Transcript

Welcome and Introductions

Cathi Thomas, MS, RN, CNRN

[Slide 1] Welcome everyone and thank you so much for joining us today. **[Slide 2]** My name is Cathi Thomas, and I am the Program Director of the Parkinson Disease and Movement Disorder Center and also the Coordinator of the American Parkinson Disease Association Information and Referral Center at Boston University Medical Campus. I am pleased to welcome you to this Web education program designed for people with Parkinson's disease, their care partners, family members, and healthcare providers.

I would like to thank Acorda, Boston Scientific, and Lundbeck for sponsoring this important program and acknowledge their appreciation for the critical need to provide educational programs like this one to people impacted by Parkinson's disease (PD). During this time of uncertainty, we know that you will have concerns regarding your Parkinson's treatment and identifying ways to continue to live your best life with Parkinson's disease. The American Parkinson Disease Association, or APDA for short, 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. APDA distinguishes itself as a national organization working one on one with the Parkinson's community to make each day better.

[Slide 3] And now to our program. I would like to welcome Dr. Marie Saint-Hilaire who is Professor of Neurology and Medical Director for the Parkinson's Disease and Movement Disorders Program and Director of the APDA Center for Advanced Research at Boston University, Boston University Medical Center.

She will join me today in discussing what's new in Parkinson's disease treatment. After the presentation, we will open the program for questions from all participants.

Presentation

Marie Saint-Hilaire, MD, FRCPC

Hi, I'm Dr. Saint-Hilaire. I am the Medical Director of the APDA Advanced Center for Research in Parkinson's disease at Boston University. Thank you very much for watching this webinar today, and I want to thank the APDA for this invitation. It's always a pleasure to participate in these programs.

[Slide 4] So these are our financial disclosures.

[Slide 5] So, over the past few years, there have been a few new medications that came out for Parkinson's, including some that were approved just before the COVID (coronavirus disease [COVID-19]) pandemic and will be available this fall. So, what I will do is that I will start by doing a quick overview of the current treatments, and then I will talk more in detail about the new medications and the new developments also in the surgical therapies.

[Slide 6] So first, let's review the current treatments. **[Slide 7]** So this is a very busy slide. You will notice that the medications work in many parts of the basal ganglia or the area of the brain that is lacking dopamine. This is a schema where all the PD medications act in the brain. There are several mechanisms of action, but the goal is to increase and prolong the levels of the dopamine or the action of the dopamine in the brain. So that can be done by giving the precursor of dopamine, levodopa, which you see at the top of the slide; and the levodopa goes into the brain and is turned into dopamine.

There are also medications that prevent the degradation of levodopa called COMT (catechol-O-methyltransferase) inhibitors, like entacapone and tolcapone there on the left, on top, on the left of the levodopa there on the screen.

There are also medications that prevent the degradation of dopamine in the brain so that boost the levels of dopamine in the brain. And these are MAO-B (monoamine oxidase-B) inhibitors like rasagiline and selegiline, so you will see them sort of like in the middle of the slide in teal.

There are also medications that mimic the effect of dopamine in the brain by stimulating the receptors for dopamine, and these are the dopamine agonists such as pramipexole and ropinirole. So, you will see them also in the middle of the screen in teal next to the MAO-B inhibitors.

The anticholinergics, which are shown on the left in brown, like trihexyphenidyl or Artane, they reestablish the balance between the acetylcholine and the dopamine in the brain. There's not enough dopamine, and by consequence the action of the acetylcholine is predominating.

The amantadine, which is next to the anticholinergic in green, has a mixed mechanism of action. It acts on the dopamine neurons. It is an antagonist of a receptor called the NMDA receptor, which is a glutamate receptor, which increases the release of dopamine and blocks the dopamine reuptake by the neurons so there's more dopamine around and also has some anticholinergic properties and side effects, and it is the only medication that helps for dyskinesias in Parkinson's disease.

