

Understanding Parkinson's Disease

The Ohio State University Parkinson's Disease Quarterly Educational Series

Q & A Session Follow – Up: April 2021

Answers prepared by Dr. Aristide Merola and Clarisse Goas, MS, APRN-CNP

How widely disseminated among general practitioners are the early precursors of Parkinson's (e.g., loss of smell, constipation, tiredness)?

Although most providers learn this during training, sometimes the signs are missed as PD, unfortunately.

Many of the early non-motor symptoms are also associated with age, not to mention other diseases. Is there a trigger point at which Parkinson's should be considered worthy of consideration?

Some tipping points for Movement Disorders specialists include reduced arm swing, inability to smell things well and at least 3 out of 4 of the cardinal symptoms: rigidity, postural instability, tremor, bradykinesia (slowness of movement). Please consult your physician if you are experiencing these symptoms.

I'm interested in info about the ENLIGHT-PD trial. How can I get more information about participating?

Our center is involved in several clinical trials, observational studies and nonpharmacological treatments. If you're interested in participating in research, please contact us at PDRESEARCH@osumc.edu There's general information about this trial here: <https://neuronext.org/projects/nn110-enlite-pd>.

Does dopamine replacement medication help address the cognitive symptoms of PD along with the motor symptoms?

Excellent question! Sometimes these can help as well, but we have special medications that also can help with cognition. See Jessica Truelove's presentation for more information.

What is the definition of "long-term use" of dopamine therapy?

"Long-term use" typically means several years, but every patient is different.

Do medications contribute to psychosis?

Some medications can cause or worsen psychosis. Levodopa tends to be the best tolerated.

Adapting to decline: Is there a central, ideally medical, source for identifying Columbus-area eldercare facilities that may specialize in dealing with Parkinson's?

Reaching out to our social worker, Erica Wright, is a great place to start. Your provider can place a referral to chat with her. You can contact us

I suffer from nightmares and lively dreams.

That can be difficult; there are medications to help. Reach out to your provider.

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At what point does hospice need to be considered when dealing with a PD patient? Will patients with atypical Parkinson's be considered by Medicare for hospice?

This is an excellent question. It can be tricky to qualify for hospice; typically, we use our social worker to help us manage this. Sometimes, if they meet other qualifications, atypical Parkinsonism patients will qualify.

Can pelvic floor issues after increased constipation be related to Parkinson's?

Potentially. Our physical therapist Stephanie Bobinger is an excellent resource.

Is there a correlation between the severity of non-motor and motor symptoms?

Not always, particularly in regards to tremor. Tremor can be very bad and other non-motor symptoms not bothersome.

How is dopamine measured and tracked?

We can get an idea if it's decreased in the brain on a scan called a DaTscan. In general, we do not need to track it as we are treating the physical symptoms.

How do caregivers find out about support groups? Parkinson's Foundation? Doctors? County Office on Aging?

Yes, all of the above. You can find a list of support groups by county in Ohio here:

www.parkinson.org/Living-with-Parkinsons/Resources-and-Support.

I was recently diagnosed with binocular vision dysfunction/vertical heterophoria. Is this related to Parkinson's disease?

No. Even though Parkinson's disease can be associated with some abnormalities in the vision, these are mostly related to the perception of colors.

The current issue of *Chemical & Engineering News* has an article titled "Skin oil carries signatures of Parkinson's disease." Seems that this is diagnostic and also tells of progression of disease could be exposure to PE?

Parkinson is associated with certain types of dermatitis and alpha-synuclein deposits have been found also in the skin. This suggests that the analysis of the skin can provide valuable information about the diagnosis and monitoring of the disease. However, most of these applications are still in an early phase of development and require further research to test their sensitivity and specificity.

See also "Discovery of Volatile Biomarkers of Parkinson's Disease from Sebum," *ACS Cent Sci.* 2019, 5, 599-606. Comments?

Again, the area of biomarker research in Parkinson's disease is in very rapid expansion. A biomarker is an indicator of disease and disease progression. Identifying reliable indicators is critical to improve our diagnostic abilities and capability to track changes in the disease progression and test the efficacy of disease-modifying therapies. Multiple biomarkers are under investigation, with particular interest in those that do not require invasive blood or cerebrospinal fluid collection.

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Dr. Merola, thank you so much for mentioning sensitivity to cold as a symptom to PD. Other than Sinemet is there another drug that will help with this symptom?

