



## *The Basic Facts*

# Hormones

### **SEX HORMONES**

#### **Do sex hormones play a role in MS?**

Yes. Studies and clinical observations involving people with MS reveal that young women are more susceptible to MS than young men and that women have fewer MS attacks during the third trimester of pregnancy.

#### **Do male sex hormones play a role in MS?**

Scientists believe that the reason young women are more likely to get MS than young men is, in part, because MS is an autoimmune disease. There is a higher prevalence of other autoimmune diseases, such as lupus and rheumatoid arthritis, among young women than among young men. Men who get MS tend to get it later in life than women.

Some animal studies suggest that this may be because testosterone levels are high enough in young men to prevent these diseases. Studies in mice with an MS-model disease show a distinct link between low testosterone and worsening disease. Testosterone levels in men begin to decline modestly after the age of 30. There

is also some evidence that MS may take a more aggressive course in men, once it begins. This sex-related difference warrants more research.

#### **Do female sex hormones play a role in MS?**

A number of studies of women with MS give us inconclusive results. Fluctuating levels of female sex hormones have not been shown to affect relapses or MRI results. In a 1992 study of women with MS during menopause, women reported feeling worse with menopause and better with hormone replacement therapy. But these changes in subjective symptoms may or may not be related to MS.

### **PREGNANCY**

#### **Pregnancy and MS relapses**

Over the years, studies have clearly shown that women with autoimmune diseases including MS tend to do better during pregnancy. The diseases rebound during the postpartum period.



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In a 1998 study of 254 pregnant women with MS, Pregnancy in Multiple Sclerosis (or PRIMS), a 71% reduction in relapses was reported during the third trimester. Rates then increased during the first three months postpartum, returning to pre-pregnancy rates.

### **Can we predict who is most likely to relapse after giving birth?**

In a recent follow-up report of the PRIMS study, the researchers attempted to predict which women would or would not relapse during the postpartum period. The most significant predictor was the individual's level of MS activity prior to pregnancy. If a woman had a relatively active relapsing form of the disease, she was more likely to relapse postpartum.

### **Does pregnancy affect MS-related disability?**

If the number of relapses during the third trimester is reduced by 71%, what about the effect of pregnancy on the accumulation of disability? Does pregnancy ultimately slow down the onset of disability?

We don't know yet. The PRIMS study showed that disability continued to accumulate for the next two years at a rate unaffected by pregnancy and the postpartum period. However, two smaller studies that followed participants for longer periods of time, found that later development of disability was reduced with pregnancy, and one of these studies showed

that a full-term pregnancy increased the time interval to reach a common disability end-point, such as needing a cane or crutch.

An earlier study from 1995, which followed women with relapsing-remitting MS, found a significantly decreased risk of the disease evolving into secondary progressive MS in those women who became pregnant after MS onset.

### **Can pregnancy prevent MS?**

No. Studies to date suggest that there are no correlations between pregnancy and a lowered risk of developing MS.

### **Why is pregnancy temporarily protective?**

Pregnancy is a complex event that involves numerous changes in body chemistry. Leading candidates that may play a role in disease improvement include estrogens, progesterone, alpha-fetoprotein, and vitamin D.

Two estrogens, estradiol and estriol, have been shown to be protective in animal models of MS when given in doses equal to or greater than those found in pregnancy. Estradiol is an estrogen associated with the menstrual cycle and estriol is unique to pregnancy.

Studies in 2002 and 2003 of estriol in pill form taken by women with MS showed that treatment caused a decrease in lesions on MRI and induced a favorable effect on immune responses. Further trials

of estriol treatment for MS are now in the planning stages.

Treatment with a combination of pregnancy factors is becoming an increasingly attractive idea, and estrogens, progesterone, and/or others are primary candidates for use in future trials looking for ways to prevent the postpartum relapse.

## **ESTROGENS**

### **Could estrogens in oral contraceptives protect in MS?**

The use of oral contraceptives in healthy women has shown no effect on the risk of developing MS. This suggests that the estrogens in oral contraceptives may not be the right type, combination, and/or dosage.

### **What does the future hold for estrogens and MS treatment?**

Many more studies need to be done before we begin to know. One area of future investigation will be to determine whether estrogens may be more than just anti-inflammatory, but actually directly neuroprotective. It is possible that one day a drug that sustains the pregnancy levels of estrogen may help to protect against disease activity in MS.

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