Melanie: Welcome to the podcast series from the specialists at Penn Medicine. I'm Melanie Cole, and I invite you to listen as we discuss MS and women's health at Penn Medicine. Joining me today is Dr. Rachel Brandstadter. She's an assistant professor of Clinical Neurology at Penn Medicine.

Dr. Brandstadter, I'm so glad to have you join us today. This is a really good topic. Tell us a little bit about what you're seeing in the trends. Let's just start with sort of a summary about the average age of onset, diagnosis. What are you seeing with MS and women in particular?

Dr. Rachel Brandstadter: Thank you for having me. So multiple sclerosis is more common in women than men. There is a female to male ratio of about 3:1 in most studies.

Melanie: Well, thank you. So what makes a woman particularly susceptible to the effects of MS? Are they more at risk for MS than men?

Dr. Rachel Brandstadter: So the heritability of multiple sclerosis is rather complex. There are genome-wide association studies that have implicated over 200 independent genetic loci for multiple sclerosis. One single nucleotide polymorphism on the X chromosome has been associated with multiple sclerosis. There have not been any such susceptibility alleles found on the Y chromosome. We don't fully understand the scope of that gene's function, but it is interesting that it's seen on the X-chromosome rather than the Y chromosome and may explain a little bit about why multiple sclerosis is more common in women.

There's also very likely an interaction between the genome and sex-specific biological and environmental factors that may underlie the possible increase in MS incidence seen in women. Sex hormones very clearly play a role in the development of MS as we see that puberty represents a risk factor for MS as does earlier age of menarche, though these biological mechanisms have to be more fully fleshed out.

There's also a strong link between pregnancy and MS. As one study found that having children reduced the risk of MS in women, but not in men, by about 46% in the following five years. It's possible that low levels of estrogen that are associated with menstruation have a more stimulating effect on the immune system while higher estrogen levels like those seen during pregnancy might exhibit a more immunosuppressive effect.

And as I mentioned, there are several environmental factors that have been identified as increasing the risk for multiple sclerosis, including smoking, Epstein-Barr virus, seropositivity, low serum vitamin D levels and low sunlight exposure. So these factors may also interact with biological sex to increase the risk for multiple sclerosis in women.

Melanie: Wow. That's so interesting. So do MS symptoms onset occur in predictable patterns in women, doctor? Are there times of life when they're more likely to experience these symptoms or that the symptoms are exacerbated?

Dr. Rachel Brandstadter: Yes. MS is more likely to impact women between the ages of 20 and 40 years old this highlights the importance actually of discussing family planning with our patients, including pregnancy and breastfeeding. There have been several studies also that have attempted to determine if menopause affects MS disease course. Some of these studies have noted a worsened disability accrual around menopause, but others have not borne that out.

Melanie: So then speak a little bit about the commonality in both sexes. You've already spoken about how they're worse in women. Are there any common symptoms, things that you've noticed that you'd like other providers to know where you could link the two sexes?

Dr. Rachel Brandstadter: So multiple sclerosis presents with a very common set of symptoms that we see equally in men and women. Those are impairments of visual functioning, symptoms related to spinal cord dysfunction like weakness, numbness or tingling, spasticity or muscle tightness, gait dysfunction. We also see other symptoms such as brainstem symptoms, such as double vision or vertigo and cognitive dysfunction in all of our patients with MS.

But again, many of the symptoms of MS are common to men and women, but they might be experienced a bit differently. For example, neurologic bladder dysfunction from MS may be heightened by bladder dysfunction related to pelvic floor weakness from prior childbirth in women.

Melanie: So now, let's talk about treatments that are specifically available for women with MS.

Dr. Rachel Brandstadter: We have so many medications now to help treat multiple sclerosis. Most of these are common to men and women, but there are a few interesting research interests for women specifically. So research conducted in animal models of multiple sclerosis suggested a protective effect of high doses of estrogen.

Two randomized phase II clinical trials evaluated the impact of exogenous hormones on MS disease course. In these studies, an oral estrogen called ethinyl estradiol was added to standard injectable disease-modifying MS therapies and patients were treated both with the traditional MS therapy and estrogen. And those that got both treatments demonstrated fewer inflammatory lesions on brain MRI and a lower rate of clinical relapses than those who were treated with the MS therapy alone.

There was encouragingly a suggestion of a positive impact on cognitive disability in these studies as well. This is being further investigated with dedicated clinical trials. Here at Penn Medicine, we are part of these phase III clinical trial efforts to better study the effect of exogenous hormones to help our women with MS.

Melanie: So tell us a little bit about what makes your program stand apart. What's unique about the program at Penn Medicine? Tell us a little bit about the multidisciplinary team and what that means for these patients.

Dr. Rachel Brandstadter: Here at Penn Medicine, we are a dynamic multidisciplinary team that are here first and foremost to help patients with multiple sclerosis and related disorders. We follow this comprehensive care model in order to address all of our patient's needs. So we have attending neurologists. We have three expert nurse practitioners who help us take care of patients. We have nurses who coordinate care and care for our patients. We have a social worker who is dedicated, knowledgeable, and empathic, and there to help our patients with the many ways that MS affects their personal and professional lives. And we have clinical pharmacists who are experts on all of our MS disease-modifying and symptomatic medications that are there just to educate, counsel and support our patients and help them navigate their drug treatment for MS.

Melanie: Do you have any final thoughts you'd like to leave other providers with when you feel it's important they refer to the specialists at Penn Medicine and what you'd like them to know about women's health and MS?

Dr. Rachel Brandstadter: The field of multiples sclerosis care has become ever more complex. And there are so many treatments, both disease-modifying and symptomatic, that we offer our patients here at Penn Medicine. So a consultation with us is a great idea when somebody is newly diagnosed to confirm diagnosis, when someone's about to initiate a treatment or even when somebody is facing some symptoms that might be challenging. We are here to provide that additional layer of support and use all of the resources that I mentioned earlier to help improve the lives of our patients with MS.

There are many opportunities for a referral to our team at Penn Medicine for a patient where we need to confirm the diagnosis of multiple sclerosis, initiate a treatment, or for patients who are having difficulty with symptom management. Importantly, a good time to refer your patient for a consultation with us at Penn Medicine would be to discuss complex issues around family planning and pregnancy, and to help women with MS deal with symptoms during the menopausal period. The specialists at Penn Medicine are always here for your patients with multiple sclerosis.

Melanie: Thank you so much, doctor, for joining us today and telling us about the program 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.

That concludes this episode from the specialists at Penn Medicine. Please remember to subscribe, rate and review this podcast and all the other Penn Medicine podcasts. I'm Melanie Cole.