Moderator Rachel Breidster: Hello and welcome to Public Health Live!, the Thursday Breakfast Broadcast. I am Rachel Breidster, and I'll be your moderator today. Before we get started I ask that you please fill out your online evaluations at the end of the webcast. Continuing education credits are available after you complete our short post-test, and your feedback is helpful in planning future programs. The planners and other speakers have no financial arrangements or affiliations with commercial entities whose products, research or services may be discussed in this program. Dr. Salgado serves for speakers bureau for Teva Pharmaceuticals and Allergan Incorporated, and is a consultant for Teva Pharmaceuticals and Allergan Incorporated. We will be taking your questions throughout the hour by phone, the toll-free number is 1800-452-0662 (this webcast is over and questions are no longer being taken on this topic), or you may e-mail your written questions to phlive.ny@gmail.com (this webcast is over and questions are no longer being taken on this topic). Please send your questions at any time throughout the hour. Today's program is, “Parkinson's Disease: The Importance of An Interdisciplinary Approach for Identification, Treatment and Patient support.” Our guest today is Dr. Miran Salgado, who is the Chairman at the Department of Neurosciences at New York Methodist Hospital, and the Medical Director at the American Parkinson Disease Association Information and Resource Center at New York Methodist Hospital. Welcome, doctor.

Miran Salgado, MD: Thank you. Thank you for having me on the program.

RB: To get us started today, can you tell us what it is we hope to accomplish with today’s broadcast?

MS: At the end of this program, we should be able to list the early clinical manifestations of Parkinson's disease, at least identify two treatment options available for patients with Parkinson's, and recall at least three examples of local support and resources which are available to patients with Parkinson’s disease and caregivers.

RB: I think many people have heard of or are familiar with the term Parkinson's disease but most of us don't know much about the history or background of the disease. Can you tell us when it was first identified?

MS: The history is very interesting—not only for the illness, but also for the man who described this. It was James Parkinson who was a family physician in England, and he was a member of the Royal Court of Surgeons who first described six patients afflicted with this disease. Parkinson himself was interested because he was a rebel physician who was fighting with the government and later on in life he started writing. So Parkinson who describes six cases of shaking palsy in 1817, not only published on this but
appendicitis, gout and other illnesses as well. About 60 years later Shaw Cole, a very famous French neurologist once again saw this illness and once he looked to the literature, he saw Parkinson had already mentioned this and written about it and named it Parkinson's disease.

**RB:** Who is more likely to be diagnosed with Parkinson's disease? Is there a difference in men and women? How much of a factor does age play?

**MS:** Age plays an important role. We see increased incidence of Parkinson's in an ageing population. It is the second most common neurodegenerative disease after Alzheimer's. It affects approximately a million people in North America and about 4 million people throughout the world. The majority of the patients get their initial symptoms in their 60s. For incidence, you might see 0.5 people between the age of 30 to 39, if you go up to 80 to 89 people, it will be up to 120. So you see this enormous Increase of incidence as we get older.

**RB:** And does gender play a factor?

**MS:** Gender does play a factor. It was slight extent. There's slightly more male predominance than female.

**RB:** What about the progression of the disease? Does Parkinson's fairly to progress fairly rapidly or a slow progression?

**MS:** It is highly variable. There are patients who develop Parkinson's at a younger age who might progress at a slower rate. Certain forms of Parkinson's which are inherited might have a much higher rate of progression. Some of the forms have slower progression. So it's a highly variable progression. But in gender terms, younger patients probably have a slower progression. All the patients might have developed after 70 might have a faster progression of the illness. People who have more tremor might have a slower progression as opposed to people who start with walking difficulties, they have higher faster progression.

**RB:** Now, I think we hear a great deal about neurodegenerative disease and its impact on the aging population. Can you talk to us about Parkinson's disease as compared to other diseases such as Alzheimer's and what can we expect in the future in terms of prevalence?

**MS:** Prevalence of both of these illnesses are going to increase. If you know right now from public health perspective, Alzheimer's is going to consume the most amount of health care dollars as we go along. If we were to take prevalence of Parkinson's as I mentioned, we based on the age group, if you take patients at 70 years you'll see a prevalence about 120 per 100,000. Gender prevalence is about 20 per 100,000. You see the difference in aging age group with the age of the population, the prevalence will increase.

**RB:** Now, what are the main causes of Parkinson's disease?
**MS:** Causes of Parkinson’s is multifactorial. So, there's a genetic component and there's environmental component. We feel that familial forms of Parkinson's account for about 20%. Out of that, one-third—5-8%—are what we call monogenic inheritance, meaning a single gene would account for the illness. And the rest of the 20% would be polygenic, multiple genes involved. The others are sporadic as far as we know. But there can be some genetic influence on those as well, which are unknown.

