



Understanding MS Relapses and MS Progression

Presented by:
Barry A. Singer, MD

Marie LeGrand:

Good evening, everyone, and welcome to the MSAA's live webinar: "Understanding MS Relapses and MS Progression" presented by Dr. Barry Singer. I would like to take this opportunity to thank you for joining us this evening. I'm Marie LeGrand, Associate Vice President of Mission Delivery, Health Equity, and Education for MSAA and your host for the program this evening. Before turning it over to our speaker, I would like to take this opportunity to go over a few of the services that MSAA provides and some housekeeping items.

As you may know, MSAA is a national nonprofit organization dedicated to improving lives today through vital services and support for the entire MS community. Our services include a national helpline, providing English and Spanish services Monday through Friday, 8:30 a.m. to 8 p.m. Eastern. Additionally, MSAA provides equipment and cooling products designed to improve safety and mobility and to also help with heat sensitivity. We also offer an MRI access program to help cover some of the costs for individuals with MS who qualify for assistance. We provide a variety of educational programs, such as this, including webinars and on-demand videos, online tools, publications and digital resources. And part of that includes the Ultimate MS Treatment Guide, which you can also find on our website. Now, this interactive guide describes and compares 19 FDA approved MS treatments and will help people living with MS make informed decisions and choices. MSAA offers support through community connection to help you stay connected with other members of the MS community. To learn more about MSAA's programs and services, please do visit our website or give us a call to speak with one of our specialists.

Now, as a reminder, throughout tonight's program, you will have the opportunity to ask questions by typing them into the chat box. We encourage you to submit questions throughout the program and we'll do our very best to answer during the Q&A portion of tonight's webinar. At the end of the program, we ask that you please complete a brief survey. Your feedback is extremely important and it will help us in developing future programs and content. A link to the survey will also be included in the chat box. Please note that this program is for educational and informational purposes only and does not constitute as formal recommendations. Please do speak with your doctor or healthcare provider if you have any questions or concerns. As part of tonight's discussion, we are providing our viewers with a deeper understanding of the markers of progression and the effects of progression in people living with MS, including relapsing forms of MS. Dr. Singer will answer questions on the importance of early treatment and factors that

can affect the progression of MS and relapses. He will also discuss how to have conversations with your healthcare team to ensure that these issues are addressed promptly and efficiently.

Without further ado, I'd like to introduce our speaker, Dr. Barry Singer is the director and founder of The MS Center for Innovations in Care at Missouri Baptist Medical Center. He is an associate professor of clinical neurology at Washington University School of Medicine. He has been an investigator in more than 35 multiple sclerosis trials focused on new therapeutic options, including demyelination. He currently serves on the board of directors of the MSAA and has a position on its executive committee. Dr. Singer received a congressional proclamation for MS research in 2008 and his award winning MS patient education website, www.MSLivingWell.org, started in 2007, has been a valuable resource in 200 countries. Dr. Singer is also the host of the MS Living Well podcast. Welcome, Dr. Singer. We are so excited to have you here with us today to discuss this very important topic.

Dr. Barry Singer:

Well, thank you so much, Marie. It's great to be invited and I'm happy to share the latest information with all our people listening-in.

Marie LeGrand:

Wonderful. Well, Dr. Singer, I'd like to begin our conversation by having you talk to us about MS relapses and MS progression and provide us with an overview and background. What are the differences between an MS relapse and MS progression?

Dr. Barry Singer:

So MS relapses are when you are cruising along and everything's fine, no change in your MS, and then suddenly something happens. So, you might lose vision in one eye, it starts to get blurred over a few days and then you can't see out of that eye for a day or two or a month or two. And so a relapse would be more than 24 hours of a neurologic symptom that you haven't had before or something you haven't had in a while, at least 30 days. So when you have this new neurologic symptom, you know, sometimes in relapsing remitting disease, sometimes it remits and goes away, but sometimes people are left with residual disability after a relapse. So, for example, some people might have numbness in their legs that comes up their torso, lingers on for two weeks, and then starts to go away. But they may have permanent numbness in their feet. So sometimes after a relapse, you're left with some disability.

The biggest... When we talk about progression, we're talking about, kind of, like this relentless moving-forward in terms of disability, where things are slowly getting worse over time. So you're talking about like your leg is getting slowly weaker over time or your memory is slowly getting worse over time. So progression means it's continuously getting worse. It's not like you had this bump in the road and then you're recovering. It's more slowly changing and things are getting worse over time. So that's how we define progression versus relapses.

It's interesting, there's something called RAW, which is relapse associated worsening. So you have a relapse and you're not fully recovered from that attack and you have residual disability. And then we have progression that happens independently of relapses so that without a relapse you can still get worse. And we call that progression independent of relapse activity, or PIRA. So there's a lot of interest in the field at looking at what's driving that progression that's independent of the relapses.

Marie LeGrand:

Okay, I see. Now, can you have a relapse with progressive MS?

Dr. Barry Singer:

Yes, so we do know that some patients do have progressive MS, and so they're slowly getting worse over time. And so you definitely see that where someone is slowly getting worse, and then boom, all of a sudden they have a relapse. We even see it in primary progressive patients. So they were kind of labeled as this primary progressive course. And then they have occasionally a superimposed relapse. So it's not black and white. I think, you know, the original definitions of primary progressive and relapsing remitting came long before the era of MRI. And I think we over time, we realized that we can't put people in boxes. I think some of the drugs get FDA approved for specific diagnosis, but it's not so simple in the real world, as many of the people listening to this program will understand.

Marie LeGrand:

I see. And that is very true. I mean, as we've learned over the years, that MS is very unique to different individuals.

Dr. Barry Singer:

Yeah.

Marie LeGrand:

Is there an average length of time between MS relapses?