Finally, there's a medication that is in a category all by itself called istradefylline or an adenosine inhibitor, which is in purple at the bottom of the screen. It's an adenosine A2A receptor antagonist, so it's a nondopaminergic therapy. It's the only one so far. So, its precise mechanism by which it can improve Parkinson's disease symptoms is unclear, but it is thought to reestablish the balance between the pathways of motor control in the basal ganglia of the brain. There are some very complicated pathways in these basal ganglia, and when you have a lack of dopamine, there is an imbalance between these pathways, causing the symptoms of Parkinson's. And it is thought that the adenosine A2A antagonists will reestablish the balance between the two pathways. So, it was also observed that there's an increase in these adenosine receptors in Parkinson's disease, so they might have a role to play.

So, patients wonder why they're on so many medications as the disease progress. Why am I on the dopamine agonist and on levodopa and on amantadine, and now you just added an adenosine inhibitor. It's because all these medications work on a different pathway to increase the dopaminergic activity in the brain, and the effects complement each other, so it is very frequent for people who have Parkinson's to be on several medications as the disease progresses to control their symptoms.

[Slide 8] So, this is the list of all the levodopa preparations. So besides levodopa-carbidopa immediate release or Sinemet®, and there's a controlled-release form, there's a form called Parcopa® which melts in the mouth, and it's useful for people who have difficulty swallowing. We're going to talk more in detail about the extended-release capsule, Rytary®, in green there and the inhalable form of levodopa called Inbrija®. We're also going to talk about the intestinal drug called Duopa™.

The COMT inhibitors, the category behind the levodopa, are given with levodopa. They prolong the effect but have no effect if given alone, so you don't take any of these medications by itself. You take it combined with levodopa. Now there's one pill called Stalevo® that combines the levodopa and a COMT inhibitor together, so you just have to take one pill instead of two pills. There's a newly approved medication in that COMT inhibitor category called opicapone or Ongentys®, and we're going to discuss more in detail.

[Slide 9] Now the dopamine agonists, there are several. The ones that are used most are ropinirole and pramipexole, which are generic; and there's an immediate-release form and a long-acting form for each of these medications. These long-acting forms are taken once a day.

These dopamine agonists are effective by themselves, so given as a first-line therapy to help the symptoms of Parkinson's, and they can be used also, added to this levodopa later on if the person has more complications.

Rotigotine is a patch, and apomorphine is either injectable or sublingual. So, the apomorphine is used as a rescue medication. The new sublingual form of apomorphine, Kynmobi™, was very recently approved; and we're going to discuss more about it later.

[Slide 10] We're going to talk also more about Nourianz™ or istradefylline, recently approved as an adjunct to levodopa. It's the only medication in its category because it doesn't have a dopaminergic mechanism. It's that adenosine A2A inhibitor I discussed before.

The MAO-B inhibitors include selegiline and rasagiline and the form of selegiline that is absorbed in the mouth called Zelapar™. They may be used early in the disease without levodopa or later on in the disease to help levodopa last longer. Xadago™ or safinamide has activities of an MAO-B inhibitor as well as other activities.

Finally, amantadine improves tremors, stiffness, and can be given alone to relieve the symptoms of Parkinson's before starting levodopa. We are going to talk more about the extended-release forms, Gocovri™ and Osmolex®; and as I mentioned before, amantadine is also the only medication that we have that can improve dyskinesia.

[Slide 11] So as anybody who has Parkinson's knows, there are medications for motor symptoms of Parkinson's; but a lot of people who have Parkinson's also have nonmotor symptoms, whether they have mood disorders, low blood pressure, constipation.

So, there are two recent medications that have been approved. One is for hallucinations in Parkinson's. It's called pimavanserin or Nuplazid® and one medication for low blood pressure called droxidopa or Northera®, so we're going to discuss these medications more in detail.

There's one medication that has been approved a long time ago for cognitive issues in Parkinson's disease called rivastigmine. There's a generic pill but there is also a patch called Exelon®, and the patch form is not generic, but the pill is generic.

[Slide 12] So, let's discuss more about the newly approved medication. You may have noticed these medications address the events in motor symptoms of Parkinson's such as fluctuations and dyskinesias as well as the nonmotor complications of Parkinson's.

[Slide 13] So, Rytary is an extended-release form of levodopa-carbidopa in the capsule. So, each capsule contains both beads of immediate-release levodopa and extended-release. So, you can even open the capsule and put the beads in the applesauce if you have difficulty swallowing. But I just want to warn you not to give them through a gastric tube or G-tube because it will clog it. Trust me, I tried it, and it didn't work well.

