Living Fully with Multiple Sclerosis: Keys to a Healthy Life through Nutrition, Brain Health, Exercise and Culture

Presented by:
Rhaisa M. Castrodad-Molina, MD

Yahaira Rivera:
Hello. Good night or good afternoon depending on where you are connecting from. On behalf of the Multiple Sclerosis Association of America, I warmly welcome you all to our seminar, “Living Fully with Multiple Sclerosis: Keys to a Healthy Life through Nutrition, Brain Health, Exercise and Culture.” This program will be presented by multiple sclerosis neurologist Dr. Rhaisa Castrodad Molina, and this seminar is part of our Together Finding Resilience, Living with Multiple Sclerosis series. This series is dedicated to our Hispanic and Latino community. My name is Yahaira Rivera and I am the Director of Mission and Program Development for the Multiple Sclerosis Association of America and I have the pleasure of being the moderator tonight.

This program is made possible thanks to the generosity and support of our sponsors Genentech and Novartis. We want to join in the celebration of National Hispanic Heritage Month, celebrating and recognizing our history, our culture and the contributions of our people in this country of the United States. So congratulations to everyone. Before we begin our talk today, I want to take a moment to give you some information about who we are and the services we offer.

The Multiple Sclerosis Association of America is a national nonprofit organization dedicated to improving the quality of life for the community living with multiple sclerosis, and we do so through vital services and support. Our services include a toll-free telephone line that provides services nationwide in English and Spanish Monday through Friday from 8:30 a.m. to 8:00 p.m. Eastern Time. We also have an equipment distribution program with products designed to improve safety, mobility and also to help with heat sensitivity. We also offer educational programs, digital resources, and publications to keep you, your family, and your caregivers informed. Our programs and services are available to people living with multiple sclerosis in the United States and its territories. Many of our resources are available in Spanish and are free through our website. So for more information about our programs and services, I invite you to visit our website, as you see on the screen, mymsaa.org. You can also call us, send us an email, and don't forget to follow us on social media.

Now for some reminders. I want to let you know that during tonight's program you will have the opportunity to send us questions. You can use the icon or tool for questions and answers, or “Q&A,” as we say in English. We will do our best to answer questions at the end of the presentation. And I also want to let you know that when the seminar is over you will have access to a link that will take you to a short survey. We appreciate it if you fill out the survey and let us know what you thought of the program, what you thought of the learning, and if you have recommendations for future programs as well. And lastly, I also want to let you know that this program is being recorded and will be available in our digital library in the coming weeks.

And please know that this program is for informational and educational purposes and does not constitute recommendations provided above. If you have questions or concerns specific to your diagnosis or treatment, we recommend that you consult with your doctor or healthcare provider.

And now, without further ado, I want to introduce you to our guest speaker tonight. Today we are joined by Dr. Rhaisa Castrodad Molina. She studied medicine and completed her specialty in Neurology at the University of Puerto Rico. Medical Sciences Campus. He then went on to pursue his multiple sclerosis subspecialty at Baylor College of Medicine in Houston, Texas. The doctor has been providing in-hospital services for two years and has her private practice at the Menonita Medical Center in Cayey and Menonita Hospital in Aibonito, Puerto Rico. Welcome, Dr. Castrodad. It is a pleasure to have you with us tonight, and now we pass it over to you.

Dra. Rhaisa Castrodad Molina:
Thank you so much. Thank you very much for the introduction. I feel very honored to be able to be here and be able to provide this educational talk to the population, to Hispanic patients with multiple sclerosis. I'm going to share the presentation. Can you see it?

Yahaira Rivera:
Not yet, doctor.

Dra. Rhaisa Castrodad Molina:
Now yes. I'm going to start. I wanted to give a brief introduction about what multiple sclerosis is. I imagine that you, as family patients, already know what the condition is. But as a summary, multiple sclerosis is an autoimmune, chronic, degenerative condition. At the moment there is no cure for the disease. And what happens is that there is a response from our own immune system. Due to multiple factors, we have not yet been able to identify a specific cause, but we know that genetic, infectious, environmental, and geographic factors can influence the risk of developing the condition. And what happens is that this immune system, for some reason, creates a response towards myelin. Myelin is a component of the neuron's axon, which is what we are seeing here in more intense yellow, and it provides that neuron with that axon, the ability to conduct electricity or that neurological signal that we want to transmit quickly and effectively. We know that the neuron jumps between the little bumps, which are the Nodes of Ranvier, and this allows it to conduct very quickly instead of going through the entire axon. When we have multiple sclerosis, there is a disruption of that myelin and that conduction through that neuron is no longer going to be as effective, and the damage may even be so severe that that signal does not reach where it needs to go. And that neuron can even die.

We know that multiple sclerosis affects around 2.3 million people around the world. And it is more predominant in women with a male to female ratio of 2 to 3. Two women for every three individuals affected with the condition. Now, I wanted to make the presentation a little more

interactive, and I wanted to ask you and I will soon tell you when you can scan the QR code. But, do we understand that the management of multiple sclerosis should only involve disease-modifying therapies or should we go a little further? You can start scanning now. I'm going to give it five seconds. 3... 2... 1. The majority answered false, and they are correct. And that's what this conference is about. There is something that has taken off a lot in recent years in brain health, or what is known as neurological reserve. And this has been studied in previous years for conditions such as Alzheimer's and normal aging processes, because there is development of dementia, because our motor and cognitive abilities decrease as we age and because it happens to some people and not to other people. .