Dr. Barry Singer:

So MS relapses can really vary. Now before there was treatment, you know, early in my career when we just had basically interferons and glatiramer acetate, we had very few options, we used to think one relapse a year was pretty normal. And some of the clinical trials, you could see that on placebo. And so, off of treatment, relapses can be every one to two years sometimes. The good news is we have highly effective treatment now and some of our medications we're getting down to relapse rates in the clinical trials of one relapse every ten years. So it's really amazing that many of our medications are one relapse every five years to one relapse every ten years. So we now have the power to really help reduce those relapses.

Marie LeGrand:

And that's a very important thing to know for our patient community and our care partners. How would a person know that they are having a relapse? Are there perhaps specific symptoms of relapsing remitting MS?

Dr. Barry Singer:

Yeah. Can you repeat that one more time?

Marie LeGrand:

Yeah, sure. How would a person know that they are having a relapse?

Dr. Barry Singer:

So you basically know that you're having a relapse if you, if you're like, you know, just... everything's fine. You know, maybe you have a little weakness in your leg, but then all of a sudden something happens. So you develop double vision. You develop spinning sensation, going round and round. Your face goes numb. You have shooting pain in your face. So all those symptoms, double vision, vertigo, shooting pain in the face could be a sign, a brain stem attack.

Or if your spinal cord is affected, it tends to affect both sides of your body. So you may get numbness coming up your torso into your hands. We talk about the MS hug where you get the squeezing sensation. As one of my patients said, it's not a nice hug, someone just told me that this evening. So it's a squeezing, tight sensation. So that could be something in your thoracic spinal cord. If you get shocks down your spine when you bend your neck, called Lhermitte's Sign, it could be cervical spinal cord inflammation going on. So if you're having a new symptom more than 24 hours, that could be an attack.

Now, it's important to keep in mind there is something called pseudo exacerbations. And this is if you are... you've got a bladder infection, you get COVID. I had a lot of patients in the pandemic show up in the E.R. - I have an MS flare up, and I'm like, you do? And then the E.R. doc calls me, and I said do they have a mild cough? Yes. So it was COVID, because of the fever COVID can make your symptoms of MS worse, but that's not a real relapse. A real relapse would not be with an infection. And so we would call those a pseudo relapse. So, again, more than 24 hours of symptoms and it is important to contact your provider and your healthcare team as soon as possible, because, maybe, we may want to treat that with steroids.

Marie LeGrand:

Good to know. Now, you mentioned treatments earlier and how we've advanced, you know, we do have quite a number of treatments that are FDA approved. Now, are there specific treatments to treat relapsing remitting MS?

Dr. Barry Singer:

Yes. So a lot of treatments. So we've done well on relapsing remitting MS. So, you know, we have the injectable, self injected medications, the first line treatments that we had, including interferon and glatiramer acetate, we have an array of oral medications and different classes. So one called teriflunomide. We have a class called S1P medications, another class called fumarates, we have Cladribine, so we have a variety of these different medications in the oral field. And then we have antibody therapies which may be our most potent class of medications, which are antibodies that are either infused or given underneath the skin in an injection.

Marie LeGrand:

Okay. I'd like to circle back to progression. How fast does progressive MS progress, and can you stop an MS progression?

Dr. Barry Singer:

Yeah. So progression can really be variable in terms of how fast it moves. I have some patients that I think have been slowly progressing for decades, for at least a couple of decades I've been taking care of them, where they used to run and now they can't run anymore, but they could walk, you know, five miles. And then, you know, then they'd be on the treadmill. They took it inside because it was hard outside, the balance would be a little off. And now they walk on a treadmill for 30 minutes. And over time, you could hear, you know, how what they could do has just slowly gotten worse. But they're still ambulatory, you know, still walking 20 years later. And so some patients, it's very slow in terms of how it goes. And unfortunately, in some other people it goes much faster. I think the problem is that once you start using a cane and your balance is off, it doesn't take much to push someone over. If the leg is pretty weak, and the leg that's a little weaker pushes them over to the edge where they really need a wheelchair to get around.

So some people do progress a little faster. The important thing is trying to pick that up as soon as possible. Like if there's a change going on. I think it's sometimes very hard for doctors to pick

up, and I think it's sometimes very hard for people living with MS to understand the subtle signs of progression and disability. And a lot of times, it's easy to pick up a relapse, you know, you suddenly get double vision and vertigo, it's pretty obvious. But progression can sneak up on people over time and you go, Whoa, you know, you're now like, you know, really using a cane to get around. When did this happen? And it can sneak up on people.

Marie LeGrand:

Hmm. Okay. We had a few questions come in regarding MS remission. So can progressive MS go into remission?

Dr. Barry Singer:

It can. So there can be times where it starts to plateau out. So, Marie, you can have people that have like an attack and then it can plateau over time. So you definitely can see that where things plateau.

Marie LeGrand:

Okay. We had another question come in earlier asking if it's worse to have a relapse or if it's worse to have relapsing remitting MS or progressive MS.

Dr. Barry Singer:

Well, you know, relapsing remitting MS is a little easier to control. So ideally, you know, we want to try to control it in the relapsing remitting phase. You know, if we don't give people treatment and you follow people over time, up to 90% of patients will go on to develop progressive MS, which we call secondary progressive. So you start out with having relapsing disease and then it slowly, things can start slowly getting worse at some point, you still may have new relapses, despite being in the progressive phase, particularly earlier in the progressive phase.