**RB:** So you can tell us a bit more in detail about the genetic causes of Parkinson's disease.

**MS:** Out of the genetic forms we have identified certain chromosomal areas, and they have been sequentially named from park-1 to park-18. That basically means a certain area of the chromosome that is affected. That doesn't necessarily mean that we have identified the gene. We've identified at least six genes which are known to cause Parkinson's. First one was the alpha-synuclien gene which was also known as park-1. Park-2 was the parking mutation which we have identified as a parking protein. Now, alpha-synuclien was first identified in an Italian family and subsequently in Greek families a faster Progression illness—autosomal dominant—starting at a young age. It was early onset. Park-2 was autosomal recessive once again in the young populations we have seen this. The commonest is leucine rich reverse kinase, which is what is called park-8. Which is seen in a autosomal dominant patterns in older individuals. We have also identified another mutation called pink which is park-6 and park 7 is called Dj-1. So these are the genes specifically identified, but as for now about 18 chromosomal areas have been identified. Sometimes there is overlap, in fact park 1 and park 2 subsequent people realize it's the same gene you're talking about even though the chromosomal areas were identified separately.

**RB:** In addition to the genetic contributions or contributor, there's environmental factors as well. Can you talk to us about those?

**MS:** Environmental probably plays a big role. Environmental factors might be modifying our genes. So these are susceptible individuals in their genetic makeup. Then they get exposed to something in the environment that caused change in the genes which would result in abnormal proteins which would double up toxic. We know that people who live in rural areas are much more likely to get Parkinson's. One of the reasons might be the exposure to pesticides. People who are exposed to carbon disulfide have been known. Manganese has been known to cause Parkinson's. There are so many other solvents and chemicals that might be resulting in increasing incidents of Parkinson’s.

**RB:** So we need to consider the genetic and environmental. Giving these factors, are there things we can definitively say about what causes Parkinson's?

**MS:** I don't know whether one can frame it may way, as if it is something that for 100% sure you're going to get Parkinson's. But we know that MTPT which was a by-product of heroine that was cooked by addicts in California back in the '70s, and when they got exposed a significant number of patients came down with Parkinson's either sooner or later. So that is what we use for animal models today, MTPT-induce Parkinson's for animal models to create Parkinson’s.

**RB:** Can you tell us what exactly is happening in the brain of someone who has Parkinson's and what's the pathology of the disease?
**MS:** The pathology of the disease—and we always define Parkinson’s as a motor illness. The motor manifestation which are mainly the stiffness, slowness, tremor and balance issues come because of the problems we encounter in the basal ganglia and the dopaminergic neurons you find in the mid-brain. These are the cells which when they start dying and about 60% of these cells get affected, you first manifest with the motor manifestations of the illness. But the illness itself might be starting way before you really get the motor manifestations and then key things in this is to emphasize how to recognize even before you manifest with the motor symptoms.

**RB:** And is that—you talked a little or I know you were going to talk about the presence of Lewy bodies.

**MS:** So Lewy body is a pathological hallmark of Parkinson's. This is aggregate of abnormal proteins in the cell. They're not 100% sure if it's the cause or the effect. We have former packages of normal proteins to protect the cells or is this toxic in itself? But these are abnormal alpha-synuclein which we see in the Lewy bodies. We also know at this time that huge hypothesis is Parkinson's really a prion disease because we know if you take this substance in the Lewy bodies that inoculate another cell, you can get Parkinson's changes happening in those cells. So these become kind of infectious particle. But Lewy body path logically is a hallmark of Parkinson’s.

**RB:** What can you tell us about the way the disease progresses within the patient?

**MS:** This is once again a very interesting hypothesis. There's a pathologist in Germany called Braak who classified Alzheimer’s disease pathologically. About 10 years ago, he came with a hypothesis. He looked at brains of Parkinson's patients at different stages and also he looked at other organs like the gut and the olfactory system. He hypothesized that actually Parkinson's earliest changes probably occur in the gut, what we call the enteric autonomic nervous system. And Lewy bodies are found in those. Subsequently there's a spread to your olfactory bulb, to the brain stem and ultimately the cortex. Based on this, he classified Parkinson’s into six pathological stages—in fact it is in stage 3b where the mid-brain gets affected. In stage 1, it will be the peripheral nervous system that it starts with.

**RB:** Are there specific phases of progression in terms of how Parkinson's affects the patient?

**MS:** Yes. We can once again look at how your dopaminergic system gets affected. And even before the dopaminergic system I have to emphasize this is primarily the motor symptoms are due to the dopamine other systems such as your serotonergic system, and other systems get affected in Parkinson's. So you have a premotor phase where symptoms are seen and they're usually non-motor manifestations of Parkinson’s. Your dopamine producing cells will be falling as you see on the graph and with that your symptoms with non-motor symptoms start first. At a certain stage when dopamine producing cells are affected to 60%, you start getting the motor symptoms. That is when the first initial diagnosis is usually made. But we might be able to see what are how these non-motor manifestations which you may be able to see way before you get the motor manifestations.
RB: So based on that description it certainly sounds like there's a lot that's happening within the patient and as the disease is progressing. And it's not just impacting motor symptoms. So you can talk a little bit more about that?