In multiple sclerosis, we have the same question: why do some people reach the point where they begin to progress, while other people have had the condition for many years, remain stable and perhaps never reach that stage of disease progression? And it has been seen that in multiple sclerosis in these conditions that involve a neuropathology, the greater the neurological reserve, the lower the risk that that person will suffer neurological deterioration and be able to compensate for the damage that is occurring associated with the disease for a longer period of time.

I took this slide from an interactive module of the MSAA, it is excellent. And it first explains the natural history of the condition of multiple sclerosis. We know that there are three types, and that has been changing a little with the introduction of the concept of “PIRA,” *progression independent of relaxed activity*, but roughly speaking we know that there is a relaxing-remitting stage where patients suffer, they improve, they can improve completely, reach their base state, but they can be left with some neurological deficit and if they do not receive treatment or sometimes even against treatment. They may have another relapse and accumulate more disability until it reaches the point where our brain is no longer able to compensate for the neuronal damage that is occurring and enters a progressive stage. And in those progressive stages, the thing we usually see most affected is that patient's ability to walk.

And well, this neurological reserve is what postpones the development of this disease and if these relapses and new lesions are occurring, the brain somehow has that reserve and does not enter a degenerative stage. We know that medications help reduce the risk of this degenerative stage, but many times we still reach that progressive stage and we want to add other ways, in addition to medications, to reduce that risk of disease progression, which is what we are going to discuss today.

I am going to explain this again, that concept of neuronal volume loss that we know is more severe in multiple sclerosis patients who are not treated. We can see how over the years patients with multiple sclerosis have a deterioration or decline in that brain volume, while a healthy patient has less decline associated with the disease. But in both cases, if they had a greater neuronal reserve, this decline in brain volume would be smaller.

So we want to preserve that neurological reserve as much as we can, both with medications and with a healthy lifestyle. And there are several ways or several domains that affect this brain health. We have mental health, we have intellectual health, we have physical and behavioral health, which includes diet and supplements and exercise, and we also have sociocultural and spiritual factors.

This is more or less the same. So, I wanted to ask you, don't scan yet, I'm going to tell you. Did your doctor, during any of your visits or once the diagnosis was made, ever talk to you about modifying nutritional patterns? Three more seconds. Super interesting. I'm going to close. I

know you can't see it, but 60% answered no. It worries me, and it is the purpose of why the importance of this type of conference and that patients are informed and take these topics to their specialist.

So let's start talking about diet. Diet has been found to significantly influence multiple sclerosis pathology, the development of the disease and how severe that disease can be. We have also identified that there are certain dietary modifications that can have an anti-inflammatory effect and possibly impact that disease progression. But as we saw in these questions, despite the fact that there is increasing evidence that a pattern in eating habits, although we do not have enough evidence, could affect the course of that disease, we are focusing only on treatments and modification of lifestyle.

And I wanted to start talking about oxidative stress. This is one of the causes of neuronal damage in patients with multiple sclerosis, both from the early stage to the progressive forms, although more subtle, it becomes more prominent as the disease progresses. And this oxidative stress causes damage to that cell and can lead to neuronal death. And we know that a diet rich in antioxidants could impact oxidative stress and protect our neurons.

This slide. This is available for free on YouTube. This was during the pandemic, they wanted me to say that it is available online for everyone. And this is a slide from Dr. Calabresi where he explains in part this damage, to all kinds of free radicals and the mitochondria. Above we can see that there is a neuron that is intact. We can see the myelin in the nodules, look well, we see that those little red dots are sodium channels and those sodium channels help conduction of that nerve signal, that action potential. And what happens is that it is even more effective, because the signal that leaves the body of the neuron and jumps around is why they did not find it well until they reached the end and it requires almost no energy.

But when there is myelination, we see that then that signal is going to have to jump here, there is no longer that electrical insulation and it has to go through all this until it reaches the other side. And well, the neuron tries to compensate for this increased need to carry that signal for all this and increases the number of mitochondria. But that has an energetic cost and if there is more of this, there is no remyelination and there is more demyelination, more mitochondria, more sodium channels, more energy will have to be produced, and if the neuron lasts for a while, if it remains chronically demyelinated, well, the mitochondria, which is what we see here in green, begin to swell, free radicals begin to be produced, the neuron swells and dies. So it is understood that diet could have an impact on these patterns of oxidative damage.

Some of the foods that have been seen to be able to impact this oxidative damage, this oxidative stress due to free radicals, are turmeric, vitamin D and fatty acid, and we are going to discuss them now little by little. Turmeric is derived from curcuma longa, it is understood to promote cytokines, inhibit proinflammatory cytokines. I am going to explain to you that all this is not asked and we have seen that in animal models there are few models in humans that the consumption of turmeric could reduce the clinical severity and the infiltration of that inflammatory cell in the central nervous system. So it is understood that it has antioxidant and anti-inflammatory properties. It has even been studied in diseases such as Alzheimer's, Parkinson's, they are also trying to analyze the possible impact of the antioxidant effects of turmeric on this condition.