So, it's supposed to be a long-acting medication, but that doesn't mean that it is given only once a day as some of the dopamine agonists. Most people take it a minimum of three times a day but often four to five times a day. The dosage, as you see, is quite different than the regular levodopa-carbidopa. It's almost like starting a different medication, and the patient may need quite a few adjustments to get the dosage right. So, you have to work with your neurologist before you find the right schedule and be patient with it. You cannot just change it milligram per milligram from an immediate regular-release levodopa to the Rytary.

It's good for people who take their medication very often, some people, as the disease progresses, have to take their Sinemet like every two hours, eight to ten doses a day sometimes. So that decreases the number of times you have to take your medication and hopefully smooth out the off time.

[Slide 14] Another way to help with the off time if you have bad motor fluctuations, is with Duopa. It's an intestinal gel containing levodopa and is given through a tube inserted in the small intestine. So, it allows to provide continuous delivery of levodopa for 16 hours of the day, so during the waking hours [and]has to be started at night. The infusion rate is programmed to provide continuous on time for patients who have motor fluctuations. And there's also the possibility for the patient to give themselves little boosts if necessary, like first thing in the morning to get started or before doing exercise, for example, could give yourself a little boost or if you feel that you're wearing off a little bit. That's another possibility. There's also reports that long-term use of Duopa® will decrease dyskinesias.

[Slide 15] Inbrija® is another form of levodopa. It is a rescue form. Levodopa is put into a powder that is inhaled, and it's directly absorbed through the lungs, which may be absorbed much faster than taking it as a pill by mouth. And it can be used up to five times a day. It works best when the patients feel the off coming, so don't wait until your off is really bad to take the Inbrija. It might be too late. When you feel your off coming, either the tremor coming back or the stiffness or the gait difficulties, that's when you can use your Inbrija. There's only one dose of Inbrija. It's two capsules. That's just the standard dose.

[Slide 16] So it's used as a rescue medication. So, if you have off periods, either that you cannot predict or that could happen a half-hour or an hour before your next dose, that's when to use it. It's to give relief of these PD symptoms before you're due for your next dose or sometimes your oral dose takes a long time to kick in. Some patients take it first thing in the morning with their oral dose of Sinemet because they know that their Sinemet takes a long time to work in the morning. So, they use the Inbrija, and the Inbrija gives them some relief until their oral Sinemet kicks in.

It lasts about an hour, the effect, and one of the main things to get used to with the Inbrija is that it can cause some coughing. So, you have to get used to it. You can just take a small puff and rebreathe it in after again to be sure that everything went in. Follow each puff with a glass of water to be sure you clean your mouth. So, there are tricks that can work around to help with the coughing.

You cannot preload the capsules in the inhaler because when you put the capsules in the inhaler, it makes holes in the capsules, and then you will lose the powder. So, I think it's something that's useful to carry around if you're concerned about being somewhere and having some off time. I tell people it's a bit like a safety type medication.

[Slide 17] So Gocovri® is a form of amantadine that is long-acting, taken once a day, and it is approved to treat dyskinesias and off time. It's given at bedtime, and the level rises before the patient gets up in the morning. The full dose is 274 milligrams at bedtime, but there are some people, because of some medical issues or because of their age, that can tolerate only a lower dose. So, there are other capsules. There's a 68.5 milligram tablet, and you can start with that if you're concerned about the potential side effects. So, it has similar side effects as the regular amantadine, but it gives higher and more sustained blood levels than the regular amantadine.

[Slide 18] Now Osmolex® is another form of long-acting amantadine which is taken once a day. This one is taken in the morning. The way the pill is built is that the outside is an immediate-release outer layer, and inside the pill, the core is the long-acting medication. So, you take your pill in the morning,

have an immediate-release effect from the medication and then a sustained effect for the rest of the day from the long-acting part of the medication. So, the dose also depends on the tolerability and the reaction to the medication, and it is indicated for the treatment of Parkinson's disease symptoms.

