

[Multiple Sclerosis Center of Oregon](#)[Index of current releases](#) | [News release archive](#)

OHSU-VAMC STUDY SHEDS LIGHT ON ESTROGEN'S BENEFIT FOR MS

High hormone levels, particularly during pregnancy, boost T cells that lead to remission

PORTLAND, Ore. - For years, doctors have suggested the best treatment for multiple sclerosis is pregnancy. Now, an Oregon study is delivering solid evidence to support the theory.

Researchers at Oregon Health & Science University and the Portland Veterans Affairs Medical Center have uncovered the mechanism by which estrogen, produced in high volumes during pregnancy, boosts the expression and number of regulatory cells that are key to fighting MS and other autoimmune diseases, such as arthritis and diabetes.

The study, published in the "Cutting Edge" section of the current issue of *The Journal of Immunology*, shows the hormone augments a compartment containing T cells known as CD4+CD25+, and a regulatory protein called FoxP3. The cells are important for protecting mice against a model for human MS called experimental autoimmune encephalomyelitis (EAE).

Autoimmune disease has been associated with a deficiency of FoxP3, whose expression is a reliable indicator of the regulatory T cells' function and development.

"This is the first report that this single, benign compound - estrogen - can increase regulatory cells," said study co-author **Halina Offner**, Ph.D., professor of neurology, and anesthesiology and peri-operative medicine, OHSU School of Medicine and the Portland VA Medical Center. "When you remove (the CD4+CD25+ cells), animals get autoimmune disease. They're very important to maintaining a healthy state."

Dennis Bourdette, M.D., professor and chairman of neurology, OHSU School of Medicine, and director of OHSU's MS Center of Oregon, says understanding how estrogens boost protective T cells to fight MS will lead to the development of "estrogen-like" drugs that could increase the cells without the female hormone's side effects.

"Dr. Offner and her research team have made a major breakthrough in understanding how estrogens help MS," Bourdette said. "This breakthrough will provide a critical 'tool' for developing these new estrogen-like drugs."

The study found that estrogen treatment simulates pregnancy in increasing T cell levels. It also demonstrated that estrogen boosts expression of the FoxP3 protein not only in a mouse model, but also in cell culture. "In vitro, estrogen can induce regulatory cells," Offner added.

In their research, the OHSU-VAMC scientists saw a "significant increase" in the number of CD4+CD25+ regulatory T cells - 43 percent - and a correlated boost in FoxP3 expression in mice treated for 14 days with estrogen versus untreated mice. Pregnancy increased the CD4+CD25+ count and amplified FoxP3 expression as well.

Scientists have long been interested in the role sex hormones play in the body's ability to fight autoimmune diseases like MS, particularly since these disorders occur more frequently in females than in males. But the link between pregnancy and MS has been hotly debated.

In 1998, scientists in France went a step closer to putting the issue to rest when they conducted the first large study aimed at assessing pregnancy and delivery on the course of the disease. The group found there was a marked reduction in the rate of MS relapse during pregnancy, especially in the third trimester.

Three years later, Offner and a team of OHSU and Portland VA Medical Center neurologists published a study showing treatment with low doses of estrogen protects mice from developing EAE, but the mechanism of the effect hadn't been fully characterized. And earlier this year, researchers in the United Kingdom found that human pregnancy elevated levels of the disease-fighting CD4+CD25+ T cells.

However, "They didn't say it was (due to) estrogen," Offner said.

Estrogen levels during pregnancy can be 50 to 100 times higher than normal, Offner said. Scientists attribute this jump to the body's natural defense against its own immune system, whose reaction to self-antigen proteins, or "self-Ags," in fetal tissue can lead to fetal rejection, as well as the chronic inflammation that is the root of autoimmune disease.

"It's very well known that pregnant women are in remission. They do feel better," Offner said. "If you could mimic pregnancy somehow, it would be great" as a therapy.

Bourdette said many of his patients have told him their MS symptoms improved dramatically during pregnancy. And a small clinical trial at the University of California, Los Angeles, showed estriol, the estrogen hormone produced during pregnancy and available as an oral therapy, showed "some benefit" for MS patients.

"However, long-term estrogen therapy has potential side effects," and developing estrogen-like drugs can help patients avoid these potentially detrimental effects, he said.

Research is continuing on regulatory T cells - "T-regs," as they're often called - and their potential benefit for other autoimmune diseases, Offner said.

"It would be nice to look at regulatory T cells in an animal model for arthritis," she said. "There's still a lot to do."

The study was supported by grants from the National Institutes of Health, the National Multiple Sclerosis Society, the Nancy Davis MS Center Without Walls, the Department of Veterans Affairs, the American Diabetes Association and the Juvenile Diabetes Research Foundation.

###

Last updated on Thu, 24 Feb 2005 22:50:42 GMT by [News and Publications](#)

[OHSU Home](#) | [About OHSU](#) | [Search](#) | [Site Map](#) | [Contact OHSU](#)
[Health Care Services](#) | [Research Programs](#) | [Academic & Students](#) | [Regional Outreach](#)

OHSU is an equal opportunity, affirmative action institution.

© 2001-2005, Oregon Health & Science University

[OHSU Notice of Privacy Practices](#)

