Advances in Parkinson's Disease Management

Parkinson's disease is a neurological disorder that affects the ability of a person to control body movements. It is caused by loss of nerve cells in the region of the brain that produces the neurotransmitter dopamine. Dopamine, the messenger between the brain and nervous system, is responsible for coordinating body movements.

Decreased levels of dopamine in the brain may lead to physical symptoms such as tremors, slowness of movement, muscle stiffness amongst many others, as well as, cognitive symptoms such as anxiety, depression, dementia and impaired cognition.

Medications and therapy can help control the symptoms of parkinson's disease. The CureTalks panel is talking to Dr Andres F. Deik of University of Pennsylvania to learn about the basics of managing Parkinson's disease, available treatment approaches and clinical trials in Parkinson's disease.

Full Transcript:

Shweta Mishra: Hello and welcome to CureTalks. This is Shweta Mishra your host and today we are discussing advances in Parkinson's disease management. We have with us Dr. Andres Deik from the University of Pennsylvania. Dr. Deik is Associate Professor of Clinical Neurology, Director of Experimental Therapeutics and Associate Director of Movement Disorders Fellowship Program at the University of Pennsylvania. Joining Dr. Deik on the patient panel are Patient advocates Dr. Frank Church, who is a Professor of Pathology and Lab medicine and was diagnosed with Parkinson's at the age of 60 and Beverly Ribaudo, a traveler and author who cheers people up with her funny stories on Parkinson's and was diagnosed at the age of 47. Welcome to CureTalks everyone.

Dr. Andres F. Deik: Thank you.

Shweta Mishra: So, Dr. Deik to set a bit of a background for today's discussion could you please begin by telling us what is Parkinson's disease and what are the underlying causes and mechanisms that drive the disease process in Parkinson's?

Dr. Andres F. Deik: Sure. So, thank you again for the invitation. Parkinson's disease is one of the most common neurodegenerative conditions in the United States and in the world, and it's characterised by the onset of motor symptoms including slowness, stiffness, tremor and balance problems, which are progressive over time and can lead to disability. There are also a large number of non-motor symptoms that come with the disease that have been recently recognized and that can be as or even more disabling than the motor symptoms. The disease itself has no cure at this point. We do have a host of symptomatic drugs that we use to manage this condition. The causes of PD are a little bit obscure; it is not fully understood why every patient gets this condition. However, for a subset of people around ten to fifteen percent, it is due to a genetic mutation, stuff running in their families. So, there is now more recognized bourbon of genetic mutations that can lead to disease. For folks who don't really have a family history it is also thought that their exposures in the environment that could lead to the disease. The ones that are most accepted upon are exposures to pesticides. So, patients, who work as farmers spreading crops that has been recognized as a very strong predictor of disease. Some other exposures like heavy metal fumes, so patients, who are welders or exposure to heavy metals and well water have also been recognized as a cause of the disease.

However, for the majority of the patients that we see in our clinic, and this is, of course, a very common question that they ask. We don't really have an answer as a why this actually happened to them.

Shweta Mishra: Could you please throw some light on the mechanisms? The underlying mechanisms that drive this process.

Dr. Andres F. Deik: Yes. So, Parkinson's disease is thought to be due to the accumulation of a protein called alpha-synuclein. Alpha-synuclein is a protein that we all have in our brains, and it is actually involved in a number of different tasks in the brain. It is about to be involved in neuro chemical signalling between neurons, as well as in the metabolism and energy creation of the brain. But in patients with Parkinson's, there has been noticed to be an accumulation of this protein, an abnormal accumulation leading to these clumps of you may of protein that end up "clogging up" the mechanisms that happen within the cell, what we call the metabolic chain of the cell and this leads to the generation of cell loss, and it is the cell loss of a specific type of cell, which is the logo mean cell which lives in an area of the brain called, the substantia nigra that leads to most of the motor symptoms of Parkinson's. However, the substantia nigra cells are not the only cells that are susceptible to accumulation of this protein and has also been seen to be spread throughout the brain and in other types of neurons including neurons that use a chemical called serotonin another type of neurons that use a chemical called acetylcholine to communicate among themselves. So, it's really a widespread multicellular type of process, but the hallmark, the motor symptoms are thought to be mostly related to the drop in the chemical called dopamine due to degeneration of the cells that produce this chemical.