And so we want to ideally, you know, we want to keep people in the relapsing phase of the disease and try to prevent people getting progressive. We're doing a pretty good job of it. We've definitely made some strides. If you look at people that were put on highly effective treatment early, they're less likely to go on to form, go into the secondary progressive phase. So we're making some progress. But I think we need we're going to need some new treatments. And unfortunately, there's a lot of new treatments. There's dozens of trials going on in progressive MS right now. So the idea is to kind of slow down that progression. Now that we've done a good job in shutting down new MRI activity and new relapses, we're kind of really focused on trying to prevent that slow progression over time.

Marie LeGrand:

Okay. Now, still talking about progressive MS, what is the difference between the primary progressive MS and secondary progressive MS?

Dr. Barry Singer:

So the difference is how your MS starts. So someone that has primary progressive MS may say like, you know, somewhere in their late thirties, in their forties, they notice that their leg is a little weak. And then when they walk, they go for a walk, they might get a little foot drop or the foot catches on the ground. And so they may see the, you know, like their foot, basically because their leg is getting a little weak, when they walk distance. And gradually over time, they find that, you know, they used to be able to walk three miles before the foot drop pit, and now they can only walk about a mile before their leg starts to hit. And just over time, it's just slowly getting worse. They never have an attack with primary progressive MS, never start out with, oh, I had,

you know, vision loss out of one eye for two weeks or I had double vision for two months, or I had numbness on one side of my body. One of my patients today said that they had numbness on one side of their body as their first attack. So you don't hear that first relapse, it's just slow progression.

And then a secondary progressive would be someone that had relapses initially, had an attack, maybe one or more, and then went on to the progressive phase where their balance is getting worse, their memory is getting worse, their legs are getting weaker. So then they go into that progressive phase. So it is important that you, you know, a lot of times to find out if it's really secondary progressive is really listening to my patients. So you have to kind of think back. You know, I got patients that start remembering things that happened in high school, you know, that they had bad balance problems and/or vertigo, which are spinning sensations, and they went to their, you know, they saw their pediatrician and it went on for like three weeks, and they did tests and they couldn't figure it out. And then, you know, when you look back and you're like, whoa, that may have been their first relapse. So I think we always have to kind of go back and it's almost like digging through time to see if there were any relapses. I see some people that get diagnosed with MS in their sixties and even seventies, and it's like going back and thinking about were there any clear attacks in the past.

Marie LeGrand:

Yeah. I know that's one of the questions that came in was, what are the changes when moving from relapsing to secondary progressive MS?

Dr. Barry Singer:

So, you know, one of the things that we want to do is start thinking about, you know, what are the changes going on in your body? And so when I, one of the first questions I ask when I see people in the exam room is, you know, how's your MS doing? Is there any change in your MS? And it's important to think about all the different aspects of how MS can affect you. Definitely, cognition is a huge issue, so cognitive processes meaning like memory, word finding ability, are you having a harder time finding those words, like when you're in conversation, do you have a harder time multitasking, if you have to learn something new at work, are you struggling with that? And so we know that about half of people with MS have cognitive problems, and if that's slowly getting worse, that could be a sign of progressive disease.

And one of the things that we see in the brain tissue when we see this is that they're... well, all our brains, unfortunately, are shrinking as we age, so I can look at a 20 year old brain from a 40 year old brain to an 80 year old brain and see shrinkage over time. But with MS it can happen a little faster, especially off of medication. And so this can start to affect the memory and how fast you can process information. So we have to monitor that. And one of the things they do in the clinic, actually I do, I bring an iPad in, I've been doing this since 2019, and people match symbols and numbers together over 2 minutes and we see how people are doing in terms of their processing ability. So we want to kind of monitor that.

We also want to monitor, ask questions about your strength and your balance. You know, how far can you walk, you know, can you... what kind of distance can you walk? Some people do a 25 foot walk where you measure 25 feet in the clinic and have people walk and kind of monitor that over time. So we definitely want to look at balance and strength to see if there's a change over time.

You know, vision can deteriorate over time. You know, just personally, I don't see a lot of patients with their visual acuity, you know, they don't tend to go from 20/20 to 20/40 to 20/80 to

20/200. I don't see a lot of that. Ophthalmologists say they can see some changes that are progressive on the back of the eye in terms of the retina. But you know, but we tend not to see a lot of that. We do see worsening bladder function, worsening bowel function and sexual function. So we have to ask these questions. And I think it's important to be candid with your neurologist, if you're seeing changes, so you're having a harder time emptying your bladder, recurrent bladder infections, your fatigue is getting worse and we need to address those.

One are the things with progressive MS, the meds work so well. Some of them do slow down the progression of progressive disease, but there is a lot we can do in terms of managing the symptoms of the disease and ways to improve quality of life and trying to manage all these different aspects, ways to improve gait, ways to improve fatigue, nerve pain. So one of the things we really focus on is trying to improve those symptoms of progressive MS to improve quality of life.

Marie LeGrand:

So you talked about ways in which to improve quality of life. Do you have anything specific? Because I'm sure some people are wondering, is there anything specifically that I can do to improve my quality of life?

Dr. Barry Singer:

Yeah, definitely. So, okay, a big issue is strength and balance. So the meds are only going to do so much. So very important that you come up with an exercise regimen. You know, it really depends on your level of disability, what you can and cannot do. You know, if you have a lot of balance problems or leg weakness, I had people that are swimming. So getting into water aerobics or water swimming, exercise class can help. I love recumbent bikes for progressive patients because they can get on a recumbent bike, exercise bike, and pedal, and so that can really help build up the strength in the legs. Stretching is important because a lot of people get muscle spasms, particularly like cramping or spasms at night. So stretching can really help. If it gets bad enough that we use muscle relaxants, such as... one is called baclofen, another one called tizanidine, to kind of loosen up the muscles. But stretching can be really, really important. If it gets bad enough we use Botox.

