with the rotigotine patch because it's transdermal and absorbed through the skin. So that would be one thought.

Other options, if it really came to it and it was really quite severe, you could think about things like the Duopa pump because that does bypass the stomach; and that medication is delivered directly in the intestines. Now, whether that's really necessary for you or not, I'm not quite sure I could answer; but that is at least two strategies that we can use that don't involve absorbing pills through your stomach.

### **Stephanie Paul**

Okay, terrific. We have another caller. Let's take that question please.

### **Operator**

Our next call is from Joseph from New Jersey. Joseph, please state your question. Your line is now live.



### ***Joseph, from New Jersey***

Yes, I'd like to ask about severe weight loss and loss of appetite. Food is not appealing.

### ***David G. Standaert, MD, PhD***

Yes, so weight loss is a problem in Parkinson's, and I get quite concerned when my patients lose a lot of weight because if you lose a few pounds, that may actually be a good thing. But if you get into severe weight loss, usually you're losing muscle and you're losing strength, and that sets you up for falling and all kinds of other problems. So, I always consider really marked weight loss in Parkinson's to be a serious problem.

In terms of the food not tasting like anything, usually that is the loss of sense of smell. The smell of food is actually what drives a lot of our perception of the taste. And losing sense of smell can be a big problem.

In terms of fixing that, we can't really fix the sensation of it. I do recommend people with weight loss get checked out by their doctor to make sure something else isn't going on. Weight loss can also be a sign of other serious gastrointestinal disease or even cancer. But once that's been ruled out, then it involves working with foods, focusing on more savory foods, calorie counts, going to some high-density foods. But it's important to maintain your weight in Parkinson's, and that can be a chore. It can get to be challenging.

### ***Stephanie Paul***

Okay, another question from the Web. This comes from Marie. "Are there any vision problems associated with Parkinson's?"

### ***David G. Standaert, MD, PhD***

Yes, there are some vision problems associated with Parkinson's. So early on you can see a little bit loss of color sensitivity, so loss of red color particularly. Most people don't notice that, but we can see that testing it.

The common problem I hear about is double vision. So, in Parkinson's, what can happen is there's some slight slowing of the eyes; and because one eye may slow just a little bit more than the other, there's double vision, particularly looking quickly from one spot to another. This can be very annoying. It doesn't usually get severe, but it's annoying. When it's a problem, I do sometimes refer to some of our neuro-ophthalmologists who can adjust this with lenses, by adjusting of the glasses, and putting prisms in, these kinds of things. But I think it's one of these mild but annoying problems you can develop in Parkinson's.

### ***Stephanie Paul***

Okay, terrific. We have another caller. If we could take that please.



## ***Operator***

Our next call is from AI from New York. AI, please state your question. Your line is now live.

## ***AI, from New York***

Yes, hello. I've been diagnosed for about four years now. I'm considering DBS, but I'm wondering if having the procedure this early will affect my treatment options later on, and my Sinemet doses are very close together at this point.

## ***David G. Standaert, MD, PhD***

Right, so this is a question about what is the timing of deep brain stimulation. So certainly, the traditional approach to this has been to use deep brain stimulation once we've exhausted medical therapy. So, patients who are taking a lot of carbidopa-levodopa, having worn off, having dyskinesia, those are the patients who have generally been recommended to have DBS in the past.

Now there is some research recently and there's a movement afoot to do DBS earlier in the course of the disease, and there's actually been several studies published suggesting there may be a benefit to doing it earlier than we traditionally would. And those are small numbers, but I think the data are interesting; and as the technology for DBS gets better one of the challenges right now is you have to replace the batteries every two or three years in DBS. But if we get to where the battery is rechargeable, and it might last 15 years or more, that would change that as well.

So, in the end, it's an individual decision; but as with many things in Parkinson's, I think you have to ask how is this disease affecting my life? Is this really holding me back? And if it's holding me back, I ought to think about taking the next step in the course because a lot of people save treatments for a rainy day when it's pouring outside. And it's important to focus on moving ahead today sometimes with these treatments.

## ***Stephanie Paul***

Okay, thank you. We have time for one more question, and it's from the Web. It comes from Sandy, and the question is, "I am concerned about my husband's focus and driving abilities. He refuses to discuss it. Any suggestions would be helpful."

## ***David G. Standaert, MD, PhD***

Yes, this is a major problem. People with Parkinson's can have trouble driving, either because of the cognitive symptoms or simply the physical symptoms. But as we all know, taking away driving privileges is a major problem in our culture and our communities. Many of our cities are not set up for people who don't drive.

What we do in the clinic when this question comes up is, we recommend a formal driving evaluation, usually done by an occupational therapist or a driving instructor, because that really takes all the personalities out of the question. And most of my patients will accept the idea that if they can pass a



driving exam, they can go back on the road; and if they can't, they should stay off. And I think that route is much more helpful in a lot of these situations.

## Closing Remarks

### *Stephanie Paul*

**[SLIDE 25]** Dr. Standaert, thank you so much for this wonderful information today. And my thanks to everyone for participating in today's telephone and Web education program. I do apologize that we couldn't get to all of the wonderful questions, but if you have a question or would like to speak with someone from our Scientific and Medical Affairs Department, **[SLIDE 26]** I encourage you to visit our website at [apdaparkinson.org](http://apdaparkinson.org) or call 1-800-223-2732 and you can ask your questions there.

I want to emphasize to everyone on the phone that we really do appreciate your feedback and comments and want to make sure you complete the program evaluation form.

APDA is proud to support those living with Parkinson's disease by helping them live life to the fullest every day. We do this each year by providing more than 1,700 support groups that serve more than 75,000 people with Parkinson's disease and their family members and through running 770+ exercise groups attended by more than 21,000 participants.

These exercise programs help improve the symptoms of Parkinson's and lessen the impact of the disease. We also offer educational symposia across the country on living well with the disease. These programs have been attended annually by more than 5,500 people impacted by the disease, and we rely on the support of the entire Parkinson's community to accomplish all of this.

To join us in the fight against Parkinson's and to learn more about the support APDA provides across the country through our network of chapters and information and referral centers, as well as our National Research Grant Program and Centers for Advanced Research, please visit us at [APDAparkinson.org](http://APDAparkinson.org).

We all agree that being informed about your disease and treatment options is the best way to empower yourself and take control of your care. Have a wonderful day.