



**MS Learn Online
Feature Presentation
Hormones, Gender, and MS – part two
Nancy Sicotte, M.D.**

Tracey>> Welcome to MS Learn Online, I'm Tracey Kimball.

Tom>> And I'm Tom Kimball. MS affects women two to three times more often than men. Researchers are starting to learn more about the impact testosterone may have on that statistic.

Tracey>> Let's continue our series on Hormones, Gender and MS with Dr. Nancy Sicotte as she talks about the male side of the equation.

>> Rick Sommers: As I was telling you before we started, I was at a presentation a couple of years ago in New York City, where a doctor was addressing a room full of women MS patients, and talked about the benefits of estrogen and how being pregnant -- I mean, it's exactly what you and I are talking about. He said this conceivably could be very good news for everybody in the room, at which point I raised my hand and he said, "Except for you." But that's not necessarily true now, because we're talking about estrogen on this side, and because we're equal opportunity, we have testosterone on this side.

>>Nancy Sicotte: Absolutely. And we know that it's not only women that get MS. Men get MS as well. But what's interesting, if you look at MS and other autoimmune diseases, is that women are more susceptible to these diseases.

I've also seen some interesting posters at this presentation, at this meeting, suggesting that that sex ratio is actually increasing. So, there is more women than men who are being diagnosed with MS, and this has not been explained. But in general, the old numbers suggest that it's about a 2:1 ratio.

So, while men still get MS, they are less likely to. So, that raises some interesting observations or questions that you might ask as to why that is. It could be that there's a factor that men have that could be protective for preventing them from developing an autoimmune disease like MS.

So, if you're thinking about hormone differences, clearly one of the big differences between men and women is that men have testosterone and women have some testosterone but very, very low levels compared to men. And, in fact, if you think about it, in terms of clinical observations, men tend to be a little bit older when they get the disease, and I know this is sometimes hard to hear or accept, but testosterone levels do start to decrease relatively early, around age 30. And this is around the time that men who are going to be diagnosed with MS tend to be diagnosed.

>> **Rick Sommers:** That's exactly how it happened for me.

>> **Nancy Sicotte:** So, again, thinking about this in terms of could this be a disease modifier, or could testosterone have a beneficial effect on immune function, my colleague, Dr. Voskuhl, went back into the lab and did the same types of experiments using testosterone, to see if this might have a beneficial effect on disease activity in the animal model, and in fact saw that testosterone was protective and decreased the severity of the EAE, or the animal model, of MS.

So, we then took that into a pilot trial and have done a study where we used a testosterone gel. So, this is not an injection, not even a pill. It's a gel that's rubbed on the shoulders, and we did a study where we took men with relapsing-remitting MS and observed them for about six months without treatment, and then treated them for one year using this gel. And this was a study that was funded by the National MS Society, and then with some donor money we originally were going to do six months of treatment, we ended up extending it to 12 months of treatment, which turned out to be very, very important in terms of the findings that we had. Because we really started to see benefits of this testosterone therapy toward the later end, the last -- really, the last nine to twelve months of treatment.

>> **Rick Sommers:** This is a therapy applicable to both sexes, then, or --

>> **Nancy Sicotte:** So, testosterone itself would not be advised for women, in part, because there are masculinizing effects of testosterone. And, again this is really in the experimental phase, in the exploratory phase. There are certainly risks associated with hormone supplementation, as we're well aware from estrogen studies that have been done, and the Women's Health Initiative, and so on. And testosterone, there are certain contraindications in terms of prostate cancer. It can increase hematocrit, and so on. So, it's not that we are suggesting that people should be using this therapy now, but it's an interesting potential treatment that we're exploring further.

>> **Rick Sommers:** Some of your research at UCLA also talks about the performance of hormones having a possible dual role, anti-inflammatory and neuroprotective. Let's talk about that a little bit.

>> **Nancy Sicotte:** So, this is really exciting, and I think this is really where hormone therapy has a benefit. Because the truth is, right now there are no really purely neuroprotective treatments for multiple sclerosis. And as we recognized, MS is really a disease that has two pathologies. One, of course, is inflammation, and this causes the acute exacerbations and worsening of symptoms. But we know that over the long term, really what is the major player in disability development is neurodegeneration. So, there is loss of nerve cells, there is atrophy within the brain, there is atrophy within gray matter areas of the brain, and none of the treatments that we have currently seem to target that process of neurodegeneration directly.

So, the treatments that we have that are anti-inflammatory are secondarily neuroprotective, because you stop inflammation, you stop the process that damages axons that ultimately leads to this neurodegenerative change. But could we have therapies that we could put onboard that keep the nerves healthy without having to have this first effect on inflammation? And

hormones are really an interesting choice and interesting possibility to have these both neuroprotective and anti-inflammatory effects.

And, again, looking at a therapy such as estriol or estradiol, there are different kinds of receptors within the brain that mediate estrogen effects. There is ER-alpha and ER-beta, and it seems that these two receptors have different kinds of effects, and it may be that one of these receptors has a more neuroprotective effect that's separate from the anti-inflammatory effect.

So, we've been looking at this in my lab, specifically looking at this from an imaging perspective to see if these treatments that we're trying could have benefits on MRI markers of neurodegeneration. So, that would be brain atrophy or specific gray matter structures. And, for example, in our testosterone study, while we didn't see a pronounced affect on inflammation, so the enhancing lesion activity didn't change too much during the course of the study, and that may have been because the men in general had lower levels of inflammation. What we did see was that brain atrophy slowed in the men who were treated with testosterone to a level that was more consistent with healthy aging rather than the disease process of MS, suggesting perhaps that testosterone could have a more neuroprotective effect that might be separate from the anti-inflammatory effect.

>>Interviewer: There is contagious enthusiasm in your voice as you talk about this. It's all very, very exciting and well above my head, which is why you're the M.D. and I'm sitting here asking the questions. But I can't thank you enough for sharing some of your expertise with us and some of your study findings. We look forward to hearing big things from you down the road.

>>Nancy Sicotte: Great. Thanks very much for having me.

Tom>> Dr. Sicotte's enthusiasm about what they're learning regarding the relationship of hormones on MS brings yet another ray of hope for those of us dealing with this disease.

Tracey>> Yes indeed, it's truly exciting to think that perhaps someday they'll be able to use hormone therapy to treat MS.

Tom>> And as always for more information on this and other MS related topics, check out NationalMSSociety.org.

Tracey>> Thanks for joining us.