



**National
Multiple Sclerosis
Society**

**MS Learn Online
Feature Presentation
Understanding Primary-Progressive MS
John Richert, MD**

Tracey>> Welcome to MS Learn Online I'm Tracey Kimball.

Tom>> And I'm Tom Kimball. Understanding the different disease courses is part of living with multiple sclerosis. However for those living with the primary-progressive course of MS there simply has not been as much information available as for those with other courses of MS.

Tracey>> In this program, "Understanding Primary-Progressive MS", Dr. John Richert helps us understand how Primary Progressive MS is different than the other courses.

>>John Richert: Primary-Progressive MS is a clinical diagnosis and it depends largely on the course in terms of the timing of what happens when. And it is a form of MS that is in most cases represented by a gradual downhill course, gradually accumulating more and more neurologic deficits without any clear-cut exacerbations and remissions.

The rate at which somebody worsens may vary over time. Sometimes it will be a little faster, sometimes it will be a little slower.

Usually, it's relatively slow overall. Rarely it's precipitous and rapid. But the hallmarks are gradual worsening without exacerbations and remissions.

>>**Kate Milliken:** How is Primary-Progressive MS different than the other courses?

>>**John Richert:** There are a total of four different forms of MS, Primary-Progressive is one, and it is the only one that is not characterized by relapses and remissions. About 10% of people with MS will have Primary-Progressive MS, and about 80% or 85% of people with MS will begin with a Relapsing-Remitting MS, in which they have fairly rapid onset of new neurologic signs and symptoms that may come on over a matter of usually hours or days, and then from which the person will fully or partially recover.

As long as between exacerbations somebody is rock-solid stable, we continue to call that Relapsing-Remitting MS. But most people who begin with Relapsing-Remitting MS, at some point in the future will begin to also slowly go downhill between exacerbations, or instead of exacerbations. Exacerbations become less frequent or they may disappear altogether. And once someone reaches the point during which their baseline slowly worsens, that's the point at which they have entered into what we call Secondary-Progressive phase.

So, people may begin with Relapsing-Remitting and eventually become secondarily-progressive as opposed to people with Primary-Progressive, who never have relapses. And then a small number of people, maybe 5%, will begin with a progressive course, but then have relatively few superimposed exacerbations. So, we call them Progressive-Relapsing MS, because they begin with a progressive course, but then have a few relapses.

>>**Kate Milliken:** Do you find that the demographics dealing with Primary-Progressive MS, are they similar than the other courses?

>>**John Richert:** For the relapsing forms of MS, the ratio, the gender ratio is roughly 2:1, maybe 3:1, women to men. But for people with Primary-Progressive MS, it is more of a 1:1 ratio, equal men and women.

The people with Primary-Progressive MS tend to have their onset somewhat later in life than those who have a Relapsing-Remitting onset. And the progressive form of MS, Primary-Progressive form of MS tends more often to be concentrated in the spinal cord and not as much in the brain, in the cerebral hemispheres.

>>**Kate Milliken:** So, when someone does have Primary-Progressive MS, are they diagnosed at onset, or is it a little bit different?

>>**John Richert:** The diagnosis of Primary-Progressive MS takes a bit longer to make the diagnosis in part because one has to follow these people for a longer period of time to be more certain of what their course is, and in part because there are more -- there is a larger number of other diseases that may mimic this form of the disease that may take a while to rule out. By convention, someone has to have had this progressive course for at least a year before we can be reasonably certain that what they have Primary-Progressive MS.

For the relapsing forms of MS, for the most part now with the advent of MRI scans, if someone has a pretty classic story and findings on exam and MRI scans, we usually don't need to do spinal taps anymore for people with the relapsing forms of MS. But for the progressive forms of MS, for either Progressive-Relapsing or Primary-Progressive, usually we need to also get spinal fluid data to see whether or not the immunologic abnormalities in the spinal fluid are consistent with MS.

So, it takes a longer time to go through the diagnostic workup often, and we do have to make sure that when, as the disease progresses,

that it really is in a pattern consistent with MS and not something else.

>>**Kate Milliken:** Is it also possible, if one is diagnosed initially with Relapsing-Remitting over time to have it slide into a primary form?

>>**John Richert:** It doesn't slide into a primary form, but it may slide into a progressive form. And because it begins with relapses and remissions and then subsequently becomes progressive, we call it Secondary-Progressive rather than Primary.

So, when we talk about Primary-Progressive, we're talking about a form of MS that is Progressive from onset and remains Progressive throughout. When we talk about Secondary-Progressive MS, we're talking about a form of MS that begins with relapses and remissions and only secondarily develops a more progressive, slowly, gradual downhill course.

>>**Kate Milliken:** So, from a clinical standpoint, when did people start getting diagnosed with Primary-Progressive MS?

>>**John Richert:** So, the diagnosis of Primary-Progressive MS, or the realization that there was an entity that we now call Primary-Progressive MS, is only something that we've largely realized and defined since approximately the mid-1990s. Prior to that, most, in fact all of the progressive forms of MS tended to be lumped together in an entity that we all referred to as Chronic-Progressive MS. And that included people with Secondary-Progressive MS, with Primary-Progressive MS, with Progressive-Relapsing MS, and some people even used that terminology to describe people who had Relapsing-Remitting MS but were accumulating severe permanent neurologic deficits as a result of the Relapsing-Remitting process.

In the early to mid-1990s, the MS Society called together a group of experts and decided they really needed to redo the nomenclature, because it appeared that what we were calling Chronic-Progressive

MS really constituted more than one form of MS. And this had practical consequences because in clinical trials, one wants to be able to study people with either Relapsing-Remitting or Secondary-Progressive or Primary-Progressive. You don't want to lump them together. By lumping them together, one essentially stacks the deck against the therapy, because people with Primary-Progressive MS tend not to have as good a response to the immunomodulatory therapies as people who have relapsing forms of MS.

And so when people with Primary-Progressive MS were lumped together with the others in what was called Chronic-Progressive MS, many of the clinical trials in that lumped group of patients showed no benefit. Yet when the different forms of MS were differentiated from one another, we subsequently found that the people who have Secondary-Progressive MS do in fact respond to some degree to the immunomodulatory therapies. They don't respond as well as people do with the Relapsing-Remitting forms, but they respond better than people with Primary-Progressive.

So, it had practical consequences not only for the development of therapies for MS, but also for deciding which people with MS are likely to have a reasonable response to therapy in clinical practice. So, it had very important practical consequences for us to delineate these four different forms of MS.

Tom>> Thank you Dr. Richert for helping us to better understand primary-progressive MS.

Tracey>> But there is much more to learn. You can watch additional programs that explore primary progressive MS by checking out the menu to the right of the screen.

Tom>> Thanks for joining us.