Melatonin is also understood to have anti-inflammatory or antioxidant properties. We know that melatonin is produced by the pineal gland which regulates our circadian pattern and regulates the sleep cycle. But estrogen can also be formed, so by supplementing with tryptophan, which is

a precursor of melatonin and serotonin, we can also increase the amount of melatonin. Melatonin can also be obtained from foods such as meat, high-fat fish such as salmon, eggs, milk, seeds, nuts, soy products and it is understood that it regulates these antioxidant defenses, increasing the synthesis of glutathione. But they are precursors of this mechanism, enzymes of that antioxidant mechanism. They are one of the two most important enzymes in this antioxidant mechanism and it has been seen that they could have a greater impact on patients with this progressive form of multiple sclerosis.

Also vitamin D, as I mentioned, vitamin D, in addition to an antioxidant effect, has been seen to have a neuromodulatory effect. Even vitamin D is talked about a lot in multiple sclerosis. It is extremely important that patients with multiple sclerosis have their optimal levels of vitamin D, but also the general population, because we know that it is a risk factor for developing multiple sclerosis. It is common that patients with vitamin D deficiency, for example, those who live far from Ecuador, Caucasian patients with little exposure to the sun, are at greater risk of developing multiple sclerosis. So that's why it's suggested that, in addition to what we know it has a role in calcium homeostasis, it also has an immunomodulatory role. And it has been found, that the majority of patients with multiple sclerosis have a deficiency of vitamin D. I am going to teach you now what these cytokines or those pro-inflammatory and anti-inflammatory mechanisms are so that I can explain to you well how vitamin D works.

There are pro-inflammatory cytokines and anti-inflammatory cytokines, and these cytokines are secreted by immune cells that we know as T cells, specifically from those T cells, CD4 cells. Of these CD4 cells, they differentiate into TH-1 cells. TH-17, TH-2, and regulatory THs. The TH-1 are pro-inflammatory and the TH-2 and the regulatory T are anti-inflammatory and secrete all these cytokines, which will cause a lot of the tumor in others in the alpha factor, IL-6 and IL-17 throughout the presentation. And IL-4 and IL-10 taking the beta factor in the presentation also suggest those anti-inflammatory and pro-inflammatory mechanisms. These T cells are part of the adaptive system of our immune system, that is, they are modified as we are exposed to environmental factors, to certain antigens.

But we also have the innate system with which we already know that this first line of defense and there are the macrophages, that little onion that you see here, that says M1. And that alone has also been found to be macrophages, they can have an anti-inflammatory function that cleans all that myelin, they are like little mice, like Pac-Man that eats the balls, because it eats all that myelin that has been destroyed by that immune system and that would be a positive response from that macrophage cell, because it allows space for remyelination to occur again, but it can also release this pro-inflammatory cytokine and cause neuronal damage.

To continue, in multiple sclerosis and in many of the autoimmune conditions, we know that there is a regulation of this cell, an imbalance, or they are supposed to be balanced, those pro-inflammatory cells and those anti-inflammatory cells. But in multiple sclerosis, these anti-inflammatory cells become more reactive for the reason that it is infections, this genetic environment, something leads them to be more active and cause autoimmunity.

So knowing this, we see that vitamin D stimulates when it is normal. What it does is that it stimulates those CD4 cells that we said are those active T cells that differentiate between H2 that are anti-inflammatory and regulatory T cells that are also anti-inflammatory, they inhibit the differentiation of those cells to H1 and TH-17, which are pro-inflammatory, also help to reduce these free radicals so that there is more activity, macrophages to eat all those balls, and that these glial cells also have an anti-inflammatory function, protective and not causing neurotoxicity.

So vitamin D deficiency leads to the exact opposite that we see here. So what I explained to them. So although the data is inconsistent, knowing these functions of vitamin D and that vitamin D deficiency has been seen to be a risk factor, it is very important that we recommend our patients supplementation with vitamin D in high doses, always monitoring that we do not reach toxic levels of vitamin D, because we can cause hyperglycemia and that will accumulate in the arteries, in the kidneys, cause stones, clog the arteries and we do not want that. But monitoring closely, we want patients to simply be on high doses of vitamin D. The general recommendation is 4000 units daily.

In addition to turmeric, melatonin and vitamin D, we have polyunsaturated fatty acids. Within these polyunsaturated fatty acids we have omega-3, which has been found to have an antioxidant effect and can slow or reduce degeneration in patients with multiple sclerosis. We can consume these fatty acids through fish, nuts, and seeds and it has been found that they can reduce demyelination. In animal models, supplementation with omegas has been found to decrease inflammation, maintain that immunomodulation that we talked about, TH-1, TH-17, TH-2, regulatory T, and promote neuroprotection and re-myelination, that myelin regenerates again.

But still the data we have is little and inconsistent. It has been found that it does not significantly help with the progression of the disease, but it has been found in some meta-analyses that it could help with the reduction of relapses in patients with multiple sclerosis while supplementing. Also, in some patients in human studies it was noted that there was an improvement in the quality of life of those patients. Other studies showed that it could reduce markers of inflammation and neurodegeneration, although we do not see an improvement in this pattern of progression. Other patients in that same study showed a decrease, but did not show improvement in the disability scale or in fatigue.

What are the Omegas that we should consume? We have 11 types of omega, but of these 11 types of Omega we have three main ones, which are ALA, EPA and DHA. I'm sure you've seen EPA and DHA in most of the little bottles you buy from Omega. We don't see the ALA as much and I'm going to explain why. But it is consumed mostly through plants, while EPA and DHA are consumed mostly through animal products, mainly high-fat fish and sometimes less in meat. ALA is a precursor to EPA and DHA. ALA has been found to be beneficial, decreasing inflammation markers, while DHA decreases MMP.-9. What's that? This protein has been found to be elevated in patients with multiple sclerosis and it is understood that it could be involved in demyelination.