MS: Yes. Some of the non-motor manifestations, let's go to the pathology of what Braak described. What happens when the gut autonomic nervous system gets affected? You get constipation. You see people who get constipation 10, 15 years before you get the tremor, stiffness. Sleep very important. REM-behavior disorder where people act out their dream sleep. Where they scream or normally in dream sleep you are paralyzed. You lose the paralysis when you have REM-behavior disorder and you might see this five, ten years before you develop Parkinson's. Similarly, you might get cardiac rhythm changes which is when the cardiac autonomic nervous system gets affected. Hypertension might be seen. Depression very common before you develop Parkinson's not only in Parkinson's even Alzheimer's depression precedes the neurodegenerative diseases because the mid-brain gets affected both in Parkinson's as well as in Alzheimer's. Erectile dysfunction in men which needs treatment, again another risk factor. Rheumatological complaints are very common, including shoulders, elbows. These have been weighed into the classification of diagnosing Parkinson's.

RB: Certainly I think for a lot of us we think of the motor symptoms but those non-motor features are fairly significant. Can you talk about the differences between the two?

MS: Differences between the—

RB: Between motor symptoms and non-motor symptoms. What are the early motor features?

MS: The early motor features are you might see a variability of your gait pattern. These are a little bit more difficult to assess than non-motor. Flexion/extension of the wrist, reaction time, movement time. If you can measure. These are motor tests. Some of the dexterity tests like the peg board test which are given in jobs to see how quickly you can perform tasks, this kind of reaction movement association task will be affected from the motor aspect. And these might occur once again before you truly see the true motor features of the illness.

RB: Now, you've certainly gone through a lot of non-motor and motor features, given all of that, how is the disease clinically diagnosed when we consider all the information you've shared?

MS: So the clinical diagnosis there's an age-old way of clinical diagnosis. The main body—had a task force which was convened to come up with the diagnostic criteria. They just published it about three months ago. A lot of us wondered, well, how are we going to bring the non-motor markers to the process of diagnosis? In fact, they designed it to kind of leave it alone and form a separate category called prodromal Parkinson's. Give hypothesis and the odds how to calculate if you have a number of those high-risk factors which I described. From the motor aspect, it's a two-step process. First is that you are to establish you have Parkinsonism. To say you have Parkinsonism you would have slowness—which is bradykinesia—and two of the three major manifestations, which are rigidity, tremor and postural instability. So you have slowness and one of the other three, then you say you have definite Parkinsonism. How do you make a diagnosis of Parkinson's disease from there? Everything that looks
like Parkinson’s may not be Parkinson’s. To make that diagnosis, first of all, you cannot have any definite exclusion criteria, and they listed a number of them which actually these markers for other look-alike syndromes. Then they said there are red flags. If there are red flags you cannot make a certain clinical diagnosis, only be possible or probable diagnosis. Once you take those two out, if you have a good response to L-Dopa, if your symptoms are symmetric and your onset is asymmetric, which are called supportive criteria, you can make a diagnosis. First you have Parkinsonism, then you have the ones with simple Parkinson’s disease—who usually have a resting tremor which is a supporting criteria—resting tremor, asymmetric onset, and a good response to L-Dopa which I think is extremely important.

**RB:** Are there blood markers? What are tests are available that can help with the diagnosis?

**MS:** Clinical tests with blood, CSF, skin tests, looking for alpha-synuclein, particularly, none of them are really established at this time. So they’re good in a research way. Out of the radiological disease markers we have, the DaTscan and PET scan are probably the most useful. MRI can sometimes show changes in the middle brain. Sonograms might show that you have hyperechoic areas but I think we should more emphasize on the DaTscan which is kind of the latest tool in the toolbox in this country. It came in 2011, and it has been here five years in the United States. It has been in Europe for the last 15 years. And with DaTscans you are basically looking at the dopamine reuptake sites. Therefore indirectly looking at the dopaminergic neurons or terminals.

**RB:** Is that one of the more new or exciting diagnostic tools you wanted to share with us today?

**MS:** I think it is one of the newer diagnostic tools which are available. It has been increasingly used. You understand in this country the FDA has given it labeling—it is to differentiate between essential tremor and Parkinson’s. But what we are looking at is in an indirect way the amount of dopaminergic nerve terminals which are there, it’s a very visual test. Right now it’s only a qualitative test. You look at the picture and say, “well, we think this is abnormal shape. This has not been seen in a normal person.” We have a head and a tail. If you look at the picture on the slide you'll see that. If the tail is vanishing first, you say, “oh, this area, there’s less dopaminergic nerve terminals and therefore this patient might have Parkinson’s disease.” It’s not a good test to differentiate between Parkinsonism Syndrome. It might be able to differentiate drug induced Parkinson’s from idiopathic Parkinson’s disease because if psychiatric drugs are producing it, the DaTscans will be normal, if it’s vascular issues like in vascular Parkinson’s, it might be useful in differentiating.

