



Can Do MS Podcast Transcript

Research Update: Epstein-Barr Virus and MS

Episode 65

[music intro]

[[0:11]] Host: Welcome to the Can Do MS Podcast. This is episode number 65 and I'm your host, Dr. Rosalind Kalb. Today, I have the great fortune to be talking with our guest Dr. Alberto Ascherio of the Harvard School of Public Health, where he is a professor of Epidemiology and Nutrition. Alberto has had a special focus in his long career on the positive and negative risk factors for MS and other diseases, including smoking, low vitamin D levels, childhood obesity, and the Epstein-Barr virus, which is what he and I are going to be talking about today.

[[1:06]] Dr. Rosalind Kalb (Roz): So, thank you very much, Alberto, for being with us today. I really appreciate it. I've been a fan for a long time so I'm thrilled to have this opportunity to talk to you. Many of us have been following your work on the Epstein-Barr virus for a very long time. Could you share a bit about the path that brought you to this point?

[[1:29]] Dr. Alberto Ascherio: Yes. Thank you, Roz, and I'm happy to be here sharing this information with you. So, the Epstein-Barr virus is a common virus. It is nearly ubiquitous, meaning infects nearly all of us. Once you're infected with the virus, the virus will remain in your body for the rest of your life. And it persists in B-cells which are an important component of the immune system. That is also extremely important in causing MS and driving the disease progressing in individuals with MS.

Many years ago, we go back to the 1980s, it was not that mononucleosis, which is the clinical manifestation of infection with the Epstein-Barr virus. It's a distribution that is very similar to the data of MS. This prompted several investigators to think, well, there may be a link between the two diseases. In fact, the individual with a history of mononucleosis has two to threefold higher risk of developing MS. This was sort of the beginning of a long journey, starting to look at the relation and the possible association of how the virus is related to MS risk. So we've done studies for over 20 years and until now I think we've been able to finally provide definitive evidence of a causal association.

[[3:05]] Dr. Kalb: So, increasing the risk of a disease like MS is different from causing the disease of MS. How close are we to understanding what other factors combined with Epstein-Barr infection to cause a person to get MS?

[(3:26)] Dr. Ascherio: Yes. Let me first to say that, you know, causing may have a different meaning for different people. So, in epidemiology, when we say that the virus causes a disease, what we mean literally is that if you prevent infection with the virus, you prevent the disease. So, let me give you an example. The human papillomavirus is thought to be the cause of cervical cancer. And we actually believe it is the cause of the large majority of cervical cancer, not necessarily all of them. In other example, the Hepatitis B virus is a strong cause of liver cancer. And again, maybe 90% of the cases in some countries are caused by the Hepatitis B virus, not necessarily all of them. So, in the same way, when I say that EBV is the leading cause of MS, what I mean is that to the large majority of MS cases, virtually all MS cases, could be prevented if we prevented EBV infection.

Now, that does not mean that there are no other factors involved? There are always other factors. It's never the case that the virus will be sufficient to cause disease. For example, the virus of paralytic poliomyelitis used to infect virtually all the children in the United States before the vaccine. But only one in 400 would develop paralytic disease. So I think the situation is similar for EBV. EBV is the leading cause of MS and other factors including genetic predisposition and other environmental factors, like vitamin D deficiency, cigarette smoking, and childhood obesity, all factors that we've been investigating for the past 20 years contribute to determine the risk. But if you could prevent the infection with EBV, you would prevent MS.

[(5:27)] Dr. Kalb: So, would it be accurate to say that the EBV virus is essential to causing MS but is only one of several things that come together to cause it?

[(5:50)] Dr. Ascherio: I think some people like to put it the way, saying that is essential organization. I think to avoid the... it's almost true but they tend to avoid that language because that is always... Again, let me give you the example of poliomyelitis, paralytic poliomyelitis. The disease was defined by the virus. So if you define the disease, you call it poliomyelitis. It's called by definition by the polio virus. Let's say instead of calling it poliomyelitis, you describe the disease in clinical way, you know, acute flaccid paralysis with fever in children, then you will find out a few cases even in, you know, in the past were caused by some other virus, like an intra virus that is not the polio virus, which is true today when the polio virus is not in the circulation anymore. So I believe the same is for MS. When you define MS clinically by MRI, there will be one case in a thousand that even if clinically radiologically perfectly fit the description that is not caused by Epstein-Barr virus. In fact, in our own study, out of 801 cases with one case that was not caused by EBV because it was EBV [inaudible].

[(7:09)] Dr. Kalb: Okay. Interesting. So what does our current understanding of Epstein-Barr virus mean for people who already have MS? All of the folks out there who are listening. What does it mean for them?

