QUESTIONs
Who gets MS? Why do I have MS? Why do I have MS? I never asked why I contracted this, but I wondered how I contracted it. How did I get MS? What did I do wrong to enable me to have MS? Did I do something in my past, put myself in a situation that could have caused me to develop MS? How would you explain multiple sclerosis to your friends and other people that don’t know what multiple sclerosis is? I want to know what causes MS because it fills in a blank for me but it also helps other people, and I am encouraged that people are trying all around the world to find out what causes MS.

WHAT IS MS?
Dr. Segal: Multiple sclerosis is an inflammatory disease of the central nervous system - the central nervous system including the brain, the spinal cord and the optic nerves.

Dr. Hafler: It doesn’t affect other organs. It’s strictly limited to the myelin which surrounds the nerves in the brain.

Dr. O’Looney: What happens in MS for some unknown reason is that the signal that travels to and from the brain is interrupted.

Dr. O’Connor: The result neurological symptoms and disability.

Dr. Bennett: Multiple sclerosis is the most common chronic inflammatory disorder of the central nervous system.

Dr. Segal: Since the inflammation can occur virtually anywhere within the central nervous system, there’s a wide range of symptoms that patients experience that
include decreased vision in an eye, double vision, numbness, tingling, weakness, vertigo.

**Dr. O’Connor:** For those people whose disease begins in their teens or 20s or 30s, it tends to take a pattern that we call relapsing-remitting where patients have worsenings, which we call attacks or relapses, followed by improvements in how they feel, which are called remissions. If MS begins after the age of 40, it’s more likely to take a different form and in that form it tends to be more of a purely progressive illness where the symptoms slowly worsen with time.

Cancer, MS, heart disease - these are complex illnesses in which there are multiple factors that work to produce the illness, but in a given patient these factors interact in ways that we don’t really understand.

**WHAT CAUSES MS?**

**Dr. O’Looney:** We believe that there are several risk factors that may trigger the disease and cause the inflammation, but we don’t completely understand what causes MS.

**Dr. Tremlett:** There are many studies out there, and people are looking at many different aspects of MS and potentially what might cause MS, but essentially we don’t know.

**Dr. Wolinsky:** We know an awful lot about what goes on in the course of individual attacks and what goes on overtime, both in the immune system of patients with MS as well as in the central nervous system where the pathologic changes are taking place.

**Dr. Segal:** I think we’re getting closer and closer to uncovering the answers of why multiple sclerosis develops, which gives us clues on developing drugs to stop it. It is a very complicated disease that involves interactions between the immune system and the central nervous system.

**Dr. Wolinsky:** Now there’s a question as to whether there may be another system, that is in terms of the vascular system. If there’s a role for the vascular system in multiple sclerosis, I think it needs to be explored enough to know what that role might be.

**Dr. Segal:** There are environmental factors. There are genetic factors that influence whether someone is at risk for multiple sclerosis. And putting all this information together into one story is a big undertaking,
Dr. Bennett: The only way to explain all this complexity is to think that there is going to be multiple different causes for these multiple different types of progressions and forms that we see.

Dr. Segal A In the past researchers have thought that multiple sclerosis was caused by a very similar process from one individual to another, and that notion is being revised, and it's going to lead, I believe, to great advances in the future.

WHY STUDY THE CAUSE?
Dr. O’Connor: We have very greatly increased our understanding of what causes MS, and we also have treatments for MS nowadays which really do slow down the disease. But what we’d really like to find is a way of completely stopping or reversing the damage that MS causes.

Dr. Tremlett: If you can find out what triggers MS, then you always hope that that’s a factor you can modulate. And if you can modulate that factor, then you can alter someone’s risk of developing MS.

Dr. Hafler: To come up effective treatments you have to understand what causes the disease.

Dr. Bennett: I think it’s critical to study the cause of multiple sclerosis because it’s the only way to understand how the disease begins and to develop important preventative strategies for people who are at risk.

Dr. O’Connor: Once we find a cause, we’ll be able to figure out how to cure the disease.

QUESTIONS
What is it about my immune system? Is it my immune system? Do I have some sort of underlying condition that made me susceptible to MS? I’ve heard something about a vascular theory. I’ve wondered for a long time if there’s any correlation between MS and the fact that I have never had chicken pox or measles or mumps? If MS is an autoimmune disease why look for other causes?

