



**MS Learn Online
Feature Presentation
Research News – Part Two
Peter Calabresi, MD**

Tom>> Hello, I'm Tom Kimball

Tracey>> and I'm Tracey Kimball. Welcome to MS Learn Online where correspondent Rick Sommers continues his conversation on Research News with neurologist Dr. Peter Calabresi.

Tom>> He talks about advances in imaging, the different characteristics of MS lesions and the latest on Tysabri. We begin with Tysabri.

>>Rick Sommers: Let's talk about Tysabri. It's been in the news lately. Studies showing improvement in cognition and fatigue for those who have been on Tysabri. Tell me about that.

>>Dr. Calabresi: Right. Tysabri, or natalizumab, is one of the monoclonal antibodies that blocks how cells migrate from the blood into the brain and spinal cord. And, of course, it's now approved, back on the market. There was and has been concern about cases of PML, which is a viral infection of the brain, but the good news is that we've seen very limited number of cases of that, and there are now, I'm told, almost 50,000 people around the world on the drug. And I

think patients speak for themselves. When they feel well on a drug and their quality of life improves, they want it and they tell their friends.

Our experience locally has been that it is effective, and we have seen a variety of different beneficial responses. It's not designed to repair anything, but when you stop the inflammation so effectively, I think some natural mechanisms of repair -- we know there can be natural remyelination kick in. So, we've seen people after being on it for a year come back and say, "You know, my fatigue is gone and I can think more clearly, and I can walk without having to stop all the time." And so it's been very rewarding for the patients who are early in their course of the disease.

>> **Rick Sommers:** That's exciting. I mean, to hear remyelination and the thought that there may be some regeneration from these drugs that we've been taking, or at least this drug. So, we'll keep our eyes watchfully on that.

Doctor, your research team has also been testing specific channel blockers that are akin to the beta-blockers that cardiologists use to treat their patients. Explain to me how that all comes together in the study with MS.

>>**Dr. Calabresi:** Right. So, all cells in the body have channels on their surface that regulate the flow of transmitters and ions in and out of the cells. And we've been very interested in ion channels, specifically, potassium channels, which regulate intracellular levels of calcium. This is important for what cells do. And we found specifically that the T cells that get into MS brain tissue have very high levels of a particular channel that we're learning how to block. And we think that this may allow us to more specifically target those bad cells without compromising the good ones that are there to fight off infection.

>> **Rick Sommers:** Let's talk about acute lesions in MS patients and some research -- I'm not sure if it's research that you've been doing or just aware of -- that have shown that some lesions show different characteristics. What's been discovered and how would that knowledge make a difference in moving forward?

>>**Dr. Calabresi:** A number of neuropathologists around the world have been looking very extensively at MS lesions and have found that they're not all the same, which is not surprising, because we see people with MS that behave in many different ways. But it's exciting because it may lead us towards, again, more specific therapies.

So, it's been proposed that there may be four types of MS lesions, and there are different stages of those lesions, so that an acute stage that may be characterized by a lot of the immune white blood cells that are what we call inflammation, but in the later stages there are different types of cells in the lesions and a different process going on. And so in progressive MS, now the focus is looking at remyelination or protecting the nerves, or targeting different types of cells called glial cells.

>> **Rick Sommers:** Typically, doctors send us for maybe an annual, every couple of years, an MRI to see how the progression of these lesions may be being impacted by drugs we're taking or drugs that we aren't taking. There's been some research done looking at optic nerves and how that plays into MS and its progression. Tell me about that.

>>**Dr. Calabresi:** Well, MRI is extremely useful in diagnosing MS and tracking the disease, but it's clear it's not the whole story. And so one of the shortcomings of MRI is that it doesn't see the very small nerves in the back of the eye, the optic nerve or the spinal cord.

We've recently become very interested in a technique called OCT, or optical coherence tomography that can visualize the nerves in the back of the eye and basically take a microscopic picture of those

nerves right at the bedside, in the clinic, and gives information immediately. It's painless and there is no radiation involved, so we think it's very safe and it's relatively inexpensive as compared to MRIs.

So, we've been doing this for the last three years and found that it's a good way of looking at these nerves, and it's linked with other outcome measures in MS, the EDSS rating scale, and it's even linked to some extent with what we see by MRI. So, the thought is that the eye may be a window into the brain.

>> **Rick Sommers:** And explain to me how that test is actually done.

>>**Dr. Calabresi:** So, it uses a light that is shined through the pupil much like if you've ever been to the eye doctor and have a slit lamp exam, and that light bounces back and gives a picture that looks somewhat like an ultrasound, but instead of using sound waves it's using light waves. So, we get a picture of the different layers of what we call the retina, or the back of the eye. And specifically we can look at the axons in the retina and even the cell bodies and determine whether they're just unhappy and thinned, or whether they're actually permanently damaged.

>> **Rick Sommers:** So, is it getting to the point where technology has advanced so that maybe my ophthalmologist might be able to tell me I should see a neurologist because I may have MS?

>>**Dr. Calabresi:** Well, it certainly could be, and many people do present with clinical episodes of optic neuritis with vision loss, but what we're finding is that about half of the patients with MS never knew they had optic nerve problems and so they wouldn't necessarily go to an eye doctor. It comes on more slowly and they have subtle manifestations, such as they notice that their vision at night is not so good. So, they just stop driving. Some people have attributed that to aging and say, well, I'm getting into my forties, maybe I'm just getting

old. I hope that's not the case, but we're finding that there are some very subtle things that this machine can pick up. So, I envision that neurologists are going to have this in the office and that MS clinics will have an OCT right there and will be able to do as part of their MS evaluation.

>> Rick Sommers: One of the ongoing debates that I'm sure as a researcher and as a practitioner you can't get away from is did I inherit this? Is it environmental? What can you tell me about any new information that may have been revealed about environmental triggers?

>>Dr. Calabresi: Well, it's really both. We know that there's a genetic predisposition, but they probably have a variety of environmental triggers. There has been a lot of focus on viruses, because MS is not so common at the equator and more common in northern temperate latitudes where viruses are more prevalent. The monovirus, like Epstein-Barr virus has been studied for many, many years, and there is some new data suggesting that kids who get MS may have particularly abnormal responses to that virus, so they don't clear it as well. And they have higher antibodies to the virus.

Another really interesting area of research is vitamin D, the sunshine vitamin. So, of course, as I just said, that at the equator where there is more sun, there is less MS, and one of the characteristics of the northern, damp latitudes and coastal areas where there is a lot of MS, like in the Mid-Atlantic Northeast of the US and the West Coast of the US is the less sunlight exposure. And it turns out that vitamin D is not only good for your bones, but it's very important for regulating immune cells. And there is a lot of exciting research going on to understand how we could use vitamin D to actually perhaps treat MS.

Tracey>> Researchers and clinicians today know so much more than they did when I was first diagnosed. It seem progress is being made every day.

Tom>> And these programs on Research News are just snippets of a much larger MS research picture. If you'd like to know more about the different areas of research on MS click on the "Resources" button below.