**RB:** Now, in addition to these different motor features that we've discussed, can we talk about cognitive changes that might occur in an individual as the disease progresses.

**MS:** Cognitive changes even might incur before you have motor manifestations in a group of patients. Now, we have two forms of cognitive changes. One is Parkinson’s disease, the other is Dementia which occurs years after you develop the motor manifestations. Some of the changes you'll see is in attention—your attention span might become shorter. You might have visual/spatial skills which may get affected. You might be getting lost in space. If you're asked to copy a complex diagram, you may not be able to put the spatial sequence in a proper manner. Also, you might get autonomic changes with blood pressure fluctuations. Your retrieval abilities—what we call ‘tip-of-the-tongue phenomenon’—
your retention is usually okay but your retrieval can be affected to a bigger extent. Memory is not a major feature that gets affected early in Parkinson's dementia as opposed to Alzheimer’s, which is primary memory problems, but memory can get affected as well.

RB: Well, thank you. Now, we recently had the opportunity to visit with Dr. Albert Ortega, a New York Methodist Hospital’s in-house Neuropsychologist. Dr. Ortega focuses on the interface between physical and psychology response to illness and injury. Let’s take a look.

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 Albert Ortega, MD: What’s fascinating about Parkinson’s most people consider it a motor diseases—unfortunately it’s more than that. There are two major aspects of Parkinson’s which are not motor which affect individuals in a serious manner. One of them are the cognitive changes that occur with Parkinson’s and the other one are the mood/behavior changes. Now, the cognitive changes unfortunately start pretty mild and often manifest itself as something called mild cognitive impairment. But over time worsens to an eventual dementia. Some of the symptoms of Parkinson's actually occur before the motor symptoms. Cognitive deficits are some of them, and depression as well. Now, we make a distinction between mild cognitive impairment and dementia when it comes to Parkinson's. The difference really is, in one case you do have the cognitive deficits—mild cognitive impairment, but they don't affect functioning. They might be annoying—you might forget where your keys are or where you parked your car—but it's the kind of thing where you can still do your bills, get to locations and so on and so forth. Unfortunately, it evolves to a dementia where you’re going to need help to do the basic things in life. Now, people often ask, isn’t depression with Parkinson’s really a reaction to the Parkinson’s? I mean, if I couldn’t walk, I’d be depressed. Well, that may be the case. But they've done some interesting studies where they worked with individuals who have difficulties with movement. A lot of rheumatology patients have difficulties with movement and they compared them with Parkinson's patients who also have movement issues, and they looked at the depression between the two. As it turns out Parkinson’s folks are more depressed. So there’s something more to it than just the fact that it’s changed your functioning.

In addition, the role of dopamine in Parkinson’s understood by everyone, but people tend to forget that dopamine is also implicated in depression. In fact, one of the popular medications for depression, Wellbutrin, works on dopamine receptors. So, yes, depression after Parkinson’s could be a reaction, but we also understand it's caused by Parkinson’s. I will be honest, the success of cognitive intervention for Parkinson’s may not be as successful as an acquired injury—because basically we’re fighting a degenerative disorder and the individual gets worse. But at least the hope with cognitive remediation is we’ll keep the individual at a certain level for a longer time. If you have a Parkinson’s patient who’s having memory difficulties as a family member when you get home, you may want to ask, “Hey, did anyone call?” to help trigger the Parkinson’s patient’s memory. And if they say yes but can't recall who, you might want to give them an alternative possibilities—was it a family member? Was it someone calling for business? So these serve as prompts that help the individual come up with the answers. So remediation, compensatory strategies for the patient, as well as the family.

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**RB:** certainly a lot of good information there in that video. Now, earlier you mentioned briefly Lewy body dementia. I wonder if you could talk to us a little bit more in detail about what that is.

**MS:** The term Lewy body dementia was coined when people saw a process of dementia occurring early with features of Parkinsonism. The clinical diagnosis of Lewy body dementia was made when either dementia occurred first or dementia occurred within the first year of being diagnosed as Parkinson’s. These patients had vivid hallucinations. They had fluctuating cognitive functions. They had episodes of confusion. Some of them came to the emergency room with confusional episodes. They had a significant amount of autonomic dysfunctions with episodes of fainting. They were very sensitive to neuroleptic drugs which made their Parkinsonian symptoms worse. So these were classified as different illnesses, they found Lewy bodies in their cerebral cortex. Today the thought process has evolved that we are just seeing another Lewy body disease. This is in the same spectrum. If you see the neoclassification, they say Parkinson’s dementia with the Lewy body variant or the subtype with Lewy bodies. Many of us believe this is in the same spectrum as Parkinson’s, dementia but the dementia component is occurring fairly early but the pathology is very similar and the clinical manifestations of both of these is very similar as well.

