## Referring an MS Patient to the Multiple Sclerosis and Related Disorders Center at Penn Medicine - An Interview with Christopher Perrone, MD

**Melanie Cole:** Welcome to the podcast series from the specialists at Penn Medicine. I'm Melanie Cole and I invite you to listen in as we discuss how and when to refer an MS patient to Penn Medicine. Joining me is Dr. Christopher Perrone. He's an Assistant Professor of Clinical Neurology at Penn Medicine.

Dr. Perrone, it's a pleasure to have you join us today. We know that primary care providers should refer to a neurologist when they suspect MS in a patient. But how do they know which neurologist to refer to? Please start by defining a multiple sclerosis expert for us.

**Dr Perrone:** Many neurologists have subspecialty training. So it's beneficial to inquire about further expertise in multiple sclerosis if that is the condition of concern. Some of the symptoms in multiple sclerosis can actually be seen across a number of conditions. For instance, numbness and tingling can come from multiple sclerosis, but also peripheral neuropathy. In those settings, a general neurologist will actually try to distinguish between these conditions. But if there's additional evidence concerning for multiple sclerosis, with MRI for instance or other studies, it may actually be better to refer that patient to an MS expert.

Typically, they've spent a lot of time with multiple sclerosis patients, but their related inflammatory diseases, that they will also likely have exposure to. And they've done this specialty training with at least one year of clinical fellowship, sometimes longer.

And so while some general neurologists are comfortable treating patients with multiple sclerosis, it's pretty common that there are questions that arise during a patient's course that could ultimately prompt for referral. And that referral should go to a neurologist that has specialty training in multiple sclerosis. Because when it comes to diagnosis and treatment, the earlier the condition is identified and managed, there's likely a greater benefit to the patient.

**Melanie:** Thank you for that answer. Dr. Perrone, what makes MS so difficult to diagnosis? As you're telling us about how and when to refer an MS patient to Penn Medicine, what combination of symptoms in a previously unaffected patient would suggest the need for referral? And why is it so difficult to diagnose?

**Dr Perrone:** Part of the reason why MS is such a difficult condition to diagnosis is because the symptoms can be seen across a number of neurologic conditions. Oftentimes there's actually a constellation of symptoms that constitutes an initial MS-related attack.

And so some of those common examples would be optic neuritis, where a patient may have a dark spot in the vision of one of their eyes or pain when looking around with one eye. And they might also complain of double vision that improves when one eye is covered or they might have one-sided numbness or weakness. They could also have leg weakness bilaterally, so in both legs and also bladder dysfunction. These are usually the unilateral symptoms, whether it be numbness, weakness, or the bilateral symptoms of leg weakness and also having some bladder dysfunction typically indicate transverse myelitis or an inflammatory lesion of the spinal cord. So it's these kinds of symptoms, sometimes one, sometimes many, that constitute typical signs of an initial MS-related attack.

And it's also important to consider the cadence of symptoms, how quickly they came on and how they ultimately evolve, because the symptoms in multiple sclerosis typically have a relatively acute onset over days. They then reach hit peak intensity or spread out, and then subsequently improve over weeks to months. And so these are the most common types of symptoms for multiple sclerosis and how they evolve. And this is specifically for the most common type of multiple sclerosis known as relapsing-remitting multiple sclerosis. About 85% of patients will have these kinds of symptoms as the presenting signs.

**Melanie:** Thank you Dr Perrone for that answer. We know there are other forms of multiple sclerosis that providers should be aware of—do these forms have the same symptoms and cadence?

**Dr Perrone:** There are forms of MS that feature more of a slow decline in functional capacity over time. And this is what we call progressive MS as opposed to relapsing-remitting. The most common example of someone with a slow decline in a certain functional capacity is with regard to ambulatory dysfunction where a patient might notice that they, you know, started tripping initially, and then they start requiring potentially use of a cane and then maybe ultimately a walker, but this is over years of time. In these kinds of instances, imaging is extremely helpful of the brain and the spinal cord, because there's actually many different causes of difficulties walking. But if there's evidence of inflammation in the central nervous system with MRI and this kind of a story, the slow functional decline, that's concerning for progressive MS and would indicate grounds for a referral.

**Melanie:** Well, then what's the tipping point for a referral in a patient with relapsing-remitting MS. How can a primary care provider tell the difference between poor compliance, for example, or a drug that's waning in efficacy? Tell us about that.

