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Aging and Multiple Sclerosis: Insights from the 2024 CMSC Consensus Statement

Announcer:
You're listening to *On the Frontlines of Multiple Sclerosis* on ReachMD. And now, here's your host, Dr. Charles Turck.

Dr. Turck:
This is *On the Frontlines of Multiple Sclerosis* on ReachMD, and I'm Dr. Charles Turck. Today we'll be taking a look at the 2024 Consensus Statement on MS and aging from the Consortium of Multiple Sclerosis Centers. Joining me in this discussion are two Chairs of the Consensus Conference, Dr. Yinan Zhang and Dr. Sarah Morrow. Dr. Zhang is an Assistant Professor of Neurology at the Wexner Medical Center in Columbus.

Dr. Zhang, welcome to the program.

Dr. Zhang:
Thank you for having me.

Dr. Turck:
And Dr. Morrow is the Director of the Multiple Sclerosis Program at the University of Calgary in Alberta, Canada.

Dr. Morrow, it's great to have you with us.

Dr. Morrow:
Thank you so much for inviting us to talk about this important document.

Dr. Turck:
Well, Dr. Zhang, let's start with you. What inspired you to focus on MS and aging?

Dr. Zhang:
When I was a resident in neurology, I knew I wanted to do MS, but I wasn't sure what the important topics were at the time within MS. Eventually, as I did my fellowship training, I realized that it's really the older adults with MS who we have the biggest gaps in knowledge and treatment options about. Our disease-modifying therapies are not very effective in progressive forms of MS, which tend to be more prevalent in older adults, and we know that older adults are underrepresented in clinical trials, so there's a lot of gaps in care for this population, and that's where I decided to focus my efforts on.

Dr. Turck:
So starting to dig into some of the key themes of this consensus statement, Dr. Zhang, what are the most significant pathophysiological changes that occur in older adults with MS and how do they impact disease progression?

Dr. Zhang:
So as people with MS get older, many of them transition from the relapsing-remitting form of MS to a progressive form of the disease, as characterized by gradual and irreversible accrual of disability. And for this type of progression, we don't have any effective therapies that reliably slow down disease progression compared to the over 20 disease-modifying therapies that we have to prevent new relapses or decrease the risk of new lesions on the MRI. And that's because the pathophysiology of progressive MS is, in many ways, different from in relapsing-remitting MS, whereas in progressive forms of MS, it's a process that's predominantly characterized by neurodegeneration. There is chronic inflammation compared to the focal, acute episodes of inflammation in relapsing-remitting MS. So in progressive MS, there is accumulation of tertiary lymphoid-like structures behind the close blood-brain barrier that contributes to a chronic, inflammatory

state. And this is very detrimental for myelin repair and promotes neurodegeneration, so our disease-modifying therapies have a difficult time targeting these processes.

And as we're learning more with emerging research, there is evidence of accelerated biological aging in people with MS as well, particularly in the progressive MS phenotypes. This tends to be more associated with worse disease outcomes, as MS is a very age-driven condition and aging plays a large role in the conversion of relapsing-remitting MS to secondary progressive MS.

Dr. Turck:
And turning to you now, Dr. Morrow, Dr. Zhang started to touch on disease-modifying therapies, or DMTs. Would you tell us a little bit about the risks and benefits of DMTs for older adults with MS?

Dr. Morrow:
That's an excellent question, Dr. Turck, partly because we don't fully know the answer to it. So most of our disease-modifying trials have been done with younger people with MS. Most of the time, the inclusion criteria only included people with MS up to the age of 50, sometimes 55, so we are just learning now about these risks and benefits in our older population.

We know that as people age, there is what we call immunosenescence, or aging of the immune system, and that both increases the risk of infections—it's why we use things like boosters, the shingles vaccine, or pneumovax to make sure they're fully protected against infections and also why they are more prone to getting infections and less able to fight them off—but can also affect their MS activity. So the inflammatory part of the disease—the relapsing part that Dr. Zhang was talking about—is also immunosenescent, meaning that overstimulation of the immune system that our disease-modifying therapies target tends to wane over time as well, so there has to be a balance between trying to ensure that we are protecting our MS patients from disease activity but also protecting them by not putting them at unneeded risks by suppressing their immune system beyond what is needed to control it.

It was one of the hot topics that we talked about in this Consensus Conference because it was such a huge issue with those of us who are seeing MS patients on a regular basis. And based on the evidence that is currently available, our recommendations are that after the age of 60, disease-modifying therapies are less likely to show benefit if these people with MS have been stable for five to 10 years before that. This means that they are likely in an immunosenescent phase. And by using these disease-modifying therapies, we are probably suppressing them to a point where we could be putting them at risk without providing any benefit from the disease-modifying therapies.

Having said that, there's, of course, a wide range of things that happen with people with MS. No two people have the same MS, so it's quite possible some people who are younger are immunosenescent and don't need something, and it's quite possible that people who are older still have inflammatory activity and may require disease-modifying therapy, so it still should be on a case-by-case basis. But certainly, based on the evidence we have to date—retrospective studies as well as prospective studies such as the DISCO-MS study—we have made this recommendation in the best interest of our MS patients.

Dr. Turck:
Now, comorbidities and polypharmacy are major concerns in aging. So, Dr. Morrow, what can you tell us about how those challenges affect patients with MS?

