



***MS Learn Online Internet Program***  
**Current Options in Disease Modifying Therapies**  
**(Part One)**  
**Featuring Dr. John Richert**  
**Length ~ 13:46**

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>> Welcome, and thank you for joining the National Multiple Sclerosis Society's MS Learn Online Internet Program. I'm Kate Milliken, host and medical correspondent.

Although there is still no cure for MS, there are various strategies available to modify the disease course, treat exacerbations, manage symptoms, and improve function and safety. In combination, these treatments enhance the quality of life for people living with MS.

Today's webcast is the first of a two-part series focusing on current options available in disease-modifying therapies. We are very pleased to have as our guest for this series, Dr. John Richert. Dr. Richert is Executive Vice President for Research and Clinical Programs for the National Multiple Sclerosis Society headquartered in New York City.

Welcome, to MS Learn Online, Dr. Richert.

>>**Dr. Richert:** Thank you, Kate.

>>**Kate Milliken:** Dr. Richert, begin by giving us a broad overview of the current disease-modifying agents available today.

>>**Dr. Richert:** It has only been in the past 15 years that we've had any drugs available capable of altering the long-term course of MS. The first ones were the beta interferons and Copaxone, and have been followed by mitoxantrone and Tysabri. There are now a large number of new drugs in the pipeline, including a

number of oral therapies, and we are very optimistic that a number of these will prove to be successful.

>>**Kate Milliken:** Four of them, Avonex, Rebif, Betaseron and Copaxone are classified as immune modulators. Novantrone and Tysabri are classified as immunosuppressants. Explain to us the difference between these classifications.

>>**Dr. Richert:** An immunosuppressant drug tends to suppress immune responses across-the-board. So, a drug like Novantrone actually kills immune cells. A drug like Tysabri prevents immune cells from getting out of the bloodstream and into the tissues. All of their effects on the immune system are to dampen immune function.

The immune modulators, on the other hand, dampen some immune functions and increase others. They turn on some genes and turn off other genes. And it's that combination of genes being turned on and off that leads to the immunomodulation that has the beneficial effect on MS.

>>**Kate Milliken:** Let's walk through some of these therapies one by one. Why don't we start with the group of therapies called the interferons?

>>**Dr. Richert:** All of the interferons, Avonex, Rebif and Betaseron, are relatively similar in their effects over the long run, but each has advantages and disadvantages that makes it important for all three to be available when your doctor is tailor-making your therapy to best fit your situation. So, we'll talk a little bit about the differences and similarities.

One of the major differences is simply the logistics of how the drugs are administered. So, Avonex, for example, is given intramuscularly on a weekly basis, once a week. Whereas, both Betaseron and Rebif are given subcutaneously. Betaseron every other day, Rebif three times a week.

So, people who like the infrequent dosing, infrequent injections, tend to gravitate to Avonex; whereas, those who like a smaller needle tend to gravitate to Betaseron and Rebif.

Betaseron and Rebif are used at a higher dose than Avonex. This has advantages and disadvantages. One of the advantages is that it seems to get them out of the starting blocks somewhat faster than Avonex. But the downside is that these increased doses all lead to an increased incidents of neutralizing antibodies. And so if you start making neutralizing antibodies that neutralize the effect of the beta interferon that you're taking, it neutralizes the effects of all beta interferons, so you

are no longer able to take any of the beta interferons and have them be of any value to you. So, there are pluses and minuses.

Also, there's an increase incidences of abnormal liver function and abnormal blood cell counts. These tend to be more common in the higher dosing interferons. But these can usually be managed safely. They're monitored carefully by your doctor and usually for most people they are not that much of a problem.

All of them have evidence of decreasing relapse rates and decreasing the development of eventual disability due to MS. And all have evidence that starting therapy as early in the course of the disease as possible is beneficial.

We used to think that it was better to hold off on therapies until one could see how aggressive the disease might be in a given person. But what we learned was that once that happens, if somebody is starting to accumulate disability, that the horse is already out of the barn and then it's much more difficult to get the disease under control.

We now have studies of what we refer to as Clinically Isolated Syndrome. And that is when somebody has had their first neurologic event that looks a lot like MS, but you can't definitely make the diagnosis of MS until somebody has a second event, if you start someone on one of these therapies, after that clinically isolated event it delays the onset of Clinically Definite MS. It delays that next episode.

And so when somebody has a Clinically Isolated Syndrome, we say they're at increased risk of developing Clinically Definite MS, and starting these drugs at that point delays the onset of Clinically Definite MS.

>>**Kate Milliken:** Patients who are on these therapies how do they know if these antibodies are neutralizing the drugs?

