



National  
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Society

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# Clinical Bulletin

Information for Health Professionals

## Reproductive Issues in Persons with Multiple Sclerosis

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Multiple sclerosis (MS) is diagnosed most commonly in young adulthood, when men and women are in the process of making important lifestyle, career, and family decisions. Reproductive issues are among those of greatest concern to those living with this unpredictable, chronic disease, and the concerns are both medical and psychosocial.

### WOMEN WITH MS

The majority of persons with MS are young, premenopausal women. In this population, questions regarding fertility, pregnancy, childbirth, and contraception—and their interaction with disease activity and disease-modifying therapy—are of paramount importance for both the patient and her health care team.

#### The Effects of MS on Pregnancy

Multiple sclerosis does not appear to affect a woman's ability to conceive or bear children. There is also no indication that congenital malformations are increased in the MS population. Therefore, the effects of MS on pregnancy are minimal. Some reports suggest that women with MS may have babies with slightly lower birth weight (Dahl et al. 2005). What then, are the effects of pregnancy on MS?

#### The Effects of Pregnancy on MS

Decades of data have been collected on women with MS who become pregnant. (Damek & Shuster, 1997). These studies indicate that disease activity, as measured by relapse rate and/or MRI activity, is significantly decreased during pregnancy, particularly in the third trimester. The relapse rate then rises in the three to six months post partum, followed thereafter by a return to the pre-pregnancy level (Confavreux et al., 1998). A small pilot study has suggested that intravenous immunoglobulin (IVIG) administered for five consecutive days during the first week postpartum, and at six and twelve

weeks thereafter, can help prevent postpartum relapses (Achiron, Rotstein, Noy, et al., 1996). Most important, however, is the finding that despite the higher postpartum risk of relapse, women with MS who have had children demonstrate the same level of long-term disability as women who have not had children.

In an effort to understand, and perhaps capitalize on, the apparent immunosuppressive effects of pregnancy, Sicotte and her colleagues conducted a small pilot study of estriol, a hormone that is only produced in appreciable amounts during pregnancy. This study demonstrated significant reduction in MRI activity in women with relapsing/remitting MS, and larger trials are in progress (Sicotte et al., 2002).

## Symptom Management During Pregnancy

Many symptoms of MS may become more prominent during pregnancy, including 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, as long as it is safe for use in pregnancy.

## Disease Management During Pregnancy

The use of disease-modifying agents (DMA) for prophylactic therapy of MS is also a significant issue for women of child-bearing age. Beta-interferon and natalizumab are considered category "C" drugs, meaning that there are animal data that indicate potential for harm to the offspring (an increased rate of miscarriage with beta-interferon and decreased survival and hematologic effects with natalizumab). Glatiramer acetate is a category "B" agent, indicating that there is no evidence of fetal damage from animal studies, but no human data are available. There are currently no evidence-based guidelines for use of DMA in the months prior to pregnancy, although the manufacturers of these medications are in the process of collecting data about women who have inadvertently become pregnant while on medication. Women on any of the DMAs are generally advised by their neurologists to discontinue their use for at least one to two menstrual cycles before attempting conception. Women on DMA who discover that they are pregnant should promptly discontinue these drugs. DMA may be resumed as soon as desired after delivery, except by women who plan to breastfeed. Because it is not known if beta-interferon, natalizumab or glatiramer acetate are secreted in breast milk, their use is not recommended in nursing mothers.

The use of mitoxantrone (an immunosuppressive agent that is approved for use in patients with secondary-progressive, progressive-relapsing, or worsening relapsing-remitting MS) poses additional issues. Mitoxantrone, like other immunosuppressants that are sometimes used in MS (e.g., methotrexate, cyclophosphamide, azathioprine), is considered a category "D" drug, meaning that studies in humans and/or investigational or post-marketing data have demonstrated fetal risk. Women should be given a pregnancy test prior to initiating this or any other immunosuppressive medication. Since the impact on future fertility is unclear, young women initiating treatment with mitoxantrone or any other immunosuppressive agent should be counseled as to the advisability of harvesting eggs for

future use. Mitoxantrone is known to pass into the breast milk, with potentially significant effects on the infant. Breastfeeding should be stopped before treatment begins.

## **Delivery**

All forms of anesthesia are considered safe for women with MS during childbirth. 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, and might require additional assistance during labor and delivery.

## **Breastfeeding**

There are very few studies about the effects of breastfeeding on disease activity, but the available data do not indicate a negative impact. One small study has reported a reduced postpartum relapse rate in women who breastfeed exclusively for at least two months (Langer-Gould et al. 2009). Women who wish to breastfeed should be encouraged to do so unless it is judged critical for them to resume their disease-modifying agent immediately or their fatigue and/or disability level is likely to make it impractical.

## **Contraception**

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 indicate 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, anti-convulsants or antibiotics, can interfere with the effectiveness of oral contraceptives. Women should be encouraged to use 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.

## **Menstrual Cycle**

Self-report studies have indicated that many women with MS experience a worsening of neurologic symptoms several days immediately before onset of menses, with resolution of symptoms once the period begins (Giesser, 2003). Larger, controlled studies with objective outcome measures are needed to confirm these observations.

## **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 interferes with conception. These problems are amenable to a variety of therapeutic strategies, including medication for erectile dysfunction, artificial insemination, and electronic ejaculatory stimulation.

To date, there are no 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. Since the

impact on spermatogenesis and fetal development has never been studied, men should be counseled about the possibility of stopping their medication while trying to conceive. For those 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.

## **GENETIC FACTORS**

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, and for children of a woman with MS than of a man). Thus, the risk increases significantly for a person whose parent has MS, but still remains relatively low.

These simple risk estimates, however, are oversimplifications that can easily be misinterpreted. We now know, for example, that 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.

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 fact that identical twins of people with MS who share all the same genes don't always get MS, and that more than 80% of people with MS do not have a first-degree relative with MS, demonstrates conclusively that MS is not directly inherited and that factors other than genetics must be involved (Ebers & Sadovnick, 1998).

While couples who express concerns about the genetic risk for their children should be reassured that the risk is relatively low, they need to be reminded that the risk is present and that there is no genetic testing available at this time to provide them with a definitive answer.

## **SOCIAL AND EMOTIONAL ISSUES: Decision-Making in the Face of Uncertainty**

In addition to the emotional, social, and economic issues that all of us need to take into account when planning a family, young men and women with MS have to factor in the uncertainties of a chronic, unpredictable disease. In talking with couples about this complex decision, it is important to encourage them to think through the negative as well as the positive possible outcomes—e.g., if the parent's disability were to progress significantly, and if the parenting and wage-earning roles and activities were to require some changes. They may also need to be reminded to think beyond the initial few weeks or months of a child's life. 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. Couples that have taken the time to think through possible strategies and resources for dealing with future disease-related changes, have a far easier time meeting the challenges when they do occur.

Important factors for partners to consider include:

- ◆ Personal priorities and needs
- ◆ Strength and flexibility of their relationship
- ◆ Available support system
- ◆ Financial resources
- ◆ Parenting and child-rearing goals and ideals

Under the best of circumstances, some couples may find it difficult to communicate about these important issues. The unpredictability of MS can make it even more challenging, especially if partners are unwilling to think or talk about the possibility of worsening symptoms or disease progression. A family therapist familiar with MS can help partners express their feelings and concerns with one another, identify options, and develop effective communication and problem-solving strategies.

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