**RB:** We've spent a lot of time talking about symptoms and ways to diagnose. Let's shift gears and talk about the options that exist for treatment.

**MS:** The treatment options I think can be broadly divided. One could be just nonpharmacological methods in the early phases of the disease. Then you have the medical options—which are available, and surgical options that are available. Secondly, we have to look and say, this is a progressive neurological disease can we slow progression of this illness which will be the key, and are there any new protective strategies we can use if they're available? So then as I mentioned, you have symptom relief. What are the medications or non-medical strategies we have for symptomatic relief? For early Parkinson’s patients, we can use a wait and watch policy. This is what we followed for many, many years. People said, “You have a little tremor, who cares? Wait and see.” I think the thought process has since evolved. We pay a lot of attention to quality of life. If somebody says, “Doc, my tremor really makes me ashamed of myself. I cannot go into public.” You have a problem. You are not disabled. You’re able to do everything, but that really affects your life. So then we feel, oh, you should treat because it affects your quality of life. And we have made quality of life and we have made quality of life parameters like the pdq 39 a quality of life questionnaire assesses these areas. From the non-pharmacological approach you can have counseling. You can have exercise regiments which are initiated very early in the illness. You can treat things like depression very early as well, which might help Parkinson’s patients not cope with the illness, they'll be much more conducive to taking part in managing the illness as well.

**RB:** Now, what would you say are the goals for medical treatment of Parkinson’s?

**MS:** So once again the goals are can we retard the progression of the illness in any way? We should institute them early. In the short term, we are trying to alleviate symptoms and give you back your functionality. Improve quality of life. And in the long term we want to make these treatments effective for as long as we can go on and with the least amount of side effects. Those are the main goals for medical management.
RB: You discussed a number of different treatment options. As a doctor, can you talk to us about, how do you make decisions about treating different patients?

MS: This is a key in managing Parkinson's patients. No two patients with Parkinson’s disease are the same. As I mentioned before, some people progress faster, some people progress slower, some have more tremor, some have more gait difficulties. So each person, some have cognitive problems, some don't until later. The age is a primary concern, a younger person the way you manage would be quite different from managing an older individual. Your lifestyle, are you active? Are you retired? Or are you still working? Are you a CEO of your company and you’re in your 50s and you want 10 good years in your life to make that retirement nest egg bigger? And that's a big consideration. You might use drugs different to keep the functionality different not thinking of 20 years from now because he wants 10 years. I have had this in patients each come with a different employee status. They may want to keep their job, which is quite different from a person who is retired. Comorbidities, do you have other concurrent illnesses? Some of these medications may interact with other drugs. Cognition—very important. Certain drugs we don’t want to use in something who is cognitively impaired because you have a high chance of developed hallucinations and psychiatric manifestations in those patients. Caregivers. Do you have anybody at home, or are you living alone? You don't want to try out a medication which might make you confused or hallucinate or you might go very, very slow based on that. And from the treatment side, the efficacy of the medication. We always weigh the risk and benefits of a medication. That's key to giving any medications. How will this patient tolerate that and what are the side effect profiles? And then when to start the medications. So these are all kind of broader treatment considerations when you select medications and non-medical forms of management.

RB: Now, you mentioned there are medical treatments some of which are neuroprotective and some of which may tend to alleviate symptoms. Can you tell us more about those different options?

MS: So this is kind of a lecture by itself, but if I kind of narrow it down, if there’s anything neuroprotective, you should use them early. Is there anything that has been known and FDA has approved so far as an agent that will retard disease progression? No. But we have tried a couple of things. When selegiline came out first in 1980 and 1990, the study was published with selegiline compared to placebo as well as Vitamin E, they found that people with selegiline would offer short period did better. So at that time they came to the conclusion, well selegiline it might be neuroproductive. They didn't consider one thing. They didn't consider that selegiline by itself had symptom relieving properties and they might last in the system longer than what they anticipated. However, there's enough animal experiments by pretreating symptoms with selegiline and then exposing them to other toxic substances that you might have some protective benefit. So is rasagiline, it is another monoamine oxidase inhabitant with a large study in Europe with one milligram and two milligram dose. One milligram dose showed three end points but again it has been challenged. FDA did not give the labeling that this neuroprotective. We tried ant oxidants. We know that one of the mutations which we see in dj-1 actually is related to oxidative stress. So this is a big hypothesis that oxidative stress might be bringing it on. But we know at least one of the genetically acquired ones may be through this mechanism but again we don't have antioxidants like Vitamin E, Vitamin C which we use in large quantities to be of any benefit. Mitochondrial biogenetics, such as CoQ10, and creatine, once
again the studies have failed to show. We really don't have anything for sure, but we can do guesswork and see with maybe some may be a little bit more useful than the others.