Dr. Morrow:
It's one of those things we have to remember that we're not just treating someone with MS; we're often treating someone with MS with many other health issues going on. It's something we're used to focusing on in MS practice in younger patients who are of childbearing age—having pregnancies, breastfeeding, or trying to manage things with a young family or while working—but as we get older, we, unfortunately, accumulate other health issues as well. And we know based on some of the work done by Ruth Ann Marrie that people with MS and comorbidities do worse than you would expect from just having MS, so it seems to be more than an additive effect; these comorbidities have a negative effect on people living with MS more than you'd expect from just having those comorbidities. It means it's really important for us as MS clinicians to think of the patient as a whole—not just their MS—and think of their other comorbidities that might be affecting their health and MS as well. Additionally, the same work by Dr. Marrie has shown that people with MS and other comorbidities are often undertreated or underscreened for these comorbidities, which means that we as an MS community need to advocate for MS patients to ensure that we're treating all of their healthcare issues, not just their MS, since these other healthcare issues can affect their MS just as much, and it's important not to ignore them.

In terms of polypharmacy, that I think is an issue for anyone who is aging. As we age, we have more health issues and aches and pains, and we have more things going on, and it's often easy to start a medication and then continue with it without always addressing whether we need to stay on it or not. So polypharmacy really affects anyone who's on more than five prescribed medications, and this is not uncommon in an aging population, let alone those who are also on disease-modifying therapies for their MS. And they're often on

medications to treat many other MS symptoms, so we thought it was really important to address in this aging population with MS because we want to maximize their health and minimize the harm we might be causing. So we think about, are these medications that are needed? Are they things we can deescalate? Are there medications that could have more than one mechanism of action, so perhaps treating two things so that we can minimize the number of drugs they're on? And we try to consider the side effects that these medications may cause, especially in the context of the varied symptoms you can have from living with multiple sclerosis.

Dr. Turck:
For those just tuning in, you're listening to *On the Frontlines of Multiple Sclerosis* on ReachMD. I'm Dr. Charles Turck, and I'm speaking Drs. Yinan Zhang and Sarah Morrow about the 2024 Consensus Statement on MS and aging from the Consortium of Multiple Sclerosis Centers.

So, Dr. Zhang, now that we have a better understanding of some of the key challenges facing older adults with MS, let's talk a bit more about how we can address them. In the clinical setting, how can we best collaborate with our patients and provide them with comprehensive care?

Dr. Zhang:
So, as we know, the management of adults with MS, and particularly older adults with MS, requires a multidisciplinary team addressing different symptoms that affect parts of the body, initiated by the central nervous system. So this includes rehab therapies like physical, occupational, and speech therapy, as well as neuropsychology, psychiatry, urology, ophthalmology, sleep medicine, diet, social work, and the list goes on. And we have over a dozen different specialties that are commonly involved in the management of symptoms, so it can be burdensome for patients to see all these specialists, and sometimes they may not be sure who they should see or which specialties are available for managing which MS-related symptoms.

So at OSU we have developed what's called the Aging with MS Clinic. This is a clinic that I started and I direct. It's a multidisciplinary clinic for older adults with MS over the age of 60 where they are seen by six different specialists, and that includes a physical therapist, pharmacist, social worker, dietician, neuropsychologist, and MS nurse practitioner. And we go over things like doing a comprehensive geriatric assessment, reviewing their medications, identifying risks about polypharmacy, talking about deprescribing, going over comorbidities, doing a frailty assessment, and assessing social work needs and advanced directives: anything related to aging and MS that would benefit the patient.

So we have seen in studies that multidisciplinary care improves patient satisfaction outcomes in MS. However, we don't have enough studies to really say for certain whether multidisciplinary care improves MS outcomes such as disease progression and so forth, just because it's difficult to conduct randomized controlled trials in that manner. But nevertheless, I encourage providers and patients to discuss multidisciplinary care in MS.

Dr. Turck:
Now, we're almost out of time for today, but before we close, Dr. Morrow, let's look ahead for just a moment. What are the future directions for clinical research that might fill our gaps in knowledge about aging and MS?

Dr. Morrow:
There are so many that we could focus on. As I said earlier, we are still learning about aging with MS, and I feel like it's a privilege for us as people caring for people with MS that we can learn with them while they age, but it does mean that we are acting somewhat in a vacuum without evidence. So looking at when it's the appropriate time to stop disease-modifying therapies for people with MS, we've based our recommendations on the evidence we have to date, but it is limited. Looking at the aspects of the MS disease, these disease-modifying therapies affect the inflammatory part of the disease, and yet they do not work as people age with MS. They still tend to progress. And so what are we missing? Are there other targets that we should be focusing on with our research that could prevent this progression over time that really affects our aging MS population? And I think, finally, looking at how we can best support our people living with MS who have these comorbidities and ensuring that they don't feel like they're being bounced around from one medical practitioner to another, and working as a team to ensure we're treating all of their health at one time rather than just their MS—and perhaps their hypertension, cardiac disease, or diabetes—and ensuring that we're looking at them as one person rather than their health in different silos.

Dr. Turck:
Well, with those forward-looking thoughts in mind, I want to thank my guests, Drs. Yinan Zhang and Sarah Morrow, for joining me to share key takeaways and strategies from the Consortium of Multiple Sclerosis Centers 2024 Consensus Statement on MS and aging.

Dr. Zhang, Dr. Morrow, it was great having you both on the program.

Dr. Zhang:
Thank you. It's a pleasure.

Dr. Morrow:
Absolutely. Thank you for having us.

Announcer:
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