

Transcript Details

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Expanding Options for the Management of Multiple Sclerosis

Announcer:

Welcome to *Medical Breakthroughs from Penn Medicine*, Advancing Medicine Through Precision Diagnostics and Novel Therapy.

Dr. Caudle:

This is Medical Breakthroughs from Penn Medicine on ReachMD. I'm your host, Dr. Jennifer Caudle, and joining me on this episode is Dr. Amit Bar-Or, Chief of the Multiple Sclerosis Division and Director for the Center of Neuroinflammation and Neurotherapeutics at Penn Medicine. Dr. Bar-Or, welcome to the program.

Dr. Bar-Or:

Thanks for having me.

Dr. Caudle:

Absolutely. So, let's begin by reviewing the scope and the burden of multiple sclerosis, or MS. So, who is most at risk of developing MS, and what kind of effect does this have on their life?

Dr. Bar-Or:

So, unlike many other neurological conditions that people think of as affecting individuals later in life, MS tends to affect relatively young individuals, typically young adults, more women than men, about a two or three to one ratio of women to men, and is more prevalent in Caucasian populations than in African-American populations or Hispanics, although when it does occur in those populations, it tends sometimes to be more aggressive. People can have very different experiences with multiple sclerosis as they live with it over the lifetime. Some have relatively mild MS that doesn't cause much problem, but others may end up with very substantial neurological difficulties and become quite dependent in terms of their mobility and ability to function. Importantly, the new era of treatments with various treatments that limit new MS activity and injury have resulted in us referring now to the new MS. The prospect of living with MS with a diagnosis made now is very different than the prospect of living with MS with a diagnosis made even five, certainly ten years ago.

Dr. Caudle:

What are some of the typical symptoms of MS? And when should clinicians refer patients to a specialist?

Dr. Bar-Or:

MS affects the central nervous system pathways of the spinal cord and the brain, and so the type of symptom depends very much on the area or the location where a new MS lesion may develop, and so common features include loss of vision in one eye, for instance, often referred to as optic neuritis. The involvement of the spinal cord can cause issues with bladder, with mobility. Issues of incoordination, or sensory changes, may also be fairly common, for individuals who experience the MS activity. MS has been treated by clinicians, both in academic centers and in the community very well over the years, and many clinicians in the community are quite comfortable treating individuals with MS. With the development and availability now of more treatment options, some of which are more complicated and require greater assessment, monitoring and so on, more and more of the community clinicians may be referring MS patients to specialists either to transfer the care or even just for, a one-time, input in order to then refer back with some particular suggestions.

Dr. Caudle:

Excellent. Now, can you walk us through the current treatment landscape for MS and how it's been traditionally managed?

Dr. Bar-Or:

So, MS, had not been a treatable neurological condition until the early 1990s when it transitioned with the advent of the interferon beta

therapies to, a treatable condition but one that's very partially treatable with it, the decrease in about 30-40 percent of new MS activity with these injections. The injectables that are referred to sometimes as the platform therapy are ones that we've had experience with now for, for a couple of decades, and they all limit MS activity to a similar degree partially and may be sufficient for some people with MS, but for many, there is MS activity that overcomes these treatments.

We've had the development over the years of several oral therapies in pill form, which are much easier for people to take. They have some burden associated in terms of monitoring that's required just to keep people safe though they're generally well-tolerated, and then there are several infusible therapies that have emerged that are very effective at limiting new MS-relapsing activity, and they have actually come without much more, if any, added risk in the sense that the balance between the efficacy and the safety of the more recently approved treatments is actually quite, favorable

the approach to treating MS, has always involved two general philosophies with both patients and clinicians feeling differently. One would be the gradual escalation – "Let's try the treatment that is the mildest but may be sufficient for my MS" – versus treating more actively or proactively up front to try to really put the stop to the MS process. The latter may have some additional risks but the former, of course, means that you may try a treatment that doesn't work and you try another and so on, and you keep accumulating some injury that we don't yet know how to fix. More and more people are shifting to trying to treat MS more actively up front in order to really limit and minimize new activity, and limit new injury, and that has changed the prospect long term for people living with MS.

Dr. Caudle:

Excellent. Dr. Bar-Or, there have been several advances in terms of expanding our treatment options for MS how do the new immune reconstitution therapies, or IRTs, compare to the established ongoing therapies for multiple sclerosis, which involve persistent immunosuppression and ongoing immunomodulation?