Bladder problems are huge with MS. You know, one of the downsides with MS is bladder urgency. You got to run to the bathroom. Well, if you're more progressive, it's harder to, you know, when you have disability, it's hard to get there fast enough. So you have to worry about incontinence. Should I leave my house? You know, how do I manage that? So if you can manage it without medication, great. Pee before you get in the car. People learn the tricks to help manage that. Avoiding caffeine, which makes your bladder more urgent. And then if you get to the point where it's not working, then we use medication to kind of manage that. So there's different classes of medications that can work and even Botox in the bladder can keep you dry for six months. So bladder is another huge issue. So we have to kind of work through all these different symptoms we have to work through.

And, you know, even sexual dysfunction, I think it's very important to have candid conversations with your doctors. I think neurologists don't do a great job of that. There's very little training. But I find that's an important candid conversation to have with patients. And there's a lot we can do on that front in terms of women tend to have less sensitivity, less sensation. So there are ways that we can address that. Sometimes the anti-depressant medications block someone's ability to have an orgasm, and it's not their MS. Men tend to have a low testosterone and erectile

dysfunction that can be treated with medications, even injections, testosterone replacement. So all these things can impact your quality of life. And there's a lot we could do on that front.

Marie LeGrand:

Okay. Okay. Good to know. Thank you so much for sharing that. And that was going to be one of my questions in terms of are there any treatments specifically to help with sexual dysfunction? So you've addressed that for sure. Now, we did have some questions come in prior to tonight's webinar, and I wanted to go ahead and ask some of these questions. So we'll start with this one. How do you know for sure without an MRI that you are experiencing a relapse or flare up? I know you mentioned that, a little bit about that earlier in the conversation.

Dr. Barry Singer:

Yeah. So, I mean, again, MS attack, we call them attack, relapse, exacerbation, are all the same thing. So it's basically more than 24 hours of a symptom of a new neurologic symptom that you haven't had for at least 30 days or never had before. So you've got to have at least, you want to at least get that, you know, you want to have at least that amount of time. So again, it's not when you're just overheated; you go out, do some yard work, it's 100 degrees, and you get out there and mow the lawn, and then I get a call - my leg is weak and my balance is off. Yeah, well, it's 103 in St Louis today. This was not the time to mow the lawn. And, you know, I had one person that actually called me through the exchange, they fell three times in one day because it was 100 degrees. So if you're overheated, it's going to make your symptoms worse. But it's not a true relapse.

There's also this phenomenon called Uhthoff's phenomenon, which means when your body gets overheated, you might have transient worsening of an old symptom. For example, I've had patients who play basketball and they get out on a basketball court and their eye, like the right eye might get blurred, and that's because they're overheated, and it's an old damage to the optic nerve, but it's not a true relapse because as soon as you cool down, you're better. And you're not hurting yourself. You should exercise. It's not damaging anything, but it's bringing out some old symptoms. But again, we're looking for more than 24 hours. Obviously, you know, if you're blind in one eye for 12 hours, don't, you know, you don't have to wait 24 hours to contact a healthcare provider. But definitely let us know if you're seeing changes, whether it's slow and progressive or it's sudden, speak up. And then maybe there's some intervention that we need to do.

Marie LeGrand:

Okay. Now, can you do anything to prevent a flare up?

Dr. Barry Singer:

Yeah, it's... well, there's a couple of things you can do. One is take your medication. So that's the best way to prevent it. We have highly effective disease modifying therapies. You know, I can tell you over my career, the people that do well are the ones that consistently take their medications. And unfortunately, I've seen so many patients that have done very, very well for a long time and just got tired of taking the medication. "Do I really need it?" And then have a bad relapse, you know, some people have permanent burning on one side of their body from that relapse or permanent balance problems. So the best way to prevent relapses is really to be on disease modifying therapy.

There's some data with vitamin D, that levels of vitamin D are associated with higher risk of having an MS relapse. So we do frequently check your vitamin D level to see where you are. So

that can help. But it's kind of "we still don't really know," like, why specifically one part of the nervous system that your immune system all of a sudden attacks, you know, why is it in the optic nerve, why, you know, one part of the brain and what brings it on? We don't really know. Not a lot of good data for stress and triggering MS exacerbations. So I think it's still a bit of a mystery why it attacks certain parts of the nervous system and why some people have much more active disease. than others, I mean, I see people with very mild disease and some people with very active disease.

Marie LeGrand:

Yeah. Talking about stress, one of the questions asks what are the impacts of extreme job stress on relapsing remitting MS?

Dr. Barry Singer:

I think we're... we don't think that it causes new MRI lesions. There's not a lot of great data there. But we do know that if you're under a lot of stress, it makes it sure hard to cope with your disease. So, you know, you basically, if you have fatigue issues, if you have processing information, processing problems, you know, memory problems, you're dealing with depression, so half of people with MS have some depression, over 40% of anxiety, and then you throw on a boss who's a bear, you know, that's driving you crazy, it just is very hard for people with MS. You're just... bandwidth is less. And so to deal with that, it's very hard. And, you know, and I see a lot of people in great work environments, very supportive work environments. But then sometimes we see the toxic work environment. You know, sometimes I think I spend more time doing therapy about the job, the boss, and the office. Their MS is fine.

That and families, I think that's the other issue. I've been hearing a lot of family issues going on, so dealing with their kids and teenagers and stress and, you know, family member issues. Sometimes all those issues go on in life, but unfortunately, we can't escape stress in our world. So how to cope with it? You know, and you got to find your strategies, whether it's finding a therapist, you know, mindfulness, yoga, you know, whatever therapy works for you to kind of help you chill out and cope. It's very, very important. So find... if exercise, you know, is the way you wind down, then do that. And, you know, in the evening, get off the screens, you know, read a book, chill out, get some good sleep. I think that's all very, very important.

