

About Health TV with Jeanne Blake
Parkinson's Disease
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DR. SIMON: Parkinson's disease is a neurodegenerative disorder, meaning it involves progressive loss of a small set of brain cells in a part of the brain called the substantia nigra, and this part of the brain produces dopamine, and the loss of that dopamine leads to certain difficulties, predominantly with movement.

JEANNE BLAKE: Welcome to About Health. I'm Jeanne Blake. Parkinson's disease is familiar to many of us, in part because Michael J. Fox and Muhammad Ali are so public about their struggle with it. Every year, 50,000 Americans are diagnosed with Parkinson's disease, a disorder that slowly robs one of his or her ability to move or function independently. On this edition of About Health, we'll learn a lot more about Parkinson's disease, with the help of Dr. Bruce Lamar, who is living with Parkinson's, and a little bit later with internationally respected Dr. Ole Isacson from Harvard Medical School, who will talk with us about exciting developments in the treatment for this disorder. Bruce, thank you so much for coming in today. Tell us just a little bit, first, about your work as a mathematician.

DR. LAMAR: Certainly. I work in a federally funded research and development center. I am an operations research analyst and apply operations research techniques to government agencies, to try to help them run more efficiently and more effectively.

JEANNE BLAKE: So, with that, you first started noticing symptoms of Parkinson's disease how many years ago?

DR. LAMAR: Almost three years ago, I guess. I was finding my arm was somewhat stiff, my leg was somewhat stiff, and I wasn't quite sure what the problem was. I talked to my general practitioner, and

she had gone through various tests, including an MRI, to see if there was any brain tumor or other things that might be causing that, and gradually, through a process of elimination, they came down to the diagnosis of Parkinson's.

JEANNE BLAKE: Just to back up a bit, when you first started feeling these symptoms, did you just think, I hurt myself lifting something? Did you pass it off, or did you see your doctor soon?

DR. LAMAR: Initially, with my right arm feeling stiff and just harder to move, I guess I went through denial at first and said it'll probably go away, and it didn't go away, I checked to see what was the cause. I guess my symptoms, in that case, I didn't have a tremor, which I guess is one of the classic symptoms. I know Michael J. Fox had said he had noticed his finger, a small tremor in it, and that was sort of his initial noticing of something wrong. I didn't have the tremors to start with, I developed some of those later, but at the onset those weren't the case. I guess it was finding things that were causing – trying to find what the cause of it was. Actually when I did get diagnosed, it was a mixed feeling. It was a concern, certainly, about having that diagnosis, but also it was almost some slight feeling of relief. I remember calling my wife after I got the diagnosis to let her know what they thought the causes were, just that it was something I could focus on to treat and work with.

JEANNE BLAKE: So how long from the time that you first felt the symptoms to the time at Beth Israel with Dr. Simon, who we saw at the top of the program, that you received a final diagnosis?

DR. LAMAR: Probably about six months was going on between when I had some initial symptoms, when I noticed them and when I had the diagnosis. But looking back, I can actually see there were other situations that were probably indicative of the fact that I had Parkinson's.

JEANNE BLAKE: What was your initial thought? You use your brain for your work. We all do, but I think of you as an accomplished mathematician, as someone who particularly uses one's brain. And I'm wondering what your thoughts were upon getting your initial diagnosis. You say that there was a bit of relief, but what were your concerns and what did you know about Parkinson's disease when you finally learned that you had it?

DR. LAMAR: That's a good question. It was sort of a mixed feeling. Part of it was, certainly, the concern of having something that was going on deep down in my brain that was causing me to not function as well as I had in the past, physically not be able to move around, and worries about how that would develop over the years. At the same time, it would seem like it was an opportunity, sort of a challenge that I could use my skills of analysis to try to either combat it, or at least being able to analyze it and make decisions about what to do in the future.

JEANNE BLAKE: I want to go back to how you've done that, but first, we were with you, with Dr. Simon, as you underwent an exam, but I also had an opportunity to talk with Dr. Simon about some of the primary, initial concerns that people who come to him and are diagnosed with Parkinson's have. Let's hear what Dr. Simon has to say.

