Transcript Details

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Multiple Sclerosis: A Look at Disease Progression Over Time

Announcer Introduction:
Welcome to ReachMD. This medical industry feature, titled “Multiple Sclerosis: A Look at Disease Progression Over Time”, is sponsored by Novartis Pharmaceuticals Corporation. This program is intended for health care professionals. Here’s your host.

Welcome to the Novartis Multiple Sclerosis Disease Progression Audio Tool. In this 5-minute recording, we will explore changes in MS symptoms as the disease progresses over time.

Multiple sclerosis is an autoimmune disease with inflammatory and neurodegenerative processes leading to damage in the central nervous system.[1] Relapsing-remitting MS, or RRMS, is the most common type of MS, accounting for approximately 85% of cases.[2] It’s characterized by discrete attacks that evolve and can last from days to weeks, followed by some degree of recovery that can last from weeks to months.[2]

In this recording, we’ll describe disease progression over a 20-year period. Over the years as the disease progresses, patients experience increased impairment in the body, as measured by changes to mobility, and axonal damage, and neurodegeneration, which can be assessed as cumulative damage over time using MRI scanning technology. In this example, the timeline of disease progression following initial diagnosis is characterized by early RRMS for the first 5 years, late relapsing-remitting MS from years 6 to 10, and secondary progressive MS from years 10 to 20.[1,3]

We will focus on the MS patient journey from 3 different perspectives, specifically:

- the whole body, to describe mobility issues and changes in physical disability
- the whole brain, to describe changes in cortical volume
- and at the neuronal level, to illustrate how neuroinflammation and neurodegeneration correlate with these more measurable disease outcomes

Early RRMS

Gait dysfunction is a common symptom in MS, reported by almost 90% of patients after 20 years of disease progression.[4,5] The Expanded Disability Status Scale, or EDSS, is a method used to quantify physical disability in MS and monitor changes in the level of disability over time.[6] Based on the examination of a range of neurological functions, results are presented on a scale from 0 to 10, with 0 indicating normal neurologic function, 7 being confined to a wheelchair, and progressing to death at [10.6,7]

In the early stages of RRMS, neuropathology is dominated by focal inflammatory lesions often associated with subtle symptoms, most commonly fatigue, vision, and sensory issues.[5] This clinical expression of subtle symptoms characterizes the relapsing stage of RRMS. However, in some cases, sub-threshold lesions may not manifest clinically, especially in the early course of the disease. [1,7] In between relapses, the patient may not have worsening neurological function, although some patients may still experience some degree of physical and cognitive decline.[2]

At the neuronal level in RRMS, autoreactive immune cells trigger proinflammatory processes that disrupt oligodendrocyte activity and cause damage to the myelin sheath,[3,8] which is the fatty layer that protects the axons in the brain and promotes communication between neurons.[9] Damage to the myelin sheath can cause lesions in specific brain regions that are associated with the relapsing phase of MS.

This neuronal damage can be improved by anti-inflammatory mechanisms that are associated with improved physical symptoms, which characterize the remitting phase of disease.[8] Despite these anti-inflammatory mechanisms, the damage that occurs during a relapse can linger in the patient sub-clinically, leading to accumulation of deficits over time.[10] After about 5 years, patients enter the late phase of RRMS.[1]

Late RRMS

As the disease progresses to this stage, patients are likely to experience increasing gait variability—walking speed is also impacted.[4,11] Additionally, periods of remission become less frequent and eventually stop altogether as the patient exhibits a slow, steady decline in physical symptoms.[10]

At the same time, neuroinflammatory activity decreases, and active lesions become less common. As neuroinflammation leads to irreversible neuronal damage, increased neurodegeneration, and sustained disability,[10,12] the patient transitions to secondary progressive MS, or SPMS.[8]

SPMS

The consensus among practitioners has been that approximately 50% of patients with RRMS will advance to an irreversible form of the disease—secondary progressive MS, or SPMS—within 10 to 20 years of onset.[3,13] Gait disturbance in SPMS is marked by asymmetry, ataxia, muscular weakness, and impaired dynamic stability.[4] At this stage, the patient will likely require a walking device, such as a cane or a walker.[6] Within 20 years of disease onset, approximately 17% of patients will experience disease progression requiring the use of a wheelchair.[5]

Patients with SPMS also show accelerated cortical grey matter atrophy compared to patients with RRMS.[12] These cortical changes correlate with increasing levels of physical disability.[1,6]

In SPMS, diffuse pathological features are more prominent in the white and grey matter, including microglial activation and neurodegeneration on cortical histopathology.[7] Inflammation becomes, at least in part, trapped within the CNS behind an intact blood-brain barrier.[14]

At the neuronal level, the neuropathology that defines progressive MS is brain atrophy, which is related to axonal loss, cortical demyelination, microglial activation, and failure of remyelination. This cortical atrophy progresses due to ongoing axonal degeneration that eventually cannot be repaired.[8]

Therefore, early diagnosis and use of high-efficacy disease-modifying therapy are critical in potentially helping slow the progression of this disease.[10]

References and Disclaimer

By exploring mobility, brain imaging, and neuronal health at different times throughout the MS disease continuum, we can better understand progression of physical symptoms in patients, while also gaining a deeper knowledge of the neuropathology that underlies these changes.

Thank you for listening to the Novartis Multiple Sclerosis Disease Progression Audio Tool.

Announcer Close:
This program was sponsored by Novartis Pharmaceuticals Corporation. If you missed any part of this discussion, visit reach-m-d-dot-com/industry-feature. This is ReachMD. Be part of the knowledge.

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