Shweta Mishra: All right, thank you. So, you mentioned that the pathology involves misfolded alpha-synuclein proteins which are toxic to the neurons and leads to loss of dopamine producing nerve cells. So, what are the treatments, what are the treatments currently available to manage Parkinson's disease, and its symptoms?

Dr. Andres F. Deik: Right. So, as I mentioned before, we do not have a cure. So, at this point, our technology has not advanced to the point that we're able to replace the cells that are lost. However, we are able to replete the dopamine levels that are running low in patients with Parkinson's. We have synthetic medications, some of which resemble the effect of dopamine in the brain, others that slow down the breakdown of dopamine, and we have, of course, levodopa, which is the gold standard of treatment of Parkinson's disease, which once it crosses the blood-brain barrier and enters the brain actually turns into dopamine. So, the mainstay of treatment I would say from a pharmacologic perspective is really the repletion of this chemical that is running low. There are also other treatments that non-pharmacological and those are more interventions, FDA approved interventions that exists in the US and across the world at this point include deep brain stimulation surgery in which, an electrode is inserted in the brain and stimulates the area of the brain where we think the motor symptoms are coming from and there is a more reasoned procedure called focused ultrasound or high frequency, high intensity, focused ultrasound, that can be very helpful in the treatment of tremor in patients with Parkinson's disease. So, there's a host of symptomatic therapies that we have. Exercise I will say maybe the one and only intervention at this point that might slow down the disease and should also be considered as a very important complement to whatever other therapy that the patient is receiving.

Shweta Mishra: Right. Thank you. Could you also share some research advances happening in the field of Parkinson's disease? Talk about some of the clinical trials that are going on at Penn that our audience can keep track of and touch upon some of the promising drugs and therapies in the pipeline?

Dr. Andres F. Deik: Sure. So, we have a robust portfolio of clinical trials, here at Penn. We have clinical trials, both for compounds that might slow down the course of the disease, as well as compounds that are not disease-modifying, but can actually be effective in the management of the symptoms of Parkinson's disease. If we think of the clinical trials that we have available here at Penn. I would say we have three main categories in which we subdivide them. One group of studies are for patients, who are diagnosed within three years, who have never taken medication for Parkinson's. The second category would be for patients

who have been diagnosed in the last three years but are already taking medications for Parkinson's. And then the third category would be for patients who have been diagnosed more than three years, most of whom or all of whom I would say are likely to be taking some sort of medication. Within the group of patients diagnosed for less than three years, that's where we have the bulk of our disease-modifying trials. So, the compounds that might slow down the disease. We have studies that are looking at interventions, exercise interventions for disease modification. We also have infusion trials for compounds that might hopefully target the root cause of Parkinson's. And allow the brain to get rid of those proteins that are accumulated. In terms of drugs that are used for symptomatic therapy. We have drugs for the treatment or that might be helpful for the treatment of Dyskinesia these involuntary movements that sometimes happen further in the course of the disease. We also have medications that might prevent the onset of or delay the onset of changes in cognitive function and falls. So, as you can see, we have a really, a potpourri of you may of clinical trials that can really fit many of our different patient characteristics.

Shweta Mishra: Right. Thank you. Thanks for that detail, Dr. Deik. So, you mentioned dopamine replacement therapy is the mainstay treatment for Parkinson's Disease right now, but we know that it has several side effects and also does not delay the progression of the disease and it doesn't slow degeneration. So, could you please shed some light about the status of gene therapy in the management of Parkinson's disease?