DR. SIMON Probably the most common concern the patients express, especially early on, is the fear of losing independence, no longer being able to do everything for themselves, but starting to have to depend on others, whether it's at work, depending on co-workers, or, more often, at home. Sometimes it can be just a few things, like pulling on your socks, tying your shoes, and then when people have more severe or advanced disease, sometimes it can become a much more prominent loss of independence, to the point that they're unable to drive, unable to walk, even, in some cases. But fortunately, the medicines can help quite a bit and keep many patients quite functional for decades.

JEANNE BLAKE: When you hear Dr. Simon talk of the concerns that are so often voiced in his office, do you remember thinking about those things? You brought your analytical approach to it, but did you also fear for the day that would come when you would lose your independence?

DR. LAMAR: Yeah, I guess that's something that's been on my mind quite a bit, and I do experience that day to day, some things I used to be able to do easily and not even thinking about, and now I either struggle with it or I'm less able to do.

JEANNE BLAKE: For example?

DR. LAMAR: Buttoning my collar, trying to do shoelaces, things like that that are sometimes easily frustrating. Just typing on the computer is slower and I miss the keys more often, so that it takes longer to produce things than I did in the past.

JEANNE BLAKE: So there is, I would imagine, an emotional component to having this disease.

DR. LAMAR: Yes. It's partly sort of the concern about the uncertainty of what's going to happen in the future, part of it is frustration of not being able to do things, and part of it, the other side of it is the challenge to make sure I can – it is something that, an adversity, to be able to meet that and to find a way to get around it and cope with it. Find little things, like if I have trouble buttoning collars, start experimenting with Velcro, of having a button that's on the outside and Velcro underneath, so I can get around it. Turn it around, instead of being something of frustration, something that's an opportunity to find ways to circumvent the problem. And so I can use that both for myself and other people could perhaps benefit from it too.

JEANNE BLAKE: You've got young children. You've got children who are two teenagers and an 11-year-old, and I think it's obvious that when one person is living with a disorder like Parkinson's, that the entire family is experiencing it, wouldn't you say?

DR. LAMAR: Yeah, I guess both directly and indirectly, I think that it's on their minds too, even if they don't talk about it. I think sometimes they go through denial too. I remember when I first was diagnosed and I was at the dinner table telling them, I have something to tell you about this disease I have and how it's going to be affecting my ability to move, and I asked my kids if anybody had any questions, and my son said, "Yes, can I have some more French fries?" I think at that point they were trying to either not deal with it or weren't familiar with the impact of it. At the same time, now they offer to help to do things and if they notice that I'm having a harder time moving something they would offer to help do it. So I think it's on their minds too, and they try in little ways to help as well.

JEANNE BLAKE: Sometimes denial is a valuable mechanism, but I've spoken with other families where one parent is living with a disease and they're not talking about it, and it really worries me, just for the whole family, especially, I think, for the children, because children do know that there's something going on, and to not give them the opportunity to be part of the process doesn't seem fair to me, either in the short term or in the long run. So you've obviously made a decision to be very open about it.

DR. LAMAR: Yeah, I think it was partly that – in some ways there wasn't a full choice, because I think they would notice it anyhow, so it seemed like it was better just discussing it with them, and as I learn things I bring it up to them. Sometimes they find out things that they've seen on the Web or the newspaper and they point it out to me too.

JEANNE BLAKE: Dr. Lamar, you said that you brought your analytical mind to the way that you go about seeking treatment for this. Can you give me an example of how you've done that?

DR. LAMAR: I guess part of the type of analysis that we'd go through is the sort of medication that I would be taking, and I try to keep track of what the effect of that was so I would know, I would advise Dr. Simon of what the impact was, so he could then fine-tune the medicines. It seems a little bit like a see-saw or saw edge, that I would take a medicine that the level would be appropriate, and after a while the symptoms would progress further, and so I'd need a change in the dosage, but it wouldn't be clear, since I have a mix of medicines, exactly whether I should increase one or decrease the other, or add another one to it. So I would try to note what my symptoms were as I was taking the medicines so I could refer that to Dr. Simon.

JEANNE BLAKE: I think a doctor likes a good patient, one who's very involved. You have to be involved in your own health care, no matter what.

DR. LAMAR: That's true, yes.