[Slide 19] Now we have Xadago® (safinamide). So, Xadago is mostly an MAO-B inhibitor like rasagiline or selegiline, so it should not be combined with them. But it also probably has other activities, and it's not totally clear how it works. It's used as an add-on therapy to levodopa to help improve the off periods. So, it's not approved to be given by itself, contrary to rasagiline for example. And it's given once a day, and you start by 15 milligrams, and depending on the response, you can go up to 100 milligrams.

[Slide 20] So Nourianz®, istradefylline, has, as I mentioned, a unique mechanism of action that it's the only nondopaminergic medication that we have. It does not add by increasing dopamine. It is approved for off periods, and the dose is given once a day, and it's 20 to 40 milligrams. The side effects include dyskinesias and hallucinations. Although it's not a nondopaminergic medication, it seems to potentiate dopaminergic side effects. So, if you have dyskinesias and hallucinations from your levodopa, it could get worse on the Nourianz.

[Slide 21] Now we have opicapone or Ongentys®, which is a COMT inhibitor like entacapone and tolcapone, but it's given only once a day. It's also given with levodopa to decrease the off period. It was very recently approved, just before COVID came. The most common side effects are dyskinesias, low blood pressure, and weight loss. So far from the studies I've read, it doesn't appear to increase the risk of diarrhea like entacapone and tolcapone, but it seems instead to cause constipation.

[Slide 22] Another medication very recently approved is sublingual apomorphine or Kynmobi™. Like the injectable form of apomorphine, it is a rescue medication for off periods; but instead of an injection like the regular apomorphine or like inhalation like the Inbrija®, it's given under the tongue. It's a little strip that looks like Listerine strips, and it melts under the tongue. So, it's a rescue medication for the off periods.

And there are several available doses, depending on their response, and the maximal dose is 30 milligrams, five times a day. Like the injectable apomorphine, it causes nausea and vomiting. So, patients must be premedicated with an antinausea medication called Tigan® for three days before starting the Kynmobi. And they continue their Tigan till they get used to the Kynmobi. Eventually, most patients get used to it and are able to stop the Tigan. You get used to it much faster if you are on another dopamine agonist such as pramipexole or ropinirole.

The other specific side effect is irritation of the mucosa of the mouth, and it does not appear to get better as people use it. In fact, it can get worse, so that can be a limiting side effect for this medication. And the other side effects of Kynmobi are very similar to the side effect of the other dopamine agonists like ropinirole and pramipexole. And the Kynmobi will be available, I understand, in October.

[Slide 23] So Nuplazid® or pimavanserin is the only medication approved by the [United States] FDA (Food & Drug Administration) for hallucinations in Parkinson's disease. So, these hallucinations are

often associated with long-term treatment with the various Parkinson's disease medications, but it is often difficult to decrease the Parkinson's disease medications because the mobility, the motor symptoms get worse. But unlike the traditional medications given for hallucinations, Nuplazid does not block the dopamine receptor. So, it does not worsen the motor symptoms of Parkinson's disease. It's given once a day, and the usual dose is 34 milligrams, although there's a 10-milligram tablet if you want to start slowly. It does not cause somnolence like many medications for hallucinations, such as the Seroquel® or quetiapine, and it is given in the morning.

[Slide 24] The last medication I will mention is Northera® or droxidopa, which is a medication given to treat low blood pressure in Parkinson's disease. Low blood pressure is very common in Parkinson's disease, and it can cause lightheadedness or dizziness when getting up from the bed or from a chair. It can cause loss of consciousness, fog, or even confusion. Unfortunately, it is also underdiagnosed because some patients do not feel the symptoms of low blood pressure. They don't feel dizzy even when their blood pressure is quite low. It's why when you go see the physician, you should always check their blood pressure sitting and standing. The sitting blood pressure may look totally perfect, but it drops when the person stands. And some studies have shown that when the orthostatic hypertension is treated, it can improve cognition. So, it is important to monitor the blood pressure sitting and standing when you go see your physician.

The dose of droxidopa are 100, 200, or 300 milligram tablets; and the dose is increased progressively as the person, following the response of the blood pressure. The blood pressure has to be monitored, so it might be helpful to have a blood pressure monitor at home.

