



**MS Learn Online  
Feature Presentation  
Genetics and MS  
Featuring Dr. Dessa Sadovnick**

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

**Tom>>** And I'm Tom Kimball. We're happy to have Dr. Dessa Sadovnick speaking with our medical correspondent Kate Milliken on genetic research.

**Tracey>>** The genetics factor is intriguing to me because my sister also has MS.

**Tom>>** Dr. Sadovnick begins by addressing the question I think we all have, what's the relationship between our genetic make-up and MS?

**>>Dr. Sadovnick:** There is not one gene that causes MS. It's not what's called a monogenic disease, where you have one gene, one gene change. You have this change, you get the disease; you don't have this change, you don't get the disease.

In MS it's part of what are called the common complex disorders. That means there are many genes involved, there are nongenetic factors involved, and there are probably interactions between genes and environment as well.

So, in MS, trying to determine if there really were genetic factors was not really straightforward, because you couldn't just identify one specific gene. So, what we did is we started using what are called the genetic epidemiological approach, which is where you study families and you study subgroups within families to try to tease out whether there seems to be a role for heredity in the disease.

And how this was done initially in MS is, if you went back and you asked someone who had MS, "Do you think there's a genetic factor involved?" They would have said yes. And the reason they'd say yes is because they would say, "Well, I have MS and my cousin has MS, and I know this other family where two sisters have MS. And I know another family where a mother and a son have MS."

And when we looked at the literature, and this is going back to the mid to early 1980s, what you found is that there were anecdotal reports of MS occurring in more than one family member. But there was never a real study to try to tease out whether there is really an excess of MS in relatives of patients compared to the general population, or whether maybe if there is an excess it's because families do things together. They share a family environment much more compared to the general population.

So, what we wanted to do was set out to separate genes and family environment, and see if we could do that.

And so in Canada we have a large, ongoing Canadian MS study that includes over 30,000 families in which at least one individual has MS. We also have information on unaffected family members including biologically related, such as brothers, sisters, parents, as well as people who are less biologically related, such as perhaps a half sibling rather than a full sibling.

We also have information on people who live in the family unit but you don't have genetic sharing, such as a person who is adopted, or step siblings who are all raised together.

And so what we set out to do was in many large series of studies, we set out to look at what -- if someone in the family had MS, did their relatives develop MS more often or less often than the general population? And could you tie that in with genetic sharing versus family environment sharing?

>>**Kate Milliken:** And why don't you give an example of family environment sharing.

>>**Dr. Sadovnick:** Okay. So, family environment sharing, for example, you're eating the same food, you're exposed to the same indoor/outdoor activities. Even things like your education is probably much similar. Things like alcohol exposure. All these things -- smoking -- all these family environment factors are equally affecting all people in the household.

>>**Kate Milliken:** So, what did you discern as a result of this study?

>>**Dr. Sadovnick:** Well, the first thing we did is, we wanted to find out is whether family members did have a higher rate of MS compared to the general population. So, we started studying biological family members. That would be brothers, sisters, parents, aunts, uncles, first cousins, etc., of people who had MS, and we said knowing the background rate for our population, the lifetime risk to develop MS, that's from the time you're born until the time you die.

Knowing that, we ask the very simple question, "If you were a family member of someone who had MS, did you get a higher rate of MS?" And we found this was true. We found, for example, even first cousins who only share an eighth of their genetic material, their risk of MS was maybe around 7 out of 1,000, compared to the background risk of 2 out of 1,000.

When you looked at brothers and sisters of people who had MS, you found they had risks of, say, 35 to 50 out of 1,000 to get MS, compared to the background rate of 2 in 1,000.

>>**Kate Milliken:** Do you feel in light of what you know, finding out with even this part of the study, that there thereby is a genetic component?

>>**Dr. Sadovnick:** Well, this was the interesting part, is because when you look at identical twins, you share 100 percent of their genetic material. They only have a risk of about 35 percent, if one twin has MS, for the other twin. So, it didn't look like it was purely genetic, because then you would expect identical twins to have 100 percent risk. But we could definitely see this elevated risk within families.

So, we thought there was a genetic component existing, but we had to rule out this common family environment. So, we then looked at families where you had people living together in the family environment sharing all the same experiences, but the only differences was they were not biologically related or they had less biological relationship.

>>**Kate Milliken:** And what were the results on that?

>>**Dr. Sadovnick:** The results of those showed very clearly, we did half sibling studies, we did adopted studies, we did step sibling studies, and what was showed very clearly is it wasn't the living together in the family environment; it was the amount of genetic sharing you had. Could I give you a couple of examples?

>>**Kate Milliken:** In light of what you found out about the genetic percentage, let's say, would you say that in the future with these types of studies, that MS may be perceived as having a genetic component that would actually start changing the way that MS is

described? Because I feel like when I got MS, they were like there's no genetic component and it's not genetic or whatever else. But in the future, do you feel that's going to come into play?

>>**Dr. Sadovnick:** I would say even now it is accepted that there is a strong genetic component, that given your family history, depending on whatever your family history is, I would be able to give you an estimate of what are the risks that your children would develop MS in the future. That's actually called genetic counseling. And some of the risks really depend on family structure.

For example, if you're a female with MS and you have nobody else in the family, and you want to know the risks for your children, I would tell you probably about 5 percent, which is about 5 in 1,000, which is -- 5 in 100.

>>**Kate Milliken:** Five in 100.

>>**Dr. Sadovnick:** Which is a relatively low risk, but it is still higher than the 0.1% for the general population.

>>**Kate Milliken:** And do you feel that that's a little bit of a change, just quickly, a little bit of a change of how MS has been perceived in the past?

>>**Dr. Sadovnick:** I think this has been a change in about the last 10, 15 years, yes. Unfortunately, there are no -- even with all the work done in genetic research, there are no biomarkers. There is nothing in genes and there's nothing in other biological material that we can predict who is going to get MS in the future.

But that would be, like my risk figure to you, for example, if you were coming in and all you wanted to know was about the risk, no other information, and there is nobody else in the family. Then if you gave me a different family structure --

>>**Kate Milliken:** It would be different.

>>**Dr. Sadovnick:** Say you told me your mother had MS and you have MS, and maybe a cousin has MS.

>>**Kate Milliken:** The numbers would change.

>>**Dr. Sadovnick:** The numbers would change.

>>**Kate Milliken:** That's the thing.

>>**Dr. Sadovnick:** If you told me that you had MS and your partner had MS, and you wanted to have children, the numbers would change.

>>**Kate Milliken:** Wonderful. I think that's -- again, this is something that's very new, at least in my world. It's not something I've heard about and I think it's fascinating, so I really appreciate your time. Thank you so much.

**Tracey>>** Dr. Sadovnick gives us lots to think about regarding family planning.

**Tom>>** What stood out for me, is how important it is to be proactive, getting as much good information as possible, and making the decision that's right for your family.

**Tracey>>** We'd like to thank Kate and Dr. Sadovnick for this candid and insightful interview.

**Tom>>** And thank you for joining us. We hope to see you again soon.