**RB:** Can you give us more detail on various drug options specifically the Levo-Dopa?

**MS:** Levo-Dopa is the most useful or most powerful agent, and the most potent agent for the treatment of Parkinson's disease. It is dopamine that you are replenishing in the Levo-Dopa form, it is taken up by the nerve cells and then released in the nerve terminals. There are numerous preparations of Levo-Dopa available. We have the short acting form, and we have the long acting form. We have also now a new drug which is sold by [A Company] which combines both long acting and short acting. There are little pellets inside the capsule that dissolves at different speeds. An intranasal form of the drug is being formulated and has been submitted to the FDA for approval in the near future. And they're even forming a long acting patch form. So these are different formulations of the same Levo-Dopa which are available.

**RB:** So with all of that information in mind, can you tell us how you as a physician make decisions about the use of Levo-Dopa?

**MS:** So as I told you it's the most effective drug, but when you are making a decision who would I start on it first. I would probably say we normally try to start in a young individual not to give it very early because we know that although it's extremely effective, Levo-Dopa can cause what we call motor fluctuations or problems in the longer term. So we kind of not so much shy away not using Levo-Dopa right off the bat, but in older individuals it becomes a choice. There are studies to show that starting Levo-Dopa might give you the best bang for your buck in the elderly. People with cognitive impairment, you don't want to try dopaminergic which might give rise to more hallucinations and psychosis, so Levo-Dopa becomes a choice in the cognitive impaired. These are two main categories that you try Levo-Dopa. The other categories you start with different drugs. And at a certain stage almost everybody you need to start on Levo-Dopa. And they will come to a point that the first drug that you use or the first two drugs you have used are not giving sufficient motor movements so you try to use Levo-Dopa. One of the key things to remember is, if you are using it, do not use large doses. Use the minimum possible dose. By trying to keep the dose below 400 milligrams will avoid some of the complications of motor fluctuations. That has evolved into a concept called rational polypharmacy, which is a big break now.

**RB:** How do these treatment options change as the disease progresses within a patient?

**MS:** That's not a very good question. As I mentioned, at the beginning of the illness, you might start with your monoamine oxidase inhibitor or dopamine agonist and then you might get on to your Levo-Dopa. When you start it initially there's enough nerve cells which might be able to store this Levo-Dopa and release. Similarly, after use of Levo-Dopa for some time, your receptors also undergo certain changes. So your therapeutic window becomes narrower as the disease goes on. So you have to hit a narrow target with medications. So that would result in either you exceeding the amount you should be giving and people having involuntary movements, or you are too slow and you can't move. So then you come to the point you are using medications that would work very evenly throughout the day and you might have result to multiple dosing at that time. Rather than three times you may be giving every three or
four hours a dose, and adding things like dopamine agonist if they’re not already on it because
dopamine agonist is much longer lasting. The long acting preparations, similarly monoimmunex oxidase
inhibitors also useful at that stage. So when you come to that stage, you are almost always on a
combination of medications unless you are cognitively impaired and you cannot use multiple
medications for that reason.

**RB:** In addition to the medical options, I know you had referenced there were surgical options. Can you
briefly describe these for us?

**MS:** Surgical options, once again, I would like to divide into two categories. One is, is there anything we
can restore function? We can either bring back cells, put in new cells, and we have tried many of these.
Go back to 1995—'94, '95—a large study was conducted at Columbia Presbyterian when I was a fellow,
where they took fetal cells and transplanted into Parkinson’s disease patients. We thought it would
work with the dopaminergic cells. Unfortunately, that study fell apart because, yes, the cells took hold in
the new brains but they caused very bizarre, abnormal movements due to what we think is aberrant
connections. So it was replicated and that kind of fell out of favor. Since then numerous transplants.
Right now the big thing is stem cells. But we will encounter the same problems. The advisory from
the American Academy of Neurology on stem cells and we understand with stem cells there’s a lot of
hope but probably not ready for prime time yet. On the palliative side—so on the restorative size also
you I have to mention they have tried infusing growth factors into the brain. Preliminary studies show
some benefit double blind study fell apart. So we don't have anything on the restorative side which we
can talk about. On the palliative side, the number...pallidotomy where you make a little lesion in your
basal ganglia existed before Levo-Dopa existed. In fact, Surgery fell out of favor when Levo-Dopa came
because they thought they found the answer, only to find that long-term Levo-Dopa caused all the
problems. At that time surgery came back into work and we started doing pallidotomies. With
thalamotomies, you can make a little lesion in the thalamus in the brain which can relieve tremor but
not the other Parkinson's symptoms. So the main target right now has become the subthalamic nucleus,
or the STN, and we do deep brain stimulation. But stimulating you can change the parameters. You can
stop the stimulation. It's not a permanent lesion you're making. Although there are some changes which
occur in the brain which might be kind of semi-permanent in nature. Gene therapy is another option for
palliative care. It's for those not suitable for DBS. Gene therapy is still experimental—research is still
going on with gene therapy.