[Slide 25] Now let's discuss updates in surgical treatments for Parkinson's disease. We'll start with deep brain stimulation or DBS, the most widely used surgery. As you know, an electrode is implanted in an area of the brain. The main two areas that are implanted are the subthalamic nucleus or STN or the Globus pallidus or GPi. Wires attached to the electrode goes to the chest under the skin and attaches to a battery or we call IPG, implantable pulse generator, which is very similar to a pacemaker, if you know people who have had pacemakers. So, it is this IPG which contains the computer that controls the electrode, and we program it according to the response of the various symptoms through the stimulation of each electrode.

[Slide 26] There are three systems on the market, so they're systems from Medtronic, Abbott, and Boston Scientific. Initially, DBS was reserved for advanced Parkinson's disease when all medications were tried and were deemed not to be effective; but it has been demonstrated that it benefits more when it's used earlier in the disease. And in 2016, the FDA approved DBS for earlier stages of Parkinson's. Now all of these systems are what we call MRI-conditional (magnetic resonance imaging), so meaning you can have an MRI with them under certain conditions, depending on the machine and so on.

Medtronic and Boston Scientific have a choice of rechargeable battery, and surgery is classically done with the patient awake and microelectrode recordings where we record the activity of the brain when we implant the electrode, but it can be done in an MRI or CAT (computerized axial tomography) scan or a CT (computerized tomography) scan or a CAT scan while the patient is asleep.

[Slide 27] So I'll talk briefly about the various systems. The Boston Scientific Vercise™ system was approved in 2017. So, each electrode, which you see on the bottom right, has eight contacts; and the patient can make some changes on their own if preprogrammed by the neurologist. It's a very customizable field of stimulation.

[Slide 28] The Cartesia™ system was approved in 2019; it's also a Boston Scientific system, and it uses directional leads, which means you can direct where the current is going. So, you can direct the current from each point in the electrode to go in a different direction. So, there are three sections on the two middle contacts, as you see on bottom right, and they can be stimulated independently. So, this can decrease the side effect of the stimulation. If you find that one direction causes more side effects, you can cut off the current to that direction and direct it in the two other directions, for example, and you can isolate the section that is responsible for the side effect.

[Slide 29] The Abbott system is the first one to use directional leads like this, but they do not have a rechargeable battery. The advantage of the directional leads is that you can stimulate a target without activating an unintended pathway that can cause side effects. For example, the STN, the subthalamic nucleus, is in a dense area with many adjacent structures that when you stimulate can cause side effects such as double vision, numbness, tingling, mood changes, muscle contractions. So, having the potential to direct the current from the contact in the electrode, it gives more flexibility to the person programming the stimulator.

[Slide 30] The Medtronic system was the first one on the market. In 2020, the new Percept™ system was approved. The electrode records the activity of the brain cells or the neurons in the vicinity of the electrode, and the DBS can be adjusted based on this activity, which can change depending on the symptoms or when the person took their medication. So, this gives you a sort of feedback loop. The new battery is also thinner and has a longer life than the previous battery. And there's one battery for both sides, so one battery delivers stimulation to both sides of the brain. The two leads are attached to one battery.

[Slide 31] Finally, in the surgical therapies, we have to mention the MRI-guided ultrasound. It's performed in the MRI machine, and a beam of ultrasound makes a lesion in the region of the brain called the thalamus. It's an intervention, but it's not classically a surgery because there's no opening of the skull. It's approved for tremors, so it was first approved for essential tremor, but it's also approved for Parkinson's disease tremor. There are clinical trials underway to see if it's helpful for other symptoms of Parkinson's disease.

There are some limitations. For example, you must have the right shape of skull because some people have too thick a skull, and they don't think the ultrasound will go through. And it can be done classically only on one side of the brain because if you do it on both sides of the brain, it can cause some speech and swallowing difficulties, although there are some recent reports that maybe if you wait a while between doing one side and the other, you can get away with it. But this is still under investigation.

Cathi Thomas, MS, RN, CNRN

[Slide 32] Okay, thank you, Dr. Saint-Hilaire for that wonderful overview of therapies. I think you and I can both appreciate the advances that have been made in therapies to address not only the motor problems but nonmotor problems.