But what about ALA? In ALA, in humans, the ability to convert it to EPA and DHA is very low. So it is not recommended to supplement it. It has also been found that although it reduces the risk of heart disease, it could also increase the risk of prostate cancer. So it is not recommended to supplement ALA so much as to supplement with EPA and DHA. That's why the little boats see it mostly. We can also consume omegas or these polyunsaturated fatty acids through fish oil. It has been found to be equally effective and performs the same function as EPA and DHA in reducing MMP-9 levels.

We also have polyphenols, we find polyphenols mostly in vegetables, fruits, wines and teas. And it has also been found that we can obtain it in less than these supplements are already more familiar to you than ginkgo biloba and resveratrol. In polyphenols, he has found that they can be beneficial by modulating that immune response and decreasing those genes that code for enzymes that promote oxidative stress. In animal studies it has been seen that it can

promote protection against this oxidative damage and that it can also protect against demyelination and axonal damage.

So, although we do not have enough evidence to establish and tell the patient you have to take this, since there are studies that have positive results regarding these supplements, yes, vitamin D supplementation should be recommended primarily, but it should also be suggested to supplement omega three, melatonin, and polyphenols. But we need more research to truly provide more accurate recommendations.

Now let's talk about the pro-inflammatory diet. We know that a pro-inflammatory diet can have effects on the immune system and increases the production of these inflammatory cytokines that we discuss now such as tumor necrosis factor, inflammatory cytokines, MMP9 and other inflammatory factors that can also lead to this initiative. For inflammatory diet components, such as saturated fats, saturated fats have been found to cause dysbiosis in the intestinal flora. I am not going to explain all this later, but they can have an impact on that intestinal flora and we will see what the relevance of this is.

We also have vegetable oils that are rich in trans fats and can lead to inflammation in the intestine and also have an impact on those inflammatory cells, and we will also see how this occurs. Red meat has been found to form water components and increase chronic inflammation. These chains contain arachidonic acid which truly increases inflammatory vessels and increases those inflammatory cells, in this case, TH-17.

High sugar drinks, refined grains can lead to the production of insulin and in this way promote the synthesis and production of arachidonic sugar, which we saw increases TH-17. There are also studies on high salt consumption that can also promote the differentiation and production of TH-17 cells and proinflammatory cytokines and also dairy products derived from cows, cow's milk may also play a role in those mechanisms that can lead to multiple sclerosis, particularly the feline type that can induce, can be used to... or can induce multiple sclerosis, right? This is the animal model of multiple sclerosis that is used in rats. You can induce it and it is understood to be through molecular mimicry. That's basically if our immune system is exposed to the... in this case, butyrophilin and affinity have a similarity to the myelin protein and that immune cell that your exposure to butyrophilin is exposed to the myelin becomes confused and attacks it, and that generates an immune response against that myelin and eventually multiple sclerosis.

We already talked about that, but arachidonic acid, in addition to TH-17, promotes demyelination, palliation and oligodendrocytes, which is the cell in the central nervous system that produces myelin, axonal pathology and eventually neurological deficit and the characteristic symptoms of sclerosis. multiple. So let's talk a little bit about the gut-brain axis. The brain-gut axis is made up of our central nervous system, which is the brain of the spinal cord, that enteric nervous system that controls the motility of that intestinal system. The autonomic system that manages functions such as pressure, pulse, urine and stool control. This is also the immune system that is directly tied, as we are going to see to that gastric system, that intestinal flora and that intestinal flora.

The intestinal flora or intestinal microbiota has gained significant interest in recent years and is under investigation. This intestinal flora has multiple roles, including the metabolism of nutrients, especially carbohydrates, but it can also produce neurotransmitters and vitamins. And it can compete with some other pathogen that is wild in our intestine to maintain that flora in them, which we are going to see now, which is the normal intestinal flora that keeps that gastric wall intact. It is understood that this intestinal flora may be associated with the homeostasis of the

central nervous system and the development of neurodegenerative and neuroimmunological diseases. And diet can be a factor that can compromise or favor that intestinal flora and can compromise our ability to defend ourselves against those pathogens and therefore, the production of those vitamins, those neurotransmitters and predispose us to those neurodegenerative and neuroimmunological diseases. It has been found that the intestinal flora can also regulate this immune system and if it is deregulated it can lead to the activation of this inflammatory cell, and cause chronic inflammation.

And this was what I was telling them about eubiosis and dysbiosis. Eubiosis is the intestinal flora when that flora truly colonizes our intestine from the moment we are born. And it is supposed to remain in that stable condition throughout our lives. Here we can see that we have the flora that is not seriously pathogenic, that the intestinal wall is intact, that there is no permeability and this is what we want to have to have a healthy immune homeostasis. But through the use of antibiotics, infections, poor eating habits, they can lead to an alteration of the intestinal flora, causing pathogenic bacteria to prevail and therefore affecting the intestinal wall and causing greater permeability. And that leads to the access of pathogens and the release of those inflammatory cytokines, as we saw, remember in IL6, interleukin six and tumor necrosis factor alpha that eventually lead to chronic inflammation and can cause diseases such as inflammatory bowel disease, metabolic diseases, autoimmune disorders, food intolerances and even colon cancer.

