CAUSES OF PARKINSON'S DISEASE PART ONE

In a two part series on the possible causes of PD, KQED's Dave Iverson talks to Dr. William Langston of the Parkinson's Institute about the current state of research in this area, with a focus on environmental risk factors.

A transcript of the interview follows. To listen to a podcast version, visit http://www.michaeljfox.org/newsEvents_podcasts.cfm

Opening Narration: This is Dave Iverson and welcome to another in our continuing series of reports about the latest in Parkinson's disease research. What causes Parkinson's? Over the next month we're going to look at what we know about both environmental and genetic factors. In this report we focus on the search for environmental triggers, a search that had its first big breakthrough back in the mid 1980s when Dr. Bill Langston was called in to see a young patient who had seemingly come down with Parkinson's overnight. It turned out the patient had taken a synthetic form of heroin called MPTP. And that in turn led to a research breakthrough because MPTP was chemically identical to a commonly used herbicide, paraquat.

William Langston: Well paraquat is used all over — it is used by farmers to burn fields, it was used to get rid of marijuana crops by the government, widely used herbicide. And the fact that something that similar to a toxin that caused Parkinson's was in our environment — in fact, we were putting it there — caused an explosion of interest in the possibility that environmental toxins, both manmade and natural by the way, could trigger a cause to the disease.

Dave Iverson: Bill Langston's discovery set in motion a quest to find a definitive environmental link. Twenty-fve years later that quest is still ongoing, but scientists have identified a number of pesticides that are at least associated with higher incidences of Parkinson's, ranging from those favored by organic farmers like rotenone to a key ingredient in agent orange .

William Langston: Well it would be fair to say that we don't have a smoking gun—yet. However there are an increasing number of studies that are starting to show significant risk from a variety of things in the environment. Pesticides are the most powerful right now. There are probably 40 or 50 studies that show that different pesticides or pesticide use can increase your risk. Rotenone is particularly interesting since it's been used in over 2,000 products in the U.S. It is the favorite of organic farmers because it occurs naturally in plants. Pyrethrum, which is actually used in all military uniforms to avoid bugs and insects and varmints. An interesting one is 2-4D. Why is it interesting? Recently the military finally decided there was an association between Agent Orange and Parkinson's. Well 2-4-D is one of the major agents in Agent Orange. So we may have found the culprit in Agent Orange. This is a story that isn't going away but in fact I think it is getting more powerful.

Dave Iverson: For most of the last 25 years, the search for what causes Parkinson's has focused largely on environmental factors, from pesticides to dry cleaning solvents. But now the search for a smoking gun is relying on an additional form of ammunition: genetics.

William Langston: Yes, in fact the old adage that you've heard me say before is that genetics loads the gun but environment pulls the trigger.

Dave Iverson: In other words, genetic factors might make some people vulnerable to Parkinson's, but they'd be okay until something in the environment triggers the disease. Consider something called the LRRK2 mutation, the leading cause of genetically based Parkinson's.

William Langston: However only about one third of the people that carry this gene ever get Parkinson's. So, here is a strong genetic component yet two thirds don't get it. Is there something in the environment that is triggering it? This is a perfect population to start testing some of these hypotheses.

The home run would be if we found both genetic factors that increased your risk combined with pretty strong environmental exposures. Then you could start to do risk assessment, genetically based risk assessments. You shouldn't be out in fields, you shouldn't be using pesticides, etc. The conclusion down the road some day, and I think this is one of the things that our institute is based on, is prevention, literally keeping people from getting the disease in the first place. So if we can identify a number of things in the environment, identify those people at risk and take precautions, we could really see this disease prevented. That's the Holy Grail in Parkinson's disease.

Dave Iverson: We're still a long ways from the Holy Grail, in part because the environmental factors associated with Parkinson's are so varied — and sometimes seemingly wholesome, like milk.

William Langston: A few years ago one of our investigators working with some other teams discovered that in a big population, that increased milk consumption increased your risk for Parkinson's. They saw that mainly in men, it wasn't obvious in women. Now, why milk? We don't know. One theory is that—we've been talking about pesticides, herbicides—the food chain there. We're trying to study whether things could get through that food chain. You know, cows are in fields, pesticides are sprayed. Could it be things that are just literally going that route? We don't know

Dave Iverson: And then there's the case of head trauma. People who've had a head injury are at greater risk of Parkinson's but combine genetic risk and head injury and the odds really go up.

William Langston: Your risk of Parkinson's goes up 11fold. That's huge. In fact, that's the biggest risk we've seen so far in any study. So, a genetic predisposition and an

environmental event suddenly have big numbers. So I think that's where we will ultimately figure this out.

Dave Iversion: Unfortunately, the key word in that last comment is "ultimately". We're still not at a point where people can be counseled to avoid this or don't do that.

William Langston: No, I think we're not close enough to start making specific recommendations. Could we be in three or five years? Yeah, I think we could be. But, I get asked this question a lot. "What can I do?" There are only two things I'm recommending at the moment: one, lots of exercise. You should be doing it anyway. It's not invasive, it's free, and it's good for you. And there is a fair amount of evidence that it may help slow or protect the brain. The other one, and this may sound a little crazy, is coffee. There's a number of studies now showing that the more coffee you drink, it reduces your risk for Parkinson's. I happen to love coffee anyway, so not a big deal for me! But if you like coffee, there's nothing wrong with drinking it. Green tea may also have a similar effect, although the evidence isn't as strong.

Dave Iverson: I think people at Starbucks and Pete's just said "We like this guy Bill Langston!"

William Langston: (laughs) We've been talking about going to Starbucks for a grant! We haven't gotten there yet.

Dave Iverson: What to consume and what to avoid — key environmental questions researchers like Bill Langston will continue to explore. And in an upcoming podcast, we'll delve more deeply into the other aspect of the Parkinson's puzzle — genetics. In the meantime, to learn more about Parkinson's disease research, visit www.michaeljfox.org. I'm Dave Iverson.