



**National
Multiple Sclerosis
Society**

**MS Learn Online
Feature Presentation
Strategies, Research and Hope for Primary-Progressive MS
John Richert, MD**

Tom>> Hello, I'm Tom Kimball

Tracey>> and I'm Tracey Kimball. Welcome to MS Learn Online. Of all the courses of MS, primary progressive is perhaps the most challenging ... for both the people living with it and those who are working at finding ways to treat or even cure this disease.

Tom>> Dr. John Richert, Executive Vice President of Research and Clinical Programs at the National MS Society, joins Kate Milliken to talk about what they are learning in research and the prospects for the future.

>>Kate Milliken: Is there a chance that PPMS actually shifts more toward the mold of these other neurodegenerative diseases versus MS?

>>John Richert: The issue of whether Primary-Progressive MS is the same disease as MS that begins with relapses or whether it's a different disease altogether has been debated. And we don't really have the answers yet. There is evidence that could push one in either direction. It is quite similar, the Secondary-Progressive MS, which

begins with relapses and remissions, and so that argues for it being the same disease.

When we see MS in families, multiple people in a family with MS, we may see people in that same family have both Primary-Progressive MS and Relapsing-Remitting MS. So, those two forms of MS may show up in the same family, which makes us think again that there are different versions of the same disease.

On the other hand, since Primary-Progressive MS does have more of a degenerative component than an inflammatory component compared with relapsing forms, it makes us think there may be something fundamentally different.

The studies that may answer that the fastest may turn out to be the genetic studies. So, when our genetics researchers are able to do some of these very large scale genetic screens on people with Primary-Progressive MS and compare them with people who have relapsing forms of MS, if different genetic patterns show up, that will be very strong evidence that they are really two different diseases. But we really don't know the answer to that yet.

>>**Kate Milliken:** Can you discuss why the current disease-modifying therapies are not approved by the FDA for PPMS?

>>**John Richert:** The current disease-modifying therapies are not approved for Primary-Progressive MS in large part because they don't work for Primary-Progressive MS. So, the question then is, well, why is Primary-Progressive MS different? And it's really only been in the last 10 years or so, and I might say largely through studies funded by the National MS Society, that we've learned a lot more about what's going on pathologically in the brain and spinal cord in a way that we can envision them under the microscope.

So, we used to say MS is an inflammatory, demyelinating disease of the central nervous system that spares axons, doesn't affect the rest

of the nerve, just the insulation, the myelin insulation. And we used to say that the reason people with MS got symptoms was only because they had slowing of nerve conduction because of the loss of myelin. What we have learned in the last 10 years or so is that in addition to loss of the myelin sheath, there is also loss of axons.

In an electrical wire, you've got your copper wire that is surrounded by insulation, and you need both of those components in order to conduct an electrical impulse along the wire. In the nervous system, the copper wire analog us the axon, and the insulation is the myelin sheath, and you need both.

We used to think just the insulation, just the myelin sheath, was destroyed. And now we know that the copper wire, the axon, can be damaged as well. And what we've learned is that while that axonal damage can occur early in the disease, it becomes more prominent as the disease gets into the progressive forms. Not only does axonal damage become more prominent, but the inflammation becomes less prominent.

So, what we used to think was an inflammatory, demyelinating disease throughout its course, now we know that the inflammation and demyelination is predominant in the early phases of the disease. But as one gets -- progresses into the progressive phases of the disease, there's less inflammation, less new loss of myelin, and there's more of a degenerative process in the axons that appears not to be immune-mediated, or at least not predominantly immune-mediated. We think it's more akin to the kind of degeneration of axons and nerves that can occur in other neurodegenerative diseases, like Alzheimer's, like Parkinson's.

A new terminology that -- at least it's new in the MS field in the last five years or so. You may hear the terminology neuroprotective therapies. And so much of our effort in devising new therapies for the progressive forms of MS, both Primary- and Secondary- Progressive forms of MS, much of that effort now is aimed at

understanding that neurodegenerative process and learning how to protect the nervous system against the degenerative forces, and also to learn how to protect the nervous system against damage from the immune system, too. But much of it is very analogous to the research that is being done in Alzheimer's and in Huntington's disease and in Parkinson's. Because we all want to learn how do we protect the nervous system from those neurodegenerative forces? It also means that much of our research that is aimed at the progressive forms of MS is related to how to repair the nervous system.

We often hear from our constituents is why aren't you doing more to devise treatments for the progressive forms of MS, the Primary-Progressive forms of MS? People with Primary-Progressive MS say, "We feel like we're left out." They -- it's understandable why they feel left out, because we don't have treatments for them. But, in fact, a very large proportion of our funding from the MS Society for research is for research into the neurodegenerative processes, how to prevent it, how to repair it.

So, all of that work is really aimed at trying to help people with the progressive forms of MS. And in addition, those areas of research will help people with Relapsing-Remitting MS as well, but it's important for people who have the progressive forms of MS know that there is a very vigorous effort to be able to devise new treatments for them.

>>**Kate Milliken:** So, because medication for PPMS has not been FDA approved, what is the reason why you encourage patients to continue to go to their neurologists and their doctors?

>>**John Richert:** There are several important reasons why someone with Primary-Progressive MS should continue to see his or her neurologist on a routine basis. The first is that there are really two major categories of treatment that we have for people with MS. Up until now we've been talking about the disease modifying therapies,

the therapies that cut down on inflammation, or that may be neuroprotective, or may be research on reparative processes.

>>John Richert: The second category of therapies for MS in general are the symptomatic therapies, and these are very useful for people with Primary-Progressive MS. These are therapies aimed at various symptoms of MS, such as neurogenic pain, fatigue, spasticity, bladder problems, cognitive problems, sexual problems. And so these are symptoms that can be very troublesome to people with MS, sometimes incapacitating for people with Primary-Progressive MS. But they can be treated very often quite successfully. And so it's important that someone with Primary-Progressive MS continue to be followed by his or her neurologist so that these symptoms and combinations of symptoms can be treated in a symptomatic way.

Secondly, there are more and more clinical trials of new therapies aimed at Primary-Progressive MS. These will, as we go forward in the future, will more and more be related to neuroprotective strategies and reparative strategies. So, it's important that someone with Primary-Progressive MS be in close touch with a neurologist so that if a clinical trial comes along that would be appropriate for that person, that that person doesn't miss out on the opportunity to take part in that clinical trial.

Tracey>> It is truly fascinating to hear what researchers are learning about the different courses of MS.

Tom>> And for people living with primary-progressive MS this research is their best hope for the future.

Tracey>> In the meantime, there are a number of symptom management strategies that they can use to lessen the impact of the disease.

Tom>> You can learn more by checking out some of our other programs dealing with primary progressive MS or by contacting the National MS Society. Thanks for joining us.