Unfortunately, no drug particularly helps with this symptom.

Does the long-term use of Sinemet contribute to PD dementia?

No, this is more related to progression of disease than Sinemet.

I've noticed my incontinence has become pretty severe since the diagnosis of PD. I've always had a problem with incontinence... I tried several things before being diagnosed for the incontinence, which did not help. Now that it's gotten worse with the PD, is there anything that can help? I have an upcoming appointment with a urogynecologist but just wondering if it's going to be a waste of time?

I would certainly still go to see them — there are several options including Botox and PT. We have an excellent urologist here, and we often refer patients to PT as well.

Is there a team program to manage multiple meds from different doctors for prostate hyperplasia, cholesterol drugs, anxiety drugs, in addition to high Sinemet medications?

Excellent question — ideally your PCP should do this. Also gerontologists can be a great help. We're also hopeful that our new multidisciplinary clinic scheduled to open later this year will help.

Could exposure to Agent Orange in the late 1960s not show tremors till the 2000s? If so, why?

Regarding Agent Orange, it is possible as the exposure to toxins can accelerate the progression of neurodegeneration, but this does not mean that the consequences are immediate. If, for instance, the exposure to Agent Orange depleted 35%-40% of dopaminergic neurons, the body still had the ability to compensate for some time thanks to the residual population of neurons, which eventually degenerated due to physiological aging.

Hello, I understand there is some new research regarding when medication should be started. One theory says we should delay L-dopa as long as possible, the other says we should start it early but just make sure it's at the right dose. Dr. Merola, should we start PD medication as early as possible, or wait as long as possible to start?

Research shows that we should not delay treatment if the patient is having frustrating or bothersome symptoms. However, if the symptoms are mild and non-bothersome, it is OK to wait.

Do medications such as Wellbutrin and Paxil affect the results of DaTscan?

Not typically. In trials they tend to want them held. If they have an effect it's believed to be so small, it would not affect the outcome of the scan.

What is the average age of PD diagnosis? And are the symptoms different for someone diagnosed at 30 as opposed to someone diagnosed at 80?

Age 60 is the average age. PD symptoms can certainly vary from person to person, even regardless of age. We do tend to see more limb dystonia in young onset patients.

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What is the minimally therapeutic daily dose of carbidopa-levodopa? What is the maximum amount of carbidopa-levodopa a person can safely take a day?

We tend to think Sinemet 25/100mg 1 tablet by mouth three times a day, but we do have some patients able to take a bit less. There really is no maximum dosage — side effects tend to keep folks less than 250mg at each dosage.

What are reasons for not taking carbidopa-levodopa?

Some folks are afraid if they take it early, it won't help later on. This has been proven false. For others, it doesn't help their tremor, so they don't find it useful.

It has been suggested that mitochondrial dysfunction is a critical event in PD pathogenesis. What do you think of the studies in a PD mouse model using mitochondrial uncoupling agent 2,4-dinitrophenol (DNP) or DNP producing MP201 to protect dopaminergic neurons?

Multiple metabolic pathways have been involved in the pathogenesis of Parkinson's, and mitochondria are certainly one of the most important. The idea of targeting these intracellular organelles makes a lot of sense and multiple laboratories are working on this.

My question is about so-called "atypical Parkinson's." When symptoms don't respond to carbidopa-levodopa we usually are told that this is not "classic" PD. Is there, in such cases, a different cause of Parkinsonism? If levodopa doesn't help, is it safe to assume that lack of dopamine is not the problem in this case?

This is an excellent question! Both Parkinson's and atypical Parkinsonisms have a dopaminergic deficit. However, in Parkinson's this is related to a pre-synaptic damage, which means that the neuron that produces dopamine is not working properly. In this case, we can replace its functionality with carbidopa-levodopa. In MSA, the damage is at a post-synaptic level, which means that the second neuron of the chain, the one that receives the dopamine produced by the first neuron, doesn't work. In this case, the replacement of dopamine with carbidopa-levodopa is inefficient because the problem is on the receptor.

Is there an intensity or frequency of exercise — for example daily 30 to 60 minutes of high-intensity interval training on a stationary bike — that provides therapeutic benefits similar and/or supplemental to carbidopa-levodopa?

We highly recommend this as a supplement to medication treatment as well. This is currently the only thing we have data on that slows the progression of disease.

Are there specific combinations of medications that will help improve freezing and movement disorders? That is, create a target to help decrease freezing?