Dr. Andres F. Deik: Yes. So, gene therapy is a promising and exciting new Field in the management of PD. There are a number of different clinical trials, around the country, looking at different ways of fixing the genes that we think increase the risk of Parkinson's. One of those studies we do have here at Penn where we are looking at a specific type of patient with Parkinson's who is they have the conditions secondary to mutation in a gene that is one of the most common causes of genetic forms of Parkinson's. And basically, the study is looking at ways of delivering that gene, the normal version of the gene back to the patients, in the hope that correcting the gene mutation will ultimately translate into a reduction in the progression of symptoms and the disease itself. These types of clinical trials are early in their development. We're talking about mostly phase one studies. So, we will have to see whether these studies actually are successful but we're certainly very excited about it. And I think as we recognize more and more genetic causes for Parkinson's will probably have a larger option or larger amount of options of Gene therapies for these trials. There's also a prospect that some of these Gene therapies may actually also work for patients who don't necessarily have a gene mutation. So that I think is also very exciting because we're talking about being able to provide this cutting-edge technology to the broader Parkinson's population.

Shweta Mishra: Right**.** That's very interesting Dr. Deik. At this point now, I would like to invite the patient panel Dr. Deik to the discussion. First up we have Dr. Frank C Church, Professor of Pathology and Lab Medicine who was diagnosed at the age of 60 and as a long-time educator and scientist he is committed to helping others learn more about Parkinson's. Dr. Church, you have the floor.

Dr. Frank C. Church: Thank you. Dr. Deik, I enjoyed your presentation. My first question would be you talked about the role and the importance of aerobic exercise as being neuroprotective. And what strategy can you do to convince your patients to actually exercise? Most of the people that I know with Parkinson's of my age are older and they don't like to exercise. How do you convince them how important it is?

Dr. Andres F. Deik: That's a great question. It's a challenge I will say. Some patients who come to see us already have the habit of exercising so that's easy. Right? Just tell them, keep doing what you're doing. But how do we convert if you may the non-exerciser or to an exerciser. There's are few strategies, I will say I usually think about it depending on whether patients still working or not. So, for patients who are still working, I usually tell them to try to fit it in the morning before they go to work just to carve out about 20, 25, 30 minutes every morning, even if it means waking up a little bit earlier, which is kind of getting it out of the way and then just going on with your daytime routine. Now, patients who are retired or were no longer working and do have some more flexibility with time. So, the benefit there is that you don't have to tell them to wake up earlier, which many people don't like to do, but I usually still tell them to try to fit it in the morning. I feel like most patients after they exercise, develop a feeling about of-being and sort of an energizing sort of effect

that carries out throughout the day. So, I tell them that it's like taking an extra pill, like the same sort of motor benefit that a pill could provide, a little bit of exercise could provide to you, and you want to capitalize on that and make sure that you front-load that in the day. Something I do see is that there are patients who like to exercise at night, and they tell me that after they exercise, they do have this rush of energy but then they have trouble going to sleep because there is sort of snow ripped up from having it a good exercise later in the day. So, as I was saying, I usually encourage it earlier in the day or rather later, if there are patients, who like it at night, and they find that it doesn't interfere with sleep then again, whatever works for you works for you, but I have seen that sort of trying to put it in earlier in the day tends to work for most patients.

Dr. Frank C. Church: Okay. Good. That was helpful. Okay. My next question may not have an answer. Are you concerned at all about covid-19 promoting or accelerating Parkinson's?

Dr. Andres F. Deik: That's a great question. And I think the jury still out. There was a review I want to say was published last year by a Brazilian group, looking at movement disorders happening after covid-19, and contrary to the side that parkinsonism was a big one. It was actually on minority locations that were seen to be parkinsonian the most likely movement disorder seen in patients after covid-19 was actually myoclonus, which is another movement disorder completely different from Parkinson's. But I do worry that we might be headed towards the situation similar to the 1920s pandemic where there was this delayed effect from the Spanish Flu with patients developing what's now known as Encephalitis lethargica or post and syphilitic parkinsonism. Again, we haven't seen those cases yet but more and more, we have evidence that even mild cases of covid-19 can have an impact in brain function to some extent that we don't quite understand yet. So, I think the community in general is very much in the lookouts to see whether there will be an uptake of cases in the next few years. And I guess the jury, as I said, the jury still out. But yes, it is a source of concern and hoping that the virus is this similar enough to the virus from a century ago that we will not be headed in that direction.