So, there are certain foods that we have seen that are also produced by that intestinal flora that is in eubiosis and one of them is single short-chain fatty acids, short-chain fatty acids, like butyrate, and these short-chain fatty acids. short ones have anti-inflammatory properties and can inhibit the ability of the intestine or decrease the ability of those white cells to adhere to the wall of the intestine and cross into our blood system and throughout our body.

So, we can also consume these fatty acids in addition to the production we have of that flora, but we can consume them through high-fibers. The consumption of fiber in the diet can produce butyrate and improve these anti-inflammatory capacities of our system. gastric. In animal studies, as you see, in most animal studies in humans we have limited data, but in reality, introducing this to humans, it has been shown that stuffing all butyrate production has some factors important and protective with that microbiota and that central nervous system. In patients with multiple sclerosis who had it, it has been found that, and this has been studied, fecal transplants are being studied. For this reason, it has been found that in patients with multiple sclerosis they have low levels of short-chain fatty acids in their feces. And well, one of the things that has been studied is fecal transplants to see if this intestinal flora and the production of these components produced by this intestinal flora are improved.

So we already talked about the intestinal flora. Now we are going to talk about comorbidities in patients with multiple sclerosis. The comorbidity of multiple sclerosis patients has some of them that become more common as the patient becomes more disabled, the less they walk, the greater the risk of obesity, suffering, high cholesterol, uncontrolled sugar. But we also know that culturally, we may be predisposed by our lifestyle, our diet to suffer from these vascular abilities as well as mood abilities, as we are going to discuss. But I am going to focus now on the vascular probabilities and these vascular probabilities such as obesity and high cholesterol, which are the most common in multiple sclerosis patients, can represent a greater risk of hospitalization and to patients and it has been seen that they can be correlated with greater disability and by the prognosis of the disease. Thus, it is very important to address these issues.

As for hyperlipidemia, high cholesterol, high triglycerides were found to be common in patients with multiple sclerosis, a high-fat diet has been found to promote inflammation and this inflammation, as it can lead to the activation of those T cells and those macrophages and the production of more inflammatory cytokines. Cholesterol and cholesterol components may also correspond to adverse effects in multiple sclerosis patients. And very important patients who have vascular comorbidities, such as high cholesterol, which leads to coronary heart disease, which causes heart attack, which causes cerebral infarction. Uncontrolled sugar is also a limiting factor for us to be able to use a certain medication, it can predispose us to damage to the heart, damage to the eye and we cannot use it, so, after promoting inflammation, treatment alternatives also decrease. And not only do they promote inflammation, but it has also been found to promote neurodegeneration and disease progression, as we said previously in multiple sclerosis patients, and it has been found that a decrease in the consumption of these saturated fats is associated with less disability and the opposite.

I'm going to skip that. And so let's talk now about obesity. Being overweight and obesity lead to chronic inflammation and it is understood that this is partly due to the production of adipokines. There are adipokines, I will explain, that are pro-inflammatory and there are adipokines that are anti-inflammatory. Well, in obesity there is an imbalance and there is a greater production of those pro-inflammatory adipokines, and we can see in this slide that an inflammatory look is created by adipose tissue. This adipose tissue produces adipokines that are transferred to the blood and there are very few of them in the blood. They alter the permeability of the blood-brain barrier and allow a transfer of those pro-inflammatory cells to the central nervous system and cause neuroinflammation and cause demyelination. They cause multiple sclerosis and that. It leads to more inflammation and if the adipokines keep coming out, a chronic cycle of inflammation is maintained.

Even in children it has been seen that this is a risk factor for developing not only a poor prognostic factor, but a risk factor for multiple sclerosis. Yes, the leptin of this adipokine is one of the proinflammatory adipokines, as are adipsin and resistin. And with regard to anti-inflammatory drugs, we truly see that they are so diminished and that this proinflammatory pattern that leads to an increase in TH1 and TH17 leads to this patient who has this relationship from remitter to degeneration due to this chronic inflammation. It has been seen that obese patients begin to practice calorie restriction, which we are going to talk about, because it leads to a decrease in leptin levels and a reduction in inflammation, demyelination and axonal damage. This is what we are talking about, about adiponectin in obese patients who have decreased levels of adiponectin, we have seen that there is a greater risk of pediatric multiple sclerosis, greater disability and progression of the disease, higher scores on the disability and this is especially seen in obese female patients, but can also occur in men.

And on this slide we can see what he just explained to you and much more. We see how those pro-inflammatory adipokines are released, there is a decrease so that is why it is a line. In this production of anti-inflammatory adipokines, there is less absorption of vitamin D in obese patients and I know that with the distribution of the true volume of the body of a patient who is overweight, they are diluted in vitamin D and those levels decrease. And as we discussed, there is an increase in that production of those inflammatory cells and a decrease in those anti-inflammatory cells. An affectation of this intestinal microbiota occurs in obese patients. There is greater production of these inflammatory cytokines, reminiscent of TNF, IL-6, IL-17, saturated fat increases and therefore production, as we discussed about all that dysbiosis, pre-inflammation, and oxidative stress. And an increase in those macrophages, I don't know if you remember, which may also have that proinflammatory capacity. Obesity is an important factor that we have to address.