Question & Answer

[Slide 33] So at this point, it's now time for the Question & Answer session. So, I would like to start. We have some wonderful questions that have already been presented or typed in, and I would like to start.

Michael asked, "Does delaying taking medications cause further degradation of dopamine production versus taking medications early?" So, should one delay taking medications, Dr. Saint-Hilaire?

Marie Saint-Hilaire, MD, FRCPC

That's a very important question of something we deal with every time we diagnose somebody with Parkinson's disease.

At this point, I feel medication is slowing down the progression of the disease. We can talk about neuroprotection. Some people might have questions about that, but all the medications we have are for the symptomatic treatment of Parkinson's. So, delaying taking medication, you're not worsening the progression, you're not worsening the disease. I just tell people, "You have to be able to function to do your activities of daily living and participate in hobbies." So, think about that if you want to start medication. You want to be able to be participating in exercise. We all know exercise is very important. If the symptoms prevent you from doing an adequate amount of exercise, it might be a reason to start medication. So, it's a discussion you have with your doctor; and by delaying, you're not doing any harm to the disease process itself, but you might be affecting your ability to do things that you enjoy.

Cathi Thomas, MS, RN, CNRN

Great. And another common question from Al that people wonder about, "Can the amount of natural dopamine be measured for diagnosing purposes?"

Marie Saint-Hilaire, MD, FRCPC

No, we cannot measure that directly. We can measure it indirectly. So, there's a test called a DaTscan, which indirectly measures the dopamine in the brain. It measures the, how do you say, the integrity of the dopamine-producing cells. So, if it's decreased, if the cells are decreased, the DaTscan will be positive. So, at this point, the DaTscan is approved as a yes/no test. So, yes, it's positive; no, it's negative, you don't have Parkinsonian syndrome. It is being studied to see if we can follow the progression of the disease with the DaTscan, but that's really used in investigational trials and biomarker studies, for example.

Cathi Thomas, MS, RN, CNRN

Great. And we also have a question related to anxiety in Parkinson's disease. Are there any new treatments for anxiety?

Marie Saint-Hilaire, MD, FRCPC
No, the treatments for anxiety in Parkinson's are really the treatments that we'd use for anxiety in any other condition or in the people who have just basic anxiety. There are medications such as benzodiazepine, like lorazepam and clonazepam. There are what we call SSRI (selective serotonin reuptake inhibitors) like paroxetine, sertraline or Zoloft®. There is some data that cognitive behavioral therapy can be very helpful for depression and anxiety in Parkinson's. There's some research showing that, but there's nothing really specific for the anxiety in Parkinson's.

Cathi Thomas, MS, RN, CNRN

Yes, and that's a really good point that although medications are so important and other forms of treatment; but also, rehabilitation therapies, cognitive behavioral therapy also is extremely important, and most healthcare providers will use a combination of all of these things. Great question to also address exercise, etc., so we'll talk a little bit about that.

Marie Saint-Hilaire, MD, FRCPC

Exercise will help with mood also. That's true, Cathi.

Cathi Thomas, MS, RN, CNRN

So, there are some questions that address some of the side effects of medications, and you talked a little bit about hallucination. And Hon is asking, "Do you start medication if you have a very mild hallucination?"

Marie Saint-Hilaire, MD, FRCPC

That's a great question. We don't know exactly. When we have to start the medication for the hallucination, of course, the hallucination is disruptive and scary, embarrassing. People agree you have to start medication, but what to do with those benign hallucinations, very mild? You look in the bottom of your cup of coffee and you see the little eyes looking at you, and there are many interesting hallucinations. Really, I think it's important for the patient to tell their physician, and it's important for the physician to always ask the patient at every visit how things are going. There are some people who remain with those benign hallucinations for quite a while before the hallucinations get worse.

My feeling is I personally don't like people to have hallucinations, and if somebody reports that to me, I will try first to adjust the medications they are taking; see if I can peel off some of their – because people are, as I mentioned at the beginning, on many medications for their Parkinson's. So, see if I can peel off a little, decrease a little bit the dose of certain medications, see if I can improve that. And then I watch the patient very closely, but if really the hallucinations seem to be getting worse, I would start the medication again for them.

Cathi Thomas, MS, RN, CNRN

And here's a question maybe to any new medications to treat fatigue, which as we know is a common complaint for people.