Freezing can respond to any medications for Parkinson's disease, but it tends to be less responsive over time. Physical therapy, U-Step walker with light and laser cane are often treatment options.

Is there any current research on the use of coconut oil and specifically MCT oil (medium chain triglyceride) in the diet to treat Parkinson's?

There is some research on this topic. You can find information here: <https://doi.org/10.1007/s11062-020-09866-1> or we would be happy to make an appointment to discuss this research further.

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Do PD patients have a problem with urinary accidents?

They often do. A good urologist is an excellent addition to any care team.

Is constipation without a sense of feeling bloated, full, etc., also linked to PD?

Absolutely.

A few years ago there was a test online in which you said a number of phrases. From your verbal results, the test could supposedly determine whether you have PD. Have you heard of this test? And if so, what did you think of the test?

The test you are referring to aims at testing verbal fluency, which is one of the main neuropsychological aspects involved in PD. However, this test alone does not have sufficient accuracy to be used for differential diagnosis. We regularly administer this and other tests to patients undergoing deep brain stimulation (DBS) and we are working on a plan to have these tests available for all patients, if interested.

I'd like to hear about overmedication. I believe a lot of PD patients have more issues/side effects from too much medication than actually side effects of PD.

Absolutely, patients can have dyskinesia, impulsivity, low blood pressure, hallucinations from taking too much levodopa. It's important to find a good balance.

Is there always loss of smell in early PD?

Typically, but not always.

Are in-person speech therapy sessions done without masks? Also, are caregivers required to wear a mask during in-person sessions?

Yes to both.

Please give the website for the free Zoom classes on Thursdays.

wexnermedical.osu.edu/pdfitness

If you're bedridden and having constipation issues and have tried MiraLAX and prunes, are there other options to try that aren't medication?

Excellent question — hydration, yogurt and even minor movement of the arms and legs to help move things along.

Is an elliptical as good as a bike to exercise on?

We think all exercise is good. However, the research has focused on the bike, so we just aren't sure in a head-to-head comparison.

Boxing has been shown to be a good exercise for PD patients. Can you comment on this?

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This is another great therapy. It hasn't been as studied as riding a bike, but we've also seen great results in patients.

Are small sips of liquids more beneficial when dealing with swallowing issues?

Yes, typically smaller sips and bites are more beneficial, safer and easier to swallow.

What is the procedure for getting in touch with a bladder specialist for physical therapy?

Excellent question. You can ask your movement disorder provider to refer you.

We are hearing about the benefits of exercise. Is it a PD symptom to be experiencing such severe fatigue that even 5 minutes of exercise feels like it's difficult?

It can be. Of course, we always recommend that you follow up with your PCP to ensure that you don't have any other causes for the fatigue. Starting with 5 minutes is fantastic. It can get easier.

When beginning Sinemet, how soon should one begin to see changes to consider it effective?

Typically within 20 minutes it should kick in. The benefit may take a few weeks in general while we figure out the optimal dose for you. So when starting the drug, you may not see benefit at first, until we get the dose to a level that helps your symptoms.

One of my PD symptoms is tightness around my neck. It comes and goes. It feels like someone is lightly choking me and I cannot vocalize in a normal way. Is this common? Can it improve through speech therapy?

This is not common, so it is hard to say if it would improve. I believe it would be worth it to see a speech therapist.

Does excess phlegm and constantly clearing your throat have anything to do with PD?

It does. You tend to not swallow as often, so you feel as though you have more phlegm. Your nose also runs more often.

What if a person with PD has taken the best medicines available and they don't help with tremor, which is worsening?

At this time you may want to talk to your neurologist about deep brain stimulation, which is better at treating tremor than medication.

What is the youngest age seen in diagnosing Parkinson's disease? Are children diagnosed with PD?

Parkinson's is called: "juvenile" when diagnosed before the age of 30, and this is usually associated with rare genetic mutations. The youngest patient I've seen diagnosed with Parkinson's was 18. However, the vast majority of patients are diagnosed between the ages of 50 and 70.

If you have had DBS, would Duopa intestinal be indicated or contraindicated?

We can do Duopa intestinal infusion system on patients with DBS. This is something that can be done for persistent motor fluctuations despite the DBS.

Can ropinirole and carbidopa-levodopa be taken at the same time?

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Yes, they can. It is common in PD to be on a "cocktail" of many medications that all act synergistically to help your symptoms.