And now we are going to talk about specific diets. At present there is not enough evidence on any diet that can be recommended specifically for patients with multiple sclerosis. My recommendation is always that the patient go hand in hand with a nutritionist if they are going to proceed to follow a specific diet pattern. Because these diet patterns can often lead to nutritional problems that can cause other problems. The Mediterranean diet is one of the ones that has the most evidence with multiple sclerosis and consists of an increased consumption of fruits and vegetables, whole grains, and olive oil, which we are going to talk about because olive oil is important, and an increase the consumption of fish, dairy products, and a decrease in red meat. Olive oil produces phenols that have been found to have an anti-inflammatory effect and can protect the nervous system from that oxidative stress. It can also decrease markers of inflammation, it can decrease those comorbidities, and those vascular comorbidities, and also regulate the intestinal microbiota. So, again, if someone wishes, they could always proceed to do it with the help of a nutritionist.

There is the paleo diet that I imagine everyone or many have heard of, the Wahls protocol, and it is the diet that the Wahls protocol was based on with some modifications and lifestyle changes. And the diet is mainly composed of increasing the consumption of vegetables, green leaves, vegetable proteins, soy, nuts and excluding the consumption of dairy and processed foods. There has been an improvement in fatigue, the benefit we have seen in patients with multiple sclerosis, but there is a high risk of nutritional deficiencies, so you have to be careful if you are going to proceed with this diet. The diet was developed by Swank because not everyone and in countries that had a low consumption of saturated fats had a lower incidence of multiple sclerosis. So the diet is based on a decreased consumption of saturated fats. And it has been seen that this diet could have an anti-inflammatory effect and could protect against demyelination.

Caloric restriction is based on the fact that overconsumption of postprandial food can have a pro-inflammatory response and by restricting this excess of postprandial food it could have an anti-inflammatory response. But we need more evidence to know how long this period of fasting should be and also some more specific recommendations. But it has also been found that it could have, as we mentioned, an anti-inflammatory effect by restricting calories.

The ketogenic diet is based on increasing fat consumption and decreasing carbohydrate consumption. It may have an anti-inflammatory effect, but it can lead to vitamin deficiency effects, excessive weight loss, and can affect the gastrointestinal system. So, I never recommend the ketogenic diet and if someone wants to follow the ketogenic diet, they have to be an expert nutritionist who is an expert in the ketogenic diet.

And the gluten-free diet, which many of us have seen, is now very fashionable, it has not been found to have a significant effect on multiple sclerosis. There are very few interventions with a gluten-free diet that showed any improvement, but it is understood that those studies that showed improvement, there could have been a risk of this and the control of those randomized studies.

So, although the diet is, the evidence is limited, we can see that it could have an anti-inflammatory and beneficial effect for multiple sclerosis patients. Follow my recommendation for my patients, it is not a specific diet, but a diet that is made up of high fruit consumption, vegetables, and is low in fat. At the moment, diet should not replace disease-modifying therapy, but should go hand in hand with treatment.

Now, I'm going to talk a little about physical activity and I wanted to ask you if you exercise. You can begin to respond. Five more seconds. 5... 4... 3... 2... 1. Very good. A majority answered yes. Now I would like to ask you if at any time your doctor has recommended that you exercise? Today I'm going there. Aha. I'm going with... Not yet. Now. 5... 4... 3... 2... 1... 0. That makes me very happy. 60% answered yes and 30% said no. And finally, I wanted to ask you: How many minutes a week do you exercise? Well, now you can. 5... 4... 3... 2... 1. The response was quite mixed, but the majority answered more than 150 minutes. And that's excellent. It is a topic that I am passionate about. I love CrossFit, I love there are CrossFit classes and I put it in this photo because among the individuals there, one of them is my patient and for me exercise is one of my main recommendations In conjunction with the nutritional changes and lifestyle changes.

So, if exercise is important for many patients, you may find it a little difficult either because of exposure to heat, because of worsening fatigue, because of restrictions in movement, true that it can cause the disease. And this can lead to the population of patients with multiple sclerosis exercising less than what is recommended or less than the general population. But we do really reinforce the benefits that exercise can have, such as fatigue, quality of life, improvement of the cognitive part in mood, improvement of mobility and balance. I think we can convince them to gradually increase physical activity until it reaches the recommended levels.

This is a study that was done, which was found in a database analysis in a European country, that vigorous exercise means that there is an increase in the respiratory rate, and in breathing, I don’t know if it was right, for instance, mild physical activity was inversely correlated with the risk of developing multiple sclerosis. In animal studies, as I told you, in the EAE, where a myelin antigen is injected into the rats, they made the rats swim or run on the wheel before being injected with the antigen and for one time they were injected with the antigen before developing demining disease or multiple sclerosis in the rat and found that exercise was associated with a delay in the onset of the development of these clinical symptoms and that once they had the relapse, that relapse will last less. And they also found that there was a moment in that hippocampal neurogenesis and therefore a decrease in memory decline. But we must take into account that in these studies the animals were taken at their maximum functional moment and that it is impossible to do these studies with animals that have a mobility restriction. So, translating this data to humans who have greater disabilities, the truth is not going to directly correlate.