**Dr Perrone:** There are certain circumstances in which a patient, who has relapsing-remitting MS, a situation they might have or a clinical scenario that may prompt a referral-- there's actually quite a few of these we are addressing every day at our comprehensive MS center. One of the most common reasons is actually pregnancy planning. So management of these disease-modifying therapies around pregnancy as relapsing-remitting MS often affects women of reproductive age. And we have a strong program for women's health and MS at our center as well.

Another indication for referral would be lack of response to conventional therapies. So there's a number of therapies for relapsing-remitting MS. But the patient might not be responding appropriately. And that could either indicate

that maybe there's a different disease process going on. Maybe it's not multiple sclerosis. Maybe it's something in that spectrum like NMO, which is neuromyelitis Optica or a MOG-associated disease. There's also neurosarcoidosis and other inflammatory diseases, which actually won't respond well to MS medicines. So if a patient is not responding to conventional therapies, it would be an appropriate referral, because they might not actually have relapsing-remitting MS. They might have a different neuroinflammatory disease.

And for the patients who do have relapsing-remitting MS but require more aggressive therapy or therapies that may not be available where the patient is currently being seen or that require closer monitoring, those are other patients that we typically will be seeing. And those include patients who are on certain oral medications and maybe infusions as well. And some of the newer therapies are injectable that are similar to some of the infusions. So that might also prompt a referral because it's a very new medicine and also has certain monitoring that needs to take place.

**Melanie:** Wonderful answer, Dr Perrone. How, exactly, do you manage symptoms in patients with MS, particularly when they start to see some of the troubling signs of recurrence?

**Dr Perrone:** The other thing that's important is that our MS center does a lot with symptomatic management. So while a patient may be on a disease-modifying therapy and maybe doing fairly well, maybe they're starting to notice some progressive aspects of the disease or having difficulty with symptom control from prior attacks. And so we actually do a lot with regard to symptom management, because there's really two arms of MS care. There is disease modification, which is the medications that they're taking to prevent new things from happening with regard to their MS. But then there's also treatment, what we call symptomatic management, which is treatment for areas of prior injury to the central nervous system that have left the patient with symptoms.

**Melanie:** Dr Perrone, we've been talking about physician referrals—but what would you like patients to know about the MS Center at Penn Medicine?

**Dr Perrone:** We also have a number of supportive services at our center. We have social work, MS pharmacy, that basically will counsel the patient about each of the drugs. And there's also support groups that we offer, so we can help an MS patient really have a sense of community and support. We also work with the patients in those who may have been on a therapy for years, maybe even decades, and there's a question of therapy discontinuation. We're also happy to talk with a patient about that consideration.

And then lastly, I think one of the other things that's important for patients to know is that we are a very active research center. So we have many studies going on at any given time. And our goal is really to offer research to anyone who has an interest in exploring that. Our goal is to make sure that we are at the forefront of MS care and actually making progress toward the steps of tomorrow and in terms of caring for these patients. So in terms of the instances that would prompt a referral, those are the kinds of patients that are typically coming to our center taking advantage of some of the services that we have to offer.

**Melanie:** Dr Perrone, getting back for a moment to drug therapy—what do you do when a drug simply stops working?

**Dr Perrone:** Now, just touching back on that question about breakthrough disease on a therapy that's waning in efficacy versus difficulties with adherence in terms of a therapy. So regarding that question, there are some mechanisms outside of a patient's report that can demonstrate compliance. And those kinds of things, for instance, are risk mitigation programs for some of the medications, improved adherence through regular contact with the patient through phone calls. So some of the drugs have very close monitoring mechanisms through drug mitigation programs.

Some of the medications also result in lab abnormalities, which can offer insight into adherence, such as low lymphocyte counts on fingolimod,

cladribine, alemtuzumab or ocrelizumab, some of the stronger or higher efficacy agents. And then also, infusion centers keep records of infusion dates. And so that's another way to try and determine whether there is non-compliance or if they are compliant, then that would suggest that there's waning drug efficacy in the setting of breakthrough activity.

And then lastly, our MS pharmacy team does an amazing job with outreach to ensure compliance, so that medications are switched in the appropriate circumstances.

**Melanie:** Thank you so much, Dr. Perrone, for joining us today. And that concludes this episode from the specialists at Penn Medicine. To refer your patient to a specialist at Penn Medicine, please visit our website at PennMedicine.org/refer or you can call (877) 937-PENN for more information and to get connected with one of our providers. Please remember to subscribe, rate and review this podcast and all the other Penn Medicine podcasts. I'm Melanie Cole.