Marie LeGrand:

Yeah. I was going to say, well, you know, you're very easy to talk to. So, you know, you're definitely part of that stress relief regiment for some individuals who have a lot going on where they feel comfortable to talk to you about that kind of thing.

Dr. Barry Singer:

It's tough. I think the one good thing about talking to a doctor, it's like the bartender, the priest and the doctor, you know, the bartender may have loose lips, but we don't. So I think people feel very comfortable sharing, you know, and, one of the honors of being an MS doc is that I've known my patients a long time, so some people I've known for literally, I've been taking care of patients for 23 years, some of them coming up to 24. And so, you know, when you know people over that period of time, there's a certain amount of trust. And I think that's really important with your MS providers, whether it be a P.A., a nurse practitioner or a doctor, is that you really feel comfortable, that you can share when there's problems going on, that you're listened to. I mean, that's extremely important. I think the first thing doctors should do is listen so that we understand where you're coming from and help you navigate this disease.

Marie LeGrand:

Yeah, it's so important to build a rapport with your healthcare team because they're the ones that's, you know, they see intimate parts of you, you know, and you rely on them for guidance, you know, for your health.

Dr. Barry Singer:

Yeah. In fact, I probably see more second opinions for that reason than anything else. It's feeling confident in that relationship, that they're being heard and that, you know, your concerns are being addressed. I think that's really important. I mean, I've heard some places say, oh, medically, I thought it was fine, but didn't seem like a good fit. So, yeah, I think you really want to find that right fit as you go through this journey with this disease.

Marie LeGrand:

Absolutely. Another question came in around aggressive treatments. So is it best to begin aggressive treatments to treat MS?

Dr. Barry Singer:

So there is mounting data to support that. So there's some studies going on. One that's this global MS registry of people living with MS called MSBase, and they looked at patients that were, started on highly effective treatment early versus waiting, you know, not the first couple of years but waiting past that and then looking at patients long term. And really early intervention with highly effective treatment was more likely to have fewer patients going on to have significant disability progression. So it was a sizable difference. And there's trials going on right now kind of doing a randomized trial, starting on a conservative treatment, you know, maybe a modest efficacy treatment that's very safe and then escalating to a higher potency drug if there's a breakthrough disease versus starting up strong and maintaining.

And I think the growing consensus is starting strong and maintaining is the way to go for a lot of patients. Now, everyone's different, though. Some people, for example, have very mild disease, so some people have three or four spots in their brain and nothing in their spinal cord. Some people have multiple lesions in their spinal cord and a lot on their brain. Some people are very active disease, some people have very mild disease. We know some patients are at higher risk for disability, so those with a lot of lesions. We see late onset MS tends to do, people tend to do a little worse, so if you get MS after age 40 versus 25. We also see issues with poor recovery from their first attack is a bad prognostic sign. Men tend to do a little worse. And unfortunately our black and Hispanic patients tend to have more disease activity. But not everybody reads the book. I mean, I saw a guy today, he was a black man with late onset disease and with mild MS, you know, mild disease in the brain and spinal cord. So you can have patients that don't, you know, follow the pattern. So we have to really individualize treatment. So, but we are seeing a lot more of high efficacy antibody treatment being used. First line over 40% of people in the U.S. are on these antibody therapies now.

Marie LeGrand:

Okay. You mentioned black, African-American and Hispanic patients living with MS, can you talk a little bit about perhaps the differences in the disease course?

Dr. Barry Singer:

Yeah, particularly for black patients, we've known for a long time that there's a higher risk of disability that can be... that can happen. And there's growing data as well for the Hispanic community of increased risk of disability and even earlier onset of disease in Hispanic patients.

And so we... this is a real, you know, a real part of the mission of the MSAA is really to provide information out there and improve access to care. We definitely want people to be able to access the MS specialists, and so, you know, there are definitely barriers in the Hispanic community, you know, first of all, are you American status or are you illegal? And then how do you navigate that system? You have language barriers. Fortunately, now the MSAA has information in Spanish, but you know, accessing it, there may be the neurologist in the community that speaks fluent Spanish is a general neurologist who doesn't have a lot of experience in MS. So that's part of the issue.

And with the black community, you know, access to MS specialists, you know, sometimes large urban communities have access to major teaching hospitals, but the MS specialists there may see patients, you know, one day or a half a day a week. So trying to get in through the clinic processes can be challenging. And then where I am, you know, I'm in St Louis, so we have a mix of really a big geographic mix. I have like urban patients, suburban patients, so then we have a lot of rural patients. So the rural patients are also underserved. So they may be going to a general neurologist who's managing all kinds of diseases and hard to really keep up with all the changes that are going on in the MS world. And so I see a lot of patients coming in that have been kind of undertreated for a long time, and then they go into the progressive phase. So we're improving things using telemedicine and there's ways that we can try to break down those barriers and having and getting access to all those, you know, providing access to all those people that really need more intensive care.

Marie LeGrand:

Right. It's so important to, you know, create opportunities, as you mentioned, where people can access care. And to your point in terms of the rural community, it's definitely very challenging, you know, for people in rural settings. You know, I remember once there was an individual who traveled nearly 2 hours to attend, you know, one of our in-person programs that we did some years ago. And this is very real and very true. And I believe that was in Missouri. So...

Dr. Barry Singer:

So, Marie, I see patients that drive 4 hours for an appointment on a routine basis, 4 or 5 hours. And if you look at the map, there was an interesting map that was presented at ACTRIMS, it was Marisa McGinley from the Cleveland Clinic showed where the MS centers are. And, you know, out here, out here in the heartland, there aren't a lot of centers. So people, to see a specialist, there's a lot of driving to get in to see an MS expert. So again, it's one of those ways that we want to be able to provide maximum care for patients and access is really important.

