

TALKING WITH YOUR PATIENTS ABOUT
**REPRODUCTIVE ISSUES
AND MS**

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**National
Multiple Sclerosis
Society**

The National MS Society's Professional Resource Center provides:

- Easy access to comprehensive information about MS management in a variety of formats;
- Dynamic, engaging tools and resources for clinicians and their patients;
- Clinical information to support high quality care; and
- Literature search services to support high quality clinical care.

FOR FURTHER INFORMATION:

VISIT OUR WEBSITE:

nationalMSSociety.org/PRC

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Introduction

Use this resource to help facilitate conversations with your patients about MS-related reproductive issues. Most people diagnosed with MS are young, pre-menopausal women, and questions about fertility, pregnancy, childbirth, and contraception—and their interaction with disease activity and disease-modifying therapy—may be very important to them. Men with MS who are considering becoming parents may also have concerns about this issue.

This may be a topic patients are reluctant to talk about with their doctors and other healthcare professionals, particularly if they anticipate negative or distressing answers. Patients and their partners may not know the right questions to ask or when to ask them. The physician and nurse have an important role to play in initiating the discussion and providing timely information and referrals.

How and when should I address the topic of reproductive issues and MS?

- Reproductive issues should be addressed early after diagnosis.
- Newly-diagnosed adults who may be making important family-planning decisions in the near future need accurate information about how MS might affect fertility, pregnancy, childbirth and contraception.
- Since family planning decisions affect the use of disease-modifying agents (DMAs), the best strategy is to raise the issue as soon as you begin discussing treatment. If the patient has no imminent plans to start a family, the topic may be deferred until it's more relevant. However, remind your female patients to consult with you about all their medications before trying to become pregnant. Male patients who are taking teriflunomide (an FDA pregnancy category X medication) or mitoxantrone (Category D) or other immunosuppressant medication should also be reminded to consult with you before trying to conceive a child.
- The best venue for these discussions is during an office visit, ideally with the woman and her reproductive partner both present.

What is the most important information for me to give my patients about reproductive issues and MS?

- In general, couples should be reassured that MS is likely to have little effect on their reproductive capacity, and that pregnancy itself should not negatively affect the woman's long-term MS prognosis.
- MS does not increase the risk of miscarriage, congenital malformations, or infertility.
- Two studies have suggested that babies born to women with MS may tend to have slightly lower birth weights, but more research is needed to confirm these findings.
- For a woman with MS in otherwise good health, pregnancy, labor and delivery can be managed routinely, posing no greater risk than for a woman of similar health status

without MS.

- In women with relapsing-remitting MS, the relapse rate falls by approximately 66% during pregnancy. There is a sharp rise in relapse rate in the first 3–6 months post-partum, followed by a return to pre-pregnancy levels.
- Nursing does not appear to be associated with an increased relapse rate. However, any decision regarding breastfeeding must take into account the medications a woman needs to resume taking for disease or symptom management. A recent pilot study suggested that women who breastfeed exclusively (without supplemental feedings) for at least the first two months are less likely to have a post-partum relapse than those who do not breastfeed or do not breastfeed exclusively. A larger study is needed to confirm these findings.
- An important consideration for patients to take into account when making family planning decisions is the uncertainty of MS and the possibility of future disability, with its accompanying impact on finances, family roles, and the physical ability to care for a child.
- The couple should be made aware of the high incidence of depression in people with MS, which may increase the likelihood of post-partum depression. Depression during or following a pregnancy can affect a woman's ability to care for herself and her baby. Any woman who experiences depressive symptoms during or following her pregnancy should talk with you promptly so that you can make the appropriate referral for treatment.

Are there any special considerations regarding contraception for women with MS?

- Because MS does not affect fertility, women with MS and their partners need to make the same decisions about contraceptive use as anyone else.
- Studies to date do not confirm either an increased or decreased risk of MS associated with oral contraceptive use. However, some of the medications that are used to treat MS, including steroids, anticonvulsants, or antibiotics, can interfere with the effectiveness of oral contraceptives. Women should be encouraged to consider a dosage adjustment and/or the use of additional protection while taking any of these medications.
- Some women with impaired use of their upper extremities or decreased sensation may have mechanical difficulty using barrier methods of contraception, such as a diaphragm.

Are there any special considerations regarding assisted reproductive technology (ART) treatments?

- Women with MS experience infertility issues at the same rate as the general population.
- No large-scale studies of ART in women with MS have been conducted. However, one study involving 16 women found a sevenfold increase in relapses and a ninefold increase in Gd-enhancing lesion activity on MRI. The increased relapse rate mainly occurred in women receiving gonadotrophin-releasing hormone (GnRH) agonists, but an increase has also been reported in women receiving GnRH antagonists.