And these are all benefits that we have seen in animal models and in human models. As we see, in human models we have very little data, but more and more is being studied, but we have seen that in animal models there is an increase in remyelination, OPCs are oligodendrocyte progenitor cells, which are the cells that produce oligodendrocytes. , which are the cells responsible for producing myelin. There was an increase in remyelination and an increase in the width of that myelin. There were also changes in neuroinflammation. We saw that there was an increase in anti-inflammatory cells and anti-inflammatory cytokines and a decrease in that pro-inflammatory response and pro-inflammatory cytokines and in the increase in those reactive glial cells that cause damage to neurons. There was also a moment in the segregation of those growth factors, and the cough just like what happens in the intestine, as you saw in that intestinal wall with the intestinal flora, because exercise increased the union of those cells in that blood-brain barrier, which It translated into a decrease in those immune cells, crossing the central nervous system.

There was also production of laminin through the pericytes and laminin was seen to improve or increase the repair of damage in the lesions in the pericytes increased the vascularity in those lesions in multiple sclerosis and laminin was seen to increase the repair of that damage. And

well, a decrease in this infiltration of leukocytes and a decrease in the cells in, sorry, in the molecules that use those white cells to stick together and cross that blood-brain barrier. And there was also a decrease in that oxidative stress. Human studies, we have seen that there is greater cortical excitability which can be true in patients with minimal deficit. Exercise can help restore normal brain activity and there is a decrease in loss of cortex and brain volume in matter, a decrease in loss of volume in cortex and gray matter. So it is really extremely beneficial that we need more data.

This is a summary of what I mentioned, although I am going to skip it. And something very interesting is that there is this MedXercise, there are studies that are being carried out that are administering, not only studying the impact of exercise, but the impact of exercise with medications that have been associated with remyelination. And it has been seen that up to 98% of the axons in these studies with rats are remyelinated and that there is greater survival of the axons compared to patients who exercised alone or were administered clemastine alone, which is one of the drugs that can take to the administration. For this it is very premature and there are only animal models.

It has also been seen that there is a period where exercise is not as effective and this could have an impact on when we begin this rehabilitation process. It has been seen that right after a relapse is the response to exercise. It is not the same as several days after the relapse. So, this is still very premature, but something that definitely needs to be studied more with a view to the rehabilitation of that patient.

There are some general recommendations that I personally follow and that's why I asked you how long you exercise. But in general terms, the ideal is more than 150 minutes or more a week of moderate activity, which can translate into half an hour, five days a week. There are some preliminary guidelines that we can follow for now, but they are still under investigation on the maximum time, the maximum repetitions, the optimal days that should be followed. But in general, this guide recommends 2 to 3 days per week of aerobic training for 10 to 30 minutes at moderate intensity and 2 to 3 days per week of resistance training starting 1 to 3 rounds of 8 to 15 repetitions maximum per session. Each session should last between 10 to 30 minutes, starting once that person starts with ten minutes and as the number of repetitions is tolerated, the intensity and time will increase until reaching 30 minutes. Ideally, we can quantify moderate activity using scales like this one, which are the perceived “exertion scale.” Ideally, moderate activity should range from 11 to 13. Another way to let ourselves go is with the “peak heart rate” or “peak oxygen consumption.” Ideally it should be between 40 or 60%. I'm not going to teach you how to calculate it.

Always letting ourselves be carried away by the patient's level of disability, what physical level he is at, everything must be progressive, because that can lead very quickly to demotivation and the acquisition of unnecessary injuries. So the “peak heart rate” is calculated by subtracting the patient's age from 220. For example, if we have a 50-year-old patient, we subtract 50 from 220, which is 170, and if we want to go between an intensity of 40 to 60%, he does not take 50, we multiply it by 50% and the “heart rate” target of this patient while exercising should be 85 beats per minute.

There is the “peak oxygen consumption,” which is more complicated to calculate and they usually get carried away in these centers that use the mask, but we can calculate an approximate using that “peak heart rate” and multiplying it, sorry, dividing it by the “resting”. heart rate” and that by multiplying it by the 15.3 that our patient was 43.35 milliliters per kilogram per minute and there are gadgets in this modern era that can measure. What is our “peak

oxygen consumption” while we are not exercising and we can get carried away with that. Yes, these guidelines are still preliminary, but they can serve as a guide, worth the redundancy, for specialists, trainers, and the patients themselves.

So, in conclusion, we have a lot of data in preclinical models with animal models, but we still need more data and clinical studies in humans. But so far we have seen that the effect of exercise on multiple sclerosis is very promising. We have many questions to answer. We do not know if age has any impact on the benefit of exercise in that patient. We do not know if patients in a progressive stage that we know is less inflammatory, because a young patient has the same requirements or the same response to that physical activity. We do not know if these benefits of exercise are permanent or if they are transitory. We do not yet know how we can maximize the benefits of this exercise, trying to reduce the exacerbation of symptoms as much as we can. Yes, my recommendation for my patient is to make a modification if their drowsiness, weakness or tiredness worsens in the afternoon, so that they come in in the morning or when the sun has gone down, which is to hydrate well, that they wear a vest, what they are told. the “cooling vests” that use “little air conditioners” that now come from the neck, that they take a cold bath before and after. We can use all of these factors to reduce the possible exacerbation of symptoms.

Other factors that are important in terms of that neuronal reserve, mental health. And the National MS Society provides recommendations on how we can preserve or maintain emotional well-being. Among them, focusing on the positive, setting small goals, achieving these small goals within the art of this condition that changes the patient's life, gives you a small sense of “accomplishment” and hope that you are achieving something. Staying focused on each patient is different, it has a different course, do not get carried away by what happened to the other person or what the neighbor in the store told me because it can be overwhelming if we hear all these versions. Always listen to the experts and go to references that are trusted such as the MSAA, the National MS Society, the MS Foundation, which can be overwhelming. It is common for patients to come to my office crying because they were told that definitely in a couple of years You will be unable to walk and we know that this is not the reality for all patients.