JEANNE BLAKE: I've asked Dr. Simon – actually, I'll ask you what hope you have – this is a very exciting time with Parkinson's disease. There are breakthroughs being reported. Do you have that sense of hope for yourself?

DR. LAMAR: I guess it's sort of, again, a double-edge sword. In some ways it seems like there's lots of opportunities, and yet at the same time it's not known as a curable disease yet. So sometimes those things just around the corner continue to be just around the corner, so I'm hopeful that some of the recent developments will turn out to be viable. I guess certainly my state, using the medicine has helped quite a bit, and there is the opportunity for stem cell research or something that's ongoing, that's

both controversial and also some great potential too. There are surgical procedures which could be considered, but hopefully those will be later on. At the same time, I guess I've found things that are in addition to the medicine, physical therapy, they say exercise is one of the best treatments. I actually found listening to folk music makes me want to move more, so that's sort of an indirect benefit that I find that can help with the treatment of the disease.

JEANNE BLAKE: As I began to mention, I asked Dr. Simon to tell me about the way he offers newly diagnosed people with Parkinson's disease a sense of hope. So let's hear what Dr. Simon has to say about that.

DR. SIMON: The biggest hope is in finding drugs that will slow the progression of Parkinson's disease. Our strategy is to actually slow or reverse the problems in Parkinson's disease. Right now, there's an NIH sponsored trial of four potential neuroprotective agents that all have shown great promise in laboratory studies and in animal models at slowing the progression of Parkinson's disease, and they're being tested now in clinical trials.

JEANNE BLAKE: Dr. Simon refers to new drugs. I'm imagining that in the three years that you've been treated by Dr. Simon you have – you suggested that you had tried different drugs.

DR. LAMAR: Right. I guess the several different types of medications, and I guess part of that is to treat the symptoms, of course, and Dr. Simon has sort of a go slow policy, to not do more than you have to but do as much as you need to, because the other side of that is some of the drugs themselves have some side effects which are either an annoyance or definite complications, like feeling of tiredness or drowsiness with the medications. Sometimes taking the Sinemet, which is a levodopa-carbidopa mix, can cause movements. I've noticed when I was taking a little bit larger dose of that, my

tremors started increasing in my left hand. So the medicine is certainly useful, but it has to be tempered with the right dosage too.

JEANNE BLAKE: But given the opportunity to be part of a clinical trial, do you think that you would take that step?

DR. LAMAR: I'd certainly consider it. I guess the ability to advance knowledge in that with something, if I could contribute to it I'd be interested in doing that. It's always nice to get the benefits of it right away, too, which may not be always the case, but I'd certainly be interested in considering that.

JEANNE BLAKE: We wish you the best of luck as you continue to take your analytical approach to living with Parkinson's disease, and we hope that you do well.

DR. LAMAR: Thanks very much, Jeanne. I appreciate it.

JEANNE BLAKE: Thanks so much for coming in to talk about this. When we continue with our program, we'll be joined by one of the most internationally respected researchers on Parkinson's disease, Dr. Ole Isacson from Harvard Medical School. We'll be right back.

[Public Service Announcement from the Michael J. Fox Foundation]

JEANNE BLAKE: We continue our program now, talking about Parkinson's disease, joined by Dr. Ole Isacson, who is director of the Neuroregeneration Center at Harvard Medical School. Dr. Isacson, thanks so much for coming in. We just heard Dr. Lamar talking about living with Parkinson's disease, and at the beginning of the program heard Dr. Simon talk about the fact that the part of the brain that

produces dopamine is what goes wrong in someone with Parkinson's disease. Help us understand why we need dopamine.

DR. ISACSON: Dopamine is simply a chemical that the brain uses, and the chemical is produced by cells. In the brain we have trillions and trillions and trillions of cells, and even in Parkinson's most of those cells are fine, which we heard with Dr. Lamar and he's very functional in his way of acting. In this part of the brain that degenerates, we have about one million cells on each side. Now, those millions of cells work relatively well also in a Parkinsonian brain, except that they have started to lose many of them. So they usually start off with about a million, and they can have a degeneration of at least half of those cells before they even know they have the disease. So this is a slowly ongoing process in which these cells are struggling to survive.

JEANNE BLAKE: Help me understand, dopamine actually keeps different parts of the brain talking? What does dopamine actually do?

