

HORMONES

DO SEX HORMONES HAVE A ROLE IN MS?

MS is generally thought of as an “autoimmune” disease. Autoimmune diseases, which include rheumatoid arthritis and systemic lupus erythematosus, result when the body’s immune system mistakenly attacks part of the individual’s own body. As is the case with MS, the large proportion of persons with autoimmune conditions are female.

In MS, the ratio of women to men is about 2:1. (In lupus, the ratio is 10:1.) While the reasons for this are not understood and are certainly complex, most scientists believe that hormonal differences between men and women—“sex hormones”—play an important role.

It is clear that sex hormones are very powerful modulators of the immune response. In many animal models of diseases, and in some human diseases,

testosterone, the primary male hormone, seems to protect against the development of autoimmunity.

Estrogen, one of the main female hormones, may either increase or decrease the immune response, depending on dose or concentration. Progesterone, which is produced in women cyclically and also during pregnancy, seems to decrease immune responsiveness.

ARE LEVELS OF SEX HORMONES OR THEIR ACTIVITY DIFFERENT IN PERSONS WITH MS?

There has been at least one small study which reported that some men with MS may have lower than normal levels of testosterone. To date, there have been no large scale studies to indicate that men or women with MS have abnormal function of the endocrine system which produces sex and other hormones. So currently, the answer to this question is not known.

DOES THE MENSTRUAL CYCLE AFFECT MS?

Other neurologic conditions such as migraine or epilepsy tend to be exacerbated just prior to or during menses. A small uncontrolled study suggests that this may also hold true for MS. In a sample of 149 women with MS, 70% of the women said they noted an increase in their neurologic symptoms several days prior to onset of menses. Three or four additional studies of self-reports support this observation, but there are no “robust” data on this phenomenon.

If the menstrual cycle does have effects on MS, there may be non-hormonal explanations. Right before menses and during the second half of the cycle, a woman’s core body temperature rises. Persons with MS who are particularly heat sensitive may have increased symptoms at this time as an effect of heat. On the other hand, hormonal shifts may affect immune activity at different times in a woman’s monthly cycle, and this might also produce increased symptoms.

CAN WOMEN WITH MS TAKE BIRTH CONTROL PILLS?

The short answer is yes. There are no data to indicate that health risks for women with MS who take the pill are different than anyone else’s.

A small retrospective study looked at two groups of women who subsequently developed MS. One group had taken birth control pills and one had not. The MS appeared to have developed later in the group using oral contraceptives. This possibility of a protective effect is intriguing. Large scale studies are needed to shed light on this.

A related issue concerns the use of disease-modifying therapy. These are not recommended during pregnancy, so women who are thinking of becoming pregnant may need to time the starting or stopping of their MS medication. The decision has to be made on an individual basis as there are no clear clinical guidelines.

WHAT ARE THE EFFECTS OF PREGNANCY ON MS?

This is the only gender-specific MS issue that has been extensively investigated. See, for example, “Rate of Pregnancy-Related Relapse in Multiple Sclerosis”, **The New England Journal of Medicine**, Vol. 339, No. 5; 285-291.

The majority of studies indicate that women with MS tend to do well during pregnancy. While some symptoms, such as fatigue or bladder function, may be worse, relapses tend to be fewer, particularly during the third trimester. The chance of a relapse for women in the first three to six months

postpartum tends to be higher than normal. However, overall, women with MS who have had children do not have more disabilities than similar women with MS who were never pregnant.

Pregnancy is a relatively immunosuppressed state, meaning many hormones and chemicals produced normally during pregnancy tend to decrease immune responses. This may be one reason why women with MS tend to have less disease activity while they are pregnant.

DOES BREASTFEEDING AFFECT MS RELAPSES?

No. The studies that have investigated this question report no difference in the rate of relapses among women with MS who breastfeed, compared with those who do not. But the studies did not involve women who were taking a disease-modifying drug.

Since it is not known if the disease-modifying drugs are excreted into breast milk, they are not recommended for women who wish to breastfeed. A woman and her doctor need to discuss the individual risks and benefits together.

WHAT EFFECTS DOES MS HAVE ON FERTILITY?

There is no indication that women with MS have decreased fertility,

increased rates of birth defects, increased rates of miscarriage, or other problems associated with conception. Male fertility can be compromised by some MS-related difficulties with ejaculation, but these are related to nerve conduction, not hormones.

DOES MENOPAUSE AFFECT MS?

There is almost no information on this question. One study which questioned 19 women found that a majority reported improvement of neurologic symptoms at menopause. There are no data on the effects of hormone replacement therapy on MS. At this time, menopausal women with MS should make decisions about taking hormones based on such issues as the importance of hormone benefits for bone density and cardiac function rather than for a positive effect on their MS.

IS TREATMENT WITH THE DISEASE-MODIFYING DRUGS DIFFERENT FOR WOMEN THAN MEN?

Yes. The interferon-based agents have been reported to cause menstrual irregularities as a possible side effect, and there has been some speculation that treatment with interferons may increase a woman's chances of having an abnormal PAP smear.

There have been no reports on specific

drug side effects relating to men's hormones.

None of the drugs that are currently being used to modify disease course in MS are approved for use in pregnant women. This means that women with MS need to choose between starting a family and delaying treatment, or going on immunomodulating therapy and putting off pregnancy.

THE OUTLOOK

It is becoming increasingly evident that sex hormones play an important role in the development of auto-immune diseases. In 1998, the National MS Society convened a task force of clinical and basic scientists to examine what is currently known about the "gender gap" in autoimmune diseases and to identify priorities for research. The task force reviewed what is currently known and suggested several lines of scientific investigation. For example, can sex hormones be used as therapeutic agents in MS? What are the effects of hormone replacement on persons with autoimmune disease?

There are some data which indicate that men with MS tend to have more severe forms of the disease than women. Are there, in fact, differences in hormone levels in men and women with MS compared to persons without the disease? What are the exact molecular mechanisms whereby hormones, immune cells, and brain cells interact?

Studies designed to elicit answers to some of these questions have already begun, but for now, there are many more questions than there are answers. A knowledgeable physician is an individual's best guide. The Society chapter nearest you can provide referrals to health-care professionals who have an interest in MS care.

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