Dr. Frank C. Church: Yeah, I hope so too. Okay, my next question and I talked to a lot of people that have Parkinson's and their neurologist sometimes really don't want them taking supplements. I take, I'm a scientist, I read a lot, I think a lot, and I take a lot of supplements from the literature and my neurologist have been very supportive of me and my trick to try and maintain my health, and my remaining depleting neurons from dying further and I'm just wondering what your belief is about using supplements?

Dr. Andres F. Deik: Well, some supplements we know that are ineffective for example, coenzyme Q10 has been studied thoroughly. There was a large study that was called the QE3 study, which was done a few years ago and high doses of coenzyme Q10, were studied and shown not to be effective. So, there are some supplements that we know do not help. However, for the great majority of them we do not have that evidence suggesting that they do not work, and the truth is that they are helpful for health in general. So, my approach is usually that as long as the supplement is not harmful, I am not opposed at all to patients taking supplements. I do caution my patients that supplements can be expensive. So the cost of them tends to add up and then some of our patients who unfortunately have strict finances might not have the luxury of trying out a wide variety of supplements just because it's just not financially feasible for them, but if it doesn't burn a hole in your pocket, and it's not causing any harm, I think again, there's a lot that we don't know about the benefit of these supplements. So, I'm not at all opposed to our patients using them.

Dr. Frank C. Church: Okay, good. My final question relates to DBS surgery and my neurologist have always told me that he thinks I'd be a good candidate for it in some future time and but I keep running into friends and people that have had the surgery that are having a really difficult time recovering from it. And I'm just wondering if there are algorithms or there are good ways to predict who should be a good candidate for DBS surgery. And what are the pitfalls? How do you predict somebody should have a good response? It just kind of concerns me now all the sudden.

Dr. Andres F. Deik: Yeah. That's a fantastic question actually. I think patient selection is key. Patient selection goes both ways goes, number one, how does the patient look and what are the patient's characteristics. Number two, what are the patient's goals for the surgery. And I'll kind of go into both of

those categories. So, speaking about the patient's characteristic, first, there's a few characteristics that we like to see in patients who we think are ideal candidates. Number one patients who are cognitively intact. This is a brain surgery and there is reported cognitive loss after the procedure. It is usually just a matter of a few IQ points, but for patients whose cognition is not the greatest, that could mean the difference between somebody who is cognitively intact and somebody who has mild cognitive impairment, for example. So, we usually send patients force, a test called, neuropsychological testing where we really make sure that cognition is really in good shape.

So that's number one. Number two, we look for patients, who are levodopa responsive. So, I think it's reassuring when we see that patients take levodopa, and many other symptoms improve and the degree of improvement from those of levodopa tends to be predictive of the success of the surgery. Now, they're one exception to that is Tremor. So, Tremor, can be a symptom that can be really hard to treat with the dopaminergic therapy, but it really responds in a remarkable way with surgery. So, I would say the one exception to the dopamine responsive rule is if somebody has a lot of tremor that is refractory to medication. But everything else, I would say, we do like to see the dopamine response and what we do is we do something called on off testing where patients come into the office, off their medications, we examine them, then we provide them their medications, that we examine them again, and we track the amount of improvement pre and post. And that again is predicted of benefit. And then the third patient characteristic is of the patient is otherwise healthy for surgery. So, kidneys, liver, lungs, heart, everything else should be in good shape. We also like patients who are younger than 80 if possible. Now, that doesn't mean that we don't operate in people older than 80, we do, but we are a little bit more judicious on our patient selection, once they're over the age of 80. That's category number one.