Do disease-modifying agents or symptomatic therapies have an impact on fertility, pregnancy, delivery and/or the post-partum period?

In June 2015, the FDA discontinued the use of pregnancy categories and replaced them with new pregnancy guidelines. The labeling of new medications will reflect the changes; medications approved on or after June 30, 2001 will be phased in gradually.

Disease-Modifying Therapy	FDA Pregnancy Category
alemtuzumab	C
 fingolimod	C
 glatiramer acetate	B
 interferon beta -1a	C
 interferon beta-1b	C
 mitoxantrone	D
 natalizumab	C
 ocrelizumab	No category: No human data available; in monkeys, administration during organogenesis and continuing through the neonatal period resulted in perinatal deaths, renal toxicity, lymphoid follicle formation in the bone marrow and severe decreases in circulating B-lymphocytes in neonates
 teriflunomide	X

Most of the disease-modifying therapies are Category C, which means that no adequate data in humans are available, but animal studies have shown adverse effects on the fetus. The benefits of the medication may outweigh the potential risks. Category D indicates that data from human studies or marketing experience have demonstrated evidence of fetal risk but the benefits for the mother may outweigh the potential risks. Category X indicates that animal and human studies have demonstrated fetal abnormalities or studies in humans or marketing experience have provided evidence of fetal risk. The risk to the fetus outweighs any possible benefit to the mother.

- The current recommendation is for women with MS who plan to become pregnant to stop any disease-modifying therapy before trying to conceive, although some

neurologists will permit treatment with glatiramer acetate (category B) until pregnancy is confirmed. The recommended wash-out period (time between stopping the medication and trying to conceive) varies depending on how the medication is metabolized in the body and how long it takes before half of its active elements are broken down by the body.

- A woman must wait 8-24 months after the last dose of teriflunomide (category X) before trying to conceive, although elimination of the medication from the body can be accelerated with a regimen of activated charcoal or cholestyramine.
- Women who are under consideration for treatment with the immunosuppressant agent mitoxantrone (a category D agent), should be advised that the drug may cause amenorrhea, which is permanent in a small percentage of patients, and may cause fetal harm. The FDA labeling of mitoxantrone recommends that women of child-bearing age be given a pregnancy test prior to each administration of the drug.
- In women with active disease, it may be appropriate to defer attempting pregnancy until disease activity is under satisfactory control.
- Studies indicate that those women who have had more relapses prior to pregnancy, are at greater risk for developing post-partum relapses. Therefore, the urgency of re-starting the DMA after delivery may depend on the patient's pre-pregnancy relapse rate, and her desire to breast-feed.
- It is not known if any of the DMAs are excreted in breast milk; therefore, women who are nursing should discuss their medication options with their obstetrician and/or neurologist and pediatrician.
- Many symptoms of MS may become more prominent during pregnancy, including constipation, urinary urgency and frequency, and fatigue, as well as gait difficulties as the pregnancy progresses and the center of gravity shifts. These symptoms can be managed conservatively with rehabilitative strategies, and medication—if needed, following consultation with the obstetrician and/or neurologist and pediatrician.
- Some symptomatic therapies for MS, such as anti-spasticity agents, anti-fatigue drugs, and medications for bladder control are category C drugs, and their use during pregnancy should be discussed with the obstetrician and/or pediatrician.

Are there any special considerations for labor and delivery?

- Labor and delivery are generally not affected by a woman's MS; all forms of anesthesia are considered safe for women with MS.
- Because a woman with prominent spinal cord involvement and weakness or loss of sensation below the waist may not be able to feel contractions, or be able to push effectively, she may require additional assistance during labor and delivery.
- Women with MS do not need to be given steroids during labor and delivery, unless they have been on chronic steroid treatment.

What is known about the impact of the menstrual cycle and menopause on MS?

- A small number of self-report studies suggest that some women with MS experience an increase in neurologic symptoms in the few days before the onset of menses.
- There are limited data on the effect of menopause on MS. In two small studies, approximately one-half of the women reported a worsening of their MS symptoms after menopause; however, women in a larger study did not. Women's reports of the impact of hormone replacement therapy on MS symptoms differ between studies as well.

Are there any issues regarding reproductive health for men with MS?