**RB:** Now, let's talk briefly about non-pharmacological treatments available and other options that can
help to improve the quality of life for a Parkinson's patient.

**MS:** One of the key things is education. That is what EPA does, that's what we do. We spend a lot of time
with a patient newly diagnosed with Parkinson's. He has to know the illness. You have to know the
trajectory it will take. Once again, are you sure about the diagnosis? What are the other possibilities?
Sometimes the true diagnosis will happen with time. So its evolution, if you're not sure at the beginning,
you might change. New patient education is extremely important for them to cope with the illness, and
to also know what are the options available. Then the support services that are available to the patient.
Then you treat with emotional and psychological support. If they're depressed you can send them for
counseling, etc. Exercise I emphasize, a lot of data to show exercise is beneficial. It might even have
some neuroprotective properties in exercise which should be more kind of intense kind of exercise regiments. Speech and swallowing is another aspect and we can train people with swallowing exercises because aspiration becomes a problem later on. Sometimes speech volume is low and you can intervene. Proper nutrition. A lot of people say any specific thing I should eat or drink? At this time, I could say that caffeine seems to have some benefit. Maybe you should take some extra coffee. Other than that, there's no specific data, maybe Omega-3 fatty acids. We don't have so much data obviously caffeine there's some relationship. We can do cognitive training for people with mild cognitive impairment. These are all non-pharmacological interventions question make.

**RB:** Backtracking to exercise which you just mentioned, that can have both a protective and therapeutic impact, is that correct?

**MS:** That’s true. Productive benefits are being looked at in a very close way, but there are some animal experiments which show that vigorous exercise might have neuroprotective benefits through the release of certain neurotrophic factors in the brain in response to exercise.

**RB:** Now, to learn about non-pharmacological interventions worked in the field, we traveled to New York Methodist hospital to talk about exercise and speech therapy for people with Parkinson's disease. Let's take a look.

<<CLIP BEGINS>>

**Keiko Okuda, PT, DPT:** Exercise has a lot of benefits for patients with Parkinson's disease. This includes increasing their aerobic capacity, which means they'll be able to walk from point a to point b with more ease. It also increases their ability to perform their activities of daily living. So a lot of patients with Parkinson's disease come in with a very flex posture, forward flex trunk, rounded shoulders, bent knees. We want to help open that up so they're able to stand upright. You want to open up their chest. And you want to help them straighten out their legs by strengthening the extensors or the quads and gluts. We also want to work on stretching in addition to the strengthening. So by stretching you want to stretch the muscles that have become very shortened because of this posture. So depending on the patient, many patients respond to different cues. Some of the cues we use are visual cues. A lot of freezing happens at door frames. That's where the freezing and gait occurs. So during those times we can have a bright red line that they have to see so they can step over the line.

**Naga Alomari, SPL:** LSVT-loud is a program specifically designed for people with Parkinson’s to increase their vocal intensity and improve their speech. Here at New York Methodist, we follow the LSTV-X protocol where people come in twice a week instead of four times a week that’s originally designed. The reason for that is that we found that people cannot make it to our office four times a week. It was just too difficult for them. So they come in twice a week. They follow a strict homework protocol. And we found the results to be excellent, just like LSVT. The voice handicap index is a questionnaire we give patients before they undergo the LSVT program. It asks questions about how they feel about their voice. They'll answer almost never or never, all the way to almost always or always. So questions like, “I tend to use the phone less.”, “I feel embarrassed because of my voice.” We see how they feel about their voice beforehand. Then after the protocol, we usually have them answer the questionnaire again and
then we'll see a huge difference, about 70% of people with Parkinson's have either speech and/or dysphagia, which is swallowing difficulty. Helping with the speech, doing LSVT has shown to also improve the dysphagia, improve the swallowing.

<<CLIP ENDS>>

RB: So clearly these types of programs have a great value and are very important. What more can you tell us about voice therapy and why it's important?

MS: Voice therapy a lot of Parkinson's patients have low speech volume and this bothers them. Caregivers can't hear them. Intervening in voice might be helpful probably in other aspects as well. So the most effective voice therapy program which has come to light is the LSTV or Lee Silverman Voice Technique or Therapy which basically takes one aspect of speech and intensifies it. For example, speaking loud and patients are made to scream out what they're saying. Then others aspects of speech are supposed to follow and improve. And we see this in practice. It's a very useful form of speech therapy.

RB: Excellent. Doctor, you're involved with the American Parkinson's Disease Association. Can you tell us more about APDA and your specific role as the medical director?