Category number two is, what are the symptoms you want treated? So, DBS is really great to treat some symptoms, but it's not really very good to treat some others. So, the symptoms that respond the best with Deep Brain Stimulation is as I said Tremor, but also slowness and stiffness. DBS often times has equivocal benefits in terms of gait. So walking is a little bit hard to predict, some patients notice that they actually walk worse after surgery, and that's a real risk that we usually counsel our patients. And DBS can also deteriorate cognition as I mentioned before, but it can also deteriorate speech. So, if a patient is going to DBS so that they can speak better. We usually tell them, well, maybe DBS is not the best thing for you. So, if you have a patient who fulfils all the characteristics that I mentioned in the first category, and who has a symptom that we know responds very well to the surgery, those are the folks we highly encourage to have surgery. Now, the other benefit I will say is that DBS also allows patients to have more on time and less off time. So, it also helps with motor fluctuations when patients aren't noticing that the medication is lasting for three hours or less. And the other thing is that, after DBS, it allows us to reduce the amount of medicine a patient takes and that can also with dyskinesia, so that can also be a symptom that patients are interesting in treating. So, if patients have one of these symptoms that we know respond those are the patients who do the best. I would say patients who have less than ideal outcomes after surgery are usually those who either- A- weren't good candidates from a physical point of view to begin with, OR B- were most hopeful that would have a symptom that would improve that is not one of the ones that typically improves after DBS.

Dr. Frank C. Church: That was really helpful. Thank you.

Dr. Andres F. Deik: My pleasure.

Shweta Mishra: Thank you, Dr. Church, Dr. Deik. With that I will now invite Beverly Ribaudo. Beverly was diagnosed with Parkinson's disease at the age of 47, and she continues to laugh about her life with Parkinson's and cheers others through her funny stories and song parodies. Beverly, please go ahead.

Beverly Ribaudo: Thank you. Good morning, Dr. Deik.

Dr. Andres F. Deik: Good morning.

Beverly Ribaudo: I guess someone, my first question is, why are neurologist reluctant to reduce any of the

dosages or discontinued medications. In my own case, and I said I was diagnosed 15 years ago. Every time I went to my doctor's always, like increase, increase, increase, and had, I not figured out on my own that a recent increase, was causing my severe cognitive issues. I would have been confined to Memory Care Facility years ago, but because I managed to figure it out on my own and then insisted that we discontinued or lower that dosage. I'm back to within just a matter of months. I was back to my old Brainiac self.

Dr. Andres F. Deik: Well, there's all congratulations on being back to your old brainiac self. I think you raise a very good point, as the disease progresses often times, we as treating Physicians consider that patients need more medication to make up for the symptoms. That are now not as well controlled on medication as they were before. However, it is a fine balance unfortunately, with medications as you go up in the doses, as much as you might have a motor benefit or a non-motor benefit sometimes you also run into side effect profiles. So, the side effects of the medications that we use tend to be dose dependent. Meaning the more you take of a drug, the more likely you are to experience the side effect. And it certainly is something that is always in the back of our mind, whenever we do adjustments in medicines. There are different strategies for it. So, one I would say, this applies to me, but I would say that wise my colleagues, some for most people in the movement sort of field. We actually embrace polypharmacy, meaning taking multiple medications to treat symptoms. So, if you think of high blood pressure, for example, often times, your doctor will give you a blood pressure pill and will really go up as high as they can on that blood pressure pill before adding a second one. Whereas in movement disorder we don't quite follow that approach. We might give you a small dose of this and a small dose of that and it is more pills. But the idea of doing that is you can keep the dose low enough, they can minimize the risk of side effects. And then by adding these different medications through different mechanisms of action, you can have a net motor benefit at the end. So, I think you raise a very good point about the real risk of side effects that is involved in high doses of medicines and it's something that we as treating physician should always keep in the back of the mind.

