



**National
Multiple Sclerosis
Society**

**MS Learn Online
Feature Presentation
MS: the Genetic Connection: Part 2**

Tom
Hello, I'm Tom Kimball

Tracey
and I'm Tracey Kimball. Welcome to MS Learn Online

Tom
In the first webcast on The Genetic Connection we learned about some of the possible causes of MS, who's susceptible and potential new therapy options.

Tracey
In part two, of MS: The Genetic Connection we'll focus on population studies and how this research relates to finding, ready... the cure for MS.

Host:
One of the reasons genetics is being studied worldwide is to address the concern of people with MS who are worried that their loved ones may be affected.

Joann D'Amico Stone
When I was diagnosed with this my son was only five and when I was with his father we used to sit and wonder if Kevin would wind up with MS someday // and it's still in the back of my mind; is my son going to wind up with MS when he's 20,30,40,50 years old because we don't know what causes it.

Joann D'Amico Stone
I've had MS for just over 11 years and this past October my older sister who was 44 at the time, she just turned 45 last week, was diagnosed with MS.

Joann D'Amico Stone
No other family members that we know of have MS. When I was diagnosed we searched as far back as we could. At that point both of my grandmothers were still alive and they didn't know any family members that even had anything that resembled MS.

Karen DeJoe

I come from a very large Italian family. My father had 12 brothers and sisters and there is more than 150 cousins and that's 1st, 2nd, and 3rd, cause they're all first when their in town.

Karen DeJoe

I have one cousin, a first cousin with MS. Interestingly enough she has 2 daughters, both with autoimmune processes. She has one with Lupus and one with Diabetes, but she's the only one with MS in that whole group.

Maryann Murray

My mother died in November 98, it was a few months prior that my brother Pat was diagnosed, officially with MS. And um, she, it was just then shortly before she died that we became aware of this disease. She had been in a wheel chair probably for the previous 10 years before she died. // And she did get progressively weaker throughout her lifetime. Then after we were getting more and more into the multiple sclerosis scene we started wondering, gee you know, could she have had it.

Vincent Buchanan

If there's a link between genetics and MS I know my mother has MS and I have MS but is that coincidence or is this something she passed on to me?

David Hafler

One thing that we often speak about is this question of if this is a genetic disease what about my children and what about my sibling my brother or sister. And again there is a very slight increase in the chance of developing MS if you have a sister or mother or father who has the disease. But it's still a relatively small risk.

If MS is such a genetic disease then why if one twin has the disease then why don't all identical twins have the disease? Well I think there are a number of interesting points to that. First identical twins aren't truly identical in many respects. To develop into the immune systems there are a number of random events that occur in the development of the immune system such that even 2 identical twins do not have an identical immune system. Clearly there are environmental differences.

Dessa Sadovnick

We found that in identical twins the risk seems to be highest if the twin pair is female. So if they're both females their risk to develop, the one twin to have MS and the other to develop MS is much higher than if they're both males, which is a very interesting factor and that's after controlling for the fact that we know that females develop MS more often than males. Another thing we found is with these female identical twins in general if one twin developed MS the other twin either developed MS symptoms within a window of about 5 or 6 years or if they passed that window from the age of onset there was a really good chance they wouldn't develop MS at a later age.

Dessa Sadovnick

What the exact genetic factors are, what the exact environmental trigger or agent is, we really don't know. However, we do know that if you are a biological relative, in other words, you share genetic material with someone who has MS, then your risk to develop MS is higher than the general population. We also know that whatever this environmental trigger or agent or agents is or are that it's something that occurs on a whole population level.

HOST

Dr Hauser what are population studies and how can they help us understand the genetics of MS?

Dr Hauser:

Population studies look at the occurrence of a medical problem in a particular part of the world // by looking at one region in great detail we can learn very much about both the environment and the genetic contributions to a medical problem. And these studies have been very important for MS research, they've taught us that MS tends to aggregate in certain families and we think that aggregation is due to inherited and not environmental factors, for example, we now know that the sibling of a person with MS has about a 30 fold increase risk for MS or about a 3% lifetime prevalence. The prevalence for parents or children of MS patients is a bit lower and the prevalence of MS has increased compared with the background population even in 2nd and 3rd degree relatives of people with MS. This is consistent with the idea that multiple different genetic variance come together to make some people *susceptible* to MS.

Host:

Dr Rickert are there some populations who get MS more than others?

Dr Rickert:

MS is a disease that is predominately of northern European origin. There are some populations that are relatively resistant to developing MS, for example, Asians and people who are native to Africa. The study of groups of people who share the genetic backgrounds of both high and low risk populations provides a unique opportunity to discover some of the genes that confer *susceptibility* to MS.

David Hafler 04:00.43 –

So a very interesting question is if Africans don't get the disease and it's a disease that is European ancestry, what about African Americans? Well African Americans have on the average, and in wide variation obviously, about 20% European ancestry, // If MS is a genetic disease and if its due to European ancestry and African Americans have about 20% ancestry can we go back and scan African Americans with MS and look for pockets of European ancestry that are common to the African Americans with MS compared to African Americans without MS because if we can find that, those regions may represent genes that are associated with MS.