Marie LeGrand:

Absolutely. So before turning it over to our audience for a couple more Q&As, I did have one last question that came in prior to this webinar. If you are older and have not had progressive MS for a long time, is it likely that you will not get progressive MS?

Dr. Barry Singer:

The million dollar question. So I definitely get some patients... I get some patients that get away with no treatment. So, occasionally someone will show up to me, I don't know why they're coming in, they're 75 and they've done well, they had two relapses and they never had any significant disability. They have great quality of life and they somehow dodged it. You know, we actually see some people that we find MS in an autopsy and now a hot area of MS is called radiologically isolated syndrome, which means people, you know, hit their head on a door and get a scan and, lo and behold, they have lesions. Or they were in a car accident or even just get

migraines and they get a headache and we see lesions on the brain. And they look classic for MS event though someone hasn't had a symptom yet. You know, some of those people definitely go on to develop MS and there's a trial that just showed early intervention with treatment for the right patient could slow down the risk of going on to have attacks. So there's this early stage of the disease. And so sometimes the disease is under the radar.

But, you know, I have seen relapses in patients up to 80 with new active disease on the MRI scan of the brain. So it's always hard to know when the disease is over for people. There was a recent trial called the DISCOMS, and so it was about discontinuing MS treatment. And there was some patients that had breakthrough disease after they discontinued treatment, the patients were like 55 to 75. But a lot of those patients were on the old injectable medications and had been very, very stable. So it wasn't after stopping, you know, a lot of patients were not on highly effective medications and we just stopped it.

So I think it's very important to have a great conversation with your provider about if you're at the point of discontinuing medications. One of the things we are seeing is pretty good support after 65 for treatments. And we now have some that have gone generic. So we're seeing a little bit better Medicare coverage. And there's also plans with the pharmaceutical companies to help get people access to drug if they want to continue taking them.

Marie LeGrand:

Okay. There was actually a question that came in not too long ago and you addressed it about relapses if it decreases with age. And you mentioned the patient who was 80 and had relapses.

Dr. Barry Singer:

Yeah, they do decrease with age, though. Yeah. And then there was some questions in the chat, you know like how do we treat a relapse. We haven't really talked much about that. So generally the treatment is 3 to 5 days of intravenous steroids. So we generally treat, which can be either high dose I.V., which I think it's tolerated better, or oral. And there's different regimens, whether it be prednisone or intravenous or oral. I use oral methylprednisolone and we can give equivalent doses as to what we give I.V., sometimes a little harder on the stomach. Side effects of that - sometimes you get wired and have trouble sleeping. The oral ones tend to cause a little more gastric irritation. Irritation in the stomach. Blood sugar can go up. Huge problem if you're diabetic. Sometimes I have to hospitalize people if we can't manage their insulin, you know, if their blood sugar shoots up, it could be dangerous. So we may have to monitor that with insulin coverage, and rare hipbone injury, and rare psychosis, where people have hallucinations. So, but that's generally the treatment. And if you don't respond to that, and it's a real severe relapse, we can do something called plasmapheresis, which is almost like dialysis.

And if you can't tolerate steroids, there is something called Achthar, which is an injection, and that could be a backup. Very expensive, but can be a backup if needed. So there are options for acute relapse. We like to get on top of it as soon as possible. If you've got a bad relapse, I'd like to start it, you know, frankly, within days of that attack, it's not good to sit on, you know, relapses and wait to see if they go away after, you know, by two or three months, you're not going to get much benefit of the steroids. So we like to really get it going as soon as possible. So we don't want to wait, you know, don't come in, you know, to your appointments, you know, four months later and say, oh, by the way, I had a bad relapse and I'm still, my balance is still bad. So let's try to get on top of it and speak up early. You know, even if you don't like steroids, you may not need it, but at least let your doctor know. We may need to change up your meds.

Marie LeGrand:

Absolutely. One question that came in tonight - I believe I have had MS for 17 years. I am 59 years old and started treatment last year. My question is, because I was not getting treatment, how much damage has been done?

Dr. Barry Singer:

Well, one way we can figure that out is look at your MRI scans. So, we can... your provider could sit down, look at your scan. You know, some people have only a few spots on their brain. At 50, we all get a few white matter spots on our brain, so we can take a look and see how much is going on in terms of your disease. And then, unfortunately, some people get diagnosed late in life and I see a lot of disease that was under the radar and never picked up. But some people have mild disease. So we have to really kind of individualize it. So I think it's really great to see your scans with your provider. I look at my MRI scans with my patients. I mean, you got to take the medication, that has risk. So it's kind of nice to see what's going on visually so that you understand why you want to take your medication regularly to prevent that attack on the brain and spinal cord.

Marie LeGrand:

Okay. To our audience, if you haven't already done so, please feel free to put in your questions and drop it in the chat box and we'll get to those as quickly as we possibly can, time permitting. So, Dr. Singer, there was another question that came in. Are there any tests, evaluations, in addition to MRI, that can indicate where in the nervous system the progression is likely?

Dr. Barry Singer:

So really a lot of it's clinical. So if your legs are slowly getting weaker over time, both legs, then it tends to be spinal cord. So one side of the brain controls the other side of the body. So, but in the spinal cord it tends to be more symmetric. So if you have numbness in both legs, it's creeping up the body on both sides into your torso, then that would be spinal cord disease. And so spinal cord tends to affect both sides of the body, the brain, one side or the other. So sometimes we can kind of sort it out. Bladder dysfunction, like bladder urgency, you got to run to the bathroom or then you get to the bathroom and you have trouble emptying it, recurrent bladder infections, constipation, sexual dysfunction, that tends to be spinal cord. So if you're having progressive problems on that front. On the other hand, cognition, you know, if memory and word finding difficulties are your challenges, then it could be definitely, we look at the brain and see what kind of disease activity. So that's important.