MS: APDA stands for American Parkinson's Disease Association. It is based in Staten Island, New York. It was started in 1961 with two objectives in mind. One is to ease the burden and secondly to find a cure. Ease the burden is to provide resources to both families and patients on how to manage Parkinson's so it's not only information and referral service in our hospital. They have support a number of other initiatives we have. We have dance therapy for them, Thai Chi classes, cogitative training classes all partially supported by the APDA. They have annual seminars for patients and we run patient support groups through the APDA for our patients. From finding a cure they have supported research activities. And the APDA research funding becoming less each year with federal cuts, these nonprofit organizations have come to the forefront given that support particularly to young researchers, APDA are promoting young researchers in Parkinson's disease. So they do a tremendous service to the population at large.

RB: Excellent. Thank you so much. Now, we have time for just a few questions that have come in from our audience. Let me pull up the first one here. Does the intensity of exercise matter, or is it just important for patients to have some type of exercise?

MS: Intensity matters. Two years ago we looked at all the data and wrote an article on this, what are the best forms of exercise that one should do. We know that it should be kind of aerobic exercise. Exercises with high intensity—moderate to high intensity are useful. This could be on a treadmill. If your disease has progressed, treadmill i don't say is the safest exercise. You can do bicycle. I often encourage people to exercise bicycle. What i say is go faster and faster. The higher the intensity, probably the better it is. You can do other forms of exercise also like strengthening exercises have been shown to be helpful so you can do some light weights, weightlifting, etc. We've seen for balance Thai Chi is probably the best form of exercise one can do, to improve balance.
RB: Great. Thank you. We have another question. How do you determine the best dose of Levo-Dopa for a patient? When would you suggest a patient move from oral to having it delivered by a pump?

MS: So Levo-Dopa going from oral to pump is in a completely different stage of the illness. This is a new dual pump which has come into play. It is usually for later stages of the illness when we see disease fluctuations or motor fluctuations which you cannot manage with oral preparations. And at that stage you might. But understand the pump may not be for people who are cognitively impaired because you have to know how to use the pump. There is also the pump has to get washed in the night. There's a process involved. But it delivers Levo-Dopa exactly to the jejunum the good thing is it bypasses your stomach and stomach can play a huge role in how oral medications are released to the gut where absorption takes place. Sometimes you take the medicine, it may take an hour to work. It may not work. Here you have what we call a jejunal extension from a tube put into your stomach and the pump is connected. So it is usually in the later stages of the illness that you make use of the pump.

RB: Thank you. We have another question. If someone has several relatives with Parkinson’s disease but has no motor symptoms, is it beneficial to have this patient screened? Also, when would you recommend a patient get a DaTscan?

MS: ...So let me answer the first question.

RB: Sure.

MS: When will you screen a person for Parkinson’s if your Relatives have it? We know that certain types of Parkinson's are autosomal dominant, some are autosomal recessive, and some are polygenic inheritance. Every familiar form is not a monogenic inheritance—something we may seen in families. First ever all, you can see how the Mendelian pattern goes. If you’re autosomal dominant, you have to have in every generation somebody has to get affected. In autosomal recessive, it’s different. Both parents will carry the recessive gene and you have one-fourth chance. If you're young with on-set Parkinson’s, and you strongly suspect, you can screen for genes. First you are to get a geneticist, you can map out who are the affected family members—then you can see is it autosomal dominant or autosomal recessive. We have about six genes which you can test in a commercial way. And this argument goes back and forth. Whatever the result, the management isn't going to change. Is it useful? I think in certain situations it's useful because knowing what kind of Parkinson’s you have can project the progression and prognosis. So also it might be useful to know because if a treatment becomes available, then you know for this abnormal gene product we have a treatment.

RB: Thank you. Now, we have another question. Are there any correlations between traumatic injuries and the risk for Parkinson’s disease?

MS: So traumatic injuries, multiple head trauma which we call punch-drunk syndrome, there seems to be a relationship between repetitive head trauma and the development of Parkinson’s. We also know it causes Alzheimer's. Now we have a separate category of chronic traumatic enteropathy we've seen in football players.
RB: Thank you so much for all the information you’ve shared with us today. I think we got a lot of great information to increase awareness about the disease, the causes, diagnoses, and potential options for treatment. Thank you for being with us today.

MS: Thank you for having me. I enjoyed the program.

RB: Excellent. Now, thank you very much for joining us today. Please remember to fill out your evaluations online. Your feedback is always helpful for the development of our programs and continuing education credits are available. To obtain nurse continuing education hours, CME, social work, and CHES credits, learners must visit www.phlive.org and complete an evaluation and the post test for today’s offering. Additional information on upcoming webcasts and relevant public health topics can be found on our Facebook page—don’t forget to like us on Facebook to stay up to date. This webcast will be available on demand on our website within two weeks of today’s show. Please join us for our next webcast on February 18, 2016, focused on finding patients with undiagnosed hypertension. I’m Rachel Breidster, thanks for joining us on Public Health Live!