- Male fertility does not appear to be impaired in MS, although some men may have problems with impotence or ejaculatory dysfunction that interfere with conception. These problems are often amenable to a variety of therapeutic strategies, including medication for erectile dysfunction, artificial insemination, and electronic ejaculatory stimulation.
- To date, there are limited published data concerning the impact of the disease-modifying therapies on conception or fetal development when it is the father who is taking the medications.
- Men must wait 8-24 months after the last dose of teriflunomide (category X) before trying to conceive a child, although elimination of the medication from the body can be accelerated with a regimen of activated charcoal or cholestyramine.
- For men who take any of the immunosuppressant medications, including mitoxantrone (Novantrone), it is advisable for them to freeze sperm for future use in the event that the medication causes partial or complete sterility.

What should I tell patients about the risk of their children developing MS?

- Epidemiologic surveys have determined that an individual's risk of developing MS increases several-fold if a close family member has MS. While the average person in the United States has about 1 chance in 750 of developing MS, the risk for a person who has a parent with MS increases to 1 in 40 (with the risk being higher for girls than boys). Thus, the risk increases significantly for a person whose parent has MS, but still remains relatively low.
- Risk estimates can vary greatly depending upon the structure of a person's family. In families in which MS occurs in many relatives, the risks for any given individual are significantly higher than they are for an individual who has no family members with MS.
- Risk for MS is also affected in part by a person's ethnic background and other factors that haven't yet been clearly identified. MS is more common in Caucasians of northern European background than in other groups, however a recent study suggested that African-American women have a higher than previously reported risk of developing MS. In addition, several studies have suggested that African-Americans and Hispanics may

have a more active, rapidly progressive disease course.

- While genes are important determinants of a person's risk for MS, they are not the only factor. The identical twin of a person with MS has a 1 in 4 chance of developing the disease (with the concordance being higher in female twins than in male twins). The findings that identical twins of people with MS who share all the same genes do not always get MS, and that more than 80% of people with MS do not have a first-degree relative with MS, demonstrate conclusively that MS is not directly inherited and that factors other than genetics must be involved.
- Couples who express concerns about the genetic risk for their children should be told that the risk is relatively low. However, at the present time, there is no genetic testing available to provide them with a definitive answer.

How can I help my patients deal with some of the emotional issues related to this topic?

- Young men and women with MS face the additional stress of a chronic, unpredictable disease when making family planning decisions. Encourage your patient and his or her partner to talk frankly with each other about:
 - Their personal priorities and needs
 - The strength and flexibility of their relationship
 - The availability of a support system
 - Their financial resources
 - Their parenting and child-rearing goals and ideals
- Encourage your patients to think through all possible outcomes, both positive and negative—e.g., if the parent's disability were to progress significantly, or if the parenting and wage-earning roles and activities were to require some adjustments.
- Encourage your patients to think beyond the initial few weeks or months of a child's life. Remind them that too often, prospective parents focus on bringing the baby home from the hospital, forgetting that babies grow rather quickly into very active children and busy teens.
- Encourage couples to think through possible strategies and resources for dealing with future disease-related changes.
- If you feel that your patient and his/her partner are struggling with these issues, refer the couple to a family therapist familiar with MS, who can help partners express their feelings and concerns with one another, identify options, and develop effective communication and problem-solving strategies. The National MS Society (1-800-344-4867) can provide referrals to counselors who are familiar with the challenges couples and families with MS may face.

What other resources are available on this topic?

- The National MS Society (1-800-344-4867; nationalMSSociety.org) offers:
 - Educational programs and support groups
 - Referrals to professionals in the community who specialize in counseling families and are familiar with MS
 - Print and web-based materials about sexuality, pregnancy, parenting and other topics available free of charge by calling an MS Navigator at 1-800-344-4867 or online at nationalMSSociety.org/Intimacy, nationalMSSociety.org/Pregnancy, or nationalMSSociety.org/Brochures

About the author

Barbara Giesser, MD, is Professor of Clinical Neurology at the UCLA School of Medicine. She received her bachelor's degree from the University of Miami, a master's degree from the University of Texas at Houston, and her medical degree from the University of Texas Medical School at San Antonio. She trained at the MS Research & Training Center of the Albert Einstein College of Medicine, under the direction of Dr. Labe Scheinberg, and has specialized in the care of persons with MS since 1982.

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Other resources for
Talking with Your MS Patients include:

Cognitive Dysfunction
Diagnosis of Multiple Sclerosis
Progressive Disease
Elimination Problems
Sexual Dysfunction
Depression and Other Emotional Changes
Initiating and Adhering to Treatment with Injectable Disease Modifying Agents
Family Issues
Reproductive Issues
The Role of Rehabilitation
Life Planning
Primary Progressive MS (PPMS)
Palliative Care, Hospice and Dying
Wheeled Mobility



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