Beverly Ribaudo: Thank you and Dr. Church might like to hear this DBS has actually been life-changing for me. I had bilateral STN and it'll be 10 years ago in October. My settings are extremely low, and I have been off all Parkinson's meds for over two years. And yet, I find that it's not recommended very often, especially for people who are young, onsets. Any reason why it's not suggested?

Dr. Andres F. Deik: Yeah, sure. I think, as neurologist, we tend to be probably overly conservative. I think we now understand the risks and benefits of DBS, and we probably as movement specialist do advocate for its use and try to find the right patients, who would most benefit from this therapy, but it is an invasive procedure. So, I think being that we're not surgeons ourselves. But rather just prescribing physicians, we do try to rely on medications for a while before sort of suggesting the idea of an invasive procedure. But as you mentioned, I mean, for some people, it really can be life changing. So, people can really get a great benefit out of it. I think we tend to be conservative also, because we want to make sure that we have the diagnosis right. So, in the first five years after people start having their symptoms there is always the possibility that patients don't actually have Parkinson's but have one of the atypical parkinsonian syndromes. And at the beginning it can just be very difficult to tell clinically whether somebody has one or the other. Now, the reason why I mentioned this caveat is because patients with atypical parkinsonian syndrome, do not respond to DBS and actually can do worse after surgery. So, I think many of us really want to make sure we have the diagnosis right before we offer this therapy, but as you mentioned I think for the right patient it can really be a home run.

Beverly Ribaudo: Thank you. And also, to Dr. Church I would like to say to him, the neurosurgeon's skill is a good priority but if you don't have an excellent programmer than the surgery is pretty much worthless.

Dr. Frank C. Church: Okay, thank you.

Beverly Ribaudo: Are there any treatments for drooling? And I get a lot of people with Parkinson's asking me about this and of course, I'm affected with it, as well as sometimes which is one of the few upsides to wearing these covid masks.

Dr. Andres F. Deik: Yes, a lot of my patients told me that nowadays. So, it hides the drooling, and it hides when they have like a tongue tremor or a jaw tremor. So those are the small silver Linings here. Yeah. There's actually a number of different treatments for the treatment of drooling, there are medications oral medications that can help. We tend not to use them very much because they do tend to systemic side effects. The one that we worry the most about is confusion or hallucinations. Low doses are usually not a problem but as you escalate, it becomes more of a concern. There are also topical treatments, these are off-label treatments where people use drops that go in the mouth under the tongue, and it can help dry the mouth up for about 12 to 24 hours. And then there are injections botulinum toxin injections have been shown to be effective in the treatment of drooling. Usually, those injections go in the cheeks or under the jaw and that can help with drooling for about three months at a time. So, many of our patients use one of these treatments or combinations of them and they can be very effective.

Beverly Ribaudo: Thank you. And then, I guess my other question is basically most of my doctors and most of the other people here, locally, their doctors always recommending PT, OT speech therapy, the big program, the loud program, but there are not any certified therapists in our area, even though we have well over a 150 to 300 people show up whenever we do big Parkinson seminars here. So, in some ways I wish our neurologist understood that we lack access to treatment because of where we live and our finances. My own movement disorder specialist is 250 miles away and I haven't seen her since 2019 due to Covid. So, a lot of us, we must take care of ourselves.

Dr. Andres F. Deik: Yeah, you raise a very good point and I think it just shows how specialized care for Parkinson's is really confined to large metropolitan areas and how they're all these pockets within the country where it's really difficult to access care. It's a very big problem in this country and really across the world. Speaking of silver linings of the pandemic, I think the other silver lining is the access to telemedicine. So, before Covid-19, telemedicine was seen as this luxury that was inaccessible. But now, it's really open to everybody. I mean today we're doing this interview and none of us are in the same room, right? So, I think this digital Revolution is really something that is going to change the face of healthcare for the better. And I think that also includes access to exercise programs online or zumba classes, yoga classes, things that patients can now access from the comfort of their home without having to expose themselves to catching a contagious disease or traveling hundreds and hundreds of miles. I'm hoping that something that will come from the pandemic is a little bit more equity in the way that care is delivered across the country and I'm hoping too that there will be loss that will follow, that will allow this to be a permanent change as opposed to this emergency authorization in the face of the pandemic.