Dr. Bar-Or:

So, that's an excellent question, and it really opens, a window into what we now may be able to achieve, at least in some people, and that is treating their MS initially in a way that does not require ongoing treatment thereafter for the most part, the treatments that we have require ongoing treatment in order to maintain MS activity at bay, but there are a couple of treatments already approved and more that we are studying, that may offer promise where an initial treatment regimen can be followed by a period that may be quite extended without any treatment if effective, this type of approach will allow people to not have any MS activity and with no treatment, many people will consider this a form of cure. The therapies that have had that capacity are ones in which we change the immune system, largely by depleting or getting rid of some of the cells, and then allowing them to come back, and what's been very interesting to try to understand is how the cells that come back, or reconstitute, differ from the cells that were there before. If the cells that were there before the treatment were participating and contributing to the MS activity, the ones that come back may in fact, have properties that keep other cells quiescent. They might even be regulatory cells, as we refer to them in the field. This prospect would effectively translate into not having to have people exposed long term to these immune therapies, while still benefiting from essential arrest of their MS.

Dr. Caudle:

Interesting. Now, you know, it's been long suspected that MS has a viral etiology, are we drawing closer to a confirmation of these suspicions?

Dr. Bar-Or:

Well, we've long suspected some infectious agent, and Epstein-Barr virus, or EBV has been at the top of the list and really is there to stay. There's little question that Epstein-Barr virus infection is somehow involved in the initial development of MS. We don't know exactly how it does so, and we also don't know whether it continues to be relevant for ongoing MS activity. We know, there are cells of the immune system that are more involved in the MS activity process – these include T-cells and B-cells of the immune system – and Epstein-Barr virus, or EBV, tends to affect B-cells of the immune system, and that may well be how the EBV contributes to new MS activity with time. One of the only ways to really know will be try to get rid of EBV, either by preventing the infection initially, and there's some people who are very interested in EBV vaccines to try to prevent multiple sclerosis, and the other is to try to get rid of those cells that are affected by the virus and then see whether MS is arrested. So, these initiatives are of interest and being pursued, and we hope to have a better sense of how EBV indeed contributes to MS over the next few years.

Dr. Caudle:

Excellent. Now, I think that we can all agree that we've certainly made progress through these kinds of research efforts, but there's really still plenty to learn. So, what are researchers currently investigating that could give us more answers about MS?

Dr. Bar-Or:

Well, the, I would divide that into several categories. One has to do with the relapsing and remitting biology of MS, and, and most of the treatments to date that are approved are approved on the basis of their ability to decrease relapses, and we do have some treatments

that are very good at doing that and can even [?] some these relapses completely in a fair portion of patients. We haven't achieved all the answers for relapsing-remitting MS yet, and one of the important things that we're working on is this concept of precision treatment, meaning identifying how people differ from one another with their MS this will help us select the most appropriate treatment for their relapsing-remitting MS better than we can do now and also be able to make better decisions when it comes to considering a switch from one treatment of relapsing-remitting MS to another. One of the interesting still unmet needs is understanding the reconstitution immunology treatments. What is it about the cells that are allowed to come back that, in fact, results in a prolonged, durable treatment effect essentially a cure for many patients? That would be terrific to understand, and then choose treatments and develop those further. So, that's for relapsing-remitting MS.

Another very important unmet need relates to better understanding the biologies that contribute to progressive MS, and though we now have some treatments already approved for progressive MS, they work relatively modestly at limiting the rate of progression. They certainly have not been able to halt progression entirely. So, understanding mechanisms and developing and validating treatments for progressive MS – another important unmet need. And finally, we would love to learn how to fix things that are already injured because all the treatments that we were discussing are aimed at limiting or stopping new injury but don't address fixing injury that is already there, and there are a lot of initiatives, all the way from preclinical to early phase clinical trials, of approaches and at enhancing repair, be it repair of myelinating cells or repair of the neurons and axons that are also injured in the context of MS.

Dr. Caudle:

Wonderful. Now, finally before we wrap up, Dr. Bar-Or, how and when should physicians refer their patients to a Penn specialist?

Dr. Bar-Or:

Well, an easy way to get to us either through the physician-to-physician referral or if patients wish to reach out this is best done through the information available at the MS Society, the National MS Society, or NMSS, website, which identifies the Penn MS program as one of the US Centers of Excellence for comprehensive MS care.

Dr. Caudle:

Well, I'd like to thank my guest, Dr. Amit Bar-Or, for sharing his insights to these advances in treatments for our patients with multiple sclerosis. It was a pleasure speaking with you, Dr. Bar-Or.

Dr. Bar-Or:

The pleasure was mine. Thank you.

Dr. Caudle:

Absolutely. I'm Dr. Jennifer Caudle with ReachMD. Thank you for listening.

Announcer:

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