Marie Saint-Hilaire, MD, FRCPC

Great question because this is a very frequent symptom. There's no great medication for fatigue. So, I can tell you that off the record, no medication is approved for fatigue for Parkinson's; but I can tell you what has been tried by neurologists. One is amantadine. Amantadine has been used for fatigue in multiple sclerosis for quite a while, and it might be something that you can try if there is no problem using the amantadine. So that's one possibility. It might help the Parkinson's also and the dyskinesias.

One other thing is some people feel sleepy from the Parkinson's medication, so we can try a medication that wakes you up, such as modafinil or Provigil or Ritalin (methylphenidate). Some people respond to that. It's really you have to try it. It's difficult to know if you are going to respond to it or not.

Another thing is be certain that your sleep is okay at night. Some people have fatigue but have other sleep disruptions like obstructive sleep apnea, interrupted sleep, they have to get up often to go to the bathroom at night. So, try to improve the sleep at night is another thing to do.

Another thing is to look at what medications you're taking, look at your medications in general. Be sure that, some of them don't cause fatigue. For example, dopamine agonists can cause fatigue and somnolence more than some other Parkinson's medication, so that's something to look into. Review your medications.

And it's very frequent that people who have Parkinson's have to take a nap in the afternoon. There's nothing wrong with having to take a nap in the middle of the afternoon as long as that it's no more than an hour. But it is a very frequent symptom and a very challenging symptom sometimes to treat.

Cathi Thomas, MS, RN, CNRN

Absolutely, and I think another indication where you have to have several approaches to conquer a problem. So, Dave asks a good question, asking, "How does a person know if a rescue drug is important for them?"

Marie Saint-Hilaire, MD, FRCPC

My feeling is that if you have motor fluctuations, you need a rescue drug because you never know. So, motor fluctuations, let me explain for those who don't have them, is that you respond to your levodopa, you have a good response. It helps your tremor, your walking, your stiffness; but sometime before you're due for your next dose, the effect wears off, and then the tremor comes back and then you start shuffling again. And then you take your oral dose, and then it takes a little while for the next pill to kick in. So, you go through these peaks and valleys during the day.

And it doesn't have to be many peaks and valleys. It could be one valley. It could be the middle of the afternoon. It's always in the middle of your afternoon. You feel horrible because your pills don't work. Until you take your evening pill, you're really not feeling well. Or it could be first thing in the morning you take your morning pill, but it takes a long, long time to kick in; and you don't feel good until the end of the morning. So, you don't have to have a lot of these peaks and valleys to have wearing off and motor fluctuations.

And what people are bothered by sometimes the unpredictability. Some people complain that they never know when that's going to happen. And that really kind of limits your ability to knowing when you're going to go out, going to the restaurant. It can limit the activity to go exercise. So, I think if you have motor fluctuations, it's nice to have a rescue medication always with you that you can use so you feel it's a little bit like a safety blanket. So, these rescue medications, I think, are helpful for people experiencing fluctuations.

Cathi Thomas, MS, RN, CNRN

Okay. And another great question from Martin, and this is a difficult question to answer but, "What rate of success have you seen for deep brain stimulation?" I know you commented that it's now available as an option earlier in the disease course. But overall, how do you feel about that?

Marie Saint-Hilaire, MD, FRCPC

I think most people respond to the deep brain stimulation, but you have to do it for the right reason. So if you do it because you respond well to Sinemet, but you have motor fluctuations, you have to take your Sinemet many times a day, you have disabling off period, and you have dyskinesias, I think that's the idea and you will respond to that. You will respond to the DBS.

Now if the main reason you're having DBS is because you're having falls and balance problems and you have speech problems and swallowing problems; we know that these symptoms don't respond well to the deep brain stimulation. So, if that's the reason why you have your DBS, you will not respond to it. So, it's really, really important to really choose well the person who will have the DBS. And also, remember that DBS is like a medication. So, it helps with the off time and decreases the Parkinson's symptoms. People can decrease their medication often. It will decrease the dyskinesia. But it does not prevent the progression of the disease. So as time goes on, other symptoms of Parkinson's occur that do not respond to medication and will not respond to DBS. So, everybody I've seen who had DBS recently, if chosen wisely, will have a good response or some response.