We know that stress is a factor that can affect the course of the disease and can exacerbate symptoms. So either through reading, with the help of a specialist, you have to learn to manage stress. Try to avoid unnecessary stressors because this promotes emotional balance and prevents us from falling into anxiety or depression. And focus on a specific problem. So similar to what we said on nine, stay centered and focus on the positive. It is very important that we are very alert to our emotions. Emotions are not just emotions, we know that other symptoms can affect us and how we feel the cognitive part, fatigue can even cause relapses and not until those symptoms improve that other associated symptoms improve.

What symptoms should we be aware of and that constantly affect us in our daily lives? That sense of sadness, worry, fear, that we are fluctuating our mood, that we are irritable, anxious, depressed, that we have lost, we feel that we have lost our identity, that we have anxiety due to abandonment, that we have anxiety, fear, of being a burden for another. These are all risk factors for also developing more anxiety and depression. Let us feel at work that no one understands us. That not only do we no longer feel capable of doing what we did before. Or that they do not provide us with the necessary means to be able to deal with the symptoms and the condition and be able to be our best version. We often cannot handle all of these things ourselves and we have to have the courage to seek help.

We take advantage and this says 2022, but today is National Mental Health Day, so all the more reason I emphasize addressing these symptoms. Depression is known to be more common in multiple sclerosis patients, the prevalence is 50% compared to 16% in the general population, so it is quite common and it has been seen that in Hispanic patients and black patients it is even more prominent and they may be even more refractory due to those other cultural factors, which we will talk about later, cause that despite treatments such as CBT, medication, they are more refractory and do not respond like a non-Hispanic and non-black patient. Anxiety is also more common in multiple sclerosis patients and is usually comorbid with depression and is usually more common in women and is associated with a lack of social support and fluctuates between 15 to almost 60%, 1.8 to 6% more higher than the general population.

Without treatments for when these symptoms already take control of our lives, they can include counseling, CBT, exercise, medication and reinforcement. These symptoms have to be addressed because it can affect quality of life, it can affect adherence to treatment, it can increase hospitalizations, it can increase fatigue, pain, cognitive symptoms, worsen walking speed, manual austerity, speed of information processing. It is not a sign of weakness, on the contrary, it took place to really make the decision. To seek help if these symptoms take control of our functionality.

I always say that, remember, I tell my patients all this, a patient told me that “I have multiple sclerosis, but multiple sclerosis doesn't have me,” so don't let the condition take control of you. his life. And I turn over the presentation.

Yahaira Rivera:
Thank you, doctor. I'm going to ask you two important questions that came today and then we will finish. You talked about vitamin D, they asked: vitamin D2 or vitamin D3? Which of the two do you recommend? Because it seems that the patient has been recommended two different ones.

Dra. Rhaisa Castrodad Molina:
D3

Yahaira Rivera:
Thank you. And then, what about the Omega? You recommend…All of the supplements that you recommended, aren't they going to interfere if the patient is on a disease-modifying medication? Should you take them or should you consult with your doctor before taking them?

Dra. Rhaisa Castrodad Molina:
They do not interfere with the therapy, but turmeric does have to be careful because patients who suffer from gastric ulcer, gastric disease, could cause problems, but other than that.

Yahaira Rivera:
Perfect. And before we say goodbye, there is a patient who tells us that she does exercises, but after 20 minutes her foot seems to weaken and the question is, should she continue challenging or should she listen to her body and then that is the moment to stop?

Dra. Rhaisa Castrodad Molina:

Yes, you must continue to reach the time you tolerate, building tolerance and increasing that muscular resistance is going to take longer because the limb is weak. Strengthen it, and once you feel comfortable, increase the time little by little.

Yahaira Rivera:
Thank you, Dr. Castrodad. You talked about so many important and necessary topics for our community, especially because you brought this information in Spanish. So on behalf of our Association we thank you very much. Before we say goodbye, one last piece of advice you want to give to our audience?

Dra. Rhaisa Castrodad Molina:
Yes, always go hand in hand with your specialist, stay organized, take advantage of your medical visits, and be prepared. When we are not prepared and we have barriers such as language, cultural barriers, then that can affect the care and the questions and concerns we have and that can lead to more anxiety and not feeling in control. So, go hand in hand with your specialists, listen to your specialist, and always be prepared and stay as organized as possible so that you do not feel overwhelmed by the condition.

Yahaira Rivera:
Thank you for that advice, and again, Dr. Castrodad, on behalf of the Multiple Sclerosis Association of America, we thank you very much for spending all this time with us, providing such important information, research that is almost never shared with patients. So thank you very much for all the tips and strategies so that people who listened to us today can add them to their daily routine, consult with their healthcare provider and improve the quality of life, which is so necessary and so important. Thank you for your time, your dedication.

To our audience, thank you very much for being here with us, for participating. I promise you again that I will share all the questions with Dr. Castrodad, so that we can add it as another resource when we add this video to our website. So have a nice night. Thanks for joining us! Blessings and until next time.

Dra. Rhaisa Castrodad Molina:
Bye.

Yahaira Rivera:
Bye-bye