

Transcript Details

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A Closer Look at the Biology Behind MS Progression

Announcer:

You're listening to *NeuroFrontiers* on ReachMD. On this episode, we'll hear from Dr. Ethan Meltzer, Assistant Professor in the Department of Neurology and the Program Director of the Neurology Residency at the University of Texas at Austin. He'll be discussing our evolving understanding of the biology behind multiple sclerosis. Here's Dr. Meltzer now.

Dr. Meltzer:

We've been using clinical descriptors such as "relapsing" and "progressive" MS for decades now, and the challenge is that these descriptors don't necessarily line up one-to-one with what's happening on a biological level. And I think there can often be a false perception, either in persons with MS or in the conversations we have, that, for example, relapsing MS implies inflammation, and that progressive MS implies neurodegeneration—that this is a binary disease, and that there's this somewhat imaginary inflection point that a patient may experience during the course of their disease where they go from relapsing to progression, and that it's a one-way street.

And really what we know now is that if we look histopathologically and we look at these patterns of inflammation, demyelination, axonal injury, and neurodegeneration, this is occurring across the full spectrum of disease, whether it's relatively early or relatively late, and this is really unified. And so it's not that these descriptors don't have a role clinically, but they are a tool, and they can be a tool used, for example, in clinical trials to identify certain populations. But they do fall short of really capturing what is happening at a disease-state level. And in that sense, there can be some limitations in terms of both prognosis as well as identifying which patients might respond to which treatments.

So patients with MS do accumulate disability, and there's several mechanisms. So with relapse-associated worsening, this is disability that tends to follow a clinical relapse, and often we associate that with an incomplete recovery. The other term that is frequently used is progression independent of relapse activity, and this is a person with MS who accumulates disability but without a preceding relapse.

And one thing that we really know, especially in this era of high-efficacy disease-modifying therapies, is that we're very good at controlling those relapses. And then what we see is rather than this "remission," and I have that in quotes, where everything remains totally stable, we unmask this progression independent of relapse activity. And this is really a phenomenon that begins very early, even in persons who are maybe clinically labeled as relapsing-remitting MS. And often, over the course of an individual's lifetime, the longer into the diagnosis, this progression independent of relapse activity tends to become the more dominant driver of disability.

Now, I do think it is important to note that often, in the MS world, we ask this question: is MS a disease that's inside out, or is it outside in? In the sense of, where is the pathology happening? Is this something being driven from peripheral immune activation? Is this something that is within the central nervous system itself? And I think the answer is really yes, it's both. And sometimes we could even try and distinguish this relapse-associated worsening as being potentially more driven by this peripheral inflammatory process.

And so we have activated immune cells that are trafficking across the blood-brain barrier and are often associated with those very classic clinical features of a new attack, relapse, or MRI lesion. And we know that this responds quite well to our disease-modifying therapies, especially the highly effective ones.

On the other hand, progression independent of relapse activity, this is a bit more compartmentalized, and this is the sort of thing we think of when we think of neurodegeneration, meningeal follicles, microglial activation, and all of these other mechanisms that are really intrinsic and inherent to that compartment of the central nervous system and that may or may not respond as well to some of these disease-modifying therapies. I think it really invokes this potential of this era of treatments that may be targeting more of that inside out phenomenon and potentially improving care for people with MS.

Announcer:

That was Dr. Ethan Meltzer talking about the biology behind multiple sclerosis. To access this and other episodes in our series, visit *NeuroFrontiers* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!