Beverly Ribaudo: That would be nice because with my medicare advantage plan, televisits are covered for mental health and for primary care, but not specialist.

Dr. Andres F. Deik: Yes, so I think

Beverly Ribaudo: And once again location is the problem for where I live. We do not even have a board-certified neurologist in our town. We have two psychiatrists, who pretend to be a neurologist and no one with Parkinson's will go see them.

Dr. Andres F. Deik: Yeah, I think we need to do some door-knocking to our local state Senates, and really advocate for ourselves, and for the community and to raise this awareness, and it's not just Parkinson's, it's all the neurodegenerative conditions and really other conditions too knowing that we have these resources it just seems silly to me that we would go back to a world where we would cut access the way we have it now.

Beverly Ribaudo: Thank you.

Shweta Mishra: Thank you, Bev. Dr. Deik, I have just a few more questions before we wrap up for today, and I want to circle back and talk a little bit about the diagnosis and early signs of Parkinson's disease. I know you mentioned gait, right? Experts diagnose, it by gait of the patients, right. They just ask them to walk

and they're able to diagnose if they have Parkinson's. Could you please talk a little bit more about other symptoms or other parameters that are used to diagnose Parkinson's disease? And are there any blood tests or scans that help in definitive diagnosis?

Dr. Andres F. Deik: Yes, so the diagnosis of Parkinson's disease remains a clinical diagnosis. To make a diagnosis of Parkinson's disease you must have one symptom, that is a cardinal sign of Parkinson's, which is slowness or Bradykinesia. And to make a diagnosis of Parkinson's, you may have Bradykinesia, you have plus one of the following either tremor, stiffness, or changes in walking imbalance. So, slowness, plus, any of those three is enough to make a clinical diagnosis of Parkinson's. So, you can see it's not a lot of requirements to make a diagnosis. And this also contributes to why sometimes we get them wrong; you could make these diagnoses clinically and they could fit a patient. A patient could have slowness and stiffness, but that doesn't necessarily mean that they have Parkinson's, right. So, it's an overly sensitive way of diagnosing these syndromes. However, it is the standard of care, and it has been for the last 50 years. Now that's changing with the advent of new technologies will allow us to more readily identify patients who have Parkinson's. There is a scan that has been available in the US since around 2011, call it a DaTscan. DaTscan stands for a Dopamine Transporter Scan, and it allows to visualize the integrity of the dopamine circuits in the brain. So, it can be very black-and-white to distinguish between patients who have some form of Parkinson's versus no form of Parkinson's, and we do use a DaTscan sometimes in patients, usually the indication is for patients who have a Tremor but not much else and you're not sure if it's a tremor from Parkinson's or is it tremor from another tremor condition. So that's what I would say is the main reason why we do that scan. There are more recent technologies that now allow to analyse samples to look for the presence of alpha-synuclein. These are more recent technologies available in the last year or two, looking at the presence of alpha-synuclein in cerebrospinal fluid, which is the fluid that bathes, the Brain and the Spinal cord as whereas in skin biopsies, so people are getting little samples of the skin looking under the microscope and finding some alpha-synuclein there. So, I think especially for clinical trials, as we develop these technologies, my guess is that many of the trials are going to request some sort of confirmation, especially for those trials that are recruiting patients during early in the course of the disease just to make sure that we're able to have a unified, homogeneous population within the studies.

Shweta Mishra: That's very interesting to follow. Let's talk about the progression of Parkinson's, a bit Dr. Deik. So across what stages could this disease progress? And what are the symptoms that differentiate the various stages of Parkinson's?

