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Time needed to complete: 1h 04m

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Navigating the Diagnostic Maze: Strategies for Excluding MS Disease Mimics

#### Announcer:

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## Dr. Freedman:

Hello, everyone. My name is Mark Freedman. I'm a Professor of Neurology at the University of Ottawa and a Senior Scientist at The Ottawa Hospital Research Institute in Ottawa, Ontario, Canada. And I'm here to talk to you about navigating the diagnostic maze, which is basically, how do you use the diagnostic criteria to make a clear diagnosis of MS? And the first and most important criterion is no better explanation. So, otherwise exclude things that could look like multiple sclerosis. And that's key.

So, these criteria have been developed over the years not to look at sensitivity. So, it's not to pick up every case but it's to be absolutely sure that the cases that we put the label on are, in fact, MS. So, it's all about specificity.

In another talk, we talked about the need for dissemination in space and time, and those are criteria that are really important. But there are a lot of things that can look like MS. And in those circumstances, you need to use ancillary criteria, ancillary tests that will help you in not so much making a diagnosis of MS but making sure that it's not something else. And people keep thinking, 'Oh, the MRI confirms MS. The spinal fluid confirms MS.' That is not true. You can't confirm MS. These tests are not 100% specific. But in the right context, they are suggestive of the disease; they're more important in eliminating other things that can look like MS. So, let's walk through a few of these things.

The most important thing is to look at the history. If the history suggests something that's central nervous system demyelination, you've got a good start. But if there's something else that could look like that, if there was pain, maybe it was a disc, the clinical situation has to be carefully evaluated before you start applying the tests. There's too much reliance on technology, just doing the MRI and making a diagnosis would be a real problem. And that's one of the reasons why the MRI has been key to making sure that we're dealing with MS. There are certain shapes of lesions, as you can see here. And I'm going to go through a couple of these, to give you some examples. And the reports can never say confirm. If you see that, the radiologist doesn't know what they're talking about. They can support but they do not confirm.

So, what are we looking for? One of the key things now to differentiate some of the vascular-type white matter lesions that we see is the use of the so-called central vein sign. And in the new rendition of the McDonald criteria that are going to come out next year, almost certainly these central veins are going to be part and parcel of this diagnostic criteria. The little white matter lesion that you see should have a little dark vein going through the center of it using susceptibility weighted imaging, and that will differentiate it from a white matter lesion that is due to anything else. So, in the central vein sign, usually if 40% of the lesions or more show the central vein sign, then you're going to see probably that's in keeping with diagnostic criteria. And you can see that that number, 40%, has been generated from a clinical study where they looked at defining MS lesions from non-MS lesions as shown here.

What else? So, the diagnostic value has been evaluated a number of things that could look like MS. You don't see these in the – some of these other conditions like lupus or migraines. Even in NMO, you don't see it. It's even seen in RIS, that pre-MS kind of MRI sign.

So, if you use the central vein sign, you probably won't make mistakes.

What else? Doing the spinal tap. Well, the spinal tap is composed of a number of things. And so, you're looking for something that's characteristic, but you're also looking for red flags that might indicate something else. It's very unusual to have a high cell count, that means there's an inflammatory situation that should probably be evaluated beyond MS, right? You know, make sure that your tap isn't traumatic; otherwise, you can't make a diagnosis properly. The biochemistry, the protein should really not be elevated. The albumin index should be normal, that's usually indication of the leakiness of the blood-brain barrier. And then finally, you're going to see things that more or less is the immunological signature of MS with a raised IgG index, and the presence of what we call CSF-specific oligoclonal bands, looking over here to the right. Those are bands that are present in the CSF and not in the serum or there are more of these in the CSF and not in the serum. Those are characteristics of MS.

When you see this mirror pattern, the same bands in both, there's something probably wrong; those are bands that have drifted in from outside, likely the albumin index is increased and there's some inflammation as well, so it probably points to another condition.

So, use these tests effectively and you won't mistake MS for another disease.

Thanks for listening today. I'm Mark Freedman from Ottawa, Canada.

#### Announcer:

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