We are working on other ways to monitor the disease. I mentioned the cognitive testing that we do, you can do walking testing. We're working on technology to better assess it between appointments. So looking for progression with smart technology. So looking at your phone that you carry around with you, you know how active you are walking around, how much are you sleeping? Starting to look at that data in between visits to kind of give us a sense and there is also some gaming tools that are being looked at so you can have fun playing games, but meanwhile, we're keeping track of your cognition over time, make sure you're not losing anything. So there are going to be some good ways to monitor that.

And then another hot area is called biomarkers, which are blood tests to monitor the disease. So you think about diabetes and you do a blood test called a hemoglobin A1C to monitor your blood sugar or for prostate cancer, you look at PSA or cholesterol levels. So there are some blood tests that we are looking at that might be able to tell us if you have higher or increased risk of having new MRI activity, relapses or are you at risk for progression. And so one of those

tools I'm actually starting to use in the clinic, looking at a blood test for disease progression or disease activity. So I think this is going to be an interesting area that will be able to monitor people more carefully.

Marie LeGrand:

Okay. One individual asked if you could talk a little bit about and provide some information about level three MRI.

Dr. Barry Singer:

Okay. So there's three tesla MRI. So with MRIs, we have different strengths. Okay. So typical closed MRI will be a 1.5 tesla magnet. So tesla, not the car company, but the power of the magnet. So a three tesla magnet gives you really beautiful pictures of the brain and the spinal cord, particularly spinal cord because it's very, very small. So you want good pictures. On a three tesla magnet I can definitely say, Oh, you got a lesion here, here or there, on at 1.5, you're kind of guessing. Sometimes it's obvious, sometimes it's not. And then some open MRI's are like .7, so they're, you know, much worse resolution. So it really kind of depends on the scanner, you know, how... and there's even seven tesla magnets that can give you some beautiful images which I've seen coming out of research at the National Institutes of Health.

So you can get these variety of scans, so the stronger the magnet, the better the picture is. It really helps us as providers. But we have to think about costs, right? So some people, hospitals can charge \$2,500 or more. So if you have a \$5,000 deductible, that's going to cost you a lot of money. So then we have to start thinking about open MRIs, and fortunately, the Multiple Sclerosis Association of America, our sponsors tonight, have the MRI access fund. So you can go online and you can get a free MRI, if you financially qualify, of your brain or spinal cord to get diagnosed with MS or to monitor MS. So, which is huge. And so we take, we use that resource for our patients that can't afford the MRI or have high out-of-pocket costs. Medicare usually covers the MRI and hospital, so it's usually not an issue, but it is important and that's how we can tell if your disease is in-check or you have new activity.

Marie LeGrand:

Okay. Now, one person was asking if you are having new symptoms, how can you... or new sensations such as muscle pain, how can you tell the difference if it's MS or if it's aging or another health related issue?

Dr. Barry Singer:

So it's probably good just to touch base with your doc, and it can be confusing. You know, I can give you a good example is, like, you know, menopause. Women who are going through menopause and they have all these symptoms that can overlap with MS symptoms. And it's like, well, what's what? You know, and we're trying to figure it out. Or you can have a pinched nerve in your back with pain running down your leg. Is it MS or is it... you know. So this comes up a lot. And so it's really important just to touch base if you're having new symptoms. Sometimes we can do this, you know, with an appointment, sometime over the phone. But it is important if you have new symptoms coming on to kind of sort through it out. I know a lot of primary care docs they say, Oh, talk to your MS doctor, it must be MS related, but not everything MS related. But I think we pay a little... we're a little bit like primary care docs sometimes, the MS doc trying to sort through what's what. So trying to keep track of all that.

Marie LeGrand:

Of course. Are there any promising remyelination drugs in trial?

Dr. Barry Singer:

Yeah. So this is an exciting area. We like to... I got a lot of patients myself that I'd like to fix and a lot of people out there living with MS would really love to have their... recoat their nerves with new myelin. Some myelin is the coating of the nerves that's attacked in MS. So remyelination would be making new myelin. So recoding the nerves, which might help prevent progression over time. So those nerve cells, when they're lacking myelin, over time, they are not supported as well and they may die or get injured, and so new myelin might actually prevent progression as well. And so I've got about five clinical trials in my center on New Therapeutics. We haven't hit yet, but there are more research going on and contact with investigators and some things in development.

So we've got a lot of work to go. But you know, it's kind of like the Man on the Moon project. It's definitely doable. 5 to 8% of the cells in the central nervous system and the brain, spinal cord are myelin-making cells, immature cells. So we just need to get them into the plaques and make new myelin. And so there are some factors preventing that from happening. And and so there's a lot of interest in trying to come up with the right compound.

Marie LeGrand:

Okay. Now, talking about treatments. And we'll just take a couple more questions before we close. What are your feelings about stem cell treatments in treating MS?

Dr. Barry Singer:

Oh, okay. So we're getting all kinds of topics. Well, there's a few types of stem cells, so I think it's important to define what we're talking about. So there's hematopoietic stem cell transplant, autologous stem cell transplant, which is basically you take your bone marrow, you take cells out of the bone marrow, which include your stem cells. You.... then someone goes through chemotherapy, you basically knock out the immune system and then reboot the immune system. And so having this bone marrow transplant, autologous stem cell bone marrow transplant can work. And there's some good data out there that shows it can be very effective in preventing new disease activity. Unfortunately, not for everybody it's a cure. There's some breakthrough disease over time for some patients, including developing new MRI lesions, but very, very effective, at least for a lot of patients.

