A beneficial role for sex hormones in multiple sclerosis (MS) was first proposed because of observations that symptoms in MS improved during pregnancy.

In addition, the transient improvement in MS during pregnancy is most pronounced during the third trimester, and MS occurs 2-3 times more often in women than men.

**Estriol**

In the 1990s, Dr. Rhonda Voskuhl the Director of UCLA’s MS Program discovered that the hormone estriol, which rises in pregnancy, suppressed symptoms in MS. As a treatment estriol holds an advantage because it can be taken orally. In addition, estriol reduces the ability of immune cells to attack the brain, and it makes the brain more resistant to damage. Dr. Voskuhl calls this a two-prong approach in which there’s an anti-inflammatory prong that reduces attacks on the brain and a neuroprotective plug that helps the brain heal in case of an attack.

**Phase I Clinical Trial**

In 2002 Dr. Voskuhl conducted a phase I clinical trial involving 12 non-pregnant women (average age 44 yrs) with either relapsing-remitting (RRMS) or secondary progressive MS (SPMS) who were treated with 8 mg estriol daily. Two women withdrew from the study, one for concurrent steroid use, and one because she didn’t want to refrain from medications during the post-treatment phase of the study.

**The Results**

The results showed an impressive 80 percent reduction in gadolinium-enhancing inflammatory brain lesions on monthly cerebral magnetic resonance imaging (MRI) tests in women with relapsing-remitting MS. Cognitive improvement was also noted in all patients with RRMS. During the six-month posttreatment period, median total enhancing lesion volumes and numbers became variable in the first three months off treatment, before returning to near-baseline levels in the last three months. Patients with SPMS showed no measurable improvements.

Patients retreated over the course of four months showed a decrease in enhancing lesion volumes and in numbers compared with original baseline scores. After publication of the study, Dr. Voskuhl reported that additional studies performed on the six patients with RRMS showed an increase in IL-5 and a decrease in TNF.

**Phase II Study**

In March, 2007, Dr. Voskuhl began recruiting patients for a 2-year long, placebo controlled, double blind estriol study. The study involves 130-150 women with relapsing-remitting who are being treated at 7 different MS centers in the United States.
Patients in the study are being given either estriol or a placebo along with Copaxone. Investigators will measure the relapse rate for patients.

**The Significance**

Earlier studies in pregnant women and animal models suggested that estriol might be beneficial in MS by causing an immune shift from T helper 1 to T helper 2, potentially improving symptoms in a number of autoimmune diseases. If estriol works well for patients with MS, researchers believe that estriol will improve other diseases known to improve during pregnancy such as Graves’ disease and rheumatoid arthritis.

**Preliminary Results**

On September 19, 2008 at the World Congress on Treatment and Research in Multiple Sclerosis Meeting (ACTRIMS, ECTRIMS and LACTRIMS) in Montreal, Canada, Dr. Voskuhl presented results of Phase II a of her clinical trial. Estriol is the active ingredient in TRIMESTA. In a presentation from her laboratory, new findings were shown which demonstrated that estriol treatment decreases matrix metalloproteinase (MMP). MMP plays a critical role in the migration of inflammatory cells into the central nervous system. Elevated levels of MMP-9 have been described in serum and cerebrospinal fluid of multiple sclerosis patients, and they predict the occurrence of new active lesions on brain MRIs.

**Resources:**


Clinical Trial Of Sex Hormone Estriol Recruiting Women With MS To Participate, Medical News Today, June 20, 2007.

Pipex Pharmaceuticals' Oral TRIMESTA Phase IIa Clinical and Preclinical Findings Presented at World Congress on Treatment and Research in Multiple Sclerosis Meeting, Market Watch, September 19, 2008.