IMMUNOLOGIC THEORIES
Dr. Segal: It is now believed that multiple sclerosis is what is called an autoimmune disease in which the immune system attacks our body’s own tissues. In particular, there seems to be an immune response directed against proteins in a protective sheath that’s wrapped around nerve fibers called the myelin sheath.
Dr. Segal: There’s a lot of research that is focused on understanding how autoimmune attacks against the central nervous system arise and exactly what types of inflammatory cells are causing the damage. There’s also research directed at understanding how the inflammatory cells traffic into the central nervous system from the bloodstream. And those lines of research are useful in developing new drugs because you can target the inflammation at different stages, perhaps prevent it from occurring in the first place or prevent the cells from releasing the toxic factors, neutralizing the toxic factors or inactivating them, and preventing the inflammatory cells from entering the central nervous system.

Dr. Segal: Multiple sclerosis is believed to be caused by an autoimmune disease. However, that doesn’t mean that the autoimmune disease occurs in isolation from other events. The autoimmune response could be triggered by environmental factors.

QUESTIONS

What is the predisposition of people from certain parts of the world to get MS? I grew up in Africa, in Morocco. It’s a hot country. There is a lot of vitamin D. Does vitamin D levels have anything to do with MS? Did I get MS because of where I live? I wasn’t a particularly great eater when I was a kid. I didn’t eat a lot of fruits and vegetables. So I wondered about whether that was a factor. Does diet really play a part? Could smoking have given me MS? How do you pinpoint something like this? Is it one action, or is it a series of events? Is it a perfect storm of events?

ENVIRONMENTAL FACTORS

Dr. Tremlett It is very challenging to conduct a really proper, robust study, particularly looking at the factors that trigger multiple sclerosis. Particularly when you’re looking at a disease where, say, the onset in the average individual is around about age 30, it’s really, really difficult to look back over that full 30 years of their history to see what environmental factors they’re exposed to.

Dr. Bennett D Right now three major things that we know of in terms of environmental exposures appear to be certain viral infections, particularly right now a major focus on Epstein-Barr virus. In terms of diet and environmental exposure, vitamin D is gaining a lot of interest in terms of its influence on MS risk. And even acquired habits like cigarette smoking appear to affect risk as well.
**Dr. O’Looney:** The farther away you live from the equator you have less sunlight throughout the year. You also have less vitamin D because vitamin D is made through sunlight exposure. And so there is an interesting hypothesis that that might be one of the many risk factors associated with MS. Low sunlight means less vitamin D, and vitamin D regulates the immune system.

**Dr. O’Connor:** You’ll get an individual person who was born in a very sunny place, and they all come to your office, they’ve got MS too, and they say, "Why do I have it?" So these statements are all sort of generally true, but not necessarily true in an individual.

**Dr. O’Connor:** More recently it’s been shown that smoking increases your risk of getting MS, and one study suggested that those who smoke tend to have more severe MS.

**Dr. Tremlett:** There was a study actually in France that looked at passive smoking. Parents who smoked and exposed their children to smoking at home, those children were actually at increased risk of childhood onset multiple sclerosis.

**QUESTIONS**

Was I exposed to a virus that may have caused the MS? Well, I had rheumatic fever when I was 15, and I was wondering if there’s any connection between rheumatic fever and multiple sclerosis. Do you think MS is contagious?

**INFECTIOUS TRIGGERS**

**Dr. Bennett:** There are two possibilities for how exposure to an infectious agent might be causative in MS. The first possibility is that the infection takes root and it’s chronic in the nervous system, such as measles virus in the nervous system that can destroy both the white matter and even the gray matter parts of the brain. The second possibility is that a virus could take root and lay dormant in the immune system. Those types of viruses take in an initial infection and then lie dormant in the nervous system where they can reactive sporadically, and that sporadic reactivation with the body’s immune response could be these relapses and remissions of disease.

There’s been no evidence that the disease is contagious. Some investigators have argued that that points against an infectious agent being responsible for the disease, but I think that we need to keep in mind that this infectious agent may be ubiquitous. The other person may have already been exposed or have a genetic constitution that makes them different in how they respond to that
infection, and the actual load of infectious agent and the immune response of that individual also determines whether someone may or may not come down with the disease.