[[7:24]] Dr. Ascherio: That's a good question because what we don't know is whether EBV drives the disease process. We know it cause the disease, but there are different ways in which can cause the disease. It could be a hit and run as we say. For example, EBV can cause different type of cancer. It causes [inaudible]. It causes nasopharyngeal carcinoma. It causes some cases odd disease. But it's unclear whether the virus is needed to continue the growth of the tumor. Once the virus causes the transformation then targeting the virus is too late. Now, the other mechanism whether EBV continuously drive the process, for example, by triggering out immunity, stimulating the immune system to attack EBV, and by attack EBV causing collateral damage to the myelin. We don't have a definitive answer on this. There is evidence, you know, in favor of the molecular mimicry, meaning this out immune cross activity but it's also evidence for other mechanism. So until we solve that, you know, we will not know whether targeting EBV, for example, with antiviral cracks in people with MS will or will not be beneficial. This is something we are working on. It will take several years to figure it out. We are trying also to propose trials of antiviral, you know, to see whether that is true. But at this point it's difficult to tell.

[[9:03]] Dr. Kalb: So, just to make sure I understand. Once a person is infected with EBV, that stays in their body forever for the rest of their lives. What we don't know is whether its presence in the body is triggering disease progression or disease activity over time. We don't know that yet. We know that it helps to start the disease process.

[[9:31]] Dr. Ascherio: Right. What we think is almost, you know, well, almost certainly is probable that the new response against EBV plays a role. So, continuing on your question on implication for individual with MS, it is possible that therapeutic vaccine against EBV that is a vaccine that modifies the immune response against the virus could be beneficial in MS. There is also another possibility. So I think we have three possibilities; an antiviral drug or an anti-body drug could work; a therapeutic vaccine that modify the immune response to EBV could work; and third, you cannot really treat MS by targeting EBV and we don't know which of the three, too.

[[10:22]] Dr. Kalb: So, do you think we're going to have that answer in my lifetime or yours? And for people who can't see us, I think we're fairly close to the same age. So what are you thinking about when we might know?

[[10:37]] Dr. Ascherio: I would give it five years' time to sort this out because the recent work really generated a lot of interest. Now a lot of people including drug companies and academic center are redirecting the research toward the role of EBV, and I think this will help to find an answer within a few years. But I think, you know, five years still.

[[11:06]] Dr. Kalb: Well, as I said before, I've been following this for a long time. So you must

feel as though you've been like Sisyphus pushing a boulder up a hill. And now, finally, people are hearing when you and your colleagues have been talking about for a long time. So it's pretty exciting. What does this emerging information mean for children, of people who have MS or children in general? What does this knowledge tell us given that we know how many kids get mononucleosis and live with EBV?

[[11:50]] Dr. Ascherio: Well, first of all, I want to reassure everyone that having mononucleosis, you know, doesn't mean that you will get MS. Let me make it clear. So even in children who have mononucleosis, the risk of developing MS is less than 1 in 100. You know, we have a strong family history like a parent or a sibling with MS, the risk may be higher but it's still in the 5 to 10% rate. Meaning 90% of the cases will never get MS in their lifetime. So I don't think you have to worry if your child had mononucleosis. Second, virtually everyone is EBV-infected and is not possible to prevent EBV infection. It's not really feasible. So until we have a vaccine we cannot really prevent the EBV. So, for children, the implication is, one, there is ongoing work on a vaccine. Moderna and other companies are working on it. If there will be a vaccine against EBV, there are two types of vaccine. There is a vaccine for individuals who are not infected with EBV. So needs to be given in childhood to prevent EBV infection, and that would be clearly the most effective way to prevent MS if the vaccine prevents EBV infection. There is also the possibility of a vaccine that modify the response to EBV infection in individual already carrying the virus. That is a bit farther down the way.

But for now, I think we still have to rely for MS prevention on what we discovered in the past 20 years. Like vitamin D is important in preventing MS. So, vitamin D deficiency or insufficiency can double the risk. So, I would recommend individual at high risk of MS because of family history, children, to assure a good, you know, vitamin D level, either by judicious sun exposure or most likely by taking supplements, particularly in the northern latitudes during the winter, where you cannot get enough sunlight. Second, of course, you want to avoid cigarette smoking but I hope I don't even need to say that. Child obesity is actually a risk factor for MS that is now well demonstrated. Obesity during childhood and adolescence which, of course, we want to prevent for many other reasons, diabetes and other complication. So those are the three things that are really important. What is emerging now most recently that even other dietary factors, particularly alpha-linolenic acid, which is a fatty acid that is found in walnuts and flaxseeds and an omega-3 fatty acid, is associated with a lower risk of developing MS. This is a bit more recent that the evidence is getting stronger and stronger. So, I think it's something to track.

[[14:53]] Dr. Kalb: So we should all be eating walnuts.

[[14:56]] Dr. Ascherio: I think it's most likely, you know, it's not 100%, I would say maybe 80% certain that high intake of alpha-linolenic acid would also reduce the risk of MS.

[[15:08]] Dr. Kalb: What are some other sources of that important fatty acid?

[[15:12]] Dr. Ascherio: In addition to walnut, flaxseeds, some vegetables, canola oil. So there is a variety of sources.

[[15:24]] Dr. Kalb: Okay. So you've highlighted smoking, of course, low exposure to vitamin D or inadequate exposure to vitamin D, childhood obesity, and these all come together along with genetic predisposition to increase a person's risk of MS. So, if you could say one thing to people listening about risk factors in MS. You had one takeaway message from all of your work around respecters. What would you say to people?