It's probably a good potential option for highly active patients that are young, probably going to get the most out of that. And there are clinical trials looking at it in the U.S., but it's not widely available like through an FDA approved protocol. So most of the transplants done in the U.S. are done through, you know, hospital protocols, clinical trial programs. So but there are sites outside the United States that do it, including in Canada, Mexico and other places. So it's definitely a potential option.

Then the other one is taking mesenchymal stem cells where these come out of your like fat or your blood. There's no chemotherapy. They're just re-injected, they're taken out of... the stem cells are taken out of the body and then readministered. And there's not a lot of data here. There's some data that came out of Israel of giving it in the spinal fluid that showed some benefit in a nice small clinical trial. But we have some work to do on that. Unfortunately, sometimes that causes, you know, some people charge \$10,000 a pop for one of those mesenchymal stem cells. And I tend to see that my patients are about the same after they get it. So bone marrow transplant could be effective, but it does have, again, some risk, including, you

know, unfortunately some centers have had some deaths. So it's a good option for a highly active patient, particularly those that are not responding to traditional treatments.

Marie LeGrand:

Okay. Now, how can someone who works with MS patients support individuals who are perhaps living with depression? One person specifically said they have a patient who is very depressed, isolate themselves, have pain in feet, legs, and hands, at times bowel and bladder incontinence. How do I support him?

Dr. Barry Singer:

Yeah, so that's really important, if you have loved ones or friends and you're on this, you know, how to help someone that's really struggling. And I think part of it is, you know, bring a... help get that person into a healthcare provider team, you know, help bring them to the appointment, sit down and talk. I know a lot of people with MS, they come in and they say, oh, everything's fine, everything's the same.

And then the spouse or the, you know, the daughter's in the room like, No, not everything's the same. And so we can start to deal with that. For example, I can give you an example. There's a medicine, a generic medication called Cymbalta or Duloxetine, works for nerve pain, and it's an antidepressant. So, sometimes you could start a medication like that and boom, all of a sudden, the pain's controlled, the mood's better. Once the mood gets better, then, oh, I feel like doing some things and starting exercising and interacting with family again and friends again, participate in activities. So, small things can change things dramatically. For example, if you're peeing five times at night because your bladder's overactive, treating that overactive bladder, all of a sudden you can drink water, you have less constipation, you're sleeping better at night, so you have more energy, you can exercise more. So, sometimes a small intervention can change this whole cycle of not doing well.

And, but if you're a family member out there, really important to kind of come to the appointment, step up, and, you know... a lot of my patients, when they're stable, you know, sometimes no one else comes with them. But I think it is important to have someone around to help support the person living with MS. I think the other, you know, huge challenge with MS is that frequently the symptoms of MS are silent. And so a lot of people with MS are dealing with fatigue - 90% have fatigue, 50% have cognitive problems, bladder problems, burning pins and needles, spasms, tightness in your legs. You can't see all that. So, you know, if you're walking around looking normal, people say, Oh, you're doing great from your MS. But they don't know what it's like to live with all the neurologic, the inner symptoms. And so I think it's important to be understanding and patient and know there's going to be good days and bad days.

Marie LeGrand:

Yeah, well, we have so many questions that came in and were already at the hour, so I'll...

Dr. Barry Singer:

Come on Marie, we'll go all night. I still have some office notes, it's 8 o'clock here, but we could go all night.

Marie LeGrand:

I don't know, you know, how many individuals will stay with us. But, you know, we certainly can.

Dr. Barry Singer:

Unfortunately, it looks like we have over 60... that's just the Q&A. But I think we've got over 100 questions here.

Marie LeGrand:

Yeah, we do. We do have quite a bit. So I'll just ask you this one last question and then we'll go ahead and close. So, people want to know, does Dr. Singer accept remote patients?

Dr. Barry Singer:

Ah! So a little bit depends on states. So unfortunately, there's some barriers to doing virtual appointments. So I like to... during the pandemic, I did some virtual appointments, you know, at the height of COVID as first patients. But I like to see patients the first time, and really, you know, get to do a thorough exam and look at scans together. But after that, I can do virtual ones. I do it for Missouri and Illinois right now. I had like for a while I was authorized in California at the beginning of the pandemic and some other states. But, I do, you know, we do see patients from all over the country and actually some international patients as well. So we do see patients in our center. But not all remote in different states. We're hoping, you know, the problem is the states have licenses, so you have to be licensed in the state to do virtual appointments. So we're hopeful, we need to advocate, the MSAA as well as other healthcare advocacy to kind of break down those barriers so we can do telemedicine reach out across the broader area so we can reach all those underserved patients, including all of the rural patients out there.

Marie LeGrand:

Wonderful. Well, there you go, folks. Dr. Singer accepts patients in certain parts of the country and some international. All right. Well, you know what? We are definitely at time and this has been so wonderful, so amazing. So thank you so much again, Dr. Singer, for sharing and providing such insight into MS, into MS relapses, progression, your expertise will most certainly give patients and care partners the tools that they need to make informed decisions together with their healthcare team. So thank you so much once again.

Dr. Barry Singer:

All right. Thanks, Marie. I appreciate you hosting this and inviting me on.

Marie LeGrand:

Of course. Now, this concludes the webcast. Tonight's webinar was recorded and will be made available on our website. Please visit MSAA's calendar of events for our upcoming webinars and events. On behalf of MSAA, we'd like to thank you once again, Dr. Singer, for your time and your expertise. And to our wonderful audience, we'd like to thank you for joining us this evening and filling our chat box with wonderful questions. Please take a few minutes to complete the brief survey, which will appear on your screen momentarily and know that we are thinking of the entire MS community and hope that you and your families continue to stay safe. Thank you and have a good night.

Dr. Barry Singer:

Good night everybody.