Is there a better medication for someone with constipation and resting tremors only in the early stages of PD?

Constipation can be managed with MiraLAX powder, Colace, eating fruits with skins (grapes, prunes), drinking lots of water and remaining active. For severe constipation, try Linzess or Amitiza medications (prescribed by doctor). Early PD can be treated with MAOB inhibitors (rasagiline, etc.), amantadine, or dopamine agonists.

Is restless legs a side effect of overmedication?

No. Restless leg is often seen in PD patients. We actually use the same medications used to treat Parkinsonism for restless leg. Dopamine agonists and levodopa can curb the symptoms of restless leg.

When are Botox injections beneficial for dystonia, and is this procedure recommended and performed at The Ohio State University Wexner Medical Center?

Botox injections are injected paralytics that last 3 months. These are used for posturing (dystonia) in PD when medications fail to curb symptoms. They must be injected by an expert familiar with this technique, every 3 months.

What about headaches and indigestion from carbidopa-levodopa in the middle of the night

Headaches are not a typical side effect. This could be due to another problem and you should talk to your doctor about this. You could have obstructive sleep apnea or another issue. Upset stomach can happen from levodopa. You may want to decrease the dose overnight or take a medication for nausea, constipation, or acid reflux. Talk to your family doctor and neurologist about these.

What is the sign to increase carbidopa-levodopa? O, when is the right time to adjust?

The time to adjust the dose is when you have breakthrough symptoms of slowness, stiffness or tremor despite taking your medication.

Does DBS increase the likelihood of voice volume weakening?

Not necessarily. DBS does affect some voice in some patients. However, with new technology, this is less common.

What does it mean if you have chronic muscle pain, particularly in the extremities?

Good question. Unfortunately, this is not typically associated with PD.

Why does exercise help? Does it delay the substantial migration breakdown?

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Exercise helps with brain plasticity, which means helps keep the connections between neurons active and healthy. This is important in a disease in which the neuronal pool is progressively depleted. Exercising, we ensure that the remaining pool of neurons maintains the highest number of connections to overcome the progressive neuronal loss. Benefits are most evident on balance, gait and overall physical performance.

How would you determine which of the three MAOB inhibitors to take?

The best thing is to talk to your neurologist about your specific disease. It may also depend on your medical insurance (what is covered).

From Dr. Changizi's presentation, it seems like not taking the drugs that stop the breakdown of dopamine would be harmful. I'm not taking any medication because my symptoms are mild, but this makes me feel like I need to prevent the loss of more dopamine.

It's fine for your brain to be breaking down dopamine in early stages of disease. This is a normal function of the brain. There is no harm done by NOT taking these medications. These drugs just make use of this mechanism to help PD symptoms.

Sometimes I feel as if my dose of medications wouldn't get absorbed at all, when in general my four hours ON/OFF doses works well.

You may have motor fluctuations from advancing disease. Please talk to your neurologist about this. You may want to try Rytary, or even consider DBS or Duopa.

To qualify for DBS, do you still have to respond to levodopa?

Great question. You do have to respond in some manner. However, tremor is different. If tremor doesn't respond to levodopa, you may still be a good candidate for DBS.

Can DBS be used first, without using medications at all?

No, you must try medications first. Surgery is low-risk, but still higher than that of taking medications. You must be failing optimal medications before we consider a brain surgery.

The chart on deep brain stimulations suggests medical therapy has a higher percentage. Is that of success? Can someone go back to that chart and illustrate the difference between the two trend lines?

This chart showed the burden in quality of life. DBS resulted in lower burden than the best medical treatment.

Please explain the prep for the surgery, whether you're totally out, and recovery.

This is a complex process. We will have an upcoming presentation for the process of surgery in the fall.

Is DBS a one-time procedure? How long does it last?

DBS is a one-time procedure. Patients may need battery replacement. DBS is meant to last the lifetime of PD patients.

What is the age range for successful DBS?

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There's a broad range of age for successful DBS. We routinely perform DBS in patients in their 50s, 60s and 70s. We carefully evaluate patients over the age of 80 and offer DBS if it has the promise of improving a patient's quality of life.

I've heard about spinal cord stimulation (SCS) that relieves pain and improves motor symptoms. Is the Ohio State Wexner Medical Center using this method of PD treatment? If so, what has been your results?

This can be evaluated for each patients. We've had good results with SCS in PD patients. Typically, this would not improve motor symptoms.