>>**Dr. Richert:** The only way to know for sure is to do a blood test and measure for the antibodies. So the question is when should you check for the antibodies. There is not complete consensus on this among MS experts. A small number of people think that everyone on an interferon should be checked at a certain time for antibodies. Because the test is pretty expensive, that is not very practical for many people. The most common practice is if someone on an interferon is starting to have some disease activity then the issue is it because of neutralizing antibodies to have eliminated the benefit. Sometimes the decision that the doctor is trying to make is do I switch to another interferon or do I get off an interferon and switch to something else like Tysabri or Copaxone.

A neutralizing antibody test may help to make that decision because if there is a high level of neutralizing antibodies and if they persist then there is no reason to switch to another interferon.

>>**Kate Milliken:** What about Copaxone?

>>**Dr. Richert:** Copaxone is administered subcutaneously every day. So you have one of the same dichotomies -- frequent administration but with a shorter needle. It reduces relapse rates and there is also recent data to indicate that like the interferons, early treatment after a first episode can delay the onset of Clinically Definite MS.

It is a reasonably tolerated drug. Most people tolerate it pretty well. With all the subcu injectable drugs there are some degree of skin reactions that can occur. But some people on Copaxone may develop transient brief episodes of chest discomfort, maybe shortness of breath that sometimes sound like a heart attack after an injection. But careful observation over many years now has shown absolutely no evidence of either cardiac or pulmonary problems. And these episodes usually do not recur after additional doses.

So, while this may be a frightening episode for someone with MS, it does not mean that one has to stop taking the medication.

>>**Kate Milliken:** And I'm actually a Copaxone user, and every time I shoot myself I think, "Oh, God, is the one? Is this the one?" Because it in theory only happens once; is that correct?

>>**Dr. Richert:** For most people, that's right.

>>**Kate Milliken:** All of these drugs have their benefits and all seem to have almost equal effectiveness in how they work. But it is possible that sometimes a drug doesn't work for somebody and it's worth going to another drug. Can you talk about that?

>>**Dr. Richert:** One of the things that's difficult for us, and it was more difficult before Tysabri came along, for example, and before mitoxantrone came along. But one of the issues we used to face was if somebody is on one of those first four drugs and it doesn't work, is the best option to change to another one of those first four drugs or to start adding on additional therapies? And there are off-label therapies that have at least some data to suggest efficacy, although it's not Phase III data, so they aren't FDA approved.

And so in the older days and still sometimes now, people will add on something like monthly steroid infusion or low-dose oral chemotherapeutic agent like methotrexate. Now that we have Tysabri available and mitoxantrone available, one can make a case for moving on to one of those drugs if the first drug doesn't work as well as we'd like.

It's very important to know that Tysabri should not be used in combination with another immunomodifying agent or immunosuppressant agent. The data on superimposed severe infections, particularly one infection of the nervous system, a viral infection of the nervous system, has only occurred in people who have been on combination therapies. We don't know for sure that combination therapies are the key here, but the recommendation from the FDA is very strong that it should be used as a monotherapy, by itself, and not in combination with the other immunomodulatory agents. It can be used with treatments of steroids for exacerbations, but that is the only instance in which another immune-mediating drug can be -- or immune active drug can be used with Tysabri.

Very often -- this is worth making an ancillary comment here -- is that these drugs may be working, but they may not be working as well as we'd like. So, we know that, for example, the interferons and Copaxone reduce relapse rates only by a third. So, you could still have a drug that's working but you're still having disease activity. So, it's not working as well as you'd like. So, it's a mistake to say the drug's not working; it's just not working as well as we'd like when somebody has more disease activity.

And so now we've got the options of depending on what the stage in disease activity is of MS to move on to either Tysabri or to mitoxantrone. And so those are issues that we will discuss in another program. But we now have more options. And so each time, because therapeutic decisions are really very individualized, unique to an individual, that all these decisions need to take into consideration a variety of circumstances, and you and your doctor should decide together what's the best option for you.

>>**Kate Milliken:** Awesome, Dr. Richert. That's all the time we have for today. However, in our next webcast, we will definitely look forward to hearing more about these other disease-modifying therapies. Thank you so much for being with us.

>>**Dr. Richert:** Thank you, Kate. It was great talking with you.

>>**Kate Milliken:** The National MS Society is proud to be a source of information for you about multiple sclerosis. Our comments are based on professional advice, published experience and expert opinion, but do not represent individual therapeutic recommendation or prescription. For specific information and advice, consult a qualified physician.

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For the National MS Society, I am Kate Milliken, wishing you health and happiness.