Dr. Andres F. Deik: Right. So, the staging is also clinical, and we go really by the symptoms that the patients have. So, stage one is, when patients have symptoms only on one side of the body. So, Parkinson's disease, is that condition that usually starts on one side and then spreads to the other, the side where it starts is usually the side that the symptoms are always the worst on. When the symptoms go to the opposite side, which talk about stage two. We think of stage three, when the balance is affected, we think of stage four when patients require some sort of device to ambulate like a walker, for example, and then we think of stage five, when patients are on wheelchair or bed bound. So, the progression of their ability to ambulate, really determines the clinical staging of the disease.

Shweta Mishra: Right. Thank you so much. So, Dr. Deik, let's talk about the risk factors a little bit. And one of the biggest risk factors of this disease is age, right? We see it as a geriatric disease, but we do also see the disease in younger populations as young as 20- to 30-year-olds, right? We know Michael J. Fox was diagnosed at 30. So, I'm just curious, what could be triggering the occurrence of Parkinson's at such a young age.

Dr. Andres F. Deik: Yeah. So, we now recognize that there is this entity called young onset Parkinson's disease where patients have really early symptoms of Parkinson's and largely patient with young onset Parkinson's disease are thought to be due to genetic causes. So now with the sort of refinement of Gene sequencing technology, we're able to really scan the patient's genomes and really find mutations that we've did not really know before that existed. So, patient with young onset Parkinson's disease, have always existed. We now just do a better job in knowing exactly what Gene is causing them.

Shweta Mishra: Interesting. So, Dr. Deik, I have one last question before we wrap up for today. And that's about neurogenic orthostatic hypotension, one in five people with Parkinson's have this condition. So, could you, please talk about what it is? And why does that happen to Parkinson's patients? And how is it that managed?

Dr. Andres F. Deik: Yeah. So orthostatic hypotension is relatively common in patients with Parkinson's. We think that as the autonomic nervous system, which is the part of the nervous system that is in charge of sort of automatic bodily functions, including the regulation of blood pressure. We think that the autonomic nervous system is affected in patients with Parkinson's. Not only with Parkinson's, other Parkinsonian syndromes also feature this. But since we're talking about Parkinson's today, that's one of the conditions that also feature this, and it is manifested by a drop in blood pressure that is noticed when the patient stands up. The patient stands, feels lightheaded, oftentimes but not always, and that translates into a drop of around 20 points in their systolic blood pressure. The causes are multifactorial, one, as I said, is the involvement of the autonomic nervous system. Two, the medications that we use also, sometimes can trigger orthostatic hypotension. So, going back to the question before about medication side effects. That's one of the ones that we are very much in the lookout for. And we routinely check blood pressure, sitting and standing in our patients to see whether that's something that's coming up. It could also be other medications that the patients are taking. They're not necessarily for the treatment of Parkinson's that are also lowering blood pressure so that can also happen. And then a very big one is dehydration. So, patients with Parkinson's are more prone to dehydration and in the hot summer months that's certainly true, I would say June, July, August, and September are the toughest months for my patients. And what I try to do is as the summer approaches around now, actually, I start really advocating for aggressive hydration in my patients as long as they don't have any reasons not to keep themselves well hydrated, like kidney problems or heart problems or lung problems, or things like that. But I think keeping yourself very well-hydrated if you can, avoiding medications that can further lower blood pressure, and being mindful that you have this condition can certainly prevent the biggest thing that we dread with hypotension, which falls on the complications that come with that.

Shweta Mishra: Right. Thank you so much. Thanks for that information doctor. With that it's time to wrap up for today. Thank you. Dr. Deik for educating us on Parkinson's disease today. Dr. Church and Bev, thanks for joining and guiding the panel with your very insightful questions. We also thank the University of Pennsylvania, and this talk will be available on curetalks.com. So, until next time we meet. Thank you everyone and have a great day.

Thank you.