DR. ISACSON: Dopamine is a substance that we call a signal substance. Every brain cell communicates with other brain cells, and they do that by electrically firing a substance over to the other cells, so they're communicating that way. So in this case, dopamine, the cells that produce dopamine are lost, and so you've lost the connection, essentially.

JEANNE BLAKE: And we don't know, really, what causes it, do we?

DR. ISACSON: We don't know exactly what causes this, but like most medical research, we know a lot about the details. And in fact maybe we do know more than some people think, because the dopamine cell that dies is actually vulnerable to a lot of things. We know that it can die by certain things

that simulate toxins, like pesticides. We also know about seven different genetic causes that in a rare set of people, a rare set of families, produce the same syndrome as we saw earlier today.

JEANNE BLAKE: So Dr. Lamar technically may have to be concerned about one of his three children developing Parkinson's disease.

DR. ISACSON: Perhaps not, in the sense that maybe one-quarter of the people with Parkinson's have some genetic component. But it's actually a disease that follows more an aging pattern, an independent pattern, maybe it's an environmental course, or simply that the dopamine cells are quite vulnerable to age.

JEANNE BLAKE: You said that because of so many things that can go wrong with cells, that apparently is why so many different agents or medicines can potentially help either slow the progress or help, I guess, not restore it – stem cell therapy, which we'll get to in a moment, would probably be the only way to restore function, right?

DR. ISACSON: Correct.

JEANNE BLAKE: OK, so the medicines that you're developing in your lab are to target some of the things that are going wrong with the cells.

DR. ISACSON: Yes, so we actually know about the dopamine nerve cell, and we are studying its health, its disease, and its ability to function well or not well. One of the basic principles is that since you have lost maybe at least 60 percent of those nerve cells when you present in the clinic, you've already gone down that slope towards a lot of dysfunction, actually. And some of the drugs that we heard that Mr. Lamar takes actually require that the remaining cells have to work a little bit of overtime.

They actually have to convert the drug into its active signaling type, the dopamine, and then signal through that normal cell type. So what we do in the laboratory and in research today is try to slow down that slope of degeneration and try to halt it so that we can hold the cells that are still functioning as long as possible. And we have many ways of doing that.

JEANNE BLAKE: I was just about to say, just explain one.

DR. ISACSON: What we've learned over the years is that one of the most vulnerable parts of the dopamine cell, it's what we call the mitochondria. Basically a little bit of a power transistor inside the cell. We have thousands of them in each cell, and these tend to become compromised in these particular nerve cells in Parkinson's disease. In fact, if the rest of the brain has some trouble too, we can easily cope with this problem. So what we are targeting is trying to help the mitochondria, the power house, to function better, so as to put less pressure on the dopamine cells, to keep them functioning longer. There are also very standard things that we've heard about in popular literature, anti-oxidants that would protect cells from free radical oxidation of cells. But practically anything that makes the cell healthier would probably help the cell somewhat.

JEANNE BLAKE: Let's shift to some of the animal studies that you're doing, because you're doing some really exciting work that holds, from a lot of people's opinions, great promise for people living with Parkinson's, with stem cell research.

DR. ISACSON: The next challenge, in fact almost every Parkinson's patient that's currently living – and you know there are many of them, about a million in the United States alone – the cells continue to lose their function and die off. At the end, you simply can't use drugs very well. And this is actually a revolution not only in neuroscience but also in the way we look at the brain and functioning and other diseases. One of the new ideas is actually to put the cells back that have died, because they are

actually the best way to make systems function. If I may digress a little bit, in diabetes there is also one cell type that dies that produces insulin. It's very hard to control the level of insulin by injection or taking drugs, so the goals for those scientists are to produce the cell, or get the cell and put it back into the patient again. In fact, that's what we're trying to do for Parkinson's disease.

JEANNE BLAKE: You've been challenged in your laboratory by the fact that there – and this is very scientific, so I'm going to need your help to simplify this – that there are tremendous volumes of cells, and you've developed a way to target the specific cell and the specific part of the cell that is going to be most useful when the transplantation is possible.