Cathi Thomas, MS, RN, CNRN

Thank you so much. We also have some questions about potential new therapies that are maybe being studied now. Can you comment, Dr. Saint-Hilaire, about some of the promising clinical trials currently recruiting subjects in general?

Marie Saint-Hilaire, MD, FRCPC

Yes. So, interestingly, the new medications or other new treatments I talked about today are for people who are more advanced and have motor fluctuations, but the new trials are really for people who are early on in the disease.

So, there's some very promising trials, one of them being done by a company called Biogen, but there are other companies doing similar trials where they give a substance that is like an antibody to the alpha-synuclein. It gets rid of the alpha-synuclein. Alpha-synuclein is the abnormal protein that accumulates in the brain of people with Parkinson's so it like attaches to this alpha-synuclein and then clears it from the brain. Anyway, that's what we hope.

So, this trial is taking place. There's a trial starting by Neuraly. It's a medication that is used for diabetes, but it's an injectable that people are given once a week that it seems promising to slow down the progression of Parkinson's disease. So that trial is actually starting. It was a bit delayed because of COVID, but now we're starting the trial.

There's a trial taking place – and all these trials take place at many centers throughout the country, so people I know call from all over the place that you can find, hopefully, a center in your area that does those trials.

There's a very interesting trial called SPARX3, which is a NIH-funded trial, to see if intensive exercise slows down the progression of Parkinson's. Absolutely important question. Everybody wonders about that, but, hopefully, we'll answer that question with this trial.

There's a trial, for example, for more advanced patients, a trial by a company called Voyager genetic therapy trial where they put the gene to produce dopamine in the brain of people with Parkinson's. So that's more for advanced Parkinson's patients.

So, I would absolutely encourage people, if you're interested in any of those trials, to look at your local APDA page. I know in Massachusetts we put all the trials that are available on our page so people can participate.

Cathi Thomas, MS, RN, CNRN

Thank you so much for that. And there are a number of questions around the best time to take medications in relationship to food. And I know that it really depends on which medication you're taking, but there are questions asking about carbidopa/levodopa and taking with food.

Marie Saint-Hilaire, MD, FRCPC

Really, the only medication which is affected by food in Parkinson's is really the carbidopa/levodopa. The others you can take with food; you don't have to worry about it. But carbidopa/levodopa is affected by the food intake because levodopa is an amino acid, and when you take it with a big meal, there are other amino acids in the meal. Usually they come from the protein in the meal, and it competes with the levodopa for the absorption.

So, we try to tell people to take the medication on an empty stomach, the levodopa. The others are less important, but the levodopa is the most important to take on an empty stomach, either a half-hour before the meal or at least an hour after the meal. But you can still take it with something, just not with the meal. A glass of juice and some graham crackers, providing that is fine. A piece of fruit is okay if you want to have something in your stomach

And some people are very, very sensitive to the effect of food on the levodopa, and they know that. They say, "Oh, if I take my levodopa with food, I know it's not going to work." And people do notice it. Other people, it's less obvious; but, in general, it will be better absorbed if you take the levodopa away from the meal. Sometimes it's complicated because if you take your levodopa every two hours, it's difficult to know when it requires some adjustment of when you take your meals. It makes things a little more complicated.

Cathi Thomas, MS, RN, CNRN

Thank you very much for that.

Closing Remarks

Cathi Thomas, MS, RN, CNRN

[Slide 34] And at this time, I want to thank Dr. Saint-Hilaire for joining us today and my many thanks to everyone for participating in today's Web education program. **[Slide 35]** I do apologize that we couldn't get to all of the wonderful questions, **[Slide 36]** but if you have a question or would like to speak with someone from our Scientific and Medical Affairs Department, I encourage you to visit our website at apdaparkinson.org or call 1-800-223-2732, and you can ask your questions there.

[Slide 37] If you enjoyed today's webinar, we hope that you will consider supporting APDA with a donation. With your help, APDA can deliver more programs and services like this one which are needed now more than ever during these challenging times.

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 referral centers, as well as our National Research Grant Program and Centers for Advanced Research, please visit us at 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.