Dr Hauser

African American are understudied as a group with multiple sclerosis because MS is a little less common in African Americans than caucasian Americans, however, MS tends to be more severe in African Americans and maybe a little bit different in that the optic

nerve and spinal cord is more often involved. In caucasians with MS the major genetic factor that has been identified thus far is a master switch gene controlling the immune system and how it turns on and off, this is a gene called DR2, there are more than 1000 different flavors or varieties of the DR gene, but only one, DR2 is associated with genetic susceptibility to MS. In African Americans with MS there may be either this DR2 gene which is a caucasian gene primarily or a very close African relative of this gene that is inherited by individuals who are African American and develop MS. This data have been very exciting to us and suggest that we need to focus, uh in even more detail on understanding how DR2 might turn on inflammation in the white matter in people with MS.

HOST

As researchers continue to unravel the mysteries of the genetic links to MS, millions of people with MS are continuing to deal with this disease. They are going on with their lives ... waiting, hoping, and wondering when the fruits of the research will affect their lives. And they're asking some very pointed questions.

Debbie Hazlett

The questions that I would like to ask would be where does it come from? What causes, what causes it to happen? What is the make up of it that causes it? Is it a virus, is it a certain age that it happens? And also I would like to know how close they are to finding a cure. Truthfully how close they are to finding a cure?

Karen DeJoe

“What’s your time line? Where do you think we’re headed and how soon can we get there?” “Do you think that the genetic puzzle will be solved in my lifetime?” “Do you think that we will be able to change our therapeutic options because of your research in the next few years?” and “Do you think a cure is in the not to distant future?”

HOST:

Dr Rickert Debbie and Karen have asked some very important questions uh tell me what would a cure for MS look like.

Dr Rickert:

The concept of a cure is different for different people. For the person with newly diagnosed MS who has little or no permanent neurological deficit a cure for that person is stopping the disease cold, preventing new disease activity preventing development of new disabilities. For a person who has had MS for many years and who has accumulated considerable neurological disability, a cure for that person is regenerating a nervous system, regenerating a healthy nervous system, allowing that person to get up out of their wheel chair and walk again. For the person who is concerned predominately about whether their daughter, or son, or grandchild will develop MS a cure for that person is preventing the disease from the start. In each of these definitions of a cure genetics will play a significant role, so for the person who wants to stop the disease cold the study of genetics in MS will identify new therapeutic targets that will allow us to treat the disease better. For the person who’s interested in regeneration of Milan or regeneration of the nervous system, the study of genetics in MS will identify new genes that are involved in the process of re-myelination, for example, for the person who is concerned about

preventing the disease from the get go the study of genetics will identify the genetic predisposition to the disease and the things that occur at the time of the initial trigger of the disease and how the environmental factors will interact with genetic factors and will allow the eventual development measures such as vaccines.

Host:

Dr Hauser where is all this heading, how will genetics help us understand the future of MS?

Dr Hauser:

For number of other autoimmune diseases genetic discoveries have already changed the face of research in these problems, for example, in inflammatory bowel disease a wonderful discovery found last year that a totally unexpected gene that controls how the intestine reacts to bacteria is a major culprit in causing inflammation in inflammatory bowel disease. This gives great hope to people who suffer with this condition that better treatments will be soon on the horizon. I think for MS a very similar sea change will happen with a new genetic discovery that takes us to a new, probably, unexpected mechanism that sets MS in motion. This could be for the MS community like what the walk on the moon was to NASA, I think a discovery like this would revolutionize our understanding of the early developments in MS could bring to all of us new treatments and perhaps down the road even give us cause to believe we could prevent MS from occurring before it even begins. I think that the future is very bright.

Vincent Buchanan

I hope that someday I can go hike up a mountain. I hope that I can go back to work. I hope I can be strong again.

Joann D'Amico Stone

I hope that someday that I will be able to dance at my son's wedding with him.

Frederick McKoy

I pray to God everyday if I have kids that they won't get something like this in their life you know.

Karen DeJoe

I would have to say that my greatest hope is that there will be a cure for MS. That in the not to distant future that we will be able to eliminate it as a section of medical text books.

Debbie Hazlett

I hope that someday there's no MS.

Maryann Murray

I hope that someday that they fix this thing. And I know it's more than hope because I'm lucky enough to be here at the National MS Society and to be able to hear everything that's going on and how hard everyone is working and um, the research that is being done, so I know it's more than hope, I'm confident that they're going to do it, they're going to cure it.

Maryann Murray

Though MS can be such an isolating disease we are not alone, we are all in this together, so you know, keep fighting, keep up the good work.

Tracey

It's so hopeful to hear how so many researchers from around the world are working together to get to the bottom of MS.

Tom

Hopeful indeed! Thank you for joining us today and please visit us again soon.