DR. ISACSON: On the horizon, and I actually think that Mr. Lamar had a realistic view of looking at new treatments, they seem around the corner but for us, being scientists or medical doctors, we struggle very much to reach the next step. And the next step for Parkinson's disease, and maybe other diseases, is to try to replace or regenerate the dopamine cell. There is nothing better than a normally functioning dopamine cell. Drugs are a way of sort of mimicking the drugs or the chemistry of the brain, but they can never really play or interact like the normal connections do. So what we do in the laboratory is actually to try to derive the dopamine cells that have died, or it's degenerating in Mr. Lamar's brain, from stem cells. And stem cells, as you know, Jeanne, are basically the building blocks of the body. At the most immature state they're called embryonic. That's when they're just 300, 400 cells in a ball of cells, and they can become any cell in the body. What we have done in my laboratory in 2002 was to generate the first dopamine neurons from those balls of cells. And the reason that we're very eager to try this is that a ball of cells, when it's that immature, can be divided almost infinitely. So you almost have sort of an unlimited supply of raw material, if you will. And the trouble, however, is to try to learn what nature normally does, that is to generate exactly the cell type we want. It's not just that we want dopamine, we want the cell that knows exactly how to transmit messages in that, what we call, circuitry. In the future of biomedicine, what you actually have to produce now is not a drug, but a cell.

So when we grow the cells in a dish, we actually have to find ways of sorting them, or purifying them, and what we typically try to do is to find a chemical identity that we can flag with a color, and then use efficient machines to sort them.

JEANNE BLAKE: But how can you do that? How can you make one part of the cell become a little color? I was in your lab, and it's almost impossible to imagine that you can work with something that you can't see with the human eye, and yet you can have one part of it turn a special color.

DR. ISACSON: For us, it's pretty much everyday work, so it's very easy. In fact, you just add a fluorescent substance in front of what we call a gene promoter. So you know you have thousands and tens of thousands of genes turned on in every one of your cells, and if you want to have a specific characteristic, you can actually add a fluorescent tag that lights up every time that substance is produced. So it's something that's not easy, but it's something that probably is very common in most typical biological laboratories today.

JEANNE BLAKE: OK, that's a lot of science, and I hope there will be people in our viewing audience that can understand that, because it's very exciting. But the obstacles to that are obviously being able to – and we're in a precarious time in this country with being able to use stem cells, so that must be in some ways very frustrating as a scientist, when you know that if there were access, and you had unlimited access, that people like Dr. Lamar could be helped maybe more readily.

DR. ISACSON: Yes, I feel that most scientists and doctors believe that stem cells need to be researched on, and as openly as possible. Obviously it's one of those opportunities where we can contribute to medicine by using research, and since what we would have used to expand our research would be discarded previously frozen embryos, it seems pretty obvious to scientists that they will take the position that this is something that should be done vigorously.

JEANNE BLAKE: Dr. Lamar was diagnosed three years ago, and I think it's fair to say that there have been a lot of advances in the past three years, and for someone who's living with the disorder, I'm sure it's frustrating that, as he said, he'd like to see things more readily available. Obviously, one would. What do you think? Is it fair to ask you if there is, if some of the limitations on stem cells are lifted and that, combined with the work that you're doing on the other agents, what do you think the landscape looks like for Parkinson's disease over the next two years?

DR. ISACSON: The next two years may not make such a difference, unfortunately. But what I really believe and know is that the kind of research that currently is carried out, for example by the Michael J. Fox Foundation, that actually spearheads the more goal-oriented research, and many scientists would like to participate in that, that encourages me, they have many good team members, that the effort and the focus on trying to solve, slow down the progression, if we can't do that, and most patients have gone very far, to replace the nerve cells and their connections, is on a very good track. One can never know when the major discovery or the last hurdle is actually accomplished, but I feel that there's a very strong interest, and very strong progression in the science and medicine for Parkinson's disease.

JEANNE BLAKE: We hope so, and we hope it comes out of your lab.

DR. ISACSON: Yes, I hope so too.

JEANNE BLAKE: Dr. Isacson, thanks for coming in and shedding some light on a very common and important issue in this country.

DR. ISACSON: Thank you for having me.

JEANNE BLAKE: And we thank you for joining us on About Health. I'm Jeanne Blake. Our website is abouthealth.com. I'll see you next time.

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