Melanie Cole (Host): While pregnancy is safe to undertake, there are specific risks for women with MS trying to conceive. Welcome to the podcast series from the specialists at Penn Medicine. I'm Melanie Cole, and joining me today is Dr. Rachel Brandstadter. She's an Assistant Professor of Clinical Neurology at Penn Medicine, and she's part of the Penn Multiple Sclerosis Center.

We're discussing MS and pregnancy today. And Dr. Brandstadter, thank you so much. You've been on with us before, so welcome back. When we last spoke, you explained that MS is more likely to impact women between the ages of 20 and 40 years old, and you noted the importance of discussing family planning with patients. You mentioned that while pregnancy is safe to undertake, there are specific risks for women with MS when they're trying to conceive. Can you please speak about those concerns and how they can be addressed for women with MS that are planning a family?

Dr. Rachel Brandstadter: Certainly, and thank you for having me back. Firstly, for patients interested in pursuing pregnancy, it's important to note that multiple sclerosis itself does not seem to increase the risk for infertility, adverse pregnancy outcomes or adverse neonatal outcomes. For many years, the effect of pregnancy on MS disease was somewhat uncertain. However, this did change with the landmark pregnancy in MS or PRIMS study that was published in the *New England Journal of Medicine* in the late 1990s, which examined 256 pregnancies and demonstrated a decreased risk for MS relapse during pregnancy, particularly in the third trimester. This finding has since been corroborated in more modern investigations and has been encouraging for patients and providers alike.

The PRIMS study also heralded work that revealed an increased risk for relapse in the first three to four months postpartum, particularly for women with active disease prior to pregnancy, which includes clinical symptoms or MRI activity. This highlights the importance of achieving good control of MS in advance of pregnancy and the need to discuss family planning with patients as early as possible, even around the time of diagnosis.

Host: So, if a patient with MS is beginning to think about starting her family, what would be your recommended next steps? And tell us about the services that Penn Medicine offers along the way.

Dr. Rachel Brandstadter: So, if a patient with MS is considering starting a family, I would recommend that they discuss this as early as possible with their MS neurologist to ensure that there has not been any recent MS disease activity, again clinical or MRI. And for those on disease-modifying treatments for their

multiple sclerosis, it's important to discuss the safety of either continuing these medications through conception or the appropriate interval for discontinuation or washout from the drug in advance of conception.

The Penn MS Center has providers and pharmacists who are experts in preconception and intrapartum counseling, and can help provide an individualized approach for a patient and their family throughout this process.

Host: So doctor, relapse is always a concern for any individual with MS. Are there therapies that can help mitigate that risk of relapse before or during conception and pregnancy?

Dr. Rachel Brandstadter: As I mentioned earlier, good control of MS disease in advance of pregnancy is very important for mitigating the risk for relapse, both during conception and during pregnancy. There are MS disease-modifying therapies, which can provide a more durable or long-lasting protection against relapse without fetal exposure to the medication.

One example is ocrelizumab, which is a B-cell targeting immunotherapy delivered via an intravenous infusion every six months. It is one of several highly effective disease-modifying therapies in our treatment toolkit for preventing relapses and new MRI lesions. This medication could be administered and patients can wait an appropriate interval before attempting conception.

My practice is around two to three months after infusions and have some security that they are both protecting themselves from MS disease activity, but not exposing their baby to the medication. There are several other strategies for lowering the risk for relapse during pregnancy, including continuation of some MS disease-modifying therapies, even during conception and pregnancy.

Host: And what about the postpartum period and if women are breastfeeding, where do those medications fit into this picture?

Dr. Rachel Brandstadter: So in the postpartum period, we aim to prevent inflammatory activity and that's going to involve individualized decisions regarding the patient's breastfeeding plan, when to resume disease-modifying therapy and how to select the appropriate treatment. I often recommend a surveillance MRI of the brain at around four to six weeks postpartum to monitor for subclinical disease activity.

If a woman elects not to breastfeed, we may aim to resume treatment as early as two to four weeks postpartum. There are data, however, that suggests that exclusive breastfeeding extends the protective period against relapse. And that if a patient does elect to breastfeed, there are options to either remain off of disease-modifying therapy while nursing, particularly if that postpartum MRI is stable without new lesions. Or for those patients with high risk for postpartum relapse, there is an option to breastfeed while on certain disease-modifying therapies.

More data is needed in our field to confirm the safety of this strategy. It's also important for MS providers to comprehensively evaluate the patient's functioning postpartum, evaluating her mood, physical function, sphincter issues, and to utilize a multidisciplinary approach to care as needed.

Host: Well, that leads me well into my next question, and how do you advise patients and their providers, whether it's their gynecologist and obstetrician or their MS neurologist, about managing physical health side effects and mental health? Because it can be pretty scary to be pregnant with MS.

Dr. Rachel Brandstadter: Well, I certainly encourage close care with both the MS neurologist and the obstetricians as part of the team and to manage all of these symptoms as they come up and to remain attentive to them also in the postpartum period. There is not any specific strategy, for instance, treating postpartum depression in patients with MS compared with patients who don't have MS. But just to remember that a woman with MS is still a woman going through all of the other challenges of pregnancy and to stay as attentive to those as possible.

And for instance, one specific example would be if a patient already has some impacts of MS on the bladder to think about the way urinary symptoms might be exacerbated in the postpartum period after delivery and be more likely to consider strategies such as pelvic floor rehabilitation for such a patient.

Melanie Cole: That's very good advice. What about long-term impacts of pregnancy on the MS disease course? What do we know about that now?

Dr. Rachel Brandstadter: So despite the potential for increased relapse risk postpartum, the majority of individuals do not experience relapses in the postpartum period. And pregnancy does not appear to alter long-term relapse rate or the risk for disease progression. However, the impact of pregnancy on long-term MS outcomes does remain less clear, and there are some mixed data. So, we have more to learn about this for sure.

Host: Dr. Brandstadter, as we get ready to wrap up, is there anything else you'd like referring providers to know of before they refer a patient to the MS and Women's Health Center and the specialists at Penn Medicine? What would you like the lasting message to be about MS and pregnancy?

Dr. Rachel Brandstadter: I encourage all providers to start preconception counseling for MS patients early on, even at diagnosis. Providers should feel empowered to refer to our Women's Health Division within our MS Center for support in this counseling at any stage of family planning, but particularly early on when the decision regarding disease-modifying therapies are being made.

I also would empower those providers to give an optimistic message to their patients with MS, that they can pursue family planning safely, and that there are a lot of strategies in place to help them have happy and healthy pregnancies.

Host: Thank you so much, Dr. Brandstadter, for joining us today. To refer your patient to Dr. Brandstadter at Penn Medicine, please call our 24/7 provider-only line at 877-937-7366 or you can submit your referral via our secure online referral form by visiting our website at pennmedicine.org/referyourpatient.

That concludes this episode from the specialists at Penn Medicine. For updates on the latest medical advancements, breakthroughs and research, please follow us on your social channels. I'm Melanie Cole.