[[16:05]] Dr. Ascherio: Well, you know, obviously EBV is the leading cause but as of today, vitamin D in terms of prevention. Because vitamin D insufficiency is the most common, right? Most people don't smoke and most children adolescent are not obese. But a large proportion, particularly in winter, vitamin D level that fall below the optimal level. So I think if I have to think one thing I would suggest or recommend, probably vitamin D supplement to prevent or reduce the risk.

[[16:40]] Dr. Kalb: So I'm going to ask you one follow-up question about that. Because we know that many people when they hear about the importance of vitamin D, go out and begin taking mega-doses. So, can you please share what you think is the best way for people to approach making sure they have adequate vitamin D?

[[17:04]] Dr. Ascherio: Yeah. No, absolutely. There is no indication for mega-doses, which are dangerous. So the strong message: Avoid mega-doses of vitamin D. Now, for individual with MS or individuals at risk of MS, I think an oral dose of vitamin D between 2000 and 3000 IU per day is sufficient to achieve the optimal levels, and this should be clear with a treating doctor because some people have contraindication. So, again, it worked for everyone but it needs to be checked with your doctor, You need to make sure that you don't have any contraindication to take supplement at that level.

[[17:45]] Dr. Kalb: Okay. So, we know that Epstein-Barr virus is linked to other autoimmune conditions besides MS. And we know that people who have MS are also at risk for other autoimmune conditions. We often see individuals and families with several autoimmune conditions going on. So, what does this finding about EBV mean for people living with other autoimmune conditions in addition to or besides MS?

[[18:19]] Dr. Ascherio: Yeah. I know that this link is being proposed and it may be true that EBV could also increase the risk particularly of Lupus. But the evidence for other autoimmune diseases is rather weak. There is no compelling study, like the study that we recently published on MS, which doesn't exclude the possibility. But I think we shouldn't think about all autoimmune diseases as being related to EBV. I think that is almost certainly not the case, with the possible exception of lupus.

[[18:56]] Dr. Kalb: So, before we end, I think I just need to ask again. How close you think we are, given that Moderna and other companies are working on EBV vaccine, how close do you think we are today to having a vaccine?

[[19:14]] Dr. Ascherio: Yeah. I think, you know, this revolution of the RNA vaccine has really changed the, you know, it's been a game-changing discovery. Now, there is a lot of complexity. Everybody now knows with COVID, right, what does the vaccine do. As we have seen, the vaccine for COVID, for example, does not prevent COVID infection rather largely. It prevents the complication, the severity of the disease. So it could be the same for an EBV vaccine. So I think we are pretty close to having a vaccine that will reduce the severity of EBV infection. Right? So we may not be closed with a vaccine that will completely prevent, but the vaccine that will reduce the severity is likely to become available soon. Now, a vaccine that reduce the severity of infection most likely will reduce the risk of MS, but it's not certain. It's not a hundred percent. I say most likely because, you know, it's a little bit of, you know, common sense, right? Severe infection, mononucleosis increases the risk of MS. Severe infection, you have many more cells infected, the new response is much stronger. So, a vaccine that will dilute or this will attenuate most likely will contribute to prevent MS.

So I think we are in a pretty good shape again, you know, the five-year framework I expect that we will see. Now I have to say, to demonstrate that the vaccine prevents MS, even if it does, it will take longer. Only today we are starting to have the final proof that the HPV vaccine, the vaccine against human papillomavirus that is given to all the kids [inaudible] actually prevent cervical cancer. It took-- I forgot which year the vaccination started-- but it took many, many years because the cervical cancer is, you know, a disease of young adult women or adult women and the vaccine is given in children. So, with MS, we will have a transition. We will be giving a vaccine to prevent mononucleosis and for many years we will not be sure if it does really prevent MS.

[[21:38]] Dr. Kalb: We have to be patient. So when I started working MS 40 years ago, the rumor had it that we would have an end to MS within the decade, and the decades keep passing. And so I will continue to be patient.

[[21:52]] Dr. Ascherio: Yes.

[[21:52]] Dr. Kalb: Is there any other question I should be asking you Alberto that I haven't?

[[22:00]] Dr. Ascherio: I think we covered pretty much everything that is important. You know, I hope in the next couple of years we will have new findings. We'll be able to chat again and give an update to all the listener what is going on here.

[[22:16]] Dr. Kalb: I will look forward to that. Thank you so much again for your time, and for

your expertise, and for your persistence in working on EBV. Thank you.

[(22:27)] Dr. Ascherio: Thank you. Nice to talk to you. Bye.

[music outro]

[(22:46)] Host: We've reached the end of another episode of the Can Do MS Podcast. I'm your host, Rose Kalb, and I want to thank you for listening and being with us today. We'd also like to thank our sponsors for their very generous support. Thank you to EMD Serono, Novartis Pharmaceuticals, Sanofi Genzyme and Genentech. And if you've enjoyed this episode of the Can Do MS Podcast, we'd love for you to subscribe and rate and leave a review on Apple podcast. That helps us plan for our podcast's future. It is very much appreciated. Thank you.

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